The GALE ENCYCLOPEDIA *of* MEDICINE

SECOND EDITION

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VOLUME

2

C-F

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PLEASE READ—IMPORTANT INFORMATION

The *Gale Encyclopedia of Medicine 2* is a medical reference product designed to inform and educate readers about a wide variety of disorders, conditions, treatments, and diagnostic tests. The Gale Group believes the product to be comprehensive, but not necessarily definitive. It is intended to supplement, not replace, consultation with a physician or other healthcare practitioner. While the Gale Group has made substantial efforts to provide information that is accurate, comprehensive, and up-to-date, the Gale Group makes no representations or warranties of any kind, including without limitation, warranties of merchantability or fitness for a particular purpose, nor does it guarantee the accuracy, comprehensiveness, or timeliness of the information contained in this product. Readers should be aware that the universe of medical knowledge is constantly growing and changing, and that differences of medical opinion exist among authorities. Readers are also advised to seek professional diagnosis and treatment for any medical condition, and to discuss information obtained from this book with their health care provider.

INTRODUCTION

The *Gale Encyclopedia of Medicine 2 (GEM2)* is a one-stop source for medical information on nearly 1,700 common medical disorders, conditions, tests, and treatments, including high-profile diseases such as AIDS, Alzheimer's disease, cancer, and heart attack. This encyclopedia avoids medical jargon and uses language that laypersons can understand, while still providing thorough coverage of each topic. The *Gale Encyclopedia of Medicine 2* fills a gap between basic consumer health resources, such as single-volume family medical guides, and highly technical professional materials.

SCOPE

Almost 1,700 full-length articles are included in the *Gale Encyclopedia of Medicine 2*, including disorders/conditions, tests/procedures, and treatments/therapies. Many common drugs are also covered, with generic drug names appearing first and brand names following in parentheses, eg. acetaminophen (Tylenol). Throughout the *Gale Encyclopedia of Medicine 2*, many prominent individuals are highlighted as sidebar biographies that accompany the main topical essays. Articles follow a standardized format that provides information at a glance. Rubrics include:

Disorders/Conditions	Tests/Treatments
Definition	Definition
Description	Purpose
Causes and symptoms	Precautions
Diagnosis	Description
Treatment	Preparation
Alternative treatment	Aftercare
Prognosis	Risks
Prevention	Normal/Abnormal results
Resources	Resources
Key terms	Key terms

In recent years there has been a resurgence of interest in holistic medicine that emphasizes the connection between mind and body. Aimed at achieving and maintaining good health rather than just eliminating disease, this approach has come to be known as alternative medicine. The *Gale Encyclopedia of Medicine 2* includes a number of essays on alternative therapies, ranging from traditional Chinese medicine to homeopathy and from meditation to aromatherapy. In addition to full essays on alternative therapies, the encyclopedia features specific **Alternative treatment** sections for diseases and conditions that may be helped by complementary therapies.

INCLUSION CRITERIA

A preliminary list of diseases, disorders, tests and treatments was compiled from a wide variety of sources, including professional medical guides and textbooks as well as consumer guides and encyclopedias. The general advisory board, made up of public librarians, medical librarians and consumer health experts, evaluated the topics and made suggestions for inclusion. The list was sorted by category and sent to *GEM2* medical advisors, certified physicians with various medical specialities, for review. Final selection of topics to include was made by the medical advisors in conjunction with the Gale Group editor.

ABOUT THE CONTRIBUTORS

The essays were compiled by experienced medical writers, including physicians, pharmacists, nurses, and other health care professionals. *GEM2* medical advisors reviewed the completed essays to insure that they are appropriate, up-to-date, and medically accurate.

HOW TO USE THIS BOOK

The *Gale Encyclopedia of Medicine 2* has been designed with ready reference in mind.

- Straight **alphabetical arrangement** allows users to locate information quickly.
- Bold-faced terms function as **print hyperlinks** that point the reader to related entries in the encyclopedia.

- **Cross-references** placed throughout the encyclopedia direct readers to where information on subjects without entries can be found. Synonyms are also cross-referenced.
- A list of **key terms** are provided where appropriate to define unfamiliar terms or concepts.
- Valuable **contact information** for organizations and support groups is included with each entry. The appendix contains an extensive list of organizations arranged in alphabetical order.
- **Resources section** directs users to additional sources of medical information on a topic.
- A comprehensive **general index** allows users to easily target detailed aspects of any topic, including Latin names.

GRAPHICS

The *Gale Encyclopedia of Medicine 2* is enhanced with over 675 color images, including photos, charts, tables, and customized line drawings.

ADVISORY BOARD

A number of experts in the library and medical communities provided invaluable assistance in the formulation of this encyclopedia. Our advisory board performed a myriad of duties, from defining the scope of coverage to reviewing individual entries for accuracy and accessibility. The editor would like to express her appreciation to them.

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C

CABG surgery *see* **Coronary artery bypass graft surgery**

CAD *see* **Coronary artery disease**

Caffeine

Definition

Caffeine is a drug that stimulates the central nervous system.

Purpose

Caffeine makes people more alert, less drowsy, and improves coordination. Combined with certain **pain** relievers or medicines for treating **migraine headache**, caffeine makes those drugs work more quickly and effectively. Caffeine alone can also help relieve headaches. **Antihistamines** are sometimes combined with caffeine to counteract the drowsiness that those drugs cause. Caffeine is also sometimes used to treat other conditions, including breathing problems in newborns and in young babies after surgery.

Description

Caffeine is found naturally in coffee, tea, and chocolate. Colas and some other soft drinks contain it. Caffeine also comes in tablet and capsule forms and can be bought without a prescription. Over-the-counter caffeine brands include No Doz, Overtime, Pep-Back, Quick-Pep, Caffedrine, and Vivarin. Some pain relievers, medicines for migraine headaches, and antihistamines also contain caffeine.

Recommended dosage

Adults and children age 12 years and over

100–200 mg no more than every 3–4 hours. In timed-release form, the dose is 200–250 mg once a day. Timed-release forms should not be taken less than six hours before bedtime.

Children under 12 years

Not recommended.

Other considerations

Avoid taking too much caffeine when it is being taken as an over-the-counter drug. Consider how much caffeine is being taken in from coffee, tea, chocolate, soft drinks, and other foods that contain caffeine. Check with a pharmacist or physician to find out how much caffeine is safe to use.

Precautions

Caffeine cannot replace sleep and should not be used regularly to stay awake as the drug can lead to more serious **sleep disorders**, like **insomnia**.

People who use large amounts of caffeine over long periods build up a tolerance to it. When that happens, they have to use more and more caffeine to get the same effects. Heavy caffeine use can also lead to dependence. If the person then stops using caffeine abruptly, withdrawal symptoms may occur. These can include throbbing headaches, **fatigue**, drowsiness, yawning, irritability, restlessness, vomiting, or runny nose. These symptoms can go on for as long as a week if caffeine is avoided. Then the symptoms usually disappear.

If taken too close to bedtime, caffeine can interfere with sleep. Even if it does not prevent a person from falling asleep, it may disturb sleep during the night.

The notion that caffeine helps people sober up after drinking too much alcohol is a myth. In fact, using caffeine and alcohol together is not a good idea. The combination can lead to an upset stomach, nausea, and vomiting.

Older people may be more sensitive to caffeine and thus more likely to have certain side effects, such as irritability, nervousness, **anxiety**, and sleep problems.

KEY TERMS

Arrhythmia—Abnormal heart rhythm.

Central nervous system—The brain, spinal cord and nerves throughout the body.

Fetus—A developing baby inside the womb.

Palpitation—Rapid, forceful, throbbing, or fluttering heartbeat.

Withdrawal symptoms—A group of physical or mental symptoms that may occur when a person suddenly stops using a drug to which he or she has become dependent.

Special conditions

Caffeine may cause problems for people with certain medical conditions or who are taking certain medicines.

ALLERGIES. Anyone with **allergies** to foods, dyes, preservatives, or to the compounds aminophylline, dyphylline, oxtriphylline, theobromine, or theophylline should check with a physician before using caffeine. Anyone who has ever had an unusual reaction to caffeine should also check with a physician before using it again.

PREGNANCY. Caffeine can pass from a pregnant woman's body into the developing fetus. Although there is no evidence that caffeine causes **birth defects** in people, it does cause such effects in laboratory animals given very large doses (equal to human doses of 12–24 cups of coffee a day). In humans, evidence exists that doses of more than 300 mg of caffeine a day (about the amount of caffeine in 2–3 cups of coffee) may cause **miscarriage** or problems with the baby's heart rhythm. Women who take more than 300 mg of caffeine a day during **pregnancy** are also more likely to have babies with low birth weights. Any woman who is pregnant or planning to become pregnant should check with her physician before using caffeine.

BREASTFEEDING. Caffeine passes into breast milk and can affect the nursing baby. Nursing babies whose mothers use 600 mg or more of caffeine a day may be irritable and have trouble sleeping. Women who are breastfeeding should check with their physicians before using caffeine.

OTHER MEDICAL CONDITIONS. Caffeine may cause problems for people with these medical conditions:

- peptic ulcer
- heart **arrhythmias** or **palpitations**
- heart disease or recent **heart attack** (within a few weeks)
- high blood pressure
- liver disease
- insomnia (trouble sleeping)
- anxiety or panic attacks
- agoraphobia (fear of being in open places)
- premenstrual syndrome (PMS)

USE OF CERTAIN MEDICINES. Using caffeine with certain other drugs may interfere with the effects of the drugs or cause unwanted—and possibly serious—side effects.

Side effects

At recommended doses, caffeine can cause restlessness, irritability, nervousness, shakiness, **headache**, lightheadedness, sleeplessness, nausea, vomiting, and upset stomach. At higher than recommended doses, caffeine can cause excitement, agitation, anxiety, confusion, a sensation of light flashing before the eyes, unusual sensitivity to touch, unusual sensitivity of other senses, ringing in the ears, frequent urination, muscle twitches or **tremors**, heart arrhythmias, rapid heartbeat, flushing, and convulsions.

Interactions

Certain drugs interfere with the breakdown of caffeine in the body. These include **oral contraceptives** that contain estrogen, the antiarrhythmia drug mexiletine (Mexitil), the ulcer drug cimetidine (Tagamet), and the drug disulfiram (Antabuse), used to treat **alcoholism**.

Caffeine interferes with drugs that regulate heart rhythm, such as quinidine and propranolol (Inderal). Caffeine may also interfere with the body's absorption of iron. Anyone who takes iron supplements should take them at least an hour before or two hours after using caffeine.

Serious side effects are possible when caffeine is combined with certain drugs. For example, taking caffeine with the decongestant phenylpropanolamine can raise blood pressure. And very serious heart problems may occur if caffeine and **monoamine oxidase inhibitors** (MAO) are taken together. These drugs are used to treat **Parkinson's disease**, depression, and other psychiatric conditions. Consult with a pharmacist or physician about which drugs can interact with caffeine.

Because caffeine stimulates the nervous system, anyone taking other central nervous system (CNS) stimulants should be careful about using caffeine.

Nancy Ross-Flanigan

CAH *see* **Congenital adrenal hyperplasia**

Caisson disease *see* **Decompression sickness**

Calcaneal spurs *see* **Heel spurs**

Calcitonin *see* **Bone disorder drugs**

Calcium carbonate *see* **Antacids**

Calcium channel blockers

Definition

Calcium channel blockers are medicines that slow the movement of calcium into the cells of the heart and blood vessels. This, in turn, relaxes blood vessels, increases the supply of oxygen-rich blood to the heart, and reduces the heart's workload.

Purpose

Calcium channel blockers are used to treat high blood pressure, to correct abnormal heart rhythms, and to relieve the type of chest **pain** called **angina** pectoris. Physicians also prescribe calcium channel blockers to treat panic attacks and **bipolar disorder** (manic depressive illness) and to prevent **migraine headache**.

Precautions

Seeing a physician regularly while taking calcium channel blockers is important. The physician will check to make certain the medicine is working as it should and will watch for unwanted side effects. People who have high blood pressure often feel perfectly fine. However, they should continue to see their prescribing physician even when they feel well so that he can keep a close watch on their condition. They should also continue to take their medicine even when they feel fine.

Calcium channel blockers will not cure high blood pressure, but will help to control the condition. To avoid the serious health problems associated with high blood pressure, patients may have to take this type of medication for the rest of their lives. Furthermore, the blockers alone may not be enough. People with high blood pressure may also need to avoid certain foods and keep their weight under control. The health care professional who is treating the condition can offer advice as to what measures may be necessary. Patients being treated for high blood pressure should not change their **diets** without consulting their physicians.

Anyone taking calcium channel blockers for high blood pressure should not take any other prescription or over-the-counter medication without first checking with the prescribing physician, as some of these drugs may increase blood pressure.

Some people feel drowsy or less alert than usual when taking calcium channel blockers. Anyone who takes these drugs should not drive, use machines, or do anything else that might be dangerous until they have found out how the drugs affect them.

People who normally have chest pain when they **exercise** or exert themselves may not have the pain when they are taking calcium channel blockers. This could lead them to be more active than they should be. Anyone taking calcium channel blockers should therefore consult with the prescribing physician concerning how much exercise and activity may be considered safe.

Some people get headaches that last for a short time after taking a dose of this medication. This problem usually goes away during the course of treatment. If it does not, or if the headaches are severe, the prescribing physician should be informed.

Patients taking certain calcium channel blockers may need to check their pulse regularly, as the drugs may slow the pulse too much. If the pulse is too slow, circulation problems may result. The prescribing physician can show patients the correct way to check their pulse.

This type of medication may cause the gums to swell, bleed, or become tender. If this problem occurs, a medical physician or dentist should be consulted. To help prevent the problem, care should be taken when brushing and flossing the teeth. Regular dental check-ups and cleanings are also recommended.

Older people may be unusually sensitive to the effects of calcium channel blockers. This may increase the chance of side effects.

Special conditions

People with certain medical conditions or who are taking certain other medicines may develop problems if they also take calcium channel blockers. Before taking these drugs, the prescribing physician should be informed about any of these conditions:

ALLERGIES. Anyone who has had a previous unusual reaction to any calcium channel blocker should let his or her physician know before taking the drugs again. The physician should also be notified about any **allergies** to foods, dyes, preservatives, or other substances.

PREGNANCY. The effects of taking calcium channel blockers during **pregnancy** have not been studied in

KEY TERMS

Angina pectoris—A feeling of tightness, heaviness, or pain in the chest, caused by a lack of oxygen in the muscular wall of the heart.

Bipolar disorder—A severe mental illness, also known as manic depression, in which a person has extreme mood swings, ranging from a highly excited state—sometimes with a false sense of well-being—to depression.

Migraine—A throbbing headache that usually affects only one side of the head. Nausea, vomiting, increased sensitivity to light, and other symptoms often accompany migraine.

humans. However, in studies of laboratory animals, large doses of these drugs have been reported to cause **birth defects**, **stillbirth**, poor bone growth, and other problems when taken during pregnancy. Women who are pregnant or who may become pregnant should check with their physicians before using these drugs.

BREASTFEEDING. Some calcium channel blockers pass into breast milk, but there have been no reports of problems in nursing babies whose mothers were taking this type of medication. However, women who need to take this medicine and want to breastfeed their babies should check with their physicians.

OTHER MEDICAL CONDITIONS. Calcium channel blockers may worsen heart or blood vessel disorders.

The effects of calcium channel blockers may be greater in people with kidney or liver disease, as their bodies are slower to clear the drug from their systems.

Certain calcium channel blockers may also cause problems in people with a history of heart rhythm problems or with depression, **Parkinson's disease**, or other types of parkinsonism.

USE OF CERTAIN MEDICINES. Taking calcium channel blockers with certain other drugs may affect the way the drugs work or may increase the chance of side effects.

As with most medications, certain side effects are possible and some interactions with other substances may occur.

Side effects

Side effects are not common with this medicine, but some may occur. Minor discomforts, such as **dizziness**, lightheadedness, flushing, **headache**, and nausea, usually go away as the body adjusts to the drug and do not require medical treatment unless they persist or they are bothersome.

If any of the following side effects occur, the prescribing physician should be notified as soon as possible:

- breathing problems, coughing or wheezing
- irregular, fast, or pounding heartbeat
- slow heartbeat (less than 50 beats per minute)
- skin rash
- swollen ankles, feet, or lower legs

Other side effects may occur. Anyone who has unusual symptoms after taking calcium blockers should contact the prescribing physician.

Interactions

Calcium channel blockers may interact with a number of other medications. When this happens, the effects of one or both of the drugs may change or the risk of side effects may increase. Anyone who takes calcium channel blockers should not take any other prescription or nonprescription (over-the-counter) medicines without first checking with the prescribing physician. Substances that may interact with calcium channel blockers include:

- Diuretics (water pills). This type of medicine may cause low levels of potassium in the body, which may increase the chance of unwanted effects from some calcium channel blockers.
- Beta-blockers, such as atenolol (Tenormin), propranolol (Inderal), and metoprolol (Lopressor), used to treat high blood pressure, angina, and other conditions. Also, eye drop forms of **beta blockers**, such as timolol (Timoptic), used to treat **glaucoma**. Taking any of these drugs with calcium channel blockers may increase the effects of both types of medicine and may cause problems if either drug is stopped suddenly.
- Digitalis heart medicines. Taking these medicines with calcium channel blockers may increase the action of the heart medication.
- Medicines used to correct irregular heart rhythms, such as quinidine (Quinidex), disopyramide (Norpace), and procainamide (Procan, Pronestyl). The effects of these drugs may increase if used with calcium channel blockers.
- Anti-seizure medications such as carbamazepine (Tegretol). Calcium channel drugs may increase the effects of these medicines.
- Cyclosporine (Sandimmune), a medicine that suppresses the immune system. Effects may increase if this drug is taken with calcium channel blockers.
- Grapefruit juice may increase the effects of some calcium channel blockers.

The above list does not include every drug that may interact with calcium channel blockers. The prescribing physician or pharmacist will advise as to whether combining calcium channel blockers with any other prescription or nonprescription (over-the-counter) medication is appropriate or not.

Description

Calcium channel blockers are available only with a physician's prescription and are sold in tablet, capsule, and injectable forms. Some commonly used calcium channel blockers include amlopidine (Norvasc), diltiazem (Cardizem), isradipine (DynaCirc), nifedipine (Adalat, Procardia), nicardipine (Cardene), and verapamil (Calan, Isoptin, Verelan).

The recommended dosage depends on the type, strength, and form of calcium channel blocker and the condition for which it is prescribed. Correct dosage is determined by the prescribing physician and further information can be obtained from the pharmacist.

Calcium channel blockers should be taken as directed. Larger or more frequent doses should not be taken, nor should doses be missed. This medicine may take several weeks to noticeably lower blood pressure. The patient taking calcium channel blockers should keep taking the medicine, to give it time to work. Once it begins to work and symptoms improve, it should continue to be taken as prescribed.

This medicine should not be discontinued without checking with the prescribing physician. Some conditions may worsen when patients stop taking calcium channel blockers abruptly. The prescribing physician will advise as to how to gradually taper down before stopping the medication completely.

Risks

A report from the European Cardiology Society in 2000 found that patients taking certain calcium channel blockers had a 27% greater risk of **heart attack**, and a 26% greater risk of **heart failure** than patients taking other high blood pressure medicines. However, there are many patients affected by conditions that still make calcium channel blockers the best choice for them. The patient should discuss this issue with the prescribing physician.

Normal results

The expected result of taking a calcium channel blocker is to either correct abnormal heart rhythms, return blood pressure to normal, or relieve chest pain.

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Deanna M. Swartout-Corbeil, R.N.

Calcium imbalance *see* **Hypercalcemia; Hypocalcemia**

Calcium polycarbophil *see* **Laxatives**

California flower essences *see* **Flower remedies**

Calluses *see* **Corns and calluses**

Calorie-modified diet *see* **Diets**

Calymmatobacteriosis *see* **Granuloma inguinale**

Campylobacter jejuni infection *see* **Campylobacteriosis**

Campylobacteriosis

Definition

Campylobacteriosis refers to infection by the group of bacteria known as *Campylobacter*. The term comes from the Greek word meaning "curved rod" referring to the bacteria's curved shape. The most common disease caused by these organisms is **diarrhea**, which most often affects children and younger adults. *Campylobacter* infections account for a substantial percent of food-borne illness encountered each year.

Description

There are over 15 different subtypes, all of which are curved Gram-negative rods. *C. jeuni* is the subtype that

KEY TERMS

Antibiotic—A medication that is designed to kill or weaken bacteria.

Anti-motility medications—Medications such as loperamide (Imodium), dephenoxylate (Lomotil), or medications containing codeine or narcotics which decrease the ability of the intestine to contract. This can worsen the condition of a patient with dysentery or colitis.

Fluoroquinolones—A relatively new group of antibiotics that have had good success in treating infections with many Gram-negative bacteria. One drawback is that they should not be used in children under 17 years of age, because of possible effect on bone growth.

Food-borne illness—A disease that is transmitted by eating or handling contaminated food.

Gram-negative—Refers to the property of many bacteria that causes them to not take up color with Gram's stain, a method which is used to identify bacteria. Gram-positive bacteria which take up the stain turn purple, while Gram-negative bacteria which do not take up the stain turn red.

Guillain-Barré syndrome—Progressive and usually reversible paralysis or weakness of multiple muscles usually starting in the lower extremities and often ascending to the muscles involved in respiration. The syndrome is due to inflammation and loss of the myelin covering of the nerve fibers, often associated with an acute infection.

Meninges—Outer covering of the spinal cord and brain. Infection is called meningitis, which can lead to damage to the brain or spinal cord and even death.

Oral Rehydration Solution (ORS)—A liquid preparation developed by the World Health Organization that can decrease fluid loss in persons with diarrhea. Originally developed to be prepared with materials available in the home, commercial preparations have recently come into use.

Stool—Passage of fecal material; a bowel movement.

most often causes gastrointestinal disease. However, some species such as *C. fetus* produce disease outside the intestine, particularly in those with altered immune systems, such as people with **AIDS**, **cancer**, and liver disease.

Campylobacter are often found in the intestine of animals raised for food produce and pets. Infected animals often have no symptoms. Chickens are the most common source of human infection. It is estimated that 1% of the general population is infected each year.

Causes and symptoms

Improper or incomplete food preparation is the most common way the disease is spread, with poultry accounting for over half the cases. Untreated water and raw milk are also potential sources.

The incubation period after exposure is from one to 10 days. A day or two of mild **fever**, muscle aches, and **headache** occur before intestinal symptoms begin. Diarrhea with or without blood and severe abdominal cramps are the major intestinal symptoms. The severity of symptoms is variable, ranging from only mild fever to **dehydration** and rarely **death** (mainly in the very young or old). The disease usually lasts about one week, but persists longer in about 20% of cases. At least 10% will have a relapse, and some patients will continue to pass the bacteria for several weeks.

Complications

Dehydration is the most common complication. Especially at the extremes of age, this should be watched for and treated with either Oral Rehydration Solution or intravenous fluid replacement.

Infection may also involve areas outside the intestine. This is unusual, except for infections with *C. fetus*. *C. fetus* infections tend to occur in those who have diseases of decreased immunity such as AIDS, cancer, etc. This subtype is particularly adapted to protect itself from the body's defenses.

Areas outside the intestine that may be involved are:

- Nervous system involvement either by direct infection of the meninges (outer covering of the spinal and brain) or more commonly by producing the **Guillain-Barré syndrome** (progressive and reversible **paralysis** or weakness of many muscles). In fact, *Campylobacter* may be responsible for 40% of the reported cases of this syndrome.

- Joint inflammation can occur weeks later (leading to an unusual form of arthritis).
- Infection of vessels and heart valves is a special characteristic of *C. fetus*. Immunocompromised patients may develop repeated episodes of passage of bacteria into the bloodstream from these sites of infection.
- The gallbladder, pancreas, and bone may be affected.

Diagnosis

Campylobacter is only one of many causes of acute diarrhea. Culture (growing the bacteria in the laboratory) of freshly obtained diarrhea fluid is the only way to be certain of the diagnosis.

Treatment

The first aim of treatment is to keep up **nutrition** and avoid dehydration. Medications used to treat diarrhea by decreasing intestinal motility, such as Loperamide or Diphenoxylate are also useful, but should only be used with the advice of a physician. **Antibiotics** are of value, if started within three days of onset of symptoms. They are indicated for those with severe or persistent symptoms. Either an erythromycin type drug or one of the **fluoroquinolones** (such as ciprofloxacin) for five to seven days are the accepted therapies.

Prognosis

Most patients with *Campylobacter* infection rapidly recover without treatment. For certain groups of patients, infection becomes chronic and requires repeated courses of antibiotics.

Prevention

Good hand washing technique as well as proper preparation and cooking of food is the best way to prevent infection.

Resources

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OTHER

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David Kaminstein, MD

Cancer

Definition

Cancer is not just one disease, but a large group of almost one hundred diseases. Its two main characteristics are uncontrolled growth of the cells in the human body and the ability of these cells to migrate from the original site and spread to distant sites. If the spread is not controlled, cancer can result in **death**.

Description

One out of every four deaths in the United States is from cancer. It is second only to heart disease as a cause of death in the states. About 1.2 million Americans are diagnosed with cancer annually; more than 500,000 die of cancer annually.

Cancer can attack anyone. Since the occurrence of cancer increases as individuals age, most of the cases are seen in adults, middle-aged or older. Sixty percent of all cancers are diagnosed in people who are older than 65 years of age. The most common cancers are skin cancer, lung cancer, **colon cancer**, **breast cancer** (in women), and **prostate cancer** (in men). In addition, cancer of the kidneys, ovaries, uterus, pancreas, bladder, rectum, and blood and lymph node cancer (leukemias and lymphomas) are also included among the 12 major cancers that affect most Americans.

Cancer, by definition, is a disease of the genes. A gene is a small part of DNA, which is the master molecule of the cell. Genes make "proteins," which are the ultimate workhorses of the cells. It is these proteins that allow our bodies to carry out all the many processes that permit us to breathe, think, move, etc.

Throughout people's lives, the cells in their bodies are growing, dividing, and replacing themselves. Many genes produce proteins that are involved in controlling the processes of cell growth and division. An alteration (mutation) to the DNA molecule can disrupt the genes and produce faulty proteins. This causes the cell to become abnormal and lose its restraints on growth. The abnormal cell begins to divide uncontrollably and eventually forms a new growth known as a "tumor" or neoplasm (medical term for cancer meaning "new growth").

In a healthy individual, the immune system can recognize the neoplastic cells and destroy them before they get a chance to divide. However, some mutant cells may escape immune detection and survive to become tumors or cancers.

Tumors are of two types, benign or malignant. A benign tumor is not considered cancer. It is slow growing, does not spread or invade surrounding tissue, and once it is removed, it doesn't usually recur. A malignant tumor, on the other hand, is cancer. It invades surrounding tissue and spreads to other parts of the body. If the cancer cells have spread to the surrounding tissues, then, even after the malignant tumor is removed, it generally recurs.

A majority of cancers are caused by changes in the cell's DNA because of damage due to the environment. Environmental factors that are responsible for causing the initial mutation in the DNA are called carcinogens, and there are many types.

There are some cancers that have a genetic basis. In other words, an individual could inherit faulty DNA from his parents, which could predispose him to getting cancer. While there is scientific evidence that both factors (environmental and genetic) play a role, less than 10% of all cancers are purely hereditary. Cancers that are known to have a hereditary link are breast cancer, colon cancer, **ovarian cancer**, and uterine cancer. Besides genes, certain physiological traits could be inherited and could contribute to cancers. For example, inheriting fair skin makes a person more likely to develop skin cancer, but only if they also have prolonged exposure to intensive sunlight.

There are several different types of cancers:

- Carcinomas are cancers that arise in the epithelium (the layers of cells covering the body's surface and lining the internal organs and various glands). Ninety percent of human cancers fall into this category. Carcinomas can be subdivided into two types: adenocarcinomas and squamous cell carcinomas. Adenocarcinomas are cancers that develop in an organ or a gland, while squamous cell carcinomas refer to cancers that originate in the skin.
- Melanomas also originate in the skin, usually in the pigment cells (melanocytes).
- Sarcomas are cancers of the supporting tissues of the body, such as bone, muscle and blood vessels.
- Cancers of the blood and lymph glands are called leukemias and lymphomas respectively.
- Gliomas are cancers of the nerve tissue.

Causes and symptoms

The major risk factors for cancer are: tobacco, alcohol, diet, sexual and reproductive behavior, infectious agents, family history, occupation, environment and pollution.

According to the estimates of the American Cancer Society (ACS), approximately 40% of the cancer deaths in 1998 will be due to tobacco and excessive alcohol use. An additional one-third of the deaths will be related to diet and **nutrition**. Many of the one million skin cancers that are expected to be diagnosed in 1998 will be due to over-exposure to ultraviolet light from the sun's rays.

Tobacco

Eighty to ninety percent of the lung cancer cases occur in smokers. **Smoking** has also been shown to be a contributory factor in cancers of upper respiratory tract, esophagus, larynx, bladder, pancreas, and probably liver, stomach, and kidney as well. Recently, scientists have also shown that second-hand smoke (or passive smoking) can increase one's risk of developing cancer.

Alcohol

Excessive consumption of alcohol is a risk factor in certain cancers, such as **liver cancer**. Alcohol, in combination with tobacco, significantly increases the chances that an individual will develop mouth, pharynx, larynx and esophageal cancers.

Diet

Thirty-five percent of all cancers are due to dietary causes. Excessive intake of fat leading to **obesity** has been associated with cancers of the breast, colon, rectum, pancreas, prostate, gall bladder, ovaries and uterus.

Sexual and reproductive behavior

The human papilloma virus, which is sexually transmitted, has been shown to cause cancer of the cervix.

Having too many sex partners and becoming sexually active early has been shown to increase one's chances of contracting this disease. In addition, it has also been shown that women who don't have children or have children late in life have an increased risk for both ovarian and breast cancer.

Infectious agents

In the last 20 years, scientists have obtained evidence to show that approximately 15% of the world's cancer deaths can be traced to viruses, bacteria, or parasites. The most common cancer-causing pathogens and the cancers associated with them are shown in table form.

Family history

Certain cancers like breast, colon, ovarian and uterine cancer recur generation after generation in some families. A few cancers, such as the **eye cancer** "retinoblastoma," a type of colon cancer, and a type of breast cancer known as "early-onset breast cancer," have been shown to be linked to certain genes that can be tracked within a family. It is therefore possible that inheriting particular genes makes a person susceptible to certain cancers.

Occupational hazards

There is evidence to prove that certain occupational hazards account for 4% of all cancer deaths. For example, asbestos workers have an increased incidence of lung cancer. Similarly, a higher likelihood of getting **bladder cancer** is associated with dye, rubber and gas workers; skin and lung cancer with smelters, gold miners and arsenic workers; leukemia with glue and varnish workers; liver cancer with PVC manufacturers; and lung, bone and bone marrow cancer with radiologists and uranium miners.

Environment

Radiation is believed to cause 1–2% of all cancer deaths. Ultra-violet radiation from the sun accounts for a majority of melanoma deaths. Other sources of radiation are x rays, radon gas, and ionizing radiation from nuclear material.

Pollution

Several studies have shown that there is a well-established link between asbestos and cancer. Chlorination of water may account for a small rise in cancer risk. However, the main danger from pollution occurs when dangerous chemicals from the industries escape into the surrounding environment. It has been estimated that 1% of cancer deaths are due to air, land and water pollution.

Frequency Of Cancer-Related Death

Cancer Site	Number of Deaths Per Year
Lung	160,100
Colon and rectum	56,500
Breast	43,900
Prostate	39,200
Pancreas	28,900
Lymphoma	26,300
Leukemia	21,600
Brain	17,400
Stomach	13,700
Liver	13,000
Esophagus	11,900
Bladder	12,500
Kidney	11,600
Multiple myeloma	11,300

Cancer is a progressive disease, and goes through several stages. Each stage may produce a number of symptoms. Some symptoms are produced early and may occur due to a tumor that is growing within an organ or a gland. As the tumor grows, it may press on the nearby nerves, organs and blood vessels. This causes **pain** and some pressure which may be the earliest warning signs of cancer.

Despite the fact that there are several hundred different types of cancers, producing very different symptoms, the ACS has established the following seven symptoms as possible warning signals of cancer:

- changes in the size, color, or shape of a wart or a mole
- a sore that does not heal
- persistent **cough**, hoarseness, or **sore throat**
- a lump or thickening in the breast or elsewhere
- unusual bleeding or discharge
- chronic **indigestion** or difficulty in swallowing
- any change in bowel or bladder habits

Many other diseases, besides cancer, could produce the same symptoms. However, it is important to have these symptoms checked, as soon as possible, especially if they linger. The earlier a cancer is diagnosed and treated, the better the chance of it being cured. Many cancers such as breast cancer may not have any early symptoms. Therefore, it is important to undergo routine screening tests such as breast self-exams and mammograms.

Diagnosis

Diagnosis begins with a thorough **physical examination** and a complete medical history. The doctor will observe, feel and palpate (apply pressure by touch) different parts of the body in order to identify any variations from the normal size, feel and texture of the organ or tissue.

As part of the physical exam, the doctor will inspect the oral cavity or the mouth. By focusing a light into the mouth, he will look for abnormalities in color, moisture, surface texture, or presence of any thickening or sore in the lips, tongue, gums, the hard palate on the roof of the mouth, and the throat. To detect **thyroid cancer**, the doctor will observe the front of the neck for swelling. He may gently manipulate the neck and palpate the front and side surfaces of the thyroid gland (located at the base of the neck) to detect any nodules or tenderness. As part of the physical examination, the doctor will also palpate the lymph nodes in the neck, under the arms and in the groin. Many illnesses and cancers cause a swelling of the lymph nodes.

The doctor may conduct a thorough examination of the skin to look for sores that have been present for more than three weeks and that bleed, ooze, or crust; irritated patches that may itch or hurt, and any change in the size of a wart or a mole.

Examination of the female pelvis is used to detect cancers of the ovaries, uterus, cervix, and vagina. In the visual examination, the doctor looks for abnormal discharges or the presence of sores. Then, using gloved hands the physician palpates the internal pelvic organs such as the uterus and ovaries to detect any abnormal masses. Breast examination includes visual observation where the doctor looks for any discharge, unevenness, discoloration, or scaling. The doctor palpates both breasts to feel for masses or lumps.

For males, inspection of the rectum and the prostate is also included in the physical examination. The doctor inserts a gloved finger into the rectum and rotates it slowly to feel for any growths, tumors, or other abnormalities. The doctor also conducts an examination of the testes, where the doctor observes the genital area and looks for swelling or other abnormalities. The testicles are palpated to identify any lumps, thickening or differences in the size, weight and firmness.

If the doctor detects an abnormality on physical examination, or the patient has some symptom that could be indicative of cancer, the doctor may order diagnostic tests.

Laboratory studies of sputum (sputum cytology), blood, urine, and stool can detect abnormalities that may indicate cancer. Sputum cytology is a test where the phlegm that is coughed up from the lungs is microscopically examined. It is often used to detect lung cancer. A blood test for cancer is easy to perform, usually inexpensive and risk-free. The blood sample is obtained by a lab technician or a doctor by inserting a needle into a vein and is relatively painless. Blood tests can be either specific or non-specific. Often times, in certain cancers, the cancer cells release particular proteins (called **tumor markers**) and blood tests can be used to detect the presence of these tumor markers. However, with a few exceptions, tumor markers are not used for routine screening of cancers, because several non-cancerous conditions also produce positive results. Blood tests are generally more useful in monitoring the effectiveness of the treatment, or in following the course of the disease and detecting recurrent disease.

Imaging tests such as **computed tomography scans** (CT scans), **magnetic resonance imaging** (MRI), ultrasound and fiberoptic scope examinations help the doctors determine the location of the tumor even if it is deep within the body. Conventional x rays are often used for initial evaluation, because they are relatively cheap, painless and easily accessible. In order to increase the information obtained from a conventional x ray, air or a dye (such as barium or iodine) may be used as a contrast medium to outline or highlight parts of the body.

The most definitive diagnostic test is the biopsy, wherein a piece of tissue is surgically removed for microscope examination. Besides confirming a cancer, the biopsy also provides information about the type of cancer, the stage it has reached, the aggressiveness of the cancer and the extent of its spread. Since a biopsy provides the most accurate analysis, it is considered the gold standard of diagnostic tests.

Screening examinations conducted regularly by healthcare professionals can result in the detection of cancers of the breast, colon, rectum, cervix, prostate, testis, tongue, mouth, and skin at early stages, when treatment is more likely to be successful. Some of the routine screening tests recommended by the ACS are **sigmoidoscopy** (for colorectal cancer), **mammography** (for breast cancer), pap smear (for **cervical cancer**), and the PSA test (for prostate cancer). Self-examinations for cancers of the breast, testes, mouth, and skin can also help in detecting the tumors before the symptoms become serious.

A recent revolution in molecular biology and cancer genetics has contributed a great deal to the development of several tests designed to assess one's risk of getting cancers. These new techniques include **genetic testing**, where molecular probes are used to identify mutations in certain genes that have been linked to particular cancers. At present, however, there are a lot of limitations to genetic testing and its utility appears ambiguous, emphasizing the need to develop better strategies for early detection.

Treatment

The aim of cancer treatment is to remove all or as much of the tumor as possible and to prevent the recurrence or spread of the primary tumor. While devising a treatment plan for cancer, the likelihood of curing the

Common Pathogens And The Cancers Associated With Them

Causative Angent	Type of Cancer
Viruses	
Papillomaviruses	Cancer of the cervix
Hepatitis B virus	Liver cancer
Hepatitis C virus	Liver cancer
Epstein-Barr virus	Burkitt's lymphoma
Cancers of the upper pharynx	Hodgkin's lymphoma, Non-Hodgkin's lymphoma, Gastric cancers
Human immunodeficiency virus (HIV)	Kaposi's sarcoma lymphoma
Bacteria	
Helicobacter pylori	Stomach cancer lymphomas

cancer has to be weighed against the side effects of the treatment. If the cancer is very aggressive and a cure is not possible, then the treatment should be aimed at relieving the symptoms and controlling the cancer for as long as possible.

Cancer treatment can take many different forms, and it is always tailored to the individual patient. The decision on which type of treatment is the most appropriate depends on the type and location of cancer, the extent to which it has already spread, the patient's age, sex, general health status and personal treatment preferences. The major types of treatment are: surgery, radiation, **chemotherapy**, immunotherapy, hormone therapy, and bone-marrow transplantation.

Surgery

Surgery is the removal of a visible tumor and is the most frequently used cancer treatment. It is most effective when a cancer is small and confined to one area of the body.

Surgery can be used for many purposes.

- Treatment. Treatment of cancer by surgery involves removal of the tumor to cure the disease. This is typically done when the cancer is localized to a discrete area. Along with the cancer, some part of the normal surrounding tissue is also removed to ensure that no cancer cells remain in the area. Since cancer usually spreads via the lymphatic system, adjoining lymph nodes may be examined and sometimes they are removed as well.
- Preventive surgery. Preventive or prophylactic surgery involves removal of an abnormal looking area that is likely to become malignant over time. For example, 40% of the people with a colon disease known as **ulcerative colitis**, ultimately die of colon cancer. Rather than live with the fear of developing colon cancer, these people may choose to have their colons removed and reduce the risk significantly.
- Diagnostic purposes. The most definitive tool for diagnosing cancer is a biopsy. Sometimes, a biopsy can be performed by inserting a needle through the skin. However, at other times, the only way to obtain some tissue sample for biopsy is by performing a surgical operation.
- Cytoreductive surgery is a procedure where the doctor removes as much of the cancer as possible, and then treats the remaining with **radiation therapy** or chemotherapy or both.
- Palliative surgery is aimed at curing the symptoms, not the cancer. Usually, in such cases, the tumor is so large or has spread so much that removing the entire tumor is not an option. For example, a tumor in the abdomen may be so large that it may press on and block a portion of the intestine, interfering with digestion and causing pain and vomiting. "Debulking surgery" may remove a part of the blockage and relieve the symptoms. In tumors that are dependent on hormones, removal of the organs that secrete the hormones is an option. For example, in prostate cancer, the release of testosterone by the testicles stimulates the growth of cancerous cells. Hence, a man may undergo an "orchiectomy" (removal of testicles) to slow the progress of the disease. Similarly, in a type of aggressive breast cancer, removal of the ovaries (**oophorectomy**) will stop the synthesis of hormones from the ovaries and slow the progression of the cancer.

Radiation

Radiation kills tumor cells. Radiation is used alone in cases where a tumor is unsuitable for surgery. More often, it is used in conjunction with surgery and chemotherapy. Radiation can be either external or internal. In the external form, the radiation is aimed at the tumor from outside the body. In internal radiation (also known as brachytherapy), a radioactive substance in the form of pellets or liquid is placed at the cancerous site by means of a pill, injection or insertion in a sealed container.

Chemotherapy

Chemotherapy is the use of drugs to kill cancer cells. It destroys the hard-to-detect cancer cells that have spread and are circulating in the body. Chemotherapeutic drugs can be taken either orally (by mouth) or intravenously, and may be given alone or in conjunction with surgery, radiation or both.

When chemotherapy is used before surgery or radiation, it is known as primary chemotherapy or "neoadjuvant chemotherapy." An advantage of neoadjuvant chemotherapy is that since the cancer cells have not been exposed to anti-cancer drugs, they are especially vulnerable. It can therefore be used effectively to reduce the size of the tumor for surgery or target it for radiation. However, the toxic effects of neoadjuvant chemotherapy are severe. In addition, it may make the body less tolerant to the side effects of other treatments that follow such as radiation therapy. The more common use of chemotherapy is adjuvant therapy, which is given to enhance the effectiveness of other treatments For example, after surgery, adjuvant chemotherapy is given to destroy any cancerous cells that still remain in the body.

Immunotherapy

Immunotherapy uses the body's own immune system to destroy cancer cells. This form of treatment is being intensively studied in clinical trials and is not yet widely available to most cancer patients. The various immunological agents being tested include substances produced by the body (such as the interferons, interleukins, and growth factors), monoclonal antibodies and vaccines. Unlike traditional vaccines, cancer vaccines do not prevent cancer. Instead, they are designed to treat people who already have the disease. Cancer vaccines work by boosting the body's immune system and training the immune cells to specifically destroy cancer cells.

Hormone therapy

Hormone therapy is standard treatment for some types of cancers that are hormone-dependent and grow faster in the presence of particular hormones. These include cancer of the prostate, breast, and uterus. Hormone therapy involves blocking the production or action of these hormones. As a result the growth of the tumor slows down and survival may be extended for several months or years.

Bone marrow transplantation

The bone marrow is the tissue within the bone cavities that contains blood-forming cells. Healthy bone marrow tissue constantly replenishes the blood supply and is essential to life. Sometimes, the amount of drugs or radiation needed to destroy cancer cells also destroys bone marrow. Replacing the bone marrow with healthy cells counteracts this adverse effect. A bone marrow transplant is the removal of marrow from one person and the transplant of the blood-forming cells either to the same person or to someone else. Bone-marrow transplantation, while not a therapy in itself, is often used to "rescue" a patient, by allowing those with cancer to undergo very aggressive therapy.

Many different specialists generally work together as a team to treat cancer patients. An oncologist is a physician who specializes in cancer care. The oncologist provides chemotherapy, hormone therapy, and any other non-surgical treatment that does not involve radiation. The oncologist often serves as the primary physician and coordinates the patient's treatment plan.

The radiation oncologist specializes in using radiation to treat cancer, while the surgical oncologist performs the operations needed to diagnose or treat cancer. Gynecologist-oncologists and pediatric-oncologists, as their titles suggest, are physicians involved with treating women's and children's cancers respectively. Many other specialists may also be involved in the care of a cancer patient. For example, radiologists specialize in the use of x rays, ultrasounds, computed tomography scans (CT scans), MRI imaging and other techniques that are used to diagnose cancer. Hematologists specialize in disorders of the blood and are consulted in case of blood cancers and bone marrow cancers. The samples that are removed for biopsy are sent to a laboratory, where a pathologist examines them to determine the type of cancer and extent of the disease. Only some of the specialists who are involved with cancer care have been mentioned above. There are many other specialties, and virtually any type of medical or surgical specialist may become involved with care of the cancer patient should it become necessary.

Alternative treatment

There are a multitude of alternative treatments available to help the person with cancer. They can be used in conjunction with, or separate from, surgery, chemotherapy, and radiation therapy. Alternative treatment of cancer is a complicated arena and a trained health practitioner should be consulted.

Although the effectiveness of complementary therapies such as **acupuncture** in alleviating cancer pain has not been clinically proven, many cancer patients find it safe and beneficial. Bodywork therapies such as massage and **reflexology** ease muscle tension and may alleviate the side effects such as **nausea and vomiting**. **Homeopathy** and herbal remedies used in Chinese traditional

herbal medicine have also been shown to alleviate some of the side effects of radiation and chemotherapy and are being recommended by many doctors.

Certain foods including many vegetables, fruits and grains are believed to offer protection against various cancers. However, isolation of the individual constituent of vegetables and fruits that are anti-cancer agents has proven difficult. In laboratory studies, **vitamins** such as A, C and E, as well as compounds such as isothiocyanates and dithiolthiones found in broccoli, cauliflower, and cabbage, and beta-carotene found in carrots have been shown to protect against cancer. Studies have shown that eating a diet rich in fiber as found in fruits and vegetables reduces the risk of colon cancer. **Exercise** and a low fat diet help control weight and reduce the risk of endometrial, breast, and colon cancer.

Certain drugs, which are currently being used for treatment, could also be suitable for prevention. For example, the drug tamoxifen (Nolvadex), which has been very effective against breast cancer, is currently being tested by the National Cancer Institute for its ability to prevent cancer. Similarly, retinoids derived from vitamin A are being tested for their ability to slow the progression or prevent head and neck cancers. Certain studies have suggested that cancer incidence is lower in areas where soil and foods are rich in the mineral selenium. More trials are needed to explain these intriguing connections.

Prognosis

"Lifetime risk" is the term that cancer researchers use to refer to the probability that an individual over the course of a lifetime will develop cancer or die from it. In the United States, men have a one in two lifetime risk of developing cancer, and for women the risk is one in three. Overall, African-Americans are more likely to develop cancer than whites. African-Americans are also 30% more likely to die of cancer than whites.

Most cancers are curable if detected and treated at their early stages. A cancer patient's prognosis is affected by many factors, particularly the type of cancer the patient has, the stage of the cancer, the extent to which it has metastasized and the aggressiveness of the cancer. In addition, the patient's age, general health status and the effectiveness of the treatment being pursued are also important factors.

To help predict the future course and outcome of the disease and the likelihood of recovery from the disease, doctors often use statistics. The five-year survival rates are the most common measures used. The number refers to the proportion of people with cancer who are expected to be alive, five years after initial diagnosis, compared with a similar population that is free of cancer. It is important to note that while statistics can give some information about the average survival experience of cancer patients in a given population, it cannot be used to indicate individual prognosis, because no two patients are exactly alike.

A transmission electron micrograph (TEM) of two spindle cell nuclei from a human sarcoma. Sarcomas are cancers of the connective tissue (bone, nerves, smooth muscle). *(Photograph by Dr. Brian Eyden, Photo Researchers, Inc. Reproduced by permission.)*

Prevention

According to nutritionists and epidemiologists from leading universities in the United States, a person can reduce the chances of getting cancer by following some simple guidelines:

- eating plenty of vegetables and fruits
- exercising vigorously for at least 20 minutes every day
- avoiding excessive weight gain
- avoiding tobacco (even second hand smoke)
- decreasing or avoiding consumption of animal fats and red meats
- avoiding excessive amounts of alcohol
- avoiding the midday sun (between 11 A.M. and 3 P.M.) when the suns rays are the strongest
- avoiding risky sexual practices
- avoiding known carcinogens in the environment or work place

KEY TERMS

Benign—A growth that does not spread to other parts of the body. Recovery is favorable with treatment.

Biopsy—The surgical removal and microscopic examination of living tissue for diagnostic purposes.

Bone marrow—Spongy material that fills the inner cavities of the bones. The progenitors of all the blood cells are produced in this bone marrow.

Carcinogen—Any substance capable of causing cancer by mutating the cell's DNA.

Chemotherapy—Treatment with drugs that are anti cancer.

Epithelium—The layer of cells covering the body's surface and lining the internal organs and various glands.

Hormone therapy—Treatment of cancer by inhibiting the production of hormones such as testosterone and estrogen.

Immunotherapy—Treatment of cancer by stimulating the body's immune defense system.

Malignant—A general term for cells that can dislodge from the original tumor, invade and destroy other tissues and organs.

Metastasis—The spread of cancer from one part of the body to another.

Radiation therapy—Treatment using high-energy radiation from x-ray machines, cobalt, radium, or other sources.

Sore—An open wound or a bruise or lesion on the skin.

Tumor—An abnormal growth resulting from a cell that lost its normal growth control restraints and started multiplying uncontrollably.

X rays—High-energy radiation used in high doses, either to diagnose or treat disease.

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Rosalyn Carson-DeWitt

Cancer chemotherapy drugs *see* **Anticancer drugs**

Cancer therapy, definitive

Definition

Definitive **cancer** therapy is a treatment plan designed to potentially cure cancer using one or a combination of interventions including surgery, radiation, chemical agents, or biological therapies.

Purpose

The primary purpose of definitive care is to establish a cure and to destruct and remove all cancer cells from the infected person.

Surgery is not only a diagnostic tool, but also used for **tumor removal**. The surgeon usually identifies potential candidates for tumor removal and repairs intraoperatively (during the operation procedure). Surgery can be curative for some stomach, genital/urinary, thyroid, breast, skin, and central nervous system cancers. The best chance for a surgical cure is usually with the first opera-

tion. It is essential that the cancer surgeon (oncologic surgeon) be experienced in the specific procedure.

Radiation therapy is commonly administered to approximately 50% of cancer patients during the course of illness. It can be used as the sole method of cure for tumors in the mouth and neighboring structures in the oral cavity, vagina, prostate, cervix, esophagus, **Hodgkin's disease**, and certain types of cancer in the spinal cord and brain. Research and clinical trials have demonstrated that combination treatment is more effective than radiotherapy alone.

Chemotherapy is curative for only a small percentage of cancers. It is most effective for **choriocarcinoma**, cancer of the testis, some types of lymphomas, and cancer of skeletal muscles.

Biological therapies are a new and promising direction for cancer cures. Usually when cancer cells grow they manage to derive a blood supply that allows passage of nutrients promoting continuation of abnormal cancer growth. Research that focuses on destroying these blood vessels is called angiogenesis. Cutting off the blood supply has been shown to destroy tumors, since this stops the flow of essential nutrients required for cancer growth. Use of certain growth factors can also stimulate self-destructive pathways in cancer cells (apoptosis). **Gene therapy** is directed towards inhibiting specific cellular signals that promote cancer cell multiplication.

Precautions

Surgical resection requires an experienced surgeon, preoperative assessment, imaging studies, and delicate operative technique. Care should be taken during the procedure to avoid unnecessary tumor manipulation, which can cause cancer cells to infiltrate adjacent structures. If manipulation is excessive, cells can enter nearby areas for future re-growth. Accurate isolation of the tumor can also help to avoid contamination of the surgical area. Early ligation of the blood supply to the tumor is an essential component of a surgical cure.

Radiotherapy requires extensive treatment planning and imaging. Care must be taken to localize the cancer field while attempting to spare destruction of normal tissue. This requires image monitoring and exact positioning during radiation treatment sessions.

Chemotherapy usually causes destruction of normal cells, and cancer cells can become immune to chemical destruction. Side effects and patient tolerance issues are typically anticipated and dosages may have to be specifically altered. Very few chemotherapeutic agents offer curative responses.

Biological therapies may cause patient toxicity resulting in extensive side effects. This can occur since the optimal dose may be exceedingly elevated above patient tolerance.

Description

Surgery

Surgical removal of the tumor must be performed with care and accuracy. The surgeon must avoid over manipulation of the surgical field. Too much movement within the area can cause cancer cell displacement into surrounding tissue. If this occurs and no further treatment is indicated, the tumor may grow again. The surgeon should also perform an assessment concerning tissue removal around the cancer site. Tissue around the site may not by inspection seem cancerous, but adjacent structures may have cancer cells and surrounding tissue removal is usually part of the operative procedure. Pieces of tumor and the surrounding area are analyzed microscopically during the operation for cell type. An adequate resection (removal of tissue) will reveal normal cells in the specimens analyzed from areas bordering the cancerous growth. Surgery can also help to decrease the tumor bulk and, along with other treatment measures, may provide a cure for certain cancers.

Not only can surgery be curative for some cancers, but it is an essential diagnostic tool that must be assessed intraoperatively since microscopic analysis will guide the surgeon concerning tumor and surrounding tissue removal. These diagnostic procedures include an aspiration biopsy, which inserts a needle to extract (aspirate) fluid contained inside a cancerous growth; a needle biopsy uses a specialized needle to obtain a core tissue specimen; an incision biopsy removes a section from a large tumor; and an excision biopsy removes the entire tumor. The surgeon can also take samples of neighboring lymph nodes. Cancer in surrounding lymph nodes is an important avenue for distant spread of cancer to other areas. If microscopic analysis determines the presence of cancer cells in lymph nodes then the surgeon may decide to perform a more aggressive surgical approach.

Radiation therapy

Similar to surgical intervention, radiotherapy is a localized treatment. It involves the administration of ionizing radiation to a solid tumor location. This generates reactive oxygen molecules, causing the destruction of DNA in local cells. There are three commonly used radiotherapy beams: gamma rays from a linear accelerator machine produce a focused beam; orthovoltage rays are of less energy, thus penetrate less and typically deliver higher doses to superficial tissues (efficient for treating skin cancers); and megavoltage rays are high energy producing beams and can penetrate deeply situated inter-

KEY TERMS

Bone marrow suppression—A decrease in cells responsible for providing immunity, carrying oxygen and those responsible for normal blood clotting.

DNA—The molecule responsible for cell multiplication.

Titrate—To analyze the best end point (for dose) for a medication.

nal organs, while sparing extensive skin damage. Two common routes can deliver radiation. Brachytherapy delivers radiation to a local area by placing radioactive materials within close proximity to the cancerous site. Teletherapy delivers radiation to a specific area using an external beam machine.

Chemotherapy

Curative chemotherapy usually requires multiple administrations of the chemical agent. Chemotherapy or systemic therapy is administered in the blood and circulates through the entire body. The choice of chemotherapeutic agents depends on the specific type of cancer. Chemotherapy is more commonly used for metastatic (malignant cancer which has spread to other areas beyond the primary site of cancer growth) disease, since very few cancers are cured by systemic therapy.

Biologic therapy

Biologic therapies primarily function to alter the patient's response to cancer. These treatments are mostly investigations and there are numerous research protocols studying the effects of biologic treatments. These protocols usually have strict admission criteria that may exclude potential candidates who can benefit from treatment. These treatments tend to stimulate specific immune cells or immune chemicals to destroy cancer cells.

Preparation

For all treatment modalities imaging studies, biopsy, and constant blood analysis is essential before, during, and after treatments. Surgical candidates should undergo extensive pre-operative evaluation with imaging studies, blood chemistry analysis, stabilized health status, and readiness of staff for any potential complications and cell biopsy analysis. Patients with other pre-existing chronic disease may require intensive post-operative monitoring.

For radiotherapy, the patient undergoes extensive imaging studies. Additional planning strategies include beam localization to spare normal tissues, calibration of fractionated doses, and specific positioning during treatment sessions.

Patients who receive curative chemotherapy should be informed of possible side effects associated with the chemotherapeutic agent. Patients should also be informed of temporary lifestyle changes and medications that may offer some symptomatic relief.

Patients undergoing biologic therapies are usually advised of potential side effects, treatment cycles and specific tests for monitoring progress according to the specific research protocol.

Aftercare

Patients will typically be evaluated by imaging studies, blood analysis, **physical examination**, and health improvement. These follow-up visits usually occur at specific time intervals during the course of treatment. Surgical patients may require closer observation during the initial post-operative period to avoid potential complications. Reconstructive surgery can be considered to improve appearance and restore function. Certain surgical procedures (such as flaps and microsurgery of blood vessels) can restore new tissues to a previous surgery site.

Risks

Surgical risks

Surgical therapy can be both disfiguring and disabling. Many normal tissues can be adversely affected by radiotherapy. Side effects that commonly occur shortly after a treatment cycle include nausea, vomiting, **fatigue**, loss of appetite, and bone marrow suppression (a decrease in the cells that provide defense against infections and those which carry oxygen to cells).

Radiation risks

Radiotherapy can also cause difficulty swallowing, oral gum disease, and **dry mouth**. Additionally, radiation therapy can cause damage to local structures within the irradiated field.

Chemotherapy risks

Chemotherapy commonly causes bone marrow suppression. Additionally, a cell called platelets—important for normal blood clotting—may be significantly lowered, causing patients to bleed. This may be problematic enough to limit the treatment course. Bone marrow suppression can increase susceptibility to infection and also cause **infertility**. Patients commonly have bouts of **nausea and vomiting** shortly after a treatment session. Rapidly multiplying normal cells are also affected such as skin cells (causing blistering and ulceration) and hair cells (causing loss of hair, a condition called **alopecia**).

Biologic therapies risks

Biologic therapies can cause patients to develop suppression of cells that help the body fight against infection. Administration of certain chemicals that have anticancer effects can cause heart damage. Injection of killer immune cells (lymphokine-activated killer cells) may cause bone marrow suppression, and the host may reject the newly introduced cells.

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Cancer therapy, palliative

Definition

Palliative **cancer** therapy is treatment specifically directed to help improve the symptoms associated with terminal cancer.

Purpose

Palliative care is directed to improving symptoms associated with incurable cancer. Care can include surgery, **radiation therapy**, **chemotherapy**, symptomatic treatments resulting from cancer, and side effects of treatment. The primary objective of palliative care is to improve the quality of remaining duration of life. Treatment usually involves a combination of modalities (multimodality approach) and numerous specialists are typically involved in the treatment planning process. Therapeutic planning usually involves meticulous coordination with the treatment team.

Surgery can be utilized for palliation after careful evaluation and planning. The use of surgery in these cases may reduce the tumor bulk and help improve the quality of life by relieving **pain**, alleviating obstruction, or controlling bleeding. Radiotherapy for terminal cancer patients can also alleviate pain, bleeding, and obstruction of neighboring areas. Chemotherapy may be helpful to reduce tumor size and provide some reduction to metastatic disease. Long-term chemotherapy patients develop drug resistance, a situation that renders chemotherapeutic treatments ineffective. If this occurs patients are usually given a second line medication or, if admission criteria are met, they may participate in an experimental research protocol. Palliative treatments and terminal cancer in combination can cause many symptoms that can become problematic. These symptoms commonly include pain, nausea, vomiting, difficulty in breathing, **constipation**, dehydration, agitation, and **delirium**. The palliative treatment-planning goal focuses to reduce these symptoms.

Precautions

Surgery for the purpose of **tumor removal**, biopsy, or size reduction is associated with postoperative pain and local nerve damage, which may be both severe and difficult to alleviate. Chemotherapy and radiation therapy can also produce nerve damage and severe pain. Additionally, patients with malignant cancer are susceptible to infections like herpes, **pneumonia**, urinary tract infections, and wound **abscess**, all of which can cause severe pain. Pain associated with cancer and/or treatments can significantly impair the patient's capabilities for performing daily tasks and hence impair quality of life. These complications may negatively impact the patient's psychological well being.

Description

Pain is one of the common symptoms associated with cancer. Approximately 75% of terminal cancer patients have pain. Pain is a subjective symptom and thus it cannot be measured using technological approaches. Pain can be assessed using numeric scales (from one to 10, one is rated as no pain while 10 is severe) or rating specific facial expressions associated with various levels of pain. The majority of cancer patients experience pain as a result of tumor mass that compresses neighboring nerves, bone, or soft tissues, or from direct nerve injury (neuropathic pain). Pain can occur from affected nerves in the ribs, muscles, and internal structures such as the abdomen (cramping type pain associated with obstruction). Many patients also experience various types of pain as a direct result of follow-up tests, treatments (surgery, radiation, and chemotherapy) and diagnostic procedures (i.e., biopsy).

Preparation

Patients are typically informed that their diagnosis is terminal and treatments are directed to improve quality of life for the remaining time and to minimize emotional suffering associated with pain.

KEY TERMS

Opioids—Narcotic pain killing medication.

World Health Organization (WHO)—An international organization concerned with world health and welfare.

A careful history is necessary to assess duration, severity, and location of pain. A **physical examination** may verify the presence of pain. Imaging analysis may further confirm the presence of potential causes of pain. The World Health Organization (WHO) recommends an analgesic ladder. This treatment approach provides medication selections based on previous analgesic use and severity of pain. The ladder starts with the use of non-opioid (non-morphine) drugs such as **aspirin**, acetaminophin, or non-steroidal anti-inflammatory medications for control of mild pain. Chronic pain must be treated with constant and consistently administered medication(s). The "take as needed" approach is not advised. Supplemental doses may be recommended in addition to the standard dose for circumstances that may worsen pain. Opioids (i.e., morphine and codeine) are the medications of choice for moderate to severe pain. Doses are adjusted to produce maximum pain relief while minimizing side effects. These medications are conveniently administered orally. Administering steroids can help reduce **nausea and vomiting**. Delirium and **anxiety** may be improved by psychoactive medications.

Aftercare

Care for palliation is continuous and consistent for the remainder of life. Patients who have less than six months of life remaining may choose a hospice to stop treatment and control pain.

Risks

Patients taking opioids for pain relief can develop tolerance and dependence. Tolerance develops when a patient requires increasing amounts of medication to produce pain reduction. Dependence shows characteristic withdrawal symptoms if medications are abruptly stopped. These symptoms can be avoided by tapering down doses in the event that these medications should be stopped.

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Cancer therapy, supportive

Definition

Supportive **cancer** therapy is the use of medicines to counteract unwanted effects of cancer treatment.

Purpose

Along with their beneficial effects, many cancer treatments produce uncomfortable and sometimes harmful side effects. For example, cancer drugs may cause nausea or vomiting. They may also destroy red or white blood cells, resulting in a low **blood count**. Fortunately, many of these side effects can be relieved with other medicines.

Description

Different kinds of drugs are used for different purposes in supportive cancer therapy. To relieve **nausea and vomiting**, a physician may prescribe dolasetron (Anzemet), granisetron (Kytril) or ondansetron (Zofran). Drugs called colony stimulating factors are used to help the bone marrow make new white blood cells to replace those destroyed by cancer treatment. Examples of colony stimulating factors are filgrastim (Neupogen) and sargramostim (Leukine). Another type of drug, epoetin (Epogen, Procrit), stimulates the bone marrow to make new red blood cells. It is a synthetically made version of human erythropoietin that is made naturally in the body and has the same effect on bone marrow.

Some physicians who treat cancer recommend that their patients use **marijuana** to relieve nausea and vomiting. This practice is controversial for several reasons. Using marijuana, even for medicinal purposes, is illegal in most states. Also, most of the evidence that marijuana effectively relieves nausea and vomiting comes from reports of people who have used it, not from carefully designed scientific studies. An oral medication that contains one of the active ingredients of marijuana is available with a physician's prescription and sometimes is used to treat nausea and vomiting in patients undergoing cancer treatment. However, the drug, dronabinol (Marinol), takes longer to work than smoked marijuana and may be difficult for patients with nausea and vomiting to swallow and keep down.

In 1997, the National Institutes of Health issued a report calling for more research into medical uses of marijuana. The panel of experts who wrote the report also recommended that researchers investigate other ways of getting the active ingredients of marijuana into the body, such as nasal sprays, skin patches and inhalers.

Patients who want to use marijuana to relieve side effects of cancer treatment should talk to their physicians and should carefully consider the benefits and risks, both medical and legal.

Recommended dosage

The recommended dosage depends on the type of supportive cancer therapy. Check with the physician who prescribed the drug or the pharmacist who filled the prescription for the correct dosage.

Precautions

Dolasetron, granisetron and ondansetron

If severe nausea and vomiting occur after taking this medicine, check with a physician.

The use of ondansetron after abdominal surgery may cover up symptoms of stomach problems.

People with liver disease may be more likely to have side effects from ondansetron.

Colony stimulating factors

Certain cancer drugs reduce the body's ability to fight infections. Although colony stimulating factors help restore the body's natural defenses, the process takes time. Getting prompt treatment for infections is important, even while taking this medicine. Call the physician at the first sign of illness or infection, such as a **sore throat**, **fever** or chills.

Seeing a physician regularly while taking this medicine is important. This will give the physician a chance to make sure the medicine is working and to check for unwanted side effects.

People with certain medical conditions may have problems if they take colony stimulating factors. In people who have kidney disease, liver disease, or conditions caused by inflammation or immune system problems, colony stimulating factors may make these problems worse. People with heart disease may be more likely to have side effects such as water retention and heart rhythm problems when they take these drugs. And people with lung disease may be more likely to have **shortness of breath**. Anyone who has any of these medical conditions should check with his or her physician before using colony stimulating factors.

Epoetin

This medicine may cause seizures (convulsions), especially in people with a history of seizures. Anyone who takes these drugs should not drive, use machines or do anything else that might be dangerous if they have had a seizure.

Epoetin helps the body make new red blood cells, but it cannot do its job unless there is plenty of iron in the body. The physician may recommend taking iron supplements or certain **vitamins** that help get iron into the body. Follow the physician's orders to make sure the body has enough iron for this medicine to work. Do not take iron supplements unless they are prescribed by a physician.

In studies of laboratory animals, epoetin taken during **pregnancy** caused **birth defects**, including damage to the bones and spine. However, the drug has not been reported to cause problems in human babies whose mothers take it. Women who are pregnant or who may become pregnant should check with their physicians for the most up-to-date information on the safety of taking this medicine during pregnancy.

People with certain medical conditions may have problems if they take this medicine. For example, the chance of side effects may be greater in people with high blood pressure, heart or blood vessel disease or a history of blood clots. Epoetin may not work properly in people who have bone problems or sickle cell anemia.

Dronabinol

This medicine contains sesame oil and one of the active ingredients of marijuana. Anyone who has had allergic or unusual reactions to sesame oil or marijuana products should let his or her physician know before taking dronabinol.

KEY TERMS

Bipolar disorder—A severe mental illness in which a person has extreme mood swings, ranging from a highly excited state—sometimes with a false sense of well-being—to depression

Bone marrow—Soft tissue that fills the hollow centers of bones. Blood cells and platelets (disk-shaped bodies in the blood that are important in clotting) are produced in the bone marrow.

Hallucination—A false or distorted perception of objects, sounds, or events that seems real. Hallucinations usually result from drugs or mental disorders.

Immune system—The body's natural defenses against disease and infection.

Inflammation—Pain, redness, swelling, and heat that usually develop in response to injury or illness.

Schizophrenia—A severe mental disorder in which people lose touch with reality and may have illogical thoughts, delusions, hallucinations, behavioral problems and other disturbances.

Sickle cell anemia—An inherited disorder in which red blood cells contain an abnormal form of hemoglobin, a protein that carries oxygen. The abnormal form of hemoglobin causes the red cells to become sickle- or crescent-shaped. The misshapen cells may clog blood vessels, preventing oxygen from reaching tissues and leading to pain, blood clots and other problems. Sickle cell anemia is most common in people of African descent and in people from Italy, Greece, India, and the Middle East.

Because dronabinol works on the central nervous system, it may add to the effects of alcohol and other drugs that slow down the central nervous system. Examples of these drugs are **antihistamines**, cold medicine, allergy medicine, sleep aids, medicine for seizures, tranquilizers, some **pain** relievers, and **muscle relaxants**. Dronabinol may also add to the effects of anesthetics, including those used for dental procedures. Anyone taking dronabinol should not drink alcohol and should check with his or her physician before taking any of the drugs listed above.

This drug makes some people feel drowsy, dizzy, lightheaded or "high," with a sense of well-being. Because of these possible reactions, anyone who takes dronabinol should not drive, use machines or do anything else that might be dangerous until they have found out how the drug affects them. The **dizziness** and lightheadedness are especially likely when getting up after sitting or lying down. Getting up gradually and holding onto something for support should lessen the problem.

In laboratory studies, giving high doses of dronabinol to pregnant animals increased the risk of the unborn baby's **death**. The medicine's effects on pregnant women have not been studied. Women who are pregnant or who may become pregnant should check with their physicians before taking this medicine.

Dronabinol passes into breast milk and may affect nursing babies whose mothers take the medicine. Women who are breastfeeding their babies should check with their physicians before using dronabinol.

Because of its possible mind-altering effects, dronabinol should be used with care in children and older people. Both children and older people should be watched carefully when they are taking this medicine.

Using dronabinol may worsen some medical conditions, including high blood pressure, heart disease, **bipolar disorder** and **schizophrenia**.

General precautions for all types of supportive cancer therapy

Anyone who previously has had unusual reactions to drugs used in supportive cancer therapy should let his or her physician know before taking the drugs again. The physician should also be told about any **allergies** to foods, dyes, preservatives, or other substances.

Side effects

Dolasetron, granisetron and ondansetron

The most common minor side effects are **headache**, dizziness or lightheadedness, drowsiness, **dry mouth**, **diarrhea**, **constipation**, abdominal pain or stomach cramps and unusual tiredness or weakness. These problems usually do not require medical treatment.

Check with a physician as soon as possible if fever occurs after taking granisetron.

If any of these symptoms occur after taking ondansetron, check with a physician immediately:

- breathing problems or **wheezing**
- chest pain or tightness in chest
- skin rash, **hives** or **itching**

Colony stimulating factors

As this medicine starts to work, it may cause mild pain in the lower back or hips. This is nothing to worry about, and it will usually go away within a few days. If the pain is too uncomfortable, the physician may pre-

scribe a painkiller. Be sure to let the physician know if the painkiller does not help.

Other possible side effects include headache, joint or muscle pain, and skin rash or itching. These side effects usually go away as the body adjusts to the medicine and do not need medical treatment. If they continue or they interfere with normal activities, check with a physician.

Epoetin

This medicine may cause flu-like symptoms, such as muscle aches, bone pain, fever, chills, shivering, and sweating, within a few hours after it is taken. These symptoms usually go away within 12 hours. If they do not, or if they are troubling, check with a physician. Other possible side effects that do not need medical attention are diarrhea, nausea or vomiting, and tiredness or weakness.

Certain side effects should be brought to a physician's attention as soon as possible. These include headache, vision problems, increased blood pressure, fast heartbeat, weight gain, and swelling of the face, fingers, lower legs, ankles or feet.

Anyone who has chest pain or seizures after taking epoetin should check with a physician immediately.

Dronabinol

Side effects such as dizziness, drowsiness, confusion and clumsiness or unsteadiness usually do not need medical attention unless they are long-lasting or they interfere with normal activities.

Other side effects or signs of overdose should have immediate medical attention. These include:

- fast or pounding heartbeat
- constipation
- trouble urinating
- red eyes
- slurred speech
- mood changes, including depression, nervousness or **anxiety**
- confusion
- forgetfulness
- changes in sight, smell, taste, touch or hearing
- a sense that time is speeding up or slowing down
- **hallucinations**

General advice on side effects for all types of supportive cancer therapy

Other side effects are possible with any type of supportive cancer therapy. Anyone who has unusual symptoms during or after treatment with these drugs should get in touch with his or her physician.

Interactions

Anyone who has supportive cancer therapy should let the physician know all other medicines he or she is taking. Some combinations of drugs may interact, which may increase or decrease the effects of one or both drugs or may increase the risk of side effects. Ask the physician whether the possible interactions can interfere with drug therapy or cause harmful effects.

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Nancy Ross-Flanigan

Candida albicans infection *see* **Candidiasis**

Candidiasis

Definition

Candidiasis is an infection caused by a species of the yeast *Candida*, usually *Candida albicans*. This is a common cause of vaginal infections in women. Also, *Candida* may cause mouth infections in people with reduced immune function, or in patients taking certain **antibiotics**. *Candida* can be found in virtually all normal people but causes problems in only a fraction. In recent years, however, several serious categories of candidiasis have become more common, due to overuse of antibiotics, the rise of **AIDS**, the increase in organ transplantations, and the use of invasive devices (catheters, artificial joints and valves)—all of which increase a patient's susceptibility to infection.

Description

Vaginal candidiasis

Over one million women in the United States develop vaginal yeast infections each year. It is not life-threatening, but it can be uncomfortable and frustrating.

Oral candidiasis

This disorder, also known as thrush, causes white, curd-like patches in the mouth or throat.

This patient's tongue is infected with candidiasis. *(Photograph by Edward H. Gill, Custom Medical Stock Photo. Reproduced by permission.)*

Deep organ candidiasis

Also known as invasive candidiasis, deep organ candidiasis is a serious systemic infection that can affect the esophagus, heart, blood, liver, spleen, kidneys, eyes, and skin. Like vaginal and oral candidiasis, it is an opportunistic disease that strikes when a person's resistance is lowered, often due to another illness. There are many diagnostic categories of deep organ candidiasis, depending on the tissues involved.

Causes and symptoms

Vaginal candidiasis

Most women with vaginal candidiasis experience severe vaginal **itching**. They also have a discharge that often looks like cottage cheese and has a sweet or bread-like odor. The vulva and vagina can be red, swollen, and painful. Sexual intercourse can also be painful.

Oral candidiasis

Whitish patches can appear on the tongue, inside of the cheeks, or the palate. Oral candidiasis typically occurs in people with abnormal immune systems. These can include people undergoing **chemotherapy** for **cancer**, people taking immunosuppressive drugs to protect transplanted organs, or people with HIV infection.

Deep organ candidiasis

Anything that weakens the body's natural barrier against colonizing organisms—including stomach surgery, **burns**, nasogastric tubes, and catheters—can predispose a person for deep organ candidiasis. Rising numbers of AIDS patients, organ transplant recipients, and other individuals whose immune systems are compromised help account for the dramatic increase in deep organ candidiasis in recent years. Patients with granulocytopenia (deficiency of white blood cells) are particularly at risk for deep organ candidiasis.

Diagnosis

Often clinical appearance gives a strong suggestion about the diagnosis. Generally, a clinician will take a sample of the vaginal discharge or swab an area of oral plaque, and then inspect this material under a microscope. Under the microscope, it is possible to see characteristic forms of yeasts at various stages in the lifecycle.

Fungal blood cultures should be taken for patients suspected of having deep organ candidiasis. Tissue biopsy may be needed for a definitive diagnosis.

Treatment

Vaginal candidiasis

In most cases, vaginal candidiasis can be treated successfully with a variety of over-the-counter antifungal creams or suppositories. These include Monistat, Gyne-Lotrimin, and Mycelex. However, infections often recur. If a women has frequent recurrences, she should consult her doctor about prescription drugs such as Vagistat-1, Diflucan, and others.

Oral candidiasis

This is usually treated with prescription lozenges or mouthwashes. Some of the most-used prescriptions are nystatin mouthwashes (Nilstat or Nitrostat) and clotrimazole lozenges.

Deep organ candidiasis

The recent increase in deep organ candidiasis has led to the creation of treatment guidelines, including, but not limited to, the following: Catheters should be removed from patients in whom these devices are still present. Antifungal chemotherapy should be started to prevent the spread of the disease. Drugs should be prescribed based on a patient's specific history and defense status.

Alternative treatment

Home remedies for vaginal candidiasis include vinegar douches or insertion of a paste made from *Lactobacillus acidophilus* powder into the vagina. In theory,

A transmission electron microscopy (TEM) of *Candida albicans*. *(Custom Medical Stock Photo. Reproduced by permission.)*

these remedies will make the vagina more acidic and therefore less hospitable to the growth of *Candida*. Fresh garlic (*Allium sativum*) is believed to have antifungal action, so incorporating it into the diet or inserting a gauze-wrapped, peeled garlic clove into the vagina may be helpful. The insert should be changed twice daily. Some women report success with these remedies; they should try a conventional treatment if an alternative remedy isn't effective.

Prognosis

Vaginal candidiasis

Although most cases of vaginal candidiasis are cured reliably, these infections can recur. To limit recurrences, women may need to take a prescription anti-fungal drug such as terconazole (sold as Terazol) or take other anti-fungal drugs on a preventive basis.

Oral candidiasis

These infections can also recur, sometimes because the infecting *Candida* develops resistance to one drug. Therefore, a physician may need to prescribe a different drug.

Deep organ candidiasis

The prognosis depends on the category of disease as well as on the condition of the patient when the infection strikes. Patients who are already suffering from a serious underlying disease are more susceptible to deep organ candidiasis that speads throughout the body.

Prevention

Because *Candida* is part of the normal group of microorganisms that co-exist with all people, it is impossible to avoid contact with it. Good vaginal hygiene and good **oral hygiene** might reduce problems, but they are not guarantees against candidiasis.

Because hospital-acquired (nosocomial) deep organ candidiasis is on the rise, people need to be made aware of it. Patients should be sure that catheters are properly maintained and used for the shortest possible time length. The frequency, length, and scope of courses of antibiotic treatment should also be cut back.

KEY TERMS

Biopsy—The removal and examination of tissue from a live body.

Colonize—To become established in a host.

Granulocytopenia—A condition characterized by a deficiency of white blood cells.

Nasogastric—Tube inserted through the nasal passages into the stomach.

Opportunistic—Infection caused by microorganisms that are usually harmless, but which can cause disease when a host's resistance is lowered.

Systemic—Afflicting an entire body system or the body in general.

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Richard H. Lampert

Candidosis *see* **Candidiasis**

Canker sores

Definition

Canker sores are small sores or ulcers that appear inside the mouth. They are painful, self-healing, and can recur.

KEY TERMS

Inflammation—A local reaction to tissue injury or damage, usually characterized by pain, swelling, and redness.

Sore—A wound, lesion, or ulcer on the skin.

Ulcer—A site of damage to the skin or mucous membrane that is characterized by the formation of pus, death of tissue, and is frequently accompanied by an inflammatory reaction.

Description

Canker sores occur on the inside of the mouth, usually on the inside of the lips, cheeks, and/or soft palate. They can also occur on the tongue and in the throat. Often, several canker sores will appear at the same time and may be grouped in clusters. Canker sores appear as a whitish, round area with a red border. The sores are painful and sensitive to touch. The average canker sore is about one-quarter inch in size, although they can occasionally be larger. Canker sores are not infectious.

Approximately 20% of the U.S. population is affected with recurring canker sores, and more women than men get them. Women are more likely to have canker sores during their premenstrual period.

Canker sores are sometimes confused with cold sores. Cold sores are caused by herpes simplex virus. This disease, also known as oral herpes or **fever** blisters, can occur anywhere on the body. Most commonly, herpes infection occurs on the outside of the lips and the gums, and much less frequently on the inside the mouth. Cold sores are infectious.

Causes and symptoms

The exact cause of canker sores is uncertain, however, they seem to be related to a localized immune reaction. Other proposed causes for this disease are trauma to the affected areas from toothbrush scrapes, **stress**, hormones, and food **allergies**. Canker sores tend to appear in response to stress. The initial symptom is a tingling or mildly painful **itching** sensation in the area where the sore will appear. After one to several days, a small red swelling appears. The sore is round, and is a whitish color with a grayish colored center. Usually, there is a red ring of inflammation surrounding the sore. The main symptom is **pain**. Canker sores can be very painful, especially if they are touched repeatedly, e.g., by the tongue. They last for one to two weeks.

Diagnosis

Canker sores are diagnosed by observation of the blister. A distinction between canker sores and cold sores must be made because cold sores are infectious and the herpes infection can be transmitted to other people. The two sores can usually be distinguished visually and there are specific diagnostic tests for herpes infection.

Treatment

Since canker sores heal by themselves, treatment is not usually necessary. Pain relief remedies, such as topical anesthetics, may be used to reduce the pain of the sores. The use of corticosteroid ointments sometimes speeds healing. Avoidance of spicy or acidic foods can help reduce the pain associated with canker sores.

Alternative treatment

Alternative therapies for canker sores are aimed at healing existing sores and preventing their recurrence. Several herbal remedies, including calendula (*Calendula officinalis*), myrrh (*Commiphora molmol*), and goldenseal (*Hydrastis canadensis*), may be helpful in the treatment of existing sores. Compresses soaked in teas made from these herbs are applied directly to the sores. The tannic acid in a tea bag can also help dry up the sores when the wet tea bag is used as a compress. Taking dandelion (*Taraxacum officinale*) tea or capsules may help heal sores and also prevent future outbreaks. Since canker sores are often brought on by stress, such stress-relieving techniques as **meditation**, **guided imagery**, and certain **acupressure** exercises may help prevent canker sores or lessen their severity.

Prognosis

There is no cure for canker sores. They do not get larger or occur more frequently with age.

Resources

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John T. Lohr, PhD

Captopril *see* **Angiotensin-converting enzyme inhibitors**

Carbamazepine *see* **Anticonvulsant drugs**

Carbidopa *see* **Antiparkinson drugs**

Carbohydrate intolerance

Definition

Carbohydrate intolerance is the inability of the body to completely process the nutrient carbohydrate (a classification that includes sugars and starches) into a source of energy for the body, usually because of the deficiency of an enzyme needed for digestion. **Lactose intolerance**, the inability to digest the sugar found in milk, is widespread and affects up to 70% of the world's adult population.

Description

Carbohydrates are the primary source of energy and, along with fats and proteins, one of the three major nutrients in the human diet. Carbohydrates are classified according to their structure based on the number of basic sugar, or *saccharide* units they contain.

A monosaccharide is the simplest carbohydrate and called a simple sugar. Simple sugars include glucose (the form in which sugar circulates in the blood), fructose (found in fruit and honey), and galactose (produced by the digestion of milk). These simple sugars are important because they can be absorbed by the small intestine. Two simple sugars linked together make a disaccharide. The disaccharide sugars present in the diet are maltose (a product of the digestion of starch), sucrose (table sugar), and lactose (the sugar in milk). These disaccharides must be broken down by enzymes into two simple sugars so that they can be absorbed by the intestine. Polysaccharides are much more complex carbohydrates made up of many simple sugars, the most important of which are glycogen, which is stored in the liver, and starch.

Digestion of sugars

Digestion of food begins in the mouth, moves on to the stomach, and then into the small intestine. Along the way, specific enzymes are needed to process different types of sugars. An enzyme is a substance that acts as a catalyst to produce chemical changes without being changed itself. The enzymes lactase, maltase, and isomaltase (or sucrase) are needed to break down the disaccharides; when one or more is inadequate, the result is carbohydrate intolerance.

Types of intolerance

Carbohydrate intolerance can be primary or secondary. Primary deficiency is caused by an enzyme defect present at birth or developed over time. The most common is lactose intolerance. Secondary deficiencies are caused by a disease or disorder of the intestinal tract, and disappear when the disease is treated. These include protein deficiency, **celiac disease**, and some intestinal infections.

Adult lactose intolerance is the most common of all enzyme deficiencies, and it is estimated that 30–50 million Americans have this condition. Some racial and ethnic populations are affected more than others. Lactose intolerance is found in as many as 75% of African Americans, Jewish Americans, Mexican Americans, and Native Americans, and in 90% of Asian Americans. Descendants of Northern Europeans and some Mediterranean peoples usually do not develop the condition. Deficiencies in enzymes other than lactase are extremely rare.

Causes and symptoms

Enzymes play an important role in breaking down carbohydrates into forms that can pass through the intestine and be used by the body. Usually they are named by adding *ase* to the name of the substance they act on, so lactase is the enzyme needed to process lactose. Cooked starch is broken down in the mouth to a disaccharide by amylase, an enzyme in the saliva. The disaccharides maltose, sucrose, and lactose cannot be absorbed until they have been separated into simple sugar molecules by their corresponding enzymes present in the cells lining the intestinal tract. If this process is not completed, digestion is interrupted.

Although not common, a deficiency in the enzymes needed to digest lactose, maltose, and sucrose is sometimes present at birth. Intestinal lactase enzymes usually decrease naturally with age, but this happens to varying degrees. Because of the uneven distribution of enzyme deficiency based on race and ethnic heritage, especially in lactose intolerance, genetics are believed to play a role in the cause of primary carbohydrate intolerance.

Digestive diseases such as celiac disease and tropical sprue (which affect absorption in the intestine), as well as intestinal infections and injuries, can reduce the amount of enzymes produced. In **cancer** patients, treatment with **radiation therapy** or **chemotherapy** may affect the cells in the intestine that normally secrete lactase, leading to intolerance.

The severity of the symptoms depends on the extent of the enzyme deficiency, and range from a feeling of mild bloating to severe **diarrhea**. In the case of a lactase deficiency, undigested milk sugar remains in the intestine, which is then fermented by the bacteria normally present in the intestine. These bacteria produce gas, cramping, bloating, a "gurgly" feeling in the abdomen, and flatulence. In a growing child, the main symptoms are diarrhea and a failure to gain weight. In an individual with lactase deficiency, gastrointestinal distress begins

KEY TERMS

Celiac disease—A disease, occurring in both children and adults, which is caused by a sensitivity to gluten, a protein found in grains. It results in chronic inflammation and shrinkage of the lining of the small intestine.

Digestion—The mechanical, chemical, and enzymatic process in which food is converted into the materials suitable for use by the body.

Enzyme—A substance produced by the body to assist in a chemical reaction. In carbohydrate intolerance, lack of an enzyme makes it impossible for one type of sugar to be broken down into a simpler form so that it can be absorbed by the intestines and used by the body.

Metabolism—All the physical and chemical changes that take place within an organism.

Nutrient—Food or another substance that supplies the body with the elements needed for metabolism.

Sugars—Those carbohydrates having the general composition of one part carbon, two parts hydrogen, and one part oxygen.

about 30 minutes to two hours after eating or drinking foods containing lactose. Food intolerances can be confused with food **allergies**, since the symptoms of nausea, cramps, bloating, and diarrhea are similar.

Sugars that aren't broken down into one of the simplest forms cause the body to push fluid into the intestines, which results in watery diarrhea (osmotic diarrhea). Diarrhea may sweep other nutrients out of the intestine before they can be absorbed, causing **malnutrition**.

Diagnosis

Carbohydrate intolerance can be diagnosed using oral tolerance tests. The carbohydrate being investigated is given by mouth in liquid form and several blood levels are measured and compared to normal values. This helps evaluate the individual's ability to digest the sugar.

To identify lactose intolerance in children and adults, the hydrogen breath test is used to measure the amount of hydrogen in the breath. The patient drinks a beverage containing lactose and the breath is analyzed at regular intervals. If undigested lactose in the large intestine (colon) is fermented by bacteria, various gases are produced. Hydrogen is absorbed from the intestines and carried by the bloodstream into the lungs where it is exhaled. Normally there is very little hydrogen detectable in the breath, so its presence indicates faulty digestion of lactose.

When lactose intolerance is suspected in infants and young children, many pediatricians recommend simply changing from cow's milk to soy formula and watching for improvement. If needed, a stool sample can be tested for acidity. The inadequate digestion of lactose will result in an increase of acid in the waste matter excreted by the bowels and the presence of glucose.

Treatment

Carbohydrate intolerance caused by temporary intestinal diseases disappears when the condition is successfully treated. In primary conditions, no treatment exists to improve the body's ability to produce the enzymes, but symptoms can be controlled by diet.

Because the degree of lactose intolerance varies so much, treatment should be tailored for the individual. Young children showing signs of intolerance should avoid milk products; infants should switch to soy-based formula. Older children and adults can adjust their intake of lactose depending on how much and what they can tolerate. For some, a small glass of milk will not cause problems, while others may be able to handle ice cream or aged cheeses such as cheddar or Swiss, but not other dairy products. Generally, small amounts of lactose-containing foods taken throughout the day are better tolerated than a large amount consumed all at once.

For those individuals who are sensitive to even very small amounts of lactose, the lactase enzyme is available without a prescription. It comes in liquid form for use with milk. The addition of a few drops to a quart of milk will reduce the lactose content by 70% after 24 hours in the refrigerator. Heating the milk speeds up the process, and doubling the amount of lactase liquid will result in milk that is 90% lactose free. Chewable lactase enzyme tablets are also available. Three to six tablets taken before a meal or snack will aid in the digestion of solid foods. Lactose-reduced milk and other products are also available in stores. The milk contains the same nutrients as regular milk.

Because dairy products are an important source of calcium, people who reduce or severely limit their intake of dairy products may need to consider other ways to consume an adequate amount of calcium in their **diets**.

Prognosis

With good dietary management, individuals with carbohydrate intolerance can lead normal lives.

Prevention

Since the cause of the enzyme deficiency leading to carbohydrate intolerance is unknown, there is no way to prevent this condition.

Resources

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Karen Ericson, RN

Carbon monoxide poisoning

Definition

Carbon monoxide (CO) **poisoning** occurs when carbon monoxide gas is inhaled. CO is a colorless, odorless, highly poisonous gas that is produced by incomplete combustion. It is found in automobile exhaust fumes, faulty stoves and heating systems, fires, and cigarette smoke. Other sources include woodburning stoves, kerosene heaters, improperly ventilated water heaters and gas stoves, and blocked or poorly maintained chimney flues. CO interferes with the ability of the blood to carry oxygen. The result is **headache**, nausea, convulsions, and finally **death** by asphyxiation.

Description

Carbon monoxide, sometimes called coal gas, has been known as a toxic substance since the third century B.C. It was used for executions and suicides in early Rome. Today it is the leading cause of accidental poisoning in the United States. According to the *Journal of the American Medical Association*, 1,500 Americans die each year from accidental exposure to CO, and another 2,300 from intentional exposure (suicide). An additional 10,000 people seek medical attention after exposure to CO and recover.

Anyone who is exposed to CO will become sick, and the entire body is involved in CO poisoning. A developing fetus can also be poisoned if a pregnant woman breathes CO gas. Infants, people with heart or lung disease, or those with anemia may be more seriously affected. People such as underground parking garage attendants who are exposed to car exhausts in a confined area are more likely to be poisoned by CO. Firemen also run a higher risk of inhaling CO.

Causes and symptoms

Normally when a person breathes fresh air into the lungs, the oxygen in the air binds with a molecule called hemoglobin (Hb) that is found in red blood cells. This allows oxygen to be moved from the lungs to every part of the body. When the oxygen/hemoglobin complex reaches a muscle where it is needed, the oxygen is released. Because the oxygen binding process is reversible, hemoglobin can be used over and over again to pick up oxygen and move it throughout the body.

Inhaling carbon monoxide gas interferes with this oxygen transport system. In the lungs, CO competes with oxygen to bind with the hemoglobin molecule. Hemoglobin prefers CO to oxygen and accepts it more than 200 times more readily than it accepts oxygen. Not only does the hemoglobin prefer CO, it holds on to the CO much more tightly, forming a complex called carboxyhemoglobin (COHb). As a person breathes CO contaminated air, more and more oxygen transportation sites on the hemoglobin molecules become blocked by CO. Gradually, there are fewer and fewer sites available for oxygen. All cells need oxygen to live. When they don't get enough oxygen, cellular metabolism is disrupted and eventually cells begin to die.

The symptoms of CO poisoning and the speed with which they appear depend on the concentration of CO in the air and the rate and efficiency with which a person breathes. Heavy smokers can start off with up to 9% of their hemoglobin already bound to CO, which they regularly inhale in cigarette smoke. This makes them much more susceptible to environmental CO. The Occupational Safety and Health Administration (OSHA) has established a maximum permissible exposure level of 50 parts per million (ppm) over eight hours.

With exposure to 200 ppm for two to three hours, a person begins to experience headache, **fatigue**, nausea, and **dizziness**. These symptoms correspond to 15–25% COHb in the blood. When the concentration of COHb reaches 50% or more, death results in a very short time. Emergency room physicians have the most experience diagnosing and treating CO poisoning.

KEY TERMS

Carboxyhemoglobin (COHb)—Hemoglobin that is bound to carbon monoxide instead of oxygen.

Hemoglobin (Hb)—A molecule that normally binds to oxygen in order to carry it to our cells, where it is required for life.

Hypothermia—Development of a subnormal body temperature.

pH—A measurement of the acidity or alkalinity of a fluid. A neutral fluid, neither acid nor alkali, has a pH of 7.

The symptoms of CO poisoning in order of increasing severity include:

- headache
- shortness of breath
- dizziness
- fatigue
- mental confusion and difficulty thinking
- loss of fine hand-eye coordination
- nausea and vomiting
- rapid heart rate
- hallucinations
- inability to execute voluntary movements accurately
- collapse
- lowered body temperature (**hypothermia**)
- coma
- convulsions
- seriously low blood pressure
- cardiac and **respiratory failure**
- death

In some cases, the skin, mucous membranes, and nails of a person with CO poisoning are cherry red or bright pink. Because the color change doesn't always occur, it is an unreliable symptom to rely on for diagnosis.

Although most CO poisoning is acute, or sudden, it is possible to suffer from chronic CO poisoning. This condition exists when a person is exposed to low levels of the gas over a period of days to months. Symptoms are often vague and include (in order of frequency) fatigue, headache, dizziness, sleep disturbances, cardiac symptoms, apathy, nausea, and memory disturbances. Little is known about chronic CO poisoning, and it is often misdiagnosed.

Diagnosis

The main reason to suspect CO poisoning is evidence that fuel is being burned in a confined area, for example a car running inside a closed garage, a charcoal grill burning indoors, or an unvented kerosene heater in a workshop. Under these circumstances, one or more persons suffering from the symptoms listed above strongly suggests CO poisoning. In the absence of some concrete reason to suspect CO poisoning, the disorder is often misdiagnosed as **migraine headache**, **stroke**, psychiatric illness, **food poisoning**, alcohol poisoning, or heart disease.

Concrete confirmation of CO poisoning comes from a carboxyhemoglobin test. This blood test measures the amount of CO that is bound to hemoglobin in the body. Blood is drawn as soon after suspected exposure to CO as possible.

Other tests that are useful in determining the extent of CO poisoning include measurement of other arterial blood gases and pH; a complete **blood count**; measurement of other blood components such as sodium, potassium, bicarbonate, urea nitrogen, and lactic acid; an electrocardiogram (ECG); and a **chest x ray**.

Treatment

Immediate treatment for CO poisoning is to remove the victim from the source of carbon monoxide gas and get him or her into fresh air. If the victim is not breathing and has no pulse, **cardiopulmonary resuscitation** (**CPR**) should be started. Depending on the severity of the poisoning, 100% oxygen may be given with a tight fitting mask as soon as it is available.

Taken with other symptoms of CO poisoning, COHb levels of over 25% in healthy individuals, over 15% in patients with a history of heart or lung disease, and over 10% in pregnant women usually indicate the need for hospitalization. In the hospital, fluids and electrolytes are given to correct any imbalances that have arisen from the breakdown of cellular metabolism.

In severe cases of CO poisoning, patients are given hyperbaric oxygen therapy. This treatment involves placing the patient in a chamber breathing 100% oxygen at a pressure of more than one atmosphere (the normal pressure the atmosphere exerts at sea level). The increased pressure forces more oxygen into the blood. Hyperbaric facilities are specialized, and are usually available only at larger hospitals.

Prognosis

The speed and degree of recovery from CO poisoning depends on the length and duration of exposure to

the gas. The half-life of CO in normal room air is four to five hours. This means that, in four to five hours, half of the CO bound to hemoglobin will be replaced with oxygen. At normal atmospheric pressures, but breathing 100% oxygen, the half-life for the elimination of CO from the body is 50-70 minutes. In hyperbaric therapy at three atmospheres of pressure, the half-life is reduced to 20-25 minutes.

Although the symptoms of CO poisoning may subside in a few hours, some patients show memory problems, fatigue, confusion, and mood changes for two to four weeks after their exposure to the gas.

Prevention

Carbon monoxide poisoning is preventable. Particular care should be paid to situations where fuel is burned in a confined area. Portable and permanently installed carbon monoxide detectors that sound a warning similar to smoke detectors are available for under $50. Specific actions that will prevent CO poisoning include:

- stop **smoking**. Smokers have less tolerance to environmental CO
- have heating systems and appliances installed by a qualified contractor to assure that they are properly vented and meet local building codes
- inspect and properly maintain heating systems, chimneys, and appliances
- do not use a gas oven or stove to heat the home
- do not burn charcoal indoors
- make sure there is good ventilation if using a kerosene heater indoors
- do not leave cars or trucks running inside the garage
- keep car windows rolled up when stuck in heavy traffic, especially if inside a tunnel

Resources

ORGANIZATIONS

American Lung Association. 1740 Broadway, New York, NY 10019. (800) 586-4872. <http://www.lungusa.org>.

OTHER

"Carbon Monoxide Headquarters." *Wayne State University School of Medicine*. <http://www.phypc.med.wayne.edu/>.

Tish Davidson

Carbunculosis *see* **Boils**

Carcinoembryonic antigen test

Definition

The carcinoembryonic antigen (CEA) test is a laboratory blood study. CEA is a substance which is normally found only during fetal development, but may reappear in adults who develop certain types of **cancer**.

Purpose

The CEA test is ordered for patients with known cancers. The CEA test is most commonly ordered when a patient has a cancer of the gastrointestinal system. These include cancer of the colon, rectum, stomach (gastric cancer), esophagus, liver, or pancreas. It is also used with cancers of the breast, lung, or prostate.

The CEA level in the blood is one of the factors that doctors consider when determining the prognosis, or most likely outcome of a cancer. In general, a higher CEA level predicts a more severe disease, one that is less likely to be curable. But it does not give clear-cut information. The results of a CEA test are usually considered along with other laboratory and/or imaging studies to follow the course of the disease.

Once treatment for the cancer has begun, CEA tests have a valuable role in monitoring the patient's progress. A decreasing CEA level means therapy is effective in fighting the cancer. A stable or increasing CEA level may mean the treatment is not working, and/or that the tumor is growing. It is important to understand that serial CEA measurements, which means several done over a period of time, are the most useful. A single test result is difficult to evaluate, but a number of tests, done weeks apart, shows trends in disease progression or regression.

Certain types of cancer treatments, such as hormone therapy for **breast cancer**, may actually cause the CEA level to go up. This elevation does not accurately reflect the state of the disease. It is sometimes referred to as a "flare response." Recognition that a rise in CEA may be temporary and due to therapy is significant. If this possibility is not taken into account, the patient may be unnecessarily discouraged. Further, treatment that is actually effective may be stopped or changed prematurely.

CEA tests are also used to help detect recurrence of a cancer after surgery and/or other treatment has been completed. A rising CEA level may be the first sign of cancer return, and may show up months before other studies or patient symptoms would raise concern. Unfortunately, this does not always mean the recurrent cancer can be cured. For example, only a small percentage of patients with colorectal cancers and rising CEA levels will benefit from

another surgical exploration. Those with recurrence in the same area as the original cancer, or with a single metastatic tumor in the liver or lung, have a chance that surgery will eliminate the disease. Patients with more widespread return of the cancer are generally not treatable with surgery. The CEA test will not separate the two groups.

Patients who are most likely to benefit from nonstandard treatments, such as bone marrow transplants, may be determined on the basis of CEA values, combined with other test results. CEA levels may be one of the criteria for determining whether the patient will benefit from more expensive studies, such as CT scan or MRI.

Precautions

The CEA test is not a screening test for cancer. It is not useful for detecting the presence of cancer. Many cancers do not produce an increased CEA level. Some noncancerous diseases, such as hepatitis, inflammatory bowel disease, **pancreatitis**, and obstructive pulmonary disease, may cause an elevated CEA level.

Description

Determination of the CEA level is a laboratory blood test. Obtaining a specimen of blood for the study takes only a few minutes. CEA testing should be covered by most insurance plans.

Preparation

No preparation is required.

Aftercare

None.

Risks

There are no complications or side effects of this test. However, the results of a CEA study should be interpreted with caution. A single test result may not yield clinically useful information. Several studies over a period of months may be needed.

Another concern is the potential for false positive as well as false negative results. A false positive result means the test shows an abnormal value when cancer is not present. A false negative means the test reveals a normal value when cancer actually is present.

Normal results

The absolute numbers which are considered normal vary from one laboratory to another. Any results reported should come with information regarding the testing facility's normal range.

Abnormal results

A single abnormal CEA value may be significant, but must be regarded cautiously. In general, very high CEA levels indicate more serious cancer, with a poorer chance for cure. But some benign diseases and certain cancer treatments may produce an elevated CEA test. Cigarette **smoking** will also cause the CEA level to be abnormally high.

Resources

BOOKS

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Ellen S. Weber, MSN

Carcinoid tumors *see* **Neuroendocrine tumors**

Cardiac arrest *see* **Sudden cardiac death**

Cardiac arrhythmias *see* **Arrhythmias**

Cardiac blood pool scan

Definition

A cardiac blood pool scan is a non-invasive test that uses a mildly radioactive marker to observe the functioning of the left ventricle of the heart.

Purpose

The left ventricle is the main pump for distributing blood through the body. A cardiac blood pool scan is used to determine how efficiently the left ventricle is working. The scan can detect aneurysms of the left ventricle, motion abnormalities caused by damage to the heart wall, cardiac shunts between the left and right ventricle, and coronary occlusive artery disease.

Precautions

Pregnant women are the only patients who should not participate in a cardiac blood pool scan. However, the accuracy of the results may be affected if the patient moves during imaging, has had other recent nuclear scans, or has an irregular heartbeat.

Description

A cardiac blood pool scan is sometimes called equilibrium radionuclide angiocardiography or gated (synchronized) cardiac blood pool imaging. A **multiple-gated acquisition (MUGA) scan** is a variation of this test.

To perform a cardiac blood pool scan, the patient lies under a special gamma scintillation camera that detects radiation. A protein tagged with a radioactive marker (usually technetium-99m) is injected into the patient's forearm.

The camera is synchronized with an electrocardiogram (ECG) to take a picture at specific times in the cycle of heart contraction and relaxation. When data from many sequential pictures is processed by a computer, a doctor can analyze whether the left ventricle is functioning normally.

The patient needs to remain silent and motionless during the test. Sometimes the patient is asked to **exercise**, then another set of pictures is taken for comparison. This test normally takes about 30 minutes.

Preparation

No changes in diet or medication are necessary. An ECG will probably be done before the test.

Aftercare

The patient may resume normal activities immediately.

Risks

Cardiac blood pool scans are a safe and effective way of measuring left ventricle function. The only risk is to the fetus of a pregnant woman.

Normal results

A computer is used to process the information from the test, then the results are analyzed by a doctor. A normally functioning left ventricle will contract symmetrically, show even distribution of the radioactively tagged protein, and eject about 55–65% of volume of blood it holds on each contraction.

Abnormal results

Patients with damage to the ventricle or heart wall will show an uneven distribution of the radiopharmaceutical. The volume of blood ejected in each contraction will be less than 55%.

KEY TERMS

Aneurysm—A sac or bulge that forms because of a weak spot in the wall of an artery or heart chamber.

Cardiac shunt—A defect in the wall of the heart that allows blood from different chambers to mix.

Coronary occlusive artery disease—Blockage of the arteries that supply blood to the heart; frequently a precursor to a heart attack.

Electrocardiogram (ECG)—A graph that shows the electrical charges that trigger the heart to contract. Heart abnormalities alter the graph, giving clues to the source of the abnormality.

Ventricle—One of the two bottom chambers of the heart (the heart has four chambers). The left ventricle acts as the body's main pump for blood.

Resources

BOOKS

"Cardiac Blood Pool Imaging." In *Illustrated Guide to Diagnostic Tests*, ed. J. A. Lewis. Springhouse, PA: Springhouse Corp., 1994.

Pagana, Kathleen Deska. *Mosby's Manual of Diagnostic and Laboratory Tests*. St. Louis: Mosby, Inc., 1998.

Tish Davidson

Cardiac catheterization

Definition

Cardiac catheterization (also called heart catheterization) is a diagnostic procedure which does a comprehensive examination of how the heart and its blood vessels function. One or more catheters is inserted through a peripheral blood vessel in the arm (antecubital artery or vein) or leg (femoral artery or vein) with x-ray guidance. This procedure gathers information such as adequacy of blood supply through the coronary arteries, blood pressures, blood flow throughout chambers of the heart, collection of blood samples, and x rays of the heart's ventricles or arteries.

A test that can be performed on either side of the heart, cardiac catheterization checks for different functions in both the left and right sides. When testing the heart's right side, tricuspid and pulmonary valve function

are evaluated, in addition to measuring pressures of and collecting blood samples from the right atrium, ventricle, and pulmonary artery. Left-sided heart catheterization is performed by way of a catheter through an artery which tests the blood flow of the coronary arteries, function of the mitral and aortic valves, and left ventricle.

Purpose

The primary reason for conducting a cardiac catheterization is to diagnose and manage persons known or suspected to have heart disease, a frequently fatal condition that leads to 1.5 million heart attacks annually in the United States.

Symptoms and diagnoses that may lead to performing this procedure include:

- chest **pain**, characterized by prolonged heavy pressure or a squeezing pain
- abnormal treadmill **stress test**
- myocardial infarction, also known as a **heart attack**
- congenital heart defects, or heart problems that originated from birth
- a diagnosis of valvular-heart disease
- a need to measure the heart muscle's ability to pump blood

Typically performed along with **angiography**, a technique of injecting a dye into the vascular system to outline the heart and blood vessels, a catheterization can aid in the visualization of any blockages, narrowing, or abnormalities in the coronary arteries. If these signs are visible, the cardiologist may assess the patient's need and readiness for coronary bypass surgery, or perhaps a less invasive approach, such as dilation of a narrowed blood vessel either surgically or with the use of a balloon (**angioplasty**).

When looking at the left side of the heart, fluoroscopic guidance also allows the following diagnoses to be assessed:

- enlargement of the left ventricle
- ventricular aneurysms (abnormal dilation of a blood vessel)
- narrowing of the aortic valve
- insufficiency of the aortic or mitral valve
- the detour of blood from one side of the heart to the other due to septal defects (also known as shunting)

Precautions

Cardiac catheterization is categorized as an "invasive" procedure which involves the heart, its valves, and coronary arteries, in addition to a large artery in the arm or leg. Due to the nature of the test, it is important to evaluate for the following conditions before considering this procedure:

- A diagnosis of a bleeding disorder, poor kidney function, or debilitation. Any of these pre-existing conditions typically raises the risk of the catheterization procedure and may be reason to cancel the procedure.
- A diagnosis of heart valve disease. If this is detected, **antibiotics** may be given before the test to prevent inflammation of the membrane which lines the heart (endocarditis).

Description

To understand how a cardiac catheterization is able to diagnose and manage heart disease, the basic workings of the heart muscle must also be understood. Just as the body relies on a constant supply of blood to aid in its everyday functions, so does the heart. The heart is made up of an intricate web of blood vessels (coronary arteries) that ensure an adequate supply of blood rich in oxygen and nutrients. It is easy to see how an abnormality in any of these arteries can be detrimental to the heart's function. These abnormalities cause the heart's blood flow to decrease and result in the condition known as **coronary artery disease** or coronary insufficiency.

Catheterization is a valuable tool in detecting and treating abnormalities of the heart. Through the use of fluoroscopic (x ray) guidance, a catheter, which may resemble a balloon-tipped tube, is strung through the veins or arteries into the heart, so the cardiologist can monitor a body's various functions at each moment.

Generally a test that lasts two to three hours, a patient should expect the following prior to and during the catheterization procedure:

- A mild sedative may be given that will allow the patient to relax but remain conscious during the test.
- An intravenous needle will be inserted in the arm to administer medication. Electrodes will be attached to the chest to enable the painless procedure known as an electrocardiograph.
- Prior to inserting a catheter into an artery or vein in the arm or leg, the incision site will be made numb by injecting a local anesthetic. When the anesthetic is injected it may feel like a pin-prick followed by a quick stinging sensation. Pressure may also be experienced as the catheter travels through the blood vessel.
- After the catheter is guided into the coronary-artery system, a dye (also called a radiocontrast material) is injected to aid in the identification of any abnormalities

of the heart. During this time, the patient may experience a hot, flushed feeling or a quickly passing nausea. Coughing or breathing deeply aids in any discomfort.

- Medication may be given during the procedure if chest pain is experienced, and nitroglycerin may also be administered to allow expansion of the heart's blood vessels.
- When the test is complete, the physician will remove the catheter and close the skin with several sutures or tape.

Preparation

Prior to the cardiac catheterization procedure, it is important to relay information to the physician or nurse regarding **allergies** to shellfish (such as shrimp or scallops) which contain iodine, iodine itself, or the dyes that are commonly used in other diagnostic tests.

Because this procedure is categorized as a surgery, the patient will be instructed not to eat or drink anything for at least six hours prior to the test. Just before the test begins, the patient will urinate and change into a hospital gown, then lie flat on a padded table that may also be tilted in order for the heart to be examined from a variety of angles.

Aftercare

While cardiac catheterization may be performed on an outpatient basis, a patient may require close monitoring following the procedure while remaining in the hospital for at least 24 hours. The patient will be instructed to rest in bed for at least eight hours immediately after the test. If the catheter was inserted into a vein or artery in the leg or groin area, the leg will be kept extended for four to six hours. If a vein or artery in the arm was used to insert the catheter, the arm will need to remain extended for a minimum of three hours.

The patient should expect a hard ridge to form over the incision site that diminishes as the site heals. Bluish discoloration under the skin at the point of insertion should also be expected but fades in two weeks. It is also not uncommon for the incision site to bleed during the first 24 hours following surgery. If this should happen, the patient should apply pressure to the site with a clean tissue or cloth for 10–15 minutes.

Risks

Similar to all surgical procedures, the cardiac catheterization test does involve some risks. Complications that may occur during the procedure include

- cardiac **arrhythmias** (an irregular heart beat)
- pericardial tamponade (a condition that causes excess pressure in the pericardium which affects the heart due to accumulation of excess fluid)

The cardiac catheter runs from the groin to the heart. *(Illustration by Argosy Inc.)*

- the rare occurrence of myocardial infarction (heart attack) or **stroke** may also develop due to clotting or plaque rupture of one or more of the coronary or brain arteries.

Before left-side catheterization is performed, the anticoagulant medication heparin may be administered. This drug helps decrease the risk of the development of a blood clot in an artery (thrombosis) and blood clots traveling throughout the body (embolization).

The risks of the catheterization procedure increase in patients over the age of 60, those who have severe **heart failure**, or persons with serious **valvular heart disease**.

Normal results

Normal findings from a cardiac catheterization will indicate no abnormalities of heart chamber size or configuration, wall motion or thickness, the direction of blood flow, or motion of the valves. Smooth and regular outlines on the x ray indicate normal coronary arteries.

An essential part of the catheterization is measuring intracardiac pressures, or the pressure in the heart's chambers and vessels. Pressure readings that are higher

KEY TERMS

Aneurysm—An abnormal dilatation of a blood vessel, usually an artery. It can be caused by a congenital defect or weakness in the vessel's wall.

Angiography—In cardiac catheterization, a picture of the heart and coronary arteries is seen after injecting a radiopaque substance (often referred to as a dye) throughout the veins and arteries.

Angioplasty—An alternative to vascular surgery, a balloon catheter is used to mechanically dilate the affected area of the artery and enlarge the constricted or narrowed segment.

Aortic valve—The valve between the heart's left ventricle and ascending aorta that prevents regurgitation of blood back into the left ventricle.

Catheter—A tube made of elastic, elastic web, rubber, glass, metal, or plastic used to evacuate or inject fluids into the body. In cardiac catheterization, a long, fine catheter is used for passage through a blood vessel into the chambers of the heart.

Coronary bypass surgery—A surgical procedure which places a shunt to allow blood to travel from the aorta to a branch of the coronary artery at a point past an obstruction.

Left anterior descending coronary artery (LAD)—One of the heart's coronary artery branches from the left main coronary artery which supplies blood to the left ventricle.

Mitral valve—The bicuspid valve which is between the left atrium and left ventricle of the heart.

Pulmonary valve—The heart valve which is positioned between the right ventricle and the opening into the pulmonary artery.

Shunt—A passageway (or an artificially created passageway) that diverts blood flow from one main route to another.

Tricuspid valve—The right atrioventricular valve of the heart.

than normal are significant for a patient's overall diagnosis. The pressure readings that are lower, other than those which are produced as a result of **shock**, typically are not significant.

An ejection fraction, or a comparison of how much blood is ejected from the heart's left ventricle during its contraction phase with a measurement of blood remaining at the end of the left ventricle's relaxation phase, is also determined by performing a catheterization. The cardiologist will look for a normal ejection fraction reading of 60–70%.

Abnormal results

Cardiac catheterization provides valuable still and motion x-ray pictures of the coronary arteries that help in diagnosing coronary artery disease, poor heart function, disease of the heart valves, and septal defects (a defect in the septum, the wall that separates two heart chambers).

The most prominent sign of coronary artery disease is the narrowing or blockage in the coronary arteries, with narrowing that is greater than 70% considered significant. A clear indication for intervention (by angioplasty or surgery) is a finding of significant narrowing of the left main coronary artery and/or blockage or severe narrowing in the high, left anterior descending coronary artery.

A finding of impaired wall motion is an additional indicator of coronary artery disease, aneurysm, an enlarged heart, or a congenital heart problem. Using the findings from an ejection fraction test which measures wall motion, cardiologists look at an ejection fraction reading under 35% as increasing the risk of complications while also decreasing a successful long term or short term outcome with surgery.

Detecting the difference in pressure above and below the heart valve can verify heart valve disease. The greater narrowing correlates with the higher pressure difference.

To confirm septal defects, a catheterization measures oxygen content on both the left and right sides of the heart. The right heart pumps unoxygenated blood to the lungs, and the left heart pumps blood that contains oxygen from the lungs to the rest of the body. Right side elevated oxygen levels indicate left-to-right atrial or **ventricular shunt**. A left side that experiences decreased oxygen indicates a right-to-left shunt.

Resources

BOOKS

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ORGANIZATIONS

American Heart Association. 7320 Greenville Ave. Dallas, TX 75231. (214) 373-6300. <http://www.americanheart.org>.
National Heart, Lung and Blood Institute. P.O. Box 30105, Bethesda, MD 20824-0105. (301) 251-1222. <http://www.nhlbi.nih.gov>.

Beth A. Kapes

Cardiac compression *see* **Cardiac tamponade**

Cardiac conduction disorder *see* **Heart block**

Cardiac mapping *see* **Electrophysiology study of the heart**

Cardiac rehabilitation

Definition

Cardiac **rehabilitation** is a comprehensive **exercise**, education, and behavioral modification program designed to improve the physical and emotional condition of patients with heart disease.

Purpose

Heart attack survivors, bypass and **angioplasty** patients, and individuals with **angina**, congestive **heart failure**, and heart transplants are all candidates for a cardiac rehabilitation program. Cardiac rehabilitation is prescribed to control symptoms, improve exercise tolerance, and improve the overall quality of life in these patients.

Precautions

A cardiac rehabilitation program should be implemented and closely monitored by a trained team of healthcare professionals.

This 40-year-old male is working out on a treadmill, monitored by his physician, following heart surgery. *(Custom Medical Stock Photo. Reproduced by permission.)*

Description

Cardiac rehabilitation is overseen by a specialized team of doctors, nurses, and other healthcare professionals. Members of the cardiac rehabilitation team may include a dietician or nutritionist, physical therapist, exercise physiologist, psychologist, vocational counselor, occupational therapist, and social worker. The program frequently begins in a hospital setting and continues on an outpatient basis after the patient is discharged over a period of six to 12 months.

Components of a cardiac rehabilitation program vary by individual clinical need, and each program will be carefully constructed for the patient by his or her rehabilitation team.

- Exercise. Exercise programs typically start out slowly, with simple range-of-motion arm and leg exercises. Walking and stair climbing soon follow. Blood pressure is carefully monitored before and after exercise ses-

KEY TERMS

Angina—Chest pain.

Bypass surgery—A surgical procedure that grafts blood vessels onto arteries to reroute the blood flow around blockages in the arteries (arteriosclerosis).

sions, and patients are taught how to measure their heart rate and evaluate any possible cardiac symptoms during each session. Patients with advanced coronary disease may require continuous ECG monitoring throughout their exercise sessions. Once discharged from the hospital, the patient works with his cardiac team to create an individual exercise plan.

- Diet. Cardiac patients will work with a nutritionist or dietician to develop a low-fat, low-cholesterol diet plan. Patients with high blood pressure may be put on a salt-restricted diet and instructed to limit alcohol intake. Weight loss may also be a goal with obese cardiac patients.
- Counseling. A psychologist or social worker can help cardiac patients with issues that may be contributing to their heart condition, such as **stress** and **anxiety**. Relaxation techniques may be taught to patients to help them deal with these feelings. Cardiac patients frequently experience a period of depression, and group or individual counseling can be beneficial in overcoming these feelings. Vocational counselors can assist cardiac patients in returning to the workforce.
- Education. The patient and family should be fully educated on the physical limitations of the patient, his recommended diet and exercise plan, his emotional status, and the lifestyle changes required to improve the patient's overall health.
- **Smoking** cessation. Cardiac patients who smoke are twice as likely to have a heart attack in the following five years than non-smoking patients. These patients are strongly encouraged to enroll in a smoking cessation program, which typically includes patient education and behavioral counseling. Nicotine replacement therapy, which uses nicotine patches, nose spray, or gum to wean patients off of cigarettes, may also be part of the program. Antidepressants and anti-anxiety medication may be helpful in some cases.

Aftercare

Long-term maintenance is a critical feature of cardiac rehabilitation. Patients require support from their healthcare team, family, and friends to continue the lifestyle changes they implemented during the rehabilitation period.

Risks

The risks of another heart attack during cardiac rehabilitation are slight, and greatly reduced by careful, continuous monitoring of the physical status of the patient.

Normal results

The outcome of the cardiac rehabilitation program depends on a number of variables, including patient follow-through, type and degree of heart disease, and the availability of an adequate support network for the patient. Patients who successfully complete the program will ideally reach an age-appropriate level of physical activity and be able to return to the workforce and/or other daily activities.

Resources

BOOKS

The American Heart Association. *American Heart Association Guide to Heart Attack Treatment, Recovery, and Prevention*. New York: Times Books, 1996.

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PERIODICALS

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ORGANIZATIONS

American Heart Association. 7320 Greenville Ave. Dallas, TX 75231. (214) 373-6300. <http://www.americanheart.org>.

Paula Anne Ford-Martin

Cardiac tamponade

Definition

Cardiac tamponade occurs when the heart is squeezed by fluid that collects inside the sac that surrounds it.

Description

The heart is surrounded by a sac called the pericardium. When this sac becomes filled with fluid, the liquid presses on the heart, preventing the lower chambers of the heart from properly filling with blood.

Because the lower chambers (the ventricles) cannot fill with the correct amount of blood, less than normal amounts of blood reach the lungs and the rest of the body. This condition is very serious and can be fatal if not treated.

Causes and symptoms

Fluid can collect inside the pericardium and compress the heart when the kidneys do not properly remove waste from the blood, when the pericardium swells from unknown causes, from infection, or when the pericardium is damaged by **cancer**. Blunt or penetrating injury from trauma to the chest or heart can also result in cardiac tamponade when large amounts of blood fill the pericardium. Tamponade can also occur during heart surgery.

When the heart is compressed by the surrounding fluid, three conditions occur: a reduced amount of blood is pumped to the body by the heart, the lower chambers of the ventricles are filled with a less than normal amount of blood, and higher than normal blood pressures occur inside the heart, caused by the pressure of the fluid pushing in on the heart from the outside.

When tamponade occurs because of trauma, the sound of the heart beats can become faint, and the blood pressure in the arteries decreases, while the blood pressure in the veins increases.

In cases of tamponade caused by more slowly developing diseases, **shortness of breath**, a feeling of tightness in the chest, increased blood pressure in the large veins in the neck (the jugular veins), weight gain, and fluid retention by the body can occur.

Diagnosis

When cardiac tamponade is suspected, accurate diagnosis can be life-saving. The most accurate way to identify this condition is by using a test called an echocardiogram. This test uses sound waves to create an image of the heart and its surrounding sac, making it easy to visualize any fluid that has collected inside the sac.

Treatment

If the abnormal fluid buildup in the pericardial sac is caused by cancer or kidney disease, drugs used to treat these conditions can help lessen the amount of fluid collecting inside the sac. Drugs that help maintain normal blood pressure throughout the body can also help this condition; however, these drugs are only a temporary treatment. The fluid within the pericardium must be drained out to reduce the pressure on the heart and restore proper heart pumping.

The fluid inside the pericardium is drained by inserting a needle through the chest and into the sac itself. This allows the fluid to flow out of the sac, relieving the abnormal pressure on the heart. This procedure is called **pericardiocentesis**. In severe cases, a tube (catheter) can be inserted into the sac or a section of the sac can be surgically cut away to allow for more drainage.

KEY TERMS

Pericardiocentesis—A procedure used to drain fluid out of the sac surrounding the heart. This is done by inserting a needle through the chest and into the sac.

Prognosis

This condition is life-threatening. However, drug treatments can be helpful, and surgical treatments can successfully drain the trapped fluid, though it may reaccumulate. Some risk of **death** exists with surgical drainage of the accumulated fluid.

Resources

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American Heart Association. 7320 Greenville Ave. Dallas, TX 75231. (214) 373-6300. <http://www.americanheart.org>.

Dominic De Bellis, PhD

Cardiac tumors *see* **Myxoma**

Cardiogenic shock *see* **Shock**

Cardiomyopathy *see* **Congestive cardiomyopathy; Restrictive cardiomyopathy**

Cardiopulmonary resuscitation (CPR)

Definition

Cardiopulmonary resuscitation (CPR) is a procedure to support and maintain breathing and circulation for a

person who has stopped breathing (respiratory arrest) and/or whose heart has stopped (cardiac arrest).

Purpose

CPR is performed to restore and maintain breathing and circulation and to provide oxygen and blood flow to the heart, brain, and other vital organs. CPR should be performed if a person is unconscious and not breathing. Respiratory and cardiac arrest can be caused by allergic reactions, an ineffective heartbeat, asphyxiation, breathing passages that are blocked, **choking**, drowning, drug reactions or overdoses, electric shock, exposure to cold, severe shock, or trauma. CPR can be performed by trained bystanders or healthcare professionals on infants, children, and adults. It should always be performed by the person on the scene who is most experienced in CPR.

Precautions

CPR should never be performed on a healthy person because it can cause serious injury to a beating heart by interfering with normal heartbeats.

Description

CPR is part of the emergency cardiac care system designed to save lives. Many deaths can be prevented by prompt recognition of the problem and notification of the emergency medical system (EMS), followed by early CPR, **defibrillation** (which delivers a brief electric shock to the heart in attempt to get the heart to beat normally), and advanced cardiac **life support** measures.

CPR must be performed within four to six minutes after cessation of breathing so as to prevent brain damage or **death**. It is a two-part procedure that involves rescue breathing and external chest compressions. To provide oxygen to a person's lungs, the rescuer administers mouth-to-mouth breaths, then helps circulate blood through the heart to vital organs by external chest compressions. Mouth-to-mouth breathing and external chest compression should be performed together, but if the rescuer is not strong enough to do both, the external chest compressions should be done. This is more effective than no resuscitation attempt, as is CPR that is performed "poorly."

When performed by a bystander, CPR is designed to support and maintain breathing and circulation until emergency medical personnel arrive and take over. When performed by healthcare personnel, it is used in conjunction with other basic and advanced life support measures.

According to the American Heart Association, early CPR and defibrillation combined with early advanced emergency care can increase survival rates for people with a type of abnormal heart beat called **ventricular fibrillation** by as much as 40%. CPR by bystanders may prolong life during deadly ventricular fibrillation, giving emergency medical service personnel time to arrive.

However, many CPR attempts are not ultimately successful in restoring a person to a good quality of life. Often, there is brain damage even if the heart starts beating again. CPR is therefore not generally recommended for the chronically or terminally ill or frail elderly. For these people, it represents a traumatic and not a peaceful end of life.

Each year, CPR helps save thousands of lives in the United States. More than five million Americans annually receive training in CPR through American Heart Association and American Red Cross courses. In addition to courses taught by instructors, the American Heart Association also has an interactive video called Learning System, which is available at more than 500 healthcare institutions. Both organizations teach CPR the same way, but use different terms. These organizations recommend that family members or other people who live with people who are at risk for respiratory or cardiac arrest be trained in CPR. A hand-held device called a CPR Prompt is available to walk people trained in CPR through the procedure, using American Heart Association guidelines. CPR has been practiced for more than 40 years.

Performing CPR

The basic procedure for CPR is the same for all people, with a few modifications for infants and children to account for their smaller size.

PERFORMING CPR ON AN ADULT. The first step is to call the emergency medical system for help by telephoning 911; then to begin CPR, following these steps:

- The rescuer opens a person's airway by placing the head face up, with the forehead tilted back and the chin lifted. The rescuer checks again for breathing (three to five seconds), then begins rescue breathing (mouth-to-mouth artificial respiration), pinching the nostrils shut while holding the chin in the other hand. The rescuer's mouth is placed against the unconscious person's mouth with the lips making a tight seal, then gently exhales for about one to one and a half seconds. The rescuer breaks away for a moment and then repeats. The person's head is repositioned after each mouth-to-mouth breath.
- After two breaths, the rescuer checks the unconscious person's pulse by moving the hand that was under the person's chin to the artery in the neck (carotid artery). If the unconscious person has a heartbeat, the rescuer continues rescue breathing until help arrives or the per-

CPR in basic life support. Figure A: The victim should be flat on his back and his mouth should be checked for debris. Figure B: If the victim is unconscious, open airway, lift neck, and tilt head back. Figure C: If victim is not breathing, begin artificial breathing with four quick full breaths. Figure D: Check for carotid pulse. Figure E: If pulse is absent, begin artificial circulation by depressing sternum. Figure F: Mouth-to-mouth resuscitation of an infant. *(Illustration by Electronic Illustrators Group.)*

son begins breathing without assistance. If the unconscious person is breathing, the rescuer turns the person onto his or her side.

- If there is no heartbeat, the rescuer performs chest compressions. The rescuer kneels next to the unconscious person, placing the heel of one hand in the spot on the lower chest where the two halves of the rib cage come together. The rescuer puts one hand on top of the other on the person's chest and interlocks the fingers. The arms are straightened, the rescuer's shoulders are positioned directly above the hands on the unconscious person's chest. The hands are pressed down, using only the palms, so that the person's breastbone sinks in about 1.5–2 inches. The rescuer releases pressure without removing the hands, then repeats about 15 times per 10–15 second intervals.
- The rescuer tilts the unconscious person's head and returns to rescue breathing for one or two quick breaths. Then breathing and chest compressions are alternated for one minute before checking for a pulse. If the rescuer finds signs of a heartbeat and breathing, CPR is stopped. If the unconscious person is breathing but has no pulse, the chest compressions are continued. If the unconscious person has a pulse but is not breathing, rescue breathing is continued.
- For children over the age of eight, the rescuer performs CPR exactly as for an adult.

PERFORMING CPR ON AN INFANT OR CHILD UNDER THE AGE OF EIGHT. The procedures outlined above are followed with these differences:

- The rescuer administers CPR for one minute, then calls for help.
- The rescuer makes a seal around the child's mouth or infant's nose and mouth to give gentle breaths. The rescuer delivers 20 rescue breaths per minute, taking 1.5–2 seconds for each breath.
- Chest compressions are given with only one hand for a child and with two or three fingers for an infant. The breastbone is depressed only 1–1.5 in (2.5–3.8 cm) for a child and 0.5–1 in (1.3–2.5 cm) for an infant, and the rescuer gives at least 100 chest compressions per minute.

New developments in CPR

Some new ways of performing CPR have been tried. Active compression-decompression resuscitation, abdominal compression done in between chest compressions, and chest compression using a pneumatic vest have all been tested but none are currently recommended for routine use.

The active compression-decompression device was developed to improve blood flow from the heart, but clinical studies have found no significant difference in survival between standard and active compression-decompression CPR. Interposed abdominal counterpulsation, which requires two or more rescuers, one compressing the chest and the other compressing the abdomen, was developed to improve pressure and therefore blood flow. It has been shown in a small study to improve survival but more data is needed. A pneumatic vest, which circles the chest of an unconscious person and compresses it, increases pressure within the chest during external chest compression. The vest has been shown to improve survival in a preliminary study but more data is necessary for a full assessment.

Preparation

If a person suddenly becomes unconscious, a rescuer should call out for help from other bystanders, and then determine if the unconscious person is responsive by gently shaking the shoulder and shouting a question. Upon receiving no answer, the rescuer should call the emergency medical system. The rescuer should check to see whether the unconscious person is breathing by kneeling near the person's shoulders, looking at the person's chest, and placing a cheek next to the unconscious person's mouth. The rescuer should look for signs of breathing in the chest and abdomen, and listen and feel for signs of breathing through the person's lips. If no signs of breathing are present after three to five seconds, CPR should be started.

Aftercare

Emergency medical care is always necessary after successful CPR. Once a person's breathing and heartbeat have been restored, the rescuer should make the person comfortable and stay there until emergency medical personnel arrive. The rescuer can continue to reassure the person that help is coming and talk positively until professionals arrive and take over.

Risks

CPR can cause injury to a person's ribs, liver, lungs, and heart. However, these risks must be accepted if CPR is necessary to save the person's life.

Normal results

In many cases, successful CPR results in restoration of consciousness and life. Barring other injuries, a revived person usually returns to normal functions within a few hours of being revived.

Abnormal results

These include injuries incurred during CPR and lack of success with CPR. Possible sites for injuries include a person's ribs, liver, lungs, and heart. Partially successful CPR may result in brain damage. Unsuccessful CPR results in death.

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American College of Emergency Physicians. P.O. Box 619911, Dallas, TX 75261-9911. (800) 798-1822 or (972) 550-0911. Fax: (972) 580-2816. <info@acep.org>. <http://www.acep.org/>.

American College of Osteopathic Emergency Physicians. 142 E. Ontario Street, Suite 550, Chicago, IL 60611. (312) 587-3709 or (800) 521-3709. Fax: (312) 587-9951. <http://www.acoep.org>.

American Heart Association, National Center. 7272 Greenville Avenue, Dallas, TX 75231. (877) 242-4277. <http://www.americanheart.org/Heart_and_Stroke_A_Z_Guide/heim.html>.

Heimlich Institute. PO Box 8858, Cincinnati, OH 45208. <heimlich@iglou.com>. <http://www.heimlichinstitute.org/index.htm>.

National Safe Kids Campaign. 1301 Pennsylvania Avenue, Suite 1000, Washington, DC 20004-1707. <http://pedsccm.wustl.edu/All-Net/english/neurpage/protect/drown.htm>.

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Columbia Presbyterian Medical Center. <http://cpmcnet.columbia.edu/texts/guide/hmg13_0001.html>.

Learn CPR. <http://www.learn-cpr.com>.

National Registry of Cardiopulmonary Resuscitation. <http://www.nrcpr.org/>.

University of Washington School of Medicine. <http://depts.washington.edu/learncpr/>.

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KEY TERMS

Cardiac arrest—Temporary or permanent cessation of the heartbeat.

Cardiopulmonary—Relating to the heart and the lungs.

Defibrillation—A procedure to stop the type of irregular heart beat called ventricular fibrillation, usually by using electric shock.

Resuscitation—Bringing a person back to life after an apparent death or in cases of impending death.

Ventricular fibrillation—An irregular heartbeat where the heart beats very fast but ineffectively. Ventricular fibrillation is fatal if not quickly corrected.

Cardioversion

Definition

Cardioversion refers to the process of restoring the heart's normal rhythm by applying a controlled electric shock to the exterior of the chest.

Purpose

When the heart beats too fast, blood no longer circulates effectively in the body. Cardioversion is used to stop this abnormal beating so that the heart can begin normal rhythm and pump more efficiently.

Precautions

Not all unusual heart rhythms (called **arrhythmias**) are dangerous or fatal. Atrial fibrillation and atrial flutter often revert to normal rhythms without the need for car-

KEY TERMS

Atrial fibrillation—A condition in which the upper chamber of the heart quivers instead of pumping in an organized way.

Atrial flutter—A rapid pulsation of the upper chamber of the heart that interferes with normal function.

Ventricular fibrillation—A condition in which the lower chamber of the heart quivers instead of pumping in an organized way.

Ventricular tachycardia—A rapid heart beat, usually over 100 beats per minute.

dioversion. Healthcare providers may also try to correct the heart rhythm with medication or recommend a lifestyle change before trying cardioversion. However, **ventricular tachycardia** lasting more than 30 seconds and **ventricular fibrillation** require immediate cardioversion.

Description

Elective cardioversion is usually scheduled ahead of time. After arriving at the hospital, an intravenous (IV) catheter will be placed in the arm and oxygen will be given through a face mask. A short-acting general anesthetic will be administered through the vein. During the two or three minutes of anesthesia, the doctor will apply two paddles to the exterior of the chest and administer the electric shock. It may be necessary to give the shock two or three times to obtain normal rhythm.

Preparation

Medication to thin the blood is usually given for at least three weeks before elective cardioversion. Food intake should be stopped eight hours before the procedure.

Aftercare

Medical personnel will monitor the heart rhythm for a few hours, after which the patient is usually sent home. It is advisable to arrange for transportation home, because drowsiness may last several hours. The doctor may prescribe anti-arrhythmic medication to prevent the abnormal rhythm from returning.

Risks

Cardioverters have been in use for many years and the risks are few. Those unlikely risks that remain include those instances when the device delivers greater or lesser power than expected or when power setting and control knobs are not set correctly. Unfortunately, in a number of cases, the heart prefers its abnormal rhythm and reverts to it despite cardioversion.

Normal results

Most cardioversions are successful and, at least for a time, restore the normal heart rhythm.

Resources

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ORGANIZATIONS

American Heart Association. 7320 Greenville Ave. Dallas, TX 75231. (214) 373-6300. <http://www.americanheart.org>.

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Carisoprodol *see* **Muscle relaxants**

Carotid artery surgery *see* **Endarterectomy**

Carotid Doppler ultrasound *see* **Doppler ultrasonography**

Carotid endarterectomy *see* **Endarterectomy**

Carotid sinus massage

Definition

Carotid sinus massage involves rubbing the large part of the arterial wall at the point where the common carotid artery, located in the neck, divides into its two main branches.

Purpose

Sinus, in this case, means an area in a blood vessel that is bigger than the rest of the vessel. This is a normal dilation of the vessel. Located in the neck just below the angle of the jaw, the carotid sinus sits above the point where the carotid artery divides into its two main branches. Rubbing the carotid sinus stimulates an area in the artery wall that contains nerve endings. These nerves respond to changes in blood pressure and are capable of slowing the heart rate. The response to this simple procedure often slows a rapid heart rate (for example, atrial

KEY TERMS

Angina pectoris—Chest pain usually caused by a lack of oxygen in the heart muscle.

Arrhythmia—Any deviation from a normal heart beat.

Atrial fibrillation—A condition in which the upper chamber of the heart quivers instead of pumping in an organized way.

Atrial flutter—Rapid, inefficient contraction of the upper chamber of the heart.

Carotid artery—One of the major arteries supplying blood to the head and neck.

Tachycardia—A rapid heart beat, usually over 100 beats per minute.

flutter or atrial tachycardia) and can provide important diagnostic information to the physician.

Description

The patient will be asked to lie down, with the neck fully extended and the head turned away from the side being massaged. While watching an electrocardiogram monitor, the doctor will gently touch the carotid sinus. If there is no change in the heart rate on the monitor, the pressure is applied more firmly with a gentle rotating motion. After massaging one side of the neck, the massage will be repeated on the other side. Both sides of the neck are never massaged at the same time.

Preparation

No special preparation is needed for carotid sinus massage.

Aftercare

No aftercare is required.

Risks

The physician must be sure there is no evidence of blockage in the carotid artery before performing the procedure. Massage in a blocked area might cause a clot to break loose and cause a **stroke**.

Normal results

Carotid sinus massage will slow the heart rate during episodes of atrial flutter, fibrillation, and some tachycardias. It has been known to stop the arrhythmia completely. If the procedure is being done to help diagnose **angina** pectoris, massaging the carotid sinus may make the discomfort go away.

Resources

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Carpal tunnel syndrome

Definition

Carpal tunnel syndrome is a disorder caused by compression at the wrist of the median nerve supplying the hand, causing **numbness and tingling**.

Description

The carpal tunnel is an area in the wrist where the bones and ligaments create a small passageway for the median nerve. The median nerve is responsible for both sensation and movement in the hand, in particular the thumb and first three fingers. When the median nerve is compressed, an individual's hand will feel as if it has "gone to sleep."

Women between the ages of 30 and 60 have the highest rates of carpal tunnel syndrome. Research has demonstrated that carpal tunnel syndrome is a very significant cause of missed work days due to **pain**. In 1995, about $270 million was spent on sick days taken for pain from repetitive motion injuries.

Causes and symptoms

Compression of the median nerve in the wrist can occur during a number of different conditions, particularly those conditions which lead to changes in fluid accumulation throughout the body. Because the area of the wrist through which the median nerve passes is very narrow, any swelling in the area will lead to pressure on the median nerve. This pressure will ultimately interfere with the nerve's ability to function normally. **Pregnancy**, **obesity**, arthritis, certain thyroid conditions, diabetes, and certain pituitary abnormalities all predispose to carpal tunnel syndrome. Other conditions which increase the risk for carpal tunnel syndrome include some forms

The most severe cases of carpal tunnel syndrome may require surgery to decrease the compression of the median nerve and restore its normal function. This procedure involves severing the ligament that crosses the wrist, thus allowing the median nerve more room and decreasing compression. *(Illustration by Electronic Illustrators Group.)*

of arthritis and various injuries to the arm and wrist (including **fractures**, sprains, and dislocations). Furthermore, activities which cause an individual to repeatedly bend the wrist inward toward the forearm can predispose to carpal tunnel syndrome. Certain jobs which require repeated strong wrist motions carry a relatively high risk of carpal tunnel syndrome. Injuries of this type are referred to as "repetitive motion" injuries, and are more frequent among secretaries doing a lot of typing, people working at computer keyboards or cash registers, factory workers, and some musicians.

Symptoms of carpal tunnel syndrome include numbness, burning, tingling, and a prickly pin-like sensation over the palm surface of the hand, and into the thumb, forefinger, middle finger, and half of the ring finger. Some individuals notice a shooting pain which goes from the wrist up the arm, or down into the hand and fingers. With continued median nerve compression, an individual may begin to experience muscle weakness, making it difficult to open jars and hold objects with the affected hand. Eventually, the muscles of the hand served by the median nerve may begin to grow noticeably smaller (atrophy), especially the fleshy part of the thumb. Untreated, carpal tunnel syndrome may eventually result in permanent weakness, loss of sensation, or even **paralysis** of the thumb and fingers of the affected hand.

Diagnosis

The diagnosis of carpal tunnel syndrome is made in part by checking to see whether the patient's symptoms can be brought on by holding his or her hand in position with wrist bent for about a minute. Wrist x rays are often taken to rule out the possibility of a tumor causing pressure on the median nerve. A physician examining a patient suspected of having carpal tunnel syndrome will perform a variety of simple tests to measure muscle strength and sensation in the affected hand and arm. Further testing might include electromyographic or nerve conduction velocity testing to determine the exact severity of nerve damage. These tests involve stimulating the median nerve with electricity and measuring the resulting speed and strength of the muscle response, as well as recording speed of nerve transmission across the carpel tunnel.

Treatment

Carpal tunnel syndrome is initially treated with splints, which support the wrist and prevent it from flexing inward into the position which exacerbates median nerve compression. Some people get significant relief by wearing such splints to sleep at night, while others will need to wear the splints all day, especially if they are performing jobs which **stress** the wrist. Ibuprofen or other **nonsteroidal anti-inflammatory drugs** may be prescribed to decrease pain and swelling. When carpal tunnel syndrome is more advanced, injection of steroids into the wrist to decrease inflammation may be necessary.

The most severe cases of carpal tunnel syndrome may require surgery to decrease the compression of the median nerve and restore its normal function. Such a repair involves cutting that ligament which crosses the wrist, thus allowing the median nerve more room and decreasing compression. This surgery is done almost exclusively on an outpatient basis and is often performed without the patient having to be made unconscious. Careful injection of numbing medicines (local anesthesia) or nerve blocks (the injection of anesthetics directly into the nerve) create sufficient numbness to allow the surgery to be performed painlessly, without the risks associated with general anesthesia. Recovery from this type of surgery is usually quick and without complications.

KEY TERMS

Carpal tunnel—A passageway in the wrist, created by the bones and ligaments of the wrist, through which the median nerve passes.

Electromyography—A type of test in which a nerve's function is tested by stimulating a nerve with electricity, and then measuring the speed and strength of the corresponding muscle's response.

Median nerve—A nerve which runs through the wrist and into the hand. It provides sensation and some movement to the hand, the thumb, the index finger, the middle finger, and half of the ring finger.

Prognosis

Without treatment, continued pressure on the median nerve puts an individual at risk for permanent disability in the affected hand. Most people are able to control the symptoms of carpal tunnel syndrome with splinting and anti-inflammatory agents. For those who go on to require surgery, about 95% will have complete cessation of symptoms.

Prevention

Prevention is generally aimed at becoming aware of the repetitive motions which one must make which could put the wrist into a bent position. People who must work long hours at a computer keyboard, for example, may need to take advantage of recent advances in "ergonomics," which try to position the keyboard and computer components in a way that increases efficiency and decreases stress. Early use of a splint may also be helpful for people whose jobs increase the risk of carpal tunnel syndrome.

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Casts *see* **Immobilization**

CAT scan *see* **Computed tomography scans**

Cat-bite infection *see* **Animal bite infections**

Cat-scratch disease

Definition

Cat-scratch disease is an uncommon infection that typically results from a cat's scratch or bite. Most sufferers experience only moderate discomfort and find that their symptoms clear up without any lasting harm after a few weeks or months. Professional medical treatment is rarely needed.

Description

Cat-scratch disease (also called cat-scratch **fever**) is caused by the *Bartonella henselae* bacterium, which is found in cats around the world and is transmitted from cat to cat by fleas. Researchers have discovered that large numbers of North American cats carry antibodies for the disease (meaning that the cats have been infected at some point in their lives). Some parts of North America have much higher rates of cat infection than others, however. *Bartonella henselae* is uncommon or absent in cold climates, which fleas have difficulty tolerating, but prevalent in warm, humid places such as Memphis, Tennessee, where antibodies were found in 71% of the cats tested. The bacterium, which remains in a cat's bloodstream for several months after infection, seems to be harmless to most cats, and normally an infected cat will not display any symptoms. Kittens (cats less than one year old) are more likely than adult cats to be carrying the infection.

Bartonella henselae can infect people who are scratched or (more rarely) bitten or licked by a cat. It cannot be passed from person to person. Although cats are popular pets found in about 30% of American households, human infection appears to be rare. One study estimated that for every 100,000 Americans there are only 2.5 cases of cat-scratch disease each year (2.5/100,000). It is also unusual for more than one family member to become ill; a Florida investigation discovered multiple cases in only 3.5% of the families studied. Children and teenagers appear to be the most likely victims of cat-scratch disease, although the possibility exists that

KEY TERMS

Acetaminophen—A drug for relieving pain and fever.

AIDS—Acquired immunodeficiency syndrome. A disease that attacks the immune system.

Antibiotics—A category of manufactured substances used to combat infection.

Antibodies—Special substances created by the body to combat infection.

Bacterium—A tiny organism. Some bacteria cause disease.

Hepatitis—A disease that inflames the liver.

Immune system—A body system that combats disease.

Immunocompromised—Having a damaged immune system.

Lymph nodes—Small, kidney-shaped organs that filter a fluid called lymph.

Pneumonia—A disease that inflames the lungs.

Pus—A thick yellowish or greenish fluid.

the disease may be more common among adults than previously thought.

Causes and symptoms

The first sign of cat-scratch disease may be a small blister at the site of a scratch or bite three to 10 days after injury. The blister (which sometimes contains pus) often looks like an insect bite and is usually found on the hands, arms, or head. Within two weeks of the blister's appearance, lymph nodes near the site of injury become swollen. Often the infected person develops a fever or experiences **fatigue** or headaches. The symptoms usually disappear within a month, although the lymph nodes may remain swollen for several months. Hepatitis, **pneumonia**, and other dangerous complications can arise, but the likelihood of cat-scratch disease posing a serious threat to health is very small. **AIDS** patients and other immunocompromised people face the greatest risk of dangerous complications.

Occasionally, the symptoms of cat-scratch disease take the form of what is called Parinaud's oculoglandular syndrome. In such cases, a small sore develops on the palpebral conjunctiva (the membrane lining the inner eyelid), and is often accompanied by **conjunctivitis** (inflammation of the membrane) and swollen lymph nodes in front of the ear. Researchers suspect that the first step in the development of Parinaud's oculoglandular syndrome occurs when *Bartonella henselae* bacteria pass from a cat's saliva to its fur during grooming. Rubbing one's eyes after handling the cat then transmits the bacteria to the conjunctiva.

Diagnosis

A family doctor should be called whenever a cat scratch or bite fails to heal normally or is followed by a persistent fever or other unusual symptoms such as long-lasting bone or joint **pain**. The appearance of painful and swollen lymph nodes is another reason for consulting a doctor. When cat-scratch disease is suspected, the doctor will ask about a history of exposure to cats and look for evidence of a cat scratch or bite and swollen lymph nodes. A blood test for *Bartonella henselae* may be ordered to confirm the doctor's diagnosis.

Treatment

For otherwise healthy people, rest and over-the-counter medications for reducing fever and discomfort (such as **acetaminophen**) while waiting for the disease to run its course are usually all that is necessary. **Antibiotics** are prescribed in some cases, particularly when complications occur or the lymph nodes remain swollen and painful for more than two or three months, but there is no agreement among doctors about when and how they should be used. If a lymph node becomes very swollen and painful, the family doctor may decide to drain it.

Prognosis

Most people recover completely from a bout of cat-scratch disease. Further attacks are rare.

Prevention

Certain common-sense precautions can be taken to guard against the disease. Scratches and bites should be washed immediately with soap and water, and it is never a good idea to rub one's eyes after handling a cat without first washing one's hands. Children should be told not to play with stray cats or make cats angry. Immunocompromised people should avoid owning kittens, which are more likely than adult cats to be infectious. Because cat-scratch disease is usually not a life-threatening illness and people tend to form strong emotional bonds with their cats, doctors do not recommend getting rid of a cat suspected of carrying the disease.

Resources

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Howard Baker

Cat-scratch fever *see* **Cat-scratch disease**

Cataract surgery

Definition

Cataract surgery is a procedure performed to remove a cloudy lens from the eye; usually an intraocular lens is implanted at the same time.

Purpose

The purpose of cataract surgery is to restore clear vision. It is indicated when cloudy vision due to **cataracts** has progressed to such an extent that it interferes with normal daily activities.

Precautions

Cataract surgery is not performed on both eyes at once. To avoid risking blindness in both eyes in the event of infection or other catastrophe, the first eye is allowed to heal before the cataract is removed from the second eye.

The presence of cataracts can mask additional eye problems, such as retinal damage, that neither doctors nor patients are aware of prior to surgery. Since such conditions will continue to impair sight after cataract removal if they are not identified and treated, the eventual outcome of cataract surgery will depend on the outcome of other problems.

In 1997 and 1998, evidence that cataract surgery can contribute to the progression of age-related **macular degeneration** (ARMD) was published. ARMD is the degeneration of the central part of the retina. Accordingly, ARMD patients with cataracts must weigh the risks of the loss of central vision, within four or five years, against short-term improvement. When an ARMD patient chooses cataract surgery, the surgeon should shield the retina against bright light to protect it from possible light-induced damage during surgery and install an intraocular lens capable of absorbing ultraviolet and blue light, which seem to do the most damage.

KEY TERMS

Age-related macular degeneration (ARMD)—Degeneration of the macula (the central part of the retina where the rods and cones are most dense) that leads to loss of central vision in people over 60.

Cataract—Progressive opacity or clouding of an eye lens, which obstructs the passage of light to the retina.

Cornea—Clear outer covering of the front of the eye.

Intraocular lens—Lens made of silicone or plastic placed within the eye; can be corrective.

Retina—Innermost layer at the back of the eye, which contains light receptors, the rods and cones.

Description

There are two types of cataract surgery: intracapsular and extracapsular. Intracapsular surgery is the removal of both the lens and the thin capsule that surround them. This type of surgery was common before 1980, but has since been displaced by extracapsular surgery. Removal of the capsule requires a large incision and doesn't allow comfortable intraocular lens implantation. Thus, people who undergo intracapsular cataract surgery have long recovery periods and have to wear very thick glasses.

Extracapsular cataract surgery is the removal of the lens where the capsule is left in place. Each year in the United States, over a million cataracts are removed this way.

There are two methods for extracapsular cataract surgery. The usual technique is phacoemulsification. A tiny incision (about 0.12 in or 3 mm long) is made next to the cornea (the eye's outer covering), and an ultrasonic probe is used to break the cataract into minute pieces, which are then removed by suction. When the lens is too hard to be emulsified ultrasonically, the surgeon will use a different extracapsular technique requiring a larger incision. An incision about 0.37 in (9 mm) long is made, and the whole lens (without its capsule) is removed through the incision. Both kinds of extracapsular extraction leave the back of the capsule intact, so a silicone or plastic intraocular lens can be stably implanted in about the same location as the original lens.

The surgery takes about 30–60 minutes per eye.

Preparation

Patients must have a pre-operation **eye examination**, which will include ultrasound analysis to make sure the

Cataract surgery in progress. *(Photograph by David Sutton/Zuma Images, The Stock Market. Reproduced by permission.)*

retina (the innermost layer of the eye, containing the light receptors) is intact and also to measure eye curvature so that a lens with the proper correction can be implanted. The patient will also have a pre-operative **physical examination**. In addition, patients start a course of antibiotic eye drops or ointment the day before surgery.

Aftercare

Proper post-operative care is especially important after cataract surgery. Patients will need someone to drive them home after the surgery and should not bend over or do anything strenuous for about two weeks. They should refrain from rubbing the eye, should wear glasses to protect their eye, and should wear a shield while sleeping so the eye won't be rubbed or bumped accidentally. The patient will usually continue their antibiotic for two to three weeks and will also take anti-inflammatory medication for about the same length of time. If the patient experiences inflammation, redness, or **pain**, they should seek immediate medical treatment to avoid serious complications.

Risks

Cataract surgery itself is quite safe; over 90% of the time, there are no complications. Possible complications include intraocular infection (endophthalmitis), central retinal inflammation (macular **edema**), post-operative **glaucoma**, **retinal detachment**, bleeding under the retina (choroidal hemorrhage), and tiny lens fragments in the back (vitreous) cavity of the eye, all of which can lead to loss of sight.

Normal results

Ordinarily, patients experience improved visual acuity and improved perception of the vividness of colors, leading to increased abilities in many activities, including reading, needlework, driving, golf, and tennis, for example. In addition, sometimes implanted corrective lenses eliminate the need for eyeglasses or contact lenses.

Resources

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American Academy of Ophthalmology. 655 Beach Street, P.O. Box 7424, San Francisco, CA 94120-7424. <http://www.eyenet.org>.

American Society of Cataract and Refractive Surgery. 4000 Legato Road, Suite 850, Fairfax, VA 22033-4055. (703) 591-2220. <http://www.ascrs.org>.

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Lorraine Lica, PhD

Cataracts

Definition

A cataract is a cloudiness or opacity in the normally transparent crystalline lens of the eye. This cloudiness can cause a decrease in vision and may lead to eventual blindness.

Description

The human eye has several parts. The outer layer of the eyeball consists of a transparent dome-shaped cornea and an opaque, white sclera. The cornea and sclera help protect the eye. The next layer includes the iris, pupil, and ciliary body. The iris is the colored part of the eye and the pupil is the small dark round hole in the middle of the iris. The pupil and iris allow light into the eye. The ciliary body contains muscles that help in the eye's focusing ability. The lens lies behind the pupil and iris. It is covered by a cellophane-like capsule. The lens is normally transparent, elliptical in shape, and somewhat elastic. This elasticity allows the lens to focus on both near and far objects. The lens is attached to the ciliary body by fibers (zonules of Zinn). Muscles in the ciliary body act on the zonules, which then change the shape of the lens. This process is called accommodation—the lens focuses images to help make vision clear. As people age, the lens hardens and changes shape less easily. As a result, the accommodation process becomes more difficult, making it harder to see things up close. This generally occurs around the age of 40 and continues until about age 65. The condition is called **presbyopia**. It is a normal condition of **aging**, generally resulting in the need for reading glasses.

The lens is made up of approximately 35% protein and 65% water. As people age, degenerative changes in the lens' proteins occur. Changes in the proteins, water content, enzymes, and other chemicals are some of the reasons for the formation of a cataract.

The major areas of the lens are the nucleus, the cortex, and the capsule. The nucleus is in the center of the lens, the cortex surrounds the nucleus, and the capsule is the outer layer. Opacities can occur in any area of the lens. Cataracts, then, can be classified according to location (nuclear, cortical, or posterior subcapular cataracts). The density and location of the cataract determines the amount of vision affected. If the cataract forms in the area of the lens directly behind the pupil, vision may be significantly impaired. A cataract that occurs on the outer edges or side of the lens will create less of a visual problem.

Cataracts in the elderly are so common that they are thought to be a normal part of the aging process. Between the ages of 52 and 64, there is a 50% chance of having a cataract, while at least 70% of those 70 and older are affected. Cataracts associated with aging (senile or age-related cataracts) most often occur in both eyes, with each cataract progressing at a different rate. Initially, cataracts may not affect vision. If the cataract remains small or at the periphery of the lens, the visual changes may be minor.

Cataracts that occur in people other than the elderly are much less common. Congenital cataracts occur very rarely in newborns. Genetic defects or an infection or disease in the mother during **pregnancy** are among the causes of congenital cataracts. Traumatic cataracts may develop after a foreign body or trauma injures the lens or eye. Systemic illnesses, such as diabetes, may result in cataracts. Cataracts can also occur secondary to other eye diseases—for example, an inflammation of the inner layer of the eye (**uveitis**) or **glaucoma**. Such cataracts are called complicated cataracts. Toxic cataracts result from chemical toxicity, such as steroid use. Cataracts can also result from exposure to the sun's ultraviolet (UV) rays.

Causes and symptoms

Recent studies have been conducted to try to determine whether diet or the use of **vitamins** might have an effect on the formation of cataracts in older people. The results have been mixed, with some studies finding that there is a connection and other studies finding none. Much interest has been focused on the use of antioxidant supplements as a protection against cataracts. Antioxidant vitamins such as vitamins A, C, E and beta-carotene help the body clean-up oxygen-free radicals. Some vitamins are marketed specifically for the eyes. Patients should speak to their doctors about the use of such vitamins.

Smoking and alcohol intake have been implicated in cataract formation. Some studies have determined that a diet high in fat will increase the likelihood of cataract formation, while an increase in foods rich in antioxidants will reduce the incidence. More research is needed to determine if diet, smoking, alcohol consumption, or vitamins have any connection to the formation of cataracts.

A dense cataract on lens of eye. *(Photograph by Margaret Cubberly, Phototake NYC. Reproduced by permission.)*

There are several common symptoms of cataracts:

- gradual, painless onset of blurry, filmy, or fuzzy vision
- poor central vision
- frequent changes in eyeglass prescription
- changes in color vision
- increased glare from lights, especially oncoming headlights when driving at night
- "second sight" improvement in near vision (no longer needing reading glasses), but a decrease in distance vision
- poor vision in sunlight
- presence of a milky whiteness in the pupil as the cataract progresses.

Diagnosis

Both ophthalmologists and optometrists may detect and monitor cataract growth and prescribe prescription lenses for visual deficits. However, only an ophthalmologist can perform cataract extraction.

Cataracts are easily diagnosed from the reporting of symptoms, a visual acuity exam using an eye chart, and by examination of the eye itself. Shining a penlight into the pupil may reveal opacities or a color change of the lens even before visual symptoms have developed. An instrument called a slit lamp is basically a large microscope. This lets the doctor examine the front of the eye and the lens. The slit lamp helps the doctor determine the location of the cataract.

Some other diagnostic tests may be used to determine if cataracts are present or how well the patient may potentially see after surgery. These include a glare test, potential vision test, and contrast sensitivity test.

Treatment

For cataracts that cause no symptoms or only minor visual changes, no treatment may be necessary. Continued monitoring and assessment of the cataract is needed by an ophthalmologist or optometrist at scheduled office visits. Increased strength in prescription eyeglasses or contact lenses may be helpful. This may be all that is required if the cataract does not reduce the patient's quality of life.

Cataract surgery—the only option for patients whose cataracts interfere with vision to the extent of affecting their daily lives—is the most frequently performed surgery in the United States. It generally improves vision in over 90% of patients. Some people have heard that a cataract should be "ripe" before being removed. A "ripe" or mature cataract is when the lens is completely opaque. Most cataracts are removed before they reach that stage. Sometimes cataracts need to be removed so that the doctor can examine the back of the eye more carefully. This is important in patients with diseases that may affect the eye. If cataracts are present in both eyes, only one eye at a time should be operated on. Healing occurs in the first eye before the second cataract is removed, sometimes as early as the following week. A final eyeglass prescription is usually given about four to six weeks after surgery. Patients will still need reading glasses. The overall health of the patient needs to be considered in making the decision to operate. However, age alone need not preclude effective surgical treatment of cataracts. People in their 90s can have successful return of vision after **cataract surgery**.

Surgery to remove cataracts is generally an outpatient procedure. A local anesthetic is used and the procedure lasts about an hour. Removal of the cloudy lens can be done by several different procedures. The three types of cataract surgery available are:

- Extracapsular cataract extraction. This type of cataract extraction is the most common. The lens and the front portion of the capsule are removed. The back part of the capsule remains, providing strength to the eye.
- Intracapsular cataract extraction. The lens and the entire capsule are removed. This method carries an increased risk for detachment of the retina and swelling after surgery. It is rarely used.
- Phacoemulsification. This type of extracapsular extraction needs a very small incision, resulting in faster healing. Ultrasonic vibration is applied to the lens to break it up into very small pieces which are then aspirated out of the eye with suction by the ophthalmologist.

A replacement lens is usually inserted at the time of the surgery. A plastic artificial lens called an intraocular lens (IOL) is placed in the remaining posterior lens capsule of the eye. When the intracapsular extraction

method is used, an IOL may be clipped onto the iris. Contact lenses and cataract glasses (aphakic lenses) are prescribed if an IOL was not inserted. A folding IOL is used when phacoemulsification is performed to accommodate the small incision.

Antibiotic drops to prevent infection and steroids to reduce inflammation are prescribed after surgery. An eye shield or glasses during the day will protect the eye from injury while it heals. During the night, an eye shield is worn. The patient returns to the doctor the day after surgery for assessment, with several follow-up visits over the next two months to monitor the healing process.

Prognosis

The success rate of cataract extraction is very high, with a good prognosis. A visual acuity of 20/40 or better may be achieved. If an extracapsular cataract extraction was performed, a secondary cataract may develop in the remaining back portion of the capsule. This can occur one to two years after surgery. YAG capsulotomy is most often used for this type of cataract. YAG stands for yttrium aluminum garnet, the name of the laser used for this procedure. This is a painless outpatient procedure and requires no incision. The laser beam makes a small opening in the remaining back part of the capsule, allowing light through.

In a very small percentage (3–5%) of surgical cataract extractions, complications occur. Infections, swelling of the cornea (**edema**), bleeding, **retinal detachment**, and the onset of glaucoma have been reported. Some problems may occur one to two days, or even several weeks, after surgery. Any haziness, redness, decrease in vision, nausea, or **pain** should be reported to the surgeon immediately.

Prevention

Preventive measures emphasize protecting the eyes from UV radiation by wearing glasses with a special coating to protect against UV rays. Dark lenses alone are not sufficient. The lenses must protect against UV light (specifically, UV-A and UV-B). Antioxidants may also provide some protection by reducing free radicals that can damage lens proteins. A healthy diet rich in sources of antioxidants, including citrus fruits, sweet potatoes, carrots, green leafy vegetables, and/or vitamin supplements may be helpful. When taking certain medications, such as steroids, more frequent eye exams may be necessary. Patients should speak to their doctors to see if medications may affect their eyes.

Resources

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KEY TERMS

Aphakia—Absence of the lens of the eye.

Ciliary body—A structure in the eye that contains muscles which will affect the focusing of the lens.

Glaucoma—Disease of the eye characterized by increased pressure of the fluid inside the eye. Untreated, glaucoma can lead to blindness.

Phacoemulsification—Surgical procedure to remove a cataract using sound waves to disintegrate the lens which is then removed by suction.

Retina—The innermost layer of the eyeball. Images focused onto the retina are then sent to the brain.

Ultraviolet radiation (UV)—Invisible light rays which may be responsible for sunburns, skin cancers, and cataract formation.

Uveitis—Inflammation of the uvea. The uvea is a continuous layer of tissue which consists of the iris, the ciliary body, and the choroid. The uvea lies between the retina and sclera.

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ORGANIZATIONS

American Academy of Ophthalmology. 655 Beach Street, P.O. Box 7424, San Francisco, CA 94120-7424. <http://www.eyenet.org>.

American Optometric Association. 243 North Lindbergh Blvd., St. Louis, MO 63141. (314) 991-4100. <http://www.aoanet.org>.

The Lighthouse. 111 East 59th St., New York, NY 10022. (800) 334-5497. <http://www.lighthouse.org>.

Prevent Blindness America. 500 East Remington Road, Schaumburg, IL 60173. (800) 331-2020. <http://www.preventblindness.org>.

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Catatonia

Definition

Catatonia is a condition marked by changes in muscle tone or activity associated with a large number of serious mental and physical illnesses. There are two distinct sets of symptoms that are characteristic of this condition. In catatonic stupor the individual experiences a

deficit of motor (movement) activity that can render him/her motionless. Catatonic excitement, or excessive movement, is associated with violent behavior directed toward oneself or others.

Features of catatonia may also be seen in Neuroleptic Malignant Syndrome (NMS) which is an uncommon (but potentially lethal) reaction to some medications used to treat major mental illnesses. NMS is considered a medical emergency since 25% of untreated cases result in **death**. Catatonia can also be present in individuals suffering from a number of other physical and emotional conditions such as drug intoxication, depression, and **schizophrenia**. It is most commonly associated with **mood disorders**.

Description

In catatonic stupor, motor activity may be reduced to zero. Individuals avoid bathing and grooming, make little or no eye contact with others, may be mute and rigid, and initiate no social behaviors. In catatonic excitement the individual is extremely hyperactive although the activity seems to have no purpose. Violence toward him/herself or others may also be seen.

NMS is observed as a dangerous side effect associated with certain neuroleptic (antipsychotic) drugs such as haloperidol (Haldol). It comes on suddenly and is characterized by stiffening of the muscles, **fever**, confusion and heavy sweating.

Catatonia can also be categorized as intrinsic or extrinsic. If the condition has an identifiable cause, it is designated as extrinsic. If no cause can be determined following **physical examination**, laboratory testing, and history taking, the illness is considered to be intrinsic.

Causes and symptoms

The causes of catatonia are largely unknown although research indicates that brain structure and function are altered in this condition. While this and other information point to a physical cause, none has yet been proven. A variety of medical conditions also may lead to catatonia including head trauma, cerebrovascular disease, **encephalitis**, and certain metabolic disorders. NMS is an adverse side effect of certain **antipsychotic drugs**.

A variety of symptoms are associated with catatonia. Among the more common are echopraxia (imitation of the gestures of others) and echolalia (parrot-like repetition of words spoken by others). Other signs and symptoms include violence directed toward him/herself, the assumption of inappropriate posture, selective **mutism**, negativism, facial grimaces, and animal-like noises.

Catatonic stupor is marked by immobility and a behavior known as *cerea flexibilitas* (waxy flexibility) in which the individual can be made to assume bizarre (and sometimes painful) postures that they will maintain for extended periods of time. The individual may become dehydrated and malnourished because food and liquids are refused. In extreme situations such individuals must be fed through a tube. Catatonic excitement is characterized by hyperactivity and violence; the individual may harm him/herself or others. On rare occasions, **isolation** or restraint may be needed to ensure the individual's safety and the safety of others.

KEY TERMS

Barbiturates—A group of medicines that slow breathing and lower the body temperature and blood pressure. They can be habit forming and are now used chiefly for anesthesia.

Benzodiazipines—This group of medicines is used to help reduce anxiety (especially before surgery) and to help people sleep.

Electroconvulsive therapy—This type of therapy is used to treat major depression and severe mental illness that does not respond to medications. A measured dose of electricity is introduced into the brain in order to produce a convulsion. Electroconvulsive therapy is safe and effective.

Mutism—The inability or refusal to speak.

Negativism—Behavior characterized by resistance, opposition, and refusal to cooperate with requests, even the most reasonable ones.

Neuroleptic drugs—Antipsychotic drugs, including major tranquilizers, used in the treatment of psychoses like schizophrenia.

Diagnosis

Recognition of catatonia is made on the basis of specific movement symptoms. These include odd ways of walking such as walking on tiptoes or ritualistic pacing, and rarely, hopping and skipping. Repetitive odd movements of the fingers or hands, as well as imitating the speech or movements of others also may indicate that catatonia is present. There are no laboratory or other tests that can be used to positively diagnose this condition, but medical and neurological tests are necessary to rule out underlying lesions or disorders that may be causing the symptoms observed.

Treatment

Treatment of catatonia includes medications such as benzodiazipines (which are the preferred treatment) and rarely **barbiturates**. Antipsychotic drugs may be appropri-

ate in some cases, but often cause catatonia to worsen. **Electroconvulsive therapy** may prove beneficial for clients who do not respond to medication. If these approaches are unsuccessful, treatment will be redirected to attempts to control the signs and symptoms of the illness.

Prognosis

Catatonia usually responds quickly to medication interventions.

Prevention

There is currently no known way to prevent catatonia because the cause has not yet been identified. Research efforts continue to explore possible origins. Avoiding excessive use of neuroleptic drugs can help minimize the risk of developing catatonic-like symptoms.

Resources

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Catecholamines tests

Definition

Catecholamines is a collective term for the hormones epinephrine, norepinephrine, and dopamine. Manufactured chiefly by the chromaffin cells of the adrenal glands, these hormones are involved in readying the body for the "fight-or-flight" response (also known as the alarm reaction). When these hormones are released, the heart beats stronger and faster, blood pressure rises, more blood flows to the brain and muscles, the liver releases stores of energy as a sugar the body can readily use (glucose), the rate of breathing increases and airways widen, and digestive activity slows. These reactions direct more oxygen and fuel to the organs most active in responding to stress—mainly the brain, heart, and skeletal muscles.

Purpose

Pheochromocytoma (a tumor of the chromaffin cells of the adrenal gland) and tumors of the nervous system (neuroblastomas, ganglioneuroblastomas, and ganglioneuromas) that affect hormone production can cause excessive levels of different catecholamines to be secreted. This results in constant or intermittent high blood pressure (**hypertension**). Episodes of high blood pressure may be accompanied by symptoms such as **headache**, sweating, **palpitations**, and **anxiety**. The catecholamines test can be ordered, then, to determine if high blood pressure and other symptoms are related to improper hormone secretion and to identify the type of tumor causing elevated catecholamine levels.

Description

The catecholamines test can be performed on either blood or urine. If performed on blood, the test may require one or two samples, depending on the physician's request. The first blood sample will be drawn after the patient has been lying down in a warm, comfortable environment for at least 30 minutes. If a second sample is needed, the patient will be asked to stand for 10 minutes before the blood is drawn. Instead of a venipuncture, which can be stressful for the patient, possibly increasing catecholamine levels in the blood, a plastic or rubber tube-like device called a catheter may be used to collect the blood samples. The catheter would be inserted in a vein 24 hours in advance, eliminating the need for needle punctures at the time of the test.

It may take up to a week for a lab to complete testing of the samples. Because blood levels of catecholamines commonly go up and down in response to such factors as temperature, **stress**, postural change, diet, **smoking**, **obesity**, and many drugs, abnormally high blood test results should be confirmed with a 24-hour urine test. In addition, catecholamine secretion from a tumor may not be steady, but may occur periodically during the day, and potentially could be missed when blood testing is used. The urine test provides the laboratory with a specimen that reflects catecholamine production over an entire 24-hour period. If urine is tested, the patient or a healthcare worker must collect all the urine passed over the 24-hour period.

Preparation

It is important that the patient refrain from using certain medications, especially cold or allergy remedies, for two weeks before the test. Certain foods—including bananas, avocados, cheese, coffee, tea, cocoa, beer, licorice, citrus fruit, vanilla, and Chianti—must be avoided for 48 hours prior to testing. However, people should be sure to get adequate amounts of vitamin C before the test, because this vitamin is necessary for catecholamine formation. The patient should be **fasting** (nothing to eat or drink) for 10 to 24 hours before the blood test and should not smoke for 24 hours beforehand. Some laboratories may call for additional restrictions. As much as possible, the patient should try to avoid excessive physi-

KEY TERMS

Dopamine—Dopamine is a precursor of epinephrine and norepinephrine.

Epinephrine—Epinephrine, also called adrenaline, is a naturally occurring hormone released by the adrenal glands in response to signals from the sympathetic nervous system. These signals are triggered by stress, exercise, or by emotions such as fear.

Ganglioneuroma—A ganglioneuroma is a tumor composed of mature nerve cells.

Neuroblastoma—Neuroblastoma is a tumor of the adrenal glands or sympathetic nervous system. Neuroblastomas can range from being relatively harmless to highly malignant.

Norepinephrine—Norepinephrine is a hormone secreted by certain nerve endings of the sympathetic nervous system, and by the medulla (center) of the adrenal glands. Its primary function is to help maintain a constant blood pressure by stimulating certain blood vessels to constrict when the blood pressure falls below normal.

Pheochromocytoma—A pheochromocytoma is a tumor that originates from the adrenal gland's chromaffin cells, causing overproduction of catecholamines, powerful hormones that induce high blood pressure and other symptoms.

cal **exercise** and emotional stress before the test, because either may alter test results by causing increased secretion of epinephrine and norepinephrine.

Patients collecting their own 24-hour urine samples will be given a container with special instructions. The urine samples must be refrigerated.

Risks

Risks for the blood test are minimal, but may include slight bleeding from the venipuncture site, **fainting** or feeling lightheaded after blood is drawn, or blood accumulating under the puncture site (hematoma). There are no risks for the urine test.

Normal results

Reference ranges are laboratory-specific, vary according to methodology of testing, and differ between blood and urine samples. If testing is done by the method called High Performance Liquid Chromatography (HPLC), typical values for blood and urine follow.

Reference ranges for blood catecholamines

Supine (lying down): Epinephrine less than 50 pg/mL, norepinephrine less than 410 pg/mL, and dopamine less than 90 pg/mL. Standing: Values for blood specimens taken when the subject is standing are higher than the ranges for supine posture for norepinephrine and epinephrine, but not for dopamine.

Reference ranges for urine catecholamines

Epinephrine 0–20 microgram per 24 hours; norepinephrine 15–80 microgram per 24 hours; dopamine 65–400 microgram per 24 hours.

Abnormal results

Depending on the results, high catecholamine levels can indicate different conditions and/or causes:

- High catecholamine levels can help to verify pheochromocytoma, **neuroblastoma**, or ganglioneuroma. An aid to diagnosis is the fact that an adrenal medullary tumor (pheochromocytoma) secretes epinephrine, whereas ganglioneuroma and neuroblastoma secrete norepinephrine.
- Elevations are possible with, but do not directly confirm, thyroid disorders, low blood sugar (**hypoglycemia**), or heart disease.
- Electroshock therapy, or **shock** resulting from hemorrhage or exposure to toxins, can raise catecholamine levels.
- In the patient with normal or low baseline catecholamine levels, failure to show an increase in the sample taken after standing suggests an autonomic nervous system dysfunction (the division of the nervous system responsible for the automatic or unconscious regulation of internal body functioning).

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Janis O. Flores

Catheter ablation

Definition

Catheter ablation of an irregular heartbeat involves having a tube (a catheter) inserted into the heart through

During catheter ablation, a long flexible tube called a catheter is inserted into a vein in the patient's groin and guided toward the heart. A special x-ray machine called a fluoroscope helps the electrophysiologist visualize correct placement. *(Photograph by Collette Placek. Reproduced by permission.)*

which electrical energy is sent to either reset the heartbeat or stop the heart from beating so a mechanical pacemaker can be put in place.

Purpose

Irregular heartbeats can occur in healthy people without causing any dangerous symptoms or requiring medical attention. Slight changes in the normal patterns of heartbeats often reset themselves without notice.

But when the heartbeat is greatly disrupted—either because of traumatic injury, disease, **hypertension**, surgery, or reduced blood flow to the heart caused by blockages in the blood vessels that nourish the heart—the condition must be recognized and treated immediately. Otherwise, it can be fatal.

Various drugs can be used to control and help reset these abnormal heart rhythms (**arrhythmias**). The technique of catheter ablation (meaning tube-guided removal) is used to interrupt the abnormal contractions in the heart, allowing normal heart beating to resume. **Atrial fibrillation and flutter** and **Wolff-Parkinson-White syndrome** are two of the most common disorders treated with catheter ablation.

Precautions

The improper correction of abnormal heartbeats can cause additional arrhythmias and can be fatal. Abnormalities in different areas of the heart cause different types of irregular heartbeats; the type of arrhythmia must be clearly defined before this procedure can be properly done.

Description

Catheter ablation involves delivering highly focused heat (or radio frequency energy) to specific areas of the

KEY TERMS

Fluoroscope—A specialized x-ray machine used to visualize the placement of the catheter when attempting to correct irregular heartbeats.

Pacemaker—An electrical device that has electrodes attached to the heart to electrically stimulate the heart to beat normally. Pacemakers can be internal (placed under the skin) or external, with the electrodes placed on the skin or threaded through a tube placed into the heart.

heart. Radio frequency energy is very rapidly alternating electrical current that is produced at the tip of the catheter that is placed inside the heart. At the same time as the catheter is inserted, a second electrode is placed on the patient's skin. When the catheter is energized, the body conducts the energy from the catheter's tip, through the heart and to the electrode on the skin's surface, completing the circuit.

Although very little electricity is given off by the catheter, the instrument does generate a large amount of heat. This heat is absorbed by the heart tissue, causing a small localized burn and destroying the tissue in contact with the catheter tip; in this way, small regions of heart tissue are burned in a controlled manner. This controlled destruction of small sections of heart muscle actually kills the nerve cells causing the irregular heartbeat, stopping the nerve signals that are passing through this section of the heart. This usually causes the irregular heartbeat to be reset into a normal heartbeat.

Preparation

People can undergo this procedure by having general anesthesia or by taking medicines to make them relaxed and sleepy (sedatives) along with painkillers. Once the type of irregular heartbeat is identified and these medicines are given, the catheter is inserted through a blood vessel and into the heart. Importantly, correct placement of the catheter is visualized by using a specialized type of x-ray machine called a fluoroscope.

Aftercare

Being sure the patient is comfortable during and after this procedure is very important. However, because each person may have a different arrhythmia and possibly other medical problems as well, each patient's needs must be evaluated individually.

Risks

Overall, fewer than 5% of people having this procedure experience complications. The most common complications are usually related to blood vessel injury when the catheter is inserted and to different heart-related problems due to the moving of the catheter within the heart. However, in general, this technique is safe and can control many different heart arrhythmias.

Normal results

Depending upon the type of irregular heartbeat being treated, either the normal heartbeat resumes after treatment or the ability of the heart to beat on its own is lost, requiring the insertion of a pacemaker to stimulate the heart to beat regularly.

Abnormal results

Additional irregular heartbeats can occur as a result of this procedure, as can damage to the blood vessels that feed the heart. Because this procedure requires the use of the x-ray machine called a fluoroscope, there is exposure to x-ray radiation, but it's doubtful that this is harmful in adult patients. The risk versus benefit is considered with pediatric patients.

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American Heart Association. 7320 Greenville Ave. Dallas, TX 75231. (214) 373-6300. <http://www.americanheart.org>.

Dominic De Bellis, PhD

Cat's cry syndrome *see* **Cri du chat syndrome**

CBC *see* **Blood count**

CEA test *see* **Carcinoembryonic antigen test**

CEB *see* **Chronic fatigue syndrome**

Cefaclor *see* **Cephalosporins**

Cefadroxil *see* **Cephalosporins**

Cefixime *see* **Cephalosporins**

Cefprozil *see* **Cephalosporins**

Cefurox *see* **Cephalosporins**

Celiac disease

Definition

Celiac disease is a disease of the digestive system that damages the small intestine and interferes with the absorption of nutrients from food.

Description

Celiac disease occurs when the body reacts abnormally to gluten, a protein found in wheat, rye, barley, and possibly oats. When someone with celiac disease eats foods containing gluten, that person's immune system causes an inflammatory response in the small intestine, which damages the tissues and results in impaired ability to absorb nutrients from foods. The inflammation and malabsorption create wide-ranging problems in many systems of the body. Since the body's own immune system causes the damage, celiac disease is classified as an "autoimmune" disorder. Celiac disease may also be called sprue, nontropical sprue, gluten sensitive enteropathy, celiac sprue, and adult celiac disease.

Celiac disease may be discovered at any age, from infancy through adulthood. The disorder is more commonly found among white Europeans or in people of European descent. It is very unusual to find celiac disease in African or Asian people. The exact incidence of the disease is uncertain. Estimates vary from one in 5000, to as many as one in every 300 individuals with this background. The prevalence of celiac disease seems to be different from one European country to another, and between Europe and the United States. This may be due to differences in diet and/or unrecognized disease. A recent study of random blood samples tested for celiac disease in the US showed one in 250 testing positive. It is clearly underdiagnosed, probably due to the symptoms being attributed to another problem, or lack of knowledge about celiac disease by physicians and laboratories. Because of the known genetic component, relatives of patients with celiac disease are considered at higher risk for the disorder.

Because celiac disease has a hereditary influence, close relatives (especially first degree relatives, such as children, siblings, and parents) have a higher risk of being affected with the condition. The chance that a first degree relative of someone with celiac disease will have the disease is about 10%.

As more is learned about celiac disease, it becomes evident that it has many variations which may not produce typical symptoms. It may even be clinically "silent," where no obvious problems related to the disease are apparent.

Causes and symptoms

Celiac disease can run in families and has a genetic basis, although the pattern of inheritance is complicated. The type of inheritance pattern that celiac disease follows is called multifactorial (caused by many factors, both genetic and environmental). Researchers think that several factors must exist in order for the disease to occur. The patient must have a genetic predisposition to develop the disorder. Then, something in their environment acts as a stimulus, or "trigger," to their immune system, causing the disease to become active for the first time. For conditions with multifactorial inheritance, people without the genetic predisposition are less likely to develop the condition with exposure to the same triggers. Or, they may require more exposure to the stimulus before developing the disease than someone with a genetic predisposition. Some of the things which may provoke a reaction include surgery, especially gastrointestinal surgery; a change to a low fat diet, which has an increased number of wheat-based foods; **pregnancy**; **childbirth**; severe emotional **stress**; or a viral infection. This combination of genetic susceptibility and an outside agent leads to celiac disease.

Each person with celiac disease is affected differently. When food containing gluten reaches the small intestine, the immune system begins to attack a substance called gliadin, which is found in the gluten. The resulting inflammation causes damage to the delicate finger-like structures in the intestine, called villi, where food absorption actually takes place. The patient may experience a number of symptoms related to the inflammation and the chemicals it releases, and/or the lack of ability to absorb nutrients from food, which can cause **malnutrition**.

The most commonly recognized symptoms of celiac disease relate to the improper absorption of food in the gastrointestinal system. Many patients with gastrointestinal symptoms will have **diarrhea** and fatty, greasy,

unusually foul-smelling stools. The patient may complain of excessive gas (flatulence), distended abdomen, weight loss, and generalized weakness. Not all people have digestive system complications; some people only have irritability or depression. Irritability is one of the most common symptoms in children with celiac disease.

Not all patients have these problems. Unrecognized and therefore untreated celiac disease may cause or contribute to a variety of other conditions. The decreased ability to digest, absorb, and utilize food properly (malabsorption) may cause anemia (low red **blood count**) from iron deficiency or easy bruising from a lack of vitamin K. Poor mineral absorption may result in **osteoporosis**, or "brittle bones," which may lead to bone **fractures**. Vitamin D levels may be insufficient and bring about a "softening" of bones (osteomalacia), which produces **pain** and bony deformities, such as flattening or bending. Defects in the tooth enamel, characteristic of celiac disease, may be recognized by dentists. Celiac disease may be discovered during medical tests performed to investigate **failure to thrive** in infants, or lack of proper growth in children and adolescents. People with celiac disease may also experience **lactose intolerance** because they don't produce enough of the enzyme lactase, which breaks down the sugar in milk into a form the body can absorb. Other symptoms can include muscle cramps, **fatigue**, delayed growth, tingling or numbness in the legs (from nerve damage), pale sores in the mouth (called aphthus ulcers), tooth discoloration, or missed menstrual periods (due to severe weight loss).

A distinctive, painful skin rash, called **dermatitis** herpetiformis, may be the first sign of celiac disease. Approximately 10% of patients with celiac disease have this rash, but it is estimated that 85% or more of patients with the rash have the disease.

Many disorders are associated with celiac disease, though the nature of the connection is unclear. One type of epilepsy is linked to celiac disease. Once their celiac disease is successfully treated, a significant number of these patients have fewer or no seizures. Patients with **alopecia** areata, a condition where hair loss occurs in sharply defined areas, have been shown to have a higher risk of celiac disease than the general population. There appears to be a higher percentage of celiac disease among people with **Down syndrome**, but the link between the conditions is unknown.

Several conditions attributed to a disorder of the immune system have been associated with celiac disease. People with insulin dependent diabetes (type I) have a much higher incidence of celiac disease. One source estimates that as many as one in 20 insulin-dependent diabetics may have celiac disease. Patients with other conditions where celiac disease may be more commonly found include those with juvenile chronic arthritis, some thyroid diseases, and IgA deficiency.

There is an increased risk of intestinal lymphoma, a type of **cancer**, in individuals with celiac disease. Successful treatment of the celiac disease seems to decrease the chance of developing lymphoma.

Diagnosis

Because of the variety of ways celiac disease can manifest itself, it is often not discovered promptly. Its symptoms are similar to many other conditions including irritible bowel syndrome, **Crohn's disease**, **ulcerative colitis**, diverticulosis, intestinal infections, **chronic fatigue syndrome**, and depression. The condition may persist without diagnosis for so long that the patient accepts a general feeling of illness as normal. This leads to further delay in identifying and treating the disorder. It is not unusual for the disease to be identified in the course of medical investigations for seemingly unrelated problems. For example, celiac disease has been discovered during testing to find the cause of **infertility**.

If celiac disease is suspected, a blood test can be ordered. This test looks for the antibodies to gluten (called antigliadin, anti-endomysium, and antireticulin) that the immune system produces in celiac disease. Antibodies are chemicals produced by the immune system in response to substances that the body perceives to be threatening. Some experts advocate not just evaluating patients with symptoms, but using these blood studies as a screening test for high-risk individuals, such as those with relatives (especially first degree relatives) known to have the disorder. An abnormal result points towards celiac disease, but further tests are needed to confirm the diagnosis. Because celiac disease affects the ability of the body to absorb nutrients from food, several tests may be ordered to look for nutritional deficiencies. For example, doctors may order a test of iron levels in the blood because low levels of iron (anemia) may accompany celiac disease. Doctors may also order a test for fat in the stool, since celiac disease prevents the body from absorbing fat from food.

If these tests above are suspicious for celiac disease, the next step is a biopsy (removal of a tiny piece of tissue surgically) of the small intestine. This is usually done by a gastroenterologist, a physician who specializes in diagnosing and treating bowel disorders. It is generally performed in the office, or in a hospital's outpatient department. The patient remains awake, but is sedated. A narrow tube, called an endoscope, is passed through the mouth, down through the stomach, and into the small intestine. A small sample of tissue is taken and sent to the laboratory for analysis. If it shows a pattern of tissue damage characteristic of celiac disease, the diagnosis is established.

The patient is then placed on a gluten-free diet (GFD). The physician will periodically recheck the level of antibody in the patient's blood. After several months, the small intestine is biopsied again. If the diagnosis of celiac disease was correct (and the patient followed the rigorous diet), healing of the intestine will be apparent. Most experts agree that it is necessary to follow these steps in order to be sure of an accurate diagnosis.

Treatment

The only treatment for celiac disease is a gluten-free diet. This may be easy for the doctor to prescribe, but difficult for the patient to follow. For most people, adhering to this diet will stop symptoms and prevent damage to the intestines. Damaged villi can be functional again in three to six months. This diet must be followed for life. For people whose symptoms are cured by the gluten-free diet, this is further evidence that their diagnosis is correct.

Gluten is present in any product that contains wheat, rye, barley, or oats. It helps make bread rise, and gives many foods a smooth, pleasing texture. In addition to the many obvious places gluten can be found in a normal diet, such as breads, cereals, and pasta, there are many hidden sources of gluten. These include ingredients added to foods to improve texture or enhance flavor and products used in food packaging. Gluten may even be present on surfaces used for food preparation or cooking.

Fresh foods that have not been artificially processed, such as fruits, vegetables, and meats, are permitted as part of a GFD. Gluten-free foods can be found in health food stores and in some supermarkets. Mail-order food companies often have a selection of gluten-free products. Help in dietary planning is available from dieticians (healthcare professionals specializing in food and **nutrition**) or from support groups for individuals with celiac disease. There are many cookbooks on the market specifically for those on a GFD.

Treating celiac disease with a GFD is almost always completely effective. Gastrointestinal complaints and other symptoms are alleviated. Secondary complications, such as anemia and osteoporosis, resolve in almost all patients. People who have experienced lactose intolerance related to their celiac disease usually see those symptoms subside, as well. Although there is no risk and much potential benefit to this treatment, it is clear that avoiding all foods containing gluten can be difficult.

Experts emphasize the need for lifelong adherence to the GFD to avoid the long-term complications of this disorder. They point out that although the disease may have symptom-free periods if the diet is not followed, silent damage continues to occur. Celiac disease cannot be "outgrown" or cured, according to medical authorities.

KEY TERMS

Antibodies—Proteins that provoke the immune system to attack particular substances. In celiac disease, the immune system makes antibodies to a component of gluten.

Gluten—A protein found in wheat, rye, barley, and oats.

Villi—Tiny, finger-like projections that enable the small intestine to absorb nutrients from food.

Prognosis

Patients with celiac disease must adhere to a strict GFD throughout their lifetime. Once the diet has been followed for several years, individuals with celiac disease have similar mortality rates as the general population. However, about 10% of people with celiac disease develop a cancer involving the gastrointestinal tract (both carcinoma and lymphoma).

There are a small number of patients who develop a refractory type of celiac disease, where the GFD no longer seems effective. Once the diet has been thoroughly assessed to ensure no hidden sources of gluten are causing the problem, medications may be prescribed. Steroids or **immunosuppressant drugs** are often used to try to control the disease. It is unclear whether these efforts meet with much success.

Prevention

There is no way to prevent celiac disease. However, the key to decreasing its impact on overall health is early diagnosis and strict adherence to the prescribed gluten-free diet.

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American Celiac Society. 58 Musano Court, West Orange, NJ, 7052. (201) 325-8837.

Celiac Disease Foundation. 13251 Ventura Blvd., Suite 1, Studio City, CA 91604-1838. (818) 990-2354.

Celiac Sprue Association/United States of America (CSA/USA). PO Box 31700, Omaha, NE 68131-0700. (402) 558-0600.

Gluten Intolerance Group. PO Box 23053, Seattle, WA, 98102-0353. (206) 325-6980.

National Center for Nutrition and Dietetics. American Dietetic Association, 216 West Jackson Boulevard, Suite 800, Chicago, IL, 60606-6995. (800) 366-1655.

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National Institute of Diabetes & Digestive & Kidney Diseases. <http://www.niddk.nih.gov/health/digest/pubs/celiac/index.htm>.

Amy Vance, MS, CGC

Cellulitis

Definition

Cellulitis is a spreading bacterial infection just below the skin surface. It is most commonly caused by *Streptococcus pyogenes* or *Staphylococcus aureus*.

Description

The word "cellulitis" actually means "inflammation of the cells." Specifically, cellulitis refers to an infection of the tissue just below the skin surface. In humans, the skin and the tissues under the skin are the most common locations for microbial infection. Skin is the first defense against invading bacteria and other microbes. An infection can occur when this normally strong barrier is damaged due to surgery, injury, or a burn. Even something as small as a scratch or an insect bite allows bacteria to enter the skin, which may lead to an infection. Usually, the immune system kills any invading bacteria, but sometimes the bacteria are able to grow and cause an infection.

Once past the skin surface, the warmth, moisture, and nutrients allow bacteria to grow rapidly. Disease-causing bacteria release proteins called enzymes which cause tissue damage. The body's reaction to damage is inflammation which is characterized by **pain**, redness, heat, and swelling. This red, painful region grows bigger as the infection and resulting tissue damage spread. An untreated infection may spread to the lymphatic system (**acute lymphangitis**), the lymph nodes (**lymphadenitis**), the bloodstream (**bacteremia**), or into deeper tissues. Cellulitis most often occurs on the face, neck, and legs.

Orbital cellulitis

A very serious infection, called orbital cellulitis, occurs when bacteria enter and infect the tissues surrounding the eye. In 50–70% of all cases of orbital cellulitis, the infection spreads to the eye(s) from the sinuses or the upper respiratory tract (nose and throat). Twenty-five percent of orbital infections occur after surgery on the face. Other sources of orbital infection include a direct infection from an eye injury, from a dental or throat infection, and through the bloodstream.

Infection of the tissues surrounding the eye causes redness, swollen eyelids, severe pain, and causes the eye to bulge out. This serious infection can lead to a temporary loss of vision, blindness, brain abscesses, inflammation of the brain and spinal tissues (**meningitis**), and other complications. Before the discovery of **antibiotics**, orbital cellulitis caused blindness in 20% of patients and **death** in 17% of patients. Antibiotic treatment has significantly reduced the incidence of blindness and death.

Causes and symptoms

Although other kinds of bacteria can cause cellulitis, it is most often caused by *Streptococcus pyogenes* (the bacteria which causes **strep throat**) and *Staphylococcus aureus*. *Streptococcus pyogenes* is the so-called "flesh-eating bacteria" and, in rare cases, can cause a dangerous, deep skin infection called necrotizing fasciitis. Orbital cellulitis may be caused by bacteria which cannot grow in the presence of oxygen (anaerobic bacteria). In children, *Haemophilus influenzae* type B frequently causes orbital cellulitis following a sinus infection.

Streptococcus pyogenes can be picked up from a person who has strep throat or an infected sore. Other cellulitis-causing bacteria can be acquired from direct contact with infected sores. Persons who are at a higher risk for cellulitis are those who have a severe underlying disease (such as **cancer**, diabetes, and kidney disease), are taking steroid medications, have a reduced immune system (because of **AIDS**, organ transplant, etc.), have been burned, have insect bites, have reduced blood circulation to limbs, or have had a leg vein removed for coronary bypass surgery. In addition, chicken pox, human or animal bite **wounds**, skin wounds, and recent surgery can put a person at a higher risk for cellulitis.

The characteristic symptoms of cellulitis are redness, warmth, pain, and swelling. The infected area appears as a red patch that gets larger rapidly within the first 24 hours. A thick red line which progresses towards the heart may appear indicating an infection of the lymph vessels (lymphangitis). Other symptoms which may occur include **fever**, chills, tiredness, muscle aches, and a

general ill feeling. Some people also experience nausea, vomiting, stiff joints, and hair loss at the infection site.

The characteristic symptoms of orbital cellulitis are eye pain, redness, swelling, warmth, and tenderness. The eye may bulge out and it may be difficult or impossible to move. Temporary loss of vision, pus drainage from the eye, chills, fever, headaches, vomiting, and a general ill feeling may occur.

Diagnosis

Cellulitis may be diagnosed and treated by a family doctor, an infectious disease specialist, a doctor who specializes in skin diseases (dermatologist), or in the case of orbital cellulitis, an eye doctor (ophthalmologist). The diagnosis of cellulitis is based mainly on the patient's symptoms. The patient's recent medical history is also used in the diagnosis.

Laboratory tests may be done to determine which kind of bacteria is causing the infection but these tests are not always successful. If the skin injury is visible, a sterile cotton swab is used to pick up a sample from the wound. If there is no obvious skin injury, a needle may be used to inject a small amount of sterile salt solution into the infected skin, and then the solution is withdrawn. The salt solution should pick up some of the bacteria causing the infection. A blood sample may be taken from the patient's arm to see if bacteria have entered the bloodstream. Also, a blood test may be done to count the number of white blood cells in the blood. High numbers of white blood cells suggest that the body is trying to fight a bacterial infection.

For orbital cellulitis, the doctor may often perform a special x-ray scan called **computed tomography scan** (CT). This scan enables the doctor to see the patient's head in cross-section to determine exactly where the infection is and see if any damage has occurred. A CT scan takes about 20 minutes.

Treatment

Antibiotic treatment is the only way to battle this potentially life-threatening infection. Mild to moderate cellulitis can be treated with the following antibiotics taken every four to eight hours by mouth:

- penicillins (Bicillin, Wycillin, Pen Vee, V-Cillin)
- erythromycin (E-Mycin, Ery-Tab)
- cephalexin (Biocef, Keflex)
- cloxacillin (Tegopen)

Other medications may be recommended, such as **acetaminophen** (Tylenol) or ibuprofen (Motrin, Advil) to relieve pain, and **aspirin** to decrease fever.

This person's lower leg is swollen and inflamed due to cellulitis. Cellulitis is a *Streptococcus* bacterial infection of the skin and the tissues beneath it. The face, neck, or legs are common sites of cellulitis. *(Custom Medical Stock Photo. Reproduced by permission.)*

A normally healthy person is usually not hospitalized for mild or moderate cellulitis. General treatment measures include elevation of the infected area, rest, and application of warm, moist compresses to the infected area. The doctor will want to see the patient again to make sure that the antibiotic treatment is effective in stopping the infection.

Persons at high risk for severe cellulitis will probably be hospitalized for treatment and monitoring. Antibiotics may be given intravenously to patients with severe cellulitis. Complications such as deep infection, or bone or joint infections, might require surgical drainage and a longer course of antibiotic treatment. Extensive tissue destruction may require plastic surgery to repair. In cases of orbital cellulitis caused by a sinus infection, surgery may be required to drain the sinuses.

Prognosis

Over 90% of all cellulitis cases are cured after seven to 10 days of antibiotic treatment. Persons with serious disease and/or those who are taking immunosuppressive drugs may experience a more severe form of cellulitis which can be life threatening. Serious complications include blood **poisoning** (bacteria growing in the blood stream), meningitis (brain and spinal cord infection), tissue death (necrosis), and/or lymphangitis (infection of the lymph vessels). Severe cellulitis caused by *Streptococcus pyogenes* can lead to destructive and life-threatening necrotizing fasciitis.

Prevention

Cellulitis may be prevented by wearing appropriate protective equipment during work and sports to avoid

KEY TERMS

Inflammation—A local, protective response to tissue injury. It is characterized by redness, warmth, swelling, and pain.

Necrotizing fasciitis—A destructive infection which follows severe cellulitis and involves the deep skin and underlying tissues.

Sinuses—Air cavities found in the bones of the head. The sinuses which are connected to the nose are prone to infection.

skin injury, cleaning cuts and skin injuries with antiseptic soap, keeping wounds clean and protected, watching wounds for signs of infection, taking the entire prescribed dose of antibiotic, and maintaining good general health. Persons with diabetes should try to maintain good blood sugar control.

Resources

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Belinda Rowland, PhD

Cell therapy

Definition

Cell therapy is the transplantation of human or animal cells to replace or repair damaged tissue and/or cells.

Purpose

Cell therapy has been used successfully to rebuild damaged cartilage in joints, repair spinal cord injuries, strengthen a weakened immune system, treat autoimmune diseases such as **AIDS**, and help patients with neurological disorders such as **Alzheimer's disease**, **Parkinson's disease**, and epilepsy. Further uses have shown positive results in the treatment of a wide range of chronic conditions such as arteriosclerosis, congenital defects, and **sexual dysfunction**. The therapy has also been used to treat **cancer** patients at a number of clinics in Tijuana, Mexico, although this application has not been well supported with controlled clinical studies.

Description

Origins

The theory behind cell therapy has been in existence for several hundred years. The first recorded discussion of the concept of cell therapy can be traced to Phillippus Aureolus Paracelsus (1493–1541), a German-Swiss physician and alchemist who wrote in his *Der grossen Wundartzney* ("Great Surgery Book") in 1536 that "the heart heals the heart, lung heals the lung, spleen heals the spleen; like cures like." Paracelsus and many of his contemporaries agreed that the best way to treat an illness was to use living tissue to restore the ailing. In 1667, at a laboratory in the palace of Louis XIV, Jean-Baptiste Denis (1640–1704) attempted to transfuse blood from a calf into a mentally ill patient—and since blood **transfusion** is, in effect, a form of cell therapy, this could be the first documented case of this procedure. However, the first recorded attempt at non-blood cellular therapy occurred in 1912 when German physicians attempted to treat children with **hypothyroidism**, or an underactive thyroid, with thyroid cells.

In 1931, Dr. Paul Niehans (1882–1971), a Swiss physician, became known as "the father of cell therapy" quite by chance. After a surgical accident by a colleague, Niehans attempted to transplant a patient's severely damaged parathyroid glands with those of a steer. When the patient began to rapidly deteriorate before the transplant could take place, Niehans decided to dice the steer's parathyroid gland into fine pieces, mix the pieces in a saline solution, and inject them into the dying patient. Immediately, the patient began to improve and, in fact, lived for another 30 years.

Cell therapy is, in effect, a type of organ transplant which has also been referred to as "live cell therapy," "xenotransplant therapy," "cellular suspensions," "glandular therapy," or "fresh cell therapy." The procedure involves the injection of either whole fetal xenogenic (animal) cells (e.g., from sheep, cows, pigs, and sharks) or cell extracts from human tissue. The latter is known as autologous cell therapy if the cells are extracted from and transplanted back into the same patient. Several different types of cells can be administered simultaneously.

Just as Paracelsus' theory of "like cures like," the types of cells that are administered correspond in some

PAUL NIEHANS (1882–1971)

(AP/Wide World Photos. Reproduced by permission.)

Paul Niehans was born and raised in Switzerland. His father, a doctor, was dismayed when he entered the seminary, but Niehans quickly grew dissatisfied with religious life and took up medicine after all. He first studied at Bern, then completed an internship in Zurich.

Niehans enlisted in the Swiss Army in 1912. When war erupted in the Balkans, Niehans set up a hospital in Belgrade, Yugoslavia. The war provided him the opportunity to treat numerous patients, gaining a firsthand knowledge of the body and its workings.

Since 1913, Niehans had been intrigued with Alexis Carrel's experiments concerning the adaptive abilities of cells, though Niehans himself specialized in glandular transplants and by 1925 was one of the leading glandular surgeons in Europe.

Niehans referred to 1931 as the birth year of cellular therapy. That year, he treated a patient suffering from tetany whose parathyroid had been erroneously removed by another physician. Too weak for a glandular transplant, the patient was given injections of the parathyroid glands of an ox, and she soon recovered. Niehans made more injections, even experimenting on himself, and reported he could cure illnesses through injections of live cells extracted from healthy animal organs. He believed adding new tissue stimulated rejuvenation and recovery.

Niehans treated Pope Pious XII with his injections and was nominated to the Vatican Academy of Science following the pope's recovery.

Niehans remained a controversial figure throughout his life. As of 2000, the Clinique Paul Niehans in Switzerland, founded by his daughter, continues his work.

way with the organ or tissue in the patient that is failing. No one knows exactly how cell therapy works, but proponents claim that the injected cells travel to the similar organ from which they were taken to revitalize and stimulate that organ's function and regenerate its cellular structure. In other words, the cells are not species specific, but only organ specific. Supporters of cellular treatment believe that embryonic and fetal animal tissue contain active therapeutic agents distinct from **vitamins**, **minerals**, hormones, or enzymes.

Swedish researchers have successfully transplanted human fetal stem cells into human recipients, and the procedure is being investigated further as a possible treatment for repairing brain cells in Parkinson's patients. However, because the cells used in these applications must be harvested from aborted human fetuses, there is an ethical debate over their use.

Currently, applications of cell therapy in the United States is still in the research, experimental, and clinical trial stages. The U.S. Food and Drug Administration has approved the use of one cellular therapy technique for repairing damaged knee joints. The procedure involves removing healthy chondrocyte cells, the type of cell that forms cartilage, from the patient, culturing them in a laboratory for three to four weeks, and then transplanting them back into the damaged knee joint of the patient.

Preparations

There are several processes to prepare cells for use. One form involves extracting cells from the patient they are to be used on and then culturing them in a laboratory setting until they multiply to the level needed for transplant back into the patient. Another procedure uses freshly removed fetal animal tissue, which has been processed and suspended in a saline solution. The preparation of fresh cells then may be either injected immediately into the patient, or preserved by being freeze-dried or deep-frozen in liquid nitrogen before being injected. Cells may be tested for pathogens, such as bacteria, viruses, or parasites, before use.

KEY TERMS

Anaphylactic shock—A severe allergic reaction that causes blood pressure drop, racing heart, swelling of the airway, rash, and possibly convulsions.

Culturing—To grow cells in a special substance, or media, in the laboratory.

Encephalitis—Inflammation of the brain.

Precautions

Patients undergoing cell therapy treatments which use cells transplanted from animals or other humans run the risk of cell rejection, in which the body recognizes the cells as a foreign substance and uses the immune system's T-cells to attack and destroy them. Some forms of cell therapy use special coatings on the cells designed to trick the immune system into recognizing the new cells as native to the body.

There is also the chance of the cell solution transmitting bacterial or viral infection or other disease and parasites to the patient. Careful screening and testing of cells for pathogens can reduce this risk.

Many forms of cell therapy in the United States are still largely experimental procedures. Patients should approach these treatments with extreme caution, should inquire about their proven efficacy and legal use in the United States, and should only accept treatment from a licensed physician who should educate the patient completely on the risks and possible side effects involved with cell therapy. These same cautions apply for patients interested in participating in clinical trials of cell therapy treatments.

Side effects

Because cell therapy encompasses such a wide range of treatments and applications, and many of these treatments are still experimental, the full range of possible side effects of the treatments are not yet known. Anaphylactic **shock** (severe allergic reaction), immune system reactions, and **encephalitis** (inflammation of the brain) are just a few of the known reported side effects in some patients to date.

Side effects of the FDA-approved chondrocyte cell therapy used in knee joint repair may include tissue hypertrophy, a condition where too much cartilage grows in the joint where the cells were transplanted to and the knee joint begins to stiffen.

Research and general acceptance

There is a growing debate in the medical community over the efficacy and ethical implications of cell therapy. Much of the ethical debate revolves around the use of human fetal stem cells in treatment, and the fact that these cells must be harvested from aborted fetuses.

While some cell therapy procedures have had proven success in clinical studies, others are still largely unproven, including cell therapy for cancer treatment. Until more large, controlled clinical studies are performed on these procedures to either prove or disprove their efficacy, they will remain fringe treatments.

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ORGANIZATIONS

Center for Cell and Gene Therapy. Baylor College of Medicine. 1102 Bates St, Suite 1100, Houston, Texas 77030-2399. (713) 770-4663. <http://www.bcm.tmc.edu/genetherapy>.

Paula Ford-Martin

Central Mississippi Valley disease *see* **Histoplasmosis**

Central nervous system depressants

Definition

Central nervous system (CNS) depressants are drugs that can be used to slow down brain activity.

Purpose

CNS depressants may be prescribed by a physician to treat anxiety, muscle tension, pain, insomnia, acute stress reactions, panic attacks, and seizure disorders. In higher doses, some CNS depressants may be used as general anesthetics.

Description

Throughout history, humans have sought relief from anxiety and insomnia by using substances that depress brain activity and induce a drowsy or calming effect. CNS depressants include a wide range of drugs such as alcohol, narcotics, barbiturates (Amytal, Nembutal, Seconal), benzodiazepines (Ativan, Halcion, Librium, Valium, Xanax), chloral hydrate, and methaqualone (Quaaludes), as well as newer CNS depressants developed in the 1990s, such as Buspirone (Buspar) and Zolpidem (Ambien), which are thought to have the fewest sideeffects. Most CNS depressants activate a neurotransmitter called gamma-aminobutyric acid (GABA), which helps decrease brain activity. Street names for CNS depressants include Reds, Yellows, Blues, Ludes, Barbs, and Downers.

Precautions

Most CNS depressants have the potential to be physically and psychologically addictive. Alcohol is the most widely abused depressant. The body tends to develop tolerance for CNS depressants, and larger doses are needed to achieve the same effects. Withdrawal from some CNS depressants can be uncomfortable; for example, withdrawal from a depressant treating insomnia or anxiety can cause rebound insomnia or anxiety as the brain's activity bounces back after being suppressed. In some cases withdrawal can result in life-threatening seizures. Generally, depressant withdrawal should be undertaken under a physician's supervision. Many physicians will reduce the depressant dosage gradually, to give the body time to adjust. Certain CNS depressants such as barbiturates are easy to overdose on, since there is a relatively small difference between the optimal dose and an overdose. A small miscalculation can lead to coma, slowed breathing, and death. CNS depressants should be administered to elderly individuals with care, as these individuals have a reduced ability to metabolize CNS depressants.

Side Effects

Especially when taken in excess, CNS depressants can cause confusion and dizziness, and impair judgment, memory, intellectual performance, and motor coordination.

Interactions

CNS depressants should be used with other medications, such as antidepressant medications, only under a physician's supervision. Certain herbal remedies, such as Valerian and Kava, may dangerously exacerbate the effects of certain CNS depressants. Also, ingesting a combination of CNS depressants, such Valium and alcohol, for example, is not advised. When mixed together, CNS depressants tend to amplify each other's effects, which can cause severely reduced heart rate and even death.

KEY TERMS

GABA (gamma-aminobutyric acid)—A neurotransmitter that slows down the activity of nerve cells in the brain.

Neurotransmitter—A chemical compound in the brain that carries signals from one nerve cell to another.

Resources

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American Society of Addiction Medicine. 4601 North Park Avenue, Arcade Suite 101, Chevy Chase, MD 20815. (301) 656-3920. <http://www.asam.org>.

National Clearinghouse for Alcohol and Drug Abuse Information (NCADI) Center for Substance Abuse Prevention. 5600 Fishers Lane, Rockville, MD 20857. (301) 443-0365. <http://www.health.org>.

National Institute on Drug Abuse. 6001 Executive Blvd, Bethesda, MD 20892. (301) 443-1124 <http://www.nida.nih.gov>.

Ann Quigley

Central nervous system infections

Definition

The central nervous system, or CNS, comprises the brain, the spinal cord, and associated membranes. Under some circumstances, bacteria may enter areas of the CNS. If this occurs, abscesses or empyemas may be established.

Description

In general, the CNS is well defended against infection. The spine and brain are sheathed in tough, protective membranes. The outermost membrane, the dura mater, and the next layer, the arachnoid, entirely encase the brain and spinal cord. However, these defenses are not absolute. In rare cases, bacteria gain access to areas within the CNS.

KEY TERMS

Abscess—A pus-filled area with definite borders.

Arachnoid—One of the membranes that sheathes the spinal cord and brain; the arachnoid is the second-layer membrane.

Cerebrospinal fluid—Fluid that is normally found in the spinal cord and brain. Abnormal levels of certain molecules in this fluid can indicate the presence of infection or damage to the central nervous system.

CT scan (computed tomography)—Cross-sectional x rays of the body are compiled to create a three-dimensional image of the body's internal structures.

Dura mater—One of the membranes that sheathes the spinal cord and brain; the dura mater is the outermost layer.

Empyema—A pus-filled area with indefinite borders.

Lumbar puncture—A procedure in which a needle is inserted into the lower spine to collect a sample of cerebrospinal fluid.

MRI (magnetic resonance imaging)—An imaging technique that uses a large circular magnet and radio waves to generate signals from atoms in the body. These signals are used to construct images of internal structures.

Bacterial infection of the CNS can result in abscesses and empyemas (accumulations of pus). Abscesses have fixed boundaries, but empyemas lack definable shape and size. CNS infections are classified according to the location where they occur. For example, a spinal epidural **abscess** is located above the dura mater, and a cranial subdural **empyema** occurs between the dura mater and the arachnoid.

As pus and other material from an infection accumulate, pressure is exerted on the brain or spinal cord. This pressure can damage the nervous system tissue, possibly permanently. Without treatment, a CNS infection is fatal.

Causes and symptoms

Typically, bacterial invasion results from the spread of a nearby infection; for example, a chronic sinus or middle ear infection can extend beyond its initial site. Bacteria may also be conveyed to the CNS from distant sites of infection by the bloodstream. In rare cases, head trauma or surgical procedures may introduce bacteria directly into the CNS. However, the source of infection cannot always be identified.

Specific symptoms of a CNS infection hinge on its exact location, but may include severe **headache** or back **pain**, weakness, sensory loss, and a **fever**. An individual may report a stiff neck, nausea or vomiting, and tiredness or disorientation. There is a potential for seizures, **paralysis**, or **coma**.

Diagnosis

Physical symptoms, such as a fever and intense backache or a fever, severe headache, and stiff neck, raise the suspicion of a CNS infection. Blood tests may indicate the presence of an infection but do not pinpoint its location. CT scans or MRI scans of the brain and spine can provide definitive diagnosis, with an MRI scan being the most sensitive. A lumbar puncture and analysis of the cerebrospinal fluid can help diagnose an epidural abscess; however, the procedure can be dangerous in cases of subdural empyema.

Treatment

A two-pronged approach is taken to treat CNS infections. First, antibiotic therapy against an array of potential infectious bacteria is begun. The second stage involves surgery to drain the infected site. Although some CNS infections have been resolved with **antibiotics** alone, the more aggressive approach is often preferred. Surgery allows immediate relief of pressure on the brain or spinal cord, as well as an opportunity to collect infectious material for bacterial identification. Once the bacterial species is identified, drug therapy can be altered to a more specific antibiotic. However, surgery may not be an option in some cases, such as when there are numerous sites of infection or when infection is located in an inaccessible area of the brain.

Prognosis

The fatality rate associated with CNS infections ranges from 10% to as high as 40%. Some survivors experience permanent CNS damage, resulting in partial paralysis, speech problems, or seizures. Rapid diagnosis and treatment are essential for a good prognosis. With prompt medical attention, an individual may recover completely.

Prevention

Treatment for pre-existing infections, such as sinus or middle ear infections, may prevent some cases of CNS infection. However, since some CNS infections are of unknown origin, not all are preventable.

Resources

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Julia Barrett

Central nervous system stimulants

Definition

Central nervous system (CNS) stimulants are medicines that speed up physical and mental processes.

Purpose

Central nervous system stimulants are used to treat conditions characterized by lack of adrenergic stimulation, including **narcolepsy** and neonatal apnea. Additionally, methylphenidate (Ritalin) and dextroamphetamine sulfate (Dexedrine) are used for their paradoxical effect in attention-deficit hyperactivity disorder (**ADHD**).

The anerexiants, benzphetamine (Didrex), diethylpropion (Tenuate), phendimetrazine (Bontril, Plegine), phentermine (Fastin, Ionamine), and sibutramine (Meridia) are CNS stimulants used for appetite reduction in severe **obesity**. Although these drugs are structurally similar to amphetamine, they cause less sensation of stimulation, and are less suited for use in conditions characterized by lack of adrenergic stimulation.

Phenylpropanolamine and ephedrine have been used both as diet aids and as vasoconstrictors.

Description

The majority of CNS stimulants are chemically similar to the neurohormone norepinephrine, and simulate the traditional "fight or flight" syndrome associated with sympathetic nervous system arousal. **Caffeine** is more closely related to the xanthines, such as theophylline. A small number of additional members of the CNS stimulant class do not fall into specific chemical groups.

Precautions

Amphetamines have a high potential for abuse. They should be used in weight reduction programs only when alternative therapies have been ineffective. Administration for prolonged periods may lead to drug dependence. These drugs are classified as schedule II under federal drug control regulations.

The amphetamines and their cogeners are contraindicated in advanced arteriosclerosis, symptomatic cardiovascular disease, and moderate to severe **hypertension** and **hyperthyroidism**. They should not be used to treat patients with hypersensitivity or idiosyncrasy to the sympathomimetic amines, or with **glaucoma**, a history of agitated states, a history of drug abuse, or during the 14 days following administration of monoamine oxidase (MAO) inhibitors.

Methylphenidate may lower the seizure threshold.

Benzphetamine is category X during **pregnancy**. Diethylpropion is category B. Other anorexiants have not been rated; however their use during pregnancy does not appear to be advisable. Safety for use of anorexiants has not been evaluated.

Amphetamines are all category C during pregnancy. Breastfeeding while receiving amphetamines is not recommended because the infant may experience withdrawal symptoms.

There have been reports that when used in children, methylphenidate and amphetamines may retard growth. Although these reports have been questioned, it may be suggested that the drugs not be administered outside of school hours (because most children have behavior problems in school), in order to permit full stature to be attained.

The most common adverse effects of CNS stimulants are associated with their primary action. Typical responses include overstimulation, **dizziness**, restlessness, and similar reactions. Rarely, hematologic reactions, including leukopenia, agranulocytosis, and bone marrow depression have been reported. Lowering of the seizure threshold has been noted with most drugs in this class.

Withdrawal syndrome

Abrupt discontinuation following prolonged high dosage results in extreme **fatigue**, mental depression and changes on the sleep EEG. This response is most evident with amphetamines, but may be observed with all CNS stimulants taken over a prolonged period of time.

KEY TERMS

Agranulocytosis—An acute febrile condition marked by severe depression of the granulocyte-producing bone marrow, and by prostration, chills, swollen neck, and sore throat sometimes with local ulceration.

Anorexiant—A drug that suppresses appetite.

Anxiety—Worry or tension in response to real or imagined stress, danger, or dreaded situations. Physical reactions, such as fast pulse, sweating, trembling, fatigue, and weakness, may accompany anxiety.

Attention-deficit hyperactivity disorder (ADHD)—A condition in which a person (usually a child) has an unusually high activity level and a short attention span. People with the disorder may act impulsively and may have learning and behavioral problems.

Central nervous system—The brain and spinal cord.

Depression—A mental condition in which people feel extremely sad and lose interest in life. People with depression may also have sleep problems and loss of appetite, and may have trouble concentrating and carrying out everyday activities.

Leucopenia—A condition in which the number of leukocytes circulating in the blood is abnormally low and which is most commonly due to a decreased production of new cells in conjunction with various infectious diseases or as a reaction to various drugs or other chemicals.

Pregnancy category—A system of classifying drugs according to their established risks for use during pregnancy. Category A: Controlled human studies have demonstrated no fetal risk. Category B: Animal studies indicate no fetal risk, but no human studies, or adverse effects in animals, but not in well-controlled human studies. Category C: No adequate human or animal studies, or adverse fetal effects in animal studies, but no available human data. Category D: Evidence of fetal risk, but benefits outweigh risks. Category X: Evidence of fetal risk. Risks outweigh any benefits.

Withdrawal symptoms—A group of physical or mental symptoms that may occur when a person suddenly stops using a drug on which he or she has become dependent.

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ORGANIZATION

Children and Adults with Attention Deficit Disorders (CH.A.D.D.). 499 N.W. 70th Avenue, Suite 109, Plantation, FL 33317. (305) 587-3700.

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Nancy Ross-Flanigan

Central retinal artery occlusion *see* **Retinopathies**

Central retinal vein occlusion *see* **Retinopathies**

Cephalosporins

Definition

Cephalosporins are medicines that kill bacteria or prevent their growth.

Purpose

Cephalosporins are used to treat infections in different parts of the body—the ears, nose, throat, lungs, sinuses, and skin, for example. Physicians may prescribe these drugs to treat **pneumonia**, **strep throat**, staph infections, **tonsillitis**, **bronchitis**, and **gonorrhea**. These drugs will *not* work for colds, flu, and other infections caused by viruses.

Description

Examples of cephalosporins are cefaclor (Ceclor), cefadroxil (Duricef), cefazolin (Ancef, Kefzol, Zolicef),

cefixime (Suprax), cefoxitin (Mefoxin), cefprozil (Cefzil), ceftazidime (Ceptaz, Fortaz, Tazicef, Tazideme), cefuroxime (Ceftin) and cephalexin (Keflex). These medicines are available only with a physician's prescription. They are sold in tablet, capsule, liquid, and injectable forms.

Recommended dosage

The recommended dosage depends on the type of cephalosporin. Check with the physician who prescribed the drug or the pharmacist who filled the prescription for the correct dosage.

Always take cephalosporins exactly as directed by your physician. Never take larger, smaller, more frequent, or less frequent doses. Take the drug for exactly as long as directed—no more and no less. Do not save some doses of the drug to take for future infections. The medicine may not be right for other kinds of infections, even if the symptoms are the same. In addition, take all of the medicine to treat the infection for which it was prescribed. The infection may not clear up completely if too little medicine is taken. Taking this medicine for too long, on the other hand, may open the door to new infections that do not respond to the drug.

Some cephalosporins work best when taken on an empty stomach. Others should be taken after meals. Check with the physician who prescribed the medicine or the pharmacist who filled the prescription for instructions on how to take the medicine.

Precautions

Certain cephalosporins should not be combined with alcohol or with medicines that contain alcohol. Abdominal or stomach cramps, nausea, vomiting, facial flushing, and other symptoms may result within 15–30 minutes and may last for several hours. Do not drink alcoholic beverages or use other medicines that contain alcohol while being treated with cephalosporins and for several days after treatment ends.

Special conditions

People with certain medical conditions or who are taking certain other medicines can have problems if they take cephalosporins. Before taking these drugs, be sure to let the physician know about any of these conditions:

ALLERGIES. Severe allergic reactions to this medicine may occur. Anyone who is allergic to cephalosporins of any kind should not take other cephalosporins. Anyone who is allergic to penicillin should check with a physician before taking any cephalosporin. The physician should also be told about any **allergies** to foods, dyes, preservatives, or other substances.

KEY TERMS

Bronchitis—Inflammation of the air passages of the lungs.

Colitis—Inflammation of the colon (large bowel).

Gonorrhea—A sexually transmitted disease (STD) that causes infection in the genital organs and may cause disease in other parts of the body.

Inflammation—Pain, redness, swelling, and heat that usually develop in response to injury or illness.

Phenylketonuria—(PKU) A genetic disorder in which the body lacks an important enzyme. If untreated, the disorder can lead to brain damage and mental retardation.

Pneumonia—A disease in which the lungs become inflamed. Pneumonia may be caused by bacteria, viruses, or other organisms, or by physical or chemical irritants.

Sexually transmitted disease—A disease that is passed from one person to another through sexual intercourse or other intimate sexual contact. Also called STD.

Staph infection—Infection with *Staphylococcus* bacteria. These bacteria can infect any part of the body.

Strep throat—A sore throat caused by infection with *Streptococcus* bacteria. Symptoms include sore throat, chills, fever, and swollen lymph nodes in the neck.

Tonsillitis—Inflammation of a tonsil, a small mass of tissue in the throat.

DIABETES. Some cephalosporins may cause false positive results on urine sugar tests for diabetes. People with diabetes should check with their physicians to see if they need to adjust their medication or their **diets**.

PHENYLKETONURIA. Oral suspensions of cefprozil contain phenylalanine. People with **phenylketonuria** (PKU) should consult a physician before taking this medicine.

PREGNANCY. Women who are pregnant or who may become pregnant should check with their physicians before using cephalosporins.

BREASTFEEDING. Cephalosporins may pass into breast milk and may affect nursing babies. Women who are breastfeeding and who need to take this medicine

should check with their physicians. They may need to stop breastfeeding until treatment is finished.

OTHER MEDICAL CONDITIONS. Before using cephalosporins, people with any of these medical problems should make sure their physicians are aware of their conditions:

- History of stomach or intestinal problems, especially colitis. Cephalosporins may cause colitis in some people.
- Kidney problems. The dose of cephalosporin may need to be lower.
- Bleeding problems. Cephalosporins may increase the chance of bleeding in people with a history of bleeding problems.
- Liver disease. The dose of cephalosporin may need to be lower.

USE OF CERTAIN MEDICINES. Taking cephalosporins with certain other drugs may affect the way the drugs work or may increase the chance of side effects.

Side effects

Get medical attention immediately if any of these symptoms develop while taking cephalosporins:

- shortness of breath
- Pounding heartbeat
- Skin rash or **hives**
- Severe cramps or **pain** in the stomach or abdomen
- **Fever**
- Severe watery or bloody **diarrhea** (may occur up to several weeks after stopping the drug)
- Unusual bleeding or bruising

Other rare side effects may occur. Anyone who has unusual symptoms during or after treatment with cephalosporins should get in touch with his or her physician.

Interactions

Some cephalosporins cause diarrhea. Certain diarrhea medicines, such as diphenoxylate-atropine (Lomotil), may make the problem worse. Check with a physician before taking any medicine for diarrhea caused by taking cephalosporins.

Birth control pills may not work properly when taken at the same time as cephalosporins. To prevent **pregnancy**, use other methods of birth control in addition to the pills while taking cephalosporins.

Taking cephalosporins with certain other drugs may increase the risk of excess bleeding. Among the drugs that may have this effect when taken with cephalosporins are:

- blood thinning drugs (anticoagulants) such as warfarin (Coumadin)
- blood viscosity reducing medicines such as pentoxifylline (Trental)
- the antiseizure medicines divalproex (Depakote) and valproic acid (Depakene)

Cephalosporins may also interact with other medicines. When this happens, the effects of one or both of the drugs may change or the risk of side effects may be greater. Anyone who takes cephalosporins should let the physician know all other medicines he or she is taking.

Nancy Ross-Flanigan

Cerebral abscess *see* **Brain abscess**

Cerebral amyloid angiopathy

Definition

Cerebral amyloid angiopathy (CAA) is also known as congophilic angiopathy or cerebrovascular **amyloidosis**. It is a disease of small blood vessels in the brain in which deposits of amyloid protein in the vessel walls may lead to **stroke**, brain hemorrhage, or **dementia**. Amyloid protein resembles a starch and is deposited in tissues during the course of certain chronic diseases.

Description

CAA may affect patients over age 45, but is most common in patients over age 65, and becomes more common with increasing age. Men and women are equally affected. In some cases, CAA is sporadic but it may also be inherited as an autosomal dominant condition (a form of inheritance in which only one copy of a gene coding for a disease need be present for that disease to be expressed; if either parent has the disease, a child has a 50% chance of inheriting the disease). CAA is responsible for 5–20% of brain hemorrhages and up to 30% of lobar hemorrhages localized to one lobe of the brain. CAA may be found during an **autopsy** in over one-third of persons over age 60, even though they may not have had brain hemorrhage, stroke, or other manifestations of the disease during life. In **Alzheimer's disease**, CAA is more common than in the general population, and may occur in more than 80% of patients over age 60.

Causes and symptoms

The cause of amyloid deposits in blood vessels in the brain in sporadic CAA is not known. In hereditary CAA,

genetic defects, typically on chromosome 21, allow accumulation of amyloid, a protein made up of units called beta-pleated sheet fibrils. The fibrils tend to clump together, so that the amyloid cannot be dissolved and builds up in the brain blood vessel walls. One form of amyloid fibril subunit proteins is the amyloid beta protein.

Different theories have been suggested for the source of amyloid beta protein in the brain. The systemic theory suggests that amyloid beta protein in the blood stream is deposited in blood vessels in the brain, causing weakness in the blood vessel wall and breakdown in the blood-brain barrier. Normally, the blood-brain barrier keeps proteins and other large molecules from escaping from the blood vessel to the brain tissue. When there is breakdown of the blood-brain barrier, amyloid beta protein leaks through the blood vessel wall, and is deposited in the brain substance, where it forms an abnormal structure called a neuritic plaque.

A second, more likely theory is that amyloid fibrils that form amyloid beta protein are produced by perivascular microglia, or support cells in contact with the brain blood vessel wall. The third theory is that the brain tissue gives rise to amyloid beta protein. Both the nerve cells and the glia are known to produce amyloid precursor protein, which increases with **aging** and with cell **stress**.

Bleeding into the brain may occur as tiny blood vessels carrying amyloid deposits become heavier and more brittle, and are therefore more likely to burst with minor trauma or with fluctuating blood pressure. Aneurysms, or ballooning of the blood vessel wall, may develop, and may also rupture as the stretched wall becomes thinner and is under more pressure. Amyloid deposits may destroy smooth muscle cells or cause inflammation in the blood vessel wall. This may also cause the blood vessel to break more easily.

The most common form of CAA is the sporadic form associated with aging. This type of CAA usually causes lobar hemorrhage, which may recur in different lobes of the brain. The frontal lobe (behind the forehead) and parietal lobe (behind the frontal lobe) are most often affected; the temporal lobe (near the temple) and occipital lobe (at the back of the brain) are affected less often; and the cerebellum (under the occipital lobe) is rarely affected. Approximately 10–50% of hemorrhages in sporadic CAA involve more than one lobe.

Symptoms of lobar hemorrhage in CAA include sudden onset of **headache**, neurologic symptoms such as weakness, sensory loss, visual changes, or speech problems, depending on which lobe is involved; and decreased level of consciousness (a patient who is difficult to arouse), nausea, and vomiting. Sporadic CAA may be associated with symptoms unrelated to lobar hemorrhage. Petechial hemorrhages (tiny hemorrhages involving many small vessels) may produce recurrent, brief neurologic symptoms secondary to seizures or decreased blood flow, or may produce rapidly progressive dementia (loss of memory and other brain functions) that worsens in distinct steps rather than gradually. Over 40% of patients with hemorrhage secondary to CAA also have dementia.

Genetic factors play a role in certain types of CAA and in diseases associated with CAA:

- Dutch type of hereditary cerebral hemorrhage with amyloidosis (build up of amyloid protein in blood vessels): autosomal dominant, with a genetic mutation involving the amyloid precursor protein. Onset is at age 40–60 with headaches, brain hemorrhage often in the parietal lobe, strokes, and dementia. More than half of patients die from their first hemorrhage. Patients with the Dutch type of CAA may produce an abnormal anti-

KEY TERMS

Amyloid—Amyloid protein resembles a starch and is deposited in tissues during the course of certain chronic diseases.

Ataxia—Problems with coordination and walking.

Autosomal dominant—A form of inheritance in which only one copy of a gene coding for a disease need be present for that disease to be expressed. If either parent has the disease, a child has a 50% chance of inheriting the disease.

Chromosome—A cellular structure containing genetic information in the form of DNA.

Dementia—Loss of memory and other higher functions, such as thinking or speech, lasting six months or more.

Hemorrhage—Bleeding, or escape of blood through ruptured or unruptured blood vessel walls.

Lobar hemorrhage—Bleeding into one of the lobes of the brain.

Seizure—Epileptic convulsion, fit, or attack.

Sporadic—A form of disease found in persons without a family history of the disease.

Spasticity—Limb stiffness related to disease of the brain or spinal cord.

Stroke—Sudden neurological deficit related to impaired blood supply to the brain.

coagulant, or blood thinner, which makes hemorrhage more likely.

- Flemish type of hereditary cerebral hemorrhage with amyloidosis: autosomal dominant, with a mutation involving the amyloid precursor protein. Symptoms include brain hemorrhage or dementia.
- Familial Alzheimer's disease: autosomal dominant, comprising 5–10% of all Alzheimer's disease cases (a brain disease in which **death** of nerve cells leads to progressive dementia).
- **Down Syndrome**: caused by trisomy 21 (three rather than two copies of chromosome 21), causing excess amyloid precursor protein gene. Children with Down syndrome are mentally handicapped and may have heart problems.
- Icelandic type of hereditary cerebral hemorrhage with amyloidosis: autosomal dominant, with mutation in the gene coding for cystatin C. Symptoms often begin at age 30–40 with multiple brain hemorrhages, dementia, **paralysis** (weakness), and death in 10–20 years. Headache occurs in more than half of patients, and seizures occur in one-quarter. Unlike most other forms of CAA, most hemorrhages involve the basal ganglia deep within the brain (Basal ganglia are islands of tissues in the cerebellum part of the brain.).
- Familial oculo-leptomeningeal amyloidosis: autosomal dominant with unknown gene defect(s), described in Japanese, Italian, and North American families. Symptoms can include dementia, ataxia (problems with coordination), spasticity (limb stiffness), strokes, seizures, **peripheral neuropathy** (disease affecting the nerves supplying the limbs), migraine, spinal cord problems, blindness, and deafness. Brain hemorrhage is rare as the amyloid protein is deposited in blood vessels in the eye and meninges (brain coverings), but not in the brain itself. In Italian families with the disease, patients may be affected as early as 20–30 years of age.
- British type of familial amyloidosis: autosomal dominant with unknown gene defect(s), associated with progressive dementia, spasticity, and ataxia. Brain stem, spinal cord, and cerebellum all exhibit amyloid deposits, but hemorrhage typically does not occur.

Diagnosis

As in most neurologic diseases, diagnosis is made most often from the patient's history, with careful inquiry into family history and the patient's onset and pattern of symptoms, as well as neurologic examination. Brain **computed tomography scan** (CT) or **magnetic resonance imaging** (MRI) may identify lobar hemorrhage, stroke, or petechial hemorrhages, and are important in excluding arteriovenous malformation, **brain tumor**, or other causes of hemorrhage. **Angiography** (x-ray study of the interior of blood vessels and the heart) is not helpful in diagnosis of CAA, but may be needed to exclude aneurysm. **Brain biopsy** (surgical removal of a small piece of brain tissue) may show characteristic amyloid deposits, but is rarely performed, as the risk may not be justifiable in the absence of effective treatment for CAA. If diagnosis is uncertain, biopsy may be needed to rule out conditions which are potentially treatable. Definite diagnosis requires microscopic examination of brain tissue, either at biopsy, at autopsy, or at surgery when brain hemorrhage is drained. Lumbar puncture to examine cerebrospinal fluid proteins may show characteristic abnormalities, but is not part of the routine exam. In familial forms, genetic analysis may be helpful.

CAA with hemorrhage must be distinguished from other types of brain hemorrhage. In CAA, hemorrhage typically occurs in the lobar region, often ruptures into the subarachnoid space between the brain and its coverings, and occurs at night. In hemorrhage related to high blood pressure, hemorrhage is usually deeper within the brain, ruptures into the ventricles or cavities deep inside the brain, and occurs during daytime activities. Other causes of brain hemorrhage are **arteriovenous malformations**, trauma, aneurysms, bleeding into a brain tumor, **vasculitis** (inflammation of blood vessels), or bleeding disorders.

Treatment

Although there is no effective treatment for the underlying disease process of CAA, measures can be taken to prevent brain hemorrhage in patients diagnosed with CAA. High blood pressure should be treated aggressively, and even normal blood pressure can be lowered as much as tolerated without side effects from medications. Blood thinners such as Coumadin, antiplatelet agents such as **aspirin**, or medications designed to dissolve blood clots may cause hemorrhage in patients with CAA, and should be avoided if possible. If these medications are required for other conditions, such as heart disease, the potential benefits must be carefully weighed against the increased risks.

Seizures, or recurrent neurologic symptoms thought to be seizures, should be treated with anti-epileptic drugs, although Depakote (sodium valproate) should be avoided because of its antiplatelet effect. Anti-epileptic drugs are sometimes given to patients with large lobar hemorrhage in an attempt to prevent seizures, although the benefit of this is unclear.

Once brain hemorrhage has occurred, the patient should be admitted to a hospital (ICU) for neurologic monitoring and control of increased pressure within the brain, blood pressure control, and supportive medical

care. Antiplatelet agents and blood thinners should be discontinued and their effects reversed, if possible. Surgery may be needed to remove brain hemorrhage, although bleeding during surgery may be difficult to control.

CAA may be rarely associated with cerebral vasculitis, or inflammation of the blood vessel walls. In these cases treatment with steroids or immune system suppressants may be helpful. Without tissue examination, vasculitis cannot be diagnosed reliably, and probably coexists with CAA too rarely to justify steroid treatment in most cases.

Prognosis

Since CAA is associated with progressive blood vessel degeneration, and since there is no effective treatment, most patients have a poor prognosis. Aggressive neurosurgical management allows increased survival following lobar hemorrhage, but as of 1998, 20–90% of patients die from the first hemorrhage or its complications, which include progression of hemorrhage, brain **edema** (swelling) with herniation (downward pressure on vital brain structures), seizures, and infections such as **pneumonia**. Many survivors have persistent neurologic deficits related to the brain lobe affected by hemorrhage, and are at risk for additional hemorrhages, seizures, and dementia. Prognosis is worse in patients who are older, or who have larger hemorrhages or recurrent hemorrhages within a short time.

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Laurie Barclay, MD

Cerebral aneurysm

Definition

A cerebral aneurysm occurs at a weak point in the wall of a blood vessel (artery) that supplies blood to the brain. Because of the flaw, the artery wall bulges outward and fills with blood. This bulge is called an aneurysm. An aneurysm can rupture, spilling blood into the surrounding body tissue. A ruptured cerebral aneurysm can cause permanent brain damage, disability, or **death**.

Description

A cerebral aneurysm can occur anywhere in the brain. Aneurysms can have several shapes. The saccular aneurysm, once called a berry aneurysm, resembles a piece of fruit dangling from a branch. Saccular aneurysms are usually found at a branch in the blood vessel where they balloon out by a thin neck. Saccular cerebral aneurysms most often occur at the branch points of large arteries at the base of the brain. Aneurysms may also take the form of a bulge in one wall of the artery—a lateral aneurysm—or a widening of the entire artery—a fusiform aneurysm.

The greatest danger of aneurysms is rupture. Approximately 50–75% of stricken people survive an aneurysmal rupture. A ruptured aneurysm spills blood into the brain or into the fluid-filled area that surrounds the brain tissue. Bleeding into this area, called the subarachnoid space, is referred to as **subarachnoid hemorrhage** (SAH). About 25,000 people suffer a SAH each year. It is estimated that people with unruptured aneurysm have an annual 1–2% risk of hemorrhage. Under age 40, more men experience SAH. After age 40, more women than men are affected.

Most people who have suffered a SAH from a ruptured aneurysm did not know that the aneurysm even existed. Based on **autopsy** studies, medical researchers estimate that 1–5% of the population has some type of cerebral aneurysm. Aneurysms rarely occur in the very young or the very old; about 60% of aneurysms are diagnosed in people between ages 40 and 65.

Some aneurysms may have a genetic link and run in families. The genetic link has not been completely proven and a pattern of inheritance has not been determined. Some studies seem to show that first-degree relatives of people who suffered aneurysmal SAH are more likely to have aneurysms themselves. These studies reported that such immediate family members were four times more likely to have aneurysms than the general population. Other studies do not confirm these findings. Better evidence links aneurysms to certain rare diseases of the connective tissue. These diseases include **Marfan syndrome**, **pseudoxanthoma elasticum**, **Ehlers-Danlos syndrome**, and fibromuscular dysplasia. **Polycystic kidney disease** is also associated with cerebral aneurysms.

These diseases are also associated with an increased risk of aneurysmal rupture. Certain other conditions raise

Three aneurysms can be seen in this section of a cerebral artery removed from a human brain. *(Photograph by Martin Rotker, Phototake NYC. Reproduced by permission.)*

the risk of rupture, too. Most aneurysms that rupture are a half-inch or larger in diameter. Size is not the only factor, however, because smaller aneurysms also rupture. Cigarette **smoking**, excessive alcohol consumption, and recreational drug use (for example, use of **cocaine**) have been linked with an increased risk. The role, if any, of high blood pressure has not been determined. Some studies have implicated high blood pressure in aneurysm formation and rupture, but people with normal blood pressure also experience aneurysms and SAHs. High blood pressure may be a risk factor but not the most important one. **Pregnancy**, labor, and delivery also seem to increase the possibility that an aneurysm might rupture, but not all doctors agree. Physical exertion and use of oral contraceptives are not suspected causes for aneurysmal rupture.

Causes and symptoms

Cerebral aneurysms can be caused by brain trauma, infection, hardening of the arteries (**atherosclerosis**), or abnormal rapid cell growth (neoplastic disease), but most seem to arise from a congenital, or developmental, defect. These congenital aneurysms occur more frequently in women. Whatever the cause may be, the inner wall of the blood vessel is abnormally thin and the pressure of the blood flow causes an aneurysm to form.

Most aneurysms go unnoticed until they rupture. However, 10–15% of unruptured cerebral aneurysms are found because of their size or their location. Common warning signs include symptoms that affect only one eye, such as an enlarged pupil, a drooping eyelid, or **pain** above or behind the eye. Other symptoms are a localized **headache**, unsteady gait, a temporary problem with sight, double vision, or numbness in the face.

Some aneurysms bleed occasionally without rupturing. Symptoms of such an aneurysm develop gradually. The symptoms include headache, nausea, vomiting, neck pain, black-outs, ringing in the ears, **dizziness**, or seeing spots.

Eighty to ninety percent of aneurysms are not diagnosed until after they have ruptured. Rupture is not always a sudden event. Nearly 50% of patients who have aneurysmal SAHs also experience "the warning leak phenomenon." Persons with warning leak symptoms have sudden, atypical headaches that occur days or weeks before the actual rupture. These headaches are

KEY TERMS

Congenital—Existing at birth.

Ehlers-Danlos syndrome—A rare inheritable disease of the connective tissue marked by very elastic skin, very loose joints, and very fragile body tissue.

Embolization—A technique to stop or prevent hemorrhage by introducing a foreign mass, such as an air-filled membrane (balloon), into a blood vessel to block the flow of blood.

Fibromuscular dysplasia—A disorder that causes unexplained narrowing of arteries and high blood pressure.

Magnetic resonance angiography—A noninvasive diagnostic technique that uses radio waves to map the internal anatomy of the blood vessels.

Marfan syndrome—An inheritable disorder that affects the skeleton, joints, and blood vessels. Major indicators are excessively long arms and legs, lax joints, and vascular defects.

Nimodipine (Nimotop)—A calcium-channel blocker, that is, a drug that relaxes arterial smooth muscle by slowing the movement of calcium across cell walls.

Polycystic kidney disease—An abnormal condition in which the kidneys are enlarged and contain many cysts.

Pseudoxanthoma elasticum—A hereditary disorder of the connective, or elastic, tissue marked by premature aging and breakdown of the skin and degeneration of the arteries that leads to hemorrhages.

Subarachnoid hemorrhage (SAH)—Loss of blood into the subarachnoid space, the fluid-filled area that surrounds the brain tissue.

Vasospasm—Narrowing of a blood vessel caused by a spasm of the smooth muscle of the vessel wall.

referred to as sentinel headaches. Nausea, vomiting, and dizziness may accompany sentinel headaches. Unfortunately, these symptoms can be confused with tension headaches or migraines, and treatment can be delayed until rupture occurs.

When an aneurysm ruptures, most victims experience a sudden, extremely severe headache. This headache is typically described as the worst headache of the victim's life. **Nausea and vomiting** commonly accompany the headache. The person may experience a short loss of consciousness or prolonged **coma**. Other common signs of a SAH include a stiff neck, **fever**, and a sensitivity to light. About 25% of victims experience neurological problems linked to specific areas of the brain, swelling of the brain due to fluid accumulation (**hydrocephalus**), or seizure.

Diagnosis

Based on the clinical symptoms, a doctor will run several tests to confirm an aneurysm or an SAH. A **computed tomography** (CT) scan of the head is the initial procedure. A **magnetic resonance imaging** test (MRI) may be done instead of a CT scan. MRI, however, is not as sensitive as CT for detecting subarachnoid blood. A CT scan can determine whether there has been a hemorrhage and can assist in pinpointing the location of the aneurysm. The scan is most useful when it is done within 72 hours of the rupture. Later scans may miss the signs of hemorrhage.

If the CT scan is negative for a hemorrhage or provides an unclear diagnosis, the doctor will order a **cerebrospinal fluid (CSF) analysis**, also called a lumbar puncture. In this procedure, a small amount of cerebrospinal fluid is removed from the lower back and examined for traces of blood and blood-breakdown products. If this test is positive, cerebral **angiography** is used to map the brain's blood vessels and the damaged area. The angiography is done to pinpoint the aneurysm's location. About 15% of people who experience SAH have more than one aneurysm. For this reason, angiography should include both the common carotid artery that feeds the front of the brain and the vertebral artery that feeds the base of the brain. Occasionally, the angiography fails to find the aneurysm and must be repeated. If seizures occur, **electroencephalography** (EEG) may be used to measure the electrical activity of the brain.

Treatment

Unruptured aneurysm

If an aneurysm has not ruptured and is not causing any symptoms, it may be left untreated. Because there is a 1–2% chance of rupture per year, the cumulative risk over a number of years may justify surgical treatment.

However, if the aneurysm is small or in a place that would be difficult to reach, or if the person who has the aneurysm is in poor health, the surgical treatment may be a greater risk than the aneurysm. Risk of rupture is higher for people who have more than one aneurysm. Unruptured aneurysm would probably be treated with a surgical procedure called the clip ligation, as described below.

Ruptured aneurysm

The primary treatment for a ruptured aneurysm involves stabilizing the victim's condition, treating the immediate symptoms, and promptly assessing further treatment options, especially surgical procedures. The patient may require mechanical ventilation, oxygen, and fluids. Medications may be given to prevent major secondary complications such as seizures, rebleeding, and vasospasm (narrowing of the affected blood vessel). Vasospasm decreases blood flow to the brain and causes the death of nerve cells. A drug such as nimodipine (Nimotop) may help prevent vasospasm by relaxing the smooth muscle tissue of the arteries. Even with treatment, however, vasospasm may cause **stroke** or death.

To prevent further hemorrhage from the aneurysm, it must be removed from circulation. In general, surgical procedures should be performed as soon as possible to prevent rebleeding. The chances that aneurysm will rebleed are greatest in the first 24 hours, and vasospasm usually does not occur until 72 hours or more after rupture. If the patient is in poor condition or if there is vasospasm or other complication, surgical procedures may be delayed. The preferred surgical method is a clip ligation in which a clip is placed around the base of the aneurysm to block it off from circulation. Surgical coating, wrapping, or trapping of the aneurysm may also be performed. These procedures do not completely remove the aneurysm from circulation, however, and there is some risk that it may rebleed in the future. Newer techniques that look promising include balloon embolization, a procedure that blocks the aneurysm with an inflatable membrane introduced by means of a catheter inserted through the artery.

Prognosis

An unruptured aneurysm may not cause any symptoms over an entire lifetime. Surgical clip ligation will ensure that it won't rupture, but it may be better to leave the aneurysm alone in some cases. Familial cerebral aneurysms may rupture earlier than those without a genetic link.

The outlook is not as good for a person who suffers a ruptured aneurysm. Fifteen to twenty-five percent of people who experience a ruptured aneurysm do not survive. An additional 25–50% die as a result of complications associated with the hemorrhage. Of the survivors, 15–50% suffer permanent brain damage and disability. These conditions are caused by the death of nerve cells. Nerve cells can be destroyed by the hemorrhage itself or by complications from the hemorrhage, such as vasospasm or hydrocephalus. Hydrocephalus, a dilatation (expansion) of the fluid-filled cavity surrounding the brain, occurs in about 15% of cases. Immediate medical treatment is vital to prevent further complications and brain damage in those who survive the initial rupture. Patients who survive SAH and aneurysm clipping are unlikely to die from events related to SAH.

Prevention

There are no known methods to prevent an aneurysm from forming. If an aneurysm is discovered before it ruptures, it may be surgically removed. CT or MRI angiography may be recommended for relatives of patients with familial cerebral aneurysms.

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Julia Barrett

Cerebral angiography *see* **Angiography**

Cerebral palsy

Definition

Cerebral palsy (CP) is the term used for a group of nonprogressive disorders of movement and posture caused by abnormal development of, or damage to, motor control centers of the brain. CP is caused by events before, during, or after birth. The abnormalities of muscle control that define CP are often accompanied by other neurological and physical abnormalities.

Description

Voluntary movement (walking, grasping, chewing, etc.) is primarily accomplished using muscles that are attached to bones, known as the skeletal muscles. Control of the skeletal muscles originates in the cerebral cortex, the largest portion of the brain. Palsy means **paralysis**, but may also be used to describe uncontrolled muscle movement. Therefore, cerebral palsy encompasses any disorder of abnormal movement and paralysis caused by abnormal function of the cerebral cortex. In truth, however, CP does not include conditions due to progressive disease or degeneration of the brain. For this reason, CP is also referred to as static (nonprogressive) encephalopathy (disease of the brain). Also excluded from CP are any disorders of muscle control that arise in the muscles themselves and/or in the peripheral nervous system (nerves outside the brain and spinal cord).

CP is not a specific diagnosis, but is more accurately considered a description—a description of a broad but defined group of neurological and physical problems.

The symptoms of CP and their severity are quite variable. Those with CP may have only minor difficulty with fine motor skills, such as grasping and manipulating items with their hands. A severe form of CP could involve significant muscle problems in all four limbs, **mental retardation**, seizures, and difficulties with vision, speech, and hearing.

Muscles that receive defective messages from the brain may be constantly contracted and tight (spastic), exhibit involuntary writhing movements (athetosis), or have difficulty with voluntary movement (dyskinesia). There can also be a lack of balance and coordination with unsteady movements (ataxia). A combination of any of these problems may also occur. Spastic CP and mixed CP constitute the majority of cases. Effects on the muscles can range from mild weakness or partial paralysis (paresis), to complete loss of voluntary control of a muscle or group of muscles (plegia). CP is also designated by the number of limbs affected. For instance, affected muscles in one limb is monoplegia, both arms or both legs is diplegia, both limbs on one side of the body is hemiplegia, and in all four limbs is quadriplegia. Muscles of the trunk, neck, and head may be affected as well.

CP can be caused by a number of different mechanisms at various times—from several weeks after conception, through birth, to early childhood. For many years, it was accepted that most cases of CP were due to brain injuries received during a traumatic birth, known as birth asphyxia. However, extensive research in the 1980s showed that only 5–10% of CP can be attributed to birth trauma. Other possible causes include abnormal development of the brain, prenatal factors that directly or indirectly damage neurons in the developing brain, premature birth, and brain injuries that occur in the first few years of life.

Advances in the medical care of premature infants in the last 20 years have dramatically increased the rate of survival of these fragile newborns. However, as gestational age at delivery and birth weight of a baby decrease, the risk for CP dramatically increases. A term **pregnancy** is delivered at 37–41 weeks gestation. The risk for CP in a preterm infant (32–37 weeks) is increased about five-fold over the risk for an infant born at term. Survivors of extremely preterm births (less than 28 weeks) face as much as a 50-fold increase in risk. About 50% of all cases of CP now being diagnosed are in children who were born prematurely.

Two factors are involved in the risk for CP associated with **prematurity**. First, premature babies are at higher risk for various CP-associated medical complications, such as intracerebral hemorrhage, infection, and difficulty in breathing, to name a few. Second, the onset of **premature labor** may be induced, in part, by complications that have already caused neurologic damage in the fetus. A combination of both factors almost certainly plays a role in some cases of CP. The tendency toward premature delivery runs in families, but the genetic mechanisms are far from clear.

An increase in multiple pregnancies in recent years, especially in the United States, is blamed on the increased use of fertility drugs. As the number of fetuses in a pregnancy increases, the risks for abnormal development and premature delivery also increase. Children from twin pregnancies have four times the risk of developing CP as children from singleton pregnancies, owing to the fact that more twin pregnancies are delivered prematurely. The risk for CP in a child of triplets is up to 18 times greater. Furthermore, recent evidence suggests that a baby from a pregnancy in which its twin died before birth is at increased risk for CP.

Approximately 500,000 children and adults in the United States have CP, and it is newly diagnosed in about 6,000 infants and young children each year. The inci-

dence of CP has not changed much in the last 20–30 years. Ironically, advances in medicine have decreased the incidence from some causes, Rh disease for example, but increased it from others, notably, prematurity and multiple pregnancies. No particular ethnic groups seem to be at higher risk for CP. However, people of disadvantaged background are at higher risk due to poorer access to proper prenatal care and advanced medical services.

Causes and symptoms

As noted, CP has many causes, making a discussion of the genetics of CP complicated. A number of hereditary/genetic syndromes have signs and symptoms similar to CP, but usually also have problems not typical of CP. Put another way, some hereditary conditions "mimic" CP. Isolated CP, meaning CP that is not a part of some other syndrome or disorder, is usually not inherited.

It might be possible to group the causes of CP into those that are genetic and those that are non-genetic, but most would fall somewhere in between. Grouping causes into those that occur during pregnancy (prenatal), those that happen around the time of birth (perinatal), and those that occur after birth (postnatal), is preferable. CP related to premature birth and multiple pregnancies (twins, triplets, etc., not "many pregnancies") is somewhat different and considered separately.

Prenatal causes

Although much has been learned about human embryology in the last couple of decades, a great deal remains unknown. Studying prenatal human development is difficult because the embryo and fetus develop in a closed environment—the mother's womb. However, the relatively recent development of a number of prenatal tests has opened a window on the process. Add to that more accurate and complete evaluations of newborns, especially those with problems, and a clearer picture of what can go wrong before birth is possible.

The complicated process of brain development before birth is susceptible to many chance errors that can result in abnormalities of varying degrees. Some of these errors will result in structural anomalies of the brain, while others may cause undetectable, but significant, abnormalities in how the cerebral cortex is "wired." An abnormality in structure or wiring is sometimes hereditary, but is most often due to chance, or a cause unknown at this time. Whether and how much genetics played a role in a particular brain abnormality depends to some degree on the type of anomaly and the form of CP it causes.

Several maternal-fetal infections are known to increase the risk for CP, including **rubella** (German **measles**, now rare in the United States), cytomegalovirus (CMV), and **toxoplasmosis**. Each of these infections is considered a risk to the fetus only if the mother contracts it for the first time during that pregnancy. Even in those cases, though, most babies will be born normal. Most women are immune to all three infections by the time they reach childbearing age, but a woman's immune status can be determined using the so-called TORCH (for Toxoplasmosis, Rubella, Cytomegalovirus, and Herpes) test before or during pregnancy.

Just as a **stroke** can cause neurologic damage in an adult, so too can this type of event occur in the fetus. A burst blood vessel in the brain followed by uncontrolled bleeding (coagulopathy), known as intracerebral hemorrhage, could cause a fetal stroke, or a cerebral blood vessel could be obstructed by a clot (**embolism**). Infants who later develop CP, along with their mothers, are more likely than other mother-infant pairs to test positive for factors that put them at increased risk for bleeding episodes or blood clots. Some **coagulation disorders** are strictly hereditary, but most have a more complicated basis.

A teratogen is any substance to which a woman is exposed that has the potential to harm the embryo or fetus. Links between a drug or other chemical exposure during pregnancy and a risk for CP are difficult to prove. However, any substance that might affect fetal brain development, directly or indirectly, could increase the risk for CP. Furthermore, any substance that increases the risk for premature delivery and low birth weight, such as alcohol, tobacco, or **cocaine**, among others, might indirectly increase the risk for CP.

The fetus receives all nutrients and oxygen from blood that circulates through the placenta. Therefore, anything that interferes with normal placental function might adversely affect development of the fetus, including the brain, or might increase the risk for premature delivery. Structural abnormalities of the placenta, premature detachment of the placenta from the uterine wall (abruption), and placental infections (chorioamnionitis) are thought to pose some risk for CP.

Certain conditions in the mother during pregnancy might pose a risk to fetal development leading to CP. Women with autoimmune anti-thyroid or anti-phospholipid (APA) antibodies are at slightly increased risk for CP in their children. A potentially important clue uncovered recently points toward high levels of cytokines in the maternal and fetal circulation as a possible risk for CP. Cytokines are proteins associated with inflammation, such as from infection or **autoimmune disorders**, and they may be toxic to neurons in the fetal brain. More research is needed to determine the exact relationship, if any, between high levels of cytokines in pregnancy and

KEY TERMS

Asphyxia—Lack of oxygen. In the case of cerebral palsy, lack of oxygen to the brain.

Ataxia—A deficiency of muscular coordination, especially when voluntary movements are attempted, such as grasping or walking.

Athetosis—A condition marked by slow, writhing, involuntary muscle movements.

Cerebral palsy—Movement disability resulting from nonprogressive brain damage.

Coagulopathy—A disorder in which blood is either too slow or too quick to coagulate (clot).

Contracture—A tightening of muscles that prevents normal movement of the associated limb or other body part.

Cytokine—A protein associated with inflammation that, at high levels, may be toxic to nerve cells in the developing brain.

Diplegia—Paralysis affecting like parts on both sides the body, such as both arms or both legs.

Dorsal rhizotomy—A surgical procedure that cuts nerve roots to reduce spasticity in affected muscles.

Dyskinesia—Impaired ability to make voluntary movements.

Hemiplegia—Paralysis of one side of the body.

Hypotonia—Reduced or diminished muscle tone.

Quadriplegia—Paralysis of all four limbs.

Serial casting—A series of casts designed to gradually move a limb into a more functional position.

Spastic—A condition in which the muscles are rigid, posture may be abnormal, and fine motor control is impaired.

Spasticity—Increased mucle tone, or stiffness, which leads to uncontrolled, awkward movements.

Static encephalopathy—A disease of the brain that does not get better or worse.

Tenotomy—A surgical procedure that cuts the tendon of a contracted muscle to allow lengthening.

CP. A woman has some risk of developing the same complications in more than one pregnancy, slightly increasing the risk for more than one child with CP.

Serious physical trauma to the mother during pregnancy could result in direct trauma to the fetus as well, or injuries to the mother could compromise the availability of nutrients and oxygen to the developing fetal brain.

Perinatal causes

Birth asphyxia significant enough to result in CP is now uncommon in developed countries. Tight nuchal cord (umbilical cord around the baby's neck) and prolapsed cord (cord delivered before the baby) are possible causes of birth asphyxia, as are bleeding and other complications associated with **placental abruption** and **placenta previa** (placenta lying over the cervix).

Infection in the mother is sometimes not passed to the fetus through the placenta, but is transmitted to the baby during delivery. Any such infection that results in serious illness in the newborn has the potential to produce some neurological damage.

Postnatal causes

The remaining 15% of CP is due to neurologic injury sustained after birth. CP that has a postnatal cause is sometimes referred to as acquired CP, but this is only accurate for those cases caused by infection or trauma.

Incompatibility between the Rh blood types of mother and child (mother Rh negative, baby Rh positive) can result in severe anemia in the baby (**erythroblastosis fetalis**). This may lead to other complications, including severe **jaundice**, which can cause CP. Rh disease in the newborn is now rare in developed countries due to routine screening of maternal blood type and treatment of pregnancies at risk. The routine, effective treatment of jaundice due to other causes has also made it an infrequent cause of CP in developed countries. Rh blood type poses a risk for recurrence of Rh disease if treatment is not provided.

Serious infections that affect the brain directly, such as **meningitis** and **encephalitis**, may cause irreversible damage to the brain, leading to CP. A **seizure disorder** early in life may cause CP, or may be the product of a hidden problem that causes CP in addition to seizures. Unexplained (idiopathic) seizures are hereditary in only a small percentage of cases. Although rare in infants born healthy at or near term, intracerebral hemorrhage and brain embolism, like fetal stroke, are sometimes genetic.

Physical trauma to an infant or child resulting in brain injury, such as from abuse, accidents, or near

drowning/suffocation, might cause CP. Likewise, ingestion of a toxic substance such as lead, mercury, poisons, or certain chemicals could cause neurological damage. Accidental overdose of certain medications might also cause similar damage to the central nervous system.

By definition, the defect in cerebral function causing CP is nonprogressive. However, the symptoms of CP often change over time. Most of the symptoms of CP relate in some way to the aberrant control of muscles. To review, CP is categorized first by the type of movement/postural disturbance(s) present, then by a description of which limbs are affected, and finally by the severity of motor impairment. For example, spastic diplegia refers to continuously tight muscles that have no voluntary control in both legs, while athetoid quadraparesis describes uncontrolled writhing movements and muscle weakness in all four limbs. These three-part descriptions are helpful in providing a general picture, but cannot give a complete description of any one person with CP. In addition, the various "forms" of CP do not occur with equal frequency—spastic diplegia is seen in more individuals than is athetoid quadraparesis. CP can also be loosely categorized as mild, moderate, or severe, but these are very subjective terms with no firm boundaries between them.

A muscle that is tensed and contracted is hypertonic, while excessively loose muscles are hypotonic. Spastic, hypertonic muscles can cause serious orthopedic problems, including **scoliosis** (spine curvature), hip dislocation, or **contractures**. A contracture is shortening of a muscle, aided sometimes by a weak-opposing force from a neighboring muscle. Contractures may become permanent, or "fixed," without some sort of intervention. Fixed contractures may cause postural abnormalities in the affected limbs. Clenched fists and contracted feet (equinus or equinovarus) are common in people with CP. Spasticity in the thighs causes them to turn in and cross at the knees, resulting in an unusual method of walking known as a "scissors gait." Any of the joints in the limbs may be stiff (immobilized) due to spasticity of the attached muscles.

Athetosis and dyskinesia often occur with spasticity, but do not often occur alone. The same is true of ataxia. It is important to remember that "mild CP" or "severe CP" refers not only to the number of symptoms present, but also to the level of involvement of any particular class of symptoms.

Mechanisms that can cause CP are not always restricted to motor-control areas of the brain. Other neurologically based symptoms may include:

- mental retardation/learning disabilities
- behavioral disorders
- seizure disorders
- visual impairment
- hearing loss
- speech impairment (dysarthria)
- abnormal sensation and perception

These problems may have a greater impact on a child's life than the physical impairments of CP, although not all children with CP are affected by other problems. Many infants and children with CP have growth impairment. About one-third of individuals with CP have moderate-to-severe mental retardation, one-third have mild mental retardation, and one-third have normal intelligence.

Diagnosis

The signs of CP are not usually noticeable at birth. Children normally progress through a predictable set of developmental milestones through the first 18 months of life. Children with CP, however, tend to develop these skills more slowly because of their motor impairments, and delays in reaching milestones are usually the first symptoms of CP. Babies with more severe cases of CP are usually diagnosed earlier than others.

Selected developmental milestones, and the ages for normally acquiring them, are given below. If a child does not acquire the skill by the age shown in parentheses, there is some cause for concern.

- sits well unsupported—six months (eight–10 months)
- babbles—six months (eight months)
- crawls—nine months (12 months)
- finger feeds, holds bottle—nine months (12 months)
- walks alone—12 months (15–18 months)
- uses one or two words other than dada/mama—12 months (15 months)
- walks up and down steps—24 months (24–36 months)
- turns pages in books; removes shoes and socks—24 months (30 months)

Children do not consistently favor one hand over the other before 12–18 months, and doing so may be a sign that the child has difficulty using the other hand. This same preference for one side of the body may show up as asymmetric crawling or, later on, favoring one leg while climbing stairs.

It must be remembered that children normally progress at somewhat different rates, and slow beginning accomplishment is often followed by normal development. Other causes for developmental delay—some benign, some serious—should be excluded before con-

sidering CP as the answer. CP is nonprogressive, so continued loss of previously acquired milestones indicates that CP is not the cause of the problem.

No one test is diagnostic for CP, but certain factors increase suspicion. The Apgar score measures a baby's condition immediately after birth. Babies that have low Apgar scores are at increased risk for CP. Presence of abnormal muscle tone or movements may indicate CP, as may the persistence of infantile reflexes. Imaging of the brain using ultrasound, x rays, MRI, and/or CT scans may reveal a structural anomaly. Some brain lesions associated with CP include scarring, cysts, expansion of the cerebral ventricles (**hydrocephalus**), periventricular leukomalacia (an abnormality of the area surrounding the ventricles), areas of dead tissue (necrosis), and evidence of an intracerebral hemorrhage or blood clot. Blood and urine biochemical tests, as well as genetic tests, may be used to rule out other possible causes, including muscle and peripheral nerve diseases, mitochondrial and metabolic diseases, and other inherited disorders. Evaluations by a pediatric developmental specialist and a geneticist may be of benefit.

Treatment

Cerebral palsy cannot be cured, but many of the disabilities it causes can be managed through planning and timely care. Treatment for a child with CP depends on the severity, nature, and location of the primary muscular symptoms, as well as any associated problems that might be present. Optimal care of a child with mild CP may involve regular interaction with only a physical therapist and occupational therapist, whereas care for a more severely affected child may include visits to multiple medical specialists throughout life. With proper treatment and an effective plan, most people with CP can lead productive, happy lives.

Therapy

Spasticity, muscle weakness, coordination, ataxia, and scoliosis are all significant impairments that affect the posture and mobility of a person with CP. Physical and occupational therapists work with the patient, and the family, to maximize the ability to move affected limbs, develop normal motor patterns, and maintain posture. "Assistive technology," things such as wheelchairs, walkers, shoe inserts, crutches, and braces, are often required. A speech therapist, and high-tech aids such as computer-controlled communication devices, can make a tremendous difference in the life of those who have speech impairments.

Medications

Before fixed contractures develop, muscle-relaxant drugs such as diazepam (Valium), dantrolene (Dantrium), and baclofen (Lioresal) may be prescribed. Botulinum toxin (Botox), a newer and highly effective treatment, is injected directly into the affected muscles. Alcohol or phenol injections into the nerve controlling the muscle are another option. Multiple medications are available to control seizures, and athetosis can be treated using medications such as trihexyphenidyl HCl (Artane) and benztropine (Cogentin).

Surgery

Fixed contractures are usually treated with either serial casting or surgery. The most commonly used surgical procedures are tenotomy, tendon transfer, and dorsal rhizotomy. In tenotomy, tendons of the affected muscle are cut and the limb is cast in a more normal position while the tendon regrows. Alternatively, tendon transfer involves cutting and reattaching a tendon at a different point on the bone to enhance the length and function of the muscle. A neurosurgeon performing dorsal rhizotomy carefully cuts selected nerve roots in the spinal cord to prevent them from stimulating the spastic muscles. Neurosurgical techniques in the brain such as implanting tiny electrodes directly into the cerebellum, or cutting a portion of the hypothalamus, have very specific uses and have had mixed results.

Education

Parents of a child newly diagnosed with CP are not likely to have the necessary expertise to coordinate the full range of care their child will need. Although knowledgeable and caring medical professionals are indispensable for developing a care plan, a potentially more important source of information and advice is other parents who have dealt with the same set of difficulties. Support groups for parents of children with CP can be significant sources of both practical advice and emotional support. Many cities have support groups that can be located through the United Cerebral Palsy Association, and most large medical centers have special multidisciplinary clinics for children with developmental disorders.

Prognosis

Cerebral palsy can affect every stage of maturation, from childhood through adolescence to adulthood. At each stage, those with CP, along with their caregivers, must strive to achieve and maintain the fullest range of experiences and education consistent with their abilities. The advice and intervention of various professionals remains crucial for many people with CP. Although CP itself is not considered a terminal disorder, it can affect a person's lifespan by increasing the risk for certain med-

ical problems. People with mild cerebral palsy may have near-normal lifespans, but the lifespan of those with more severe forms may be shortened. However, over 90% of infants with CP survive into adulthood.

The cause of most cases of CP remains unknown, but it has become clear in recent years that birth difficulties are not to blame in most cases. Rather, developmental problems before birth, usually unknown and generally undiagnosable, are responsible for most cases. The rate of survival for preterm infants has leveled off in recent years, and methods to improve the long-term health of these at-risk babies are now being sought. Current research is also focusing on the possible benefits of recognizing and treating coagulopathies and inflammatory disorders in the prenatal and perinatal periods. The use of magnesium sulfate in pregnant women with preeclampsia or threatened preterm delivery may reduce the risk of CP in very preterm infants. Finally, the risk of CP can be decreased through good maternal **nutrition**, avoidance of drugs and alcohol during pregnancy, and prevention or prompt treatment of infections.

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March of Dimes Birth Defects Foundation. 1275 Mamaroneck Ave., White Plains, NY 10605. (888) 663-4637. resourcecenter@modimes.org. <http://www.modimes.org>.

National Easter Seal Society. 230 W. Monroe St., Suite 1800, Chicago, IL 60606-4802. (312) 726-6200 or (800) 221-6827. <http://www.easter-seals.org>.

National Institute of Neurological Disorders and Stroke. 31 Center Drive, MSC 2540, Bldg. 31, Room 8806, Bethesda, MD 20814. (301) 496-5751 or (800) 352-9424. <http://www.ninds.nih.gov>.

National Society of Genetic Counselors. 233 Canterbury Dr., Wallingford, PA 19086-6617. (610) 872-1192. <http://www.nsgc.org/GeneticCounselingYou.asp>.

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Scott J. Polzin, MS

Cerebrospinal fluid (CSF) analysis

Definition

Cerebrospinal fluid (CSF) analysis is a laboratory test to examine a sample of the fluid surrounding the brain and spinal cord. This fluid is a clear, watery liquid that protects the central nervous system from injury and cushions it from the surrounding bone structure. It contains a variety of substances, particularly glucose (sugar), protein, and white blood cells from the immune system. The fluid is withdrawn through a needle in a procedure called a lumbar puncture.

Purpose

The purpose of a CSF analysis is to diagnose medical disorders that affect the central nervous system. Some of these conditions include:

- viral and bacterial infections, such as **meningitis** and **encephalitis**
- tumors or cancers of the nervous system
- syphilis, a sexually transmitted disease
- bleeding (hemorrhaging) around the brain and spinal cord
- multiple sclerosis, a disease that affects the myelin coating of the nerve fibers of the brain and spinal cord
- Guillain-Barré syndrome, an inflammation of the nerves.

During a lumbar puncture, or spinal tap, a procedure in which cerebrospinal fluid is aspirated, the physician inserts a hollow, thin needle in the space between two vertebrae of the lower back and slowly advances it toward the spine. The cerebrospinal fluid pressure is then measured and the fluid is withdrawn for laboratory analysis. *(Illustration by Electronic Illustrators Group.)*

Precautions

In some circumstances, a lumbar puncture to withdraw a small amount of CSF for analysis may lead to serious complications. Lumbar puncture should be performed only with extreme caution, and only if the benefits are thought to outweigh the risks, in certain conditions. For example, in people who have blood clotting (coagulation) or bleeding disorders, lumbar puncture can cause bleeding that can compress the spinal cord. If there is a large **brain tumor** or other mass, removal of CSF can cause the brain to droop down within the skull cavity (herniate), compressing the brain stem and other vital structures, and leading to irreversible brain damage or **death**. These problems are easily avoided by checking blood coagulation through a blood test and by doing a **computed tomography scan** (CT) or **magnetic resonance imaging** (MRI) scan before attempting the lumbar puncture. In addition, a lumbar puncture procedure should never be performed at the site of a localized skin infection on the lower back because the infection may be introduced into the CSF and may spread to the brain or spinal cord.

Description

The procedure to remove cerebrospinal fluid is called a lumbar puncture, or spinal tap, because the area of the spinal column used to obtain the sample is in the lumbar spine, or lower section of the back. In rare instances, such as a spinal fluid blockage in the middle of the back, a doctor may perform a spinal tap in the neck. The lower lumbar spine (usually between the vertebrae known as L4–5) is preferable because the spinal cord stops near L2, and a needle introduced below this level will miss the spinal cord and encounter only nerve roots, which are easily pushed aside.

A lumbar puncture takes about 30 minutes. Patients can undergo the test in a doctor's office, laboratory, or outpatient hospital setting. Sometimes it requires an inpatient hospital stay. If the patient has spinal arthritis, is extremely uncooperative, or obese, it may be necessary to introduce the spinal needle using x-ray guidance.

In order to get an accurate sample of cerebrospinal fluid, it is critical that a patient is in the proper position. The spine must be curved to allow as much space as possi-

KEY TERMS

Encephalitis—An inflammation or infection of the brain and spinal cord caused by a virus or as a complication of another infection.

Guillain-Barré syndrome—An inflammation involving nerves that affect the extremities. The inflammation may spread to the face, arms, and chest.

Immune system—Protects the body against infection.

Manometer—A device used to measure fluid pressure.

Meningitis—An infection or inflammation of the membranes or tissues that cover the brain and spinal cord, and caused by bacteria or a virus.

Multiple sclerosis—A disease that destroys the covering (myelin sheath) of nerve fibers of the brain and spinal cord.

Spinal canal—The cavity or hollow space within the spine that contains cerebrospinal fluid.

Vertebrae—The bones of the spinal column. There are 33 along the spine, with five (called L1-L5) making up the lower lumbar region.

ble between the lower vertebrae, or bones of the back, for the doctor to insert a lumbar puncture needle between the vertebrae and withdraw a small amount of fluid. The most common position is for the patient to lie on his or her side with the back at the edge of the exam table, head and chin bent down, knees drawn up to the chest, and arms clasped around the knees. (Small infants and people who are obese may need to curve their spines in a sitting position.) People should talk to their doctor if they have any questions about their position because it is important to be comfortable and to remain still during the entire procedure. In fact, the doctor will explain the procedure to the patient (or guardian) so that the patient can agree in writing to have it done (informed consent). If the patient is anxious or uncooperative, a short-acting sedative may be given.

During a lumbar puncture, the doctor drapes the back with a sterile covering that has an opening over the puncture site and cleans the skin surface with an antiseptic solution. Patients receive a local anesthetic to minimize any **pain** in the lower back.

The doctor inserts a hollow, thin needle in the space between two vertebrae of the lower back and slowly advances it toward the spine. A steady flow of clear cerebrospinal fluid, normally the color of water, will begin to fill the needle as soon as it enters the spinal canal. The doctor measures the cerebrospinal fluid pressure with a special instrument called a manometer and withdraws several vials of fluid for laboratory analysis. The amount of fluid collected depends on the type and number of tests needed to diagnose a particular medical disorder.

In some cases, the doctor must remove and reposition the needle. This occurs when there is not an even flow of fluid, the needle hits bone or a blood vessel, or the patient reports sharp, unusual pain.

Preparation

Patients can go about their normal activities before a lumbar puncture. Experts recommend that patients relax before the procedure to release any muscle tension, since the lumbar puncture needle must pass through muscle tissue before it reaches the spinal canal. A patient's level of relaxation before and during the procedure plays a critical role in the test's success.

Aftercare

After the procedure, the doctor covers the site of the puncture with a sterile bandage. Patients must avoid sitting or standing and remain lying down for as long as six hours after the lumbar puncture. They should also drink plenty of fluid to help prevent lumbar puncture **headache**, which is discussed in the next section.

Risks

For most people, the most common side effect after the removal of CSF is a headache. This occurs in 10–30% of adult patients and in up to 40% of children. It is caused by a decreased CSF pressure related to a small leak of CSF through the puncture site. These headaches usually are a dull pain, although some people report a throbbing sensation. A stiff neck and nausea may accompany the headache. Lumbar puncture headaches typically begin within two days after the procedure and persist from a few days to several weeks or months.

Since an upright position worsens the pain, patients with a lumbar puncture headache can control the pain by lying in a flat position and taking a prescription or nonprescription pain relief medication, preferably one containing **caffeine**. In rare cases, the puncture site leak is "patched" using the patient's own blood.

People should talk to their doctor about complications from a lumbar puncture. In most cases, this test to analyze CSF is a safe and effective procedure. Some patients experience pain, difficulty urinating, infection, or leakage of cerebrospinal fluid from the puncture site after the procedure.

Normal results

Normal CSF is clear and colorless. It may be cloudy in infections; straw- or yellow-colored if there is excess protein, as may occur with **cancer** or inflammation; blood-tinged if there was recent bleeding; or yellow to brown (xanthochromic) if caused by an older instance of bleeding.

A series of laboratory tests analyze the CSF for a variety of substances to rule out possible medical disorders of the central nervous system. The following are normal values for commonly tested substances:

- CSF pressure: 50–180 mmH_2O
- glucose: 40–85 mg/dL
- protein: 15–50 mg/dL
- leukocytes (white blood cells) total less than 5 per mL
- lymphocytes: 60–70%
- monocytes: 30–50%
- neutrophils: none

Normally, there are no red blood cells in the CSF unless the needle passes though a blood vessel on route to the CSF. If this is the case, there should be more red blood cells in the first tube collected than in the last.

Abnormal results

Abnormal test result values in the pressure or any of the substances found in the cerebrospinal fluid may suggest a number of medical problems including a tumor or spinal cord obstruction; hemorrhaging or bleeding in the central nervous system; infection from bacterial, viral, or fungal microorganisms; or an inflammation of the nerves. It is important for patients to review the results of a cerebrospinal fluid analysis with their doctor and to discuss any treatment plans.

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Martha Floberg Robbins

Cerebrovascular accident *see* **Stroke**

Cerebrovascular amyloidosis *see* **Cerebral amyloid angiopathy**

Cerumen impaction

Definition

Cerumen impaction is a condition in which earwax has become tightly packed in the external ear canal to the point that the canal is blocked.

Description

Cerumen impaction develops when earwax accumulates in the inner part of the ear canal and blocks the eardrum. It affects between 2–6% of the general population in the United States. Impaction does not happen under normal circumstances because cerumen is produced by glands in the outer part of the ear canal; it is not produced in the inner part. The cerumen traps sand or dust particles before they reach the ear drum. It also protects the outer part of the ear canal because it repels water. The slow movement of the outer layer of skin of the ear canal carries cerumen toward the outer opening of the ear. As the older cerumen reaches the opening of the ear, it dries out and falls away.

Causes and symptoms

Causes

Cerumen is most likely to become impacted when it is pushed against the eardrum by cotton-tipped applicators, hair pins, or other objects that people put in their ears; and when it is trapped against the eardrum by a hearing aid. Less common causes of cerumen impaction include overproduction of earwax by the glands in the ear canal, or an abnormally shaped ear canal.

Symptoms

The most important symptom of cerumen impaction is partial loss of hearing. Other symptoms are **itching**, **tinnitus** (noise or ringing in the ears), a sensation of fullness in the ear, and **pain**.

Ear wax is removed by flushing the ear canal with warm fluid. *(Illustration by Argosy, Inc.)*

Diagnosis

The diagnosis of impacted cerumen is usually made by examining the ear canal and eardrum with an otoscope, an instrument with a light attached that allows the doctor to look into the canal.

Treatment

Irrigation is the most common method of removing impacted cerumen. It involves washing out the ear canal with water from a commercial irrigator or a syringe with a catheter attached. Although some doctors use Water Piks to remove cerumen, most do not recommend them because the stream of water is too forceful and may damage the eardrum. The doctor may add a small amount of alcohol, hydrogen peroxide, or other antiseptic. The water must be close to body temperature; if it is too cold or too warm, the patient may feel dizzy or nauseated. After the ear has been irrigated, the doctor will apply antibiotic ear drops to protect the ear from infection.

Irrigation should not be used to remove cerumen if the patient's eardrum is ruptured or missing; if the patient has a history of chronic **otitis media** (inflammation of the middle ear) or a myringotomy (cutting the eardrum to allow fluid to escape from the middle ear); or if the patient has hearing in only one ear.

If irrigation cannot be used or fails to remove the cerumen, the patient is referred to an ear, nose, and throat (ENT) specialist. The specialist can remove the wax with a vacuum device or a curette, which is a small scoop-shaped surgical instrument.

Some doctors prescribe special ear drops, such as Cerumenex, to soften the wax. The most common side effect of Cerumenex is an allergic skin reaction. Over-the-counter wax removal products include Debrox or Murine Ear Drops. A 3% solution of hydrogen peroxide may also be used. These products are less likely to irritate the skin of the ear.

Prognosis

In most cases, impacted cerumen is successfully removed by irrigation with no lasting side effects. Irrigation can, however, lead to infection of the outer or the middle ear if the patient has a damaged or absent ear drum. Patients who try to remove earwax themselves with hair pins or similar objects run the risk of perforating the ear drum or damaging the fragile skin covering the ear canal, causing bleeding and the risk of infection.

Prevention

The best method of cleaning the external ear is to wipe the outer opening with a damp washcloth folded over the index finger, without going into the ear canal itself. Two techniques have been recommended to prevent cerumen from reaccumulating in the ear. The patient may place two or three drops of mineral oil into each ear once a week, allow it to remain for two or three minutes, and rinse it out with warm water; or place two drops of Domeboro otic solution in each ear once a week after showering.

Patients who wear **hearing aids** should have their ears examined periodically for signs of cerumen accumulation.

Resources

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KEY TERMS

Cerumen—The medical term for earwax.

Curette—A small scoop-shaped surgical instrument that can be used to remove cerumen if irrigation does not work or cannot be used.

Impaction—A condition in which earwax has become tightly packed in the outer ear to the point that the external ear canal is blocked.

Irrigation—The technique of removing cerumen from the ear canal by flushing it with water.

Myringotomy—Surgical cutting of the ear drum to allow fluid to escape from the middle ear.

Otitis media—Inflammation of the middle ear. Patients who have had recurrent otitis media should not have cerumen removed by irrigation.

Tinnitus—A sensation of noise or ringing in the ears. Tinnitus may be a symptom of cerumen impaction.

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American Academy of Otolaryngology, Head and Neck Surgery. 1 Prince Street, Alexandria, VA 22314. (703) 836-4444.

Rebecca J. Frey, PhD

Cervical biopsy *see* **Cervical conization**

Cervical cancer

Definition

Cervical **cancer** is a disease in which the cells of the cervix become abnormal and start to grow uncontrollably, forming tumors.

Description

In the United States, cervical cancer is the fifth most common cancer among women aged 35–54, and the third most common cancer of the female reproductive tract. In some developing countries, it is the most common type of cancer. It generally begins as an abnormality in the cells on the outside of the cervix. The cervix is the lower part or neck of the uterus (womb). It connects the body of the uterus to the vagina (birth canal).

Approximately 90% of cervical cancers are squamous cell carcinomas. This type of cancer originates in the thin, flat, squamous cells on the surface of the ectocervix, the part of the cervix that is next to the vagina. (Squamous cells are the thin, flat cells of the surfaces of the skin and cervix and linings of various organs.) Another 10% of cervical cancers are of the adenocarcinoma type. This cancer originates in the mucus-producing cells of the inner or endocervix, near the body of the uterus. Occasionally, the cancer may have characteristics of both types and is called adenosquamous carcinoma or mixed carcinoma.

The initial changes that may occur in some cervical cells are not cancerous. However, these precancerous cells form a lesion called dysplasia or a squamous intraepithelial lesion (SIL), since it occurs within the epithelial or outer layer of cells. These abnormal cells can also be described as cervical intraepithelial neoplasia (CIN). Moderate to severe dysplasia may be called carcinoma in situ or non-invasive cervical cancer.

Dysplasia is a common condition and the abnormal cells often disappear without treatment. However, these precancerous cells can become cancerous. This may take years, although it can happen in less than a year. Eventually, the abnormal cells start to grow uncontrollably into the deeper layers of the cervix, becoming an invasive cervical cancer.

Although cervical cancer used to be one of the most common causes of cancer **death** among American women, in the past 40 years there has been a 75% decrease in mortality. This is primarily due to routine screening with Pap tests (Pap smear), to identify precancerous and early-invasive stages of cervical cancer. With treatment, these conditions have a cure rate of nearly 100%.

Worldwide, there are more than 400,000 new cases of cervical cancer diagnosed each year. The American Cancer Society (ACS) estimates that there will be 12,900 new cases of invasive cervical cancer diagnosed in the United States in 2001. More than one million women will be diagnosed with a precancerous lesion or non-invasive cancer of the cervix.

Older women are at the highest risk for cervical cancer. Although girls under the age of 15 rarely develop this

cancer, the risk factor begins to increase in the late teens. Rates for carcinoma in situ peak between the ages of 20 and 30. In the United States, the incidence of invasive cervical cancer increases rapidly with age for African American women over the age of 25. The incidence rises more slowly for Caucasian women. However, women over age 65 account for more than 25% of all cases of invasive cervical cancer.

The incidence of cervical cancer is highest among poor women and among women in developing countries. In the United States, the death rates from cervical cancer are higher among Hispanic, Native American, and African American women than among Caucasian women. These groups of women are much less likely to receive regular Pap tests. Therefore, their cervical cancers usually are diagnosed at a much later stage, after the cancer has spread to other parts of the body.

Causes and symptoms

Human papilloma virus

Infection with the common human papilloma virus (HPV) is a cause of approximately 90% of all cervical cancers. There are more than 80 types of HPV. About 30 of these types can be transmitted sexually, including those that cause **genital warts** (papillomas). About half of the sexually transmitted HPVs are associated with cervical cancer. These "high-risk" HPVs produce a protein that can cause cervical epithelial cells to grow uncontrollably. The virus makes a second protein that interferes with tumor suppressors that are produced by the human immune system. The HPV-16 strain is thought to be a cause of about 50% of cervical cancers.

More than six million women in the United States have persistent HPV infections, for which there is no cure. Nevertheless, most women with HPV do not develop cervical cancer.

Symptoms of invasive cervical cancer

Most women do not have symptoms of cervical cancer until it has become invasive. At that point, the symptoms may include:

- unusual vaginal discharge
- light vaginal bleeding or spots of blood outside of normal menstruation
- **pain** or vaginal bleeding with sexual intercourse
- post-menopausal vaginal bleeding

Once the cancer has invaded the tissue surrounding the cervix, a woman may experience pain in the pelvic region and heavy bleeding from the vagina.

Diagnosis

The Pap test

Most often, cervical cancer is first detected with a **Pap test** that is performed as part of a regular pelvic examination. The vagina is spread with a metal or plastic instrument called a speculum. A swab is used to remove mucus and cells from the cervix. This sample is sent to a laboratory for microscopic examination.

The Pap test is a screening tool rather than a diagnostic tool. It is very efficient at detecting cervical abnormalities. The Bethesda System commonly is used to report Pap test results. A negative test means that no abnormalities are present in the cervical tissue. A positive Pap test describes abnormal cervical cells as low-grade or high-grade SIL, depending on the extent of dysplasia. About 5–10% of Pap tests show at least mild abnormalities. However, a number of factors other than cervical cancer can cause abnormalities, including inflammation from bacteria or yeast infections. A few months after the infection is treated, the Pap test is repeated.

Biopsy

Following an abnormal Pap test, a **colposcopy** is usually performed. The physician uses a magnifying scope to view the surface of the cervix. The cervix may be coated with an iodine solution that causes normal cells to turn brown and abnormal cells to turn white or yellow. This is called a Schiller test. If any abnormal areas are observed, a colposcopic biopsy may be performed. A biopsy is the removal of a small piece of tissue for microscopic examination by a pathologist.

Other types of cervical biopsies may be performed. An endocervical curettage is a biopsy in which a narrow instrument called a curette is used to scrape tissue from inside the opening of the cervix. A cone biopsy, or conization, is used to remove a cone-shaped piece of tissue from the cervix. In a cold knife cone biopsy, a surgical scalpel or laser is used to remove the tissue. A loop electrosurgical excision procedure (LEEP) is a cone biopsy using a wire that is heated by an electrical current. Cone biopsies can be used to determine whether abnormal cells have invaded below the surface of the cervix. They also can be used to treat many precancers and very early cancers. Biopsies may be performed with a local or general anesthetic. They may cause cramping and bleeding.

Diagnosing the stage

Following a diagnosis of cervical cancer, various procedures may be used to stage the disease (determine

how far the cancer has spread). For example, additional pelvic exams may be performed under anesthesia.

There are several procedures for determining if cervical cancer has invaded the urinary tract. With **cystoscopy**, a lighted tube with a lens is inserted through the urethra (the urine tube from the bladder to the exterior) and into the bladder to examine these organs for cancerous cells. Tissue samples may be removed for microscopic examination by a pathologist. **Intravenous urography** (intravenous pyelogram or IVP) is an x ray of the urinary system, following the injection of special dye. The kidneys remove the dye from the bloodstream and the dye passes into the ureters (the tubes from the kidneys to the bladder) and bladder. IVP can detect a blocked ureter, caused by the spread of cancer to the pelvic lymph nodes (small glands that are part of the immune system).

A procedure called proctoscopy or **sigmoidoscopy** is similar to cystoscopy. It is used to determine whether the cancer has spread to the rectum or lower large intestine.

Computed tomography (CT or CAT) scans, ultrasound, or other imaging techniques may be used to determine the spread of cancer to various parts of the body. With a CT scan, an x-ray beam rotates around the body, taking images from various angles. It is used to determine if the cancer has spread to the lymph nodes. **Magnetic resonance imaging** (MRI), which uses a magnetic field to image the body, sometimes is used for evaluating the spread of cervical cancer. Chest x rays may be used to detect cervical cancer that has spread to the lungs.

Treatment

Following a diagnosis of cervical cancer, the physician takes a medical history and performs a complete **physical examination**. This includes an evaluation of symptoms and risk factors for cervical cancer. The lymph nodes are examined for evidence that the cancer has spread from the cervix. The choice of treatment depends on the clinical stage of the disease.

The FIGO system of staging

The International Federation of Gynecologists and Obstetricians (FIGO) system usually is used to stage cervical cancer:

- Stage 0: Carcinoma in situ; non-invasive cancer that is confined to the layer of cells lining the cervix
- Stage I: Cancer that has spread into the connective tissue of the cervix but is confined to the uterus
- Stage IA: Very small cancerous area that is visible only with a microscope
- Stage IA1: Invasion area is less than 3 mm (0.13 in) deep and 7 mm (0.33 in) wide
- Stage IA2: Invasion area is 3–5 mm (0.13–0.2 in) deep and less than 7 mm (0.33 in) wide
- Stage IB: Cancer can be seen without a microscope or is deeper than 5 mm (0.2 in) or wider than 7 mm (0.33 in)
- Stage IB1: Cancer is no larger than 4 cm (1.6 in)
- Stage IB2: Stage IB cancer is larger than 4 cm (1.6 in)
- Stage II: Cancer has spread from the cervix but is confined to the pelvic region
- Stage IIA: Cancer has spread to the upper region of the vagina, but not to the lower one-third of the vagina
- Stage IIB: Cancer has spread to the parametrial tissue adjacent to the cervix
- Stage III: Cancer has spread to the lower one-third of the vagina or to the wall of the pelvis and may be blocking the ureters
- Stage IIIA: Cancer has spread to the lower vagina but not to the pelvic wall
- Stage IIIB: Cancer has spread to the pelvic wall and/or is blocking the flow of urine through the ureters to the bladder
- Stage IV: Cancer has spread to other parts of the body
- Stage IVA: Cancer has spread to the bladder or rectum
- Stage IVB: Cancer has spread to distant organs such as the lungs
- Recurrent: Following treatment, cancer has returned to the cervix or some other part of the body

In addition to the stage of the cancer, factors such as a woman's age, general health, and preferences may influence the choice of treatment. The exact location of the cancer within the cervix and the type of cervical cancer also are important considerations.

Treatment of precancer and carcinoma in situ

Most low-grade SILs that are detected with Pap tests revert to normal without treatment. Most high-grade SILs require treatment. Treatments to remove precancerous cells include:

- cold knife cone biopsy
- LEEP
- cryosurgery (freezing the cells with a metal probe)
- cauterization or diathermy (burning off the cells)
- laser surgery (burning off the cells with a laser beam)

These methods also may be used to treat cancer that is confined to the surface of the cervix (stage 0) and other

early-stage cervical cancers in women who may want to become pregnant. They may be used in conjunction with other treatments. These procedures may cause bleeding or cramping. All of these treatments require close follow-up to detect any recurrence of the cancer.

Surgery

A simple **hysterectomy** is used to treat some stages 0 and IA cervical cancers. Usually only the uterus is removed, although occasionally the fallopian tubes and ovaries are removed as well. The tissues adjoining the uterus, including the vagina, remain intact. The uterus may be removed either through the abdomen or the vagina.

In a radical hysterectomy, the uterus and adjoining tissues, including the ovaries, the upper region (1 in) of the vagina near the cervix, and the pelvic lymph nodes, are all removed. A radical hysterectomy usually involves abdominal surgery. However, it can be performed vaginally, in combination with a laparoscopic pelvic lymph node dissection. With **laparoscopy**, a tube is inserted through a very small surgical incision for the removal of the lymph nodes. These operations are used to treat stages IA2, IB, and IIA cervical cancers, particularly in young women. Following a hysterectomy, the tissue is examined to see if the cancer has spread and requires additional radiation treatment. Women who have had hysterectomies cannot become pregnant, but complications from a hysterectomy are rare.

If cervical cancer recurs following treatment, a pelvic exenteration (extensive surgery) may be performed. This includes a radical hysterectomy, with the additional removal of the bladder, rectum, part of the colon, and/or all of the vagina. Such operations require the creation of new openings for the urine and feces. A new vagina may be created surgically. Often the clitoris and other outer genitals are left intact.

Recovery from a pelvic exenteration may take six months to two years. This treatment is successful with 40–50% of recurrent cervical cancers that are confined to the pelvis. If the recurrent cancer has spread to other organs, radiation or **chemotherapy** may be used to alleviate some of the symptoms.

Radiation

Radiation therapy, which involves the use of high-dosage x rays or other high-energy waves to kill cancer cells, often is used for treating stages IB, IIA, and IIB cervical cancers, or in combination with surgery. With external-beam radiation therapy, the rays are focused on the pelvic area from a source outside the body. With implant or internal radiation therapy, a pellet of radioactive material is placed internally, near the tumor. Alternatively, thin needles may be used to insert the radioactive material directly into the tumor.

Radiation therapy to the pelvic region can have many side effects:

- skin reaction in the area of treatment
- fatigue
- upset stomach and loose bowels
- vaginal stenosis (narrowing of the vagina due to build-up of scar tissue) leading to painful sexual intercourse
- premature **menopause** in young women
- problems with urination

Chemotherapy

Chemotherapy, the use of one or more drugs to kill cancer cells, is used to treat disease that has spread beyond the cervix. Most often it is used following surgery or radiation treatment. Stages IIB, III, IV, and recurrent cervical cancers usually are treated with a combination of external and internal radiation and chemotherapy. The common drugs used for cervical cancer are cisplatin, ifosfamide, and fluorouracil. These may be injected or taken by mouth. The National Cancer Institute recommends that chemotherapy with cisplatin be considered for all women receiving radiation therapy for cervical cancer.

The side effects of chemotherapy depend on a number of factors, including the type of drug, the dosage, and the length of the treatment. Side effects may include:

- nausea and vomiting
- fatigue
- changes in appetite
- hair loss
- mouth or vaginal sores
- infections
- menstrual cycle changes
- premature menopause
- **infertility**
- bleeding or anemia (low red blood cell count)

With the exception of menopause and infertility, most of the side effects are temporary.

Alternative treatment

Biological therapy sometimes is used to treat cervical cancer, either alone or in combination with chemotherapy. Treatment with the immune-system pro-

KEY TERMS

Adenocarcinoma—Cervical cancer that originates in the mucus-producing cells of the inner or endocervix.

Biopsy—Removal of a small sample of tissue for examination under a microscope; used for the diagnosis and treatment of cervical cancer and precancerous conditions.

Carcinoma in situ—Cancer that is confined to the cells in which it originated and has not spread to other tissues.

Cervical intraepithelial neoplasia (CIN)—Abnormal cell growth on the surface of the cervix.

Cervix—Narrow, lower end of the uterus forming the opening to the vagina.

Colposcopy—Diagnostic procedure using a hollow, lighted tube (colposcope) to look inside the cervix and uterus.

Conization—Cone biopsy; removal of a cone-shaped section of tissue from the cervix for diagnosis or treatment.

Dysplasia—Abnormal cellular changes that may become cancerous.

Endocervical curettage—Biopsy performed with a curette to scrape the mucous membrane of the cervical canal.

Human papilloma virus (HPV)—Virus that causes abnormal cell growth (warts or papillomas); some types can cause cervical cancer.

Hysterectomy—Removal of the uterus.

Interferon—Potent immune-defense protein produced by viral-infected cells; used as an anti-cancer and anti-viral drug.

Laparoscopy—Laparoscopic pelvic lymph node dissection; insertion of a tube through a very small surgical incision to remove lymph nodes.

Loop electrosurgical excision procedure (LEEP)—Cone biopsy performed with a wire that is heated by electrical current.

Lymph nodes—Small round glands, located throughout the body, that filter the lymphatic fluid; part of the body's immune defense.

Pap test—Pap smear; removal of cervical cells to screen for cancer.

Pelvic exenteration—Extensive surgery to remove the uterus, ovaries, pelvic lymph nodes, part or all of the vagina, and the bladder, rectum, and/or part of the colon.

Squamous cells—Thin, flat cells on the surfaces of the skin and cervix and linings of various organs.

Squamous intraepithelial lesion (SIL)—Abnormal growth of squamous cells on the surface of the cervix.

Vaginal stenosis—Narrowing of the vagina due to a build-up of scar tissue.

tein interferon is used to boost the immune response. Biological therapy can cause temporary flu-like symptoms and other side effects.

Some research suggests that vitamin A (carotene) may help to prevent or stop cancerous changes in cells such as those on the surface of the cervix. Other studies suggest that **vitamins** C and E may reduce the risk of cervical cancer.

Prognosis

For cervical cancers that are diagnosed in the pre-invasive stage, the five-year-survival rate is almost 100%. When cervical cancer is detected in the early invasive stages, approximately 91% of women survive five years or more. Stage IVB cervical cancer is not considered to be curable. The five-year-survival rate for all cervical cancers combined is about 70%. The death rate from cervical cancer continues to decline by about 2% each year. Women over age 65 account for 40–50% of all deaths from cervical cancer.

Prevention

Viral infections

Most cervical cancers are preventable. More than 90% of women with cervical cancer are infected with HPV. HPV infection is the single most important risk factor. This is particularly true for young women because the cells lining the cervix do not fully mature until age 18. These immature cells are more susceptible to cancer-causing agents and viruses.

Since HPV is a sexually-transmitted infection, sexual behaviors can put women at risk for HPV infection and cervical cancer. These behaviors include:

- sexual intercourse at age 16 or younger
- partners who began having intercourse at a young age
- multiple sexual partners
- sexual partners who have had multiple partners ("high-risk males")
- a partner who has had a previous sexual partner with cervical cancer

HPV infection may not produce any symptoms, so sexual partners may not know that they are infected. However, Pap tests can detect the infection. Condoms do not necessarily prevent HPV infection.

Infection with the human **immunodeficiency** virus (HIV) that causes acquired immunodeficiency syndrome (**AIDS**) is a risk factor for cervical cancer. Women who test positive for HIV may have impaired immune systems that cannot correct precancerous conditions. Furthermore, sexual behavior that puts women at risk for HIV infection, also puts them at risk for HPV infection. There is some evidence suggesting that another sexually transmitted virus, the **genital herpes** virus, also may be involved in cervical cancer.

Smoking

Smoking may double the risk of cervical cancer. Chemicals produced by tobacco smoke can damage the DNA of cervical cells. The risk increases with the number of years a woman smokes and the amount she smokes.

Diet and drugs

Diets that are low in fruits and vegetables increase the risk of cervical cancer. Women also have an increased risk of cervical cancer if their mothers took the drug diethylstilbestrol (DES) while they were pregnant. This drug was given to women between 1940 and 1971 to prevent miscarriages. Some statistical studies have suggested that the long-term use of **oral contraceptives** may slightly increase the risk of cervical cancer.

Pap tests

Most cases of cervical cancers are preventable, since they start with easily detectable precancerous changes. Therefore, the best prevention for cervical cancer is a regular Pap test. When precancerous changes are detected, appropriate treatment can prevent the development of invasive cancer. The ACS recommends that women have annual Pap tests beginning when they first start having sex or at age 18. Women who are past menopause or some women with hysterectomies continue to require Pap tests.

The National Breast and Cervical Cancer Early Detection Program provides free or low-cost Pap tests and treatment for women without health insurance, for older women, and for members of racial and ethnic minorities. The program is administered through individual states, under the direction of the Centers for Disease Control and Prevention.

Special concerns

If a woman is diagnosed with very early-stage (IA) cervical cancer while pregnant, the physician usually will recommend a hysterectomy after the baby is born. For later-stage cancers, the **pregnancy** is terminated or the baby is removed by **cesarean section** as soon as it can survive outside the womb. This is followed by a hysterectomy and/or radiation treatment. For the most advanced stages of cervical cancer, treatment is initiated despite the pregnancy.

Many women with cervical cancer have hysterectomies, which are major surgeries. Although normal activities, including sexual intercourse, can be resumed in four-eight weeks, a woman may have emotional problems following a hysterectomy. A strong support system can help with these difficulties.

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Centers for Disease Control and Prevention. National Center for Chronic Disease Prevention and Health Promotion. Mail Stop K-64. 4770 Buford Highway NE, Atlanta, GA 30341-3717. (770) 488-4751. (888) 842-6355. <http://www.cdc.gov/cancer>.

EyesOnThePrize.Org. 446 S. Anaheim Hills Road, #108, Anaheim Hills, CA 92807. <http://www.eyesontheprize.org>.

Gynecologic Cancer Foundation. 401 North Michigan Avenue, Chicago, IL 60611. (800) 444-4441. (312) 644-6610. <http://www.wcn.org/gcf/>.

National Cancer Institute. Public Inquiries Office, Building 31, Room 10A31, 31 Center Drive, MSC 2580, Bethesda, MD

20892-2580. (800) 4-CANCER. <http://www.nci.nih.gov/>. <http://cancernet.nci.nih.gov>.
National Cervical Cancer Coalition. 16501 Sherman Way, Suite #110, Van Nuys, CA 91406. (800) 685-5531. (818) 909-3849. <http://www.nccc-online.org/>.

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Cervical conization

Definition

Cervical conization is both a diagnostic and treatment tool used to detect and treat abnormalities of the cervix. It is also known as a cone biopsy or cold knife cone biopsy.

Purpose

Cervical conization is performed if the results of a cervical biopsy have found a precancerous condition in the cervix. The cervix is the small cylindrical organ at the lower part of the uterus, which separates the uterus from the vagina. Cervical conization also may be performed if there is an abnormal cervical smear test (**PAP test**). A biopsy is a diagnostic test in which tissue or cells are removed from the body and examined under a microscope, primarily to look for **cancer** or other abnormalities.

Precautions

As with any operation that is performed under general anesthesia, the patient must not eat or drink anything for six to eight hours before surgery.

Description

The patient lies on the table with her legs raised in stirrups, similar to the position when having a PAP test.

KEY TERMS

Biopsy—The removal of a small piece of living tissue for examination under a microscope.

PAP test—The short term for Papanicolaou test, this procedure tests a smear of cellular material scraped from the cervix and examined under a microscope to detect abnormal cells.

The patient is given general anesthesia, and the vagina is held open with an instrument called a speculum. Using a scalpel or laser the doctor removes a cone-shaped piece of the cervix containing the area with abnormal cells. The resulting crater is repaired by stitching flaps of tissue over the wound. Alternatively, the wound may be left open, and heat or freezing is used to stop bleeding.

Once the tissue has been removed, it is examined under a microscope for signs of cancer. If cancer is present, other tests will be needed. Surgery will be performed to remove the cervix and uterus (**hysterectomy**) and other treatments may be used as well. If the abnormal cells are precancerous, a laser can be used to destroy them.

Cold knife cone biopsy used to be the preferred treatment for removing abnormal cells in the cervix. Now, most cone biopsies are performed using **laser surgery**. Cold knife cone biopsy is generally used only for special situations. For example, if a biopsy did not remove all the abnormal cells, the cold knife cone procedure allows the physician to remove what's left.

Aftercare

An overnight stay in the hospital may be required. After the test, the patient may feel some cramps or discomfort for about a week. Women should not have sex, use tampons, or douche until after seeing their physician for a follow up appointment (a week or more after the procedure).

Risks

Because cone biopsies carry risks such as bleeding and problems with subsequent pregnancies, they have been replaced with newer technologies except in a few circumstances.

About one in 10 women experience bleeding from the vagina about two weeks after the biopsy. There is also a slight risk of infection or perforation of the uterus. In a few women, the cervical canal becomes narrowed or

completely blocked, which can later interfere with the movement of sperm. This can impair a woman's fertility.

If too much muscle tissue has been removed, the procedure can lead to an **incompetent cervix**, which can be a problem with subsequent pregnancies. An incompetent cervix cannot seal properly to maintain a **pregnancy**. If untreated, the condition increases the odds of **miscarriage** or **premature labor**.

Cervical conization also may temporarily alter cervical cells, which can make a Pap smear test hard to interpret accurately for three or four months.

Normal results

This procedure is only performed if an abnormality is known or suspected.

Abnormal results

The presence of precancerous or cancerous cells in the cervix.

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ORGANIZATIONS

Cancer Information Service. (800) 4-CANCER. <http://www.rex.nci.nih.gov>.

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Cervical disk disease

Definition

Cervical disk disease refers to a gradual deterioration of the spongy disks in the top part of the spine.

Description

The spine is made up of 33 bones called vertebrae separated by spongy rings of elastic material. These rings, known as disks, are often compared to **shock** absorbers because they help to cushion the vertebrae. Just as importantly, they also make it possible to turn the head and neck. Over time, these disks slowly become flattened and less elastic due to everyday wear and tear. When this process occurs in the disks of the neck, it is referred to as cervical disk disease. Other general terms for this process include degenerative disk disease and intervertebral disk disease.

Cervical disk disease affects everyone to some degree, often without causing any bothersome symptoms. However, this condition can also lead to specific problems related to nerve functioning. For example, the outer edge of a disk may tear, allowing the gelatinous material inside to bulge outward (**herniated disk**). This can put pressure on nerves that exit the spine. Two adjacent vertebrae may rub together (sometimes resulting in bone spurs) that can also pinch these nerves. In other cases, the inner part of the ring may push on the spinal cord itself, which passes through the disk. Any of these situations can cause **pain** and limit movement. While symptoms primarily affect the neck, they can also occur in other parts of the body.

Causes and symptoms

Cervical disk disease is a gradual process that occurs with **aging**, though poor posture, repeated lifting, and tobacco use can hasten its course. Symptoms include pain when moving the neck and limited neck movement. The condition can also affect the hand, shoulder, and arm resulting in pain, numbness/tingling, and weakness. If the spinal cord itself is affected, these symptoms may occur in the legs. Loss of bowel or bladder control may also occur.

Diagnosis

Cervical disk disease is typically diagnosed by an orthopedist or a neurologist. After taking a medical history and conducting a **physical examination**, the doctor will recommend an imaging procedure to gather more information about the nature of the problem. This may include a CT scan, an MRI, or **myelography**. In addition, an electromyogram (EMG) may be used to evaluate the functioning of nerves in the arms, hands, or legs. Cervical disk disease is typically covered by medical insurance.

Treatment

Treatment usually involves physical therapy, several weeks of drug therapy with **nonsteroidal anti-inflammatory drugs** (NSAIDs), and limited use of a cervical collar (to reduce neck movement). Neck **traction** and **heat treatments** may also be recommended. In some

KEY TERMS

Bone spur—An overgrowth of bone.

Cervical—Relating to the top part of the spine that is composed of the seven vertebrae of the neck and the disks that separate them.

Computed tomography (CT) scan—An imaging procedure that produces a three-dimensional picture of organs or structures inside the body.

Myelography—An imaging procedure involving the injection of a radioactive dye into the fluid surrounding the spine. A myelography can be used to detect herniated disks, nerve root damage, and other problems affecting the cervical spine.

Neurologist—A doctor who specializes in disorders of the brain and central nervous system.

Orthopedist—A doctor who specializes in disorders of the musculoskeletal system.

Magnetic resonance imaging—A type of imaging that uses magnetic fields to generate a picture of internal structures.

cases, steroids or anesthetic drugs may be injected into the spinal canal to help alleviate symptoms. Aside from these measures, maintaining good posture and placing a pillow under the neck and head during sleep can be helpful. Treatment may last anywhere from several weeks to three months or more. Neck surgery is not usually advised unless other therapies have failed.

Alternative treatment

Acupuncture, therapeutic massage, and **yoga** are believed by some practitioners of alternative medicine to have generalized pain-relieving effects. However, any therapy that involves manipulating the neck is not recommended and should be approved by the primary doctor beforehand.

Prognosis

In most people symptoms go away within three months if not sooner. A smaller number may require surgery to correct the problem.

Prevention

While some degree of disk degeneration is inevitable, people can reduce their risk by practicing good posture (during sitting, standing, and lifting), performing neck-stretching exercises, maintaining an ideal weight, and quitting **smoking**.

Resources

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ORGANIZATIONS

American Academy of Orthopaedic Surgeons. 6300 North River Road, Rosemont, IL 60018-4262. (800) 346-2267. <http://www.aaos.org>.

Greg Annussek

Cervical osteoarthritis *see* **Cervical spondylosis**

Cervical spondylosis

Definition

Cervical spondylosis refers to common age-related changes in the area of the spine at the back of the neck. With age, the vertebrae (the component bones of the spine) gradually form bone spurs, and their shock-absorbing disks slowly shrink. These changes can alter the alignment and stability of the spine. They may go unnoticed, or they may produce problems related to pressure on the spine and associated nerves and blood vessels. This pressure can cause weakness, numbness, and **pain** in various areas of the body. In severe cases, walking and other activities may be compromised.

Description

As it runs from the brain down the back, the spinal cord is protected by ringlike bones, called vertebrae, stacked one upon the other. The vertebrae are not in direct contact with one another, however. The intervening spaces are filled with structures called disks. The disks are made up of a tough, fibrous outer tissue with an inner core of elastic or gel-like tissue.

One of the most important functions of disks is protecting the vertebrae and the nerves and blood vessels between the vertebrae. The disks also lend flexibility to

the spinal cord, facilitating movements such as turning the head or bending the neck. As people age, disks gradually become tougher and more unyielding. Disks also shrink with age, which reduces the amount of padding between the vertebrae.

As the amount of padding shrinks, the spine loses stability. The vertebrae react by constructing osteophytes, commonly known as bone spurs. There are seven vertebrae in the neck; development of osteophytes on these bones is sometimes called cervical **osteoarthritis**. Osteophytes may help to stabilize the degenerating backbone and help protect the spinal cord.

By age 50, 25–50% of people develop cervical spondylosis; by 75 years of age, it is seen in at least 70% of people. Although shrunken vertebral disks, osteophyte growth, and other changes in their cervical spine may exist, many of these people never develop significant problems.

However, about 50% of people over age 50 experience neck pain and stiffness due to cervical spondylosis. Of these people, 25–40% have at least one episode of cervical radiculopathy, a condition that arises when osteophytes compress nerves between the vertebrae. Another potential problem occurs if osteophytes, degenerating disks, or shifting vertebrae narrow the spinal canal. This pressure compresses the spinal cord and its blood vessels, causing cervical spondylitic myelopathy, a disorder in which large segments of the spinal cord are damaged. This disorder affects fewer than 5% of people with cervical spondylosis. Symptoms of both cervical spondylitic myelopathy and cervical radiculopathy may be present in some people.

Causes and symptoms

As people age, shrinkage of the vertebral disks prompts the vertebrae to form osteophytes to stabilize the back bone. However, the position and alignment of the disks and vertebrae may shift despite the osteophytes. Symptoms may arise from problems with one or more disks or vertebrae.

Osteophyte formation and other changes do not necessarily lead to symptoms, but after age 50, half of the population experiences occasional neck pain and stiffness. As disks degenerate, the cervical spine becomes less stable, and the neck is more vulnerable to injuries, including muscle and ligament strains. Contact between the edges of the vertebrae can also cause pain. In some people, this pain may be referred—that is, perceived as occurring in the head, shoulders, or chest, rather than the neck. Other symptoms may include vertigo (a type of **dizziness**) or ringing in the ears.

The neck pain and stiffness can be intermittent, as can symptoms of radiculopathy. Radiculopathy refers to compression on the base, or root, of nerves that lead away from the spinal cord. Normally, these nerves fit comfortably through spaces between the vertebrae. These spaces are called intervertebral foramina. As the osteophytes form, they can impinge on this area and gradually make the fit between the vertebrae too snug.

The poor fit increases the chances that a minor incident, such as overdoing normal activities, may place excess pressure on the nerve root, sometimes referred to as a pinched nerve. Pressure may also accumulate as a direct consequence of osteophyte formation. The pressure on the nerve root causes severe shooting pain in the neck, arms, shoulder, and/or upper back, depending on which nerve roots of the cervical spine are affected. The pain is often aggravated by movement, but in most cases, symptoms resolve within four-six weeks.

Cervical spondylosis can cause cervical spondylitic myelopathy through stenosis- or osteophyte-related pressure on the spinal cord. **Spinal stenosis** is a narrowing of the spinal canal—the area through the center of the vertebral column occupied by the spinal cord. Stenosis occurs because of misaligned vertebrae and out-of-place or degenerating disks. The problems created by spondylosis can be exacerbated if a person has a naturally narrow spinal canal. Pressure against the spinal cord can also be created by osteophytes forming on the inner surface of vertebrae and pushing against the spinal cord. Stenosis or osteophytes can compress the spinal cord and its blood vessels, impeding or choking off needed nutrients to the spinal cord cells; in effect, the cells starve to **death**.

With the death of these cells, the functions that they once performed are impaired. These functions may include conveying sensory information to the brain or transmitting the brain's commands to voluntary muscles. Pain is usually absent, but a person may experience leg numbness and an inability to make the legs move properly. Other symptoms can include clumsiness and weakness in the hands, stiffness and weakness in the legs, and spontaneous twitches in the legs. A person's ability to walk is affected, and a wide-legged, shuffling gait is sometimes adopted to compensate for the lack of sensation in the legs and the accompanying, realistic fear of falling. In very few cases, bladder control becomes a problem.

Diagnosis

Cervical spondylosis is often suspected based on the symptoms and their history. Careful neurological examination can help determine which nerve roots are involved, based on the location of the pain and numbness, and the pattern of weakness and changes in reflex responses. To confirm the suspected diagnosis, and to rule out other possibilities, imaging tests are ordered. The first test is an x ray. X rays reveal the presence of osteophytes, stenosis,

KEY TERMS

Alexander technique—A technique developed by Frederick Alexander that focuses on the variations in body posture, muscles, and breathing. Defects in these functions can lead to stress, nervous tension or possible loss of function.

Bone spur—Also called an osteophyte, it is an outgrowth or ridge that forms on a bone.

Cervical—Referring to structures within the neck.

Computed tomography myelography—This medical procedure combines aspects of computed tomography scanning and plain-film myelography. A CT scan is an imaging technique in which cross-sectional x rays of the body are compiled to create a three-dimensional image of the body's internal structures. Myelography involves injecting a water-soluble substance into the area around the spine to make it visible on x rays. In computed tomography myelography or CT myelography, the water-soluble substance is injected, but the imaging is done with a CT scan.

Disk—A ringlike structure that fits between the vertebrae in the spine to protect the bones, nerves, and blood vessels. The outer layer is a tough, fibrous tissue, and the inner core is composed of more elastic tissue.

Feldenkrais method—A therapy based on creating a good self image by correction and improvements of body movements.

Magnetic resonance imaging (MRI)—An imaging technique that uses a large circular magnet and radio waves to generate signals from atoms in the body. These signals are used to construct images of internal structures.

Myelopathy—A disorder in which the tissue of the spinal cord is diseased or damaged.

Orthosis—An external device, such as a splint or a brace, that prevents or assists movement.

Osteophyte—Also referred to as bone spur, it is an outgrowth or ridge that forms on a bone.

Radiculopathy—Sometimes referred to as a pinched nerve, it refers to compression of the nerve root—the part of a nerve between vertebrae. This compression causes pain to be perceived in areas to which the nerve leads.

Spine—A term for the backbone that includes the vertebrae, disks, and spinal cord as a whole.

Stenosis—A condition in which a canal or other passageway in the body is constricted.

Traction—A medical treatment that exerts a pulling or extending force. Used for cervical problems, it relieves pressure on structures between the vertebrae and muscular tension.

Vertebrae—The ringlike component bones of the spine.

constricted space between the vertebrae, and misalignment in the cervical spine—in short, an x ray confirms that a person has cervical spondylosis. To demonstrate that the condition is causing the symptoms, more details are needed. Other imaging tests, such as **magnetic resonance imaging** (MRI) and computed tomography **myelography**, help assess effects of cervical spondylosis on associated nerve tissue and blood vessels.

An MRI may be preferred, because it is a noninvasive procedure and does not require injecting a contrast medium as does computed tomography myelography. MRIs also have greater sensitivity for detecting disk problems and spinal cord involvement, and the test allows the physician to create images of a larger area from various angles. However, these images may not show enough detail about the vertebrae themselves. Computed tomography myelography yields a superior image of the bones involved in cervical spondylosis. Added benefits include that it takes less time to perform and tends to be less expensive than an MRI. A good diagnosis may be reached with either a computed tomography myelography or an MRI, but sometimes complementary information from both tests is necessary. Nerve conduction velocity, electromyogram (EMG), and/or somatosensory evoked potential testing may help to confirm which nerve roots are involved.

Treatment

When possible, conservative treatment of symptoms is preferred. Conservative treatment begins with rest—either restricting normal activities to a less strenuous level or bed rest for three to five days. If rest is not adequate to relieve symptoms, a cervical orthosis may be prescribed., such as a soft cervical collar or stiffer neck brace to restrict neck movement and shift some of the head's weight from the neck to the shoulders. Cervical

traction may also be suggested, either at home with the advice of a physical therapist or in a health-care setting.

Pain is treated with **nonsteroidal anti-inflammatory drugs**, such as **aspirin** or ibuprofen. If these drugs are ineffective, a short-term prescription for **corticosteroids** or **muscle relaxants** may be given. For chronic pain, tricyclic antidepressants can be prescribed. Although these drugs were developed to treat depression, they are also effective in treating pain. Once any pain is resolved, exercises to strengthen neck muscle and preserve flexibility are prescribed.

If the pain is severe, a short treatment of epidural corticosteroids may be prescribed with discretion. A corticosteroid such as prednisone can be combined with an anaesthetic and injected with a long needle into the space between the damaged disk and the covering of the nerve and spinal cord. Injection into the cervical epidural space relieves severe pain that is not managed with conventional treatment. Frequent use of this treatment is not medically recommended and is used only if the more conservative therapy is not effective.

If pain is continuous and does not respond to conservative treatment, surgery may be suggested. Surgery is usually not recommended for neck pain, but it may be necessary to address radiculopathy and myelopathy. Surgery is particularly recommended for people who have already developed moderate to severe symptoms of myelopathy, although age or poor health may prohibit that recommendation. The specific details of the surgery depend on the structures involved, but the overall goal is to relieve pressure on the nerve root, spinal cord, or blood vessels and to stabilize the spine.

Alternative treatment

Alternative therapy is not meant to replace conventional medical treatment, but it can be a useful adjunct. Its main roles are to relieve tension, manage pain, and strengthen neck and back muscles. Massage is one way to relieve tension, and **yoga** provides the additional benefit of strengthening muscles. **Chiropractic** and **acupuncture** have been reported to relieve the pain associated with disk problems, although great care needs to be taken to avoid exacerbating them. Practitioners of the **Alexander technique** or the **Feldenkrais method** can provide instruction on correct posture and **exercise** that may help prevent further symptoms. Vitamin and mineral supplementation along with herbal therapies and **homeopathy** can help build and rebalance the weakened structure.

Prognosis

The gradual progression of cervical spondylosis cannot be stopped; however, it doesn't always cause symptoms. For the individuals who do experience problems, conservative treatment is very effective in managing the symptoms. Nearly all people with neck pain, approximately 75% of persons with radiculopathy, and up to 50% of people with myelopathy find relief through therapy alone. For the remaining people with radiculopathy or myelopathy, surgery may be recommended. Surgery is deemed successful in 70–80% of cases.

Prevention

Since cervical spondylosis is part of the normal **aging** process, not much can be done to prevent it. It may be possible to ward off some or all of the symptoms by engaging in regular physical exercise and limiting occupational or recreational activities that place pressure on the head, neck, and shoulders. The best exercises for the health of the cervical spine are noncontact activities, such as swimming, walking, or yoga. Once symptoms have already developed, the emphasis is on symptom management rather than prevention.

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Julia Barrett

Cervicitis

Definition

Cervicitis is an inflammation of the cervix.

Description

Cervicitis is a inflammation of the cervix (the opening into the uterus). This inflammation can be chronic and may or may not have an identified cause.

KEY TERMS

Cryotherapy—Freezing the affected tissue.

Electrocoagulation—Using electrical current to cauterize the affected tissue.

LEEP—Loop Electrosurgical Excision Procedure.

Causes and symptoms

The most common cause of cervicitis is infection, either local or as a result of various **sexually transmitted diseases**, such as chlamydia or **gonorrhea**. Cervicitis can also be caused by birth control devices such as a cervical cap or diaphragm, or chemical exposure. Other risk factors include multiple sexual partners or cervical trauma following birth. In postmenopausal women, cervicitis is sometimes related to a lack of estrogen.

Although a woman may not notice any signs of infection, symptoms of cervicitis include the following:

- persistent unusual vaginal discharge
- abnormal bleeding, either between periods or following sexual intercourse
- painful sexual intercourse
- vaginal pain
- frequent need to urinate
- burning or **itching** in the vaginal area

Diagnosis

The standard method of diagnosing cervicitis is through a pelvic examination or a Pap smear. During the **pelvic exam**, the physician usually swabs the affected area, and then sends the tissue sample to a laboratory. The laboratory tries to identify the specific organism responsible for causing the cervicitis. A biopsy to take a sample of tissue from the affected area is sometimes required in order to rule out **cancer**. **Colposcopy**, a procedure used to look at the cervix under a microscope, may also be used to rule out cancer.

Treatment

The first course of treatment for cervicitis is usually **antibiotics**. If these medicines do not cure the cervicitis, other treatment options include:

- Loop Electrosurgical Excision Procedure (LEEP)
- cryotherapy
- electrocoagulation
- laser treatment

Prognosis

Cervicitis will usually be cured when the course of therapy is complete. Severe cases, however, may last for a few months, even after the therapy is complete. If the cervicitis was caused by a sexually transmitted disease, both partners should be treated with medication.

Prevention

Practicing safe sexual behavior, such as monogamy, is one way of lowering the prevalence of cervicitis. In addition, women who began sexual activity at a later age have been shown to have a lower incidence of cervicitis. Another recommendation is to use a latex **condom** consistently during intercourse. If the cervicitis is caused by any sexually transmitted disease, the patient is advised to notify all sexual partners.

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American College of Obstetricians and Gynecologists. 409 12th Street, SW P.O. Box 96920, Washington, DC 20090-6920. (202) 863-2518. <http://www.acog.org>.

Kim Sharp, M.Ln.

Cesarean section

Definition

A cesarean section is a surgical procedure in which incisions are made through a woman's abdomen and uterus to deliver her baby.

This baby is being delivered by cesarean section. *(Photograph by John Smith, Custom Medical Stock Photo.)*

Purpose

Cesarean sections, also called c-sections, are performed whenever abnormal conditions complicate labor and vaginal delivery, threatening the life or health of the mother or the baby. The procedure is performed in the United States on nearly one of every four babies delivered—more than 900,000 babies each year. The procedure is often used in cases where the mother has had a previous c-section. Dystocia, or difficult labor, is the other common cause of c-sections.

Difficult labor is commonly caused by one of the three following conditions: abnormalities in the mother's birth canal; abnormalities in the position of the fetus; or abnormalities in the labor, including weak or infrequent contractions.

Another major factor is fetal distress, a condition where the fetus is not getting enough oxygen. Fetal brain damage can result from oxygen deprivation. Fetal distress is often related to abnormalities in the position of the fetus or abnormalities in the birth canal, causing reduced blood flow through the placenta. Other conditions also can make c-section advisable, such as vaginal herpes, **hypertension,** and diabetes in the mother.

Precautions

There are several ways that obstetricians and other doctors diagnose conditions that may make a c-section necessary. Ultrasound testing reveals the positions of the baby and the placenta and may be used to estimate the baby's size and gestational age. Fetal heart monitors, in use since the 1970s, transmit any signals of fetal distress. Oxygen deprivation may be determined by checking the amniotic fluid for meconium (feces)—a lack of oxygen causes an unborn baby to defecate. Oxygen deprivation may also be determined by testing the pH of a blood sample taken from the baby's scalp; a pH of 7.25 or higher is normal, between 7.2 and 7.25 is suspicious, and below 7.2 is a sign of trouble.

When a c-section is being considered because labor is not progressing, the mother should first be encouraged to walk around to stimulate labor. Labor may also be stimulated with the drug oxytocin.

When a c-section is being considered because the baby is in a breech position, the doctor may first attempt to reposition the baby; this is called external cephalic version. The doctor may also try a vaginal breech delivery, depending on the size of the mother's pelvis, the size

KEY TERMS

Breech presentation—The condition in which the baby enters the birth canal with its buttocks or feet first.

Cephalopelvic disproportion (CPD)—The condition in which the baby's head is too large to fit through the mother's pelvis.

Classical incision—In a cesarean section, an incision made vertically along the uterus; this kind of incision makes a larger opening but also creates more bleeding, a greater chance of infection, and a weaker scar.

Dystocia—Failure to progress in labor, either because the cervix will not dilate (expand) further or (after full dilation) the head does not descend through the mother's pelvis.

Low transverse incision—Incision made horizontally across the lower end of the uterus; this kind of incision is preferred for less bleeding and stronger healing.

Placenta previa—The placenta totally or partially covers the cervix, preventing vaginal delivery.

Placental abruption—Separation of the placenta from the uterine wall before the baby is born, cutting off blood flow to the baby.

Prolapsed cord—The umbilical cord is pushed into the vagina ahead of the baby and becomes compressed, cutting off blood flow to the baby.

Respiratory distress syndrome (RDS)—Difficulty breathing, found in infants with immature lungs.

Transverse presentation—The baby is laying sideways across the cervix instead of head first.

VBAC—Vaginal birth after cesarean.

of the baby, and the type of breech position the baby is in. However, a c-section is safer than a vaginal delivery when the baby is 8 lb (3.6 kg) or larger, in a breech position with the feet crossed, or in a breech position with the head hyperextended.

A woman should receive regular prenatal care and be able to alert her doctor to the first signs of trouble. Once labor begins, she should be encouraged to move around and to urinate. The doctor should be conservative in diagnosing dystocia (nonprogressive labor) and fetal distress, taking a position of "watchful waiting" before deciding to operate.

Description

The most common reason that a cesarean section is performed (in 35% of all cases, according to the United States Public Health Service) is that the woman has had a previous c-section. The "once a cesarean, always a cesarean" rule originated when the classical uterine incision was made vertically; the resulting scar was weak and had a risk of rupturing in subsequent deliveries. Today, the incision is almost always made horizontally across the lower end of the uterus (this is called a "low transverse incision"), resulting in reduced blood loss and a decreased chance of rupture. This kind of incision allows many women to have a vaginal birth after a cesarean (VBAC).

The second most common reason that a c-section is performed (in 30% of all cases) is difficult **childbirth** due to nonprogressive labor (dystocia). Uterine contractions may be weak or irregular, the cervix may not be dilating, or the mother's pelvic structure may not allow adequate passage for birth. When the baby's head is too large to fit through the pelvis, the condition is called cephalopelvic disproportion (CPD).

Another 12% of c-sections are performed to deliver a baby in a breech presentation: buttocks or feet first. Breech presentation is found in about 3% of all births.

In 9% of all cases, c-sections are performed in response to fetal distress. Fetal distress refers to any situation that threatens the baby, such as the umbilical cord getting wrapped around the baby's neck. This may appear on the fetal heart monitor as an abnormal heart rate or rhythm.

The remaining 14% of c-sections are indicated by other serious factors. One is prolapse of the umbilical cord: the cord is pushed into the vagina ahead of the baby and becomes compressed, cutting off blood flow to the baby. Another is **placental abruption**: the placenta separates from the uterine wall before the baby is born, cutting off blood flow to the baby. The risk of this is especially high in multiple births (twins, triplets, or more). A third factor is **placenta previa**: the placenta covers the cervix partially or completely, making vaginal delivery impossible. In some cases requiring c-section, the baby is in a transverse position, lying horizontally across the pelvis, perhaps with a shoulder in the birth canal.

The mother's health may make delivery by c-section the safer choice, especially in cases of maternal diabetes,

hypertension, **genital herpes**, Rh blood incompatibility, and preeclampsia (high blood pressure related to **pregnancy**).

Preparation

When a c-section becomes necessary, the mother is prepped for surgery. A catheter is inserted into her bladder and an intravenous (IV) line is inserted into her arm. Leads for monitoring the mother's heart rate, rhythm, and blood pressure are attached. In the operating room, the mother is given anesthesia—usually a regional anesthetic (epidural or spinal), making her numb from below her breasts to her toes. In some cases, a general anesthetic will be administered. Surgical drapes are placed over the body, except the head; these drapes block the direct view of the procedure.

The abdomen is washed with an anti-bacterial solution and a portion of the pubic hair may be shaved. The first incision opens the abdomen. Infrequently, it will be vertical from just below the navel to the top of the pubic bone, or more commonly, it will be a horizontal incision across and above the pubic bone (informally called a "bikini cut").

The second incision opens the uterus. In most cases a transverse incision is made. This is the favored type because it heals well and makes it possible for a woman to attempt a vaginal delivery in the future. The classical incision is vertical. Because it provides a larger opening than a low transverse incision, it is used in the most critical situations, such as placenta previa. However, the classical incision causes more bleeding, a greater risk of abdominal infection, and a weaker scar, so the low transverse incision is preferred.

Once the uterus is opened, the amniotic sac is ruptured and the baby is delivered. The time from the initial incision to birth is typically five minutes.

Once the umbilical cord is clamped and cut, the newborn is evaluated. The placenta is removed from the mother, and her uterus and abdomen are stitched closed (surgical staples may be used instead in closing the outermost layer of the abdominal incision). From birth through suturing may take 30–40 minutes. Thus the entire surgical procedure may be performed in less than one hour.

Aftercare

A woman who undergoes a c-section requires both the care given to any new mother and the care given to any patient recovering from major surgery. She should be offered **pain** medication that does not interfere with breastfeeding. She should be encouraged to get out of bed and walk around eight to 24 hours after surgery to stimulate circulation (thus avoiding the formation of blood clots) and bowel movement. She should limit climbing stairs to once a day, and avoid lifting anything heavier than the baby. She should nap as often as the baby sleeps, and arrange for help with the housework, meals, and care of other children. She may resume driving after two weeks, although some doctors recommend waiting for six weeks, the typical recovery period from major surgery.

Risks

Because a c-section is a surgical procedure, it carries more risk to both the mother and the baby. The maternal **death** rate is less than 0.02%, but that is four times the maternal death rate associated with vaginal delivery. However, many women have a c-section for serious medical problems. The mother is at risk for increased bleeding (because a c-section may result in twice the blood loss of a vaginal delivery) from the two incisions, the placental attachment site, and possible damage to a uterine artery. Complications occur in less than 10% of cases. The mother may develop infection of either incision, the urinary tract, or the tissue lining the uterus (endometritis). Less commonly, she may receive injury to the surrounding organs, like the bladder and bowel. When a general anesthesia is used, she may experience complications from the anesthesia. Very rarely, she may develop a wound hematoma at the site of either incision or other blood clots leading to pelvic **thrombophlebitis** (inflammation of the major vein running from the pelvis into the leg) or a pulmonary embolus (a blood clot lodging in the lung).

Normal results

The after-effects of a c-section vary, depending on the woman's age, physical fitness, and overall health. Following this procedure, a woman commonly experiences gas pains, incision pain, and uterine contractions—which are also common in vaginal delivery. Her hospital stay may be two to four days. Breastfeeding the baby is encouraged, taking care that it is in a position that keeps the baby from resting on the mother's incision. As the woman heals, she may gradually increase appropriate exercises to regain abdominal tone. Full recovery may be seen in four to six weeks.

The prognosis for a successful vaginal birth after a cesarean (VBAC) may be at least 75%, especially when the c-section involved a low transverse incision in the uterus and there were no complications during or after delivery.

Abnormal results

Of the hundreds of thousands of women in the United States who undergo a c-section each year, about 500

die from serious infections, hemorrhaging, or other complications. These deaths may be related to the health conditions that made the operation necessary, and not simply to the operation itself.

Undergoing a c-section may also inflict psychological distress on the mother, beyond hormonal mood swings and **postpartum depression** ("baby blues"). The woman may feel disappointment and a sense of failure for not experiencing a vaginal delivery. She may feel isolated if the father or birthing coach is not with her in the operating room, or if she is treated by an unfamiliar doctor rather than by her own doctor or midwife. She may feel helpless from a loss of control over labor and delivery with no opportunity to actively participate. To overcome these feelings, the woman must understand why the c-section was necessary. She must accept that she couldn't control the unforeseen events that made the c-section the optimum means of delivery, and recognize that preserving the health and safety of both her and her child was more important than her delivering vaginally. Women who undergo a c-section should be encouraged to share their feelings with others. Hospitals can often recommend support groups for such mothers. Women should also be encouraged to seek professional help if negative emotions persist.

Resources

ORGANIZATIONS

American Academy of Family Physicians. 8880 Ward Parkway, Kansas City, MO 64114. (816) 333-9700. <http://www.aafp.org>.

Childbirth.Org. <http://www.childbirth.org>.

International Cesarean Awareness Network. 1304 Kingsdale Ave., Redondo Beach, CA 90278. (310) 542-6400.

March of Dimes Birth Defects Foundation. 1275 Mamaroneck Ave., White Plains, NY 10605. (914) 428-7100. <http://www.modimes.org>.

National Institute of Child Health and Human Development. Bldg 31, Room 2A32, MSC 2425, 31 Center Drive, Bethesda, MD 20892-2425. (800) 505-2742. <http://www.nichd.nih.gov/sids/sids.htm>.

United States Department of Health and Human Services. 200 Independence Avenue SW, Washington DC 20201. (202) 619-0257. <http://www.hhs.gov>.

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Bethany Thivierge

Cestodiasis *see* **Tapeworm diseases**

CFS *see* **Chronic fatigue syndrome**

CGD *see* **Chronic granulomatous disease**

Chagas' disease

Definition

Chagas' disease is named after Dr. Carlos Chagas who first found the organism in the early 1900s. It involves damage to the nerves that control the heart, digestive and other organs, and eventually leads to damage to these organs. Worldwide, Chagas' disease affects over 15 million persons, and kills 50,000 each year. Researchers believe that the parasite that causes the disease is only found in the Americas.

Description

When a person is infected with Chagas' disease, the parasite known as *Trypanosoma cruzi* first causes a mild, short-lived period of "acute" illness; then after a long period without symptoms, the effects of the infection begin to appear. The heart, esophagus, and colon are most frequently involved. These organs become unable to contract properly, and begin to stretch or dilate.

Causes and symptoms

T. cruzi is carried by insects or bugs known as reduviid or "kissing bugs." These insects are very common in Central and South America where they inhabit poorly constructed houses and huts. The insects deposit their waste material, exposing inhabitants to the parasites. The parasites then enter the body by way of a cut or via the eyes or mouth. *T. cruzi* can also be transmitted by blood **transfusion**. Eating uncooked, contaminated food or breastfeeding can also transmit the disease. The reduviids, in turn, become infected with the parasite by biting infected animals and humans.

There are three phases related to infection:

- Acute phase lasts about two months, with non-specific symptoms of low grade **fever**, **headache**, **fatigue**, and enlarged liver or spleen.
- Indeterminate phase lasts 10–20 years, during which time no symptoms occur, but the parasites are reproducing in various organs.
- Chronic phase is the stage when symptoms related to damage of major organs (heart, esophagus, colon) begin.

In the chronic phase, irregularities of heart rhythm, **heart failure**, and blood clots cause weakness, **fainting**, and even sudden **death**.

KEY TERMS

Achalasia—An esophageal disease of unknown cause, in which the lower sphincter or muscle is unable to relax normally, and leads to the accumulation of material within the esophagus.

Endoscopy—Exam using an endoscope (a thin flexible tube which uses a lens or miniature camera to view various areas of the gastrointestinal tract). When the procedure is performed to examine certain organs such as the bile ducts or pancreas, the organs are not viewed directly, but rather indirectly through the injection of x ray.

Parasite—An organism that lives on or in another and takes nourishment (food and fluids) from that organism.

Regurgitation—Flow of material back up the esophagus and into the throat or lungs.

Esophageal symptoms are related to difficulty with swallowing and chest **pain**. Because the esophagus does not empty properly, food regurgitates into the lungs causing **cough**, **bronchitis**, and repeated bouts of **pneumonia**. Inability to eat, weight loss, and **malnutrition** become a significant factor in affecting survival.

Involvement of the large intestine (colon) causes **constipation**, distention, and abdominal pain.

Diagnosis

The best way to diagnose acute infection is to identify the parasites in tissue or blood. Occasionally it is possible to culture the organism from infected tissue, but this process usually requires too much time to be of value. In the chronic phase, antibody levels can be measured. Efforts to develop new, more accurate tests are ongoing.

Treatment

In most cases treatment of symptoms is all that is possible. Present medications can reduce the duration and severity of an acute infection, but are only 50% effective, at best, in eliminating the organisms.

Cardiac effects are managed with **pacemakers** and medications. Esophageal complications require either endoscopic or surgical methods to improve esophageal emptying, similar to those used to treat the disorder known as **achalasia**. Constipation is treated by increasing fiber and bulk **laxatives**, or removal of diseased portions of the colon.

Prognosis

Those patients with gastrointestinal complications often respond to some form of treatment. Cardiac problems are more difficult to treat, particularly since transplant would rekindle infection.

Prevention

Visitors traveling to areas of known infection should avoid staying in mud, adobe, or similar huts. Mosquito nets and insect repellents are useful in helping to avoid contact with the bugs. Blood screening is not always effective in many regions where infection is common. It is necessary to carefully screen people who have emigrated from Central and South America before they make blood donations.

Resources

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David Kaminstein, MD

Chalazion *see* **Eyelid disorders**

Chancroid

Definition

Chancroid is a sexually transmitted disease caused by a bacterial infection that is characterized by painful sores on the genitals.

Description

Chancroid is an infection of the genitals that is caused by the bacterium *Haemophilus ducreyi*. Chancroid is a sexually transmitted disease, which means that it is spread from person to person almost always by sexual contact. However, there have been a few cases in which healthcare providers have become infected through contact with infected patients.

Common locations for chancroid sores (ulcers) in men are the shaft or head of the penis, foreskin, the groove behind the head of the penis, the opening of the penis, and the scrotum. In women, common locations are the labia majora (outer lips), labia minora (inner lips), perianal area (area around the anal opening), and inner thighs. It is rare for the ulcer(s) to be on the vaginal walls or cervix. In about 50% of the patients with chancroid, the infection spreads to either or both of the lymph nodes in the groin.

Chancroid is most commonly found in developing and third world countries. In the United States, the most common cause of genital ulcers is **genital herpes**, followed by **syphilis**, and then chancroid. As of 1997, there were fewer than 1,500 cases of chancroid in the United States per year and it occurred primarily in African Americans, Hispanic Americans, and Native Americans. There are occasional localized outbreaks of chancroid in the United States. In addition, the practice of exchanging sex for drugs has lead to a link between crack **cocaine** use and chancroid.

Even though the incidence of chancroid in the United States decreased in the 1990s, there is an alarming connection between chancroid and human **immunodeficiency** virus (HIV) infection. HIV causes **AIDS** (acquired immunodeficiency syndrome) and is easily spread from person to person through chancroid ulcers. Uncircumcised men with chancroid ulcers have a 48% risk of acquiring HIV from sexual contact. Women with chancroid ulcers are also at a greater risk of being infected with HIV during sexual contact. Genital ulcers seem to act as doorways for HIV to enter and exit.

Causes and symptoms

Haemophilus ducreyi is spread from person to person by vaginal, anal, and oral sexual contact. Uncircumcised men are about three times more likely than circumcised men to become infected following exposure to *Haemophilus ducreyi*. Having unprotected sex, exchanging sex for drugs, and having unprotected sex with a prostitute are other risk factors. Many cases of chancroid in the United States occur in persons who had traveled to countries where the disease is more common.

A close-up view of a chancroid specimen. *(Custom Medical Stock Photo. Reproduced by permission.)*

Chancroid occurs when *Haemophilus ducreyi* penetrates the skin through an injury, like a scratch or cut. Once past the skin surface, the warmth, moisture, and nutrients allow bacteria to grow rapidly. The first sign of chancroid is a small, red papule that occurs within three to seven days following exposure to the bacteria, but may take up to one month. Usually within one day, the papule becomes an ulcer. The chancroid ulcer is painful, bleeds easily, drains a grey or yellowish pus, and has sharply defined, ragged edges. They can vary in size from an eighth of an inch to two inches in diameter. Men usually have only one ulcer, but women often have four or more. Sometimes "kissing" ulcers occur when one ulcer spreads the bacterial infection to an opposite skin surface. For example, kissing ulcers can form on the lips of the labia majora. Alternatively, women may not have any external sores but may experience painful urination, intercourse, and/or bowel movements and may have a vaginal discharge or rectal bleeding.

Signs that the infection has spread to the lymph node appear about one week after the formation of the genital ulcer. Lymph nodes are small organs in the lymphatic system that filter waste materials from nearly every organ in the body. This lymph node infection is called "lymphadenitis" and the swollen, painful lymph node is called a "bubo." The bubo, which appears as a red, spherical lump, may burst through the skin, releasing a thick pus and forming another ulcer.

Diagnosis

Chancroid may be diagnosed and treated by urologists (urinary tract doctors for men), gynecologists (for women), and infectious disease specialists. Part of the diagnosis of chancroid involves ruling out genital herpes and syphilis because genital ulcers are also symptoms of these diseases. The appearance of these three diseases

KEY TERMS

Bubo—A tender, swollen lymph node in the groin that may follow a chancroid ulcer.

Groin—The region of the body that lies between the abdomen and the thighs.

can be close enough to be confusing. However, the presence of a pus-filled lump in the groin of a patient with a genital ulcer is highly specific for chancroid.

For a clear-cut diagnosis of chancroid, *Haemophilus ducreyi* must be isolated from the ulcer. To do this, a sterile cotton swab is wiped over the ulcer to obtain a pus sample. In the laboratory, the sample is put into special media and placed in an incubator. *Haemophilus ducreyi* takes from two to five days to grow in the laboratory. In addition, the pus may be examined under the microscope to see which bacteria are in the ulcer. A sample of the pus may also be tested to see if the herpes virus is present. A blood sample will probably be taken from the patient's arm to test for the presence of antibodies to the bacteria that causes syphilis.

Treatment

The only treatment for chancroid is **antibiotics** given either once or for several days. Antibiotics taken by mouth for one to two weeks include erythromycin (E-Mycin, Ery-Tab), amoxicillin plus clavulanic acid (Augmentin), co-trimoxazole (Bactrim, Septra), or ciprofloxacin (Cipro). Antibiotics given in one dose include ceftriaxone (Rocephin), spectinomycin (Trobicin), co-trimoxazole, or ofloxacin (Floxin).

The ulcer(s) may be cleaned and soaked to reduce the swelling. Salt solution dressings may be applied to the ulcer(s) to reduce the spread of the bacteria and prevent additional ulcers. A serious infection of the foreskin may require **circumcision**. Pus would be removed from infected lymph nodes by using a needle and syringe. Very large buboes may require surgical drainage.

Prognosis

Without treatment, chancroid may either go away quickly or patients may experience the painful ulcers for many months. A complete cure is obtained with antibiotic treatment. Severe ulcers may cause permanent scars. Severe scarring of the foreskin may require circumcision. Urethral fistulas (abnormal passageways from the urine tube to the skin) may occur and requires corrective surgery.

Prevention

The best prevention for chancroid is to use a **condom** during sexual intercourse. Chancroid can also be prevented by abstinence (avoidance of any sexual contact) and by being in a monogamous relationship with a disease-free partner. To prevent the spread of chancroid, it is important that all sexual contacts of the patient are identified and treated.

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Belinda Rowland, PhD

Change of life *see* **Menopause**

Character disorders *see* **Personality disorders**

Charcoal, activated

Definition

Activated charcoal is a fine, black, odorless, and tasteless powder. It is made from wood or other materials that have been exposed to very high temperatures in an airless environment. It is then treated, or activated, to increase its ability to adsorb by reheating with oxidizing gas or other chemicals to break it into a very fine powder. Activated charcoal is pure carbon specially processed to make it highly adsorbent of particles and gases in the body's digestive system.

Activated charcoal has often been used since ancient times to cure a variety of ailments including **poisoning**.

Its healing effects have been well documented since as early as 1550 B.C. by the Egyptians. However, charcoal was almost forgotten until 15 years ago when it was rediscovered as a wonderful oral agent to treat most overdoses and toxins.

Description

Activated charcoal's most important use is for treatment of poisoning. It helps prevent the absorption of most poisons or drugs by the stomach and intestines. In addition to being used for most swallowed poisons in humans, charcoal has been effectively used in dogs, rabbits, rats, and other animals, as well. It can also adsorb gas in the bowels and has been used for the treatment of gas or **diarrhea**. Charcoal's other uses such as treatment of viruses, bacteria, bacterial toxic byproducts, snake venoms and other substances by adsorption have not been supported by clinical studies. By adding water to the powder to make a paste, activated charcoal can be used as an external application to alleviate **pain** and **itching** from **bites and stings**.

Poisons and drug overdoses

It is estimated that one million children accidentally overdose on drugs mistaken as candies or eat, drink, or inhale poisonous household products each year. Infants and toddlers are at the greatest risk for accidental poisoning. Activated charcoal is one of the agents most commonly used for these cases. It can absorb large amounts of poisons quickly. In addition, it is non-toxic, may be stored for a long time, and can be conveniently administered at home. Charcoal works by binding to irritating or toxic substances in the stomach and intestines. This prevents the toxic drug or chemical from spreading throughout the body. The activated charcoal with the toxic substance bound to it is then excreted in the stool without harm to the body. When poisoning is suspected the local poison control center should be contacted for instructions. They may recommend using activated charcoal, which should be available at home so that it can be given to the poisoned child or pet immediately. For severe poisoning, several doses of activated charcoal may be needed.

Intestinal disorders

In the past, activated charcoal was a popular remedy for gas. Even before the discovery of America by Europeans, Native Americans used powdered charcoal mixed with water to treat an upset stomach. Now charcoal is being rediscovered as an alternative treatment for this condition. Activated charcoal works like a sponge. Its huge surface area is ideal for soaking up different substances, including gas. In one study, people taking activated charcoal after eating a meal with high gas-producing foods did not produce more gas than those who did not have these foods. Charcoal has also been used to treat other intestinal disorders such as diarrhea, **constipation**, and cramps. There are few studies to support these uses and there are also concerns that frequent use of charcoal may decrease absorption of essential nutrients, especially in children.

KEY TERMS

Antidote—A remedy to counteract a poison or injury.

Adsorption—The binding of a chemical (e.g., drug or poison) to a solid material such as activated charcoal or clay.

Other uses

Besides being a general antidote for poisons or remedy for gas, activated charcoal has been used to treat other conditions as well. Based on its ability to adsorb or bind to other substances, charcoal has been effectively used to clean skin **wounds** and to adsorb waste materials from the gastrointestinal tract. In addition, it has been used to adsorb snake venoms, viruses, bacteria, and harmful materials excreted by bacteria or fungi. However, because of lack of scientific studies, these uses are not recommended. Activated charcoal, when used together with other remedies such as aloe vera, acidophilus, and psyllium, helps to keep symptoms of **ulcerative colitis** under control. While charcoal shows some anti-aging activity in rats, it is doubtful if it can do the same for humans.

Recommended dosage

For poisoning

Activated charcoal is available without prescription. However, in case of accidental poisoning or **drug overdose** an emergency poison control center, hospital emergency room, or doctor's office should be called for advice. In case that both syrup of **ipecac** and charcoal are recommended for treatment of the poison, ipecac should be given first. Charcoal should not be given for at least 30 minutes after ipecac or until vomiting from ipecac stops. Activated charcoal is often mixed with a liquid before being swallowed or put into the tube leading to the stomach. Activated charcoal is available as 1.1 oz (33 ml) liquid bottles. It is also available in 0.5 oz (15 ml) container sizes and as slurry of charcoal pre-mixed in water or as a container in which water or soda pop is added. Keeping activated charcoal at home is a

good idea so that it can be taken immediately when needed for treatment of poisoning.

For acute poisoning, the dosage is as follows:

- Infants (under 1 year of age): 1 g/kg.
- Children (1–12 years of age): 15–30 g or 1–2 g/kg with at least 8 oz of water.
- Adults: 30–100 g or 1–2 g/kg with at least 8 oz of water.

For diarrhea or gas

A person can take charcoal tablets or capsules with water or sprinkle the content onto foods. The dosage for treatment of gas or diarrhea in adults is 520–975 mg after each meal and up to 5 g per day.

Precautions

Parents should keep activated charcoal on hand in case of emergencies.

Do not give charcoal together with syrup of ipecac. The charcoal will adsorb the ipecac. Charcoal should be taken 30 minutes after ipecac or after the vomiting from ipecac stops.

Some activated charcoal products contain sorbitol. Sorbitol is a sweetener as well as a laxative, therefore, it may cause severe diarrhea and vomiting. These products should not be used in infants.

Charcoal may interfere with the absorption of medications and nutrients such as **vitamins** or **minerals**. For uses other than for treatment of poisoning, charcoal should be taken two hours after other medications.

Charcoal should not be used to treat poisoning caused by corrosive products such as lye or other strong acids or petroleum products such as gasoline, kerosene, or cleaning fluids. Charcoal may make the condition worse and delay diagnosis and treatment. In addition, charcoal is also not effective if the poison is lithium, cyanide, iron, ethanol, or methanol.

Parents should not mix charcoal with chocolate syrup, sherbet, or ice cream, even though it may make charcoal taste better. These foods may prevent charcoal from working properly.

Activated charcoal may cause swelling or pain in the stomach. A doctor should be notified immediately. It has been known to cause problems in people with intestinal bleeding, blockage or those people who have had recent surgery. These patients should talk to their doctor before using this product.

Charcoal may be less effective in people with slow digestion.

Charcoal should not be given for more than three or four days for treatment of diarrhea. Continuing for longer periods may interfere with normal **nutrition**.

Charcoal should not be used in children under three years of age to treat diarrhea or gas.

Activated charcoal should be kept out of reach of children.

Side effects

Charcoal may cause constipation when taken for overdose or accidental poisoning. A laxative should be taken after the crisis is over.

Activated charcoal may cause the stool to turn black. This is to be expected.

Pain or swelling of the stomach may occur. A doctor should be consulted.

Interactions

Activated charcoal should not be mixed together with chocolate syrup, ice cream or sherbet. These foods prevent charcoal from working properly.

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Mai Tran

Charcot Marie Tooth disease

Definition

Charcot Marie Tooth disease (CMT) is the name of a group of inherited disorders of the nerves in the peripheral nervous system (nerves throughout the body

that communicate motor and sensory information to and from the spinal cord) causing weakness and loss of sensation in the limbs.

Description

CMT is named for the three neurologists who first described the condition in the late 1800s. It is also known as hereditary motor and sensory neuropathy, and is sometimes called peroneal muscular atrophy, referring to the muscles in the leg that are often affected. The age of onset of CMT can vary anywhere from young childhood to the 50s or 60s. Symptoms typically begin by the age of 20. For reasons yet unknown, the severity in symptoms can also vary greatly, even among members of the same family.

Although CMT has been described for many years, it is only since the early 1990s that the genetic cause of many of the types of CMT have become known. Therefore, knowledge about CMT has increased dramatically within a short time.

The peripheral nerves

CMT affects the peripheral nerves, those groups of nerve cells carrying information to and from the spinal cord. CMT decreases the ability of these nerves to carry motor commands to muscles, especially those furthest from the spinal cord located in the feet and hands. As a result, the muscles connected to these nerves eventually weaken. CMT also affects the sensory nerves that carry information from the limbs to the brain. Therefore people with CMT also have sensory loss. This causes symptoms such as not being able to tell if something is hot or cold or difficulties with balance.

There are two parts of the nerve that can be affected in CMT. A nerve can be likened to an electrical wire, in which the wire part is the axon of the nerve and the insulation surrounding it is the myelin sheath. The job of the myelin is to help messages travel very fast through the nerves. CMT is usually classified depending on which part of the nerve is affected. People who have problems with the myelin have CMT type 1 and people who have abnormalities of the axon have CMT type 2.

Specialized testing of the nerves, called nerve conduction testing (NCV), can be performed to determine if a person has CMT1 or CMT2. These tests measure the speed at which messages travel through the nerves. In CMT1, the messages move too slowly, but in CMT2 the messages travel at the normal speed.

Demographics

CMT has been diagnosed in people from all over the world. It occurs in approximately one in 2,500 people, which is about the same incidence as **multiple sclerosis**. It is the most common type of inherited neurologic condition.

Signs and symptoms

CMT is caused by changes (mutations) in any one of a number of genes that carry the instructions to make the peripheral nerves. Genes contain the instructions for how the body grows and develops before and after a person is born. There are probably at least 15 different genes that can cause CMT. However, as of early 2001, many have not yet been identified.

CMT types 1 and 2 can be broken down into subtypes based upon the gene that is causing CMT. The subtypes are labeled by letters, so there is CMT1A, CMT1B, etc. Therefore, the gene with a mutation that causes CMT1A is different from that that causes CMT1B.

Types of CMT

CMT1A. The most common type of CMT is called CMT1A. It is caused by a mutation in a gene called peripheral myelin protein 22 (PMP22) located on chromosome 17. The job of this gene is to make a protein (PMP22) that makes up part of the myelin. In most people who have CMT, the mutation that causes the condition is a duplication (doubling) of the PMP22 gene. Instead of having two copies of the PMP22 gene (one on each chromosome) there are three copies. It is not known how this extra copy of the PMP22 gene causes the observed symptoms. A small percentage of people with CMT1A do not have a duplication of the PMP22 gene, but rather have a point mutation in the gene. A point mutation is like a typo in the gene that causes it to work incorrectly.

HEREDITARY NEUROPATHY WITH LIABILITY TO PRESSURE PALSIES (HNPP). HNPP is a condition that is also caused by a mutation in the PMP22 gene. The mutation is a deletion. Therefore, there is only one copy of the PMP22 gene instead of two. People who have HNPP may have some of the signs of CMT. However, they also have episodes where they develop weakness and problems with sensation after compression of certain pressure points such as the elbows or knee. Often these symptoms will resolve after a few days or weeks, but sometimes they are permanent.

CMT1B. Another type of CMT, called CMT1B, is caused by a mutation in a gene called myelin protein zero (MPZ) located on chromosome 1. The job of this gene is to make the layers of myelin stick together as they are wrapped around the axon. The mutations in this gene are point mutations because they involve a change (either deletion, substitution, or insertion) at one specific component of a gene.

CMTX. Another type of CMT, called CMTX, is usually considered a subtype of CMT1 because it affects the myelin, but it has a different type of inheritance than type 1 or type 2. In CMTX, the CMT-causing gene is located on the X chromosome and is called connexin 32 (Cx32). The job of this gene is to code for a class of protein called connexins that form tunnels between the layers of myelin.

CMT2. There are at least five different genes that can cause CMT type 2. Therefore, CMT2 has subtypes A, B, C, D and E. As of early 2001, scientists have narrowed in on the location of most of the CMT2 causing genes. However, the specific genes and the mutations have not yet been found for most types. Very recently, the gene for CMT2E has been found. The gene is called neurofilament-light (NF-L). Because it has just been discovered, not much is known about how mutations in this gene cause CMT.

CMT3. In the past a condition called Dejerine-Sottas disease was referred to as CMT3. This is a severe type of CMT in which symptoms begin in infancy or early childhood. It is now known that this is not a separate type of CMT and in fact people who have onset in infancy or early childhood often have mutations in the PMP22 or MPZ genes.

CMT4. CMT4 is a rare type of CMT in which the nerve conduction tests have slow response results. However, it is classified differently from CMT1 because it is passed through families by a different pattern of inheritance. There are five different subtypes and each has only been described in a few families. The symptoms in CMT4 are often severe and other symptoms such as deafness may be present. There are three different genes that have been associated with CMT4 as of early 2001. They are called MTMR2, EGR2, and NDRG1. More research is required to understand how mutations in these genes cause CMT.

Inheritance

CMT1A and 1B, HNPP, and all of the subtypes of CMT2 have autosomal dominant inheritance. Autosomal refers to the first 22 pairs of chromosomes that are the same in males and females. Therefore, males and females are affected equally in these types. In a dominant condition, only one gene of a pair needs to have a mutation in order for a person to have symptoms of the condition. Therefore, anyone who has these types has a 50%, or one in two, chance of passing CMT on to each of their children. This chance is the same for each **pregnancy** and does not change based on previous children.

CMTX has X-linked inheritance. Since males only have one X chromosome, they only have one copy of the Cx32 gene. Thus, when a male has a mutation in his Cx32 gene, he will have CMT. However, females have two X chromosomes and therefore have two copies of the Cx32 gene. If they have a mutation in one copy of their Cx32 genes, they will only have mild to moderate symptoms of CMT that may go unnoticed. This is because their normal copy of the Cx32 gene does make normal myelin.

Females pass on one or the other of their X chromosomes to their children—sons or daughters. If a woman with a Cx32 mutation passes her normal X chromosome, she will have an unaffected son or daughter who will not pass CMT on to his or her children. If the woman passes the chromosome with Cx32 mutation on she will have an affected son or daughter, although the daughter will be mildly affected or have no symptoms. Therefore, a woman with a Cx32 mutation has a 50%, or a one in two, chance of passing the mutation to her children: a son will be affected, and a daughter may only have mild symptoms.

When males pass on an X chromosome, they have a daughter. When they pass on a Y chromosome, they have a son. Since the Cx32 mutation is on the X chromosome, a man with CMTX will always pass the Cx32 mutation on to his daughters. However, when he has a son, he passes on the Y chromosome, and therefore the son will not be affected. Therefore, an affected male passes the Cx32 gene mutation on to all of his daughters, but to none of his sons.

CMT4 has autosomal recessive inheritance. Males and females are equally affected. In order for a person to have CMT4, they must have a mutation in both of their CMT-causing genes—one inherited from each parent. The parents of an affected person are called carriers. They have one normal copy of the gene and one copy with a mutation. Carriers do not have symptoms of CMT. Two carrier parents have a 25%, or one in four, chance of passing CMT on to *each* of their children.

The onset of symptoms is highly variable, even among members of the same family. Symptoms usually progress very slowly over a person's lifetime. The main problems caused by CMT are weakness and loss of sensation mainly in the feet and hands. The first symptoms are usually problems with the feet such as high arches and problems with walking and running. Tripping while walking and sprained ankles are common. Muscle loss in the feet and calves leads to "foot drop" where the foot does not lift high enough off the ground when walking. Complaints of cold legs are common, as are cramps in the legs, especially after **exercise**.

In many people, the fingers and hands eventually become affected. Muscle loss in the hands can make fine movements such as working buttons and zippers difficult. Some patients develop tremor in the upper limbs. Loss of sensation can cause problems such as numbness and the

inability to feel if something is hot or cold. Most people with CMT remain able to walk throughout their lives.

Diagnosis

Diagnosis of CMT begins with a careful neurological exam to determine the extent and distribution of weakness. A thorough family history should be taken at this time to determine if other people in the family are affected. Testing may also be performed to rule out other causes of neuropathy.

A nerve conduction velocity test should be performed to measure how fast impulses travel through the nerves. This test may show characteristic features of CMT, but it is not diagnostic of CMT. Nerve conduction testing may be combined with **electromyography** (EMG), an electrical test of the muscles.

A nerve biopsy (removal of a small piece of the nerve) may be performed to look for changes characteristic of CMT. However, this testing is not diagnostic of CMT and is usually not necessary for making a diagnosis.

Definitive diagnosis of CMT is made only by **genetic testing**, usually performed by drawing a small amount of blood. As of early 2001, testing is available to detect mutations in PMP22, MPZ, Cx32 and EGR2. However, research is progressing rapidly and new testing is often made available every few months. All affected members of a family have the same type of CMT. Therefore once a mutation is found in one affected member, it is possible to test other members who may have symptoms or are at risk of developing CMT.

Prenatal diagnosis

Testing during pregnancy to determine whether an unborn child is affected is possible if genetic testing in a family has identified a specific CMT-causing mutation. This can be done after 10–12 weeks of pregnancy using a procedure called **chorionic villus sampling** (CVS). CVS involves removing a tiny piece of the placenta and examining the cells. Testing can also be done by **amniocentesis** after 16 weeks gestation by removing a small amount of the amniotic fluid surrounding the baby and analyzing the cells in the fluid. Each of these procedures has a small risk of **miscarriage** associated with it, and those who are interested in learning more should check with their doctor or genetic counselor. Couples interested in these options should obtain **genetic counseling** to carefully explore all of the benefits and limitations of these procedures.

Treatment

There is no cure for CMT. However, physical and occupational therapy are an important part of CMT treatment. Physical therapy is used to preserve range of motion and minimize deformity caused by muscle shortening, or contracture. Braces are sometimes used to improve control of the lower extremities that can help tremendously with balance. After wearing braces, people often find that they have more energy because they are using less energy to focus on their walking. Occupational therapy is used to provide devices and techniques that can assist tasks such as dressing, feeding, writing, and other routine activities of daily life. Voice-activated software can also help people who have problems with fine motor control.

It is very important that people with CMT avoid injury that causes them to be immobile for long periods of time. It is often difficult for people with CMT to return to their original strength after injury.

There is a long list of medications that should be avoided if possible by people diagnosed with CMT such as hydralazine (Apresoline), megadoses of vitamin A, B_6, and D, Taxol, and large intravenous doses of penicillin. Complete lists are available from the CMT support groups. People considering taking any of these medications should weigh the risks and benefits with their physician.

Prognosis

The symptoms of CMT usually progress slowly over many years, but do not usually shorten life expectancy. The majority of people with CMT do not need to use a wheelchair during their lifetime. Most people with CMT are able to lead full and productive lives despite their physical challenges.

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CMT International. Attn: Linda Crabtree, 1 Springbank Dr. St. Catherine's, ONT L2S2K1. Canada (905) 687-3630. <http://www.cmtint.org>.

Muscular Dystrophy Association. 3300 East Sunrise Dr., Tucson, AZ 85718. (520) 529-2000 or (800) 572-1717. <http://www.mdausa.org>.

KEY TERMS

Axon—Skinny, wire-like extension of nerve cells.

Myelin—A fatty sheath surrounding nerves in the peripheral nervous system, which help them conduct impulses more quickly.

Nerve conduction testing—Procedure that measures the speed at which impulses move through the nerves.

Neuropathy—A condition caused by nerve damage. Major symptoms include weakness, numbness, paralysis, or pain in the affected area.

Peripheral nerves—Nerves throughout the body that carry information to and from the spinal cord.

Neuropathy Association. 60 E. 42nd St. Suite 942, New York, NY 10165. (212) 692-0662. <http://www.neuropathy.org>.

OTHER

HNPP—Hereditary Neuropathy with liability to Pressure Palsies. University of Washington, Seattle. <http://www.hnpp.org>.

"GeneClinics." <www.gene clinics.org>.

OMIM—Online Mendelian Inheritance in Man. <http://www.ncbi. nlm.nih.gov/Omim>.

Karen M. Krajewski, MS, CGC

Charcot's joints

Definition

Charcot's joints is a progressive degenerative disease of the joints caused by nerve damage resulting in the loss of ability to feel **pain** in the joint and instability of the joint.

Description

Charcot's joints, also called neuropathic joint disease, is the result of two conditions present in the joint. The first factor is the inability to feel pain in the joint due to nerve damage. The second factor is that injuries to the joint go unnoticed leading to instability and making the joint more susceptible to further injury. Repeated small injuries, strains and even **fractures** can go unnoticed until finally the joint is permanently destroyed. Loss of the protective sensation of pain is what leads to the disintegration of the joint and often leads to deformity in the joint.

Although this condition can affect any joint, the knee is the joint most commonly involved. In individuals with **diabetes mellitus**, the foot is most commonly affected. The disease can involve only one joint or it may affect two or three joints. More than three affected joints is very rare. In all cases, the specific joint(s) affected depends on the location of the nerve damage.

Causes and symptoms

Many diseases and injuries can interfere with the ability to feel pain. Conditions such as diabetes mellitus, spinal injuries and diseases, **alcoholism**, and even **syphilis** can all lead to a loss of the ability to feel pain in some areas. Lack of pain sensation may also be congenital.

The symptoms of Charcot's joints can go unnoticed for some time and may be confused with **osteoarthritis** in the beginning. Swelling and stiffness in a joint without the expected pain, or with less pain than would be expected, are the primary symptoms of this condition. As the condition progresses, however, the joint can become very painful due to fluid build-up and bony growths.

Diagnosis

Charcot's joints is suspected when a person with a disease that impairs pain sensation exhibits painless swelling and/or stiffness in a joint. Standard x rays will show damage to the joint, and may also show abnormal bone growth and calcium deposits. Floating bone fragments from previous injuries may also be visible.

Treatment

In the early stages of Charcot's joints, braces to stabilize the joints can help stop or minimize the damage. When the disease has progressed beyond braces, surgery can sometimes repair the joint. If the damage is extensive, an artificial joint may be necessary.

Prognosis

Treatment of the disease causing loss of pain perception may help to slow the damage to the joints.

Prevention

Preventing or effectively managing the underlying disease can slow or in some cases reverse joint damage, but the condition cannot be prevented.

Resources

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Dorothy Elinor Stonely

Charley horse *see* **Muscle spasms and cramps**

Chelation therapy

Definition

Chelation therapy is an intravenous treatment designed to bind heavy metals in the body in order to treat heavy metal toxicity. Proponents claim it also treats **coronary artery disease** and other illnesses that may be linked to damage from free radicals (reactive molecules).

Purpose

The benefits of EDTA chelation for the treatment of **lead poisoning** and excessively high calcium levels are undisputed. The claims of benefits for those suffering from **atherosclerosis**, coronary artery disease, and other degenerative diseases are more difficult to prove. Reported uses for chelation therapy include treatment of **angina**, **gangrene**, arthritis, **multiple sclerosis**, **Parkinson's disease**, **psoriasis**, and **Alzheimer's disease**. Improvement is also claimed for people experiencing diminished sight, hearing, smell, coordination, and sexual potency.

Description

Origins

The term chelation is from the Greek root word "chele," meaning "claw." Chelating agents, most commonly diamine tetraacetic acid (EDTA), were originally designed for industrial applications in the early 1900s. It was not until the World War II era that the potential for medical therapy was realized. The initial intent was to develop antidotes to poison gas and radioactive contaminants. The need for widespread therapy of this nature did not materialize, but more practical uses were found for chelation. During the following decade, EDTA chelation therapy became standard treatment for people suffering from lead **poisoning**. Patients who had received this treatment claimed to have other health improvements that could not be attributed to the lead removal only. Especially notable were comments from those who had previously suffered from intermittent claudication and angina. They reported suffering less **pain** and **fatigue**, with improved endurance, after chelation therapy. These reports stimulated further interest in the potential benefits of chelation therapy for people suffering from atherosclerosis and coronary artery disease.

If the preparatory examination suggests that there is a condition that could be improved by chelation therapy, and there is no health reason why it shouldn't be used, then the treatment can begin. The patient is generally taken to a comfortable treatment area, sometimes in a group location, and an intravenous line is started. A solution of EDTA together with **vitamins** and **minerals** tailored for the individual patient is given. Most treatments take three to four hours, as the infusion must be given slowly in order to be safe. The number of recommended treatments is usually between 20 and 40. They are given one to three times a week. Maintenance treatments can then be given at the rate of once or twice a month. Maximum benefits are reportedly attained after approximately three months after a treatment series. The cost of therapy is considerable, but it is a fraction of the cost of an expensive medical procedure like cardiac bypass surgery. Intravenous vitamin C and mercury chelation therapies are also offered.

Preparations

A candidate for chelation therapy should initially have a thorough history and physical to define the type and extent of clinical problems. Laboratory tests will be done to determine whether there are any conditions present that would prevent the use of chelation. Patients who have preexisting **hypocalcemia**, poor liver or kidney function, congestive **heart failure**, **hypoglycemia**, **tuberculosis**, clotting problems, or potentially allergic conditions are at higher risk for complications from chelation therapy. A Doppler ultrasound may be performed to determine the adequacy of blood flow in different regions of the body.

Precautions

It is important for people who receive chelation therapy to work with medical personnel who are experienced in the use of this treatment. Treatment should not be undertaken before a good physical, lifestyle evaluation, history, and any laboratory tests necessary are performed. The staff must be forthcoming about test results and should answer any questions the patient may have. Evaluation and treatment should be individualized and involve assessment of kidney function before each treatment with chelation, since the metals bound by the EDTA are excreted through the kidneys.

Although EDTA binds harmful, toxic metals like mercury, lead, and cadmium, it also binds some essential nutrients of the body, such as copper, iron, calcium, zinc, and magnesium. Large amounts of zinc are lost during chelation. Zinc deficiency can cause impaired immune function and other harmful effects. Supplements of zinc are generally given to patients undergoing chelation, but it is not known whether this is adequate to prevent deficiency. Also, chelation therapy does not replace proper **nutrition**, **exercise**, and appropriate medications or surgery for specific diseases or conditions.

KEY TERMS

Angina—Chest pain caused by reduced oxygen to the heart.

Atherosclerosis—Arterial disease characterized by fatty deposits on inner arterial walls.

Hypocalcemia—Low blood calcium.

Hypoglycemia—Low blood sugar.

Intermittent claudication—Leg pain and weakness caused by walking.

Thrombophlebitis—Inflammation of a vein together with clot formation.

Side effects

Side effects of chelation therapy are reportedly unusual, but are occasionally serious. Mild reactions may include, but are not limited to, local irritation at the infusion site, skin reactions, nausea, **headache**, **dizziness**, hypoglycemia, **fever**, leg cramps, or loose bowel movements. Some of the more serious complications reported have included hypocalcemia, kidney damage, decreased clotting ability, anemia, bone marrow damage, insulin shock, **thrombophlebitis** with **embolism**, and even rare deaths. However, some doctors feel that the latter groups of complications occurred before the safer method currently used for chelation therapy was developed.

Research and general acceptance

EDTA chelation is a highly controversial therapy. The treatment is approved by the United States Food and Drug Administration (FDA) for lead poisoning and seriously high calcium levels. However, for the treatment of atherosclerotic heart disease, EDTA chelation therapy is not endorsed by the American Heart Association (AHA), the FDA, the National Institutes of Health (NIH), or the American College of Cardiology. The AHA reports that there are no adequate, controlled, published scientific studies using currently approved scientific methods to support this therapy for the treatment of coronary artery disease. However, a pooled analysis from the results of over 70 studies showed positive results in all but one.

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Judith Turner

Chemica *see* **Skin resurfacing**

Chemical debridement *see* **Debridement**

Chemobrasion *see* **Skin resurfacing**

Chemonucleolysis

Definition

Chemonucleolysis is a medical procedure that involves the dissolving of the gelatinous cushioning material in an intervertebral disk by the injection of an enzyme such as chymopapain.

Purpose

Between each vertebra lies a disk of cushioning material that keeps the spinal bones from rubbing together and absorbs some of the **shock** to the spine from body movements. In the center of the disk is soft, gelatinous material called the nucleus pulposus (NP). The NP is surrounded by a tough fibrous coating. Sometimes when the back is injured, this coating can weaken and bulge or tear to allow the NP to ooze out. When this happens, it is called a herniated nucleus pulposus (HNP), or—in common language—a **herniated disk**.

When the disk bulges or herniates, it can put pressure on nerves which originate in the spinal column, and go to other parts of the body. This causes lower back **pain**, and/or pain to the hips, legs, arms, shoulders, and neck, depending on the location of the herniated disk. Chemonucleolysis uses chymopapain, an enzyme derived from papyrus, to dissolve the disk material that has

KEY TERMS

Chymopapain—An enzyme from the milky white fluid of the papaya, used for medical purposes in chemonucleolysis.

Myelography—An x-ray test that evaluates the subarachnoid space of the spine.

Nucleus pulposus (NP)—an elastic, pulpy mass in the center of each vertebral disk.

been displaced because of injury. Herniated disks are the cause of only a small proportion of cases of lower back pain, and chemonucleolysis is appropriate for only some cases of HNP.

Chemonucleolysis is a conservative alternative to disk surgery. There are three types of disk injuries. A protruded disk is one that is intact but bulging. In an extruded disk, the fibrous wrapper has torn and the NP has oozed out, but is still connected to the disk. In a sequestered disk, a fragment of the NP has broken loose from the disk and is free in the spinal canal. Chemonucleolysis is effective on protruded and extruded disks, but not on sequestered disk injuries. In the United States, chymopapain chemonucleolysis is approved only for use in the lumbar (lower) spine. In other countries, it has also been used successfully to treat cervical (upper spine) hernias.

Other indications that a patient is a good candidate for chemonucleolysis instead of surgery include:

- the patient is 18–50 years of age
- leg pain is worse than lower back pain
- other conservative treatments have failed
- the spot where the herniated disk presses on the nerve has been pinpointed by **myelography**, computed tomography scan (CT scan), or **magnetic resonance imaging** (MRI)
- the patient wishes to avoid surgery

Precautions

There are some situations in which chemonucleolysis should not be performed. Chymopapain is derived from the papaya. About 0.3% of patients are allergic to chymopapain and go into life-threatening shock when exposed to the enzyme. Chemonucleolysis should not be performed on patients allergic to chymopapain or papaya. It also should not be done:

- when the patient is pregnant
- if the disk is sequestered
- if the patient has had several failed back operations
- if a spinal cord tumor is present
- if the patient has a neurological disease such as multiple sclerosis

Other conditions may affect the appropriateness of chemonucleolysis, including **hypertension**, **obesity**, diabetes, and a family history of stroke.

Description

A small gauge needle is placed in the center of the affected disk. Chymopapain is introduced into the disk. The patient needs to remain still.

Preparation

Patients will need tests such as a myelogram or CT scan to pinpoint the herniated disk. Some doctors medicate the patient 24 hours prior to the operation in order to decrease the chances of post-operative lower back stiffness.

Aftercare

Patients may feel lower back stiffness, which goes away in few weeks. Heavy lifting and sports activities should be avoided for at least three months.

Risks

The greatest risk is that the patient may be allergic to chymopapain. The **death** rate for chemonucleolysis is only 0.02%. Complications overall are five to 10 times less than with conventional surgery, and the failure rate is roughly comparable to the failure rate in conventional disk surgery.

Normal results

Many patients feel immediate relief from pain, but, in about 30% of patients, maximal relief takes six weeks. The long term (seven to 20 years) success rate averages about 75%, which is comparable to the success rate for conventional surgery.

Resources

PERIODICALS

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Tish Davidson

Chemotherapy

Definition

Chemotherapy is treatment of **cancer** with **anti-cancer drugs**.

Purpose

The main purpose of chemotherapy is to kill cancer cells. It is usually used to treat patients with cancer that has spread from the place in the body where it started (metastasized). Chemotherapy destroys cancer cells anywhere in the body. It even kills cells that have broken off from the main tumor and traveled through the blood or lymph systems to other parts of the body.

Chemotherapy can cure some types of cancer. In some cases, it is used to slow the growth of cancer cells or to keep the cancer from spreading to other parts of the body. When a cancer has been removed by surgery, chemotherapy may be used to keep the cancer from coming back (adjuvant therapy). Chemotherapy also can ease the symptoms of cancer, helping some patients to have a better quality of life.

Precautions

There are many different types of chemotherapy drugs. Oncologists, doctors who specialize in treating cancer, determine which drugs are best suited for each patient. This decision is based on the type of cancer, the patient's age and health, and other drugs the patient is taking. Some patients should not be treated with certain chemotherapy drugs. Age and other conditions may affect the drugs with which a person may be treated. Heart disease, kidney disease, and diabetes are conditions that may limit the choice of treatment drugs.

Description

More than 50 chemotherapy drugs are currently available to treat cancer and many more are being tested for their ability to destroy cancer cells. Most chemotherapy drugs interfere with the ability of cells to grow or multiply. Although these drugs affect all cells in the body, many useful treatments are most effective against rapidly growing cells. Cancer cells grow more quickly than most other body cells. Other cells that grow fast are cells of the bone marrow that produce blood cells, cells in the stomach and intestines, and cells of the hair follicles. Therefore, the most common side effects of chemotherapy are linked to their effects on other fast growing cells.

Types of chemotherapy drugs

Chemotherapy drugs are classified based on how they work. The main types of chemotherapy drugs are described below:

- Alkylating drugs kill cancer cells by directly attacking DNA, the genetic material of the genes. Cyclophosphamide is an alkylating drug.
- Antimetabolites interfere with the production of DNA and keep cells from growing and multiplying. An example of an antimetabolite is 5-fluorouracil (5-FU).
- Antitumor **antibiotics** are made from natural substances such as fungi in the soil. They interfere with important cell functions, including production of DNA and cell proteins. Doxorubicin and bleomycin belong to this group of chemotherapy drugs.
- Plant alkaloids prevent cells from dividing normally. Vinblastine and vincristine are plant alkaloids obtained from the periwinkle plant.
- Steroid hormones slow the growth of some cancers that depend on hormones. For example, tamoxifen is used to treat breast cancers that depend on the hormone estrogen for growth.

Combination chemotherapy

Chemotherapy is usually given in addition to other cancer treatments, such as surgery and **radiation therapy**. When given with other treatments, it is called adjuvant chemotherapy. An oncologist decides which chemotherapy drug or combination of drugs will work best for each patient. The use of two or more drugs together often works better than a single drug for treating cancer. This is called combination chemotherapy. Scientific studies of different drug combinations help doctors learn which combinations work best for each type of cancer.

How chemotherapy is given

Chemotherapy is administered in different ways, depending on the drugs to be given and the type of cancer. Doctors decide the dose of chemotherapy drugs considering many factors, among them being the patient's height and weight.

Chemotherapy may be given by one or more of the following methods:

- orally
- by injection
- through a catheter or port
- topically

Oral chemotherapy is given by mouth in the form a pill, capsule, or liquid. This is the easiest method and can usually be done at home.

Intravenous (IV) chemotherapy is injected into a vein. A small needle is inserted into a vein on the hand or lower arm. The needle is usually attached to a small tube called a catheter, which delivers the drug to the needle from an IV bag or bottle.

Intramuscular (IM) chemotherapy is injected into a muscle. Chemotherapy given by intramuscular injection is absorbed into the blood more slowly than IV chemotherapy. Because of this, the effects of IM chemotherapy may last longer than chemotherapy given intravenously. Chemotherapy may also be injected subcutaneously (SQ or SC), which means under the skin. Injection of chemotherapy directly into the cancer is called intralesional (IL) injection.

Chemotherapy may also be given by a catheter or port permanently inserted into a central vein or body cavity. A port is a small reservoir or container that is placed in a vein or under the skin in the area where the drug will be given. These methods eliminate the need for repeated injections and may allow patients to spend less time in the hospital while receiving chemotherapy. A common location for a permanent catheter is the external jugular vein in the neck. Intraperitoneal (IP) chemotherapy is administered into the abdominal cavity through a catheter or port. Chemotherapy given by catheter or port into the spinal fluid is called intrathecal (IT) administration. Catheters and ports may also be placed in the chest cavity, bladder, or pelvis, depending on the location of the cancer to be treated.

Topical chemotherapy is given as a cream or ointment applied directly to the cancer. This method is more common in treatment of certain types of skin cancer.

Patient undergoing high dose stem cell chemotherapy.
(Custom Medical Stock Photo. Reproduced by permission.)

Treatment location and schedule

Patients may take chemotherapy at home, in the doctor's office, or as an inpatient or outpatient at the hospital. Most patients stay in the hospital when first beginning chemotherapy, so their doctor can check for any side effects and change the dose if needed.

How often and how long chemotherapy is given depends on the type of cancer, how patients respond to the drugs, patients' health and ability to tolerate the drugs, and the types of drugs given. Chemotherapy administration may take only a few minutes or may last as long as several hours. Chemotherapy may be given daily, weekly, or monthly. A rest period may follow a course of treatment before the next course begins. In combination chemotherapy, more than one drug may be given at a time, or they may be given alternately, one following the other.

Preparation

A number of medical tests are done before chemotherapy is started. The oncologist will determine how much the cancer has spread from the results of x rays and other imaging tests and from samples of the tumor taken during surgery.

Blood tests give the doctor important information about the function of the blood cells and levels of chemicals in the blood. A complete **blood count** (CBC) is commonly done before and regularly during treatment. The CBC shows the numbers of white blood cells, red blood cells, and platelets in the blood. Because chemotherapy affects the bone marrow, where blood cells are made, levels of these cells often drop during chemotherapy. The white blood cells and platelets are most likely to be affected by chemotherapy. A drop in the

white blood cell count means that the immune system cannot function properly. Low levels of platelets can cause a patient to bleed easily from a cut or other wound. A low red blood cell count can lead to anemia (deficiency of red blood cells) and **fatigue**.

When a chemotherapy treatment takes a long time, the patient may prepare for it by wearing comfortable clothes. Bringing a book to read or a tape to listen to may help pass the time and ease the **stress** of receiving chemotherapy. Some patients bring a friend or family member to provide company and support during treatment.

Sometimes, patients taking chemotherapy drugs known to cause nausea are given medications called anti-emetics before chemotherapy is administered. Anti-emetic drugs help to lessen feelings of nausea. Two anti-nausea medications that may be used are Kytril and Zofran.

Other ways to prepare for chemotherapy and help lessen nausea are:

- regularly eat nutritious foods and drink lots of fluids
- eat and drink normally until about two hours before chemotherapy
- eat high carbohydrate, low-fat foods and avoid spicy foods

Aftercare

Tips for helping to control side effects after chemotherapy include:

- follow any instructions given by the doctor or nurse
- take all prescribed medications
- eat small amounts of bland foods
- drink lots of fluids
- get plenty of rest

Some patients find it helps to breathe fresh air or get mild **exercise**, such as taking a walk.

Risks

Chemotherapy drugs are toxic to normal cells as well as cancer cells. A dose that will destroy cancer cells will probably cause damage to some normal cells. Doctors adjust doses to do the least amount of harm possible to normal cells. Some patients feel few or no side effects, and others may have more serious side effects. In some cases, a dose adjustment is all that is needed to reduce or stop a side effect.

Some chemotherapy drugs have more side effects than others. Some of the most common side effects are:

- **nausea and vomiting**
- loss of appetite
- hair loss
- anemia and fatigue
- infection
- easy bleeding or bruising
- sores in the mouth and throat
- neuropathy and other damage to the nervous system
- kidney damage

Nausea and vomiting are common, but can usually be controlled by taking **antinausea drugs**, drinking enough fluids, and avoiding spicy foods. Loss of appetite may be due to nausea or the stress of undergoing cancer treatment.

Some chemotherapy drugs cause hair loss, but it is almost always temporary.

Low blood cell counts caused by the effect of chemotherapy on the bone marrow can lead to anemia, infections, and easy bleeding and bruising. Patients with anemia have too few red blood cells to deliver oxygen and nutrients to the body's tissues. Anemic patients feel tired and weak. If red blood cell levels fall too low, a blood **transfusion** may be given.

Patients receiving chemotherapy are more likely to get infections. This happens because their infection-fighting white blood cells are reduced. It is important to take measures to avoid getting infections. When the white blood cell count drops too low, the doctor may prescribe medications called colony stimulating factors that help white blood cells grow. Neupogen and Leukine are two colony stimulants used as treatments to help fight infection.

Platelets are blood cells that make the blood clot. When patients do not have enough platelets, they may bleed or bruise easily, even from small injuries. Patients with low blood platelets should take precautions to avoid injuries. Medicines such as **aspirin** and other **pain** relievers can affect platelets and slow down the clotting process.

Chemotherapy can cause irritation and dryness in the mouth and throat. Painful sores may form that can bleed and become infected. Precautions to avoid this side effect include getting dental care before chemotherapy begins, brushing the teeth and gums regularly with a soft brush, and avoiding mouth washes that contain salt or alcohol.

Normal results

The main goal of chemotherapy is to cure cancer. Many cancers are cured by chemotherapy. It may be used in combination with surgery to keep a cancer from spread-

KEY TERMS

Adjuvant therapy—Treatment given after surgery or radiation therapy to prevent the cancer from coming back.

Alkaloid—A type of chemical commonly found in plants and often having medicinal properties.

Alykylating drug—A drug that kills cells by directly damaging DNA.

Antiemetic—A medicine that helps control nausea; also called an anti-nausea drug.

Antimetabolite—A drug that interferes with a cell's growth or ability to multiply.

Platelets—Blood cells that function in blood clotting.

ing to other parts of the body. Some widespread, fast-growing cancers are more difficult to treat. In these cases, chemotherapy may slow the growth of the cancer cells.

Doctors can tell if the chemotherapy is working by the results of medical tests. **Physical examination**, blood tests, and x rays are all used to check the effects of treatment on the cancer.

The possible outcomes of chemotherapy are:

- Complete remission or response. The cancer completely disappears. The course of chemotherapy is completed and the patient is tested regularly for a recurrence.
- Partial remission or response. The cancer shrinks in size but does not disappear. The same chemotherapy may be continued or a different combination of drugs may be tried.
- Stabilization. The cancer does not grow or shrink. Other therapy options may be explored. A tumor may stay stabilized for many years.
- Progression. The cancer continues to grow. Other therapy options may be explored.
- A secondary malignancy may develop from the one being treated, and that second cancer may need additional chemotherapy or other treatment.

Resources

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National Cancer Institute. Building 31, Room 10A31, 31 Center Drive, MSC 2580, Bethesda, MD 20892-2580. (800) 422-6237. <http://www.nci.nih.gov>.

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Toni Rizzo

Chest drainage therapy

Definition

Chest drainage therapy involves the removal of air, blood, pus, or other secretions from the chest cavity.

Purpose

Chest drainage therapy is done to relieve pressure on the lungs, and remove fluid that could promote infection. Installing a chest drainage tube can be either an emergency or a planned procedure.

Removing air or fluids from the chest involves the insertion of a tube through the skin and the muscles between the ribs, and into the chest cavity. This cavity is also called the pleural space. Insertion of this tube is called thoracostomy, and chest drainage therapy is sometimes called thoracostomy tube drainage.

Conditions that may need to be treated by chest drainage therapy include **emphysema** (air in the tissues of the lungs), **tuberculosis**, and spontaneous **pneumothorax** (air in the chest cavity) that causes more than a 25% collapse of the lung. Other conditions include **cancer** that causes excessive secretions, **empyema** (pus in the thoracic cavity), or hemothorax (blood in the thoracic cavity). Almost all chest drainage therapy is done to drain blood from the chest cavity after lung or heart surgery. In cases where the lung is collapsed, removing fluids by chest drainage therapy allows the lung to reinflate.

Oftentimes an x ray is performed prior to treatment to determine whether the problem is either fluid or air in

KEY TERMS

Empyema—Pus in the pleural cavity.

Hemothorax—Blood in the pleural cavity.

Pleural cavity—The area of the chest that includes the lining of the chest cavity, the space the lungs are located in, and the membrane covering of the lungs.

Spontaneous pneumothorax—Air in the chest cavity that occurs because of disease or other naturally occurring cause. Air and blood together in this space is called a pneumohemothorax.

the pleural space. Sometimes a procedure called **thoracentesis** is performed in an effort to avoid inserting a chest drainage tube. In this procedure a needle with a catheter is inserted into the pleural space and fluid is removed. When fluid continues to accumulate, chest drainage therapy is usually the next step. This is especially true when there is a lung infection underlying the fluid build-up.

Precautions

Chest drainage therapy is not done if a collapsed lung is not life-threatening. It also should be avoided for patients who have blood clotting problems.

Description

Most patients are awake when the chest drainage tube is inserted. They are given a sedative and a local anesthetic. Chest drainage tubes are usually inserted between the ribs. The exact location depends on the type of material to be drained and its location in the lungs.

An incision is made in the skin and through the muscles between the ribs. A chest tube is inserted and secured in place. The doctor connects one end of the tube to the chest drainage system.

The chest drainage system must remain sealed to prevent air from entering the chest cavity through the tube. One commonly used system is a water-seal drainage system, comprised of three compartments that collect and drain the fluid or air without allowing air to backflow into the tube. An alternative to this system is to connect the tube to a negative suction pump.

Once the tube and drainage system are in place, a chest x ray is done to confirm that the tube is in the right location, and that it is working. In some cases it may be necessary to insert more than one tube to drain localized pockets of fluid that have accumulated.

Preparation

A chest x ray is usually done before the chest drainage tube is inserted. Sometimes fluid becomes trapped in isolated spaces in the lung, and it is necessary to do an ultrasound to determine where to locate the drainage tube. **Computed tomography scans** (CT) are useful in locating small pockets of fluids caused by cancer or tuberculosis.

Aftercare

Normally after the material has been removed from the chest cavity and the situation is resolved, the chest drainage tube is removed. In cases where the reason for the tube was air in the pleural cavity, the tube is clamped and left in place several hours before it is removed to make sure no more air is leaking into the space. If the patient is on mechanical ventilation, the tube is often left in place until a respirator is no longer necessary. Chest drainage therapy is usually done in conjunction with treating the underlying cause of the fluid build-up.

The fluid that has been drained is examined for bacterial growth, cancer cells, pus, and blood—to determine the underlying cause of the condition and appropriate treatment.

Risks

Problems can arise in the insertion of the tube if the membrane lining the chest cavity is thick or if it has many adhesions. The tube will not drain correctly if the chest cavity contains blood clots or thick secretions that are often associated with infections. Excessive bleeding may occur during the insertion and positioning of the tube. Infection may result from the procedure. **Pain** is also a common complication.

Normal results

The gas, pus, or blood is drained from the chest cavity, and the lungs reinflate or begin to function more efficiently. The site at which the tube was inserted heals normally.

Resources

BOOKS

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Tish Davidson

Chest pain *see* **Angina**

Chest physical therapy

Definition

Chest physical therapy is the term for a group of treatments designed to improve respiratory efficiency, promote expansion of the lungs, strengthen respiratory muscles, and eliminate secretions from the respiratory system.

Purpose

The purpose of chest physical therapy, also called chest physiotherapy, is to help patients breathe more freely and to get more oxygen into the body. Chest physical therapy includes postural drainage, chest percussion, chest vibration, turning, deep breathing exercises, and coughing. It is usually done in conjunction with other treatments to rid the airways of secretions. These other treatments include suctioning, nebulizer treatments, and the administration of expectorant drugs.

Chest physical therapy can be used with newborns, infants, children, and adults. People who benefit from chest physical therapy exhibit a wide range of problems that make it difficult to clear secretions from their lungs. Some people who may receive chest physical therapy include people with **cystic fibrosis** or neuromuscular diseases like **Guillain-Barré syndrome**, progressive muscle weakness (**myasthenia gravis**), or **tetanus**. People with lung diseases such as **bronchitis**, **pneumonia**, or chronic obstructive pulmonary disease (COPD) also benefit from chest physical therapy. People who are likely to aspirate their mucous secretions because of diseases such as **cerebral palsy** or **muscular dystrophy** also receive chest physical therapy, as do some people who are bedridden, confined to a wheelchair, or who cannot breathe deeply because of postoperative **pain**.

Precautions

Chest physical therapy should not be performed on people with

- bleeding from the lungs
- neck or head injuries
- fractured ribs
- collapsed lungs
- damaged chest walls
- tuberculosis
- acute asthma
- recent heart attack
- pulmonary embolism
- lung **abscess**
- active hemorrhage
- some spine injuries
- recent surgery, open **wounds**, or **burns**

Description

Chest physical therapy can be performed in a variety of settings including critical care units, hospitals, nursing homes, outpatient clinics, and at the patient's home. Depending on the circumstances, chest physical therapy may be performed by anyone from a respiratory care therapist to a trained member of the patient's family. Different patient conditions warrant different levels of training.

Chest physical therapy consists of a variety of procedures that are applied depending on the patient's health and condition. Hospitalized patients are reevaluated frequently to establish which procedures are most effective and best tolerated. Patients receiving long term chest physical therapy are reevaluated about every three months.

Turning

Turning from side to side permits lung expansion. Patients may turn themselves or be turned by a caregiver. The head of the bed is also elevated to promote drainage if the patient can tolerate this position. Critically ill patients and those dependent on mechanical respiration are turned once every one to two hours around the clock.

Coughing

Coughing helps break up secretions in the lungs so that the mucus can be suctioned out or expectorated. Patients sit upright and inhale deeply through the nose. They then exhale in short puffs or coughs. Coughing is repeated several times a day.

Deep breathing

Deep breathing helps expand the lungs and forces better distribution of the air into all sections of the lung. The patient either sits in a chair or sits upright in bed and inhales, pushing the abdomen out to force maximum amounts of air into the lung. The abdomen is then contracted, and the patient exhales. Deep breathing exercises are done several times each day for short periods.

KEY TERMS

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Percussion—This consists of rhythmically striking the chest wall with cupped hands. It is also called cupping, clapping, or tapotement. The purpose of percussion is to break up thick secretions in the lungs so that they can be more easily removed. Percussion is performed on each lung segment for one to two minutes at a time.

Postural drainage—This technique uses the force of gravity to assist in effectively draining secretions from the lungs and into the central airway where they can either be coughed up or suctioned out. The patient is placed in a head or chest down position and is kept in this position for up to 15 minutes. Critical care patients and those depending on mechanical ventilation receive postural draingage therapy four to six times daily. Percussion and vibration may be performed in conjunction with postural drainage.

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Vibration—The purpose of vibration is to help break up lung secretions. Vibration can be either mechanical or manual. It is performed as the patient breathes deeply. When done manually, the person performing the vibration places his or her hands against the patient's chest and creates vibrations by quickly contracting and relaxing arm and shoulder muscles while the patient exhales. The procedure is repeated several times each day for about five exhalations.

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Preparation

The only preparation needed for chest physical therapy is an evaluation of the patient's condition and determination of which chest physical therapy techniques would be most beneficial.

Aftercare

Patients practice **oral hygiene** procedures to lessen the bad taste or odor of the secretions they spit out.

Risks

Risks and complications associated with chest physical therapy depend on the health of the patient. Although

chest physical therapy usually poses few problems, in some patients it may cause

- oxygen deficiency if the head is kept lowered for drainage
- increased intracranial pressure
- temporary low blood pressure
- bleeding in the lungs
- pain or injury to the ribs, muscles, or spine
- vomiting
- inhaling secretions into the lungs
- heart irregularities

Normal results

The patient is considered to be responding positively to chest physical therapy if some, but not necessarily all, of these changes occur:

- increased volume of sputum secretions
- changes in breath sounds
- improved vital signs
- improved chest x ray
- increased oxygen in the blood as measured by arterial blood gas values
- patient reports of eased breathing

Resources

PERIODICALS

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ORGANIZATIONS

Cystic Fibrosis Foundation. 6931 Arlington Road, Bethesda, MD 20814. (800) 344-4823. <http://www.cff.org>.

Tish Davidson

Chest radiography *see* **Chest x ray**

Chest x ray

Definition

A chest x ray is a procedure used to evaluate organs and structures within the chest for symptoms of disease. Chest x rays include views of the lungs, heart, small portions of the gastrointestinal tract, thyroid gland and the bones of the chest area. X rays are a form of radiation that can penetrate the body and produce an image on an x-ray film. Another name for x ray is radiograph.

A normal chest x ray of a child. (*Photograph by Peter Berndt, M.D., P.A, Custom Medical Stock Photo. Reproduced by permission.)*

Purpose

Chest x rays are ordered for a wide variety of diagnostic purposes. In fact, this is probably the most frequently performed x ray. In some cases, chest x rays are ordered for a single check of an organ's condition, and at other times, serial x rays are ordered to compare to previous studies. Some common reasons for chest x rays include:

Pulmonary disorders

Chest films are frequently ordered to diagnose or rule out **pneumonia**. Other pulmonary disorders such as **emphysema** or **pneumothorax** (presence of air or gas in the chest cavity outside the lungs) may be detected or evaluated through the use of chest x ray.

Cancer

A chest x ray may be ordered by a physician to check for possible tumors of the lungs, thyroid, lymphoid tissue, or bones of the thorax. These may be primary tumors. X rays also check for secondary spread of **cancer** from one organ to another.

Cardiac disorders

While less sensitive than **echocardiography**, chest x ray can be used to check for disorders such as congestive **heart failure** or **pulmonary edema**.

KEY TERMS

Bronchi—Plural of bronchus. The air passages in the lungs through which inhaled air passes on its way to the lungs.

Diaphragm—The large muscle that is located between the abdomen and the chest area. The diaphragm aids in breathing.

Gastrointestinal—The digestive organs and structures, including the stomach and intestines.

Interstitial lung disease—About 180 diseases fall into this category of breathing disorders. Injury or foreign substances in the lungs, (such as asbestos fibers) as well as infections, cancers, or inherited disorders may cause the diseases. They can lead to breathing or heart failure.

Lymphoid—Tissues relating to the lymphatic system. A thin, yellowish fluid, called lymph fluid, travels throughout the body. The lymphatic system helps control fluids in the body.

Portable chest x ray—An x ray procedure taken by equipment that can be brought to the patient. The resulting radiographs may not be as high in quality as stationary x ray radiographs, but allow a technologist to come to the bedridden patient.

Pulmonary—Refers to the lungs and the breathing system and function.

Serial x rays—A number of x rays performed at set times in the disease progression or treatment intervals. The radiographs will be compared to one another to track changes.

Sternum—Also referred to as the breast bone, this is the long flat bone in the middle of the chest.

Thorax—The chest area, which runs between the abdomen and neck and is encased in the ribs.

X ray—A form of electromagnetic radiation with shorter wavelengths than normal light. X rays can penetrate most structures.

Other

Tuberculosis can be observed on chest x rays, as can cardiac disease and damage to the ribs or lungs. Chest x rays are used to see foreign bodies that may have been swallowed or inhaled, and to evaluate response to treatment for various diseases. Often the chest x ray is also used to verify correct placement of chest tubes or catheters.

Precautions

Pregnant women, particularly those in the first or second trimester, should not have chest x rays unless absolutely necessary. If the exam is ordered, women who are, or could possibly be, pregnant must wear a protective lead apron. Because the procedure involves radiation, care should always be taken to avoid overexposure, particularly for children. However, the amount of radiation from one chest x ray procedure is minimal.

Description

Routine chest x rays consist of two views, the frontal view (referred to as posterioranterior or PA), and the lateral (side) view. It is preferred that the patient stand for this exam, particularly when studying collection of fluid in the lungs.

During the actual time of exposure, the technologist will ask the patient to hold his or her breath. It is very important in taking a chest x ray to ensure there is no motion that could detract from the quality and sharpness of the film image. The procedure will only take a few minutes and the time patients must hold their breaths is a matter of a few seconds.

The chest x ray may be performed in a physician's office or referred to an outpatient radiology facility or hospital radiology department. In some cases, particularly for bedridden patients, a portable chest x ray may be taken. Portable films are sometimes of poorer quality than those taken with permanent equipment, but are the best choice for some patients or situations. Bedridden patients may be placed in as upright a position as possible to get a clear picture, particularly of chest fluid.

Preparation

There is no advance preparation necessary for chest x rays. Once the patient arrives at the exam area, a hospital gown will replace all clothing on the upper body and all jewelry must be removed.

Aftercare

No aftercare is required by patients who have chest x rays.

Risks

The only risk associated with chest x ray is minimal exposure to radiation, particularly for pregnant women and children. Those patients should use protective lead aprons during the procedure. Technologists are cautioned to carefully check possible dislodging of any tubes or

monitors in the chest area from the patient's placement during the exam.

Normal results

A radiologist, or physician specially trained in the technique and interpretation of x rays, will evaluate the results. A normal chest x ray will show normal structures for the age and medical history or the patient. Findings, whether normal or abnormal, will be provided to the referring physician in the form of a written report.

Abnormal results

Abnormal findings on chest x rays are used in conjunction with a physician's physical exam findings, patient medical history and other diagnostic tests to reach a final diagnosis. For many diseases, chest x rays are more effective when compared to previous chest studies. The patient is asked to help the radiology facility in locating previous chest radiographs from other facilities.

Pulmonary disorders

Pneumonia shows up on radiographs as patches and irregular areas of density (from fluid in the lungs). If the bronchi, which are usually not visible, can be seen, a diagnosis of bronchial pneumonia may be made. Shifts or shadows in the hila (lung roots) may indicate emphysema or a pulmonary **abscess**. Widening of the spaces between ribs suggests emphysema. Other pulmonary diseases may also be detected or suspected through chest x ray.

Cancer

In nearly all patients with lung cancer, some sort of abnormality can be seen on a chest radiograph. Hilar masses (enlargements at that part of the lungs where vessels and nerves enter) are one of the more common symptoms as are abnormal masses and fluid buildup on the outside surface of the lungs or surrounding areas. Interstitial lung disease, which is a large category of disorders, many of which are related to exposure of substances (such as asbestos fibers), may be detected on a chest x ray as fiberlike deposits, often in the lower portions of the lungs.

Other

Congestive heart failure and other cardiac diseases may be indicated on the view of a heart and lung in a chest radiograph. **Fractures** of the sternum and ribs are usually easily detected as breaks on the chest x ray. In some instances, the radiologist's view of the diaphragm may indicate an abdominal problem. Tuberculosis can also be indicated by elevation of the diaphragm. Foreign bodies which may have been swallowed or inhaled can usually be located by the radiologist as they will look different from any other tissue or structure in the chest. Serial chest x rays may be ordered to track changes over a period of time.

Resources

ORGANIZATIONS

American Lung Association. 1740 Broadway, New York, NY 10019. (800) 586-4872. <http://www.lungusa.org>.

Emphysema Anonymous, Inc. P.O. Box 3224, Seminole, FL 34642. (813)391-9977.

National Heart, Lung and Blood Institute. P.O. Box 30105, Bethesda, MD 20824-0105. (301) 251-1222. <http://www.nhlbi.nih.gov>.

Teresa Norris, RN

Chickenpox

Definition

Chickenpox (also called varicella) is a common and extremely infectious childhood disease that also affects adults on occasion. It produces an itchy, blistery rash that typically lasts about a week and is sometimes accompanied by a **fever** or other symptoms. A single attack of chickenpox almost always confers lifelong immunity against the disease. Because the symptoms of chickenpox are easily recognized and in most cases merely unpleasant rather than dangerous, treatment can almost always be carried out at home. Severe complications can develop, however, and professional medical attention is essential in some circumstances.

Description

Before the varicella vaccine (Varivax) was released for use in 1995, virtually all of the four million children born each year in the United States contracted chickenpox, resulting in hospitalization in five of every 1,000 cases and 100 deaths. Chickenpox is caused by the varicella-zoster virus (a member of the herpes virus family), which is spread through the air or by direct contact with an infected person. Once someone has been infected with the virus, an incubation period of about 10–21 days passes before symptoms begin. The period during which infected people are able to spread the disease is believed to start one or two days before the rash breaks out and to continue until all the blisters have formed scabs, which usually happens fout to seven days after the rash breaks

out but may be longer in adolescents and adults. For this reason, doctors recommend keeping children with chickenpox away from school for about a week. It is not necessary, however, to wait until all the scabs have fallen off.

Chickenpox has been a typical part of growing up for most children in the industrialized world (although this may change if the new varicella vaccine becomes more widely accepted). The disease can strike at any age, but by ages nine or 10 about 80–90% of American children have already been infected. U.S. children living in rural areas and many foreign-born children are less likely to be immune. Because almost every case of chickenpox, no matter how mild, leads to lifelong protection against further attacks, adults account for less than 5% of all cases in the United States. Study results reported by the Centers for Disease Control and Prevention (CDC) indicate that more than 90% of American adults are immune to the chickenpox virus. Adults, however, are much more likely than children to suffer dangerous complications. More than half of all chickenpox deaths occur among adults.

Causes and symptoms

A case of chickenpox usually starts without warning or with only a mild fever and a slight feeling of unwellness. Within a few hours or days small red spots begin to appear on the scalp, neck, or upper half of the trunk. After a further 12–24 hours the spots typically become itchy, fluid-filled bumps called vesicles, which continue to appear in crops for the next two to five days. In any area of skin, lesions of a variety of stages can be seen. These blisters can spread to cover much of the skin, and in some cases may also be found inside the mouth, nose, ears, vagina, or rectum. Some people develop only a few blisters, but in most cases the number reaches 250–500. The blisters soon begin to form scabs and fall off. Scarring usually does not occur unless the blisters have been scratched and become infected. Occasionally a minor and temporary darkening of the skin (called **hyperpigmentation**) is noticed around some of the blisters. The degree of itchiness can range from barely noticeable to extreme. Some chickenpox sufferers also have headaches, abdominal **pain**, or a fever. Full recovery usually takes five to 10 days after the first symptoms appear. Again, the most severe cases of the disease tend to be found among older children and adults.

Although for most people chickenpox is no more than a matter of a few days' discomfort, some groups are at risk for developing complications, the most common of which are bacterial infections of the blisters, **pneumonia**, **dehydration**, **encephalitis**, and hepatitis:

- Infants. Complications occur much more often among children less than one year old than among older children. The threat is greatest to newborns, who are more at risk of **death** from chickenpox than any other group. Under certain circumstances, children born to mothers who contract chickenpox just prior to delivery face an increased possibility of dangerous consequences, including brain damage and death. If the infection occurs during early **pregnancy**, there is a small (less than 5%) risk of congenital abnormalities.
- Immunocompromised children. Children whose immune systems have been weakened by a genetic disorder, disease, or medical treatment usually experience the most severe symptoms of any group. They have the second-highest rate of death from chickenpox.
- Adults and children 15 and older. Among this group, the typical symptoms of chickenpox tend to strike with greater force, and the risk of complications is much higher than among young children.

Immediate medical help should always be sought when anyone in these high-risk groups contracts the disease.

Diagnosis

Where children are concerned, especially those with recent exposure to the disease, diagnosis can usually be made at home, by a school nurse, or by a doctor over the telephone if the child's parent or caregiver is unsure that the disease is chickenpox.

A doctor should be called immediately if:

- The child's fever goes above 102°F (38.9°C) or takes more than four days to disappear.
- The child's blisters appear infected. Signs of infection include leakage of pus from the blisters or excessive redness, warmth, tenderness, or swelling around the blisters.
- The child seems nervous, confused, unresponsive, or unusually sleepy; complains of a stiff neck or severe **headache**; shows signs of poor balance or has trouble walking; finds bright lights hard to look at; is having breathing problems or is coughing a lot; is complaining of chest pain; is vomiting repeatedly; or is having convulsions. These may be signs of **Reye's syndrome** or encephalitis, two rare but potentially very dangerous conditions.

Treatment

With children, treatment usually takes place in the home and focuses on reducing discomfort and fever. Because chickenpox is a viral disease, **antibiotics** are ineffective against it.

Applying wet compresses or bathing the child in cool or lukewarm water once a day can help the itch. Adding

four to eight ounces of baking soda or one or two cups of oatmeal to the bath is a good idea (oatmeal bath packets are sold by pharmacies). Only mild soap should be used in the bath. Patting, not rubbing, is recommended for drying the child off, to prevent irritating the blisters. Calamine lotion (and some other kinds of lotions) also help to reduce itchiness. Because scratching can cause blisters to become infected and lead to scarring, the child's nails should be cut short. Of course, older children need to be warned not to scratch. For babies, light mittens or socks on the hands can help guard against scratching.

If mouth blisters make eating or drinking an unpleasant experience, cold drinks and soft, bland foods can ease the child's discomfort. Painful genital blisters can be treated with an anesthetic cream recommended by a doctor or pharmacist. Antibiotics are often prescribed if blisters become infected.

Fever and discomfort can be reduced by **acetaminophen** or another medication that does not contain **aspirin**. *Aspirin and any medications that contain aspirin or other salicylates must not be used with chickenpox, for they appear to increase the chances of developing Reye's syndrome.* The best idea is to consult a doctor or pharmacist if one is unsure about which medications are safe.

Immunocompromised chickenpox sufferers are sometimes given an antiviral drug called acyclovir (Zovirax). Studies have shown that Zovirax also lessens the symptoms of otherwise healthy children and adults who contract chickenpox, but the suggestion that it should be used to treat the disease among the general population, especially in children, is controversial.

A five-year-old girl with chickenpox. The first symptom of the disease is the rash that is evident on the girl's back and neck. The rash and the mild fever that accompanies it should disappear in a week or two. *(Photograph by Jim Selby, Photo Researchers, Inc. Reproduced by permission.)*

Alternative treatment

Alternative practitioners seek to lessen the discomfort and fever caused by chickenpox. Like other practitioners, they suggest cool or lukewarm baths. Rolled oats (*Avena sativa*) in the bath water help relieve **itching**. (Place oats in a sock, run the bath, turn the sock to release the milky anti-itch properties.) Other recommended remedies for itching include applying aloe vera, witch hazel, or herbal preparations of rosemary (*Rosmarinus officinalis*) and calendula (*Calendual officinalis*) to the blisters. Homeopathic remedies are selected on a case by case basis. Some common remedy choices are tartar emetic (antimonium tartaricum), windflower (pulsatilla), poison ivy (*Rhus toxicodendron*), and sulphur.

Prognosis

Most cases of chickenpox run their course within a week without causing lasting harm. However, there is one long-term consequence of chickenpox that strikes about 20% of the population, particularly people 50 and older. Like all herpes viruses, the varicella-zoster virus never leaves the body after an episode of chickenpox, but lies dormant in the nerve cells, where it may be reactivated years later by disease or age-related weakening of the immune system. The result is **shingles** (also called herpes zoster), a very painful nerve inflammation, accompanied by a rash, that usually affects the trunk or the face for 10 days or more. Especially in the elderly, pain, called postherpetic **neuralgia**, may persist at the site of the shingles for months or years. As of 1998, two newer drugs for treatment of shingles are available. Both valacyclovir (Valtrex) and famciclovir (Famvir) stop the replication of herpes zoster when administered within 72 hours of appearance of the rash. The effectiveness of these two drugs in immunocompromised patients has not

KEY TERMS

Acetaminophen—A drug for relieving pain and fever. Tylenol is the most common example.

Acyclovir—An antiviral drug used for combating chickenpox and other herpes viruses. Sold under the name Zovirax.

Dehydration—Excessive water loss by the body.

Encephalitis—A disease that inflames the brain.

Hepatitis—A disease that inflames the liver.

Immune system—A biochemical complex that protects the body against pathogenic organisms and other foreign bodies.

Immunocompromised—Having a damaged immune system.

Pneumonia—A disease that inflames the lungs.

Pus—A thick yellowish or greenish fluid containing inflammatory cells. Usually caused by bacterial infection.

Reye's syndrome—A rare but often fatal disease that involves the brain, liver, and kidneys.

Salicylates—Substances containing salicylic acid, which are used for relieving pain and fever. Aspirin is the most common example.

Shingles—A disease (also called herpes zoster) that causes a rash and a very painful nerve inflammation. An attack of chickenpox will eventually give rise to shingles in about 20% of the population.

Trunk—That part of the body that does not include the head, arms, and legs.

Varicella-zoster immune globulin (VZIG)—A substance that can reduce the severity of chickenpox symptoms.

Varicella-zoster virus—The virus that causes chickenpox and shingles.

Varivax—A vaccine for the prevention of chickenpox.

Virus—A tiny particle that can cause infections by duplicating itself inside a cell using the cell's own software. Antibiotics are ineffective against viruses, though antiviral drugs exist for some viruses, including chickenpox.

been established, and Famvir is not recommended for patients under 18 years, as of 1998.

Prevention

A substance known as varicella-zoster immune globulin (VZIG), which reduces the severity of chickenpox symptoms, is available to treat immunocompromised children and others at high risk of developing complications. It is administered by injection within 96 hours of known or suspected exposure to the disease and is not useful after that. VZIG is produced as a gamma globulin from blood of recently infected individuals.

A vaccine for chickenpox became available in the United States in 1995 under the name Varivax. Varivax is a live, attenuated (weakened) virus vaccine. It has been proven to be 85% effective for preventing all cases of chickenpox and close to 100% effective in preventing severe cases. Side effects are normally limited to occasional soreness or redness at the injection site. CDC guidelines state that the vaccine should be given to all children (with the exception of certain high-risk groups) at 12–18 months of age, preferably when they receive their measles-mumps-rubella vaccine. For older children, up to age 12, the CDC recommends **vaccination** when a reliable determination that the child in question has already had chickenpox cannot be made. Vaccination is also recommended for any older child or adult considered susceptible to the disease, particularly those, such as health care workers and women of childbearing age, who face a greater likelihood of severe illness or transmitting infection. A single dose of the vaccine is sufficient for children up to age 12; older children and adults receive a second dose four to eight weeks later. In 1997 the cost of two adult doses of the vaccine in the United States was about $80. Although this cost was not always covered by health insurance plans, children up to age 18 without access to the appropriate coverage could be vaccinated free of charge through the federal Vaccines for Children program. Varivax is not given to patients who already have overt signs of the disease. The vaccine is also not recommended for those women who are pregnant, or they should delay pregnancy for three months following a complete vaccination. The vaccine is useful when given early after exposure to chickenpox and, if given in the midst of the incubation period, it can be preventative. The Infectious Diseases Society of America stated in

2000 that immunization is recommended for all adults who have never had chickenpox.

While there was initial concern regarding the vaccine's safety and effectiveness when first released, the vaccination is gaining acceptance as numerous states require it for admittance into day care or public school. In 2000, 59% of toddlers in the United States were immunized; up from 43.2% in 1998. A study published in 2001 indicates that the varicella vaccine is highly effective when used in clinical practice. Although evidence has not ruled out a booster shot later in life, all research addressing the vaccine's effectiveness throughout its six-year use indicates that chickenpox may be the first human herpesvirus to be wiped out. Although initial concerns questioned if the vaccination might make shingles more likely, studies are beginning to show the effectiveness of the vaccine in reducing cases of that disease.

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ORGANIZATION

Centers for Disease Control and Prevention. National Immunization Hotline. 1600 Clifton Rd. NE, Atlanta, GA 30333. (800) 232-2522 (English). (800) 232-0233 (Spanish). <http://www.cdc.gov>.

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Beth Kapes

Child abuse

Definition

Child **abuse** is the blanket term for four types of child mistreatment: physical abuse, sexual abuse, emotional abuse, and neglect. In many cases children are the victims of more than one type of abuse. The abusers can be parents or other family members, caretakers such as teachers and babysitters, acquaintances (including other children), and (in rare instances) strangers.

Description

Prevalence of abuse

Child abuse was once viewed as a minor social problem affecting only a handful of United States children. However, in recent years it has received close attention from the media, law enforcement, and the helping professions, and with increased public and professional awareness has come a sharp rise in the number of reported cases. But because abuse is often hidden from view and its victims too young or fearful to speak out, experts suggest that its true prevalence is possibly much greater than the official data indicate. In 1996, more than three million victims of alleged abuse were reported to child protective services (CPS) agencies in the United States, and the reports were substantiated in more than one million cases. Put another way, 1.5% of the country's children were confirmed victims of abuse in 1996. Parents were the abusers in 77% of the confirmed cases, other relatives in 11%. Sexual abuse was more likely to be committed by males, whereas females were responsible for the majority of neglect cases. More than 1,000 United States children died from abuse in 1996.

Although experts are quick to point out that abuse occurs among all social, ethnic, and income groups, reported cases usually involve poor families with little education. Young mothers, single-parent families, and parental alcohol or drug abuse are also common in reported cases. Charles F. Johnson remarks, "More than 90% of abusing parents have neither psychotic nor criminal personalities. Rather they tend to be lonely, unhappy, angry, young, and single parents who do not plan their pregnancies, have little or no knowledge of child development, and have unrealistic expectations for child behavior." About 10%, or perhaps as many as 40%, of abusive parents were themselves physically abused as children, but most abused children do not grow up to be abusive parents.

Types of abuse

PHYSICAL ABUSE. Physical abuse is the nonaccidental infliction of physical injury to a child. The abuser is

usually a family member or other caretaker, and is more likely to be male. In 1996, 24% of the confirmed cases of United States child abuse involved physical abuse.

A rare form of physical abuse is **Munchausen syndrome** by proxy, in which a caretaker (most often the mother) seeks attention by making the child sick or appear to be sick.

SEXUAL ABUSE. Charles F. Johnson defines child sexual abuse as "any activity with a child, before the age of legal consent, that is for the sexual gratification of an adult or a significantly older child." It includes, among other things, sexual touching and penetration, persuading a child to expose his or her sexual organs, and allowing a child to view pornography. In most cases the child is related to or knows the abuser, and about one in five abusers are themselves underage. Sexual abuse was present in 12% of the confirmed 1996 abuse cases. An estimated 20–25% of females and 10–15% of males report that they were sexually abused by age 18.

EMOTIONAL ABUSE. Emotional abuse, according to Richard D. Krugman, "has been defined as the rejection, ignoring, criticizing, **isolation**, or terrorizing of children, all of which have the effect of eroding their self-esteem." Emotional abuse usually expresses itself in verbal attacks involving rejection, scapegoating, belittlement, and so forth. Because it often accompanies other types of abuse and is difficult to prove, it is rarely reported, and accounted for only 6% of the confirmed 1996 cases.

NEGLECT. Neglect—failure to satisfy a child's basic needs—can assume many forms. Physical neglect is the failure (beyond the constraints imposed by poverty) to provide adequate food, clothing, shelter, or supervision. Emotional neglect is the failure to satisfy a child's normal emotional needs, or behavior that damages a child's normal emotional and psychological development (such as permitting drug abuse in the home). Failing to see that a child receives proper schooling or medical care is also considered neglect. In 1996 neglect was the finding in 52% of the confirmed abuse cases.

Causes and symptoms

Physical abuse

The usual physical abuse scenario involves a parent who loses control and lashes out at a child. The trigger may be normal child behavior such as crying or dirtying a diaper. Unlike nonabusive parents, who may become angry at or upset with their children from time to time but are genuinely loving, abusive parents tend to harbor deep-rooted negative feelings toward their children.

Unexplained or suspicious **bruises** or other marks on the skin are typical signs of physical abuse, as are **burns**. Skull and other bone **fractures** are often seen in young abused children, and in fact, head injuries are the leading cause of **death** from abuse. Children less than one year old are particularly vulnerable to injury from shaking. This is called **shaken baby syndrome** or shaken impact syndrome. Not surprisingly, physical abuse also causes a wide variety of behavioral changes in children.

Sexual abuse

John M. Leventhal observes, "The two prerequisites for this form of maltreatment include sexual arousal to children and the willingness to act on this arousal. Factors that may contribute to this willingness include alcohol or drug abuse, poor impulse control, and a belief that the sexual behaviors are acceptable and not harmful to the child." The chances of abuse are higher if the child is developmentally handicapped or vulnerable in some other way.

Genital or anal injuries or abnormalities (including the presence of **sexually transmitted diseases**) can be signs of sexual abuse, but often there is no physical evidence for a doctor to find. In fact, physical examinations of children in cases of suspected sexual abuse supply grounds for further suspicion only 15–20% of the time. **Anxiety**, poor academic performance, and suicidal conduct are some of the behavioral signs of sexual abuse, but are also found in children suffering other kinds of **stress**. Excessive masturbation and other unusually sexualized kinds of behavior are more closely associated with sexual abuse itself.

Emotional abuse

Emotional abuse can happen in many settings: at home, at school, on sports teams, and so on. Some of the possible symptoms include loss of self-esteem, sleep disturbances, headaches or stomachaches, school avoidance, and running away from home.

Neglect

Many cases of neglect occur because the parent experiences strong negative feelings toward the child. At other times, the parent may truly care about the child, but lack the ability or strength to adequately provide for the child's needs because he or she is handicapped by depression, drug abuse, **mental retardation**, or some other problem.

Neglected children often do not receive adequate nourishment or emotional and mental stimulation. As a result, their physical, social, emotional, and mental development is hindered. They may, for instance, be

Child Abuse: Signs And Symptoms

Although these signs do not necessarily indicate that a child has been abused, they may help adults recognize that something is wrong. The possibility of abuse should be investigated if a child shows a number of these symptoms, or any of them to a marked degree:

Sexual Abuse

Being overly affectionate or knowledgeable in a sexual way inappropriate to the child's age
Medical problems such as chronic itching, pain in the genitals, venereal diseases
Other extreme reactions, such as depression, self-mutilation, suicide attempts, running away, overdoses, anorexia
Personality changes such as becoming insecure or clinging
Regressing to younger behavior patterns such as thumb sucking or bringing out discarded cuddly toys
Sudden loss of appetite or compulsive eating
Being isolated or withdrawn
Inability to concentrate
Lack of trust or fear someone they know well, such as not wanting to be alone with a babysitter
Starting to wet again, day or night/nightmares
Become worried about clothing being removed
Suddenly drawing sexually explicit pictures
Trying to be "ultra-good" or perfect; overreacting to criticism

Physical Abuse

Unexplained recurrent injuries or burns
Improbable excuses or refusal to explain injuries
Wearing clothes to cover injuries, even in hot weather
Refusal to undress for gym
Bald patches
Chronic running away
Fear of medical help or examination
Self-destructive tendencies
Aggression towards others
Fear of physical contact—shrinking back if touched
Admitting that they are punished, but the punishment is excessive (such as a child being beaten every night to "make him/her study")
Fear of suspected abuser being contacted

Emotional Abuse

Physical, mental, and emotional development lags
Sudden speech disorders
Continual self-depreciation ("I'm stupid, ugly, worthless, etc.")
Overreaction to mistakes
Extreme fear of any new situation
Inappropriate response to pain ("I deserve this")
Neurotic behavior (rocking, hair twisting, self-mutilation)
Extremes of passivity or aggression

Neglect

Constant hunger
Poor personal hygiene
No social relationships
Constant tiredness
Poor state of clothing
Compulsive scavenging
Emaciation
Untreated medical problems
Destructive tendencies

A child may be subjected to a combination of different kinds of abuse. It is also possible that a child may show no outward signs and hide what is happening from everyone.

underweight, develop language skills less quickly than other children, and seem emotionally needy.

Diagnosis

Doctors and many other professionals who work with children are required by law to report suspected abuse to their state's Child Protective Services (CPS) agency. Abuse investigations are often a group effort involving medical personnel, social workers, police officers, and others. Some hospitals and communities maintain child protection teams that respond to cases of possible abuse. Careful questioning of the parents is crucial, as is interviewing the child (if he or she is capable of being interviewed). The investigators must ensure, however, that their questioning does not further traumatize the child. A **physical examination** for signs of abuse or neglect is, of course, always

necessary, and may include x rays, blood tests, and other procedures.

Treatment

Notification of the appropriate authorities, treatment of the child's injuries, and protecting the child from further harm are the immediate priorities in abuse cases. If the child does not require hospital treatment, protection often involves placing him or her with relatives or in foster care. Once the immediate concerns are dealt with, it becomes essential to determine how the child's long-term medical, psychological, educational, and other needs can best be met, a process that involves evaluating not only the child's needs but also the family's (such as for drug abuse counseling or parental skills training). If the child has brothers or sisters, the authorities must determine whether they have been abused as well. On investigation, signs of physical abuse are discovered in about 20% of the brothers and sisters of abused children.

Prognosis

Child abuse can have lifelong consequences. Research shows that abused children and adolescents are more likely, for instance, to do poorly in school, suffer emotional problems, develop an antisocial personality, become promiscuous, abuse drugs and alcohol, and attempt suicide. As adults they often have trouble establishing intimate relationships. Whether professional treatment is able to moderate the long-term psychological effects of abuse is a question that remains unanswered.

Prevention

Government efforts to prevent abuse include home-visitor programs aimed at high-risk families and school-based efforts to teach children how to respond to attempted sexual abuse. Emotional abuse prevention has been promoted through the media.

When children reach age three, parents should begin teaching them about "bad touches" and about confiding in a suitable adult if they are touched or treated in a way that makes them uneasy. Parents also need to exercise caution in hiring babysitters and other caretakers. Anyone who suspects abuse should immediately report those suspicions to the police or his or her local CPS agency, which will usually be listed in the blue pages of the telephone book under Rehabilitative Services or Child and Family Services, or in the yellow pages. Round-the-clock crisis counseling for children and adults is offered by the Childhelp USA/IOF Foresters National Child Abuse Hotline. The National Committee to Prevent Child Abuse is an excellent source of information on the many support groups and other organizations that help abused and at-risk children and their families. One of these organizations, National Parents Anonymous, sponsors 2,100 local self-help groups throughout the United States, Canada, and Europe. Telephone numbers for its local groups are listed in the white pages of the telephone book under Parents Anonymous or can be obtained by calling the national headquarters.

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ORGANIZATIONS

Childhelp USA/IOF Foresters National Child Abuse Hotline. (800) 422-4453.

National Clearinghouse on Child Abuse and Neglect Information. P.O. Box 1182, Washington, DC 20013-1182. (800) 394-3366. <http://www.calib.com/nccanch>.

National Committee to Prevent Child Abuse. 200 S. Michigan Ave., 17th Floor, Chicago, IL 60604. (312) 663-3520. <http://www.childabuse.org>.

National Parents Anonymous. 675 W. Foothill Blvd., Suite 220, Claremont, CA 91711. (909) 621-6184.

Howard Baker

Child development *see* **Children's health**

Child safety *see* **Children's health**

Childbirth

Definition

Childbirth includes both labor (the process of birth) and delivery (the birth itself); it refers to the entire process as an infant makes its way from the womb down the birth canal to the outside world.

Description

Childbirth usually begins spontaneously, following about 280 days after conception, but it may be started by artificial means if the **pregnancy** continues past 42

weeks gestation. The average length of labor is about 14 hours for a first pregnancy and about eight hours in subsequent pregnancies. However, many women experience a much longer or shorter labor.

Labor can be described in terms of a series of phases.

First stage of labor

During the first phase of labor, the cervix dilates (opens) from 0–10 cm. This phase has an early, or latent, phase and an active phase. During the latent phase, progress is usually very slow. It may take quite a while and many contractions before the cervix dilates the first few centimeters. Contractions increase in strength as labor progresses. Most women are relatively comfortable during the latent phase and walking around is encouraged, since it naturally stimulates the process.

As labor begins, the muscular wall of the uterus begins to contract as the cervix relaxes and expands. As a portion of the amniotic sac surrounding the baby is pushed into the opening, it bursts under the pressure, releasing amniotic fluid. This is called "breaking the bag of waters."

During a contraction, the infant experiences intense pressure that pushes it against the cervix, eventually forcing the cervix to stretch open. At the same time, the contractions cause the cervix to thin. During this first stage, a woman's contractions occur more and more often and last longer and longer. The doctor or nurse will do a periodic **pelvic exam** to determine how the mother is progressing. If the contractions aren't forceful enough to open the cervix, a drug may be given to make the uterus contract.

As **pain** and discomfort increase, women may be tempted to request pain medication. If possible, though, administration of pain medication or anesthetics should be delayed until the active phase of labor begins—at which point the medication will not act to slow down or stop the labor.

The active stage of labor is faster and more efficient than the latent phase. In this phase, contractions are longer and more regular, usually occurring about every two minutes. These stronger contractions are also more painful. Women who use the breathing exercises learned in childbirth classes find that these can help cope with the pain experienced during this phase. Many women also receive some pain medication at this point—either a short-term medication, such as Nubain or Numorphan, or an epidural anesthesia.

As the cervix dilates to 8–9 cm, the phase called the transition begins. This refers to the transition from the first phase (during which the cervix dilates from 0–10 cm) and the second phase (during which the baby is pushed out through the birth canal). As the baby's head begins to descend, women begin to feel the urge to "push" or bear down. Active pushing by the mother should not begin until the second phase, since pushing too early can cause the cervix to swell or to tear and bleed. The attending healthcare practitioner should counsel the mother on when to begin to push.

Stage 1: Dilation of the cervix. *(Illustration by Hans & Cassady.)*

Second stage of labor

As the mother enters the second stage of labor, her baby's head appears at the top of the cervix. Uterine contractions get stronger. The infant passes down the vagina, helped along by contractions of the abdominal muscles and the mother's pushing. Active pushing by the mother is very important during this phase of labor. If an epidural anesthetic is being used, many practitioners recommend decreasing the amount administered during this phase of labor so that the mother has better control over her abdominal muscles.

When the top of the baby's head appears at the opening of the vagina, the birth is nearing completion. First the head passes under the pubic bone. It fills the lower vagina and stretches the perineum (the tissues between the vagina and the rectum). This position is called "crowning," since only the crown of the head is visible. When the entire head is out, the shoulders follow. The attending practitioner suctions the baby's mouth and nose to ease the baby's first breath. The rest of the baby usually slips out easily, and the umbilical cord is cut.

Episiotomy

As the baby's head appears, the perineum may stretch so tight that the baby's progress is slowed down. If there is risk of tearing the mother's skin, the doctor may choose to make a small incision into the perineum to

Stage 2: Expulsion of the fetus. *(Illustration by Hans & Cassady.)*

enlarge the vaginal opening. This is called an **episiotomy**. If the woman has not had an epidural or pudendal block, she will get a local anesthetic to numb the area. Once the episiotomy is made, the baby is born with a few pushes.

Third stage

In the final stage of labor, the placenta is pushed out of the vagina by the continuing uterine contractions. The placenta is pancake shaped and about 10 inches in diameter. It has been attached to the wall of the uterus and has served to convey nourishment from the mother to the fetus throughout the pregnancy. Continuing uterine contractions cause it to separate from the uterus at this point. It is important that all of the placenta be removed from the uterus. If it is not, the uterine bleeding that is normal after delivery may be much heavier.

Breech presentation

Approximately 4% of babies are in what is called the "breech" position when labor begins. In breech presentation, the baby's head is not the part pressing against the cervix. Instead the baby's bottom or legs are positioned to enter the birth canal instead of the head. An obstetrician may attempt to turn the baby to a head down position using a technique called version. This is only successful approximately half the time.

The risks of vaginal delivery with breech presentation are much higher than with a head-first presentation and the mother and attending practitioner will need to weigh the risks and make a decision on whether to deliver via a **cesarean section** or attempt a vaginal birth. The extent of the risk depends to a great extent on the type of breech presentation—of which there are three. Frank breech (the baby's legs are folded up against its body) is the most common and the safest for vaginal delivery. The other types are complete breech (in which the baby's legs are crossed under and in front of the body) and footling breech (in which one leg or both legs are positioned to enter the birth canal) are not considered safe to attempt vaginal delivery.

Even in complete breech, other factors should be met before considering a vaginal birth. An ultrasound examination should be done to be sure the baby does not have an unusually large head and that the head is tilted forward (flexed) rather than back (hyperextended). Fetal monitoring and close observation of the progress of labor are also important. A slowing of labor or any indication of difficulty in the body passing through the pelvis should be an indication that it is safer to consider a cesarean section.

Forceps delivery

If the labor is not progressing as it should or if the baby appears to be in distress, the doctor may opt for a forceps delivery. A forceps is a spoon-shaped device that resembles a set of salad tongs. It is placed around the baby's head so the doctor can pull the baby gently out of the vagina.

Forceps can be used after the cervix is fully dilated, and they might be required if:

- the umbilical cord has dropped down in front of the baby into the birth canal
- the baby is too large to pass through the birth canal unaided
- the baby shows signs of stress
- the mother is too exhausted to push

Before placing the forceps around the baby's head, pain medication or anesthesia may be given to the mother. The doctor may use a catheter to empty the mother's bladder, and may clean the perineal area with soapy water. Often an episiotomy is done before a forceps birth, although tears can still occur.

The obstetrician slides half of the forceps at a time into the vagina and around the side of the baby's head to gently grasp the head. When both "tongs" are in place, the doctor pulls on the forceps to help the baby through the birth canal as the uterus contracts. Sometimes the baby can be delivered this way after the very next contraction.

The frequency of forceps delivery varies from one hospital to the next, depending on the experience of staff and the types of anesthesia offered at the hospital. Some obstetricians accept the need for a forceps delivery as a way to avoid cesarean birth. However, other obstetrical services don't use forceps at all.

Complications from forceps deliveries can occur. Sometimes they may cause nerve damage or temporary

bruises to the baby's face. When used by an experienced physician, forceps can save the life of a baby in distress.

Vacuum-assisted birth

This method of helping a baby out of the birth canal was developed as a gentler alternative to forceps. Vacuum-assisted birth can only be used after the cervix is fully dilated (expanded), and the head of the fetus has begun to descend through the pelvis. In this procedure, the doctor uses a device called a vacuum extractor, placing a large rubber or plastic cup against the baby's head. A pump creates suction that gently pulls on the cup to ease the baby down the birth canal. The force of the suction may cause a bruise on the baby's head, but it fades away in a day or so.

The vacuum extractor is not as likely as forceps to injure the mother, and it leaves more room for the baby to pass through the pelvis. However, there may be problems in maintaining the suction during the vacuum-assisted birth, so forceps may be a better choice if it is important to remove the baby quickly.

Cesarean sections

A cesarean section, also called a c-section, is a surgical procedure in which incisions are made through a woman's abdomen and uterus to deliver her baby.

Cesarean sections are performed whenever abnormal conditions complicate labor and vaginal delivery, threatening the life or health of the mother or the baby. The procedure is performed in the United States on nearly one of every four babies delivered—more than 900,000 babies each year. The procedure is used in cases where the mother has had a previous c-section and the area of the incision has been weakened. Dystocia, or difficult labor, is the another common reason for performing a c-section.

Difficult labor is commonly caused by one of the three following conditions: abnormalities in the mother's birth canal; abnormalities in the position of the fetus; abnormalities in the labor, including weak or infrequent contractions.

Another major factor is fetal distress, a condition where the fetus is not getting enough oxygen. Fetal brain damage can result from oxygen deprivation. Fetal distress is often related to abnormalities in the position of the fetus, or abnormalities in the birth canal, causing reduced blood flow through the placenta.

Other conditions also can make c-section advisable, such as vaginal herpes, **hypertension** (high blood pressure) and diabetes in the mother.

Stage 3: Expulsion of the placenta

Stage 3: Expulsion of the placenta. *(Illustration by Hans & Cassady.)*

Causes and symptoms

One of the first signs of approaching childbirth may be a "bloody show," the appearance of a small amount of blood-tinged mucus released from the cervix as it begins to dilate. This is called the "mucus plug."

The most common sign of the onset of labor is contractions. Sometimes women have trouble telling the difference between true and false labor pains.

True labor pains:

- develop a regular pattern, with contractions coming closer together
- last from 15–30 seconds at the onset and get progressively stronger and longer (up to 60 seconds)
- may get stronger with physical activity
- occur high up on the abdomen, radiating throughout the abdomen and lower back

Another sign that labor is beginning is the breaking of the "bag of waters," the amniotic sac which had cushioned the baby during the pregnancy. When it breaks, it releases water in a trickle or a gush. Only about 10% of women actually experience this water flow in the beginning of labor, however. Most of the time, the rupture occurs sometime later in labor. If the amniotic sac doesn't rupture on its own, the doctor will break it during labor.

Some women have **diarrhea** or nausea as labor begins. Others notice a sudden surge of energy and the urge to clean or arrange things right before labor begins; this is known as "nesting."

Diagnosis

The onset of labor can be determined by measuring how much the cervix has dilated. The degree of dilation is estimated by feeling the opening cervix during a pelvic exam. Dilation is measured in centimeters, from zero to

KEY TERMS

Amniotic sac—The membranous sac that surrounds the embryo and fills with watery fluid as pregnancy advances.

Breech birth—Birth of a baby bottom-first, instead of the usual head first delivery. This can add to labor and delivery problems because the baby's bottom doesn't mold a passage through the birth canal as well as does the head.

Cervix—A small cylindrical organ about an inch or so long and less than an inch around that makes up the lower part and neck of the uterus. The cervix separates the body and cavity of the uterus from the vagina.

Embryo—The unborn child during the first eight weeks of its development following conception.

Gestation—The period from conception to birth, during which the developing fetus is carried in the uterus.

Perineum—The area between the thighs that lies behind the genital organs and in front of the anus.

Placenta—The organ that develops in the uterus during pregnancy and that links the blood supplies of mother and baby.

10. Contractions that cause the cervix to dilate are the sign of true labor.

Fetal monitoring

Fetal monitoring is a process in which the baby's heart rate is monitored for indicators of stress during labor and birth. There are several types of fetal monitoring.

A special stethoscope called a fetoscope may be used. This is a simple and non-invasive method.

The Doppler method uses ultrasound; it involves a handheld listening device that transmits the sounds of the heart rate through a speaker or into an attached ear piece. It can usually pick up the heart sounds 12 weeks after conception. This method offers intermittent monitoring. It allows the mother freedom to move about and is also useful during contractions.

Electronic fetal monitoring uses ultrasound and provides a view of the heartbeat in relationship to the mother's contractions. It can be used either continuously or intermittently. It is often used in high risk pregnancies, and is not often recommended for low risk ones because it renders the mother immobile and requires interpretation.

Internal monitoring does not use ultrasound, is more accurate than electronic monitoring and provides continuous monitoring for the high risk mother. This requires the mother's water to be broken and that she be two to three centimeters dilated. It is used in high-risk situations only.

Telemetry monitoring is the newest type of monitoring. It uses radio waves transmitted from an instrument on the mother's thigh. The mother is able to remain mobile. It provides continuous monitoring and is used in high-risk situations.

Treatment

Most women choose some type of pain relief during childbirth, ranging from relaxation and imagery to drugs. The specific choice may depend on what's available, the woman's preferences, her doctor's recommendations, and how the labor is proceeding. All drugs have some risks and some advantages.

Regional anesthetics

Regional anesthetics include epidurals and spinals. In this technique, medication is injected into the space around the spinal nerves. Depending on the type of medications used, this type of anesthesia can block nerve signals, causing temporary pain relief, or a loss of sensation from the waist down. An epidural or spinal block can provide complete pain relief during cesarean birth.

An epidural is placed with the woman lying on her side or sitting up in bed with the back rounded to allow more space between the vertebrae. Her back is scrubbed with antiseptic, and a local anesthetic is injected in the skin to numb the site. The needle is inserted between two vertebrae and through the tough tissue in front of the spinal column. A catheter is put in place that allows continuous doses of anesthetic to be given.

This type of anesthesia provides complete pain relief, and can help conserve a woman's energy, since she can relax or even sleep during labor. This type of anesthesia does require an IV and fetal monitor. It may be harder for a woman to bear down when it comes time to push, although the amount of anesthesia can be adjusted as this stage nears.

Spinal anesthesia operates on the same principle as epidural anesthesia, and is used primarily in cases of c-section delivery. It is administered in the same way as an epidural, but the catheter is not left in place. The amount of anesthetic injected is large, since it must be injected at one time. Because of the anesthetic's effect on motor nerves, most women using it cannot push during delivery.

This is a disadvantage in labor, but not an issue during a c-section. Spinals provide quick and strong anesthesia and allow for major abdominal surgery with almost no pain.

Narcotics

Short-acting narcotics can ease pain and don't interfere with a woman's ability to push. However, they can cause **sedation**, **dizziness**, nausea, and vomiting. Narcotics cross the placenta and may slow down a baby's breathing; they can't be given too close to the time of delivery.

Natural childbirth and preparation for childbirth

There are several methods to prepare for childbirth. The one selected often depends on what is available through the healthcare provider. Overall, family involvement is receiving increased attention by the healthcare systems, and many hospitals now offer birthing rooms and maternity centers to help the entire family. There are several choices available for childbirth preparation.

Lamaze, or Lamaze-Pavlov, is the most common in the United States today. It was the first popular natural childbirth method, becoming popular in the 1960s. Breathing exercises and concentration on a focal point are practiced to allow mothers to control pain while maintaining consciousness. This allows the flow of oxygen to the baby and to the muscles in the uterus to be maintained. A partner coaches the mother throughout the birthing process.

The Read method, named for Dick Read, is a technique of breathing that was originated in the 1930s to help mothers deal with apprehension and tension associated with childbirth. This natural childbirth method uses different breathing for the different stages of childbirth.

The LeBoyer method stresses a relaxed delivery in a quiet, dim room. It attempts to avoid overstimulation of the baby and to foster mother-child bonding by placing the baby on the mother's abdomen and having the mother massage him or her immediately after the birth. Then the father washes the baby in a warm bath.

The Bradley method is called father-coached childbirth, because it focuses on the father serving as coach throughout the process. It encourages normal activities during the first stages of labor.

Resources

BOOKS

Carlson, Karen J., Stephanie A. Eisenstat, and Terra Ziporyn. *The Harvard Guide to Women's Health*. Cambridge, MA: Harvard University Press, 1996.

Cunningham, F. Gary, et.al. *Williams Obstetrics*. 20th ed. Stamford: Appleton & Lange, 1997.

Johnson, Robert V. *Mayo Clinic Complete Book of Pregnancy & Baby's First Year*. New York: William Morrow and Co., Inc., 1994.

Ryan, Kenneth J., Ross S. Berkowitz, and Robert L. Barbieri. *Kistner's Gynecology*. 6th ed. St. Louis: Mosby, 1995.

Tuteur, Amy B. *How Your Baby is Born*. Emeryville, CA: Ziff-Davis Press, 1994.

ORGANIZATIONS

American Academy of Husband-Coached Childbirth. P.O. Box 5224, Sherman Oaks, CA 91413. (800) 423-2397; in California (800) 422-4784.

American Society for Prophylaxis in Obstetrics/LAMAZE (ASP.O. /LAMAZE). 1840 Wilson Blvd., Ste. 204, Arlington, VA 22201. (800) 368-4404.

Childbirth Education Foundation. P.O. Box 5, Richboro, PA 18954. (215) 357-2792.

International Association of Parents and Professionals for Safe Alternatives in Childbirth. Rte. 1, Box 646, Marble Hill, MO 63764. (314) 238-2010.

International Childbirth Education Association. P.O. Box 20048, Minneapolis, MN 55420. (612) 854-8660.

Postpartum Support International. 927 North Kellogg Ave., Santa Barbara, CA 93111. (805) 967-7636.

Carol A. Turkington

Childhood disintegrative disorder *see* **Pervasive developmental disorders**

Children's health

Definition

Children's health encompasses the physical, mental, emotional, and social well-being of children from infancy through adolescence.

Description

All children should have regular well-child check ups according to the schedule recommended by their physician or pediatrician. The American Academy of Pediatrics (AAP) advises that children be seen for well-baby check ups at two weeks, two months, four months, six months, nine months, twelve months, fifteen months, and eighteen months. Well-child visits are recommended at ages two, three, four, five, six, eight, ten, and annually thereafter through age 21.

In addition, an immunization schedule should be followed to protect against disease and infection. As of 2001, the AAP and the U.S. Centers for Disease Control (CDC) recommended that the following childhood immunizations be administered by age two:

KEY TERMS

Bipolar disorder—Manic depressive disorder. A mood disorder characterized by manic highs and depressive lows.

Child development—The process of physical, intellectual, emotional, and social growth that occurs from infancy through adolescence. Erik Erikson, Margaret Mahler, Sigmund Freud, and Jean Piaget are among the most well-known child development theorists.

CPR—Cardiopulmonary resuscitation. A first aid technique designed to stimulate breathing and blood flow through a combination of chest compressions and rescue breathing.

Immunization—Creating immunity to a disease through a vaccine injection that stimulates the production of antibodies.

Learning disabilities—An impairment of the cognitive processes of understanding and using spoken and written language that results in difficulties with one or more academic skill sets (e.g., reading, writing, mathematics).

Motor skills—Controlled movement of muscle groups. Fine motor skills involve tasks that require dexterity of small muscles, such as buttoning a shirt. Tasks such as walking or throwing a ball involve the use of gross motor skills.

Obsessive-compulsive disorder—Also known as OCD; a disorder characterized by obsessive thoughts (e.g., fear of contamination) and compulsive behaviors (e.g., repetitive hand washing) that cause distress and/or functional impairment.

Psychological tests—Written, verbal, or visual tasks that assess psychological functioning, intelligence, and/or personality traits.

Type 1 diabetes—A chronic immune system disorder in which the pancreas does not produce sufficient amounts of insulin, a hormone that enables cells to use glucose for energy. Also called juvenile diabetes, it must be treated with insulin injections.

- Hepatitis B. Three doses.
- Diphtheria, **Tetanus**, and Pertussis (DTaP). Four doses.
- H. influenzae type b (Hib). Four doses.
- Inactivated **Polio**. Three doses.
- Pneumococcal Conjugate. Three doses.
- Measles, **Mumps**, **Rubella** (MMR). One dose.
- Varicella (chickenpox). One dose.
- Hepatitis A. (In certain geographical areas and with certain high risk groups.)

Some immunizations may cause mild side effects, or more rarely, serious adverse reactions. However, the benefits of immunization greatly outweigh the incidence of health problems arising from them.

There are serious chronic diseases and health problems that are frequently diagnosed in childhood and cannot be vaccinated against. These include, but are not limited to, **asthma**, type I diabetes (juvenile diabetes), leukemia, **hemophilia**, and **cystic fibrosis**.

Mental health

Children who have difficulty in areas of language acquisition, cognitive development, and behavior control may be suffering from mental illness. Mental health problems that may afflict children include:

- Attention Deficit Hyperactivity Disorder (**ADHD**). According to the AAP, 4–12% of school-aged children have ADHD, a condition characterized by poor impulse control and excessive motor activity.
- **Learning disorders**. Learning disabilities affect one in 10 school children.
- Depression, **anxiety**, and **bipolar disorder**. Affective, or mood, disorders can affect kids as well as adults.
- Eating disorders. **Anorexia nervosa**, **bulimia nervosa**, and binge eating disorder (BED) frequently occur in adolescent girls.
- **Schizophrenia**. A disorder characterized by bizarre thoughts and behaviors, **paranoia**, impaired sense of reality, and **psychosis** may be diagnosed in childhood.
- Obsessive-compulsive disorder. Also called OCD, this anxiety disorder afflicts one in 200 children.
- **Autism** and pervasive developmental disorder. Severe developmental disabilities that cause a child to become withdrawn and unresponsive.
- **Mental retardation**. Children under age 18 with an IQ of 70 or below and impairments in adaptive functioning are considered mentally retarded.

DR. BENJAMIN SPOCK (1903–1998)

(Library of Congress.)

Benjamin Spock, pediatrician and political activist, was most noted for his authorship of *Baby and Child Care*, which significantly changed predominant attitudes toward the raising of infants and children. He began medical school at Yale University in 1925, and transferred to Columbia University's College of Physicians and Surgeons in 1927. Spock had decided well before starting his medical studies that he would "work with children, who have their whole lives ahead of them" and so, upon taking his M.D. degree in 1929 and serving his general internship at the prestigious Presbyterian Hospital, he specialized in pediatrics at a small hospital crowded with children in New York's Hell's Kitchen area.

On a summer vacation in 1943 he began to write his most famous book and he continued to work on it from 1944 to 1946 while serving as a medical officer in the Navy. The book sharply broke with the authoritarian tone and rigorous instructions found in earlier generations of baby-care books, most of which said to feed infants on a strict schedule and not to pick them up when they cried. Spock, who spent ten years trying to reconcile his psychoanalytic training with what mothers were telling him about their children, told his readers "You know more than you think you do. Don't be afraid to trust your own common sense. Take it easy, trust your own instincts, and follow the directions that your doctor gives you." The response was overwhelming. *Baby and Child Care* rapidly became America's all-time best-seller except for Shakespeare and the Bible; by 1976 it had also eclipsed Shakespeare.

Emotional and social health

Children take their first significant steps toward socialization and peer interaction when they begin to engage in cooperative play at around age four. Their social development will progress throughout childhood and adolescence as they develop friendships, start to be influenced by their peers, and begin to show interest in the opposite sex.

Factors which can have a negative impact on the emotional and social well-being of children include:

- Violence. Bullying can cause serious damage to a child's sense of self-esteem and personal safety, as can experiences with school violence.
- Family turmoil. Divorce, **death**, and other life-changing events that alter the family dynamic can have a serious impact on a child. Even a positive event such as the birth of a sibling or a move to a new city and school can put emotional strain on a child.
- **Stress**. The pressure to perform well academically and in extracurricular activities such as sports can be overwhelming to some children.
- Peer pressure. Although it can have a positive impact, peer pressure is often a source of significant stress for children. This is particularly true in adolescence when "fitting in" seems all-important.
- Drugs and alcohol. Curiosity is intrinsic to childhood, and over 30% of children have experimented with alcohol by age 13. Open communication with children that sets forth parental expectations about drug and alcohol use is essential.
- Negative sexual experiences. Sexual **abuse** and assault can emotionally scar a child and instill negative feelings about sexuality and relationships.

Causes and symptoms

Childhood health problems may be congenital (i.e., present at birth) or acquired through infection, immune system deficiency, or another disease process. They may also be caused by physical trauma (e.g., a car accident or a playground fall) or a toxic substance (e.g., an allergen, drug, or poisonous chemical), or triggered by genetic or environmental factors.

Physical and mental health problems in childhood can cause a wide spectrum of symptoms. However, the following behaviors frequently signify a larger emotional, social, or mental disturbance:

- signs of alcohol and drug use
- falling grades
- lack of interest in activities that were previously enjoyable to the child
- excessive anxiety
- persistent, prolonged depression
- withdrawal from friends and family
- violence
- temper tantrums or inappropriate displays of anger
- self-inflicted injury
- bizarre behavior and/or speech
- trouble with the police
- sexual promiscuity
- suicide attempts

The causes of developmental disorders and delays and learning disabilities are not always fully understood. Pervasive developmental disorder (PDD) and autistic spectrum disorder (more commonly known as autism) are characterized by unresponsiveness and severe impairments in one or more of the following areas:

- Social interaction. Autistic children are often unaware of acceptable social behavior and are withdrawn and socially isolated. They frequently do not like physical contact.
- Communication and language. A child with autism or PDD may not speak or may display limited or immature language skills.
- Behavior. Autistic or PDD children may have difficulty dealing with anger, can be self-injurious, and may display obsessive behavior.

Autism is associated with brain abnormalities, but the exact mechanisms that trigger the disorder are yet to be determined. It has been linked to certain congenital conditions such as **neurofibromatosis**, **fragile X syndrome**, and **phenylketonuria** (PKU).

Diagnosis

Physical, intellectual, emotional, and social maturation are all important markers of a child's overall health and well-being. When evaluating children, pediatricians and child-care specialists assess related skill sets, such as a child's acquisition and use of language, fine and gross motor skills, cognitive growth, and socialization, and achievement of certain milestones in these areas. A developmental milestone is a task or skill set that a child is expected to reach at a certain age or stage of life. For example, by age one, most children have achieved the physical milestone of walking with the assistance of an adult. Developmental disorders may be identified and/or diagnosed by physicians, teachers, child psychologists, therapists, counselors, and other professionals who interact with children on a regular basis.

It is important to remember that all children are unique, and develop at different paces within this broad framework. Reaching a milestone early or late does not necessarily indicate a developmental problem. However, if a child is consistently lagging on achieving milestones, or has a significant deficit in one developmental area, he or she may be experiencing developmental delays.

Pediatricians and other medical professionals typically diagnose physical illness and disease in children. In cases of illness and injury, children will undergo a thorough **physical examination** and patient history. Diagnostic tests may be performed as appropriate. In cases of mental or emotional disorders, a psychologist or other mental healthcare professional will meet with the patient to conduct an interview and take a detailed social and medical history. Interviews with a parent or guardian may also be part of the diagnostic process. The physician may also administer one or more **psychological tests** (also called clinical inventories, scales, or assessments).

Treatment

Medications may be prescribed to treat certain childhood illnesses. Proper dosage is particularly important with infants and children, as medications such as **acetaminophen** can be toxic in excessive amounts. Parents and caregivers should always follow the instructions for use that accompany medications, and inform the child's pediatrician if the child is taking any other drugs or **vitamins** to prevent potentially negative drug interactions. Any side effects or adverse reactions to medication should be reported to the child's physician. If **antibiotics** are prescribed, the full course should always be taken.

Other treatments for childhood illness and/or injuries include, but are not limited to, nutritional therapy, physical therapy, respiratory therapy, medical devices (e.g., **hearing aids**, glasses, braces), and in some cases, surgery.

Counseling is typically a front-line treatment for psychological disorders. Therapy approaches include psychotherapy, cognitive therapy, behavioral therapy, family counseling, and **group therapy**. Therapy or counseling may be administered by social workers, nurses, licensed counselors and therapists, psychologists, or psy-

Leading Causes Of Illness/Injury In Adolescents

Trauma (this could be anything from sports-related injuries to gunshot wounds; alcohol or other drug abuse is frequently a factor)
Mental health issues (substance abuse, depression, etc.)
Sexually transmitted infections
Acquired immunodeficiency syndrome (AIDS)
Eating disorders

chiatrists. Psychoactive medication may also be prescribed for symptom relief in children and adolescents with mental disorders.

Support groups may also provide emotional support for children with chronic illnesses or mental disorders. This approach, which allows individuals to seek advice and counsel from others in similar circumstances, can be extremely effective, especially in older children who look towards their peers for guidance and support.

Speech therapy may be helpful to children with developmental delays in language acquisition. Children with learning disorders can benefit from special education therapy.

Alternative treatment

Therapeutic approaches that encourage self-discovery and empowerment may be useful in treating some childhood emotional traumas and mental disorders. **Art therapy**, the use of the creative process to express and understand emotion, encompasses a broad range of humanistic disciplines, including visual arts, dance, drama, music, film, writing, literature, and other artistic genres. It can be particularly effective in children who may have difficulty gaining insight to emotions and thoughts they are otherwise incapable of expressing.

Certain mild herbal remedies may also be safely used with children, such as ginger (*Zingiber officinale*) tea for nausea and aloe vera salve for **burns**. Parents and caregivers should always consult their healthcare provider before administering herbs to children.

Prognosis

The prognosis for childhood health problems varies widely. In general, early detection and proper treatment can greatly improve the odds of recovery from many childhood ailments.

Some learning disabilities and mild developmental disorders can be overcome or greatly improved through the therapies discussed above. However, as of early 2001, there was no known medical treatment or pharmacological therapy that is capable of completely eliminating all of the symptoms associated with pervasive developmental disorder (PDD), autism spectrum disorder, and mental retardation. Mental illnesses such as schizophrenia and bipolar disorder are also chronic, lifelong disorders, although their symptoms can often be well-controlled with medication.

Prevention

Parents can take some precautions to ensure the safety of their children. Childproofing the home, following a recommended immunization schedule, educating kids on safety, learning **CPR**, and taking kids for regular well-child check-ups can help to protect against physical harm. In addition, encouraging open communication with children can help them grow both emotionally and socially. Providing a loving and supportive home environment can help to nurture an emotionally healthy child who is independent, self-confident, socially skilled, insightful, and empathetic towards others.

Because they are still developing motor skills, kids can be particularly accident prone. Observe the following safety rules to protect children from injury:

- Helmets and padding. Children should always wear a properly fitted helmet and appropriate protective gear when riding a bike, scooter, or similar equipment or participating in sports. They should also ride on designated bike paths whenever possible, and learn bicycle safety rules (i.e., ride with traffic, use hand signals).
- Playground safety. Swing sets and other outdoor play equipment should be well-maintained have at least 12 in (30 cm) of loose fill materials (e.g., sand, wood chips) underneath to cushion falls, and children should always be properly supervised at play.
- Stay apprised of recalls. Children's toys, play equipment, and care products are frequently involved in product recalls. The U.S. Consumer Safety Products Commission (CSPC) is the agency responsible for tracking these recalls (see *Resources* below).
- Stay safe in the car. Up to 85% of children's car seats are improperly installed and/or used. Infants should always be in a rear-facing car seat until they are over 12 months of age and weigh more than 20 lb (9 kg). Never

Leading Causes Of Death In Adolescents

Motor vehicle crashes
Suicide (numbers 2 and 3 are approximately equal)
Homicide
Poisoning (which includes accidental poisonings due to alcohol or other drug overdose)
Drowning

put an infant or car seat in a front passenger seat that has an air bag. Once they outgrow their forward facing car seats, children between the ages of four and eight who weigh between 40–80 lb (18–36 kg) should ride in a booster seat. Every child who rides in a car over this age and weight should buckle up with a properly fitted lap and shoulder belt.

- Teach children pedestrian safety. Younger children should never be allowed to cross the street by themselves, and older kids should know to follow traffic signs and signals, cross the street at the corner, and look both ways before stepping off the curb.
- Teach children about personal safety. Kids should know what to do in case they get lost or are approached by a stranger. It is also imperative that parents talk openly with their children about their body and sexuality, and what behavior is inappropriate, to protect them against sexual predators.

Child-proofing the household is also an important step towards keeping kids healthy. To make a house a safe home:

- Ban guns. Accidental shootings in the home injure an estimated 1,500 children under age 14 each year. If a gun must be in the home, it should be securely locked in a tamper proof box or safe.
- Keep all matches, lighters, and flammable materials properly stored and out of the reach of children.
- Make sure hot water heaters are set to 120 degrees or below to prevent scalding injuries.
- Equip the home with working fire extinguishers and smoke alarms, and teach children what to do in case of fire.
- Secure all medications (including vitamins, herbs, and supplements), hazardous chemicals, and poisonous substances (including alcohol and tobacco).
- Don't smoke. Aside from causing **cancer** and other health problems in smokers, second-hand smoke is hazardous to a child's health.
- Keep small children away from poisonous plants outdoors, and remove any indoor plants that are toxic.
- Post the phone numbers of poison control and the pediatrician near the phone, and teach children about dialing 9-1-1 for emergencies.
- Children under age five should never be left alone in the bathtub, wading pool, or near any standing water source (including an open toilet). Drowning is the leading cause of death by injury for children between the ages of one and four.
- Remove lead paint. Lead is a serious health hazard for children, and houses built before 1978 should be tested for lead paint. If lead is found, the paint should be removed using the appropriate safety precautions.

These safety guidelines are not all-inclusive, and there are many age-specific safety precautions that parents and guardians of children should observe. For example, infants should never be left with a propped-up bottle in their mouths or given small play items because of the **choking** hazards involved.

Resources

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ORGANIZATIONS

National Institute of Mental Health. 6001 Executive Boulevard, Rm. 8184, MSC 9663, Bethesda, MD 20892-9663. (301) 443-4513.

National SAFE KIDS Campaign. Children's National Medical Center. (202) 662-0600. <http://www.safekids.org>.

U.S. Consumer Products Safety Commission (CPSC). 4330 East-West Highway, Bethesda, MD 20814-4408. (800) 638-2772. <http://www.cpsc.gov>.

Paula Ford-Martin

Chinese traditional herbal medicine *see* **Traditional Chinese herbalism**

Chinese traditional medicine *see* **Traditional Chinese medicine**

Chiropractic

Definition

Chiropractic is from Greek words meaning done by hand. It is grounded in the principle that the body can heal itself when the skeletal system is correctly aligned and the nervous system is functioning properly. To achieve this, the practitioner uses his or her hands or an adjusting tool to perform specific manipulations of the vertebrae. When these bones of the spine are not correctly articulated, resulting in a condition known as subluxation, the theory is that nerve transmission is disrupted and causes **pain** and illness manifested in the back as well as other areas of the body.

Chiropractic is one of the most popular alternative therapies currently available. Some would say it now qualifies as mainstream treatment as opposed to complementary medicine. Chiropractic treatment is covered by many insurance plans. It has become well-accepted treatment for acute pain and problems of the spine, including lower back pain and **whiplash**. Applications beyond that scope are not supported by current evidence, although there are ongoing studies into the usefulness of chiropractic for such problems as ear infections, **dysmenorrhea**, infant **colic**, migraine headaches, and other conditions.

Purpose

Most people will experience back pain at some time in their lives. Injuries due to overexertion and poor posture are among the most common. Depending on the cause and severity of the condition, options for treatment may include physical therapy, rest, medications, surgery, or chiropractic care. Chiropractic treatment carries none of the risks of surgical or pharmacologic treatment. Practitioners use a holistic approach to health, which is appreciated by most patients. The goal is not merely to relieve the present ailment, but to analyze the cause and recommend appropriate changes of lifestyle to prevent the problem from recurring again. They believe in a risk/benefit analysis before use of any intervention. The odds of an adverse outcome are extremely low. Chiropractic has proven in several studies to be less expensive than many more traditional routes such as outpatient physical therapy. Relief from some neuromuscular problems is immediate, although a series of treatments is likely to be required to maintain the improvement. Spinal manipulation is an excellent option for acute lower back pain, and may also relieve neck pain as well as other musculoskeletal pain. Although most back pain will subside eventually with no treatment at all, chiropractic treatment can significantly shorten the time it takes to get relief. Some types of **headache** can also be successfully treated by chiropractic.

Description

Origins

Spinal manipulation has a long history in many cultures but Daniel D. Palmer is the founder of modern chiropractic theory, dating back to the 1890s. A grocer and magnetic healer, he applied his knowledge of the nervous system and manual therapies in an unusual situation. One renowned story concerns Harvey Lillard, a janitor in the office where Palmer worked. The man had been deaf for 17 years, ever since he had sustained an injury to his upper spine. Palmer performed an adjustment on a painful vertebra in the region of the injury and Lillard's hearing was reputedly restored. Palmer theorized that all communication from the brain to the rest of the body passes through the spinal canal, and areas that are poorly aligned or under **stress** can cause physical symptoms both in the spine and in other areas of the body. Thus the body has the innate intelligence to heal itself when unencumbered by spinal irregularities causing nerve interference. After his success with Lillard, other patients began coming to him for care, and responded well to adjustments. This resulted in Palmer's further study of the relationship between an optimally functional spine and normal health.

Palmer founded the first chiropractic college in 1897. His son, B. J. Palmer, continued to develop chiropractic philosophy and practice after his father's **death**. B. J. and other faculty members were divided over the role of subluxation in disease. B. J. saw it as the cause of all disease. The others disagreed and sought a more rational way of thinking, thus broadening the base of chiropractic education. From 1910–1920, many other chiropractic colleges were established. Other innovators, including John Howard, Carl Cleveland, Earl Homewood, Joseph Janse, Herbert Lee, and Claude Watkins, also helped to advance the profession.

The theories of the Palmers receive somewhat broader interpretation today. Many chiropractors believe that back pain can be relieved and health restored through chiropractic treatment even in patients who do not have demonstrable subluxations. Scientific development and research of chiropractic is gaining momentum. The twenty-first century will likely see the metaphysical concepts such as innate intelligence give way to more scientific proofs and reform.

An example of a McTimoney chiropractic technique on patient's lumbar vertebra. The McTimoney chiropractic is a system of adjustment by hand of displacements of the spinal column and bones. It can also be applied to animals. *(Photograph by Francoise Sauze, Custom Medical Stock Photo. Reproduced by permission.)*

Many people besides the Palmers have contributed to the development of chiropractic theory and technique. Some have gone on to create a variety of procedures and related types of therapy that have their roots in chiropractic, including McTimoney-Corley chiropractic, craniosacral manipulation, naprapathy, and **applied kinesiology**. **Osteopathy** is another related holistic discipline that utilizes spinal and musculoskeletal manipulation as a part of treatment, but osteopathic training is more similar in scope to that of an M.D.

Initial visit

An initial chiropractic exam will most often include a history and a physical. The patient should be asked about what the current complaint is, whether there are chronic health problems, family history of disease, dietary habits, medical care received, and any medications currently being taken. Further, the current complaint should be described in terms of how long it has been a problem, how it has progressed, and whether it is the result of an injury or occurred spontaneously. Details of how an injury occurred should be given. The physical exam should evaluate by observation and palpation whether the painful area has evidence of inflammation or poor alignment. Range of motion may also be assessed. In the spine, either hypomobility (fixation) or hypermobility may be a problem. Laboratory analysis is helpful in some cases to rule out serious infection or other health issues that may require referral for another type of treatment. Many practitioners also insist on x rays during the initial evaluation

Manipulation

When spinal manipulation is employed, it is generally done with the hands, although some practitioners may use an adjusting tool. A classic adjustment involves a high velocity, low amplitude thrust that produces a usually painless popping noise, and improves the range of motion of the joint that was treated. The patient may lie on a specially designed, padded table that helps the practitioner to achieve the proper positions for treatment. Some adjustments involve manipulating the entire spine, or large portions of it, as a unit; others are small movements designed to affect a single joint. Stretching, **traction**, and slow manipulation are other techniques that can be employed to restore structural integrity and relieve nerve interference.

Length of treatment

The number of chiropractic treatments required will vary depending on several factors. Generally longer-term treatment is needed for conditions that are chronic, severe, or occur in conjunction with another health problem. Patients who are not in overall good health may also have longer healing times. Some injuries will inherently require more treatments than others in order to get relief. Care is given in three stages. Initially appointments are more frequent with the goal of relieving immediate pain. Next, the patient moves into a rehabilitative stage to continue the healing process and help to prevent a relapse. Finally, the patient may elect periodic maintenance, or wellness treatments, along with lifestyle changes if needed in order to stay in good health.

Follow-up care

Discharge and follow-up therapy are important. If an injury occurred as a result of poor fitness or health, a program of **exercise** or **nutrition** should be prescribed. Home therapy may also be recommended, involving such things as anti-inflammatory medication and appli-

cations of heat or ice packs. Conscious attention to posture may help some patients avoid sustaining a similar injury in the future, and the chiropractor should be able to discern what poor postural habits require correction. A sedentary lifestyle, particularly with a lot of time spent sitting, is likely to contribute to poor posture and may predispose a person to back pain and injury.

Types of practitioners

Some practitioners use spinal manipulation to the exclusion of all other modalities, and are known as straight chiropractors. Others integrate various types of therapy such as massage, nutritional intervention, or treatment with **vitamins**, herbs, or homeopathic remedies. They also embrace ideas from other health care traditions. This group is known as mixers. The vast majority of chiropractors, perhaps 85%, fall in this latter category.

Preparations

Patients should enter the chiropractic clinic with an open mind. This will help to achieve maximum results.

Precautions

Chiropractic is not an appropriate therapy for diseases that are severely degenerative and may require medication or surgery. Many conditions of the spine are amenable to manipulative treatment, but that does not include **fractures**. The practitioner should be informed in advance if the patient is on anticoagulants, or has **osteoporosis** or any other condition that may weaken the bones. There are other circumstances that would contraindicate chiropractic care, and these should be detected in the history or physical exam. In addition to fractures, **Down syndrome**, some congenital defects, and some types of **cancer** are a few of the things that may preclude spinal manipulation. On rare occasions, a fracture or dislocation may occur. There is also a very slim possibility of experiencing a **stroke** as a result of spinal manipulation, but estimates are that it is no more frequent than 2.5 occurrences per one million treatments.

Be wary of chiropractors who insist on costly x rays and repeated visits with no end in sight. Extensive use is not scientifically justifiable, especially in most cases of lower back pain. There are some circumstances when x rays are indicated, including acute or possibly severe injuries such as those that might result from a car accident.

Side effects

It is not uncommon to have local discomfort in the form of aches, pains, or spasms for a few days following a chiropractic treatment. Some patients may also experience mild headache or **fatigue** that resolves quickly.

DANIEL PALMER (1845–1913)

Chiropractic inventor, Daniel David Palmer, was born on March 7, 1845, in Toronto, Ontario. He was one of five siblings, the children of a shoemaker and his wife, Thomas and Katherine Palmer. Daniel Palmer and his older brother fell victim to wanderlust and left Canada with a tiny cash reserve in April 1865. They immigrated to the United States on foot, walking for 30 days before arriving in Buffalo, New York. They traveled by boat through the St. Lawrence Seaway to Detroit, Michigan. There they survived by working odd jobs and sleeping on the dock. Daniel Palmer settled in What Cheer, Iowa, where he supported himself and his first wife as a grocer and fish peddler in the early 1880s. He later moved to Davenport, Iowa, where he raised three daughters and one son.

Palmer was a man of high curiosity. He investigated a variety of disciplines of medical science during his lifetime, many of which were in their infancy. He was intrigued by phrenology and assorted spiritual cults, and for nine years he investigated the relationship between magnetism and disease. Palmer felt that there was one thing that caused disease. He was intent upon discovering this one thing, or as he called it: the great secret.

In September 1895, Palmer purported to have cured a deaf man by placing pressure on the man's displaced vertebra. Shortly afterward Palmer claimed to cure another patient of heart trouble, again by adjusting a displaced vertebra. The double coincidence led Palmer to theorize that human disease might be the result of dislocated or luxated bones, as Palmer called them. That same year he established the Palmer School of Chiropractic where he taught a three-month course in the simple fundamentals of medicine and spinal adjustment.

Palmer, who was married six times during his life, died in California in 1913; he was destitute. His son, Bartlett Joshua Palmer, successfully commercialized the practice of chiropractic.

Research and general acceptance

As recently as the 1970s, the American Medical Association (a national group of medical doctors) was quite hostile to chiropractic, which it deemed a cult. AMA members were advised that it was unethical to be associated with chiropractors. Fortunately that has changed, and as of 2000, many allopathic or traditionally trained physicians enjoy cordial referral relationships with chiropractors. The public is certainly strongly in

KEY TERMS

Adjustment—A very specific type of manipulation of the spine designed to return it to proper structural and functional form.

Allopathic—Conventional practice of medicine generally associated with M.D. physicians.

Dysmenorrhea—Painful menstruation.

Osteoporosis—A condition of decreased bone density, causing increased bone fragility, that is most common in elderly women.

Subluxation—Misalignment between vertebrae that structurally and functionally impairs nerve function.

favor of chiropractic treatment. An estimated 15% of people in the United States used chiropractic care in 1997. Chiropractors see the lion's share of all patients who seek medical help for back problems.

Research has also supported the use of spinal manipulation for acute low back pain. There is some anecdotal evidence recommending chiropractic treatment for ailments unrelated to musculoskeletal problems, but there is not enough research-based data to support this. On the other hand, a chiropractor may be able to treat problems and diseases unrelated to the skeletal structure by employing therapies other than spinal manipulation.

Although many chiropractors limit their practice to spine and joint problems, others claim to treat disorders that are not closely related to the back or musculoskeletal system. These include **asthma**, **bed-wetting**, **bronchitis**, coughs, **dizziness**, dysmenorrhea, earache, **fainting**, headache, hyperactivity, **indigestion**, **infertility**, migraine, **pneumonia**, and issues related to **pregnancy**. There are at least three explanations for possible efficacy for these conditions. One is that the problem could be linked to a nerve impingement, as may be possible with bed-wetting, dizziness, fainting, and headache. In a second group, chiropractic treatment may offer some relief from complicating pain and spasms caused by the disease process, as with asthma, bronchitis, coughs, and pneumonia. The discomforts of pregnancy may also be relieved with gentle chiropractic therapy. A third possibility is that manipulation or use of soft-tissue techniques may directly promote improvement of some conditions. One particular procedure, known as the endonasal technique, is thought to help the eustachian tube to open and thus improve drainage of the middle ear. The tube is sometimes blocked off due to exudates or inflammatory processes. This can offer significant relief from earaches. Some headaches also fall in this category, as skilled use of soft tissue techniques and adjustment may relieve the muscle tension that may initiate some headaches.

Dysmenorrhea, hyperactivity, indigestion, and infertility are said to be relieved as a result of improved flow of blood and nerve energy following treatment. Evidence for this is anecdotal at best, but manipulation is unlikely to be harmful if causes treatable by other modalities have been ruled out.

For conditions such as cancer, fractures, infectious diseases, neurologic disease processes, and anything that may cause increased orthopedic fragility, chiropractic treatment alone is not an effective therapy, and may even be harmful in some cases. Those who have known circulatory problems, especially with a history of thrombosis, should not have spinal manipulation.

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ORGANIZATIONS

American Chiropractic Association. 1701 Clarendon Blvd., Arlington, VA 22209. (800)986-4636. <http://www.amerchiro.org/>.

Judith Turner

Chlamydial infections *see* **Chlamydial pneumonia; Epididymitis; Nongonococcal urethritis; Sexually transmitted diseases**

Chlamydial pneumonia

Definition

Chlamydial **pneumonia** refers to one of several types of pneumonia that can be caused by various types of the bacteria known as *Chlamydia*.

Description

Pneumonia is an infection of the lungs. The air sacs (alveoli) and/or the tissues of the lungs become swollen, and the alveoli may fill with pus or fluid. This prevents the lungs from taking in sufficient oxygen, which deprives the blood and the rest of the body's tissues of oxygen.

There are three major types of *Chlamydia*: *Chlamydia psittaci*, *Chlamydia pneumoniae*, and *Chlamydia trachomatis*. Each of these has the potential to cause a type of pneumonia.

Causes and symptoms

Chlamydia trachomatis is a major cause of **sexually transmitted diseases** (called **nongonococcal urethritis** and **pelvic inflammatory disease**). When a woman with an active chlamydial infection gives birth to a baby, the baby may aspirate (suck into his or her lungs) some of the mother's bacteria-laden secretions while passing through the birth canal. This can cause a form of relatively mild pneumonia in the newborn, occurring about two to six weeks after delivery.

Chlamydia psittaci is a bacteria carried by many types of birds, including pigeons, canaries, parakeets, parrots, and some gulls. Humans acquire the bacteria through contact with dust from bird feathers, bird droppings, or from the bite of a bird carrying the bacteria. People who keep birds as pets or who work where birds are kept have the highest risk for this type of pneumonia. This pneumonia, called psittacosis, causes **fever**, **cough**, and the production of sputum containing pus. This type of pneumonia may be quite severe, and is usually more serious in older patients. The illness can last several weeks.

Chlamydia pneumoniae usually causes a type of relatively mild "walking pneumonia." Patients experience fever and cough. This type of pneumonia is called a "community-acquired pneumonia" because it is easily passed from one member of the community to another.

Diagnosis

Laboratory tests indicating the presence of one of the strains of *Chlamydia* are sophisticated, expensive, and performed in only a few laboratories across the country. For this reason, doctors diagnose most cases of chlamydial pneumonia by performing a **physical examination** of the patient, and noting the presence of certain factors. For instance, if the mother of a baby sick with pneumonia is positive for a sexually transmitted disease caused by *Chlamydia trachomatis*, the diagnosis is obvious. History of exposure to birds in a patient sick with pneumonia suggests that *Chlamydia psittaci* may be the culprit. A mild pneumonia in an otherwise healthy person is likely to be a community-acquired walking pneumonia, such as that caused by *Chlamydia pneumoniae*.

A transmission electron microscopy (TEM) of a sectioned *Chlamydia pneumoniae* bacterium. *(Photograph by Dr. Kari Lounatmaa, Custom Medical Stock Photo. Reproduced by permission.)*

Treatment

Treatment varies depending on the specific type of *Chlamydia* causing the infection. A newborn with *Chlamydia trachomatis* improves rapidly with erythromycin. *Chlamydia psittaci* infection is treated with tetracycline, bed rest, oxygen supplementation, and codeine-containing cough preparations. *Chlamydia pneumoniae* infection is treated with erythromycin.

Prognosis

The prognosis is generally excellent for the newborn with *Chlamydia trachomatis* pneumonia. *Chlamydia psittaci* may linger, and severe cases have a **death** rate of as high as 30%. The elderly are hardest hit by this type of pneumonia. A young, healthy person with *Chlamydia pneumoniae* has an excellent prognosis. In the elderly, however, there is a 5–10% death rate from this infection.

Prevention

Prevention of *Chlamydia trachomatis* pneumonia involves recognizing the symptoms of genital infection in the mother and treating her prior to delivery of her baby.

KEY TERMS

Alveoli—The small air sacs clustered at the ends of the bronchioles in the lungs, in which oxygen-carbon dioxide exchange takes place.

Aspiration—When solids or liquids that should be swallowed into the stomach are instead breathed into the respiratory system, or when substances from the outside environment are accidentally breathed into the lungs.

Sputum—Material produced within the alveoli in response to an infectious or inflammatory process.

Chlamydia psittaci can be prevented by warning people who have birds as pets, or who work around birds, to be careful to avoid contact with the dust and droppings of these birds. Sick birds can be treated with an antibiotic in their feed. Because people can contract psittacosis from each other, a person sick with this infection should be kept in **isolation**, so as not to infect other people.

Chlamydia pneumoniae is difficult to prevent because it is spread by respiratory droplets from other sick people. Because people with this type of pneumonia do not always feel very sick, they often continue to attend school, go to work, and go to other public places. They then spread the bacteria in the tiny droplets that are released into the air during coughing. Therefore, this pneumonia is very difficult to prevent and often occurs in outbreaks within communities.

Resources

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Dalhoff, Klaus, and Matthias Maass. "Chlamydia Pneumoniae Pneumonia in Hospitalized Patients: Clinical Characteristics and Diagnosis." *Chest* 110, no. 2 (Aug. 1996): 351+.

ORGANIZATIONS

American Lung Association. 1740 Broadway, New York, NY 10019. (800) 586-4872. <http://www.lungusa.org>.

Rosalyn Carson-DeWitt, MD

Chlorhexidine *see* **Antibiotics, topical**

Chloroquine *see* **Antimalarial drugs**

Chlorzoxazone *see* **Muscle relaxants**

Choking

Definition

Choking is the inability to breathe because the trachea is blocked, constricted, or swollen shut.

Description

Choking is a medical emergency. When a person is choking, air cannot reach the lungs. If the airways cannot be cleared, **death** follows rapidly.

Anyone can choke, but choking is more common in children than in adults. Choking is a common cause of accidental death in young children who are apt to put toys or coins in their mouths, then unintentionally inhale them. About 3,000 adults die each year from choking on food.

People also choke because infection causes the throat tissue to swell shut. It is believed that this is what caused George Washington's death. Allergic reactions can also cause the throat to swell shut. Acute allergic reactions are called anaphylactic reactions and may be fatal. Strangulation puts external pressure on the trachea causing another form of choking.

Finally, people can choke from obstructive **sleep apnea**. This is a condition where tissues of the body obstruct the airways during sleep. Sleep apnea is most common in obese men who sleep on their backs. **Smoking**, heavy alcohol use, lung diseases such as **emphysema**, and an inherited tendency toward a narrowed airway and throat all increase the risk of choking during sleep.

Causes and symptoms

There are three reasons why people choke. These are:

- mechanical obstruction
- tissue swelling
- crushing of the trachea

Regardless of the cause, choking cuts off the air supply to the lungs. Indications that a person's airway is blocked include:

- the person cannot speak or cry out
- the person's face turns blue from lack of oxygen
- the person desperately grabs at his or her throat

- the person has a weak **cough** and labored breathing that produces a high-pitched noise
- the person has all of the above symptoms, then becomes unconscious
- during sleep, the person has episodes of gasping, pauses in breathing, and sudden awakenings.

Diagnosis

Diagnosing choking due to mechanical obstruction is straightforward, since the symptoms are obvious even to an untrained person. In choking due to infection, the person, usually a child, will have a **fever** and signs of illness before labored breathing begins. If choking is due to an allergic reaction to medication or insect bites, the person's earlobes and face will swell, giving an external sign that internal swelling is also occurring.

Choking due to sleep apnea is usually diagnosed on reports of symptoms by the person's sleep partner. There are also alarm devices to detect the occurrence of sleep apnea. Eventually sleep may be interrupted so frequently that daytime drowsiness becomes a problem.

Treatment

Choking, except during sleep apnea, is a medical emergency. If choking is due to allergic reaction or infection, people should summon emergency help or go immediately to an emergency room. If choking is due to obstructed airways, the **Heimlich maneuver** (an emergency procedure in which a person is grasped from behind in order to forcefully expel the obstruction) should be performed immediately. In severe cases a **tracheotomy** (an incision into the trachea through the neck below the larynx) must be performed.

Patients who suffer airway obstruction during sleep can be treated with a device similar to an oxygen mask that creates positive airway pressure and delivers a mixture of oxygen and air.

Prognosis

Many people are treated successfully for choking with no permanent effects. However, if treatment is unsuccessful, the person dies from lack of oxygen. In cases where the ariway is restored after the critical period passes, there may be permanent brain damage.

Prevention

Watching children carefully to keep them from putting **foreign objects** in their mouth and avoiding giving young children food like raisins, round slices of hot dogs, and grapes can reduce the chance of choking in children. Adults should avoid heavy alcohol consumption when eating and avoid talking and laughing with food in their mouths. The risk of obstructive sleep apnea choking can be reduced by avoiding alcohol, tobacco smoking, tranquilizers, and sedatives before bed.

KEY TERMS

Trachea—The windpipe. A tube extending from below the voice box into the chest where it splits into two branches, the bronchi, that go to each lung.

Tracheotomy—The surgical creation of an opening in the trachea that functions as an alternative airway so that the patient may breathe.

Resources

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Berkow, Robert, Mark Beers, and Andrew Fletcher, eds. "Sleep Apnea Syndromes." In *The Merck Manual of Medical Information. Home Edition.* Whitehouse Station, NJ: Merck Research Laboratories, 1997.

ORGANIZATIONS

American Heart Association. 7320 Greenville Ave. Dallas, TX 75231. (214) 373-6300. <http://www.americanheart.org>.

Tish Davidson

Cholangitis

Definition

The term cholangitis means inflammation of the bile ducts. The term applies to inflammation of any portion of the bile ducts, which carry bile from the liver to the gallbladder and intestine. The inflammation is produced by bacterial infection or sometimes other causes.

Description

Bile, which is needed for digestion, is produced in the liver and then enters the common bile duct (CBD) through the hepatic ducts. Bile enters the gallbladder between meals, when the muscle or sphincter that controls flow of bile between the CBD and intestine is closed. During this period, bile accumulates in the CBD;

the pressure in the CBD rises, as would a pipe closed off at one end. The increase in pressure eventually causes the bile to flow into the gallbladder. During meals, the gallbladder contracts and the sphincter between the gallbladder and intestine relaxes, permitting bile to flow into the intestine and take part in digestion.

Bile that has just been produced by the liver is sterile (free of bacteria). This is partly due to its antibacterial properties; these are produced by the immunoglobulins (antibodies) secreted in bile, the bile acids which inhibit bacterial growth themselves, and mucus.

A small number of bacteria may be present in the bile ducts and gallbladder, getting there by moving backward from the intestine, which unlike the bile ducts, contains large numbers of bacteria. The normal flow of bile out of the ducts and into the intestine also helps keep too many organisms from multiplying. Bacteria also reach the bile ducts from the lymph tissue or from the blood stream.

When the passage of bile out of the ducts is blocked, the few bacteria that are there rapidly reproduce. A partial blockage to the flow of bile can occur when a stone from the gallbladder blocks the duct, and also allows bacteria to flow back into the CBD, and creates ideal conditions for their growth. Tumors, on the other hand, cause a more complete blockage of bile flow, both in and out, so fewer infections occur. The reproducing organisms are often able to enter the bloodstream and infect multiple organs such as the liver and heart valves.

Another source of inflammation of the bile ducts occurs in diseases of altered immunity, known as "autoimmune diseases." In these diseases, the body fails to recognize certain cells as part of its normal composition. The body thinks these cells are foreign and produces antibodies to fight them off, just as it fights against bacteria and viruses. Primary sclerosing cholangitis is a typical example of an autoimmune disease involving the bile ducts.

Causes and symptoms

As noted above, the two things that are needed for cholangitis to occur are: 1) obstruction to bile flow, and 2) presence of bacteria within the bile ducts. The most common cause of cholangitis is infection of the bile ducts due to blockage by a gallstone. Strictures (portions of ducts that have become narrow) also function in the same way. Strictures may be due to congenital (birth) abnormalities of the bile ducts, form as a result of injury to the bile duct (such as surgery, trauma), or result from inflammation that leads to scar tissue and narrowing.

The bacterium most commonly associated with infection of the bile ducts is *Escherichia coli (E. coli)* which is a normal inhabitant of the intestine. In some cases, more than one type of bacteria is involved. Patients with **AIDS** can develop infection of narrowed bile ducts with unusual organisms such as *Cryptosporidium* and others.

The three symptoms present in about 70% of patients with cholangitis are abdominal **pain**, **fever**, and **jaundice**. Some patients only have chills and fever with minimal abdominal symptoms. Jaundice or yellow discoloration of the skin and eyes occurs in about 80% of patients. The color change is due to bile pigments that accumulate in the blood and eventually in the skin and eyes.

Inflammation due to the autoimmune disease primary sclerosing cholangitis leads to multiple areas of narrowing and eventual infection. Tumors can block the bile duct and also cause cholangitis, but as noted, infection is relatively infrequent; in fact cholangitis occurs in only about one in six patients with tumors.

Another type of bile duct infection occurs mainly in Southeast Asia and is known as recurrent pyogenic cholangitis or Oriental cholangitis. It has also been identified in Asians immigrating to North America. Most patients have stones in the bile ducts and/or gallbladder, and many cases are associated with the presence of parasites within the ducts. The role of parasites in causing infection is not clear. Many researchers believe that they are just coincidental, and have nothing to do with the stones or infection.

Diagnosis

The above symptoms alone are very suggestive of cholangitis; however, it is important to determine the exact cause and site of possible obstruction. This is because attacks are likely to recur, and different causes require different treatments. For example, the treatment of cholangitis due to a stone in the CBD is different from that due to bile duct strictures. An elevated white **blood count** suggests infection, but may be normal in 20% of patients. Abnormal or elevated tests of liver function, such as bilirubin and others are also frequently present. The specific bacteria is sometimes identified from blood cultures.

X-ray techniques

A number of x-ray techniques can make the diagnosis of bile duct obstruction; these include ultrasound and **computed tomography scans** (CT scans). However, ultrasound often cannot tell if an obstruction is due to a stricture or stone, missing a stone in about half the cases. CT scans have an even poorer record of stone detection.

Another method of diagnosing and sometimes treating the cause of bile duct obstruction or narrowing is called **percutaneous transhepatic cholangiography**. In this procedure, dye is injected into the ducts by means of

KEY TERMS

Antibiotic—A medication that is designed to kill or weaken bacteria.

Bilirubin—A pigment produced by the liver that is excreted in bile which causes a yellow discoloration of the skin and eyes when it accumulates in those organs. Bilirubin levels can be measured by blood tests, and are most often elevated in patients with liver disease or a blockage to bile flow.

Computed tomography scan (CT scan)—A specialized x-ray procedure in which cross-sections of the area in question can be examined in detail. In evaluating the bile ducts, iodine-based dye is often injected intravenously. The procedure is of greatest value in diagnosing the complications of gallstones (such as abscesses, pancreatitis) rather than documenting the presence of a stone.

Endoscope—An endoscope as used in the field of gastroenterology is a thin flexible tube which uses a lens or miniature camera to view various areas of the gastrointestinal tract. When the procedure is performed to examine certain organs such as the bile ducts or pancreas, the organs are not viewed directly, but rather indirectly through the injection of x-ray dye into the bile duct.

Endoscopy—The performance of an exam using an endoscope is referred by the general term endoscopy. Diagnosis through biopsies or other means and therapeutic procedures can be done with these instruments.

Extracorporeal shock-wave lithotripsy (ESWL)—This is a technique that uses high-pressure waves similar to sound waves that can be "focused" on a very small area, thereby fracturing small solid objects such as gallstones, kidney stones, etc. The small fragments can pass more easily and harmlessly into the intestine or can be dissolved with medications.

Primary sclerosing cholangitis—A chronic disease in which it is believed that the immune system fails to recognize the cells that compose the bile ducts as part of the same body, and attempts to destroy them. It is not clear what exactly causes the disease, but it is frequently associated with another inflammatory disease of the digestive tract, ulcerative colitis. The inflammation of the ducts eventually produces formation of scar tissue, causing multiple areas of narrowing (strictures) that block bile flow and lead to bacterial infection. Liver transplant gives the best chance for long-term survival.

Ultrasound—A non-invasive procedure based on changes in sound waves of a frequency that cannot be heard, but respond to changes in tissue composition. It requires no preparation and no radiation occurs. It has become the "gold standard" for diagnosis of stones in the gallbladder, but is less accurate in diagnosing stones in the bile ducts. Gallstones as small as 2 mm can be identified. The procedure can now also be done through an endoscope, greatly improving investigation of the bile ducts.

a needle placed into the liver. It is also used to drain bile and relieve an obstruction.

ENDOSCOPIC TECHNIQUES. An endoscope is a thin flexible tube that uses a lens or mirror to look at various parts of the gastrointestinal tract. **Endoscopic retrograde cholangiopancreatography** (ERCP) can accurately determine the cause and site of blockage. It also has the advantage of being able to treat the cause of obstruction, by removing stones and dilating (stretching) strictures. ERCP involves the injection of x-ray dye into the bile ducts through an endoscope. Endoscopic ultrasound is another endoscopic alternative, but is not as available as ERCP and is not therapeutic.

Treatment

The first aim is to control the bacterial infection. Broad-spectrum **antibiotics** are usually used. If the infection does not come under control promptly, as noted by decrease in fever and pain, then other methods to relieve the obstruction and infection will be needed. Either way, definitive treatment of the cause of bile duct infection is the next step, and this has undergone revolutionary changes in the past decade. Endoscopic, radiographic and other techniques have made it possible to successfully remove stones and dilate strictures that previously required surgical intervention, often with high morbidity and mortality.

Radiologic and endoscopic techniques

Just as with diagnosis, treatment of cholangitis involves a number of similar procedures that differ mainly in the way the bile ducts are entered. The aims of these techniques are immediate relief of obstruction and infection as well as correction of any abnormalities that have

caused them. It is important to realize that even with endoscopy, x-ray dye is injected into the ducts and therefore the radiologist plays a role in both types of procedures. When endoscopy is used, the muscle between the intestine and bile duct is widened, to allow stones to pass. This is called a sphincterotomy and is often enough to relieve any obstruction and help clear infection. The widening of the muscle is needed if other procedures involving the bile duct are going to be performed.

The above techniques can be summarized as follows:

- Insertion of a catheter or thin flexible tube to drain bile and relieve obstruction. When performed by insertion of a needle into the liver the technique is called percutaneous transhepatic biliary drainage (PTBD); when performed endoscopically the catheter exits through the nose and is called a nasobiliary drain.
- Balloons can be inserted into the ducts with either method to dilate strictures.
- Insertion of a prosthesis which is a rigid or flexible tube designed to keep a narrowed area open; it is usually placed after a stricture is dilated with a balloon.
- Removal of stones can be accomplished most often by endoscopic techniques. A number of methods have been developed to perform this including laser and contact **lithotripsy** in which stones are fragmented by high-energy waves.

Surgical treatment

Fortunately, with recent advances in the above methods, this is a last option. Nonetheless, about 5–10% of patients will need to undergo surgical exploration of the bile ducts.

In some instances, the bile duct is so narrowed due to prior inflammation or tumor, that it needs connection to a different area of the intestinal tract to drain. This is rather complicated surgery and carries a mortality rate of 2%.

Other treatment

Extracorporeal shock-wave lithotripsy (ESWL) was first used to break up **kidney stones**. The technique has been extended to the treatment of **gallstones**, in both the gallbladder and bile ducts. It is often combined with endoscopic procedures to ease the passage of fragmented stones, or oral medications that can dissolve the fragments. Rarely, stones are also dissolved by instilling various chemicals such as ether directly into the bile ducts.

Prognosis

The outlook for those with cholangitis has markedly improved in the last several years due in large part to the development of the techniques described above. For those patients whose episode of infection is caused by something other than a simple stone, the future is not as bright, but still often responsive to treatment. Some patients with autoimmune disease will need **liver transplantation**.

Prevention

This involves eliminating those factors that increase the risk of infection of the bile ducts, mainly stones and strictures. If it is medically possible, patients who have their gallbladder and suffer a bout of cholangitis should undergo surgical removal of the gallbladder and removal of any stones.

For other patients, a variety of therapies as outlined above, including dissolving small stones with bile acids, are also available. A combination of several of these methods is needed in some patients. Patients should discuss the risks and alternatives of these treatments with their physicians.

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David Kaminstein, MD

A surgeon performs a laparoscopic cholecystectomy on a patient. *(Custom Medical Stock Photo. Reproduced by permission.)*

Cholecystectomy

Definition

A cholecystectomy is the surgical removal of the gallbladder. The two basic types of this procedure are open cholecystectomy and the laparoscopic approach. It is estimated that the laparoscopic procedure is currently used for approximately 80% of cases.

Purpose

A cholecystectomy is performed to treat cholelithiasis and **cholecystitis**. In cholelithiasis, **gallstones** of varying shapes and sizes form from the solid components of bile. The presence of stones, often referred to as gallbladder disease, may produce symptoms of excruciating right upper abdominal **pain** radiating to the right shoulder. The gallbladder may become the site of acute infection and inflammation, resulting in symptoms of upper right abdominal pain, **nausea and vomiting**. This condition is referred to as cholecystitis. The surgical removal of the gallbladder can provide relief of these symptoms.

Precautions

Although the laparoscopic procedure requires general anesthesia for about the same length of time as the open procedure, **laparoscopy** generally produces less postoperative pain, and a shorter recovery period. The laparoscopic procedure would not be preferred in cases where the gallbladder is so inflamed that it could rupture, or when adhesions (additional fibrous bands of tissue) are present.

Description

The laparoscopic cholecystectomy involves the insertion of a long narrow cylindrical tube with a camera on the end, through an approximately 1 cm incision in the abdomen, which allows visualization of the internal organs and projection of this image onto a video monitor. Three smaller incisions allow for insertion of other instruments to perform the surgical procedure. A laser may be used for the incision and cautery (burning unwanted tissue to stop bleeding), in which case the procedure may be called laser laparoscopic cholecystectomy.

In a conventional or open cholecystectomy, the gallbladder is removed through a surgical incision high in the right abdomen, just beneath the ribs. A drain may be inserted to prevent accumulation of fluid at the surgical site.

Preparation

As with any surgical procedure, the patient will be required to sign a consent form after the procedure is explained thoroughly. Food and fluids will be prohibited after midnight before the procedure. **Enemas** may be ordered to clean out the bowel. If nausea or vomiting are present, a suction tube to empty the stomach may be used, and for laparoscopic procedures, a urinary drainage catheter will also be used to decrease the risk of accidental puncture of the stomach or bladder with insertion of the trocar (a sharp-pointed instrument).

Aftercare

Post-operative care for the patient who has had an open cholecystectomy, as with those who have had any major surgery, involves monitoring of blood pressure, pulse, respiration and temperature. Breathing tends to be shallow because of the effect of anesthesia, and the patient's reluctance to breathe deeply due to the pain caused by the proximity of the incision to the muscles used for respiration. The patient is shown how to support the operative site when breathing deeply and coughing, and given pain medication as necessary. Fluid intake and output is measured, and the

KEY TERMS

Cholecystitis—Infection and inflammation of the gallbladder, causing severe pain and rigidity in the upper right abdomen.

Cholelithiasis—Also known as gallstones, these hard masses are formed in the gallbladder or passages, and can cause severe upper right abdominal pain radiating to the right shoulder, as a result of blocked bile flow.

Gallbladder—A hollow pear-shaped sac on the under surface of the right lobe of the liver. Bile comes to it from the liver, and passes from it to the intestine to aid in digestion.

operative site is observed for color and amount of wound drainage. Fluids are given intravenously for 24–48 hours, until the patient's diet is gradually advanced as bowel activity resumes. The patient is generally encouraged to walk 8 hours after surgery and is discharged from the hospital within three to five days, with return to work approximately four to six weeks after the procedure.

Care received immediately after laparoscopic cholecystectomy is similar to that of any patient undergoing surgery with general anesthesia. A unique post-operative pain may be experienced in the right shoulder related to pressure from carbon dioxide used through the laparoscopic tubes. This pain may be relieved by laying on the left side with right knee and thigh drawn up to the chest. Walking will also help increase the body's reabsorption of the gas. The patient is usually discharged the day after surgery, and allowed to shower on the second postoperative day. The patient is advised to gradually resume normal activities over a three day period, while avoiding heavy lifting for about 10 days.

Risks

Potential problems associated with open cholecystectomy include respiratory problems related to location of the incision, wound infection, or **abscess** formation. Possible complications of laparoscopic cholecystectomy include accidental puncture of the bowel or bladder and uncontrolled bleeding. Incomplete reabsorption of the carbon dioxide gas could irritate the muscles used in respiration and cause respiratory distress.

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Kathleen D. Wright, RN

Cholecystitis

Definition

Cholecystitis refers to a painful inflammation of the gallbladder's wall. The disorder can occur a single time (acute), or can recur multiple times (chronic).

Description

The gallbladder is a small, pear-shaped organ in the upper right hand corner of the abdomen. It is connected by a series of ducts (tube-like channels) to the liver, pancreas, and duodenum (first part of the small intestine). To aid in digestion, the liver produces a substance called bile, which is passed into the gallbladder. The gallbladder concentrates this bile, meaning that it reabsorbs some of the fluid from the bile to make it more potent. After a meal, bile is squeezed out of the gallbladder by strong muscular contractions, and passes through a duct into the duodenum. Due to the chemical makeup of bile, the contents of the duodenum are kept at an optimal pH level for digestion. The bile also plays an important part in allowing fats within the small intestine to be absorbed.

Causes and symptoms

In about 95% of all cases of cholecystitis, the gallbladder contains **gallstones**. Gallstones are solid accumulations of the components of bile, particularly cholesterol, bile pigments, and calcium. These solids may occur when the components of bile are not in the correct proportion to each other. If the bile becomes overly concentrated, or if too much of one component is present, stones may form. When these stones block the duct leaving the gallbladder, bile accumulates within the gallbladder. The gallbladder continues to contract, but the bile

cannot pass out of the gallbladder in the normal way. Back pressure on the gallbladder, chemical changes from the stagnating bile trapped within the gallbladder, and occasionally bacterial infection, result in damage to the gallbladder wall. As the gallbladder becomes swollen, some areas of the wall do not receive adequate blood flow, and lack of oxygen causes cells to die.

When the stone blocks the flow of bile from the liver, certain normal byproducts of the liver's processing of red blood cells (called bilirubin) build up. The bilirubin is reabsorbed into the bloodstream, and over time this bilirubin is deposited in the skin and in the whites of the eyes. Because bilirubin contains a yellowish color, it causes a yellowish cast to the skin and eyes that is called **jaundice**.

Gallstone formation is seen in twice as many women as men, particularly those between the ages of 20 and 60. Pregnant women, or those on birth control pills or estrogen replacement therapy have a greater risk of gallstones, as do Native Americans and Mexican Americans. People who are overweight, or who lose a large amount of weight quickly are also at greater risk for developing gallstones. Not all individuals with gallstones will go on to have cholecystitis, since many people never have any symptoms from their gallstones and never know they exist. However, the vast majority of people with cholecystitis will be found to have gallstones. Rare causes of cholecystitis include severe **burns** or injury, massive systemic infection, severe illness, diabetes, obstruction by a tumor of the duct leaving the gallbladder, and certain uncommon infections of the gallbladder (including bacteria and worms).

Although there are rare reports of patients with chronic cholecystitis who never experience any **pain**, nearly 100% of the time cholecystitis will be diagnosed after a patient has experienced a bout of severe pain in the region of the gallbladder and liver. The pain may be crampy and episodic, or it may be constant. The pain is often described as pushing through to the right upper back and shoulder. Because deep breathing increases the pain, breathing becomes shallow. **Fever** is often present, and **nausea and vomiting** are nearly universal. Jaundice occurs when the duct leaving the liver is also obstructed, although it may take a number of days for it to become apparent. When bacterial infection sets in, the patient may begin to experience higher fever and shaking chills.

Diagnosis

Diagnosis of cholecystitis involves a careful abdominal examination. The enlarged, tender gallbladder may be felt through the abdominal wall. Pressure in the upper right corner of the abdomen may cause the patient to stop breathing in, due to an increase in pain. This is called Murphy's sign. **Physical examination** may also reveal an increased heart rate and an increased rate of breathing.

A close-up view of an inflamed gallbladder. *(Custom Medical Stock Photo. Reproduced by permission.)*

Blood tests will show an increase in the white **blood count**, as well as an increase in bilirubin. Ultrasound is used to look for gallstones and to measure the thickness of the gallbladder wall (a marker of inflammation and scarring). A scan of the liver and gallbladder, with careful attention to the system of ducts throughout (called the biliary tree) is also used to demonstrate obstruction of ducts.

Rare complications of cholecystitis include:

- massive infection of the gallbladder, in which the gallbladder becomes filled with pus (called **empyema**)
- perforation of the gallbladder, in which the build-up of material within the gallbladder becomes so great that the wall of the organ bursts, with a resulting abdominal infection called **peritonitis**
- formation of abnormal connections between the gallbladder and other organs (the duodenum, large intestine, stomach), called fistulas
- obstruction of the intestine by a very large gallstone (called gallstone **ileus**)
- emphysema of the gallbladder, in which certain bacteria that produce gas infect the gallbladder, resulting in stretching of the gallbladder and disruption of its wall by gas

Treatment

Initial treatment of cholecystitis usually requires hospitalization. The patient is given fluids, salts, and sugars through a needle placed in a vein (intravenous or IV). No food or drink is given by mouth, and often a tube, called a nasogastric or NG tube, will need to be passed through the nose and down into the stomach to drain out

KEY TERMS

Bile—A substance produced by the liver, and concentrated and stored in the gallbladder. Bile contains many different substances, including bile salts, cholesterol, and bilirubin. After a meal, the gallbladder pumps bile into the duodenum (the first part of the small intestine) to keep the intestine's contents at the appropriate pH for digestion, and to help break down fats.

Bilirubin—Produced when red blood cells break down. It is a yellowish color and when levels are abnormally high, it causes the yellowish tint to eyes and skin known as jaundice.

Cholecystectomy—An operation to remove the gallbladder.

Cholecystotomy—An operation during which the gallbladder is opened, gallstones are removed, and excess bile is drained. The gallbladder is not removed.

Duct—A tube through which various substances can pass. These substances can travel through ducts to another organ or into the bloodstream.

the excess fluids. If infection is suspected, **antibiotics** are given.

Ultimately, treatment almost always involves removal of the gallbladder, a surgery called **cholecystectomy**. While this is not usually recommended while the patient is acutely ill, patients with complications usually do require emergency surgery (immediately following diagnosis) because the **death** rate increases in these cases. Similarly, those patients who have cholecystitis with no gallstones have about a 50% chance of death if the gallbladder is not quickly removed. Most patients, however, do best if surgery is performed after they have been stabilized with fluids, an NG tube, and antibiotics as necessary. When this is possible, gallbladder removal is done within five to six days of diagnosis. In patients who have other serious medical problems that may increase the risks of gallbladder removal surgery, the surgeon may decide to leave the gallbladder in place. In this case, the operation may involve removing obstructing gallstones and draining infected bile (called cholecystotomy).

Both cholecystectomy and cholecystotomy may be performed via the classical open abdominal operation (laparotomy). Tiny, "keyhole" incisions, a flexible scope, and a laser device that shatters the stones (a laparoscopic laser) can be used to destroy the gallstones. The laparoscopic procedure can also be used to remove the gallbladder through one of the small incisions. Because of the smaller incisions, laparoscopic cholecystectomy is a procedure that is less painful and promotes faster healing.

Prognosis

Hospital management of cholecystitis ends the symptoms for about 75% of all patients. Of these patients, however, 25% will go on to have another attack of cholecystitis within a year, and 60% will have another attack within six years. Each attack of cholecystitis increases a patient's risk of developing life-threatening complications, requiring risky emergency surgery. Therefore, early removal of the gallbladder, rather than a "wait-and-see" approach, is usually recommended. Cure is complete in those patients who undergo cholecystectomy.

Prevention

Prevention of cholecystitis is probably best attempted by maintaining a reasonably ideal weight. Some studies have suggested that eating a diet high in fiber, vegetables, and fruit is also protective.

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ORGANIZATIONS

Digestive Disease National Coalition. 507 Capitol Court NE, Suite 200, Washington, DC 20003. (202) 544-7497. <http://www.ddnc.org>.

National Digestive Diseases Information Clearinghouse. 2 Information Way, Bethesda, MD 20892-3570. (800) 891-5389. <http://www.niddk.nih.gov/health/digest/nddic.htm>.

Rosalyn Carson-DeWitt, MD

Cholecystography *see* **Gallbladder x rays**

Choledocholithiasis *see* **Gallstones**

Cholelithiasis *see* **Gallstones**

Cholelithotomy *see* **Gallstone removal**

Cholera

Definition

Cholera is an acute illness characterized by watery **diarrhea** that is caused by the bacterium *Vibrio cholerae*. Cholera is spread by eating food or drinking water contaminated with the bacteria. Although cholera was a public health problem in the United States and Europe a hundred years ago, modern sanitation and the treatment of drinking water have virtually eliminated the disease in developed countries. In third world countries, however, cholera is still common.

Description

Cholera is spread by eating food or drinking water that has been contaminated with cholera bacteria. Contamination usually occurs when human feces from a person who has the disease seeps into a community water supply. Fruits and vegetables can also be contaminated in areas where crops are fertilized with human feces. Cholera bacteria also live in warm, brackish water and can infect persons who eat raw or undercooked seafood obtained from such waters. Cholera is rarely transmitted directly from one person to another.

Cholera often occurs in outbreaks or epidemics. The World Health Organization (WHO) estimates that during any cholera epidemic, approximately 0.2–1% of the local population will contract the disease. Anyone can get cholera, but infants, children, and the elderly are more likely to die from the disease because they become dehydrated faster than adults. There is no particular season in which cholera is more likely to occur.

Because of an extensive system of sewage and water treatment in the United States, Canada, Europe, Japan, and Australia, cholera is generally not a concern for visitors and residents of these countries. People visiting or living in other parts of the world, particularly on the Indian subcontinent and in parts of Africa and South America, should be aware of the potential for contracting cholera and practice prevention. Fortunately, the disease is both preventable and treatable.

Causes and symptoms

Because *V. cholerae* bacteria are sensitive to acid, most cholera-causing bacteria die in the acidic environment of the stomach. However, when a person has ingested food or water containing large amounts of cholera bacteria, some will survive to infect the intestines. As would be expected, antacid usage or the use of any medication that blocks acid production in the stomach would allow more bacteria to survive and cause infection.

A false color transmission electron micrograph (TEM) of *Vibrio cholerae* bacterium magnified 6,000 times its original size. *(Photography by T. McCarthy, Custom Medical Stock Photo. Reproduced by permission.)*

In the small intestine, the rapidly multiplying bacteria produce a toxin that causes a large volume of water and electrolytes to be secreted into the bowels and then to be abruptly eliminated as watery diarrhea. Vomiting may also occur. Symptoms begin to appear between one and three days after the contaminated food or water has been ingested.

Most cases of cholera are mild, but about one in 20 patients experience severe, potentially life-threatening symptoms. In severe cases, fluids can be lost through diarrhea and vomiting at the rate of one quart per hour. This can produce a dangerous state of **dehydration** unless the lost fluids and electrolytes are rapidly replaced.

Signs of dehydration include intense thirst, little or no urine output, dry skin and mouth, an absence of tears, glassy or sunken eyes, muscle cramps, weakness, and rapid heart rate. The soft spot on an infant's head will appear to be sunken or drawn in. Dehydration occurs most rapidly in the very young and the very old because they have fewer fluid reserves. A doctor should be consulted immediately any time signs of severe dehydration occur. Immediate replacement of the lost fluids and electrolytes is necessary to prevent kidney failure, **coma**, and **death**.

Diagnosis

Rapid diagnosis of cholera can be made by examining a fresh stool sample under the microscope for the

KEY TERMS

Antibody—A specific protein produced by the immune system in response to a specific foreign protein or particle called an antigen.

Electrolytes—Salts and minerals that ionize in body fluids. Common human electrolytes are sodium, chloride, potassium, and calcium. Electrolytes control the fluid balance of the body and are important in muscle contraction, energy generation, and almost all major biochemical reactions in the body.

Toxin—A poison. In the case of cholera, a poison secreted as a byproduct of the growth of the cholera bacteria in the small intestine.

presence of *V. cholerae* bacteria. Cholera can also be diagnosed by culturing a stool sample in the laboratory to isolate the cholera-causing bacteria. In addition, a blood test may reveal the presence of antibodies against the cholera bacteria. In areas where cholera occurs often, however, patients are usually treated for diarrhea and vomiting symptoms as if they had cholera without laboratory confirmation.

Treatment

The key to treating cholera lies in preventing dehydration by replacing the fluids and electrolytes lost through diarrhea and vomiting. The discovery that rehydration can be accomplished orally revolutionized the treatment of cholera and other, similar diseases by making this simple, cost-effective treatment widely available throughout the world. The World Health Organization has developed an inexpensive oral replacement fluid containing appropriate amounts of water, sugar, and salts that is used worldwide. In cases of severe dehydration, replacement fluids must be given intravenously. Patients should be encouraged to drink when they can keep liquids down and eat when their appetite returns. Recovery generally takes three to six days.

Adults may be given the antibiotic tetracycline to shorten the duration of the illness and reduce fluid loss. The World Health Organization recommends this antibiotic treatment only in cases of severe dehydration. If **antibiotics** are overused, the cholera bacteria organism may become resistant to the drug, making the antibiotic ineffective in treating even severe cases of cholera. Tetracycline is not given to children whose permanent teeth have not come in because it can cause the teeth to become permanently discolored.

Prognosis

Today, cholera is a very treatable disease. Patients with milder cases of cholera usually recover on their own in three to six days without additional complications. They may eliminate the bacteria in their feces for up to two weeks. Chronic carriers of the disease are rare. With prompt fluid and electrolyte replacement, the death rate in patients with severe cholera is less than 1%. Untreated, the death rate can be greater than 50%. The difficulty in treating severe cholera is not in knowing how to treat it, but in getting medical care to ill people in underdeveloped areas of the world where medical resources are limited.

Prevention

The best form of cholera prevention is to establish good sanitation and waste treatment systems. In the absence of adequate sewage treatment, the following guidelines should be followed to reduce the possibility of infection:

- Boil it. Drink and brush teeth only with water that has been boiled or treated with chlorine or iodine tablets. Safe drinks include coffee and tea made with boiling water or carbonated bottled water and carbonated soft drinks.
- Cook it. Eat only thoroughly cooked foods, and eat them while they are still hot. Avoid eating food from street vendors.
- Peel it. Eat only fruit or nuts with a thick, intact skin or shell that is removed immediately before eating.
- Forget it. Do not eat raw foods such as oysters or ceviche. Avoid salads and raw vegetables. Do not use untreated ice cubes in otherwise safe drinks.
- Stay out of it. Do not swim or fish in polluted water.

A cholera vaccine exists that can be given to travelers and residents of areas where cholera is known to be active, but the vaccine is not highly effective. It provides only 25–50% immunity, and then only for a period of about six months. The vaccine is never given to infants under six months of age. The United States Centers for Disease Control and Prevention do not currently recommend cholera **vaccination** for travelers. Residents of cholera-plagued areas should discuss the value of the vaccine with their doctor.

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Tish Davidson

Cholestasis

Definition

Cholestasis is a condition caused by rapidly developing (acute) or long-term (chronic) interruption in the excretion of bile (a digestive fluid that helps the body process fat). The term is taken from the Greek *chole*, bile, and *stasis*, standing still.

Description

Cholestasis is caused by obstruction within the liver (intrahepatic) or outside the liver (extrahepatic). The obstruction causes bile salts, the bile pigment bilirubin, and fats (lipids) to accumulate in the blood stream instead of being eliminated normally.

Intrahepatic cholestasis is characterized by widespread blockage of small ducts or by disorders, such as hepatitis, that impair the body's ability to eliminate bile. Extrahepatic cholestasis can occur as a side effect of many medications. It can also occur as a complication of surgery, serious injury, tissue-destroying infection, or intravenous feeding. Extrahepatic cholestasis can be caused by conditions such as tumors and **gallstones** that block the flow of bile from the gallbladder to the first part of the small intestine (duodenum).

Pregnancy increases the sensitivity of the bile ducts to estrogen, and cholestasis often develops during the second and third trimesters of pregnancy. This condition is the second most common cause of **jaundice** during pregnancy, but generalized **itching** (pruritus gravidarum) is the only symptom most women experience. Cholestasis of pregnancy tends to run in families. Symptoms usually disappear within two to four weeks after the baby's birth but may reappear if the woman becomes pregnant again.

A similar condition affects some women who take birth-control pills. Symptoms disappear after the woman stops using **oral contraceptives**. This condition does not lead to chronic liver disease. A woman who develops cholestasis from either of these causes (pregnancy or birth control hormones) has an increased risk of developing cholestasis from the other.

Benign familial recurrent cholestasis is a rare condition characterized by brief, repeated episodes of itching and jaundice. Symptoms often disappear. This condition does not cause **cirrhosis**.

Drug-induced cholestasis may be a complication of **chemotherapy** or other medications. The two major types of drug-induced cholestasis are direct toxic injury and reactions unique to an individual (idiosyncratic reactions). In direct toxic injury, the severity of symptoms parallels the amount of medication involved. This condition:

- develops a short time after treatment begins
- follows a predictable pattern
- usually causes liver damage

Direct toxic reactions develop in 1% of all patients who take chlorpromazine (Thorazine), a tranquilizer and antinausea drug. Idiosyncratic reactions may occur at the onset of treatment or at a later time. Allergic responses are varied and are not related to the amount of medication being taken.

Causes and symptoms

Intrahepatic cholestasis is usually caused by hepatitis or by medications that can produce symptoms resembling hepatitis. Phenothiazine-derivative drugs, including chlorpromazine, can cause sudden **fever** and inflammation. Symptoms usually disappear after use of the drug(s) is stopped. In rare cases, a condition resembling chronic biliary cirrhosis (a progressive disease characterized by destruction of small bile ducts) persists even after the medication is stopped. Some patients experience a similar reaction in response to tricyclic antidepressants (amitriptyline, imipramine), phenylbutazone (Butazolidin), erythromycin estolate (Estomycin, Purmycin), and other drugs. Intrahepatic cholestasis may also be caused by alcoholic liver disease, **primary biliary cirrhosis**, **cancer** that has spread (metastasized) from another part of the body, and a number of rare disorders.

Extrahepatic cholestasis is most often caused by a stone obstructing the passage through which bile travels from the gallbladder to the small intestine (common bile duct) or by pancreatic cancer. Less often, the condition occurs as a result of non-cancerous narrowing of the common duct (strictures), ductal carcinoma, or disorders of the pancreas.

Cholestasis caused by the use of steroids causes little, if any, inflammation. Symptoms develop gradually

KEY TERMS

Bile—A bitter yellow-green substance produced by the liver. Bile breaks down fats in the small intestine so that they can be used by the body. It is stored in the gallbladder and passes from the gallbladder through the common bile duct to the top of the small intestine (duodenum) as needed to digest fat.

Biliary—Of bile or of the gallbladder and bile ducts that transport bile and make up the biliary system or tract.

Endoscopic retrograde cholangiopancreatography—A diagnostic procedure for mapping the pancreatic and common bile ducts. A flexible tube with a light transmitter (fiberoptics) is placed in the duct. A contrast dye is instilled directly into the duct and a series of x-ray images are taken.

Computed tomography scans (CT)—An imaging technique in which cross-sectional x rays of the body are compiled to create a three-dimensional image of the body's internal structures.

Hepatic—Of the liver, from the Greek *hepar*.

Liver function tests—Tests used to evaluate liver metabolism, storage, filtration, and excretion. The tests include alkaline phosphatase and serum alanine aminotransferase and aspartate aminotransferase.

Magnetic resonance imaging (MRI)—An imaging technique that uses a large circular magnet and radio waves to generate signals from atoms in the body. These signals are used to construct images of internal structures.

Percutaneous transhepatic cholangiography—An x-ray examination of the bile ducts. A needle is passed through the skin (percutaneous) across or over the liver (transhepatic) and directly into a bile duct to inject a contrast dye. The dye enhances the x-ray image mapping the system of bile ducts (cholangiography).

Phenothiazine-derivative drugs—A large family of drugs derived from phenothiazine, a compound that in itself is too poisonous for human consumption. Phenothiazine derivatives include tranquilizers, medications that prevent vomiting, antihistamines, and drugs used to enhance the effectiveness of anesthesia.

Ultrasonography—A test using sound waves to measure blood flow. Gel is applied to a hand-held transducer that is pressed against the patient's body. Images are displayed on a monitor.

and usually disappear after the drug is discontinued. Other drugs that can cause cholestasis include:

- allopurinol (Zyloprim)
- amitriptyline (Elavil)
- azathioprine (Imuran)
- benoxaprofen (Oraflex)
- capotril (Capoten)
- carbamazepine (Tegretol)
- cimetidine (Tagamet)
- hydralazine hydrochloride (Apresoline Hydrochloride)
- imipramine (Tofranil)
- penicillin
- quinidine sulfate (Quinidex)
- ranitidine (Zantac)
- sulfonamides (Apo-Sulfatrim, sulfamethoxazole)
- sulindac (Clinoril, Saldac)

Symptoms of both intrahepatic and extrahepatic cholestasis include a yellow discoloration of the skin (jaundice), dark urine, and pale stools. Itching over the skin may be severe if the condition is advanced.

Symptoms of chronic cholestasis include:

- skin discoloration
- scars or skin injuries caused by scratching
- bone **pain**
- yellowish fat deposits beneath the surface of the skin (xanthoma) or around the eyes (xanthelasma)

Patients with advanced cholestasis feel ill, tire easily, and are often nauseated. Abdominal pain and such systemic symptoms as anorexia, vomiting, and fever are usually due to the underlying condition that causes cholestasis.

Diagnosis

Determining whether obstruction exists inside or outside the liver is the essential part of diagnosis. A his-

tory of hepatitis or heavy drinking, recent use of certain drugs, and symptoms like **ascites** (abnormal abdominal swelling) and splenomegaly (enlarged spleen) suggest intrahepatic cholestasis. Pain or rigidity in the gallbladder or pancreas suggest an extrahepatic form.

Blood tests and **liver function tests** can reveal the pattern and extent of liver injury, indicate functional abnormalities, and establish the cause of the condition. However, most misdiagnoses occur when physicians rely more on laboratory analysis than on detailed medical history and the results of a thorough **physical examination**. Special attention should be paid to three liver function tests. Levels of alkaline phosphatase (ALP), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) can indicate whether the patient's condition is caused by an obstructive condition like cholestasis or a disease of the liver cells (hepatocellular disease) like viral hepatitis or cancer. ALP levels more than three times greater than normal indicate cholestasis. High levels of AST and particularly of ALT, which is found predominantly in liver cells, indicate hepatocellular disease.

Once the disease pattern has been established, ultrasound may be performed to determine whether obstruction of the large duct has caused widening of small ducts located close to it. **Computed tomography scans** (CT) and **magnetic resonance imaging** (MRI) can provide more detailed information about the source of the obstruction. If these procedures that do not enter the patient's body (non-invasive procedures) do not provide the information a family physician, internist, or gastroenterologist needs to make a diagnosis of cholestasis, one of these procedures may be performed:

- direct cholangiography, an x-ray map of the bile ducts, enhanced by the use of contrast dye
- percutaneous transhepatic cholangiography, used to identify obstructions that impede the flow of bile from the liver to the digestive system, takes x-ray images of the bile ducts after a contrast dye has been injected by a needle passed directly into a hepatic duct
- endoscopic retrograde cholangiopancreatography (ERCP), which uses a special dye to outline the pancreatic and common bile ducts and highlight the position of any obstruction; a special tube with a light transmitter is inserted into the duct and a series of x-ray images is taken

A doctor who thinks a physical obstruction is responsible for progressive deterioration of a patient's condition may consider an exploratory surgical procedure (diagnostic laparotomy). **Liver biopsy** is sometimes performed if imaging tests do not indicate why a duct is enlarged, but results of a single biopsy may not represent the status of the entire organ.

Treatment

The goal of treatment is to eliminate or control the patient's symptoms. Discontinuing the use of certain drugs can restore normal liver function, but surgery may be needed to drain or remove obstructions or to widen affected ducts.

Rifampin (Rifadin, Rimactane), an antibacterial drug; phenobarbital, a barbiturate anticonvulsant; and other drugs are sometimes prescribed to cleanse the system and eliminate bile salts and other toxic compounds.

Patients who have chronic cholestasis and have trouble digesting fat may have to restrict the amount of fat in their diet and take calcium and water-soluble vitamin supplements. A liver transplant may become necessary if complications occur.

Prognosis

Symptoms almost always disappear after the underlying condition is controlled.

Some patients who have cholestasis experience symptoms only after infection develops, but chronic bile-duct obstruction always leads to cirrhosis. It may also cause **osteoporosis** (fragile bones) or osteomalacia (soft bones).

Emergency care is not required unless inflammation of the bile ducts (**cholangitis**) develops. Cancer should be considered when an adult suddenly develops cholestasis after the age of 50.

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National Institute of Diabetes, Digestive, and Kidney Diseases of the National Institutes of Health. 31 Center Drive, Bethesda, MD 20892-2560. (301) 496-3583. <http://www.niddk.nih/gov>.

National Organization for Rare Disorders. P.O. Box 8923, New Fairfield, CT 06812-8923. (800) 999-6673. <http://www.rarediseases.org>.

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Maureen Haggerty

Cholesterol, high

Definition

Cholesterol is a fatty substance found in animal tissue and is an important component to the human body. It is manufactured in the liver and carried throughout the body in the bloodstream. Problems can occur when too much cholesterol forms an accumulation of plaque on blood vessel walls, which impedes blood flow to the heart and other organs. The highest cholesterol content is found in meat, poultry, shellfish, and dairy products.

Description

Cholesterol is the Dr. Jekyll and Mr. Hyde of medicine, since it has both a good side and bad side. It is necessary to digest fats from food, make hormones, build cell walls, and participate in other processes for maintaining a healthy body. When people talk about cholesterol as a medical problem, they are usually referring to high cholesterol. This can be somewhat misleading, since there are four components to cholesterol. These are:

- LDL, the so-called bad cholesterol
- HDL, the so-called good cholesterol
- triglycerides, a blood fat lipid that increases the risk for heart disease
- total cholesterol

High LDL (low-density lipoprotein) is a major contributing factor of heart disease. The cholesterol forms plaque in the heart's blood vessels, which restricts or blocks the supply of blood to the heart, and causes a condition called **atherosclerosis**. This can lead to a "heart attack," resulting in damage to the heart and possibly **death**. The U.S. Food and Drug Administration (FDA) estimates that 90 million American adults, roughly half the adult population, have elevated cholesterol levels.

The population as a whole is at some risk of developing high LDL cholesterol in their lifetimes. Specific risk factors include a family history of high cholesterol, **obesity**, **heart attack** or **stroke**, **alcoholism**, and lack of regular **exercise**. The chances of developing high cholesterol increase after the age of 45. One of the primary causes of high LDL cholesterol is too much fat or sugar in the diet, a problem especially true in the United States. Cholesterol is also produced naturally in the liver and overproduction may occur even in people who limit their intake of high cholesterol food. Low HDL and high triglyceride levels are also risk factors for atherosclerosis.

Types Of Cholesterol

Types	Levels	
Total cholesterol:		
	Desirable	<200
	Borderline	200 to 240
	Undesirable	>240
HDL cholesterol:		
	Desirable	>45
	Borderline	35 to 45
	Undesirable	<35
LDL cholesterol:		
	Desirable	<130
	Borderline	130 to 160
	Undesirable	>160
Ratio of total cholesterol to HDL cholesterol:		
	Desirable	<3
	Borderline	3 to 4
	Undesirable	>4

Causes and symptoms

There are no readily apparent symptoms that indicate high LDL or triglycerides, or low HDL. The only way to diagnose the problems is through a simple blood test. However, one general indication of high cholesterol is obesity. Another is a high-fat diet.

Diagnosis

High cholesterol is often diagnosed and treated by general practitioners or family practice physicians. In some cases, the condition is treated by an endocrinologist or cardiologist. Total cholesterol, LDL, HDL, and triglyceride levels as well as the cholesterol to HDL ratio are measured by a blood test called a lipid panel. The cost of a lipid panel is generally $40–100 and is covered by most health insurance and HMO plans, including Medicare, providing there is an appropriate reason for the test. Home cholesterol testing kits are available over the counter but test only for total cholesterol. The results should only be used as a guide and if the total cholesterol level is high or low, a lipid panel should be performed by a physician. In most adults the recommended levels, measured by milligrams per deciliter (mg/dL) of blood, are: total cholesterol, less than 200; LDL, less than 130; HDL, more than 35; triglycerides, 30–200; and cholesterol to HDL ratio, four to one. However, the recommended cholesterol levels may vary, depending on other risk factors such as **hypertension**, a family history of heart disease, diabetes, age, alcoholism, and **smoking**.

Doctors have always been puzzled by why some people develop heart disease while others with identical

HDL and LDL levels do not. New studies indicate it may be due to the size of the cholesterol particles in the bloodstream. A test called a nuclear magnetic resonance (NMR) LipoProfile exposes a blood sample to a magnetic field to determine the size of the cholesterol particles. Particle size can also be determined by a centrifugation test, where blood samples are spun very quickly to allow particles to separate and move at different distances. The smaller the particles, the greater the chance of developing heart disease. It allows physicians to treat patients who have normal or close to normal results from a lipid panel but abnormal particle size.

Treatment

A wide variety of prescription medicines are available to treat cholesterol problems. These include statins such as Mevacor (lovastatin), Lescol (fluvastatin), Pravachol (pravastatin), Zocor (simvastatin), Baycol (cervastatin), and Lipitor (atorvastatin) to lower LDL. A group of drugs called fibric acid derivatives are used to lower triglycerides and raise HDL. These include Lopid (gemfibrozil), Atromid-S (clofibrate), and Tricor (fenofibrate). Doctors decide which drug to use based on the severity of the cholesterol problem, side effects, and cost.

Alternative treatment

The primary goal of cholesterol treatment is to lower LDL to under 160 mg/dL in people without heart disease and who are at lower risk of developing it. The goal in people with higher risk factors for heart disease is less than 130 mg/dL. In patients who already have heart disease, the goal is under 100 mg/dL, according to FDA guidelines. Also, since low HDL levels increase the risks of heart disease, the goal of all patients is more than 35 mg/dL.

In both alternative and conventional treatment of high cholesterol, the first-line treatment options are exercise, diet, weight loss, and stopping smoking. Other alternative treatments include high doses of niacin, soy protein, garlic, algae, and the Chinese medicine supplement Cholestin (a red yeast fermented with rice).

Diet and exercise

Since a large number of people with high cholesterol are overweight, a healthy diet and regular exercise are probably the most beneficial natural ways to control cholesterol levels. In general, the goal is to substantially reduce or eliminate foods high in animal fat. These include meat, shellfish, eggs, and dairy products. Several specific diet options are beneficial. One is the vegetarian diet. Vegetarians typically get up to 100% more fiber and up to 50% less cholesterol from food than non-vegetarians. The vegetarian low-cholesterol diet consists of at least six servings of whole grain foods, three or more servings of green leafy vegetables, two to four servings of fruit, two to four servings of legumes, and one or two servings of non-fat dairy products daily.

A second diet is the Asian diet, with brown rice being the staple. Other allowable foods include fish, vegetables such as bok choy, bean sprouts, and black beans. It allows for one weekly serving of meat and very few dairy products. The food is flavored with traditional Asian spices and condiments, such as ginger, chilies, turmeric, and soy sauce.

Another regimen is the low glycemic or diabetic diet, which can raise the HDL (good cholesterol) level by as much as 20% in three weeks. Low glycemic foods promote a slow but steady rise in blood sugar levels following a meal, which increases the level of HDL. They also lower total cholesterol and triglycerides. Low glycemic foods include certain fruits, vegetables, beans, and whole grains. Processed and refined foods and sugars should be avoided.

Exercise is an extremely important part of lowering bad cholesterol and raising good cholesterol. It should consist of 20–30 minutes of vigorous aerobic exercise at least three times a week. Exercises that cause the heart to beat faster include fast walking, bicycling, jogging, roller skating, swimming, and walking up stairs. There are also a wide selection of aerobic programs available at gyms or on videocassette.

KEY TERMS

Atherosclerosis—A build-up of fatty substances in the inner layers of the arteries.

Estrogen—A hormone that stimulates development of female secondary sex characteristics.

Glycemic—The presence of glucose in the blood.

Hypertension—Abnormally high blood pressure in the arteries.

Legumes—A family of plants that bear edible seeds in pods, including beans and peas.

Lipid—Any of a variety of substances that, along with proteins and carbohydrates, make up the main structural components of living cells.

Polyunsaturated fats—A non-animal oil or fatty acid rich in unsaturated chemical bonds not associated with the formation of cholesterol in the blood.

Garlic

A number of clinical studies have indicated that garlic can offer modest reductions in cholesterol. A 1997 study by **nutrition** researchers at Pennsylvania State University found men who took garlic capsules for five months reduced their total cholesterol by 7% and LDL by 12%. Another study showed that seven cloves of fresh garlic a day significantly reduced LDL, as did a daily dose of four garlic extract pills. Other studies in 1997 and 1998 back up these results. However, two more recent studies have questioned the effectiveness of garlic in lowering "bad cholesterol."

Cholestin

Cholestin hit the over-the-counter market in 1997 as a cholesterol-lowering dietary supplement. It is a processed form of red yeast fermented with rice, a traditional herbal remedy used for centuries by the Chinese. Two studies released in 1998 showed Cholestin lowered LDL cholesterol by 20–30%. It also appeared to raise HDL and lower triglyceride levels. Although the supplement contains hundreds of compounds, the major active LDL-lowering ingredient is lovastatin, a chemical also found in the prescription drug Mevacor. The FDA banned Cholestin in early 1998 but a federal district court judge lifted the ban a year later, ruling the product was a dietary supplement, not a drug. It is not fully understood how the substance works and patients may want to consult with their physician before taking Cholestin. No serious side effects have been reported, but minor side effects, including bloating and **heartburn**, have been reported.

Other treatments

A study released in 1999 indicated that blue-green algae contains polyunsaturated fatty acids that lower cholesterol. The algae, known as alga *Aphanizomenon flos-aquae* (AFA) is available as an over-the-counter dietary supplement. Niacin, also known as nicotinic acid or vitamin B_3, has been shown to reduce LDL levels by 10–20%, and raise HDL levels by 15–35%. It also can reduce triglycerides. But because an extremely high dose of niacin (2–3 g) is needed to treat cholesterol problems, it should only be taken under a doctor's supervision to monitor possible toxic side effects. Niacin can also cause flushing when taken in high doses. Soy protein with high levels of isoflavones also have been shown to reduce bad cholesterol by up to 10%. A daily diet that contains 62 mg of isoflavones in soy protein is recommended, and can be incorporated into other diet regimens, including vegetarian, Asian, and low glycemic.

Prognosis

High cholesterol is one of the key risk factors for heart disease. Left untreated, too much bad cholesterol can clog the blood vessels, leading to chest **pain** (**angina**), blood clots, and heart attacks. Heart disease is the number one killer of men and women in the United States. By reducing LDL, people with heart disease may prevent further heart attacks and strokes, prolong and improve the quality of their lives, and slow or reverse cholesterol build-up in the arteries. In people without heart disease, lowering LDL can decrease the risk of a first heart attack or stroke.

Prevention

The best way to prevent cholesterol problems is through a combination of healthy lifestyle activities, a primarily low-fat and high-fiber diet, regular aerobic exercise, not smoking, and maintaining an optimal weight. But for people with high risk factors for heart disease, such as a family history of heart disease, diabetes, and being over the age of 45, these measures may not be enough to prevent the onset of high cholesterol. There are studies being done on the effectiveness of some existing anti-cholesterol drugs for controlling cholesterol levels in patients who do not meet the criteria for high cholesterol but no definitive results are available.

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Ken R. Wells

Cholesterol-reducing drugs

Definition

Cholesterol-reducing drugs are medicines that lower the amount of cholesterol (a fat-like substance) in the blood.

Purpose

Cholesterol is a chemical that can both benefit and harm the body. On the good side, cholesterol plays important roles in the structure of cells and in the production of hormones. But too much cholesterol in the blood can lead to heart and blood vessel disease. To complicate matters, not all cholesterol contributes to heart and blood vessel problems. One type, called high-density lipoprotein (HDL) cholesterol, or "good cholesterol," actually lowers the risk of these problems. The other type, low-density lipoprotein (LDL) cholesterol, or "bad cholesterol," is the type that threatens people's health. The names reflect the way cholesterol moves through the body. To travel through the bloodstream, cholesterol must attach itself to a protein. The combination of a protein and a fatty substance like cholesterol is called a lipoprotein.

Many factors may contribute to the fact that some people have higher cholesterol levels than others. A diet high in certain types of fats is one factor. Medical problems such as poorly controlled diabetes, an underactive thyroid gland, an overactive pituitary gland, liver disease or kidney failure also may cause **high cholesterol** levels. And some people have inherited disorders that prevent their bodies from properly using and eliminating fats. This allows cholesterol to build up in the blood.

Treatment for high cholesterol levels usually begins with changes in daily habits. By losing weight, stopping **smoking**, exercising more and reducing the amount of fat and cholesterol in the diet, many people can bring their cholesterol levels down to acceptable levels. However, some may need to use cholesterol-reducing drugs to reduce their risk of health problems.

Description

There are four different classes of cholesterol lowering drugs:

Bile acid sequesterants are drugs that act by binding with the bile produced by the liver. Bile helps the digestion and absorption of fats in the intestine. By blocking the digestion of fats, bile acid sequesterants prevent the formation of cholesterol. Drugs in this class include: cholestyramine (Questran); colestipol (Colestid); and colesevalam (Welchol).

HMG-CoA inhibitors, often called "statins," are drugs that block an enzyme called "3-hydroxy-3-methyl-glutaryl-coenzyme A reductase." This blocks one of the steps in converting fat to cholesterol. These are the most effective cholesterol lowering agents available. Drugs in this group include: atorvastatin (Lipitor); cerivastatin (Baycol); fluvastatin (Lescol); lovastatin (Mevacor); pravastatin (Pravachol); and simvastatin (Zocor).

Fibric acid derivatives include clofibrate (Atromid-S); gemfibrozil (Lopid); and fenofibrate (Tricor). Although these drugs are less effective than the statins at lowering total cholesterol, they may be able to lower the low-density lipoprotein (LDL) cholesterol while raising the high-density lipoprotein (HDL) cholesterol. Their exact mechanism of action is believed to be associated with inhibition of lipoprotein lipase activity.

Niacin, vitamin B-3, is also effective in lowering cholesterol levels. Although the normal vitamin dose of niacin is only 20 mg, the dose required to reduce cholesterol levels is at least 500 mg each day. The mechanism of action of niacin in cholesterol reduction is associated with the inhibition of VLDL secretion in the bloodstream.

Recommended dosage

The recommended dosage depends on the type of cholesterol-reducing drug used. The prescribing physician or the pharmacist who filled the prescription can advise about the correct dosage.

Cholesterol-reducing drugs should be taken exactly as directed and doses should not be missed. Double doses should not be taken to make up for a missed dose.

Physicians may prescribe a combination of cholesterol-reducing drugs, such as pravastatin and colestipol. Following the directions for how and when to take the drugs is very important. The medicine may not work properly if both drugs are taken at the same time of day.

Niacin should not be taken at the same time as an HMG-CoA inhibitor, as this combination may cause severe muscle problems. If niacin is taken in an over-the-counter form, both the prescribing physician and pharmacist should be informed. There are no problems when the niacin is taken in normal doses as a vitamin.

The prescription should not be stopped without first checking with the physician who prescribed it. Cholesterol levels may increase when the medicine is stopped, and the physician may prescribe a special diet to make this less likely.

Precautions

Seeing a physician regularly while taking cholesterol-reducing drugs is important. The physician will check to

make sure the medicine is working as it should and will decide whether it is still needed. Blood tests and other medical tests may be ordered to help the physician monitor the drug's effectiveness and check for side effects.

For most people, cholesterol-reducing drugs are just one part of a whole program for lowering cholesterol levels. Other important elements of the program may include weight loss, **exercise**, special **diets** and changes in other habits. The medication should never be viewed as a substitute for other measures ordered by the physician. Cholesterol-reducing drugs will not cure problems that cause high cholesterol; they will only help control cholesterol levels.

People over 60 years of age may be unusually sensitive to the effects of some cholesterol-reducing drugs. This may increase the chance of side effects.

Anyone who is taking an HMG-CoA reductase inhibitor should notify the health care professional in charge before having any surgical or dental procedures or receiving emergency treatment.

Special conditions

People who have certain medical conditions or who are taking certain other medications may have problems if they take cholesterol-reducing drugs. Before taking these drugs, the prescribing physician should be informed of any of the following conditions:

ALLERGIES. Anyone who has had unusual reactions to cholesterol-reducing drugs in the past should inform the prescribing physician before taking the drugs again. The physician should also be told about any **allergies** to foods, dyes, preservatives, or other substances.

PREGNANCY. Studies of laboratory animals have shown that giving high doses of gemfibrozil during **pregnancy** increases the risk of **birth defects** and other problems, including **death** of the unborn baby. The effects of this drug have not been studied in pregnant women. Women who are pregnant or who may become pregnant should check with their physicians before using gemfibrozil.

Cholesterol-reducing drugs in the group known as HMG-CoA reductase inhibitors (such as lovastatin, fluvastatin, pravastatin and simvastatin) should not be taken by women who are pregnant or who plan to become pregnant soon. By blocking the production of cholesterol, these drugs prevent a fetus from developing properly. Women who are able to bear children should use an effective birth control method while taking these drugs. Any woman who becomes pregnant while taking these drugs should check with her physician immediately.

Cholestyramine and colestipol will not directly harm an unborn baby, because these drugs are not taken into the body. However, the drugs may keep the mother's body from absorbing **vitamins** that she and the baby need. Pregnant women who take these drugs should ask their physicians whether they need to take extra vitamins.

BREASTFEEDING. Because cholestyramine and colestipol interfere with the absorption of vitamins, women who use these drugs while breastfeeding should ask their physicians if they need to take extra vitamins.

Women who are breastfeeding should talk to their physicians before using gemfibrozil. Whether this drug passes into breast milk is not known. But because animal studies suggest that it may increase the risk of some types of **cancer**, women should carefully consider the safety of using it while breastfeeding.

HMG-CoA reductase inhibitors (such as lovastatin, pravastatin, fluvastatin and simvastatin) should not be used by women who are breastfeeding their babies.

OTHER MEDICAL CONDITIONS. Cholesterol-reducing drugs may make some medical problems worse. Before using these drugs, people with any of these medical conditions should make sure their physicians are aware of their conditions:

- stomach problems, including stomach ulcer
- **constipation**
- hemorrhoids
- **gallstones** or gallbladder disease
- bleeding problems
- underactive thyroid
- heart or blood vessel disease

In addition, people with kidney or liver disease may be more likely to have blood problems or other side effects when they take certain cholesterol-reducing drugs. And some drugs of this type may actually raise cholesterol levels in people with liver disease.

Patients with any of the following medical conditions may develop problems that could lead to kidney failure if they take HMG-CoA reductase inhibitors:

- treatments to prevent rejection after an organ transplant
- recent major surgery
- seizures (convulsions) that are not well controlled

People with **phenylketonuria** (PKU) should be aware that sugar-free formulations of some cholesterol-reducing drugs contain phenylalanine in aspartame. This ingredient can cause problems in people who have phenylketonuria.

USE OF CERTAIN MEDICINES. Cholesterol-reducing drugs may change the effects of other medicines. Patients should not take any other medicine that has not been prescribed or approved by a physician who knows they are taking cholesterol-reducing drugs.

Side effects

Gemfibrozil

Studies in animals and humans suggest that gemfibrozil increases the risk of some types of cancer. The drug may also cause gallstones or muscle problems. Patients who need to take this medicine should ask their physicians for the latest information on its benefits and risks.

Patients taking gemfibrozil should check with a physician immediately if any of these side effects occur:

- fever or chills
- severe stomach **pain** with nausea and vomiting
- pain in the lower back or side
- pain or difficulty when urinating
- cough or hoarseness

HMG-CoA reductase inhibitors

These drugs may damage the liver or muscles. Patients who take the drugs should have blood tests to check for liver damage as often as their physician recommends. Any unexplained pain, tenderness or weakness in the muscles should be reported to the physician at once.

All cholesterol-reducing drugs

Minor side effects such as **heartburn**, **indigestion**, belching, bloating, gas, nausea or vomiting, stomach pain, **dizziness** and **headache** usually go away as the body adjusts to the drug and do not require medical treatment unless they continue or they interfere with normal activities.

Patients who have constipation while taking cholesterol-reducing drugs should bring the problem to a physician's attention as soon as possible.

Additional side effects are possible. Anyone who has unusual symptoms while taking cholesterol-reducing drugs should get in touch with his or her physician.

Interactions

Cholesterol-reducing drugs may interact with other medicines. When this happens, the effects of one or both of the drugs may change or the risk of side effects may be greater. Anyone who takes cholesterol-reducing drugs should let the physician know all other medicines he or she is taking and should ask whether the possible interactions can interfere with drug therapy. Examples of possible interactions are listed below.

Some cholesterol-reducing drugs may prevent the following medicines from working properly:

- thyroid hormones
- water pills (diuretics)
- certain **antibiotics** taken by mouth, such as **tetracyclines**, penicillin G and vancomycin
- the beta-blocker Inderal, used to treat high blood pressure
- digitalis heart medicines
- phenylbutazone, a nonsteroidal anti-inflammatory drug

Taking some cholesterol-reducing drugs with blood thinners (anticoagulants) may increase the chance of bleeding.

Combining HMG-CoA reductase inhibitors with gemfibrozil, cyclosporine (Sandimmune) or niacin may cause or worsen problems with the kidneys or muscles.

KEY TERMS

Cell—The basic unit that makes up all living tissue.

Cholesterol—Fatty substance found in tissue. Necessary to maintain a healthy body.

Enzyme—A type of protein, produced in the body, that brings about or speeds up chemical reactions.

Hormone—A substance that is produced in one part of the body, then travels through the bloodstream to another part of the body where it has its effect.

Phenylketonuria—(PKU) A genetic disorder in which the body lacks an important enzyme. If untreated, the disorder can lead to brain damage and mental retardation.

Pituitary gland—A pea-sized gland at the base of the brain that produces many hormones that affect growth and body functions.

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Cholesterol test

Definition

The cholesterol test is a quantitative analysis of the cholesterol levels in a sample of the patient's blood. Total serum cholesterol (TC) is the measurement routinely taken. Doctors sometimes order a complete lipoprotein profile to better evaluate the risk for **atherosclerosis** (**coronary artery disease**, or CAD). The full lipoprotein profile also includes measurements of triglyceride levels (a chemical compound that forms 95% of the fats and oils stored in animal or vegetable cells) and lipoproteins (high density and low density). Blood fats are also called "lipids."

The type of cholesterol in the blood is as important as the total quantity. Cholesterol is a fatty substance and cannot be dissolved in water. It must combine with a protein molecule called a lipoprotein in order to be transported in the blood. There are five major types of lipoproteins in the human body; they differ in the amount of cholesterol that they carry in comparison to other fats and fatty acids, and in their functions in the body. Lipoproteins are classified, as follows, according to their density:

- Chylomicrons. These are normally found in the blood only after a person has eaten foods containing fats. They contain about 7% cholesterol. Chylomicrons transport fats and cholesterol from the intestine into the liver and then into the bloodstream. They are metabolized in the process of carrying food energy to muscle and fat cells.
- Very low-density lipoproteins (VLDL). These lipoproteins carry mostly triglycerides, but they also contain 16–22% cholesterol. VLDLs are made in the liver and eventually become IDL particles after they have lost their triglyceride content.
- Intermediate-density lipoproteins (IDL). IDLs are short-lived lipoproteins containing about 30% cholesterol that are converted in the liver to low-density lipoproteins (LDLs).
- Low-density lipoproteins (LDL). LDL molecules carry cholesterol from the liver to other body tissues. They contain about 50% cholesterol. Extra LDLs are absorbed by the liver and their cholesterol is excreted into the bile. LDL particles are involved in the formation of plaques (abnormal deposits of cholesterol) in the walls of the coronary arteries. LDL is known as "bad cholesterol."
- High-density lipoproteins (HDL). HDL molecules are made in the intestines and the liver. HDLs are about 50% protein and 19% cholesterol. They help to remove cholesterol from artery walls. Lifestyle changes, including exercising, keeping weight within recommended limits, and giving up **smoking** can increase the body's levels of HDL cholesterol. HDL is known as "good cholesterol."

Because of the difference in density and cholesterol content of lipoproteins, two patients with the same total cholesterol level can have very different lipid profiles and different risk for CAD. The critical factor is the level of HDL cholesterol in the blood serum. Some doctors use the ratio of the total cholesterol level to HDL cholesterol when assessing the patient's degree of risk. A low TC/HDL ratio is associated with a lower degree of risk.

Purpose

The purpose of the TC test is to measure the levels of cholesterol in the patient's blood. The patient's cholesterol can also be fractionated (separated into different portions) in order to determine the TC/HDL ratio. The results help the doctor to assess the patient's risk for coronary artery disease (CAD). High LDL levels are associated with increased risk of CAD whereas high HDL levels are associated with relatively lower risk.

In addition, the results of the cholesterol test can assist the doctor in evaluating the patient's metabolism of fat, or in diagnosing inflammation of the pancreas, liver disease, or disorders of the thyroid gland.

The frequency of cholesterol testing depends on the patient's degree of risk for CAD. People with low cholesterol levels may need to be tested once every five years. People with high levels of blood cholesterol should be tested more frequently, according to their doctor's advice. The doctor may recommend a detailed evaluation of the different types of lipids in the patient's blood. It is ideal to check the HDL and triglycerides as well as the cholesterol and LDL. In addition, the National Cholesterol Education Program (NCEP) suggests further evaluation if the patient has any of the symptoms of CAD or if she or he has two or more of the following risk factors for CAD:

- male sex
- high blood pressure
- smoking
- diabetes
- low HDL levels
- family history of CAD before age 55

Precautions

Patients who are seriously ill or hospitalized for surgery should not be given cholesterol tests because the results will not indicate the patient's normal cholesterol level. Acute illness, high **fever**, **starvation**, or recent surgery lowers blood cholesterol levels.

KEY TERMS

Atherosclerosis—A disease of the coronary arteries in which cholesterol is deposited in plaques on the arterial walls. The plaque narrows or blocks blood flow to the heart. Atherosclerosis is sometimes called coronary artery disease, or CAD.

Fractionation—A laboratory test or process in which blood or another fluid is broken down into its components. Fractionation can be used to assess the proportions of the different types of cholesterol in a blood sample.

High-density lipoprotein (HDL)—A type of lipoprotein that protects against CAD by removing cholesterol deposits from arteries or preventing their formation.

Hypercholesterolemia—The presence of excessively high levels of cholesterol in the blood.

Lipid—Any organic compound that is greasy, insoluble in water, but soluble in alcohol. Fats, waxes, and oils are examples of lipids.

Lipoprotein—A complex molecule that consists of a protein membrane surrounding a core of lipids. Lipoproteins carry cholesterol and other lipids from the digestive tract to the liver and other body tissues. There are five major types of lipoproteins.

Low-density lipoprotein (LDL)—A type of lipoprotein that consists of about 50% cholesterol and is associated with an increased risk of CAD.

Plaque—An abnormal deposit of hardened cholesterol on the wall of an artery.

Triglyceride—A chemical compound that forms about 95% of the fats and oils stored in animal and vegetable cells. Triglyceride levels are sometimes measured as well as cholesterol when a patient is screened for heart disease.

Description

The cholesterol test requires a sample of the patient's blood. **Fasting** before the test is required to get an accurate triglyceride and LDL level. The blood is withdrawn by the usual vacuum tube technique from one of the patient's veins. The blood test takes between three and five minutes.

Preparation

Patients who are scheduled for a lipid profile test should fast (except for water) for 12–14 hours before the blood sample is drawn. If the patient's cholesterol is to be fractionated, he or she should also avoid alcohol for 24 hours before the test.

Patients should also stop taking any medications that may affect the accuracy of the test results. These include **corticosteroids**, estrogen or androgens, **oral contraceptives**, some **diuretics**, haloperidol, some **antibiotics**, and niacin. Antilipemics are drugs that lower the concentration of fatty substances in the blood. When these are taken by the patient, blood testing may be done frequently to evaluate the liver function as well as lipids. The patient's doctor will give the patient a list of specific medications to be discontinued before the test.

Aftercare

Aftercare includes routine care of the skin around the needle puncture. Most patients have no aftereffects, but some may have a small bruise or swelling. A washcloth soaked in warm water usually relieves any discomfort. In addition, the patient should resume taking any prescription medications that were discontinued before the test.

Risks

The primary risk to the patient is a mild stinging or burning sensation during the venipuncture, with minor swelling or bruising afterward.

Normal results

The "normal" values for serum lipids depend on the patient's age, sex, and race. Normal values for people in Western countries are usually given as 140–220 mg/dL in adults, although as many as 5% of the population has TC higher than 300 mg/dL. Among Asians, the figures are about 20% lower. As a rule, both TC and LDL levels rise as people get older.

Some doctors prefer to speak of "desired" rather than "normal" cholesterol values, on the grounds that "normal" refers to statistically average levels that may still be too high for good health. Desirable values are as follows:

- Total cholesterol (TC): less than 200 mg/dL
- HDL cholesterol: 40–70 mg/dL in males, 40–80 mg/dL in females
- LDL cholesterol: less than 130 mg/dL
- TC/HDL ratio: under 4.0 in males, 3.8 in females.

Abnormal results

It is possible for blood cholesterol levels to be too low as well as too high.

Abnormally low levels

TC levels less than 160 mg/dL are associated with higher mortality rates from **cancer**, liver disease, respiratory disorders, and injuries. The connection between unusually low cholesterol and increased mortality is not clear, although some researchers think that the low level is a secondary sign of the underlying disease and not the cause of disease or **death**.

Low levels of serum cholesterol are also associated with **malnutrition** or **hyperthyroidism**. Further diagnostic testing may be necessary in order to locate the cause.

Abnormally high levels

Prior to 1980, **hypercholesterolemia** (an abnormally high TC level) was defined as any value above the 95th percentile for the population. These figures ranged from 210 mg/dL in persons younger than 20 to more than 280 mg/dL in persons older than 60. It is now known, however, that TC levels over 200 mg/dL are associated with significantly higher risk of CAD. Levels of 280 mg/dL or more are considered elevated. Treatment with diet and medication has proven to successfully lower risk of **heart attack** and **stroke**.

Elevated cholesterol levels may also result from hepatitis, blockage of the bile ducts, disorders of lipid metabolism, **nephrotic syndrome**, inflammation of the pancreas, or **hypothyroidism**.

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Cholinergic drugs

Definition

Cholinergic drugs are medications that produce the same effects as the parasympathetic nervous system.

Purpose

Cholinergic drugs produce the same effects as acetylcholine. Acetylcholine is the most common neurohormone of the parasympathetic nervous system, the part of the peripheral nervous system responsible for the every day work of the body. While the sympathetic nervous system acts during times of excitation, the parasympathetic system deals with everyday activities such as salivation, digestion, and muscle relaxation.

The cholinergic drugs may be used in several ways. The cholinergic muscle stimulants are used to diagnose and treat myathenia gravis, a disease that causes severe muscle weakness. This class of drugs includes ambenonium chloride (Mytelase), edrophonium chloride (Tensilon), neostigmine (Prostigmine), and piridogstimina (Mestinón). These drugs are also widely used in surgery, both to reduce the risk of urinary retention, and to reverse the effects of the muscle relaxant drugs that are used in surgery.

Cholinergic drugs are also used in control of **glaucoma**, a disease that is caused by increased pressure inside the eye. The most common drugs used for this purpose are demecarium (Humorsol) and echthiophate (Phospholine iodide).

Description

Cholinergic drugs usually act in one of two ways. Some directly mimic the effect of acetylcholine, while others block the effects of acetylcholinesterase. Acetylcholinesterase is an enzyme that destroys naturally occurring acetylcholine. By blocking the enzyme, the naturally occurring acetylcholine has a longer action.

Recommended dosage

Cholinergic drugs are available only by prescription. They may be available as eye drops, capsules, tablets, or injections.

Precautions

Cholinergic drugs should be avoided when the patient has any sort of obstruction in the urinary or digestive tracts, such a a tumor, or severe inflammation which is causing blockage.

They should be used with caution in patients with **asthma**, epilepsy, slow heart beat, **hyperthyroidism**, or gastric ulcers.

The effects of the cholinergic drugs are to produce the same effects as stimulation of the parasympathetic nervous system. These effects include slowing of the heartbeat, increases in normal secretions including the

KEY TERMS

Cholinergic—Nerves that are stimulated by acetylcholine.

Glaucoma—a disease of the eye marked by increased pressure within the eyeball that can result in damage to the optic disk and gradual loss of vision.

Myasthenia gravis—a disease characterized by progressive weakness and exhaustibility of voluntary muscles without atrophy or sensory disturbance and caused by an autoimmune attack on acetylcholine receptors at neuromuscular junctions.

Parasympathetic nervous system—the part of the nervous system that contains chiefly cholinergic fibers, that tends to induce secretion, to increase the tone and contractility of smooth muscle, and to slow the heart rate.

digestive acids of the stomach, saliva and tears. For this reason, patients who already have a problem in one of these areas, such as a slow heartbeat or stomach ulcers should use these drugs with great caution, since the medication will make their conditions worse.

Side effects

When used properly, cholinergic drugs will increase muscle strength in patients with **myasthenia gravis**. In eye drop form, they can reduce the intraoccular pressure in glaucoma.

The possible adverse effects of cholinergic drugs are:

- slow heart beat, possibly leading to cardiac arrest
- muscle weakness, muscle cramps, and muscle pain
- convulsions
- weak breathing, inability to breath
- increased stomach acid and saliva
- nausea and vomiting
- dizziness, drowsiness, and headache

Resources

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Chondromalacia patellae

Definition

Chondromalacia patellae refers to the progressive erosion of the articular cartilage of the knee joint, that is the cartilage underlying the kneecap (patella) that articulates with the knee joint.

Description

Chondromalacia patellae (CMP), also known as patello-femoral **pain** syndrome or patello-femoral **stress** syndrome, is a syndrome that causes pain/discomfort at the front of the knee. It is associated with irritation or wear on the underside of the kneecap, or patella. In a normal knee, the articular cartilage is smooth and elastic and glides smoothly over the surface of the thighbone, or femur when the knee is bent. Erosion of the cartilage roughens the surface and prevents this smooth action.

CMP is most common in adolescent females, although older people may also develop it. An average of two out of 10,000 people develop this condition, many of them runners or other athletes.

Causes and symptoms

CMP is the result of the normal **aging** process, overuse, injury, or uneven pressures exerted on the knee joint. In teens, CMP may be caused by uneven growth or uneven strength in the thigh muscles. Growth spurts, common in teens, may result in a mildly abnormal alignment of the patella, which increases the angle formed by the thigh and the patellar tendon (Q-angle). This condition adds to the damage. Symptoms include pain, normally around the kneecap, and a grinding sensation felt when extending the leg. The pain may radiate to the back of the knee, or it may be intermittent and brought on by squatting, kneeling, going up or down stairs, especially down, or by repeated bending of the joint.

Diagnosis

Diagnosis is established during a **physical examination** performed by a general practitioner or an orthopedist, and is based on frequency of symptoms and confirmed by x rays of the knee. The CMP erosion can also

KEY TERMS

Arthroscopic knee surgery—Surgery performed to examine or repair tissues inside the knee joint through a special scope (arthroscope).

Femur—The thigh bone.

Isometric exercises—Exercises which strengthen through muscle resistance.

Osteoarthritis—Degenerative joint disease.

Quadriceps, hip flexors, hamstrings—Major muscles in the thigh area which affect knee mechanics.

be seen on an MRI, although this type of scan is not routinely performed for this purpose. The patient should inform the doctor about any previous injuries to the joint.

Treatment

Initial treatment may consist of resting the knee using crutches, along with **aspirin**, Tylenol, or a non-steroidal anti-inflammatory drug (NSAID) such as Motrin for seven to 10 days. The person should limit sports activity until the joint is healed and may use ice followed by heat to decrease inflammation. When the doctor allows the patient to resume sports, a knee brace may be prescribed in the form of a stabilizer with a hole at the kneecap.

Treatment also includes low impact exercises to strengthen the quadriceps muscles which help stabilize the knee joint. Physical therapy may be suggested at the start of this program so as to help the patient learn the correct method of performing the exercises.

Approximately 85% of people do well with conservative CMP treatment. The remainder still have severe pain and may require **arthroscopic surgery** to repair the tissues inside the knee joint. In more severe cases, open surgery may be required to realign the kneecap and perhaps other corrections.

Alternative treatments

Physical therapy offers treatments that may help CMP patients. Aqua therapy has the benefit of exercising the knee without putting stress on it and it also strengthens the thigh muscles. **Biofeedback** can be used to learn tensing and relaxing specific muscles to relieve pain. These techniques have the benefit of no side effects. **Massage therapy** might be beneficial as well. Calcium, **minerals**, and **vitamins** as part of a balanced diet will aid healing and help prevent further problems.

Prognosis

In most teens with CMP, the prognosis is excellent since the damage is reversible when treatment starts before the cartilage begins to break down. With proper treatment and preventive techniques, teenagers will complete their growth without permanent damage to the joint. Only about 15% of patients require surgical intervention. Older people may go on to develop **osteoarthritis** in the knee.

Prevention

Proper exercises are the best preventive measure. Since tightness of thigh muscles is a risk factor, warming up before athletic activities is recommended, as well as participating in a variety of sports rather than just one. Stretching exercises increase flexibility of the quadriceps, hip flexors, and hamstrings. Strengthening exercises such as short arc leg extensions, straight leg raises, quadriceps isometric exercises, and stationary bicycling are also recommended.

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Barbara J. Mitchell

Chorea *see* **Movement disorders**

Choriocarcinoma

Definition

A choriocarcinoma is type of **cancer** germ cell containing trophoblast cells.

Description

Choriocarcinomas are cancers that develop from germ cells, cells that ordinarily turn into sperm or eggs. Choriocarcinomas resemble the cells that surround an

KEY TERMS

Biopsy—A sample of an organ taken to look for abnormalities. Also, the technique used to take such samples.

Chemotherapy—The treatment of cancer with drugs.

Computed tomography (CT)—A special x ray technique that produces a cross sectional image of the organs inside the body.

Extragonadal—In a location other than the reproductive organs.

Germ cell—One of the cells that ordinarily develop into eggs or sperm (also sperm and eggs).

Gonads—The ovaries or testes.

Klinefelter syndrome—A condition caused by extra X chromosome(s) in a male, that results in small testes and infertility together with increased height, decreased facial hair, and sometimes breast enlargement.

Magnetic resonance imaging—A type of study that uses changes induced by magnets to see cells and tissues inside the body.

Mole—A mass of abnormal, partially developed tissues inside the uterus (womb). Moles develop during a pregnancy that begins with an abnormal fertilization.

Ovaries—The female sex organs that make eggs and female hormones.

Remission—The disappearance of the symptoms of cancer, although all of the cancer cells may not be gone.

Reproductive organs—The group of organs (including the testes, ovaries, and uterus) whose purpose is to produce a new individual and continue the species.

Testes—The male sex organs that make sperm and male hormones.

Testicular cancer—A cancer that originates in the testes.

Trophoblast—The tissues that surround an embryo and attach it to the uterus.

Tumor—A lump made up of abnormal cells.

Uterus—The organ where a child develops (womb).

embryo in the uterus. Most of these cancers form inside the reproductive organs. Some originate in the testes or ovaries, especially in young adults. Others develop in the uterus after a **pregnancy** or miscarriage—particularly often after a mole. A few choriocarcinomas arise in sites outside the reproductive organs. Such "extragonadal" tumors are usually found in young adults and are more common in males.

Choriocarcinomas are one of the most dangerous germ cell cancers. Choriocarcinomas usually grow quickly and spread widely. Occasionally, this cancer grows so fast that the original tumor outgrows its blood supply and dies, leaving behind only a small scar.

Causes and symptoms

Choriocarcinomas result from genetic damage to a germ cell. Males with **Klinefelter syndrome** are especially likely to develop extragonadal germ cell tumors.

The symptoms of a choriocarcinoma vary, depending on where the tumor originates and where it spreads. In the uterus, the most common symptom is bleeding. Cancers in the ovary often have only subtle signs such as widening of the waistline or **pain**. In the testes, choriocarcinomas can often be felt as small painless lumps. Choriocarcinomas that spread to other organs may reveal their presence by bleeding. In the brain, this bleeding can cause a **stroke**.

Diagnosis

Choriocarcinomas are usually referred to an oncologist, a doctor who specializes in cancer treatment. To diagnose this tumor, the doctor will do a **physical examination** and examine the internal organs with x rays or ultrasound studies. Choriocarcinomas are not always biopsied before being treated, because they tend to bleed heavily. Spreading of the cancer is detected with x rays, ultrasound studies, computed tomography (CT), or **magnetic resonance imaging** (MRI) scans.

Most choriocarcinomas make human chorionic gonadotropin (hCG), a hormone normally found only during pregnancy. The presence of hCG in the blood can help diagnose this cancer and monitor the success of treatment.

Treatment

Choriocarcinomas are usually treated by surgical removal of the tumor and **chemotherapy**. Radiation is occasionally used, particularly for tumors in the brain.

Alternative treatment

Complementary treatments can decrease **stress**, reduce the side effects of cancer treatment, and help patients feel more in control. For instance, some people find activities such as **yoga**, massage, **music therapy**, **meditation**, prayer, or mild physical **exercise** helpful.

Prognosis

The prognosis for choriocarcinomas in the uterus is very good. Although these tumors have often spread throughout the body, chemotherapy results in a cure or remission in at least 80–90% of cases. Women who have had choriocarcinomas often go on to have normal pregnancies and deliveries.

Choriocarcinomas in other sites have a poorer prognosis. These tumors tend to spread quickly and don't always respond well to chemotherapy. Although treatment can be effective, the outcome usually depends on how widely the cancer is dispersed. Generally, the prognosis is worse if the cancer can be found in the liver or brain, if hCG levels are high, or if the original tumor developed outside the gonads. Five-year survival with testicular cancers can range from 92% for tumors that have spread only to the lungs to 48% to tumors that have spread to other internal organs.

Prevention

There is no known means of prevention. However, early detection of the symptoms and prompt medical treatment can improve the odds of survival.

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Chorionic gonadotropin test *see* **Human chorionic gonadotropin pregnancy test**

Chorionic villus sampling

Definition

Chorionic villus sampling (CVS), also known as chorionic villus biopsy, is a prenatal test that can detect genetic and chromosomal abnormalities of an unborn baby.

Purpose

Chorionic villus sampling is performed on pregnant women who are at risk for carrying a fetus with a genetic or chromosomal defect. Although it carries a slightly higher risk, CVS may be used in place of **amniocentesis** for women who have one or more of the following risk factors:

- Women age 35 and older. The chance of having a child with **Down syndrome** increases with maternal age. For instance, the chance of having a baby with Down syndrome is one in 378 for a 35-year-old woman and increases to one in 30 for a 45-year-old woman.
- A history of miscarriages or children born with **birth defects**.
- A family history of genetic disease. Prenatal **genetic testing** is recommended if either the mother or father of

Chorionic villus sampling is performed on pregnant women who are at risk for carrying a fetus with a genetic or chromosomal defect. This procedure can be performed through the vagina and the cervix (transcervically) or through the abdomen (transabdominally). In the transcervical procedure, as depicted above, the physician uses ultrasound to help guide a catheter through the cervix into the uterus. By applying suction from the syringe attached to the other end of the catheter, a small sample of the chorionic villi are obtained. *(Illustration by Electronic Illustrators Group.)*

the unborn baby has a family history of genetic disease or is known to be a carrier of a genetic disease.

Precautions

Chorionic villus sampling is not recommended for women who have vaginal bleeding or spotting during the **pregnancy**. It is not typically recommended for women who have Rh sensitization from a previous pregnancy.

Description

Chorionic villus sampling has been in use since the 1980s. This prenatal testing procedure involves taking a sample of the chorion frondosum—that part of the chorionic membrane containing the villi—for laboratory analysis. The chorionic membrane is the outer sac which surrounds the developing fetus. Chorionic villi are microscopic, finger-like projections that emerge from the chorionic membrane and eventually form the placenta. The cells that make up the chorionic villi are of fetal origin so laboratory analysis can identify any genetic, chromosomal, or biochemical diseases of the fetus.

Chorionic villus sampling is best performed between 10 and 12 weeks of pregnancy. The procedure is performed either through the vagina and the cervix (transcervically) or through the abdomen (transabdominally) depending upon the preferences of the patient or the doctor. In some cases, the location of the placenta dictates which method the doctor uses. Both methods are equally safe and effective. Following the preparation time, both procedures take only about five minutes. Women undergoing chorionic villus sampling may experience no **pain** at all or feel cramping or pinching. Occasionally, a second sampling procedure must be performed if insufficient villus material was obtained.

For the transcervical procedure, the woman lies on an examining table on her back with her feet in stirrups. The woman's vaginal area is thoroughly cleansed with an antiseptic, a sterile speculum is inserted into her vagina and opened, and the cervix is cleansed with an antiseptic. Using ultrasound (a device which uses sound waves to visualize internal organs) as a guide, the doctor inserts a thin, plastic tube called a catheter through the cervix and into the uterus. The passage of the catheter through the

KEY TERMS

Chorionic villi—Microscopic, finger-like projections that emerge from the outer sac which surrounds the developing baby. Chorionic villi are of fetal origin and eventually form the placenta.

Chromosomes—Human cells carry DNA in tightly compressed rod-like structures called chromosomes. Humans have 23 pairs of chromosomes including the sex chromosomes.

Down syndrome—A chromosomal disorder caused by an extra copy or a rearrangement of chromosome 21. Children with Down syndrome have varying degrees of mental retardation and may have heart defects.

Fetus—Term for an unborn baby after the eighth week of pregnancy. Prior to seven weeks, it is called an embryo.

Rh sensitization—A woman with a negative blood type (Rh negative) who has produced antibodies against her fetus with a positive blood type (Rh positive). The mother's body considered the fetal blood cells a foreign object and mounted an immune attack on it.

Ultrasound—A safe, painless procedure which uses sound waves to visualize internal organs. A wand that transmits and receives the sound waves is moved over the woman's abdomen and internal organs can be seen on a video screen.

cervix may cause cramping. The doctor carefully watches the image produced by the ultrasound and advances the catheter to the chorionic villi. By applying suction from the syringe attached to the other end of the catheter, a small sample of the chorionic villi are obtained. A cramping or pinching feeling may be felt as the sample is being taken. The catheter is then easily withdrawn.

For the transabdominal method, the woman lies on her back on an examining table. Ultrasound enables the doctor to locate the placenta. The specific area on the woman's abdomen is cleansed thoroughly with an antiseptic and a local anesthetic may be injected to numb the area. With ultrasound guidance, a long needle is inserted through the woman's abdominal wall, through the uterine wall and to the chorionic villi. The sample is obtained by applying suction from the syringe.

The chorionic villus sample is immediately placed into nutrient medium and sent to the laboratory. At the laboratory, the sample is examined under the microscope and any contaminating cells or material is carefully removed. The villi can be analyzed immediately, or incubated for a day or more to allow for cell division. The cells are stopped in the midst of cell division and spread onto a microscope slide. Cells with clearly separated chromosomes are photographed so that the type and number of chromosomes can be analyzed. Chromosomes are strings of DNA which have been tightly compressed. Humans have 23 pairs of chromosomes including the sex chromosomes. Rearrangements of the chromosomes or the presence of additional or fewer chromosomes can be identified by examination of the photograph. Down syndrome, for instance, is caused by an extra copy of chromosome 21. In addition to the chromosomal analysis, specialized tests can be performed as needed to look for specific diseases such as **Tay-Sachs disease**. Depending upon which tests are performed, results may be available as early as two days or up to eight days after the procedure.

Chorionic villus sampling costs between $1,200 and $1,800. Insurance coverage for this test may vary.

Alternate procedures

There are alternate procedures for diagnosing genetic and chromosomal disorders of the fetus. Amniocentesis is commonly used and involves inserting a needle through the pregnant woman's abdomen to obtain a sample of amniotic fluid. Amniocentesis is usually performed in the second trimester at approximately 16 weeks gestation and the laboratory analysis may take two to three weeks. The two advantages of chorionic villus sampling are that it is performed during the first trimester and the results are available in about one week. However, as of 1997, amniocentesis is being performed in the first trimester, but this is still very rare. The risk of **miscarriage** after amniocentesis is 0.5–1% (one to two women out of 200) which is lower than that for chorionic villus sampling (1–3%).

A noninvasive alternative is the maternal blood test called triple marker screening or multiple marker screening. A sample of the pregnant woman's blood is analyzed for three different markers: alphafetoprotein (AFP), human chorionic gonadotropin, and unconjugated estriol. The levels of these three markers in the mother's blood can identify unborn babies who are at risk for certain genetic or chromosomal defects. This is a screening test which determines the chance that the fetus has the defect, but it can not diagnose defects. A negative test result does not necessarily mean the unborn baby does not have a birth defect. For instance, this screening test can only predict 60–70% of the fetuses with Down syndrome. Pregnant women who have a positive triple marker

screen are encouraged to undergo a diagnostic test, such as amniocentesis (by the time an AFP is done, it is too late to perform a CVS).

Preparation

Prior to the chorionic villus sampling procedure the woman needs to drink fluids and refrain from urinating to ensure her bladder is full. These preparations create a better ultrasound picture.

Aftercare

It is generally recommended that women undergoing chorionic villus sampling have someone drive them home and have no plans for the rest of the day. Women with Rh negative blood must receive a Rho (D) immune globulin injection following the procedure. Women should call their doctor if they experience excessive bleeding, vaginal discharge, **fever**, or abdominal pain after the procedure.

Risks

Of women who undergo transcervical chorionic villus sampling, one third experience minimal vaginal spotting and 7–10% experience vaginal bleeding. One out of five women experience cramping following the procedure. Two to three women out of 100 (or 2–3%) will miscarry following chorionic villus sampling. The risk of infection is very low. Rupture of the amniotic membranes is a rare complication. Women with Rh negative blood may be at an increased risk for developing Rh incompatibility following chorionic villus sampling.

There have been reports of limb defects in babies following chorionic villus sampling. However, in 1996 the World Health Organization reported that the incidence of babies born with limb defects from 138,966 women who had undergone chorionic villus sampling was the same as for women who had not. Therefore, this study found no connection between chorionic villus sampling and limb defects.

Normal results

No genetic, chromosomal, or biochemical abnormalities were found in the fetal cells. The gender of the fetus will be identified but will be made known to the parents only with their approval.

Abnormal results

Analysis of the cells from the chorionic villus enables the detection of over 200 diseases and disorders such as Down Syndrome, Tay-Sachs disease, and **cystic fibrosis**. Gross rearrangements of the chromosomes and chromosome additions or losses are detected.

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OTHER

Family Internet Page. <http://www.familyinternet.com>.

Belinda Rowland, PhD

Choroiditis *see* **Uveitis**

Choroiretinitis *see* **Uveitis**

Chromosome studies *see* **Genetic testing**

Chronic arthritis of childhood *see* **Juvenile arthritis**

Chronic constrictive pericarditis *see* **Pericarditis**

Chronic Epstein-Barr virus *see* **Chronic fatigue syndrome**

Chronic fatigue syndrome

Definition

Chronic **fatigue** syndrome (CFS) is a condition that causes extreme tiredness. People with CFS have debilitating fatigue that lasts for six months or longer. They also have many other symptoms. Some of these are **pain** in the joints and muscles, **headache**, and **sore throat**. CFS does not have a known cause, but appears to result from a combination of factors.

Description

CFS is the most common name for this disorder, but it also has been called chronic fatigue and immune disor-

der (CFIDS), myalgic encephalomyelitis, low natural killer cell disease, post-viral syndrome, Epstein-Barr disease, and Yuppie flu. CFS has so many names because researchers have been unable to find out exactly what causes it and because there are many similar, overlapping conditions. Reports of a CFS-like syndrome called neurasthenia date back to 1869. Later, people with similar symptoms were said to have **fibromyalgia** because one of the main symptoms is myalgia, or muscle pain. Because of the similarity of symptoms, fibromyalgia and CFS are considered to be overlapping syndromes.

In the early to mid-1980s, there were outbreaks of CFS in some areas of the United States. Doctors found that many people with CFS had high levels of antibodies to the Epstein-Barr virus (EBV), which causes mononucleosis, in their blood. For a while they thought they had found the culprit, but it turned out that many healthy people also had high EBV antibodies. Scientists have also found high levels of other viral antibodies in the blood of people with CFS. These findings have led many scientists to believe that a virus or combination of viruses may trigger CFS.

CFS was sometimes referred to as Yuppie flu because it seemed to often affect young, middle-class professionals. In fact, CFS can affect people of any gender, age, race, or socioeconomic group. Although anyone can get CFS, most patients diagnosed with CFS are 25–45 years old, and about 80% of cases are in women. Estimates of how many people are afflicted with CFS vary due to the similarity of CFS symptoms to other diseases and the difficulty in identifying it. The Centers for Disease Control and Prevention (CDC) has estimated that four to 10 people per 100,000 in the United States have CFS. According to the CFIDS Foundation, about 500,000 adults in the United States (0.3% of the population) have CFS. This probably is a low estimate since these figures do not include children and are based on the CDC definition of CFS, which is very strict for research purposes.

Causes and symptoms

There is no single known cause for CFS. Studies have pointed to several different conditions that might be responsible. These include:

- viral infections
- chemical toxins
- **allergies**
- immune abnormalities
- psychological disorders

Although the cause is still controversial, many doctors and researchers now think that CFS may not be a single illness. Instead, they think CFS may be a group of symptoms caused by several conditions. One theory is that a microorganism, such as a virus, or a chemical injures the body and damages the immune system, allowing dormant viruses to become active. About 90% of all people have a virus in the herpes family dormant (not actively growing or reproducing) in their bodies since childhood. When these viruses start growing again, the immune system may overreact and produce chemicals called cytokines that can cause flu-like symptoms. Immune abnormalities have been found in studies of people with CFS, although the same abnormalities are also found in people with allergies, autoimmune diseases, **cancer**, and other disorders.

The role of psychological problems in CFS is very controversial. Because many people with CFS are diagnosed with depression and other psychiatric disorders, some experts conclude that the symptoms of CFS are psychological. However, many people with CFS did not have psychological disorders before getting the illness. Many doctors think that patients become depressed or anxious because of the effects of the symptoms of their CFS. One recent study concluded that depression was the result of CFS and was not its cause.

Having CFS is not just a matter of being tired. People with CFS have severe fatigue that keeps them from performing their normal daily activities. They find it difficult or impossible to work, attend school, or even to take part in social activities. They may have sleep disturbances that keep them from getting enough rest or they may sleep too much. Many people with CFS feel just as tired after a full night's sleep as before they went to bed. When they **exercise** or try to be active in spite of their fatigue, people with CFS experience what some patients call "payback"—debilitating exhaustion that can confine them to bed for days.

Other symptoms of CFS include:

- muscle pain (myalgia)
- joint pain (arthralgia)
- sore throat
- headache
- **fever** and chills
- tender lymph nodes
- trouble concentrating
- memory loss

A recent study at Johns Hopkins University found an abnormality in blood pressure regulation in 22 of 23 patients with CFS. This abnormality, called neurally mediated **hypotension**, causes a sudden drop in blood pressure when a person has been standing, exercising or exposed to heat for a while. When this occurs, patients

feel lightheaded and may faint. They often are exhausted for hours to days after one of these episodes. When treated with salt and medications to stabilize blood pressure, many patients in the study had marked improvements in their CFS symptoms.

Diagnosis

CFS is diagnosed by evaluating symptoms and eliminating other causes of fatigue. Doctors carefully question patients about their symptoms, any other illnesses they have had, and medications they are taking. They also conduct a **physical examination**, neurological examination, and laboratory tests to identify any underlying disorders or other diseases that cause fatigue. In the United States, many doctors use the CDC case definition to determine if a patient has CFS.

To be diagnosed with CFS, patients must meet both of the following criteria:

- Unexplained continuing or recurring chronic fatigue for at least six months that is of new or definite onset, is not the result of ongoing exertion, and is not mainly relieved by rest, and causes occupational, educational, social, or personal activities to be greatly reduced.
- Four or more of the following symptoms: loss of short-term memory or ability to concentrate; sore throat; tender lymph nodes; muscle pain; multi-joint pain without swelling or redness; headaches of a new type, pattern, or severity; unrefreshing sleep; and post-exertional malaise (a vague feeling of discomfort or tiredness following exercise or other physical or mental activity) lasting more than 24 hours. These symptoms must have continued or recurred during six or more consecutive months of illness and must not have started before the fatigue began.

Treatment

There is no cure for CFS, but many treatments are available to help relieve the symptoms. Treatments usually are individualized to each person's particular symptoms and needs. The first treatment most doctors recommend is a combination of rest, exercise, and a balanced diet. Prioritizing activities, avoiding overexertion, and resting when needed are key to maintaining existing energy reserves. A program of moderate exercise helps to keep patients from losing physical conditioning, but too much exercise can worsen fatigue and other CFS symptoms. Counseling and **stress reduction** techniques also may help some people with CFS.

Many medications, nutritional supplements, and herbal preparations have been used to treat CFS. While many of these are unproven, others seem to provide some people with relief. People with CFS should discuss their treatment plan with their doctors, and carefully weigh the benefits and risks of each therapy before making a decision.

Drugs

Nonsteroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen and naproxen, may be used to relieve pain and reduce fever. Another medication that is prescribed to relieve pain and muscle spasms is cyclobenzaprine (sold as Flexeril).

Many doctors prescribe low dosages of antidepressants for their sedative effects and to relieve symptoms of

KEY TERMS

Arthralgia—Joint pain.

Cytokines—Proteins produced by certain types of lymphocytes. They are important controllers of immune functions.

Depression—A psychological condition, with feelings of sadness, sleep disturbance, fatigue, and inability to concentrate.

Epstein-Barr virus (EBV)—A virus in the herpes family that causes mononucleosis.

Fibromyalgia—A disorder closely related to CFS. Symptoms include pain, tenderness, and muscle stiffness.

Lymph node—Small immune organs containing lymphocytes. They are found in the neck, armpits, groin, and other locations in the body.

Lymphocytes—White blood cells that are responsible for the actions of the immune system.

Mononucleosis—A flu-like illness caused by the Epstein-Barr virus.

Myalgia—Muscle pain.

Myalgic encephalomyelitis—An older name for chronic fatigue syndrome; encephalomyelitis refers to inflammation of the brain and spinal cord.

Natural killer (NK) cell—A lymphocyte that acts as a primary immune defense against infection.

Neurally mediated hypotension—A rapid fall in blood pressure that causes dizziness, blurred vision, and fainting, and is often followed by prolonged fatigue.

Neurasthenia—Nervous exhaustion—a disorder with symptoms of irritability and weakness, commonly diagnosed in the late 1800s.

depression. **Antianxiety drugs**, such as **benzodiazepines** or buspirone may be prescribed for excessive **anxiety** that has lasted for at least six months.

Other medications that have been tested or are being tested for treatment of CFS are:

- Fludrocortisone (Florinef), a synthetic steroid, which is currently being tested for treatment of people with CFS. It causes the body to retain salt, thereby increasing blood pressure. It has helped some people with CFS who have neurally mediated hypotension.
- Beta-adrenergic blocking drugs, often prescribed for high blood pressure. Such drugs, including atenolol (Tenoretic, Tenormin) and propranolol (Inderal), are sometimes prescribed for neurally mediated hypotension.
- Gamma globulin, which contains human antibodies to a variety of organisms that cause infection. It has been used experimentally to boost immune function in people with CFS.
- Ampligen, a drug which stimulates the immune system and has antiviral activity. In one small study, ampligen improved mental function in people with CFS.

Alternative treatment

A variety of nutritional supplements are used for treatment of CFS. Among these are vitamin C, vitamin B_{12}, vitamin A, vitamin E, and various dietary **minerals**. These supplements may help improve immune and mental functions. Several herbs have been shown to improve immune function and have other beneficial effects. Some that are used for CFS are astragalus (*Astragalus membranaceus*), **echinacea** (*Echinacea* spp.), garlic (*Allium sativum*), ginseng (*Panax ginseng*), gingko (*Gingko biloba*), evening primrose oil (*Oenothera biennis*), shiitake mushroom extract (*Lentinus edodes*), borage seed oil, and quercetin.

Many people have enhanced their healing process for CFS with the use of a treatment program inclusive of one or more alternative therapies. **Stress** reduction techniques such as **biofeedback**, **meditation**, **acupuncture**, and **yoga** may help people with sleep disturbances relax and get more rest. They also help some people reduce depression and anxiety caused by CFS.

Prognosis

The course of CFS varies widely for different people. Some people get progressively worse over time, while others gradually improve. Some individuals have periods of illness that alternate with periods of good health. While many people with CFS never fully regain their health, they find relief from symptoms and adapt to the demands of the disorder by carefully following a treatment plan combining adequate rest, **nutrition**, exercise, and other therapies.

Prevention

Because the cause of CFS is not known, there currently are no recommendations for preventing the disorder.

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American Association for Chronic Fatigue Syndrome. 7 Van Buren St., Albany, NY 12206. (518) 435-1765. <http://weber.u.washington.edu/~dedra/aacfs1.html>.

The CFIDS Association. Community Health Services, P.O. Box 220398, Charlotte, NC 28222-0398. (704) 362-2343.

The National CFS Association. 919 Scott Ave., Kansas City, KS 66105. (913) 321-2278.

The National CFIDS Foundation. 103 Aletha Road, Needham, MA 02192. (781) 449-3535. <http://www.cfidsfoundation.org>.

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Toni Rizzo

Chronic granulomatous disease

Definition

Chronic granulomatous disease (CGD) is an inherited disorder in which white blood cells lose their ability to destroy certain bacteria and fungi.

Description

CGD is an X-linked genetic disease, meaning the defective gene is carried on the X chromosome (one of the sex chromosomes). Females have two copies of the X chromosome, whereas males have one X and one Y. CGD also is a recessive defect meaning that both copies of the chromosome must have the defect before it can be expressed. Females who have one X chromosome without the defect do not get this disease. Males, since they only have one X chromosome, get the disease if the defect is present. Thus, CGD affects mostly males.

CGD is an **immunodeficiency** disorder. Patients with immunodeficiency disorders suffer frequent infections. This happens because part of their immune system isn't working properly and the infectious microorganisms are not killed as rapidly as is normal. In CGD there is a defect in the ability of the white blood cells to kill bacteria and fungi. The white blood cells affected are phagocytic cells. They are part of the non-specific immune system and move via the blood to all parts of the body where they ingest and destroy microbes. Phagocytic cells are the first line of defense against microorganisms. In this disease, the decreased ability to kill microbes that they have ingested leads to a failure to effectively combat infectious diseases. Patients with CGD are subject to certain types of recurring infection, especially those of the skin, lungs, mouth, nose, intestines, and lymph nodes. With the exception of the lymph nodes, all of these areas are considered external tissues that come into contact with microorganisms from the environment. The lymph system drains all areas of the body to eliminate destroyed microorganisms and to assist the immune system in attacking microorganisms. Infections occur in the lymph nodes as a consequence of the normal draining function.

KEY TERMS

Immunodeficiency—A weakening of the body's immune system.

Phagocytic cells—A cell that ingests microorganisms and foreign particles.

Causes and symptoms

The genetic defect that causes CGD reduces the amount of hydrogen peroxide and superoxide that white blood cells can make. These chemicals are important for killing bacteria and fungi. Without them the white blood cells ingest the microorganisms, but can't kill them. In some cases, the microbes then replicate inside the white blood cell eventually causing its **death**.

Symptoms of the disease usually appear by age two. Frequent, recurrent infections of the skin, lungs (e.g. **pneumonia**), mouth (e.g. gingivitis), nose, intestines and lymph nodes are a hallmark of this disease. Patients may also develop multiple, recurrent liver abscesses and bone infections (**osteomyelitis**).

Diagnosis

Diagnosis is made based on the observation of a pattern of recurrent infections. Blood tests of lymphocyte and antibody functions will be normal. Tests of phagocytic cells will show normal ingestion, but a greatly decreased ability to kill bacteria.

Treatment

Early, aggressive treatment of all infections is critical to the successful management of CGD. Patients are treated with **antibiotics** and immune serum. Antibiotics are used at the first sign of infection. Immune serum is a source of antibodies that help fight infections. Interferon gamma is an experimental treatment for CGD that has shown promising results. There is no cure for the underlying cause of chronic granulomatous disease

Prognosis

Although antibiotics can treat most infections and may help prevent others, premature death may result, typically due to repeated lung infections.

Prevention

Since CGD is a hereditary disorder, it cannot currently be prevented. Patients and their families may ben-

efit from **genetic counseling**. Preventive (prophylactic) antibiotics may help keep some infections from occurring, and good hygiene, especially rigorous skin and mouth care, can help prevent infections in these areas. Avoiding crowds or other people who have infections are also effective preventive measures.

Resources

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ORGANIZATIONS

Chronic Granulomatous Disease Association. 2616 Monterey Road, San Marino, CA 91108-1646. (818) 441-4118.

National Organization for Rare Disorders. P.O. Box 8923, New Fairfield, CT 06812-8923. (800) 999-6673. <http://www.rarediseases.org>.

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Chronic kidney failure

Definition

Chronic kidney failure occurs when disease or disorder damages the kidneys so that they are no longer capable of adequately removing fluids and wastes from the body or of maintaining the proper level of certain kidney-regulated chemicals in the bloodstream.

Description

Chronic kidney failure, also known as chronic renal failure, affects over 250,000 Americans annually. It is caused by a number of diseases and inherited disorders, but the progression of chronic kidney failure is always the same. The kidneys, which serve as the body's natural filtration system, gradually lose their ability to remove fluids and waste products (urea) from the bloodstream. They also fail to regulate certain chemicals in the bloodstream, and deposit protein into the urine. Chronic kidney failure is irreversible, and will eventually lead to total kidney failure, also known as end-stage renal disease (ESRD). Without proper treatment intervention to remove wastes and fluids from the bloodstream, ESRD is fatal.

Causes and symptoms

Kidney failure is triggered by disease or a hereditary disorder in the kidneys. Both kidneys are typically affected. The four most common causes of chronic kidney failure include:

- Diabetes. **Diabetes mellitus** (DM), both insulin dependant (IDDM) and non-insulin dependant (NIDDM), occurs when the body cannot produce and/or use insulin, the hormone necessary for the body to process glucose. Long-term diabetes may cause the glomeruli, the filtering units located in the nephrons of the kidneys, to gradually lose functioning.
- **Glomerulonephritis**. Glomerulonephritis is a chronic inflammation of the glomeruli, or filtering units of the kidney. Certain types of glomerulonephritis are treatable, and may only cause a temporary disruption of kidney functioning.
- **Hypertension**. High blood pressure is unique in that it is both a cause and a major symptom of kidney failure. The kidneys can become stressed and ultimately sustain permanent damage from blood pushing through them at an excessive level of pressure over a long period of time.
- **Polycystic kidney disease**. Polycystic kidney disease is an inherited disorder that causes cysts to be formed on the nephrons, or functioning units, of the kidneys. The cysts hamper the regular functioning of the kidney.

Other possible causes of chronic kidney failure include **kidney cancer**, obstructions such as **kidney stones**, **pyelonephritis**, reflux nephropathy, **systemic lupus erythematosus**, **amyloidosis**, sickle cell anemia, **Alport syndrome**, and oxalosis.

Initially, symptoms of chronic kidney failure develop slowly. Even individuals with mild to moderate kidney failure may show few symptoms in spite of increased urea in their blood. Among the symptoms that may be present at this point are frequent urination during the night and high blood pressure.

Most symptoms of chronic kidney failure are not apparent until kidney disease has progressed significantly. Common symptoms include:

- Anemia. The kidneys are responsible for the production of erythropoietin (EPO), a hormone which stimulates red blood cell production. If kidney disease causes shrinking of the kidney, this red cell production is hampered.
- Bad breath or a bad taste in mouth. Urea, or waste products, in the saliva may cause an ammonia-like taste in the mouth.
- Bone and joint problems. The kidneys produce vitamin D, which aids in the absorption of calcium and keeps bones strong. For patients with kidney failure, bones may become brittle, and in the case of children, normal growth may be stunted. Joint **pain** may also occur as a result of unchecked phosphate levels in the blood.

- Edema. Puffiness or swelling around the eyes, arms, hands, and feet.
- Frequent urination.
- Foamy or bloody urine. Protein in the urine may cause it to foam significantly. Blood in the urine may indicate bleeding from diseased or obstructed kidneys, bladder, or ureters.
- Headaches. High blood pressure may trigger headaches.
- Hypertension, or high blood pressure. The retention of fluids and wastes causes blood volume to increase, which in turn, causes blood pressure to rise.
- Increased **fatigue**. Toxic substances in the blood and the presence of anemia may cause feelings of exhaustion.
- **Itching**. Phosphorus, which is typically eliminated in the urine, accumulates in the blood of patients with kidney failure. This heightened phosphorus level may cause itching of the skin.
- Lower back pain. Pain where the kidneys are located, in the small of the back below the ribs.
- Nausea, loss of appetite, and vomiting. Urea in the gastric juices may cause upset stomach. This can lead to **malnutrition** and weight loss.

Diagnosis

Kidney failure is typically diagnosed and treated by a nephrologist, a doctor that specializes in treating the kidneys. The patient that is suspected of having chronic kidney failure will undergo an extensive blood work-up. A blood test will assess the levels of creatinine, blood urea nitrogen (BUN), uric acid, phosphate, sodium, and potassium in the blood. Urine samples will also be collected, usually over a 24-hour period, to assess protein loss.

Uncovering the cause of kidney failure is critical to proper treatment. A full assessment of the kidneys is necessary to determine if the underlying disease is treatable and if the kidney failure is chronic or acute. An x ray, MRI, computed tomography scan, ultrasound, renal biopsy, and/or arteriogram of the kidneys may be employed to determine the cause of kidney failure and level of remaining kidney function. X rays and ultrasound of the bladder and/or ureters may also be taken.

Treatment

Chronic kidney failure is an irreversible condition. Hemodialysis, peritoneal dialysis, or **kidney transplantation** must be employed to replace the lost function of the kidneys. In addition, dietary changes and treatment to relieve specific symptoms such as anemia and high blood pressure are critical to the treatment process.

KEY TERMS

End-stage renal disease (ESRD)—Total kidney failure; chronic kidney failure is diagnosed as ESRD when kidney function falls to 5–10% of capacity.

Nephrotic syndrome—Characterized by protein loss in the urine, low protein levels in the blood, and fluid retention.

Ureters—The two ducts that pass urine from each kidney to the bladder.

Hemodialysis

Hemodialysis is the most frequently prescribed type of dialysis treatment in the United States. Most hemodialysis patients require treatment three times a week, for an average of three to four hours per dialysis "run" depending on the type of dialyzer used and their current physical condition. The treatment involves circulating the patient's blood outside of the body through an extracorporeal circuit (ECC), or dialysis circuit. The dialysis circuit consists of plastic blood tubing, a two-compartment filter known as a dialyzer, or artificial kidney, and a dialysis machine that monitors and maintains blood flow and administers dialysate, a chemical bath used to draw waste products out of the blood. The patient's blood leaves and enters the body through two needles inserted into the patient's vein, called an access site, and is pushed through the blood compartment of the dialyzer. Once inside of the dialyzer, excess fluids and toxins are pulled out of the bloodstream and into the dialysate compartment, where they are carried out of the body. At the same time, electrolytes and other chemicals in the dialysate solution move from the dialysate into the bloodstream. The purified, chemically-balanced blood is then returned to the body.

Peritoneal dialysis

In peritoneal dialysis (PD), the patient's peritoneum, or lining of the abdomen, acts as a blood filter. A catheter is surgically inserted into the patient's abdomen. During treatment, the catheter is used to fill the abdominal cavity with dialysate. Waste products and excess fluids move from the patient's bloodstream into the dialysate solution. After a waiting period of six to 24 hours, depending on the treatment method used, the waste-filled dialysate is drained from the abdomen, and replaced with clean dialysate. There are three types of peritoneal dialysis, which vary by treatment time and administration method: Continuous Ambulatory Peritoneal Dialysis

(CAPD), Continuous Cyclic Peritoneal Dialysis (CCPD), and Intermittent Peritoneal Dialysis (IPD).

Kidney transplantation

Kidney transplantation involves surgically attaching a functioning kidney, or graft, from a brain dead organ donor (a cadaver transplant), or from a living donor, to a patient with ESRD. Patients with chronic renal disease who need a transplant and don't have a living donor register with UNOS (United Network for Organ Sharing), the federal organ procurement agency, to be placed on a waiting list for a cadaver kidney transplant. Kidney availability is based on the patient's health status. When the new kidney is transplanted, the patient's existing, diseased kidneys may or may not be removed, depending on the circumstances surrounding the kidney failure. A regimen of immunosuppressive, or anti-rejection medication, is required after transplantation surgery.

Dietary management

A diet low in sodium, potassium, and phosphorous, three substances that the kidneys regulate, is critical in managing kidney disease. Other dietary restrictions, such as a reduction in protein, may be prescribed depending on the cause of kidney failure and the type of dialysis treatment employed. Patients with chronic kidney failure also need to limit their fluid intake.

Medications and dietary supplements

Kidney failure patients with hypertension typically take medication to control their high blood pressure. Epoetin alfa, or EPO (Epogen), a hormone therapy, and intravenous or oral iron supplements are used to manage anemia. A multivitamin may be prescribed to replace **vitamins** lost during dialysis treatments. Vitamin D, which promotes the absorption of calcium, along with calcium supplements, may also be prescribed.

Since 1973, Medicare has picked up 80% of ESRD treatment costs, including the costs of dialysis and transplantation and of some medications. To qualify for benefits, a patient must be insured or eligible for benefits under Social Security, or be a spouse or child of an eligible American. Private insurance and state Medicaid programs often cover the remaining 20% of treatment costs.

Prognosis

Early diagnosis and treatment of kidney failure is critical to improving length and quality of life in chronic kidney failure patients. Patient outcome varies by the cause of chronic kidney failure and the method chosen to treat it. Overall, patients with chronic kidney disease leading to ESRD have a shortened lifespan. According to the United States Renal Data System (USRDS), the lifespan of an ESRD patient is 18–47% of the lifespan of the age-sex-race matched general population. ESRD patients on dialysis have a lifespan that is 16–37% of the general population.

The demand for kidneys to transplant continues to exceed supply. In 1996, over 34,000 Americans were on the UNOS waiting list for a kidney transplant, but only 11,330 living donor and cadaver transplants were actually performed. Cadaver kidney transplants have a 50% chance of functioning nine years, and living donor kidneys that have two matching antigen pairs have a 50% chance of functioning for 24 years. However, some transplant grafts have functioned for over 30 years.

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American Kidney Fund (AKF). Suite 1010, 6110 Executive Boulevard, Rockville, MD 20852. (800) 638-8299. <http://www.arbon.com/kidney>.

National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). Building 31, Room 9A04, 31 Center Drive, MSC 2560, Bethesda, MD 208792-2560. (301) 496-3583. <http://www.niddk.nih.gov>.

National Kidney Foundation. 30 East 33rd St., New York, NY 10016. (800) 622-9010. <http://www.kidney.org>.

United States Renal Data System (USRDS). The University of Michigan, 315 W. Huron, Suite 240, Ann Arbor, MI 48103. (734) 998-6611. <http://www.med.umich.edu/usrds>.

Paula Anne Ford-Martin

Chronic leukemias *see* **Leukemias, chronic**

Chronic obstructive lung disease

Definition

Chronic obstructive lung disease, also known as chronic obstructive pulmonary disease (COPD), is a general term for a group of conditions in which there is persistent difficulty in expelling (or exhaling) air from the lungs. COPD commonly refers to two related, progressive diseases of the respiratory system, chronic **bronchitis** and **emphysema**. Because **smoking** is the major cause of both diseases, chronic bronchitis and emphysema often occur together in the same patient.

Description

COPD is one of the fastest-growing health problems. Nearly 16 million people in the United States, 14 million with chronic bronchitis and two million with emphysema, suffer from COPD. COPD is responsible for more than 96,000 deaths annually, making it the fourth leading cause of **death**. Although COPD is more common in men than women, the increase in incidence of smoking among women since World War II has produced an increase in deaths from COPD in women. COPD has a large economic impact on the healthcare system and a destructive impact on the lives of patients and their families. Quality of life for a person with COPD decreases as the disease progresses.

Chronic bronchitis

In chronic bronchitis, chronic inflammation caused by cigarette smoking results in a narrowing of the openings in the bronchi, the large air tubes of the respiratory system, and interferes with the flow of air. Inflammation also causes the glands that line the bronchi to produce excessive amounts of mucus, further narrowing the airways and blocking airflow. The result is often a chronic **cough** that produces sputum (mainly mucus) and **shortness of breath**. Cigarette smoke also damages the cilia, small hair-like projections that move bacteria and foreign particles out of the lungs, increasing the risk of infections.

Emphysema

Emphysema is a disease in which cigarette smoke causes an overproduction of the enzyme elastase, one of the immune system's infection-fighting biochemicals. This results in irreversible destruction of a protein in the lung called elastin which is important for maintaining the structure of the walls of the alveoli, the terminal small air sacs of the respiratory system. As the walls of the alveoli rupture, the number of alveoli is reduced and many of those remaining are enlarged, making the lungs of the patient with emphysema less elastic and overinflated. Due to the higher pressure inside the chest that must be developed to force air out of the less-elastic lungs, the bronchioles, small air tubes of the respiratory system, tend to collapse during exhalation. Stale air gets trapped in the air sacs and fresh air cannot be brought in.

Causes and symptoms

There are several important risk factors for COPD:

- Lifestyle. Cigarette smoking is by far the most important risk factor for COPD (80% of all cases). Cigar and pipe smoking can also cause COPD. Air pollution and industrial dusts and fumes are other important risk factors.
- Age. Chronic bronchitis is more common in people over 40 years old; emphysema occurs more often in people 65 years of age and older.
- Socioeconomic class. COPD-related deaths are about twice as high among unskilled and semi-skilled laborers as among professionals.
- Family clustering. It is thought that heredity predisposes people in certain families to the development of COPD when other causes, such as smoking and air pollution, are present.
- Lung infections. Lung infections make all forms of COPD worse.

In the general population, emphysema usually develops in older individuals with a long smoking history. However, there is also a form of emphysema that runs in families. People with this type of emphysema have a hereditary deficiency of a blood component, an enzyme inhibitor called alpha-1-antitrypsin (AAT). This type of emphysema is sometimes called "early onset emphysema" because it can appear when a person is as young as 30 or 40 years old. It is estimated that there are between 75,000 and 150,000 Americans who were born with AAT-deficiency. Of this group, emphysema afflicts an estimated 20,000-40,000 people (1–3% of all cases of emphysema). The risk of developing emphysema for an AAT-deficient individual who also smokes is much greater than for others.

The first symptoms of chronic bronchitis are cough and mucus production. These symptoms resemble a chest cold that lingers on for weeks. Later, shortness of breath develops. Cough, sputum production, and shortness of breath may become worse if a person develops a lung infection. A person with chronic bronchitis may later

A. lung cancer. B. pneumonia. C. emphysema. D. phlegm from chronic bronchitis. *(Illustration by Argosy, Inc.)*

develop emphysema as well. In emphysema, shortness of breath on exertion is the predominant early symptom. Coughing is usually minor and there is little sputum. As the disease progresses, the shortness of breath occurs with less exertion, and eventually may be present even when at rest. At this point, a sputum-producing cough may also occur. Either chronic bronchitis or emphysema may lead to respiratory failure—a condition in which there occurs a dangerously low level of oxygen or a serious excess of carbon dioxide in the blood.

Diagnosis

The first step in diagnosing COPD is a good medical evaluation, including a medical history and a **physical examination** of the chest using a stethoscope. In addition, the doctor may request one or more of the following tests:

Pulmonary function test

Using a spirometer, an instrument that measures the air taken into and exhaled from the lungs, the doctor will determine two important values: (1) vital capacity (VC), the largest amount of air expelled after the deepest inhalation, and (2) forced expiratory volume (FEV1), the maximum amount of air expired in one second. The **pulmonary function test** can be performed in the doctor's office, but is expensive.

Chest x ray

Chest x rays can detect only about half of the cases of emphysema. Chest x rays are rarely useful for diagnosing chronic bronchitis.

Blood gas levels

Blood may be drawn from an artery (more painful than drawing blood from a vein) to determine the amount of oxygen and carbon dioxide present. Low oxygen and high carbon dioxide levels are often indicative of chronic bronchitis, but not always of emphysema.

Tests for cause of infection

If infection is present, blood and sputum tests may be done to determine the cause of infection.

Electrocardiogram (ECG)

Many patients with lung disease also develop heart problems. The ECG identifies signs of heart disease.

Treatment

The precise nature of the patient's condition will determine the type of treatment prescribed for COPD. With a program of complete respiratory care, disability can be minimized, acute episodes prevented, hospitalizations reduced, and some early deaths avoided. On the other hand, no treatment has been shown to slow the progress of the disease, and only oxygen therapy increases survival rate.

Drugs

Medications frequently prescribed for COPD patients include:

- **Bronchodilators**. These agents open narrowed airways and offer significant symptomatic relief for many, but not all, people with COPD. There are three types of bronchodilators: Beta2 agonists, anticholinergic agents, and theophylline and its derivatives. Depending on the specific drug, a bronchodilator may be inhaled, injected, or taken orally.
- **Corticosteroids**. Corticosteroids, usually inhaled, block inflammation and are most useful for patients with chronic bronchitis with or without emphysema. Steroids are generally not useful in patients who have emphysema.
- Oxygen replacement. Eventually, patients with low blood oxygen levels may need to rely on supplemental oxygen from portable or stationary tanks.
- **Antibiotics**. Antibiotics are frequently given at the first sign of a respiratory infection, such as increased sputum production or a change in color of sputum from clear to yellow or green.
- Vaccines. To prevent pulmonary infection from viruses and bacteria, people with COPD should be vaccinated against **influenza** each year at least six weeks before flu season and have a one-time pneumococcal (**pneumonia**) vaccine.
- Expectorants. These agents help loosen and expel mucus secretions from the airways.
- Diuretics. These drugs are given to prevent excess water retention in patients with associated right **heart failure**.
- Augmentation therapy (for emphysema due to AAT-deficiency only). Replacement AAT (Prolastin), derived from human blood which has been screened for viruses, is injected weekly or bimonthly for life.

Surgery

Surgical procedures for emphysema are very rare. They are expensive and often not covered by insurance. The great majority of patients cannot be helped by surgery, and no single procedure is ideal for those who can be helped. In January of 1996, the government temporarily suspended Medicare payments for lung reduction surgery.

- **Lung transplantation**. Lung transplantation has been successfully employed in some patients with end-stage COPD. In the hands of an experienced team, the one-year survival rate is over 70%.
- Lung volume reduction. These procedures remove 20–30% of severely diseased lung tissue; the remaining parts of the lung are joined together. Mortality rates can be as high as 15% and complication rates are even higher. When the operation is successful, patients report significant improvement in symptoms.

KEY TERMS

Alpha-1-antitrypsin (AAT)—A blood component that breaks down infection-fighting enzymes such as elastase.

Alveoli—Terminal air sacs of the respiratory system, where gas (oxygen and carbon dioxide) exchange occurs.

Bronchi—Large air tubes of the respiratory system.

Bronchioles—Small air tubes of the respiratory system.

Bronchodilators—Drugs that open wider the bronchial tubes of the respiratory system.

Corticosteroids—A group of hormones that are used as drugs to block inflammation.

Forced expiratory volume (FEV1)—The maximum amount of air expired in one second.

Spirometer—An instrument used by a doctor to perform a breathing test.

Vital capacity (VC)—The largest amount of air expelled after one's deepest inhalation.

Pulmonary rehabilitation

A structured, outpatient pulmonary **rehabilitation** program improves functional capacity in certain patients with COPD. Services may include general **exercise** training, administration of oxygen and nutritional supplements, intermittent mechanical ventilatory support, continuous positive airway pressure, relaxation techniques, breathing exercises and techniques (such as pursed lip breathing), and methods for mobilizing and removing secretions.

Alternative treatment

For both chronic bronchitis and emphysema, alternative practitioners recommend diet and nutritional supplements, a variety of herbal medicines, **hydrotherapy**, **acupressure** and **acupuncture**, **aromatherapy**, **homeopathy**, and **yoga**.

Prognosis

COPD is a disease that can be treated and controlled, but not cured. Survival of patients with COPD is clearly related to the degree of their lung function when they are

diagnosed and the rate at which they lose this function. Overall, the median survival is about 10 years for patients with COPD who have lost approximately two-thirds of their lung function at diagnosis.

Prevention

Lifestyle modifications that can help prevent COPD, or improve function in COPD patients, include: quitting smoking, avoiding respiratory irritants and infections, avoiding allergens, maintaining good **nutrition**, drinking lots of fluids, avoiding excessively low or high temperatures and very high altitudes, maintaining proper weight, and exercising to increase muscle tone.

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American Lung Association. 1740 Broadway, New York, NY 10019. (800) 586-4872. <http://www.lungusa.org>.

National Heart, Lung and Blood Institute. P.O. Box 30105, Bethesda, MD 20824-0105. (301) 251-1222. <http://www.nhlbi.nih.gov>.

National Jewish Medical and Research Center. 1400 Jackson St., Denver, CO 80206. (800) 222-LUNG (Lung Line). <http://www.njc.org>.

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Chronic obstructive pulmonary disease *see* **Emphysema; Chronic obstructive lung disease**

Churg-Strauss syndrome *see* **Vasculitis**

Cingulotomy *see* **Psychosurgery**

Ciprofloxacin *see* **Fluoroquinolones**

Circadian rhythm sleep disorders *see* **Jet lag**

Circumcision

Definition

The surgical removal of the foreskin of the penis or prepuce.

Purpose

In the United States, circumcision in infant boys is performed for social, medical, or cultural/religious reasons. Once a routine operation urged by pediatricians and obstetricians for newborns in the middle of the twentieth century, circumcision has become an elective option that parents make for their sons on an individual basis. Families who practice Judaism or Islam may select to have their sons circumcised as a religious practice. Others choose circumcision for medical benefits.

Female circumcision (also known as **female genital mutilation**) is usually performed for cultural and social reasons by family members and others who are not members of the medical profession, with no anesthesia. Not only is the prepuce removed but often the vaginal opening is sewn to make it smaller. This practice is supposed to ensure the virginity of a bride on her wedding day. It also prevents the woman from achieving sexual pleasure during coitus. This practice is not universally approved by the medical profession and is considered by some as a human rights violation.

Though the incidence of male circumcision has decreased from 90% in 1979 to 60% in 1996, it is still the most common surgical operation in the United States. Circumcision rates are much lower for the rest of the industrialized world. In Britain, it is only done for religious practices or to correct a specific medical condition of the penis.

Some of the medical reasons parents choose circumcision are to protect against infections of the urinary tract and the foreskin, prevent **cancer**, lower the risk of getting **sexually transmitted diseases**, and prevent phimosis (a tightening of the foreskin that may close the opening of the penis). Though studies indicate that uncircumcised boys under the age of five are 20 times more likely than circumcised boys to have

A typical circumcision procedure involves the following steps: Figure A: The surgeon makes an incision around the foreskin. Figure B: The foreskin is then freed from the skin covering the penile shaft. Figure C: The surgeon cuts the foreskin to the initial incision, lifting the foreskin from the mucous membrane. Figure D: The surgeon sutures the top edge of the skin that covers the penile shaft and the mucous membrane. *(Illustration by Electronic Illustrators Group.)*

urinary tract infections (UTIs), the rate of incidence of UTIs is quite low. There are also indications that circumcised men are less likely to suffer from **penile cancer**, inflammation of the penis, or have many sexually transmitted diseases. Here again, the rate of incidence is low. Good hygiene usually prevents most infections of the penis. Phimosis and penile cancer are very rare, even in men who have not been circumcised. Education and good safe sex practices can prevent sexually transmitted diseases in ways that a surgical procedure cannot because these are diseases acquired through risky behaviors.

With these factors in mind, the American Academy of Pediatrics has issued a policy statement that states though there is existing scientific evidence that indicates the medical benefits of circumcision, the benefits aren't strong enough to recommended circumcision as a routine practice.

KEY TERMS

Foreskin—A covering fold of skin over the tip of the penis.

Glans—The cone-shaped tip of the penis.

Hernia—Bulging of abdominal structures through an abnormal opening in the muscular wall.

Hydrocele—Collection of fluid in the scrotum.

Hypospadias—A congenital deformity of the penis where the urinary tract opening is not at the tip of the glans.

Phimosis—A tightening of the foreskin that may close the opening of the penis.

Prepuce—A fold like the foreskin that covers the clitoris; another name for foreskin.

Precautions

Circumcision should not be performed on infants with certain deformities of the penis that may require a portion of the foreskin for repair. The most common condition for surgery using the foreskin is hypospadias, a congenital deformity of the penis where the urinary tract opening is not at the tip of the glans. Also, infants with a large hydrocoele or **hernia** may suffer important complications through circumcision. Premature infants and infants with serious infections are also poor candidates to be circumcised, as are infants with **hemophilia**, other bleeding disorders, or whose mothers had taken anticoagulant drugs. In older boys or men, circumcision is a minor procedure. Therefore, it can be performed in virtually anyone without a serious illness or unusual deformity.

Description

The foreskin of the penis protects the sensitivity of the glans and shields it from irritation by urine, feces, and foreign materials. It also protects the urinary opening against infection and incidental injury.

In circumcision of infants, the foreskin is pulled tightly into a specially designed clamp, and the foreskin pulls away from the broadened tip of the penis. Pressure from the clamp stops bleeding from blood vessels that supplied the foreskin. In older boys or adults, an incision is made around the base of the foreskin, the foreskin is

A. uncircumcised penis. B. circumcised penis. *(Illustration by Argosy Inc.)*

pulled back, and then it is cut away from the tip of the penis. Stitches are usually used to close the skin edges.

Preparation

Despite a long-standing belief that infants do not experience serious **pain** from circumcision, most authorities now believe that some form of local anesthesia is necessary. The physician injects local anesthesia at the base of the penis or under the skin around the penis (subcutaneous ring block). Both anesthetics block key nerves. EMLA cream, a topical formula of several anesthetics can also be used.

Aftercare

After circumcision, the wound should be washed daily. An antibiotic ointment or petroleum jelly may be applied to the site. If there is an incision, a wound dressing will be present and should be changed each time the diaper is changed. Sometimes a plastic ring is used instead of a bandage. The ring will usually fall off in five to eight days. The penis will heal in seven to 10 days.

Infants who undergo circumcision may be fussy for some hours afterward, so parents should be prepared for crying, feeding problems, and sleep problems. Generally these go away within a day. In older boys, the penis may be painful, but this will go away gradually. A topical anesthetic ointment or spray may be used to relieve this temporary discomfort. There may also be a "bruise" on the penis, which typically goes away with no particular attention.

Risks

Complications following newborn circumcision appear in one out of every 500 procedures. Most complications are minor. Bleeding occurs in half of the complications and is usually easy to control. Infections are rare and present with **fever** and signs of inflammation.

There may be injuries to the penis itself, and these may be difficult to repair. In 2000, there were reports that the surgical clamps used in circumcision were at fault in over 100 injuries reported between July 1996 and January 2000. In nearly all cases, the clamps were assumed to be in working order but had been repaired with replacement parts that were not of the manufacturer's specifications. Physicians were urged to inspect the clamps before use and ensure that their dimensions fit their infant patients.

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Cirrhosis

Definition

Cirrhosis is a chronic, degenerative disease in which normal liver cells are damaged and are then replaced by scar tissue.

Description

Cirrhosis changes the structure of the liver and the blood vessels that nourish it. The disease reduces the liver's ability to manufacture proteins and process hormones, nutrients, medications, and poisons.

Cirrhosis gets worse over time and can become potentially life threatening. This disease can cause:

- excessive bleeding (hemorrhage)
- impotence
- liver **cancer**
- coma due to accumulated ammonia and body wastes (liver failure)

A micrograph of a human liver showing tissue damaged by cirrhosis. *(Photograph by Professor P. Motta, Photo Researchers, Inc. Reproduced by permission.)*

• **death**

Cirrhosis is the seventh leading cause of disease-related death in the United States. It is twice as common in men as in women. The disease occurs in more than half of all malnourished chronic alcoholics and kills about 25,000 people a year. It is the third most common cause of death in adults between the ages of 45 and 65.

Types of cirrhosis

Portal or nutritional cirrhosis is the form of the disease most common in the United States. About 30–50% of all cases of cirrhosis are this type. Nine out of every 10 people who have nutritional cirrhosis have a history of **alcoholism**. Portal or nutritional cirrhosis is also called Laënnec's cirrhosis.

Biliary cirrhosis is caused by intrahepatic bile-duct diseases that impede bile flow. Bile is formed in the liver and is carried by ducts to the intestines. Bile then helps digest fats in the intestines. Biliary cirrhosis can scar or block these ducts. It represents 15–20% of all cirrhosis.

Various types of chronic hepatitis, especially **hepatitis B** and **hepatitis C**, can cause postnecrotic cirrhosis. This form of the disease affects up to 40% of all patients who have cirrhosis.

Disorders like the inability to metabolize iron and similar disorders may cause pigment cirrhosis (**hemochromatosis**), which accounts for 5–10% of all instances of the disease.

Causes and symptoms

Long-term alcoholism is the primary cause of cirrhosis in the United States. Men and women respond differently to alcohol. Although most men can safely consume two to five drinks a day, one or two drinks a day can cause liver damage in women. Individual tolerance to alcohol varies, but people who drink more and drink more often have a higher risk of developing cirrhosis. In some people, one drink a day can cause liver scarring.

Chronic liver infections like hepatitis B and particularly hepatitis C are commonly linked to cirrhosis. People at high risk of contracting hepatitis B include those exposed to the virus through contact with blood and body fluids. This includes healthcare workers and intraveneous

(IV) drug users. People in the past have contracted hepatitis C through blood transfusions.

Liver injury, reactions to prescription medications, exposure to toxic substances, and repeated episodes of **heart failure** with liver congestion can cause cirrhosis. The disorder can also be a result of diseases that run in families (inherited diseases) like:

- a lack of a specific liver enzyme (alpha$_1$-antitrypsin deficiency)
- the absence of a milk-digesting enzyme (galactosemia)
- an inability to convert sugars to energy (glycogen storage disease)
- an absorption deficit in which excess iron is deposited in the liver, pancreas, heart, and other organs (hemochromatosis)
- a disorder characterized by accumulations of copper in the liver, brain, kidneys, and corneas (Wilson's disease)

Poor **nutrition** increases a person's risk of developing cirrhosis. In about 10 out of every 100 patients, the cause of cirrhosis cannot be determined. Many people who have cirrhosis do not have any symptoms (often called compensated cirrhosis). Their disease is detected during a routine physical or when tests for an unrelated medical problem are performed. This type of cirrhosis can also be detected when complications occur (decompensated cirrhosis).

Symptoms of cirrhosis are usually caused by the loss of functioning liver cells or organ swelling due to scarring. The liver enlarges during the early stages of illness. The palms of the hands turn red and patients may experience:

- constipation
- diarrhea
- dull abdominal **pain**
- fatigue
- indigestion
- loss of appetite
- nausea
- vomiting
- weakness
- weight loss

As the disease progresses, the spleen enlarges and fluid collects in the abdomen (**ascites**) and legs (**edema**). Spider-like blood vessels appear on the chest and shoulders, and bruising becomes common. Men sometimes lose chest hair. Their breasts may grow and their testicles may shrink. Women may have menstrual irregularities.

Cirrhosis can cause extremely dry skin and intense **itching**. The whites of the eyes and the skin may turn yellow (**jaundice**), and urine may be dark yellow or brown. Stools may be black or bloody. Sometimes the patient develops persistent high blood pressure due to the scarring (portal **hypertension**). This type of hypertension can be life threatening. It can cause veins to enlarge in the stomach and in the tube leading from the mouth to the stomach (esophagus). These enlarged veins are called varices, and they can rupture and bleed massively.

Other symptoms of cirrhosis include:

- anemia
- bleeding gums
- decreased interest in sex
- fever
- fluid in the lungs
- hallucinations
- lethargy
- lightheadedness
- muscle weakness
- musty breath
- painful nerve inflammation (neuritis)
- slurred speech
- tremors

If the liver loses its ability to remove toxins from the brain, the patient may have additional symptoms. The patient may become forgetful and unresponsive, neglect personal care, have trouble concentrating, and acquire new sleeping habits. These symptoms are related to ammonia intoxication and the failure of the liver to convert ammonia to urea. High protein intake in these patients can also lead to these symptoms.

Diagnosis

A patient's medical history can reveal illnesses or lifestyles likely to lead to cirrhosis. Liver changes can be seen during a **physical examination**. A doctor who suspects cirrhosis may order blood and urine tests to measure liver function. Because only a small number of healthy cells are needed to carry out essential liver functions, test results may be normal even when cirrhosis is present.

Computed tomography scans (CT), ultrasound, and other imaging techniques can be used during diagnosis. They can help determine the size of the liver, indicate healthy and scarred areas of the organ, and detect **gallstones**. Cirrhosis is sometimes diagnosed during surgery or by examining the liver with a laparoscope. This view-

ing device is inserted into the patient's body through a tiny incision in the abdomen.

Liver biopsy is usually needed to confirm a diagnosis of cirrhosis. In this procedure, a tissue sample is removed from the liver and is examined under a microscope in order to learn more about the organ.

Treatment

The goal of treatment is to cure or reduce the condition causing cirrhosis, prevent or delay disease progression, and prevent or treat complications.

Salt and fluid intake are often limited, and activity is encouraged. A diet high in calories and moderately high in protein can benefit some patients. **Tube feedings** or vitamin supplements may be prescribed if the liver continues to deteriorate. Patients are asked not to consume alcohol.

Medication

Iron supplements, **diuretics**, and **antibiotics** may be used for anemia, fluid retention, and ammonia accumulation associated with cirrhosis. Vasoconstrictors are sometimes needed to stop internal bleeding and antiemetics may be prescribed to control nausea.

Laxatives help the body absorb toxins and accelerate their removal from the digestive tract. **Beta blockers** may be prescribed to control cirrhosis-induced portal hypertension. Because the diseased liver can no longer efficiently neutralize harmful substances, medications must be given with caution. Interferon medicines may be used by patients with chronic hepatitis B and hepatitis C to prevent post-hepatic cirrhosis.

Surgery

Medication that causes scarring can be injected directly into veins to control bleeding from varices in the stomach or esophagus. Varices may require a special surgical procedure called balloon tamponade ligation to stop the bleeding. Surgery may be required to repair disease-related throat damage. It is sometimes necessary to remove diseased portions of the spleen and other organs.

Liver transplants can benefit patients with advanced cirrhosis. However, the new liver will eventually become diseased unless the underlying cause of cirrhosis is removed. Patients with alcoholic cirrhosis must demonstrate a willingness to stop drinking before being considered suitable transplant candidates.

Supportive measures

A balanced diet promotes regeneration of healthy liver cells. Eating five or six small meals throughout the day should prevent the sick or bloated feeling patients with cirrhosis often have after eating. Alcohol and **caffeine**, which destroy liver cells, should be avoided. So should any foods that upset the stomach. Patients with brain disease associated with cirrhosis should avoid excessive amounts of protein in the diet.

A patient can keep a food diary that describes what was eaten, when it was eaten, and how the patient felt afterwards. This diary can be useful in identifying foods that are hard to digest and in scheduling meals to coincide with the times the patient is most hungry.

Patients who have cirrhosis should weigh themselves every day and notify their doctor of a sudden gain of five pounds or more. A doctor should also be notified if symptoms of cirrhosis appear in anyone who has not been diagnosed with the disease. A doctor should also be notified if a patient diagnosed with cirrhosis:

- vomits blood
- passes black stools
- seems confused or unresponsive
- shows signs of infection (redness, swelling, tenderness, pain)

Alternative treatment

Alternative treatments for cirrhosis are aimed at promoting the function of healthy liver cells and relieving the symptoms associated with the disease. Several herbal remedies may be helpful to cirrhosis patients. Dandelion (*Taraxacum officinale*) and rock-poppy (*Chelidonium majus*) may help improve the efficiency of liver cells. Milk thistle extract (*Silybum marianum*) may slow disease progression and significantly improve survival rates in alcoholics and other cirrhosis patients. Practitioners of **homeopathy** and **traditional Chinese medicine** can also prescribe treatments that support healthy liver function.

Prognosis

Cirrhosis-related liver damage cannot be reversed, but further damage can be prevented by patients who:

- eat properly
- get enough rest
- do not consume alcohol
- remain free of infection

If the underlying cause of cirrhosis cannot be corrected or removed, scarring will continue. The liver will fail, and the patient will probably die within five years. Patients who stop drinking after being diagnosed with cirrhosis can increase their likelihood of living more than a few years from 40% to 60–70%.

Prevention

Eliminating alcohol abuse could prevent 75–80% of all cases of cirrhosis.

Other preventive measures include:

- obtaining counseling or other treatment for alcoholism
- taking precautions (practicing safe sex, avoiding dirty needles) to prevent hepatitis
- getting immunizations against hepatitis if a person is in a high-risk group
- receiving appropriate medical treatment quickly when diagnosed with hepatitis B or hepatitis C
- having blood drawn at regular intervals to rid the body of excess iron from hemochromatosis
- using medicines (chelating agents) to rid the body of excess copper from Wilson's disease
- wearing protective clothing and following product directions when using toxic chemicals at work, at home, or in the garden

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ORGANIZATIONS

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United Network for Organ Sharing. 1100 Boulders Parkway, Suite 500, P.O. Box 13770, Richmond, VA 23225-8770. (804) 330-8500.

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Maureen Haggerty

Cisapride *see* **Antigastroesophageal reflux drugs**

CK test *see* **Creatine kinase test**

Clap *see* **Gonorrhea**

Clarithromycin *see* **Erythromycins**

Cleft lip and palate

Definition

A cleft is a birth defect that occurs when the tissues of the lip and/or palate of the fetus do not fuse very early in **pregnancy**. A cleft lip, sometimes referred to as a harelip, is an opening in the upper lip that can extend into the base of the nostril. A cleft palate is an opening in the roof of the mouth.

Description

Babies born with cleft lips will have an opening involving the upper lip. The length of the opening ranges from a small notch, to a cleft that extends into the base of the nostril. Cleft lips may involve one or both sides of the lip.

Babies born with cleft palates have openings in the palate, which is the roof of the mouth. The size and position of the opening varies. The cleft may be only in the hard palate, the bony portion of the roof of the mouth, opening into the floor of the nose. It may be only in the soft palate, the soft portion of the roof of the mouth. The cleft palate may involve both the hard and soft palate and may occur on both sides of the center of the palate.

Babies may have cleft lips with or without cleft palates. Cleft palates may also occur without cleft lips.

The incidence of cleft lip and palate not associated with a syndrome is one in 700 newborns. Native Americans have an incidence of 3.6 in 1,000 newborns. The incidence among Japanese newborns is 2.1 in 1,000. The incidence among whites is one in 1,000 newborns. African Americans have an incidence of 0.3 in 1,000 newborns.

Causes and symptoms

Cleft lips and palates not associated with a syndrome are caused by a combination of genetic and environmental factors. Inheritance caused by such a combination is called multifactorial. The embryo inherits genes that increase the risk for cleft lip and/or palate. When an embryo with such genes is exposed to certain environmental factors the embryo develops a cleft.

The risk of a baby being born with a cleft lip or palate increases with the number of affected relatives and increases with relatives that have more severe clefts.

Environmental factors that increase the risk of cleft lip and palate include cigarette and alcohol use during

pregnancy. Some drugs also increase the incidence of clefting, such as phenytoin, sodium valproate, and methotrexate. The pregnant mother's **nutrition** may affect the incidence of clefting as well.

Babies born with a cleft lip will be seen to have an elongated opening in the upper lip. The size of this opening may range from a small notch in the upper lip to an opening that extends into the base of the nostril. The cleft lip may be below the right or left nostril or below both nostrils.

Babies born with a cleft palate will be seen to have an opening into the roof of the mouth. The size and position of the cleft varies and it may involve only the hard palate, or only the soft palate and may occur on both sides of the center of the palate.

In some cases the cleft palate will be covered with the normal lining of the mouth and can only be felt by the examiner.

Babies with cleft lips and palates have feeding difficulties, which are more severe in babies with cleft palates. The difficulty in feeding is due to the baby being unable to achieve complete suction. In the case of clefts of the hard palate, liquids enter the nose from the mouth through the opening in the hard palate.

A cleft palate also affects a child's speech, since the palate is necessary for speech formation. The child's speech pattern may still be affected despite surgical repair.

Ear infections are more common in babies born with cleft palates. The infections occur because the muscles of the palate do not open the Eustachian tubes which drain the middle ear. This allows fluid to collect and increases the risk of infection and **hearing loss**.

Teeth may also erupt misaligned.

Diagnosis

Cleft lip and palate can be diagnosed before birth by ultrasound. After birth, cleft lip and palate are diagnosed by physical exam.

Treatment

If cleft lip and/or palate are diagnosed by ultrasound before birth, further testing may be required to diagnose associated abnormalities if present. Referral to a cleft team is essential. A cleft team consists of specialists in the management of babies with clefts and includes surgeons as well as nurses and speech therapists. Members of the team inform the parents of all aspects of management. Feeding methods are also discussed, since feeding is the first problem that must be dealt with. It may be possible to breastfeed a baby born with only a cleft lip, but babies born with cleft palates usually have more problems with feeding and frequently require special bottles and teats. A palatal obturator is a device that fits into the roof of the mouth, thus blocking the cleft opening and allowing easier suckling.

This infant has an unilateral cleft lip and palate. *(Custom Medical Stock Photo. Reproduced by permission.)*

Surgery to repair cleft lips is sometimes performed after orthodontic treatment to narrow the gap in the upper lip. The orthodontic treatment can involve acrylic splints with or without screws or may involve the use of adhesive tape placed across the gap in the lip. The orthodontic treatment for cleft lip should be started within the first three weeks of life and continue until the cleft lip is repaired.

The timing of surgical cleft lip repair depends on the judgment of the surgeon who will perform the operation. The procedure is usually performed between one and three months of age. The goals of the operation are to close the gap in the upper lip, place scars in the natural skin curves and to repair muscle so that the lip appears normal during movement. The closure is done in the three layers (skin, muscle, and mucosa) that line the inside of the lip. At the time of the procedure, if the nose is shaped abnormally due to the cleft lip, it is also corrected. Sometimes further surgery may be needed on the lip and/or nose to refine the result.

The goals of the surgeon repairing a cleft palate are normal speech, normal facial growth, and hearing for the affected infant. The repair of the cleft palate is usually performed between three and 18 months of age. The timing may extend beyond this and varies with the type of cleft palate and center where the procedure is being performed.

Depending of the type of cleft palate, more than one operation may be needed to close the cleft and improve speech.

Nonsurgical treatment of a cleft palate is available for patients who are at high risk for surgery and consists of a prosthetic appliance worn to block the opening in the palate.

Babies born with cleft palates are vulnerable to ear infections. Their Eustachian tubes do not effectively drain fluid from the middle ear so fluid accumulates and infection sets in. This may lead to hearing loss. These children require drainage tubes to be inserted to prevent fluid accumulation.

Babies born with clefts usually require orthodontic treatment between 13 and 18 years of age. They also require speech therapy.

Prognosis

Babies born with cleft lip and palate have a good prognosis, and approximately 80% will develop normal speech. There is no known means of preventing clefting. Good prenatal care is essential and avoiding harmful substances appear to reduce the risk.

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Cleft Palate Foundation. (800) 24-CLEFT. <http://www.cleftline.org>.

Farris F. Gulli, MD

Cleft palate *see* **Cleft lip and palate**

Climacteric *see* **Menopause**

Clenched fist injury

Definition

A clenched fist injury (CFI) is a bite wound on the hand, caused when a person's closed fist strikes the teeth of another person, usually in the course of a fight. CFIs are sometimes referred to as closed fist injuries or fight bites.

Description

Clenched fist injuries are most common over the metacarpo phalangeal joint. Their appearance is deceptive because they do not bleed heavily and the underlying injury is hidden by soft tissue when the patient opens his hand and straightens the injured finger. CFIs can, however, have serious consequences, including infection, **cellulitis**, inflammation of the bone or bone marrow (**osteomyelitis**), septic arthritis, and inflammation of the sheaths covering the tendons of the hand (tenosynovitis). These may lead to permanent loss of function or **amputation**.

Most CFIs result in tissue injury due to the force of impact, ragged-edged tears in the skin resulting from contact with the teeth, and contamination of the wound by the bacteria in human saliva. As the patient opens his hand, the skin of the finger is pulled backward over the deeper part of the wound, thus sealing bacteria within the injured tissue. This sealing of the wound by normal motions of the finger is the reason why clenched fist injuries have the highest rate of infection of any human bite. The rate of infection of clenched-fist injuries varies from 15–50%.

Causes and symptoms

The causes of CFIs include fighting and other forms of aggressive behavior, often combined with drug or alcohol consumption.

The symptoms of clenched fist injury include **pain** in the affected part of the hand and some stiffness of the injured finger with limitation of movement. If the patient has delayed getting medical treatment, there may be evidence of infection, including swelling, redness, and suppuration (a discharge of pus). The skin around the wound will be warm to the touch and **fever** may be present.

Diagnosis

Diagnosis of clenched fist injuries is usually made on the basis of the location of the injury and x-ray findings. The most common finding in CFI x rays is soft tissue swelling, but the x rays may also reveal air pockets in deep tissues or the joint spaces, fragments of teeth, frac-

ture lines in the bones, or small loose bone chips. Diagnosis is often complicated by the fact that the patient will be reluctant to admit how the injury happened. The treating physician must maintain a high level of suspicion and often ask directly.

Treatment

Treatment of clenched fist injuries is complicated by several factors. One factor is the anatomical structure of the human hand, which contains many small closed spaces that make it easy for infection to spread and persist. Another is the number of disease-causing bacteria transmitted by human bites; at least 42 different species have been identified. In addition, CFIs typically do not receive immediate treatment because the patient is concerned about legal consequences. The longer the delay, the higher the chances of infection and permanent damage to the hand. Patients who wait longer than 24 hours to seek treatment or have signs of infection or damage to the tendon, joint capsule, or bones are usually referred immediately to a doctor who specializes in hand surgery.

The first step in treatment of clenched fist injury is irrigation, a procedure by which the wound is flushed with a stream of water under high pressure or with an antiseptic solution. Incision and drainage of the wound (I&D) may be required as well as **debridement**, the surgical removal of dead tissue and **foreign objects** from a wound. Careful examination of the depth of the wound is essential to proper treatment. The surgeon may need to enlarge the sides of the wound in order to make an accurate evaluation. The patient will be asked to move the affected joint through its full range of motion so that the surgeon can determine whether the tendon or joint capsule has been damaged. Following these procedures, the surgeon will pack the wound and put the hand in a splint. Bite **wounds** are never sutured (sewn shut) because of the possibility of enclosing bacteria inside the injury. After 24 hours, the packing will be removed and the hand reexamined for signs of infection.

If the wound has become infected, the patient is usually hospitalized and given parenteral (injectable) **antibiotics**. The wound is irrigated and examined to determine the extent of the injury. Cultures are taken for both aerobic (requiring air or oxygen to live) and anaerobic (not requiring air or oxygen) species of bacteria. The cultures should be taken from areas deep in the wound rather than from the surface for greater accuracy. **Tetanus** toxoid should be given if the patient has not been immunized within the last 10 years. The patient should also receive treatment and follow-up for the rare possibility of HIV and hepatitis transmission. Although no well-documented cases of HIV transmission by human bites exist as of 2001, the potential for transmission by this route is still present.

KEY TERMS

Antibiotic—A chemical substance produced by a microorganism which can inhibit the growth of or kill other microorganisms.

Debridement—Surgical removal of damaged tissue and foreign objects from a wound.

I&D—Incision and drainage of a wound.

Irrigation—Cleansing a wound with large amounts of water and/or an antiseptic solution.

Parenteral—Administered inside the body but outside the digestive tract.

Tetanus toxoid—Tetanus toxoid is a vaccine used to prevent tetanus (also known as lockjaw).

Infected clenched fist injuries usually contain several disease-causing bacteria, the most common being *Streptococcus pyogenes*, *Staphylococcus aureus*, *Bacteroides sp*., *Peptostreptococcus sp*., and *Eikenella corrodens*. Broad-spectrum antibiotics are usually given. Uninfected and relatively superficial CFIs may be treated with oral penicillin plus dicloxacillin or Augmentin. For infected CFIs, parenteral penicillin G is usually given together with nafcillin or cefuroxime. CFIs infected by drug-resistant strains of *S. aureus* may require treatment with vancomycin.

Prognosis

The prognosis depends on the patient's underlying state of health and compliance with treatment; depth of the wound; the involvement of the joint capsule or tendon; and the length of time before the wound is treated. The more superficial the wound and the faster the treatment, the better the prognosis.

Prevention

The best way to prevent clenched fist injuries is to avoid fist fights, intoxication, and association with people who practice these forms of behavior. If involved in a fistfight, people should avoid directing punches at their opponent's mouth. The next best preventive measure is to get medical treatment at once for a clenched-fist injury.

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Massachusetts College of Emergency Physicians (MACEP). P. O. Box 296, Swansea, MA 02777. (508) 643-0117. Fax: (508) 643-0141.

Rebecca J. Frey, PhD

Clomiphene *see* **Infertility drugs**

Clonazepam *see* **Benzodiazepines**

Closed fracture reduction *see* **Fracture repair**

Clostridium difficile colitis *see* **Antibiotic-associated colitis**

Clotrimazole *see* **Antifungal drugs, topical**

Clotting disorders *see* **Coagulation disorders**

Clubfoot

Definition

Clubfoot is a condition in which one or both feet are twisted into an abnormal position at birth. The condition is also known as talipes.

Description

True clubfoot is characterized by abnormal bone formation in the foot. There are four variations of clubfoot, including talipes varus, talipes valgus, talipes equines, and talipes calcaneus. In talipes varus, the most common form of clubfoot, the foot generally turns inward so that the leg and foot look somewhat like the letter J. In talipes valgus, the foot rotates outward like the letter L. In talipes equinus, the foot points downward, similar to that of a toe dancer. In talipes calcaneus, the foot points upward, with the heel pointing down.

Clubfoot can affect one foot or both. Sometimes an infant's feet appear abnormal at birth because of the intrauterine position of the fetus birth. If there is no anatomic abnormality of the bone, this is not true clubfoot, and the problem can usually be corrected by applying special braces or casts to straighten the foot.

The ratio of males to females with clubfoot is 2.5 to 1. The incidence of clubfoot varies only slightly. In the United States, the incidence is approximately 1 in every 1,000 live births. A 1980 Danish study reported an overall incidence of 1.20 in every 1,000 children; by 1994, that number had doubled to 2.41 in every 1,000 live births. No reason was offered for the increase.

Causes and symptoms

Experts do not agree on the precise cause of clubfoot. The exact genetic mechanism of inheritance has been extensively investigated using family studies and other epidemiological methods. As of 1999, no definitive conclusions had been reached, although a Mendelian pattern of inheritance is suspected. This may be due to the interaction of several different inheritance patterns, different patterns of development appearing as the same condition, or a complex interaction between genetic and environmental factors. The MSX1 gene has been associated with clubfoot in animal studies. But, as of 2001, these findings have not been replicated in humans.

A family history of clubfoot has been reported in 24.4% of families in a single study. These findings suggest the potential role of one or more genes being responsible for clubfoot.

Several environmental causes have been proposed for clubfoot. Obstetricians feel that intrauterine crowding causes clubfoot. This theory is supported by a significantly higher incidence of clubfoot among twins compared to singleton births. Intrauterine exposure to the drug misoprostol has been linked with clubfoot. Misoprostol is commonly used when trying, usually unsuccessfully, to induce abortion in Brazil and in other countries in South and Central America. Researchers in Norway have reported that males who are in the printing trades have significantly more offspring with clubfoot than men in other occupations. For unknown reasons, **amniocentesis**, a prenatal test, has also been associated with clubfoot. The infants of mothers who smoke during **pregnancy** have a greater chance of being born with clubfoot than are offspring of women who do not smoke.

True clubfoot is usually obvious at birth. The four most common varieties have been described. A clubfoot has a typical appearance of pointing downward and

being twisted inwards. Since the condition starts in the first trimester of pregnancy, the abnormality is quite well established at birth, and the foot is often very rigid. Uncorrected clubfoot in an adult causes only part of the foot, usually the outer edge, or the heel or the toes, to touch the ground. For a person with clubfoot, walking becomes difficult or impossible.

Diagnosis

True clubfoot is usually recognizable and obvious on **physical examination**. A routine x ray of the foot that shows the bones to be malformed or misaligned supplies a confirmed diagnosis of clubfoot. Ultrasonography is not always useful in diagnosing the presence of clubfoot prior to the birth of a child.

Treatment

Most orthopedic surgeons agree that the initial treatment of congenital (present at birth) clubfoot should be non-operative. Non-surgical treatment should begin in the first days of life to take advantage of the favorable fibro-elastic properties of the foot's connective tissues, those forming the ligaments, joint capsules, and tendons. In a common treatment, a series of casts is applied over a period of months to reposition the foot into a normal alignment. In mild cases, splinting and wearing braces at night may correct the abnormality.

When clubfoot is severe enough to require surgery, the condition is usually not completely correctable, although significant improvement is possible. In the most severe cases, surgery may be required, especially when the Achilles tendon, which joins the muscles in the calf to the bone of the heel, needs to be lengthened. Because an early operation induces fibrosis, a scarring and stiffness of the tissue, surgery should be delayed until an affected child is at least three months old.

Much of a clubfoot abnormality can be corrected by the use of manipulation and casting during the first three months of life. Proper manipulative techniques must be followed by applications of appropriately molded plaster casts to provide effective and safe correction of most varieties of clubfoot. Long-term care by an orthopedist is required after initial treatment to ensure that the correction of the abnormality is maintained. Exercises, corrective shoes, or nighttime splints may be needed until the child stops growing.

Prognosis

With prompt, expert treatment, clubfoot is usually correctable. Most individuals are able to wear regular shoes and lead active lives. If clubfoot is not appropriately treated, the abnormality becomes fixed. This has an effect on the growth of the leg and foot, and some degree of permanent disability usually results.

Person suffering from clubfoot. About one of every 400 newborns has some form of this birth defect. *(Photo Researchers, Inc. Reproduced by permission.)*

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KEY TERMS

Enterovirus—Any of a group of viruses that primarily affect the gastrointestinal tract.

Intrauterine—Situated or occuring in the uterus.

Orthopedist—A doctor specializing in treatment of the skeletal system and its associated muscles and joints.

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ORGANIZATIONS

March of Dimes/Birth Defects Foundation. 1275 Mamaroneck Ave., White Plains, NY 10605. (888) 663-4637. resourcecenter@modimes.org. <http://www.modimes.org>.

National Easter Seal Society. 230 W. Monroe St., Suite 1800, Chicago, IL 60606-4802. (312) 726-6200 or (800) 221-6827. <http://www.easter-seals.org>.

National Organization for Rare Disorders (NORD). PO Box 8923, New Fairfield, CT 06812-8923. (203) 746-6518 or (800) 999-6673. Fax: (203) 746-6481. <http://www.rarediseases.org>.

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L. Fleming Fallon, Jr., MD, DrPH

Cluster headache

Definition

Cluster headaches are characterized by an intense one-sided **pain** centered by the eye or temple. The pain lasts for one to two hours on average and may recur several times in a day.

Description

Cluster headaches have been known as histamine headaches, red migraines, and Horton's disease, among others. The constant factor is the pain, which transcends by far the distress of the more common tension-type **headache** or even that of a **migraine headache**.

Cluster headaches afflict less than 0.5% of the population and predominantly affect men; approximately 80% of sufferers are male. Onset typically occurs in the late 20s, but there is no absolute age restriction. Approximately 80% of cluster headaches are classified as episodic; the remaining 20% are considered chronic. Both display the same symptoms. However, episodic cluster headaches occur during one- to five-month periods followed by six- to 24-month attack-free, or remission, periods. There is no such reprieve for chronic cluster headache sufferers.

Causes and symptoms

Biochemical, hormonal, and vascular changes induce cluster headaches, but why these changes occur remains unclear. Episodic cluster headaches seem to be linked to changes in day length, possibly signaling a connection to the so-called biological clock. Alcohol, tobacco, histamine, or **stress** can trigger cluster headaches. Decreased blood oxygen levels (hypoxemia) can also act as a trigger, particularly during the night when an individual is sleeping. Interestingly, the triggers do not cause cluster headaches during remission periods.

The primary cluster headache symptom is excruciating one-sided head pain centered behind an eye or near the temple. This pain may radiate outward from the initial focus and encompass the mouth and teeth. For this reason, some cluster headache sufferers may mistakenly attribute their pain to a dental problem. Secondary symptoms, occurring on the same side as the pain, include eye tearing, nasal congestion followed by a runny nose, pupil contraction, and facial drooping or flushing.

Diagnosis

Cluster headache symptoms guide the diagnosis. A medical examination includes recording headache

The primary cluster headache symptom is excruciating one-sided head pain located behind an eye or near the temple. Secondary symptoms include eye tearing, nasal congestion, and a runny nose. *(Illustration by Electronic Illustrators Group.)*

details, such as frequency and duration, when it occurs, pain intensity and location, possible triggers, and any prior symptoms. This history allows other potential problems to be discounted.

Treatment

Treatment for cluster headaches is composed of induction, maintenance, and symptomatic therapies. The first two therapies are prophylactic treatments, geared toward preventing headaches. Symptomatic therapy is meant to stop or shorten a headache.

Induction and maintenance therapies begin together. Induction therapy is intended to break the headache cycle with drugs such as **corticosteroids** (for example, prednisone) or dihydroergotamine. These drugs are not meant for long-term therapy, but rather as a jump-start for maintenance therapy. Maintenance therapy drugs include verapamil, lithium carbonate, ergotamine, and methysergide. These drugs have long-term effectiveness, but must be taken for at least a week before a response is observed. With long-term treatment, methysergide must be stopped for one month each year to avoid dangerous side effects (formation of fibrous tissue inside the abdominal artery, lungs, and heart valves).

Despite prophylactic treatment, headaches may still occur. Symptomatic therapy includes oxygen inhalation, sumatriptan injection, and application of local anesthetics inside the nose. Surgery is a last resort for chronic cluster headaches that fail to respond to therapy.

KEY TERMS

Biological clock—A synonym for the body's circadian rhythm, the natural biological variations that occur over the course of a day.

Migraine headache—An intense throbbing pain that occurs on one or both sides of the head. The headache is usually accompanied by other symptoms, such as nausea, vomiting, and aversion to light.

Prophylactic—Referring to treatment that prevents symptoms from occurring.

Tension-type headache—A dull pain that seems to exert pressure on the head; the most common form of headache.

Alternative treatment

Since some cluster headaches are triggered by stress, **stress reduction** techniques, such as **yoga**, **meditation**, and regular **exercise**, may be effective. Some cluster headaches may be an allergic response triggered by food or environmental substances, therefore identifying and removing the allergen(s) may be key to resolution of the problem. Histamine is another suspected trigger of cluster headaches, and this response may be controlled with vitamin C and the bioflavonoids quercetin and bromelain (pineapple enzyme). Supplementation with essential fatty acids (EFA) will help decrease any inflammatory response.

Physical medicine therapies such as adjustments of the spine, craniosacral treatment, and massage at the temporomandibular joint (TMJ) can clear blockages, as can traditional Chinese medical therapies including **acupuncture**. Homeopathic treatment can also be beneficial. Nervous system relaxant herbs, used singly or in combination, can allow the central nervous system to relax as well as assist in peripheral nerve response. A few herbs to consider for relaxation are valerian (*Valeriana officinalis*), chamomile (*Matricaria recutita*), rosemary (*Rosemarinus officinalis*), and skullcap (*Scutellaria baicalensis*).

Prognosis

In general, drug therapy offers effective treatment.

Prevention

Avoiding triggers, adhering to medical treatment, and controlling stress can help ward off some cluster headaches.

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Julia Barrett

CMV *see* **Cytomegalovirus infection**

CNS depressants *see* **Central nervous system depressants**

CNS stimulants *see* **Central nervous system stimulants**

Coagulation disorders

Definition

Coagulation disorders deal with disruption of the body's ability to control blood clotting. The most commonly known coagulation disorder is **hemophilia**, a condition in which patients bleed for long periods of time before clotting. There are other coagulation disorders with a variety of causes.

Description

Coagulation, or clotting, occurs as a complex process involving several components of the blood. Plasma, the fluid component of the blood, carries a number of proteins and coagulation factors that regulate bleeding. Platelets, small colorless fragments in the blood, initiate contraction of damaged blood vessels so that less blood is lost. They also help plug damaged blood vessels and work with plasma to accelerate blood clotting. A disorder affecting platelet production or one of the many steps in the entire process can disrupt clotting.

Coagulation disorders arise from different causes and produce different complications. Some common coagulation disorders are:

- Hemophilia, or hemophilia A (Factor VIII deficiency), an inherited coagulation disorder, affects about 20,000 Americans. This genetic disorder is carried by females but most often affects males.
- Christmas disease, also known as hemophilia B or Factor IX deficiency, is less common than hemophilia A with similar in symptoms.
- Disseminated intravascular coagulation disorder, also known as consumption coagulopathy, occurs as a result of other diseases and conditions. This disease accelerates clotting, which can actually cause hemorrhage.
- **Thrombocytopenia** is the most common cause of coagulation disorder. It is characterized by a lack of circulating platelets in the blood. This disease also includes idiopathic thrombocytopenia.
- Von Willebrand's disease is a hereditary disorder with prolonged **bleeding time** due to a clotting factor deficiency and impaired platelet function. It is the most common hereditary coagulation disorder.
- Hypoprothrombinemia is a congenital deficiency of clotting factors that can lead to hemorrhage.
- Other coagulation disorders include Factor XI deficiency, also known as hemophilia C, and Factor VII deficiency. Hemophilia C afflicts one in 100,000 people and is the second most common bleeding disorder among women. Factor VII is also called serum prothrombin conversion accelerator (SPCA) deficiency. One in 500,000 people may be afflicted with this disorder that is often diagnosed in newborns because of bleeding into the brain as a result of traumatic delivery.

Causes and symptoms

Some coagulation disorders present symptoms such as severe bruising. Others will show no apparent symptoms, but carry the threat of severe internal bleeding.

Hemophilia

Because of its hereditary nature, hemophilia A may be suspected before symptoms occur. Some signs of hemophilia A are numerous large, deep **bruises** and **pain** and swelling of joints caused by internal bleeding. Patients with hemophilia do not bleed faster, just longer. A person with mild hemophilia may first discover the disorder with prolonged bleeding following a surgical procedure. If there is bleeding into the neck, head, or

digestive tract, or bleeding from an injury, emergency measures may be required.

Mild and severe hemophilia A are inherited through a complex genetic system that passes a recessive gene on the female chromosome. Women usually do not show signs of hemophilia but are carriers of the disease. Each male child of the carrier has a 50% chance of having hemophilia, and each female child has a 50% chance of passing the gene on.

Christmas disease

Christmas disease, or hemophilia B, is also hereditary but less common than hemophilia A. The severity of Christmas disease varies from mild to severe, although mild cases are more common. The severity depends on the degree of deficiency of the Factor IX (clotting factor). Hemophilia B symptoms are similar to those of hemophilia A, including numerous, large, and deep bruises and prolonged bleeding. The more dangerous symptoms are those that represent possible internal bleeding, such as swelling of joints, or bleeding into internal organs upon trauma. Hemophilia most often occurs in families with a known history of the disease, but occasionally, new cases will occur in families with no apparent history.

Disseminated intravascular coagulation

The name of this disorder arises from the fact that malfunction of clotting factors cause platelets to clot in small blood vessels throughout the body. This action leads to a lack of clotting factors and platelets at a site of injury that requires clotting. Patients with disseminated intravascular coagulation (DIC) will bleed abnormally even though there is no history of coagulation abnormality. Symptoms may include minute spots of hemorrhage on the skin, and purple patches or hematomas caused by bleeding in the skin. A patient may bleed from surgery or intravenous injection (IV) sites. Related symptoms include vomiting, seizures, **coma**, **shortness of breath**, **shock**, severe pain in the back, muscles, abdomen, or chest.

DIC is not a hereditary disorder or a common one. It is most commonly caused by complications during **pregnancy** or delivery, overwhelming infections, acute leukemia, metastatic **cancer**, extensive **burns** and trauma, and even snakebites. There are a number of other causes of DIC, and it is not commonly understood why or how these various disorders can lead to the coagulation problem. What the underlying causes of DIC have in common is some factor that affects proteins, platelets, or other clotting factors and processes. For example, uterine tissue can enter the mother's circulation during prolonged labor, introducing foreign proteins into the blood, or the venom of some exotic snakes can activate one of the clotting factors. Severe head trauma can expose blood to brain tissue. No matter the cause of DIC, the results are a malfunction of thrombin (an enzyme) and prothrombin (a glycoprotein), which activate the fibrinolytic system, releasing clotting factors in the blood. DIC can alternate from hemorrhage to thrombosis, and both can exist, which further complicates diagnosis and treatment.

KEY TERMS

Clotting factor—Also known as coagulation factors. Proteins in the plasma which serve to activate various parts of the blood clotting process by being transformed from inactive to active form.

Enzyme—A substance that causes a chemical reaction, usually a protein. Enzymes are secreted by cells.

Hemorrhage—Abnormal bleeding from the blood vessels.

Heparin—An anticoagulant, or blood clot "dissolver."

Idiopathic—Refers to a disease of unknown cause, and sometime to a primary disease.

Metastatic—The term used to describe a secondary cancer, or one that has spread from one area of the body to another.

Serum reagents—Serum is fluid, or the fluid portion of the blood retained after removal of the blood cells and fibrin clot. Reagents are substances added to the serum to produce a chemical reaction.

Thrombosis—Formation of a clot in the blood that either blocks, or partially blocks a blood vessel. The thrombus may lead to infarction, or death of tissue, due to a blocked blood supply.

Thrombocytopenia

Thrombocytopenia may be acquired or congenital. It represents a defective or decreased production of platelets. Symptoms include sudden onset of small spots of hemorrhage on the skin, or bleeding into mucous membranes (such as nosebleeds). The disorder may also be evident as blood in vomit or stools, bleeding during surgery, or heavy menstrual flow in women. Some patients show none of these symptoms, but complain of **fatigue** and general weakness. There are several causes of thrombocytopenia, which is more commonly acquired as a result of another disorder. Common underlying disorders include leukemia, drug toxicity, or **aplastic ane-**

mia, all of which lead to decreased or defective production of platelets in the bone marrow. Other diseases may destroy platelets outside the marrow. These include severe infection, disseminated intravascular coagulation, and **cirrhosis** of the liver. The idiopathic form most commonly occurs in children, and is most likely the result of production of antibodies that cause destruction of platelets in the spleen and to a lesser extent the liver.

Von Willebrand's disease is caused by a defect in the Von Willebrand clotting factor, often accompanied by a deficiency of Factor VIII as well. It is a hereditary disorder that affects both males and females. In rare cases, it may be acquired. Symptoms include easy bruising, bleeding in small cuts that stops and starts, abnormal bleeding after surgery, and abnormally heavy menstrual bleeding. Nosebleeds and blood in the stool with a black, tarlike appearance are also signs of Von Willebrand's disease.

Hypoprothrombinemia

This disorder is a deficiency in prothrombin, or Factor II, a glycoprotein formed and stored in the liver. Prothrombin, under the right conditions, is converted to thrombin, which activates fibrin and begins the process of coagulation. Some patients may show no symptoms, and others will suffer severe hemorrhaging. Patients may experience easy bruising, profuse nosebleeds, postpartum hemorrhage, excessively prolonged or heavy menstrual bleeding, and postsurgical hemorrhage. Hypoprothrombinemia may also be acquired rather than inherited, and usually results from a **Vitamin K deficiency** caused by liver diseases, newborn hemorrhagic disease, or a number of other factors.

Other coagulation disorders

Factor XI deficiency, or hemophilia C, occurs more frequently among certain ethnic groups, with an incidence of about one in 10,000 among Ashkenazi Jews. Nearly 50% of patients with this disorder experience no symptoms, but others may notice blood in their urine, nosebleeds, or bruising. Although joint bleeding seldom occurs, some factor XI patients will experience bleeding long after an injury occurs. Some women will experience prolonged bleeding after **childbirth**. Patients with factor VII deficiency vary greatly in their bleeding severity. Women may experience heavy menstrual bleeding, bleeding from the gums or nose, bleeding deep within the skin, and episodes of bleeding into the stomach, intestine, and urinary tract. Factor VII patients may also suffer bleeding into joints.

Diagnosis

Several blood tests can be used to detect various coagulation disorders. There are hundreds of different tests a doctor can order to look for indications of specific diseases. In addition to blood tests, physicians will complete a medical history and **physical examination**. In the case of acquired coagulation disorders, information such as prior or current diseases and medications will be important in determining the cause of the blood disorder.

- Hemohilia A will be diagnosed with laboratory tests detecting presence of clotting factor VIII, factor IX, and others, as well as the presence or absence of clotting factor inhibitors.
- Christmas disease will be checked against normal bleeding and clotting time, as well as for abnormal serum reagents in factor IX deficiency. Other tests of **prothrombin time** and thromboplastic generation may also be ordered.
- There is no one test or group of tests that can always make (or exclude) a diagnosis of DIC. DIC can be diagnosed through a number of laboratory tests which measure concentration of platelets and fibrinogen in the blood with normal counts and prolonged prothrombin time. Other supportive data include diminished levels of factors V, fibrinogen, and VIII, decreased hemoglobin, and others. Since many of the test results also indicate other disorders, the physician may have to put together several results to reach a diagnosis of DIC. Serial tests may also be recommended, because a single examine at one moment in time may not reveal the process that is occurring.
- Tests for thrombocytopenia include coagulation tests revealing a decreased **platelet count**, prolonged bleeding time, and other measurements. If these tests indicate that platelet destruction is causing the disorder, the physician may order bone marrow examination.
- Von Willebrand's disease will be diagnosed with the assistance of laboratory tests which show prolonged bleeding time, absent or reduced levels of factor VIII, normal platelet count, and others.
- Hypothrombinemia is diagnosed with history information and the use of tests that measure vitamin K deficiency, deficiency of prothrombin, and clotting factors V, VII, IX, and X.
- Factor XI deficiency is diagnosed most often after injury-related bleeding. Blood tests can help pinpoint factor VII deficiency.

Treatment

In mild cases, treatment may involve the use of drugs that stimulate the release of deficient clotting factors. In severe cases, bleeding may only stop if the clotting factor that is missing is replaced through infusion of donated human blood in the form of fresh frozen plasma or cryoprecipitate.

- Hemophilia A in mild episodes may require infusion of a drug called desmopressin or DDAVP. Severe bleeding episodes will require transfusions of human blood clotting factors. Hemophiliacs are encouraged to receive physical therapy to help damaged joints and to **exercise** in non-contact sports such as swimming, bicycle riding, or walking.
- Christmas disease patients are treated similarly to hemophilia A patients. There are commercial products and human blood products available to provide coagulation. Cryoprecipitate was invented in 1965 to replace the need for whole plasma transfusions, which introduced more volume than needed. By the 1970s, people were able to infuse themselves with freeze-dried clotting factor. Superficial **wounds** can be cleaned and bandaged. Parents of hemophiliac children receiving immunizations should inform the **vaccination** provider in advance to decrease the possibility of bleeding problems. These children should probably not receive injections which go into the muscle.
- Treatment for disseminated intravascular coagulation patients is complicated by the large variety of underlying causes of the disorder. If at all possible, the physician will first treat this underlying disorder. If the patient is not already bleeding, this supportive treatment may eliminate the DIC. However, if bleeding is occurring, the patient may need blood, platelets, fresh frozen plasma, or other blood products. Heparin has been controversial in treating DIC, but it is often used as a last resort to stop hemorrhage. Heparin has not proven useful in treating patients with DIC resulting from heat **stroke**, exotic snakebites, trauma, mismatched transfusions, and acute problems resulting from obstetrical complications.
- Secondary acquired thrombocytopenia is best alleviated by treating the underlying cause or disorder. The specific treatment may depend on the underlying cause. Sometimes, cortocoosterids or immune globulin may be given to improve platelet production.
- Von Willebrand's disease is treated by several methods to reduce bleeding time and to replace factor VIII, which consequently will replace the Von Willebrand factor. This may include infusion of cryoprecipitate or fresh frozen plasma. Desmopressin may also help raise levels of the Von Willebrand factor.
- Hypoprothrombinemia may be treated with concentrates of prothrombin. Vitamin K may also be produced, and in bleeding episodes, the patient may receive fresh plasma products.
- Factor XI (hemophilia C) is most often treated with plasma, since there are no commercially available concentrates of factor XI in the United States. Factor VII patients may be treated with prothrombin complex concentrates. As of early 1998, factor VII concentrate was not licensed in the United States and could only be used with special permission.

Alternative treatment

This can be a very severe condition and should be managed by a practitioner of alternative medicine in conjunction with a medical doctor; this condition should not be self managed. For patients known to suffer from hemophilia A or B and other bleeding disorders, avoidance of activities that can cause severe injury should be practiced. Comprehensive care addresses the whole person by helping to deal with the psychosocial aspects of the disease.

Prognosis

The prognosis for patients with mild forms of coagulation disorders is normally good. Many people can lead a normal life and maintain a normal life expectancy. Without treatment of bleeding episodes, severe muscle and joint pain, and eventually, damage, can occur. Any incident that causes blood to collect in the head, neck, or digestive system can be very serious and requires immediate attention. DIC can be severe enough to cause clots to form and a stroke could occur. DIC is also serious enough to cause **gangrene** in the fingers, nose, or genitals. The prognosis depends on early intervention and treatment of the underlying condition. Hemorrhage from a coagulation disorder, particularly into the brain or digestive track, can prove fatal. In the past, patients who received regular transfusions of human blood products were subject to increased risk of **AIDS** and other diseases. However, efforts have been made since the early 1990s to ensure the safety of the blood supply.

Prevention

Prevention of coagulation disorders varies. Acquired disorders may only be prevented by preventing onset of the underlying disorder (such as cirrhosis). Hereditary disorders can be predicted with prenatal testing and **genetic counseling**. Prevention of severe bleeding episodes may be accomplished by refraining from activities that could cause injury, such as contact sports. Open communication with healthcare providers prior to procedures or tests that could cause bleeding may prevent a severe bleeding incident.

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National Hemophilia Foundation. 116 West 32nd St., 11th Floor, New York, NY 10001. 800-424-2634. <http://www.hemophilia.org/home.htm>.

Teresa Norris, RN

Coagulopathies *see* **Coagulation disorders**

Coal miner's disease *see* **Black lung disease**

Coal worker's pneumoconiosis *see* **Black lung disease**

Coarctation of the aorta

Definition

A defect that develops in the fetus in which there is a narrowing of the aortic arch, the main blood artery that delivers blood from the left ventricle of the heart to the rest of the body. Coarctation of the aorta is diagnosed in both newborns and adults. Approximately 10% of newborns with **congenital heart disease** have coarctation of the aorta.

Description

Blood leaves the heart by way of the left ventricle and is distributed to the body by arteries. The aortic arch is the first artery to carry blood as it leaves the heart. Other arteries to the head and arms branch off the aortic arch. A narrowing of the aorta at any spot produces resistance to the flow of blood. This causes high blood pressure before the narrowing and low pressure below the narrowing (downstream). Parts of the body supplied by arteries that branch off the aortic arch before the narrowing have high blood pressure, while most of the lower body doesn't receive enough blood supply. To compensate for this, the heart works harder, and the blood pressure rises.

Approximately half of all infants with coarctation of the aorta are diagnosed within the first two months of life. Frequently, there are other congenital cardiac complications present. Infants with **Turner syndrome** have a 45% rate of also having coarctation. There is evidence that some cases of coarctation may be inherited.

Causes and symptoms

In newborns with congenital heart disease, coarctation of the aorta develops while the baby is in the womb. Among the consequences of coarctation of the aorta is ventricular hypertrophy, an enlarging of the left ventricle in response to the increased back pressure of the blood and the demand for more blood by the body. Symptoms in infants include **shortness of breath** (dyspnea), difficulty in feeding, and poor weight gain. Older children usually don't have symptoms, but may display **fatigue**, shortness of breath, or a feeling of lameness in their legs.

Diagnosis

Infants usually have an abnormal "gallop" heart rhythm and may also have **heart murmurs**. Sometimes excessive arterial pulses can be seen in the carotid and suprasternal notch arteries, indicating increased pressure in these arteries, while the femoral pulse is weak or can't be detected. The systolic pressure is higher in the arms than in the legs. Enlargement of the heart can be seen in x rays. Similar symptoms are seen in older children and adults. A 10 mm Hg (mercury) pressure difference between the upper and lower extremities is diagnostic for coarctation of the aorta. For some patients, the systolic pressure difference is observed only during **exercise**. Infants frequently have an abnormal electrocardiogram (ECG) that indicates that the right or both ventricles are enlarged, while in older children the ECG may be normal or show that the left ventricle is enlarged. The coarctation may be detected in echocardiographic examination.

Treatment

Drugs can be used to treat the **hypertension** and **heart failure**. Surgery is recommended for infants with other, associated cardiac defects and for those infants not responding to drug therapy. Surgery is indicated for infants that don't require immediate surgery, but who develop severe hypertension during the first several months of life. Patients are advised to avoid vigorous exercise prior to surgical correction of the coarctation. Recoarctation can occur in some patients, even if they have had surgery.

Prognosis

Approximately half of all infants diagnosed with coarctation of the aorta have no other cardiac defects and will respond well to medical management. Most of these children will eventually outgrow the condition after several years of life. Although their hypertension may increase for several months early in life, it will eventually decrease as the circulatory system develops. Surgery is required for infants that have severe coarctation of the aorta or have associated cardiac defects. The average life span of children who have coarctation of the aorta is 34

KEY TERMS

Dyspnea—Difficulty in breathing. Usually associated with heart or lung diseases.

Electrocardiogram—A graph of the heart's beating produced by an instrument that detects the electrical signals made by the heart.

years of age. The most common complications for children who have not had surgery are hypertension, aortic rupture, intracranial bleeding, and congestive heart failure. Women who have an uncorrected coarctation of the aorta have a mortality rate of 10% during **pregnancy** and a 90% rate of complications.

Resources

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Cocaine

Definition

Cocaine is a highly addictive central nervous system stimulant extracted from the leaves of the coca plant, *Erythroxylon coca*.

Description

In its most common form, cocaine is a whitish crystalline powder that produces feelings of euphoria when ingested.

Now classified as a Schedule II drug, cocaine has legitimate medical uses as well as a long history of recreational abuse. Administered by a licensed physician, the drug can be used as a local anesthetic for certain eye and ear problems and in some kinds of surgery.

Forms of the drug

In powder form, cocaine is known by such street names as "coke," "blow," "C," "flake," "snow" and "toot." It is most commonly inhaled or "snorted." It may also be dissolved in water and injected.

Crack is a smokable form of cocaine that produces an immediate and more intense high. It comes in off-white chunks or chips called "rocks." Little crumbs of crack are sometimes called "kibbles & bits."

In addition to their stand-alone use, both cocaine and crack are often mixed with other substances. Cocaine may be mixed with methcathinone (a more recent drug of abuse, known as "cat," that is similar to methamphetamine) to create a "wildcat." A hollowed-out cigar filled with a mixture of crack and marijuana is known as a "woolah." And either cocaine or crack used in conjunction with heroin is called a "speedball." Cocaine used together with alcohol represents the most common fatal two-drug combination.

History

Cocaine is one of the oldest known psychoactive drugs. Coca leaves, the source of cocaine, were used by the Incas and other inhabitants of the Andean region of South America for thousands of years, both as a stimulant and to depress appetite and combat apoxia (**altitude sickness**).

Despite the long history of coca leaf use, it was not until the latter part of the nineteenth century that the active ingredient of the plant, cocaine hydrochloride, was first extracted from those leaves. The new drug soon became a common ingredient in patent medicines and other popular products (including the original formula for Coca-Cola). This widespread use quickly raised concerns about the drug's negative effects. In the early 1900s, several legislative steps were taken to address those concerns; the Harrison Act of 1914 banned the use of cocaine and other substances in non-prescription products. In the wake of those actions, cocaine use declined substantially.

The drug culture of the 1960s sparked renewed interest in cocaine. With the advent of crack in the 1980s, use of the drug had once again become a national problem. Cocaine use declined significantly during the early 1990s, but it remains a significant problem and is on the increase in certain geographic areas and among certain age groups.

Causes and symptoms

As with other forms of **addiction**, cocaine abuse is the result of a complex combination of internal and external factors. Genetic predisposition, family history, and immediate environment can all affect a person's probability of becoming addicted.

As many as three to four million people are estimated to be chronic cocaine users. The 1997 National Household Survey on Drug Abuse reported an estimated 600,000 current crack users, showing no significant change since the late 1980s.

How cocaine affects the brain

Extensive research has been conducted to determine how cocaine works on the brain and why it is so addictive. Cocaine has been found to affect an area of the brain known as the ventral tegmental area (VTA), which connects with the nucleus accumbens, a major pleasure center. Like other commonly abused addictive drugs, cocaine's effects are related to the action of the neurotransmitter dopamine, which carries information between neurons. Cocaine interferes with the normal functioning of neurons by blocking the re-uptake of dopamine, which builds up in the synapses and is believed to cause the pleasurable feelings reported by cocaine users.

Short-term effects of use

The short-term effects of cocaine can include:

- rapid heartbeat
- constricted blood vessels
- dilated pupils
- increased temperature
- increased energy
- reduced appetite
- increased sense of alertness
- euphoria
- **death** due to overdose

Long-term effects of use

The long-term effects of cocaine and crack use include:

- dependence, addiction
- irritability
- mood swings
- restlessness
- weight loss
- auditory hallucinations
- paranoia

Cocaine use and pregnancy

The rise in cocaine use as well as the appearance of crack cocaine in the late 1980s spurred fears about its effects on the developing fetus and, since then, several research reports have suggested that prenatal cocaine use could be associated to a wide range of fetal, newborn, and child development problems. According to the The Lindesmith Center-Drug Policy Foundation, many of these early reports had methodological flaws, and most researchers nowadays propose more cautious conclusions concerning prenatal cocaine effects. Much evidence would seem to point to the lack of quality prenatal care and the use of alcohol and tobacco as primary factors in poor fetal development among pregnant cocaine users. Research sponsored by the National Institute on Drug Abuse (NIDA) and the Albert Einstein Medical Center in Philadelphia corroborate the Lindensmith Center findings in reporting that the lack of quality prenatal care is associated with undesirable effects often attributed to cocaine exposure such as **prematurity**, low birth weight, and fetal or infant death. The Center for Disease Control and Prevention (CDC) however, reports that mothers who use cocaine early in **pregnancy** are five times as likely to have a baby with a malformation of the urinary tract as mothers who do not use the drug. Thus, cocaine use during pregnancy is assuredly most inadvisable, especially since it is also often associated with the use of alcohol known to cause long-term developmental problems. Supporting the cocaine-exposed expecting mother so as to discourage cocaine use remains an important task for all health caregivers.

Diagnosis

Diagnosing cocaine addiction can be difficult. Many of the signs of short-term cocaine use are not obvious. Since cocaine users often also use other drugs, it may not be easy to distinguish the effects of one drug from another.

Cocaine use has been documented in significant numbers of eighth graders as well as older teens. Over all age groups, more men than women use the drug. The highest rate of cocaine use is found among adults 18 to 25 years old.

Medical complications

Cocaine has been linked to several serious health problems, including:

- arrhythmia
- heart attacks
- chest pain
- respiratory failure
- strokes
- seizures

Other complications may vary depending on how the drug is administered. Prolonged snorting, for example, can irritate the nasal septum, producing nosebleeds, chronic runny nose, and other problems. Intravenous users face an increased risk of infectious diseases such as HIV/AIDS and hepatitis.

Testing

Drug testing can be useful in diagnosing and treating cocaine abuse. Urine testing can detect cocaine; besides providing an objective alternative to reliance on what a patient says, such tests can also be used as a follow-up to treatment to confirm that the patient has remained drug-free.

Treatment

The last two decades have seen a dramatic rise in the number of cocaine addicts seeking treatment. But like all forms of drug abuse, cocaine abuse/addiction is a multifaceted phenomenon involving environmental, social, and familial as well as physiological factors. This greatly complicates the challenge of effectively treating cocaine addiction.

Pharmacological treatments

To date, no medications have been approved specifically for treating cocaine addiction. But several were under development at this writing. Selegeline, delivered either via a time-release pill or a transdermal patch, shows promise as a possible anti-cocaine medication. Clinical studies have shown the drug disulfiram (also used to treat alcoholics) to be effective in treating cocaine abusers. In addition, antidepressant medications are sometimes used to control the mood swings associated with the early stages of cocaine withdrawal.

Behavioral approaches

A wide range of behavioral interventions have been successfully used to treat cocaine addiction. The approach used must be tailored to the specific needs of each individual patient, however.

Contingency management rewards drug abstinence (confirmed by urine testing) with points or vouchers which patients can exchange for such things as an evening out or membership in a gym. **Cognitive-behavioral therapy** helps users learn to recognize and avoid situations most likely to lead to cocaine use and to develop healthier ways to cope with stressful situations. Residential programs/therapeutic communities may also be helpful, particularly in more severe cases. Patients typically spend six to 12 months in such programs, which may also include vocational training and other features.

KEY TERMS

Apoxia—Apoxia refers to altitude sickness.

Arrhythmia—Irregular heartbeat.

Central nervous system—Part of the nervous system consisting of the brain, cranial nerves and spinal cord. The brain is the center of higher processes, such as thought and emotion and is responsible for the coordination and control of bodily activities and the interpretation of information from the senses. The cranial nerves and spinal cord link the brain to the peripheral nervous system, that is the nerves present in the rest of body.

Nasal septum—The membrane that separates the nostrils.

Neurotransmitter—A chemical that carries nerve impulses across a synapse.

Synapse—The gap between two nerve cells.

Alternative treatment

Various alternative or complementary approaches have been used in treating cocaine addiction, often in combination with more conventional therapies. In Japan, the herb acorus has been traditionally used both to assist early-stage cocaine withdrawal and in later recovery stages. Other herbs sometimes used to treat drug addictions of various kinds include kola nut, guarana seed and yohimbe (to boost short-term energy), and valerian root, hops leaf, scullcap leaf, and chamomile (to calm the patient). The amino acids phenylalanine and tyrosine have been used to reduce cocaine addicts' craving for the drug, and vitamin therapy may be used to help strengthen the patient. Gentle massage has been used to help infants born with congenital cocaine addiction. Other techniques, such as **acupuncture**, EEG **biofeedback**, and visualization, may also be useful in treating addiction.

Prognosis

Because addiction involves so many different factors, prospects for individual addicts vary widely. However, research has consistently shown that treatment can significantly reduce both drug abuse and subsequent criminal activity. The comprehensive Services Research Outcomes Study (1998) found a 45% drop in cocaine use five years after treatment, compared to use during the five years before treatment. The study also found that females generally respond better to treatment than males, and older patients tend to reduce their drug use more than younger patients.

Some research also supports the idea that 12-step programs used in conjunction with other approaches can significantly enhance the prospects for a positive outcome. One study of people in outpatient drug-treatment programs found that participation in a 12-step program nearly doubled their chances of remaining drug-free.

Prevention

Despite significant variation over time, cocaine addiction has proven to be a persistent public health problem. Interdiction and source control are expensive and have failed to eliminate the problem, and some law enforcement officials are now recommending more emphasis on demand reduction through education and other measures to address the causes of cocaine addiction.

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ORGANIZATIONS

Cocaine Anonymous. 6125 Washington Blvd. Suite 202, Culver City, CA 90232. (800) 347-8998.

Nar-Anon Family Group Headquarters, Inc. P.O. Box 2562, Palos Verdes Peninsula, CA 90274. (310) 547-5800.

Peter Gregutt

Coccidioidomycosis

Definition

Coccidioidomycosis is an infection caused by inhaling the microscopic spores of the fungus *Coccidioides immitis*. Spores are the tiny, thick-walled structures that fungi use to reproduce. Coccidioidomycosis exists in three forms. The acute form produces flu-like symptoms. The chronic form can develop as many as 20 years after initial infection and, in the lungs, can produce inflamed, injured areas that can fill with pus (abscesses). Disseminated coccidioidomycosis describes the type of coccidioidomycosis that spreads throughout the body affecting many organ systems and is often fatal.

Description

Coccidioidomycosis is an airborne infection. The fungus that causes the disease is found in the dry desert soil of the southwestern United States, Mexico, and Central and South America. Coccidioidomycosis is sometimes called San Joaquin **fever**, valley fever, or desert fever because of its prevalence in the farming valleys of California. Although commonly acquired, overt coccidioidomycosis is a rare disease. Chronic infections occur in only one out of every 100,000 people.

Although anyone can get coccidioidomycosis, farm laborers, construction workers, and archaeologists who work where it is dusty are at greater risk to become infected. People of any age can get coccidioidomycosis, but the disease most commonly occurs in the 25–55 age group. In its acute form, coccidioidomycosis infects men and women equally.

Chronic and disseminated forms of coccidioidomycosis occur more frequently in men and pregnant women. Although it is not clear why, people of color are 10-20 times more likely to develop the disseminated form of the disease than caucasians. People who have a weakened immune system (immunocompromised), either from diseases such as **AIDS** or leukemia, or as the result of medications that suppressed the immune system (**corticosteroids**, **chemotherapy**), are more likely to develop disseminated coccidioidomycosis.

Causes and symptoms

When the spores of *C. immitis* are inhaled, they can become lodged in the lungs, divide, and cause localized inflammation. This is known as acute or primary coccidioidomycosis. The disease is not spread from one person to another. Approximately 60% of people who are infected exhibit no symptoms (asymptomatic). In the other 40%, symptoms appear 10–30 days after exposure. These symptoms include a fever which can reach 104°F (39.5°C), dry **cough**, chest pains, joint and muscle aches, **headache**, and weight loss. About two weeks after the start of the fever, some people develop a painful red rash or lumps on the lower legs. Symptoms usually disappear without treatment in about one month. People who have been infected gain partial immunity to reinfection.

The chronic form of coccidioidomycosis normally occurs after a long latent period of 20 or more years during which the patient experiences no symptoms of the disease. In the chronic phase, coccidioidomycosis causes

lung abscesses that rupture, spilling pus and fluid into the lungs, and causing serious damage to the lungs. The patient experiences difficulty breathing and has a fever, chest **pain**, and other signs of **pneumonia**. Medical treatment is essential for recovery.

In its disseminated form, coccidioidomycosis spreads to other parts of the body including the liver, bones, skin, brain, heart, and lining around the heart (pericardium). Symptoms include fever, joint pain, loss of appetite, weight loss, night sweats, **skin lesions**, and difficulty breathing. Also, in 30–50% of patients with disseminated coccidioidomycosis, the tissue coverings of the brain and spinal cord become inflamed (**meningitis**).

Diagnosis

Many cases of coccidioidomycosis go undiagnosed because the symptoms resemble those of common viral diseases. However, a skin test similar to that for **tuberculosis** will determine whether a person has been infected. The test is simple and accurate, but it does not indicate whether the disease was limited to its acute form or if it has progressed to its chronic form.

Diagnosis of chronic or disseminated coccidioidomycosis is made by culturing a sample of sputum or other body fluids in the laboratory to isolate the fungus. A blood serum test is used to detect the presence of an antibody produced in response to *C. immitis* infection. Chest x rays are often used to assess lung damage, but alone cannot lead to a definitive diagnosis of coccidioidomycosis because other diseases can produce similar results on the x ray.

Treatment

In most cases of acute coccidioidomycosis, the body's own immune system is adequate to bring about recovery without medical intervention. Fever and pain can be treated with non-prescription drugs.

Chronic and disseminated coccidioidomycosis, however, are serious diseases that require treatment with prescription drugs. Patients with intact immune systems who develop chronic coccidiodomycosis are treated with the drug ketoconazole (Nizoral) or amphotericin B (Fungizone). Patients with suppressed immune systems are treated with amphotericin B (Fungizone). Amphotericin B is a powerful fungistatic drug with potentially toxic side effects. As a result, hospitalization is required in order to monitor patients. The patient may also receive other drugs to minimize the side effects of the amphotericin B.

Patients with AIDS must continue to take itraconazole (Sporonox) or fluconazole (Diflucan) orally or receive weekly intravenous doses of amphotericin B for the rest of their lives in order to prevent a relapse. Because of the high cost of fluconazole, Pfizer, the manufacturer of the drug, has established a financial assistance plan to make the drug available at lower cost to those who meet certain criteria. Patients needing this drug should ask their doctors about this program.

Alternative treatment

Alternative treatment for fungal infections focuses on creating an internal environment where the fungus cannot survive. This is accomplished by eating a diet low in dairy products, sugars, including honey and fruit juice, and foods like beer that contain yeast. This is complemented by a diet consisting, in large part, of uncooked and unprocessed foods. Supplements of **vitamins** C, E, A-plus, and B complex may also be useful. *Lactobacillus acidophilus* and *Bifidobacterium* will replenish the good bacteria in the intestines. Antifungal herbs, like garlic (*Allium sativum*), can be consumed in relatively large does and for an extended period of time in order to increase effectiveness.

KEY TERMS

Abscess—An area of inflamed and injured body tissue that fills with pus.

Acidophilus—The bacteria *Lactobacillus acidophilus* that usually found in yogurt.

Antibody—A specific protein produced by the immune system in response to a specific foreign protein or particle called an antigen.

Antigen—A foreign protein to which the body reacts by making antibodies.

Asymptomatic—Persons who carry a disease but who do not exhibit symptoms of the disease are said to be asymptomatic.

Bifidobacteria—A group of bacteria normally present in the intestine. Commercial supplements containing these bacteria are available.

Corticosteroids—A group of hormones produced naturally by the adrenal gland or manufactured synthetically. They are often used to treat inflammation. Examples include cortisone and prednisone.

Immunocompromised—A state in which the immune system is suppressed or not functioning properly.

Meningitis—An inflammation of the membranes surrounding the brain or spinal cord.

Pericardium—The tissue sac around the heart.

Prognosis

Most people who are infected with coccidiodomycosis only suffer from the mild, acute form of the disease and recover without further complications. Patients who suffer from chronic coccidiodomycosis and who have no underlying lung or immune system diseases also stand a good change of recovery, although they must be alert to a relapse.

The picture for patients with the disseminated form of the disease, many of whom have AIDS, is less positive. Untreated disseminated coccidiodomycosis is almost always fatal within a short time. With treatment, chance of survival increases, but the **death** rate remains high when meningitis or diffuse lung (pulmonary) disease is present. AIDS patients must constantly guard against relapse.

Prevention

Because the fungus that causes coccidioidomycosis is airborne and microscopic, the only method of prevention is to avoid visiting areas where it is found in the soil. Unfortunately, for many people this is impractical. Maintaining general good health and avoiding HIV infection will limit coccidioidomycosis to the acute and relatively mild form in most people.

Resources

ORGANIZATIONS

American Lung Association. 1740 Broadway, New York, NY 10019. (800) 586-4872. <http://www.lungusa.org>.

Canadian HIV/AIDS Clearinghouse. 1565 Carling Avenue, Suite 400, Ottawa, ON K1Z 8R1. (877) 999-7740. <http://www.clearinghouse.cpha.ca/clearinghouse_e.htm>.

Centers for Disease Control and Prevention. 1600 Clifton Rd., NE, Atlanta, GA 30333. (800) 311-3435, (404) 639-3311. <http://www.cdc.gov>.

National Aids Hotline. (800) 342-2437.

Project Inform. 205 13th Street, #2001, San Francisco, CA 94103. (800) 822-7422. <http://www.projinf.org>.

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Tish Davidson

Coccyx injuries

Definition

The coccyx—or tailbone—is the last bone of the vertebral column, and usually consists of three to five fused vertebrae that connect with the sacrum, a part of the pelvis.

Description

The coccyx consists of fused vertebrae, which are not flexible like the other vertebrae of the vertebral column which are all interspaced by intervertebral disks and joined together by elastic ligaments. Since the spinal cord ends just before the coccyx begins, coccygeal vertebrae also lack a central foramen (hole). In the coccyx, the vertebrae generally fuse together in early adulthood and may also fuse with the sacrum, the bone located between the 5th lumbar vertebra and the coccyx, as a person ages. In males, the coccyx curves downward, and in females, it is straighter to allow a baby to pass through the birth canal without impediment.

Pain in or around the coccyx is called coccydynia or coccygodynia. Coccydynia presents a range of symptoms associated to a variety of underlying causes and conditions.

Causes and symptoms

Causes

Coccydynia can be caused by a number of factors. Usually, patients report pain after a fall onto their buttocks, as occurs when going down stairs or while skating. Others have pain during **pregnancy** or after **childbirth**. Some experience repetitive strain from rowing or cycling, and some cite anal intercourse as the cause of pain. In many cases, pain derives from a malformation of the coccyx itself. Sometimes bony spurs appear on the coccyx, but only seem to be painful in thin patients who do not have the padding to protect the region from the spur.

Other causes of coccydynia include **cancer** or damage to the sacrum that generates referred pain, meaning pain that appears in one region but originates from another. Muscle strain or tension, pinched nerves or damaged nerves, or dislocation of the coccyx due to gross **obesity** are other causes.

Symptoms

The most common symptom of coccydynia, irrespective of the cause of the condition, is pain when sitting, or when rising from a sitting position. If the condition lasts long enough, the patient may even experience pain when standing or lying down. Sometimes, numbness occurs in the lower part of the spine. Some patients will experience pain during bowel movements, sexual intercourse, or menstruation.

Secondary symptoms include back pain from sitting in odd positions in order to relieve pain, and painful feet from standing too much, because patients avoid sitting.

KEY TERMS

Coccyx—The last bone of the spinal column, consisting of three to five fused vertebrae that connect with the sacrum, a part of the pelvis.

Coccydynia—Also called coccygodynia. Pain in or around the coccyx.

Foramen—A small opening, perforation, or orifice.

Magnetic resonance imaging (MRI)—An imaging technique that produces pictures of the inside of the body.

Sacrum—The triangle-shaped bone located between the fifth lumbar vertebra and the coccyx that consists of five vertebrae fused together. The sacrum joins on each side with the bones of the pelvis.

Spinal cord—Elongated nerve bundles that lie in the vertebral canal and from which the spinal nerves emerge.

Vertebrae—Bones in the cervical, thoracic, and lumbar regions of the body that make up the vertebral column. Vertebrae have a central foramen (hole), and their superposition makes up the vertebral canal that encloses the spinal cord.

Vertebral column—The vertebral column, also called the spinal column or spine, consists of a series of vertebrae connected by ligaments. It provides a supporting axis for the body and protects the spinal cord. The vertebral column consists of seven cervical vertebrae in the neck, followed by 12 thoracic vertebrae that connect to the ribs, five lumbar vertebrae in the lower back, the sacrum, and the coccyx.

Sometimes the entire buttocks experience pain. Rarely, exhaustion, depression, and lack of sleep may occur.

Diagnosis

Diagnosis of fracture is usually made by inserting a gloved finger in the rectum and pressing on the coccyx. X rays and **magnetic resonance imaging** (MRI) are also often used. Since coccyx pain may be the result of other factors like cancer, these must be ruled out through a variety of tests before treatment can begin.

Treatment

Treatment exists to either control the pain or eliminate the cause. Pain control may be dangerous if an underlying condition exists of which the pain is a warning sign. Nerve blocks and a variety of drugs are other options to control pain.

Elimination of the root cause of the pain is ideal. This is done through careful diagnosis and the application of manual treatments, corticosteroid injections into the coccyx vertebrae, or surgery. Injections into the fourth and fifth sacral nerves and coccygeal nerves often bring relief, but are considered more as a pain control measure than as curative treatment. Manual treatments have not been found to be effective. Surgery is a radical procedure whose indications are inconsistent and dependent on the subjectivity of the physician.

Prognosis

With current treatment, prognosis is good and patients usually are able to live pain free.

Prevention

There probably is no real prevention, expect weight control. Some women may choose to give birth through ceasarian section instead of vaginally after an episode of coccyx pain from a previous delivery.

Resources

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Janie Franz

Cochlear implants

Definition

A cochlear implant is a surgical treatment for **hearing loss** that works like an artificial human cochlea in the inner ear, helping to send sound from the ear to the brain. It is different from a hearing aid, which simply amplifies sound.

Purpose

A cochlear implant bypasses damaged hair cells and helps establish some degree of hearing by stimulating the hearing (auditory) nerve directly.

A close-up view of a cochlear implant. *(Photograph by L. Steinmark, Custom Medical Stock Photo. Reproduced by permission.)*

Precautions

Because the implants are controversial, very expensive, and have uncertain results, the U.S. Food and Drug Administration (FDA) has limited the implants to people:

- who get no significant benefit from **hearing aids**
- who are at least 2 years old (the age at which specialists can verify severity of deafness)
- with severe to profound hearing loss.

Description

Hearing loss is caused by a number of different problems that occur either in the hearing nerve or parts of the middle or inner ear. The most common type of deafness is caused by damaged hair cells in the cochlea, the hearing part of the inner ear. Normally, hair cells stimulate the hearing nerve, which transmits sound signals to the brain. When hair cells stop functioning, the hearing nerve remains unstimulated, and the person can't hear. Hair cells can be destroyed by many things, including infection, trauma, loud noise, **aging**, or **birth defects**.

All cochlear implants consist of a microphone worn behind the ear that picks up sound and sends it along a wire to a speech processor, which is worn in a small shoulder pouch, pocket, or belt. The processor boosts the sound, filters out background noise, and turns sound into digital signals before sending it to a transmitter worn behind the ear. A magnet holds the transmitter in place through its attraction to the receiver-stimulator, a part of the device that is surgically attached beneath the skin in the skull. The receiver picks up digital signs forwarded by the transmitter, and converts them into electrical impulses. These electrical impulses flow through electrodes contained in a narrow, flexible tube that has been threaded into the cochlea.

As many as 24 electrodes (depending on the type of implant) carry the impulses that stimulate the hearing nerve. The brain then interprets the signals as specific sounds.

Despite the benefits that the implant appears to offer, some hearing specialists and members of the deaf community still believe that the benefits may not outweigh the risks and limitations of the device. Because the device must be surgically implanted, it carries some surgical risk. Also, manufacturers can't promise how well a person will hear with an implant. Moreover, after getting an implant, some people say they feel alienated from the Deaf community, while at the same time not feeling fully a part of the hearing world.

The sounds heard through an implant are different from the normal hearing sounds, and have been described as artificial or "robotlike." This is because the implant's handful of electrodes cannot hope to match the complexity of a person's 15,000 hair cells.

Surgical procedure

During the procedure, the surgeon makes an incision behind the ear and opens the mastoid bone (the ridge on the skull behind the ear) leading into the middle ear. The surgeon then places the receiver-stimulator in the bone, and gently threads the electrodes into the cochlea. This operation takes between one and one-half to five hours.

Preparation

Before a person gets an implant, specialists at an implant clinic conduct a careful evaluation, including extensive hearing tests to determine how well the candidate can hear.

Unfortunately, it is not possible to predict who will benefit from an implant. In general, the later in life a person becomes deaf, and the shorter the duration of deafness, the better the person is likely to understand speech with an implant. Likewise,someone with a healthy hearing nerve will do better than someone with a damaged nerve.

First, candidates undergo a trial with a powerful hearing aid. If the aid can't improve hearing enough, a physician then performs a physical exam and orders a scan of the inner ear (some patients with a scarred cochlea aren't good candidates). A doctor may also order a psychological exam to better understand the person's expectations. Patients need to be highly motivated, and have a realistic understanding of what an implant can and cannot do.

Aftercare

The patient remains in the hospital for a day or two after the surgery. After a month, the surgical **wounds** will

have healed and the patient returns to the implant clinic to be fitted with the external parts of the device (the speech processor, microphone, and transmitter). A clinician tunes the speech processor and sets levels of stimulation for each electrode, from soft to loud.

The patient is then trained in how to interpret the sounds heard through the device. The length of the training varies from days to years, depending on how well the person can interpret the sounds heard through the device.

Risks

As with all operations, there are a few risks of surgery. These include:

- dizziness
- facial **paralysis** (rarely)
- infection at the incision site

Scientists aren't sure about the long-term effects of electrical stimulation on the nervous system. It is also possible to damage the implant's internal components by a blow to the head, which will render the device unworkable.

Normal results

Most profoundly, deaf patients who receive an implant are able to discern medium and loud sounds, including speech, at comfortable listening levels. Many use sound clues from the implant, together with speech reading and other facial cues. Almost all adults improve their communication skills when combining the implant with speech reading (lip reading), and some can understand spoken words without speech reading. More than half of adults who lost hearing after they learned to speak can understand some speech without speech reading. About 30% can understand spoken sounds well enough to use the phone.

Children who were born deaf or who lost their hearing before they could speak have the most difficulty in learning to use the implant. Research suggests, however, that most of these children are able to learn spoken language and understand speech using the implant.

KEY TERMS

Cochlea—The hearing part of the inner ear. This snail-shaped structure contains fluid and thousands of microscopic hair cells tuned to various frequencies.

Hair cells—Sensory receptors in the inner ear that transform sound vibrations into messages that travel to the brain.

Inner ear—The interior section of the ear, where sound vibrations and information about balance are translated into nerve impulses.

Middle ear—The small cavity between the eardrum and the oval window that houses the three tiny bones of hearing.

Resources

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Signor, Roger. "Sound Advice: Cochlear Implants Improve Learning for Deaf Children." *St. Louis Post-Dispatch*, 9 June 1995: 01C.

ORGANIZATIONS

Alexander Graham Bell Association for the Deaf. 3417 Volta Place NW, Washington, DC 20007. (202) 337-5220. <http://www.agbell.org>.

American Speech-Language-Hearing Association. 10801 Rockville Pike, Rockville, MD 20852. (800) 638-8255. <http://www.asha.org>.

Cochlear Implant Club International. 5335 Wisconsin Ave. NW, Suite 440, Washington, D.C. 20015-2052. (202) 895-2781. <http://www.cici.org>.

Hearing Loss Link. 2600 W. Peterson Ave., Ste. 202, Chicago, IL 60659. (312) 743-1032, (312) 743-1007 (TDD).

National Association for the Deaf. 814 Thayer Ave., Silver Spring, MD 20910. (301) 587-1788, (301) 587-1789 (TDD). <http://www.nad.org>.

Carol A. Turkington

Cognitive-behavioral therapy

Definition

Cognitive-behavioral therapy is an action-oriented form of psychosocial therapy that assumes that maladap-

tive, or faulty, thinking patterns cause maladaptive behavior and "negative" emotions. (Maladaptive behavior is behavior that is counter-productive or interferes with everyday living.) The treatment focuses on changing an individual's thoughts (cognitive patterns) in order to change his or her behavior and emotional state.

Purpose

Theoretically, cognitive-behavioral therapy can be employed in any situation in which there is a pattern of unwanted behavior accompanied by distress and impairment. It is a recommended treatment option for a number of mental disorders, including affective (mood) disorders, **personality disorders**, social phobia, **obsessive-compulsive disorder** (OCD), eating disorders, substance abuse, **anxiety** or **panic disorder**, **agoraphobia**, **post-traumatic stress disorder** (PTSD), and **attention-deficit/hyperactivity disorder** (ADHD). It is also frequently used as a tool to deal with chronic **pain** for patients with illnesses such as **rheumatoid arthritis**, back problems, and **cancer**. Patients with **sleep disorders** may also find cognitive-behavioral therapy a useful treatment for **insomnia**.

Precautions

Cognitive-behavioral therapy may not be suitable for some patients. Those who don't have a specific behavioral issue they wish to address and whose goals for therapy are to gain insight into the past may be better served by psychodynamic therapy. Patients must also be willing to take a very active role in the treatment process.

Cognitive-behavioral intervention may be inappropriate for some severely psychotic patients and for cognitively impaired patients (for example, patients with organic brain disease or a traumatic brain injury), depending on their level of functioning.

Description

Cognitive-behavioral therapy combines the individual goals of cognitive therapy and behavioral therapy.

Pioneered by psychologists Aaron Beck and Albert Ellis in the 1960s, cognitive therapy assumes that maladaptive behaviors and disturbed mood or emotions are the result of inappropriate or irrational thinking patterns, called *automatic thoughts*. Instead of reacting to the reality of a situation, an individual reacts to his or her own distorted viewpoint of the situation. For example, a person may conclude that he is "worthless" simply because he failed an exam or didn't get a date. Cognitive therapists attempt to make their patients aware of these distorted thinking patterns, or cognitive distortions, and change them (a process termed cognitive restructuring).

Behavioral therapy, or behavior modification, trains individuals to replace undesirable behaviors with healthier behavioral patterns. Unlike psychodynamic therapies, it does not focus on uncovering or understanding the unconscious motivations that may be behind the maladaptive behavior. In other words, strictly behavioral therapists don't try to find out why their patients behave the way they do, they just teach them to change the behavior.

Cognitive-behavioral therapy integrates the cognitive restructuring approach of cognitive therapy with the behavioral modification techniques of behavioral therapy. The therapist works with the patient to identify both the thoughts and the behaviors that are causing distress, and to change those thoughts in order to readjust the behavior. In some cases, the patient may have certain fundamental core beliefs, called schemas, which are flawed and require modification. For example, a patient suffering from depression may be avoiding social contact with others, and suffering considerable emotional distress because of his **isolation**. When questioned why, the patient reveals to his therapist that he is afraid of rejection, of what others may do or say to him. Upon further exploration with his therapist, they discover that his real fear is not rejection, but the belief that he is hopelessly uninteresting and unlovable. His therapist then tests the reality of that assertion by having the patient name friends and family who love him and enjoy his company. By showing the patient that others value him, the therapist both exposes the irrationality of the patient's belief and provides him with a new model of thought to change his old behavior pattern. In this case, the person learns to think, "I am an interesting and lovable person; therefore I should not have difficulty making new friends in social situations." If enough "irrational cognitions" are changed, this patient may experience considerable relief from his depression.

A number of different techniques may be employed in cognitive-behavioral therapy to help patients uncover and examine their thoughts and change their behaviors. They include:

- Behavioral homework assignments. Cognitive-behavioral therapists frequently request that their patients complete homework assignments between therapy sessions. These may consist of real-life "behavioral experiments" where patients are encouraged to try out new responses to situations discussed in therapy sessions.
- Cognitive rehearsal. The patient imagines a difficult situation and the therapist guides him through the step-by-step process of facing and successfully dealing with it. The patient then works on practicing, or rehearsing,

these steps mentally. Ideally, when the situation arises in real life, the patient will draw on the rehearsed behavior to address it.

- Journal. Patients are asked to keep a detailed diary recounting their thoughts, feelings, and actions when specific situations arise. The journal helps to make the patient aware of his or her maladaptive thoughts and to show their consequences on behavior. In later stages of therapy, it may serve to demonstrate and reinforce positive behaviors.
- Modeling. The therapist and patient engage in role-playing exercises in which the therapist acts out appropriate behaviors or responses to situations.
- Conditioning. The therapist uses reinforcement to encourage a particular behavior. For example, a child with ADHD gets a gold star every time he stays focused on tasks and accomplishes certain daily chores. The gold star reinforces and increases the desired behavior by identifying it with something positive. Reinforcement can also be used to extinguish unwanted behaviors by imposing negative consequences.
- Systematic desensitization. Patients imagine a situation they fear, while the therapist employs techniques to help the patient relax, helping the person cope with their fear reaction and eventually eliminate the anxiety altogether. For example, a patient in treatment for agoraphobia, or fear of open or public places, will relax and then picture herself on the sidewalk outside of her house. In her next session, she may relax herself and then imagine a visit to a crowded shopping mall. The imagery of the anxiety-producing situations gets progressively more intense until, eventually, the therapist and patient approach the anxiety-causing situation in real-life (a "graded exposure"), perhaps by visiting a mall. Exposure may be increased to the point of "flooding," providing maximum exposure to the real situation. By repeatedly pairing a desired response (relaxation) with a fear-producing situation (open, public spaces), the patient gradually becomes desensitized to the old response of fear and learns to react with feelings of relaxation.
- Validity testing. Patients are asked to test the validity of the automatic thoughts and schemas they encounter. The therapist may ask the patient to defend or produce evidence that a schema is true. If the patient is unable to meet the challenge, the faulty nature of the schema is exposed.

Initial treatment sessions are typically spent explaining the basic tenets of cognitive-behavioral therapy to the patient and establishing a positive working relationship between therapist and patient. Cognitive-behavioral therapy is a collaborative, action-oriented therapy effort. As such, it empowers the patient by giving him an active role in the therapy process and discourages any overdependence on the therapist that may occur in other therapeutic relationships. Therapy is typically administered in an outpatient setting in either an individual or group session. Therapists include psychologists (Ph.D., Psy.D., Ed.D. or M.A. degree), clinical social workers (M.S.W., D.S.W., or L.S.W. degree), counselors (M.A. or M.S. degree), or psychiatrists (M.D. with specialization in psychiatry) and should be trained in cognitive-behavioral techniques, although some brief cognitive-behavioral interventions may be suggested by a primary physician/caregiver. Treatment is relatively short in comparison to some other forms of psychotherapy, usually lasting no longer than 16 weeks. Many insurance plans provide reimbursement for cognitive-behavioral therapy services. Because coverage is dependent on the disorder or illness the therapy is treating, patients should check with their individual plans.

KEY TERMS

Automatic thoughts—Thoughts that automatically come to mind when a particular situation occurs. Cognitive-behavioral therapy seeks to challenge automatic thoughts.

Cognitive restructuring—The process of replacing maladaptive thought patterns with constructive thoughts and beliefs.

Maladaptive—Unsuitable or counterproductive; for example, maladaptive behavior is behavior that is inappropriate to a given situation.

Psychodynamic therapy—A therapeutic approach that assumes dysfunctional or unwanted behavior is caused by unconscious, internal conflicts and focuses on gaining insight into these motivations.

Relaxation technique—A technique used to relieve stress. Exercise, biofeedback, hypnosis, and meditation are all effective relaxation tools. Relaxation techniques are used in cognitive-behavioral therapy to teach patients new ways of coping with stressful situations.

Schemas—Fundamental core beliefs or assumptions that are part of the perceptual filter people use to view the world. Cognitive-behavioral therapy seeks to change maladaptive schemas.

Rational-emotive behavior therapy

Rational-emotive behavior therapy (REBT) is a popular variation of cognitive-behavioral therapy developed

in 1955 by psychologist Albert Ellis. REBT is based on the belief that a person's past experiences shape their belief system and thinking patterns. People form illogical, irrational thinking patterns that become the cause of both their negative emotions and of further irrational ideas. REBT focuses on helping patients discover these irrational beliefs that guide their behavior and replace them with rational beliefs and thoughts in order to relieve their emotional distress.

There are 10 basic irrational assumptions that trigger maladaptive emotions and behaviors:

- It is a necessity for an adult to be loved and approved of by almost everyone for virtually everything.
- A person must be thoroughly competent, adequate, and successful in all respects.
- Certain people are bad, wicked, or villainous and should be punished for their sins.
- It is catastrophic when things are not going the way one would like.
- Human unhappiness is externally caused. People have little or no ability to control their sorrows or to rid themselves of negative feelings.
- It is right to be terribly preoccupied with and upset about something that may be dangerous or fearsome.
- It is easier to avoid facing many of life's difficulties and responsibilities than it is to undertake more rewarding forms of self-discipline.
- The past is all-important. Because something once strongly affected someone's life, it should continue to do so indefinitely.
- People and things should be different from the way they are. It is catastrophic if perfect solutions to the grim realities of life are not immediately found.
- Maximal human happiness can be achieved by inertia and inaction or by passively and without commitment.

Meichenbaum's self-instructional approach

Psychologist Donald Meichenbaum pioneered the self-instructional, or "self-talk," approach to cognitive-behavioral therapy in the 1970s. This approach focuses on changing what people say to themselves, both internally and out loud. It is based on the belief that an individual's actions follow directly from this self-talk. This type of therapy emphasizes teaching patients coping skills that they can use in a variety of situations to help themselves. The technique used to accomplish this is self-instructional inner dialogue, a method of talking through a problem or situation as it occurs.

Preparation

Patients may seek therapy independently, or be referred for treatment by a primary physician, psychologist, or psychiatrist. Because the patient and therapist work closely together to achieve specific therapeutic objectives, it is important that their working relationship is comfortable and their goals are compatible. Prior to beginning treatment, the patient and therapist should meet for a consultation session, or mutual interview. The consultation gives the therapist the opportunity to make an initial assessment of the patient and recommend a course of treatment and goals for therapy. It also gives the patient an opportunity to find out important details about the therapist's approach to treatment, professional credentials, and any other issues of interest.

In some managed-care clinical settings, an intake interview or evaluation is required before a patient begins therapy. The intake interview is used to evaluate the patient and assign him or her to a therapist. It may be conducted by a psychiatric nurse, counselor, or social worker.

Normal results

Many patients who undergo cognitive-behavioral therapy successfully learn how to replace their maladaptive thoughts and behaviors with positive ones that facilitate individual growth and happiness. Cognitive-behavioral therapy may be used in conjunction with pharmaceutical and other treatment interventions, so overall success rates are difficult to gauge. However, success rates of 65% or more have been reported with cognitive-behavioral therapy alone as a treatment for panic attacks and agoraphobia. Relapse has been reported in some patient populations, perhaps due to the brief nature of the therapy, but follow-up sessions can put patients back on track.

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ORGANIZATIONS

Albert Ellis Institute. 45 East 65th St., New York, NY 10021. (800) 323-4738. <http://www.rebt.org>.

Beck Institute. GSB Building, City Line and Belmont Avenues, Suite 700, Bala Cynwyd, PA 19004-1610. (610) 664-3020. <http://www.beckinstitute.org>.
The National Association of Cognitive-Behavioral Therapists. P.O. Box 2195, Weirton, WV 26062. (800) 853-1135. <http://www.nacbt.org>.

Paula Anne Ford-Martin

Colchicine *see* **Gout drugs**

COLD *see* **Chronic obstructive lung disease**

Cold agglutinins test

Definition

The cold agglutinins test is performed to detect the presence of antibodies in blood that are sensitive to temperature changes. Antibodies are proteins produced by the immune system in response to specific disease agents; autoantibodies are antibodies that the body produces against one of its own substances. Cold agglutinins are autoantibodies that cause red blood cells to clump, but only when the blood is cooled below the normal body temperature of 98.6°F (37°C). The clumping is most pronounced at temperatures below 78°F (25.6°C).

Purpose

The cold agglutinins test is used to confirm the diagnosis of certain diseases that stimulate the body to produce cold agglutinins. The disease most commonly diagnosed by this test is mycoplasmal **pneumonia**, but mononucleosis, **mumps**, **measles**, **scarlet fever**, some parasitic infections, **cirrhosis** of the liver, and some types of **hemolytic anemia** can also cause the formation of cold agglutinins. Hemolytic **anemias** are conditions in which the blood is low in oxygen because the red blood cells are breaking down at a faster rate than their normal life expectancy of 120 days. In addition to these illnesses, some people have a benign condition called chronic cold agglutinin disease, in which exposure to cold causes temporary clumping of red blood cells and consequent numbness in ears, fingers, and toes.

Description

Since cold agglutinins cause red blood cells to clump only at temperatures lower than 98.6°F (37°C), the test consists of chilling a sample of the patient's blood. There is a bedside version of the test in which the doctor collects four or five drops of blood in a small tube, cools the tube in ice water for 30–60 seconds, and looks for clumping of red blood cells. If the cells clump after chilling and unclump as they rewarm, a cold agglutinin titer (concentration) greater than 1:64 is present. Bedside test results, however, should be confirmed by a laboratory. The laboratory test measures the clumping of red blood cells in different dilutions of the patient's blood serum at 39.2°F (4°C).

KEY TERMS

Agglutinin—An antibody that causes red blood cells to stick or clump together.

Antibody—A protein molecule produced by the immune system that is specific to a disease agent, such as *Mycoplasma pneumoniae*. The antibody combines with the organism and disables it.

Autoantibody—An antibody produced by the body in reaction to any of its own cells or cell products.

Cold agglutinins—Antibodies that cause clumping of red blood cells when the blood temperature falls below normal body temperature (98.6°F/37°C).

Hemolytic anemia—Oxygen deficiency in the blood, caused by shortened survival of red blood cells.

Mycoplasma—A type of free-living microorganism that has no cell wall. Mycoplasmas cause some varieties of pneumonia and urinary tract infections that stimulate the body to produce cold agglutinins.

Titer—The concentration of a substance in a given sample of blood or other tissue fluid.

Normal results

The results of the cold agglutinins test require a doctor's interpretation. In general, however, a normal value is lower than 1:32.

Abnormal results

Any value higher than 1:32 suggests a diagnosis of mycoplasmal pneumonia or one of the other viral infections or disease conditions indicated by this test.

Resources

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Rebecca J. Frey

Cold sensitivity antibodies test *see* **Cryoglobulin test**

Cold sore

Definition

A cold sore is a fluid-filled blister which usually appears at the edge of the lips. Cold sores are caused by a herpes simplex virus infection.

Description

A cold sore is a fluid-filled, painful blister that is usually on or around the lips. Other names for a cold sore are **fever** blister, oral herpes, labial herpes, herpes labialis, and herpes febrilis. Cold sores most often occur on the lips which distinguishes them from the common canker sore, which is usually inside the mouth. Cold sores do not usually occur inside the mouth except during the initial episode. **Canker sores** usually form either on the tongue or inside the cheeks.

Cold sores are caused by a herpes virus. There are eight different kinds of human herpes viruses. Only two of these, herpes simplex types 1 and 2, can cause cold sores. It is commonly believed that herpes simplex virus type 1 infects above the waist and herpes simplex virus type 2 infects below the waist. This is not completely true. Both herpes virus type 1 and type 2 can cause herpes lesions on the lips or genitals, but recurrent cold sores are almost always type 1.

Oral herpes is very common. More than 60% of Americans have had a cold sore, and almost 25% of those infected experience recurrent outbreaks. Most of these persons became infected before age 10. Anyone can become infected by herpes virus and, once infected, the virus remains latent for life. Herpes viruses are spread from person to person by direct skin-to-skin contact. The highest risk for spreading the virus is the time period beginning with the appearance of blisters and ending with scab formation. However, infected persons need not have visible blisters to spread the infection to others since the virus may be present in the saliva without obvious oral lesions.

Viruses are different from bacteria. While bacteria are independent and can reproduce on their own, viruses enter human cells and force them to make more virus. The infected human cell is usually killed and releases thousands of new viruses. The cell **death** and resulting tissue damage causes the actual cold sores. In addition, the herpes virus can infect a cell and instead of making the cell produce new viruses, it hides inside the cell and waits. The herpes virus hides in the nervous system. This is called "latency." A latent virus can wait inside the nervous system for days, months, or even years. At some future time, the virus "awakens" and causes the cell to produce thousands of new viruses that cause an active infection.

This process of latency and active infection is best understood by considering the cold sore cycle. An active infection is obvious because cold sores are present. The first infection is called the "primary" infection. This active infection is then controlled by the body's immune system and the sores heal. In between active infections, the virus is latent. At some point in the future, latent viruses become activated and once again cause sores. These are called "recurrent" infections. Although it is unknown what triggers latent virus to activate, several conditions seem to bring on infections. These include **stress**, illness, tiredness, exposure to sunlight, menstruation, fever, and diet.

Causes and symptoms

While anyone can be infected by herpes virus, not everyone will show symptoms. The first symptoms of herpes occur within two-20 days after contact with an infected person. Symptoms of the primary infection are usually more severe than those of recurrent infections. The primary infection can cause symptoms like other viral infections including tiredness, **headache**, fever, and swollen lymph nodes in the neck.

Typically, 50-80% of persons with oral herpes experience a prodrome (symptoms of oncoming disease) of **pain**, burning, **itching**, or tingling at the site where blisters will form. This prodrome stage may last anywhere from a few hours to one to two days. The herpes infection prodrome occurs in both the primary infection and recurrent infections.

In 95% of the patients with cold sores, the blisters occur at the outer edge of the lips which is called the "vermilion border." Less often, blisters form on the nose, chin, or cheek. Following the prodrome, the disease process is rapid. First, small red bumps appear that quickly form fluid-filled blisters. The painful blisters may either burst and form a scab or dry up and form a scab. Within two days of the first red bumps, all the blisters have formed scabs. The skin heals completely and without scarring within six to ten days.

Some children have a very serious primary (first episode) herpes infection called "gingivostomatitis." This causes fever, swollen lymph glands, and numerous blisters inside the mouth and on the lips and tongue that may form large, open sores. These painful sores may last up to three weeks and can make eating and drinking difficult. Because of this, young children with gingivostomatitis are at risk for **dehydration** (excessive loss of water from the body).

Most people experience fewer than two recurrent outbreaks of cold sores each year. Some people never experience outbreaks, while some have very frequent outbreaks. In most people, the blisters form in the same area each time and are triggered by the same factors (such as stress, sun exposure, etc).

Diagnosis

Because oral herpes is so common, it is diagnosed primarily by symptoms. It can be diagnosed and treated by the family doctor, dermatologists (doctors who specialize in skin diseases) and infectious disease specialists. Laboratory tests may be performed to look for the virus. Because healing sores do not shed much virus, a sample from an open sore would be taken for viral culture. A sterile cotton swab would be wiped over open sores and the sample used to infect human cells in culture. Cells that are killed by the herpes virus have a certain appearance under microscopic examination. The results of this test are available within two to 10 days.

Oral herpes may resemble a bacterial infection called impetigo. This skin infection is most commonly seen in children and causes herpes-like blisters around the mouth and nose. Also, because oral herpes can occur inside the mouth, the blisters could be mistaken for common canker sores. Therefore, the doctor would need to determine whether the blisters are oral herpes, canker sores, or **impetigo**. The diagnosis and treatment of herpes infections should be covered by most insurance providers.

Treatment

There is no cure for herpes virus infections. There are **antiviral drugs** available that have some effect on lessening the symptoms and decreasing the length of herpes outbreaks. There is evidence that some may also prevent future outbreaks. These antiviral drugs work by interfering with the replication of the viruses, and are most effective when taken as early in the infection process as possible. For the best results, drug treatment should begin during the prodrome stage before blisters are visible. Depending on the length of the outbreak, drug treatment could continue for up to 10 days.

A close-up view of a patient's mouth with gingivostomatitis cold sores. *(Custom Medical Stock Photo. Reproduced by permission.)*

Acyclovir (Zovirax) is the drug of choice for herpes infection and can be given intravenously or taken by mouth. It can be applied directly to sores as an ointment but is not very useful in this form. A liquid form for children is also available. Acyclovir is effective in treating both the primary infection and recurrent outbreaks. When taken by mouth to prevent an outbreak, acyclovir reduces the frequency of herpes outbreaks.

During an outbreak of cold sores, salty foods, citrus foods (oranges etc.), and other foods that irritate the sores should be avoided. Wash the sores once or twice a day with warm, soapy water and pat gently to dry. Over-the-counter lip products that contain the chemical phenol (such as Blistex Medicated Lip Ointment) and numbing ointments (Anbesol) help to relieve cold sores. A bandage may be placed over the sores to protect them and prevent spreading the virus to other sites on the lips or face. **Acetaminophen** (Tylenol) or ibuprofen (Motrin, Advil) may be taken if necessary to reduce pain and fever.

Alternative treatment

Vitamin and mineral supplements and diet may have an effect on the recurrence and duration of cold sores. In general, cold sore sufferers should eat a healthy diet of unprocessed foods such as vegetables, fruits, and whole grains. Alcohol, **caffeine**, and sugar should be avoided.

An imbalance in the amino acids lysine and arginine is thought to be one contributing factor in herpes virus outbreaks. A diet that is rich in the amino acid lysine may help prevent recurrences of cold sores. Foods which contain high levels of lysine include most vegetables, legumes, fish, turkey, and chicken. In one study, patients taking lysine supplements had milder symptoms during an outbreak, a shorter healing time, and had fewer outbreaks

KEY TERMS

Latent—A nonactive virus which is in a dormant state within a cell. The herpes virus is latent in the nervous system.

Prodrome—The Symptoms that warn of the beginning of disease. The herpes prodrome consists of pain, burning, tingling, or itching at a site before blisters are visible.

Recurrence—The return of an active infection following a period of latency.

than patients who did not take lysine. Patients should take 1,000 mg of lysine three times a day during a cold sore outbreak and 500 mg daily on an ongoing basis to prevent recurrences. Intake of the amino acid arginine should be reduced. Foods rich in arginine that should be avoided are chocolate, peanuts, almonds, and other nuts and seeds.

Vitamin C and bioflavonoids (a substance in fruits that helps the body to absorb and use vitamin C) have been shown to reduce the duration of a cold sore outbreak and reduce the number of sores. The vitamin B complex includes important **vitamins** that support the nervous system where viruses can hide out. B complex vitamins can also help manage stress, an important contributing factor to the outbreak of herpes viruses. Applying the oil in vitamin E capsules directly to cold sores may provide relief. Zinc lozenges appear to affect the reproduction of viruses and also enhance the immune system. Ointments containing lemon balm (*Melissa officinalis*) or licorice (*Glycyrrhiza glabra*) and peppermint (*Mentha piperita*) have been shown to help cold sores heal.

Prognosis

Oral herpes can be painful and embarrassing, but it is not a serious infection. There is no cure for oral herpes, but outbreaks usually occur less frequently after age 35. The spread of the herpes virus to the eyes is very serious. The herpes virus can infect the cells in the cornea and cause scarring that may impair vision.

Prevention

The only way to prevent oral herpes is to avoid contact with infected persons. This is not an easy solution because many people aren't aware that they are infected and can easily infect others. Currently there are no herpes vaccines available, although herpes vaccines are being tested.

Several practices can reduce the occurrence of cold sores and the spread of virus to other body locations or people. These practices are:

- Avoidance of sun exposure to the face. Before getting prolonged exposure to the sun, apply sunscreen to the face and especially to the lips. Wearing a hat with a large brim is also helpful.
- Avoid touching cold sores. Squeezing, picking, or pinching blisters can allow the virus to spread to other parts of the lips or face and infect those sites.
- Wash hands frequently. Persons with oral herpes should wash their hands carefully before touching others. An infected person can spread the virus to others even when he or she has no obvious blisters.
- Avoid contact with others during active infection. Infected persons should avoid kissing or sexual contact with others until after the cold sores have healed.
- Wear gloves when applying ointment to a child's sore.
- Be especially careful with infants. Never kiss the eyes or lips of a baby who is under six months old.
- Be watchful of infected children. Do not allow infected children to share toys that may be put into the mouth. Toys that have been mouthed should be disinfected before other children play with them.
- Maintain good general health. A healthy diet, plenty of sleep, and **exercise** help to minimize the chance of getting a cold or the flu, which are known to bring on cold sores. Also, good general health keeps the immune system strong; this helps to keep the virus in check and prevents outbreaks.

Resources

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Belinda Rowland, PhD

Cold spot myocardial imaging *see* **Thallium heart scan**

Colds *see* **Common cold**

Colic

Definition

Colic is persistent, unexplained crying in a healthy baby between two weeks and five months of age.

Description

Colic, which is not a disease, affects 10–20% of all infants. It is more common in boys than in girls and most common in a family's first child. Symptoms of colic usually appear when a baby is 14–21 days old, reach a crescendo at the age of three months, and disappear within the next eight weeks. Episodes occur frequently but intermittently and usually begin with prolonged periods of crying in the late afternoon or evening. They can last for just a few minutes or continue for several hours. Some babies who have colic are simply fussy. Others cry so hard that their faces turn red, then pale.

Causes and symptoms

No one knows what causes colic. The condition may be the result of swallowing large amounts of air, which becomes trapped in the digestive tract and causes bloating and severe abdominal **pain**.

Other possible causes of colic include:

- digestive tract immaturity
- food intolerances
- hunger or overfeeding
- lack of sleep
- loneliness
- overheated milk or formula
- overstimulation resulting from noise, light, or activity
- tension

During a colicky episode, babies' bellies often look swollen, feel hard, and make a rumbling sound. Crying intensifies, tapers off, then gets louder. Many babies grow rigid, clench their fists, curl their toes, and draw their legs toward their body. A burp or a bowel movement can end an attack. Most babies who have colic don't seem to be in pain between attacks.

Diagnosis

Pediatricians and family physicians suspect colic in an infant who:

- has cried loudly for at least three hours a day at least three times a week for three weeks or longer
- is not hungry but cries for several hours between dinnertime and midnight
- demonstrates the clenched fists, rigidity, and other physical traits associated with colic

The baby's medical history and a parent's description of eating, sleeping, and crying patterns are used to confirm a diagnosis of colic. **Physical examination** and laboratory tests are used to rule out infection, intestinal blockage, and other conditions that can cause abdominal pain and other colic-like symptoms.

Treatment

Medications do not cure colic. Doctors sometimes recommend simethicone (Mylicon Drops) to relieve gas pain, but generally advise parents to take a practical approach to the problem.

Gently massaging the baby's back can release a trapped gas bubble, and holding the baby in a sitting position can help prevent air from being swallowed during feedings. Bottle-fed babies can swallow air if nipple holes are either too large or too small.

Nipple-hole size can be checked by filling a bottle with cold formula, turning it upside down, and counting the number of drops released when it is shaken or squeezed. A nipple hole that is the right size will release about one drop of formula every second.

Babies should not be fed every time they cry, but feeding and burping a baby more often may alleviate symptoms of colic. A bottle-fed baby should be burped after every ounce, and a baby who is breastfeeding should be burped every five minutes.

When cow's milk is the source of the symptoms, bottle-fed babies should be switched to a soy milk hydrolyzed protein formula. A woman whose baby is breastfeeding should eliminate dairy products from her diet for seven days, then gradually reintroduce them unless the baby's symptoms reappear.

Since intolerance to foods other than cow's milk may also lead to symptoms of colic, breastfeeding women may also relieve their babies' colic by eliminating from their diet:

- coffee
- tea
- cocoa
- citrus
- peanuts
- wheat
- broccoli and other vegetables belonging to the cabbage family

Rocking a baby in a quiet, darkened room can prevent overstimulation, and a baby usually calms down when cuddled in a warm, soft blanket.

Colicky babies cry less when they are soothed by the motion of a wind-up swing, a car ride, or being carried in a parent's arms. Pacifiers can soothe babies who are upset, but a pacifier should never be attached to a string.

A doctor should be notified if a baby who has been diagnosed with colic:

- develops a rectal **fever** higher than 101°F (38.3°C)
- cries for more than four hours
- vomits
- has **diarrhea** or stools that are black or bloody
- loses weight
- eats less than normal

Alternative treatment

Applying gentle pressure to the webbed area between the thumb and index finger of either hand can calm a crying child. So can gently massaging the area directly above the child's navel and the corresponding spot on the spine. Applying warm compresses or holding your hand firmly over the child's abdomen can relieve cramping.

Teas made with chamomile (*Matricaria recutita*), lemon balm (*Melissa officinalis*), peppermint (*Mentha piperita*), or dill (*Anethum graveolens*) can lessen bowel inflammation and reduce gas. A homeopathic combination called "colic" may be effective, and constitutional homeopathic treatment can help strenthen the child's entire constitution.

Prognosis

Colic is distressing, but it is not dangerous. Symptoms almost always disappear before a child is six months old.

Prevention

Many doctors believe that colic cannot be prevented. Some alternative practitioners, however, feel that colic can be prevented by an awareness of food intolerances and their impact.

Resources

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ORGANIZATIONS

American Academy of Family Physicians. 8880 Ward Parkway, Kansas City, MO 64114. (816) 333-9700. <http://www.aafp.org>.

American Academy of Pediatrics. 141 Northwest Point Boulevard, Elk Grove Village, IL 60007-1098. (847) 434-4000. <http://www.aap.org>.

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Maureen Haggerty

Collapsed lung *see* **Pneumothorax**

Colloidal bath *see* **Therapeutic baths**

Colon cancer

Definition

Cancer of the colon is the disease characterized by the development of malignant cells in the lining or epithelium of the first and longest portion of the large intestine. Malignant cells have lost normal control mechanisms governing growth. These cells may invade surrounding local tissue, or they may spread throughout the body and invade other organ systems.

Synonyms for the colon include the large bowel or the large intestine. The rectum is the continuation of the large intestine into the pelvis that terminates in the anus.

Description

The colon is a tubular organ beginning in the right lower aspect of the abdomen. Anatomically, it ascends on the right side of the abdomen, traverses from right to left in the upper abdomen, descends vertically down the left side, takes an S-shaped curve in the lower left abdomen, and then flows into the rectum as it leaves the abdomen for the pelvis. These portions of the colon are named separately though they are part of the same organ:

- cecum, the beginning of the colon
- ascending colon, the right vertical ascent of the colon
- transverse colon, the portion traversing from right to left
- descending colon, the left vertical descent of the colon
- sigmoid colon, the s-shaped segment of colon above the pelvis

These portions of the colon are recognized anatomically based on the arterial blood supply and venous and lymphatic drainage of these segments of the colon. Lymph, a protein-rich fluid that bathes the cells of the body, is transported in small channels known as lymphatics that run along side the veins of the colon. Lymph nodes are small filters through which the lymph travels on its way back to the blood stream. Cancer can spread elsewhere in the body by invading the lymph and vascular systems. Therefore, these anatomic considerations become very important in the treatment of colon cancer.

The small intestine is the continuation of the upper gastrointestinal tract that is responsible for the transport of ingested nutrients into the body. The waste left after the small intestine has completed absorption of nutrients amounts to a few liters (about the same as quart) of material per day and is directly delivered to the colon (at the cecum) for processing. Physiologically, the colon is responsible for the preservation of fluid and electrolytes as it propels the increasingly solid waste towards the rectum and anus for excretion.

When cells lining the colon become malignant, they first grow locally and may invade partially or totally through the wall of the bowel and even into adjacent structures and organs. In the process, the tumor can penetrate and invade the lymphatics or the capillaries locally and it gains access to the circulation. As the malignant cells work their way to other areas of the body, they again become locally invasive in the new area to which they have spread. These tumor deposits, originating in the colon primary tumor, are then known as metastases. If metastases are found in the regional lymph nodes from the primary, they are known as regional metastases or regional nodal metastases. If they are distant from the primary tumor, they are known as distant metastases. The patient with distant metastases has systemic disease. Thus the cancer originating in the colon begins locally and, given time, can become systemic in its extent.

By the time the primary is originally detected, it is usually larger than 0.4 in (1 cm) in size and has over a million cells. This amount of growth itself is estimated to take about three to seven years. Each time the cells double in number, the size of the tumor quadruples. Thus, like most cancers, the part that is identified clinically is later in the progression than would be desired and screening becomes a very important endeavor to aid in earlier detection of this disease.

There are about 94,000 cases of colon cancer diagnosed per year in the United States. Together, colon and rectal cancers account for 10% of cancers in men and 11% of cancers in women. It is the second most common site-specific cancer affecting both men and women. (Lung cancer is the first affecting both men and women, breast is the leader in women and prostate the leader in men.) Nearly 48,000 people died from colon cancer in the United States in 2000. In recent years the incidence of this disease is decreasing very slightly, as has the mortality rate. It is difficult to tell if the decrease in mortality reflects earlier diagnosis, less **death** related to the actual treatment of the disease, or a combination of both factors.

Cancer of the colon is thought to arise sporadically in about 80% of those who develop the disease. Twenty percent of cases are thought to have genetic predisposition that ranges from familial syndromes affecting 50% of the offspring of a mutation carrier, to a risk of 6% when there is just a family history of colon cancer occurring in a first degree relative. Development of colon cancer at an early age, or at multiple sites, or recurrent colon cancer suggests a genetically transmitted form of the disease as opposed to the sporadic form.

Causes and symptoms

Causes of colon cancer are probably environmental in the sporadic cases (80%) and genetic in the heredity predisposed cases (20%). Since malignant cells have a changed genetic makeup, this means that in 80% of cases, the environment spontaneously induces change, whereas in those born with a genetic predisposition, they are either destined to get the cancer or it will take less environmental exposure to induce the cancer. Exposure to agents in the environment that may induce mutation is the process of carcinogenesis and is caused by agents known as carcinogens (cancer-causing agents). Specific carcinogens have been difficult to identify; however, dietary factors seem to be involved.

Colon cancer is more common in industrialized nations and **diets** high in fat, red meat, total calories, and alcohol seem to predispose. Diets high in fiber are associated with a decreased risk. The mechanism for protection by high-fiber diets may be related to less exposure of the colon lining to carcinogens from the environment, as the transit time through the bowel is faster with a high-fiber diet than it is with a low-fiber diet.

Age plays a definite role in the predisposition to colon cancer. Colon cancer is uncommon before age 40. This incidence increases substantially after age 50 and doubles with each succeeding decade.

There is also a slight increase risk for colon cancer in the individual who smokes.

Patients who suffer from inflammatory diseases of the colon known as **ulcerative colitis** and Crohn's colitis are also at increased risk.

As for genetic predisposition, on chromosome 5, there is a gene called the APC gene associated with the familial adenomatous polyposis syndrome. There are multiple different mutations that occur at this site, yet they all cause a defect in tumor suppression that results in early and frequent development of colon cancer. This genetic aberration is transmitted to 50% of offspring and each of those affected will develop colon cancer, usually at an early age. There is another syndrome, hereditary non-polyposis colon cancer (also known as Lynch syndrome), related to mutations in any of four genes responsible for DNA mismatch repair. In patients with colon cancer, the p53 gene is mutated 70% of the time. When the p53 gene is mutated and ineffective, cells with damaged DNA escape repair or destruction. This allows for the damaged cell to perpetuate itself, and continued replication of the damaged DNA may lead to tumor development. Though these syndromes have a very high incidence of colon cancer, family history without the syndrome is also a substantial risk factor. When considering first-degree relatives, history of one with colon cancer raises the baseline risk of 2% to 6%. (Most physicians think that this baseline is about 4%.) The presence of a second raises the risk to 17%.

The development of polyps of the colon almost always precedes the development of colon cancer by five or more years. Polyps are benign growths of the colon lining. They can be unrelated to cancer, precancerous, or malignant. Polyps, when identified, are removed for diagnosis. If the polyps are benign, the patient should undergo careful surveillance for the development of more polyps or the development of colon cancer.

Colon cancer causes symptoms related to its local presence in the large bowel or by its effect on other organs if it has spread. These symptoms may occur alone or in combination:

- a change in bowel habit
- blood in the stool
- bloating, persistent abdominal distention
- constipation
- a feeling of fullness even after having a bowel movement
- narrowing of the stool—so-called ribbon stools
- persistent, chronic **fatigue**
- abdominal discomfort
- unexplained weight loss
- very rarely, nausea and vomiting

Most of these symptoms are caused by the physical presence of the tumor mass in the colon. Similar symptoms can be caused by other processes; these are not absolutely specific to colon cancer. The key is recognizing that the persistence of these types of symptoms without ready explanation should prompt the individual to seek medical evaluation.

Many of the symptoms are understood by remembering that the colon is a tubular conduit. If a tumor develops, as it reaches a certain size it will begin to cause symptoms related to the obstruction of that conduit. In addition, the tumor commonly oozes blood that is lost in the stool. (Often, this blood is not visible.) This phenomenon results in anemia and chronic fatigue. Weight loss is a late symptom, often implying substantial obstruction or the presence of systemic disease.

Diagnosis

Screening

Of all of the major cancers, only colorectal cancer can be prevented by screening. In all other cancers (breast and prostate, for example), screening tests look for small, malignant lesions. Screening for colorectal cancers, however, is the search for pre-malignant, benign polyps. This screening can be close to 100% effective in preventing cancer development, not just in detecting small cancers.

Screening involves physical exam, simple laboratory tests, and the visualization of the lining of the colon. The ways to visualize the colon epithelium are with x rays (indirect visualization), and endoscopy (direct visualization).

The **physical examination** involves the performance of a digital rectal exam (DRE). The DRE includes manual examination of the rectum, anus, and the prostate. During this examination, the physician examines the anus and the surrounding skin for **hemorrhoids**, abscesses, and other irregularities. After lubricating the gloved finger and anus, the examiner gently slides the finger into the anus and follows the contours of the rectum. The examiner notes the tone of the anus and feels the walls and the edges for texture, tenderness and masses as far as the examining finger can reach. At the time of this exam, the physician checks the stool on the examining glove with a chemical to see if any occult (invisible), blood is present. At home, after having a bowel movement, the patient is asked to swipe a sample of stool obtained with a small stick on a card. After 3 such specimens are on the card, the card is then easily chemically tested for occult blood also. (The stool analysis mentioned here is known as a **fecal occult blood test**, or FOBT, and, while it can be helpful, it is not 100% accurate—only about 50% of cancers are FOBT-positive.) These exams are accomplished as an easy part of a routine yearly physical exam.

Proteins are sometimes produced by cancers, and these may be elevated in the patient's blood. When this occurs, the protein produced is known as a tumor marker. There is a tumor marker for some cancers of the colon; it is known as carcinoembryonic antigen, or CEA. Unfortunately, this protein may be made by other adenocarcinomas as well, or it may not be produced by a particular colon cancer. Therefore, screening by chemical analysis for CEA has not been helpful. CEA has been helpful when used in a follow-up role for patients treated for colon cancer if their tumor makes the protein.

Indirect visualization of the colon may be accomplished by placing barium through the rectum and filling the colon with this compound. Barium produces a white contrast image of the lining of the colon on x ray and thus, the contour of the lining of the colon may be seen. Detail can be increased if the barium utilized is thinned and air also introduced. These studies are known as the **barium enema** (BE) and the double contrast barium enema (DCBE).

Direct visualization of the lining of the colon is accomplished using a scope or endoscope. The physician introduces the instrument through the rectum and passes it proximally, visualizing the colon epithelium in the process. Older, shorter scopes were rigid. Today, utilizing fiberoptic technology, the scopes are flexible and can reach much farther. If the left colon only is visualized, it is called flexible **sigmoidoscopy**. When the entire colon is visualized, the procedure is known as **colonoscopy**.

Unlike the indirect visualizations of the colon (the BE and the DCBE), the endoscopic screeenings allow the physician to remove polyps and biopsy suspicious tissue. (A biopsy is a removal of tissue for examination by a pthologist.) For this reason, many physicians prefer endoscopic screening. All of the visualizations, the BE, DCBE, and each type of endoscopy require pre-procedure preparation (evacuation) of the colon.

The American Cancer Society has recommended the following screening protocol for those of normal risk over 50 years of age:

- yearly DRE with occult blood in stool testing
- flexible sigmoidoscopy at age 50
- flexible sigmoidoscopy repeated every five years

Many physicians, however, recommend full colonoscopy every five to seven years. Screening evaluations should start sooner for patients who have predisposing factors, such as family history, history of polyps, or a familial syndrome.

Evaluation of patients with symptoms

For those whose symptoms prompt them to visit their physician, and if their symptoms could possibly be related to colon cancer, the entire colon will be inspected. The combination of a flexible sigmoidoscopy and DCBE may be performed but the preferred evaluation of the entire colon and rectum is that of complete colonoscopy. Colonoscopy allows direct visualization, photography, and the opportunity to obtain a biopsy of any abnormality visualized. If, for technical reasons, the entire colon is not visualized endoscopically, a DCBE should complement the colonoscopy.

A colon with a cancerous growth. *(Illustration by Argosy Inc.)*

The diagnosis of colon cancer is actually made by the performance of a biopsy of any abnormal lesion in the colon. When a tumor growth is identified, it could be either a benign polyp (or lesion) or a cancer; the biopsy resolves the issue. The endoscopist may take many samples so as to exclude any sampling errors.

If the patient presents with advanced disease, or has advanced disease at the time of diagnosis, areas where the tumor has spread (such as the liver) may be amenable to biopsy. Such biopsies are usually obtained using a special needle under local anesthesia.

Once a diagnosis of colon cancer has been established by biopsy, in addition to the physical exam, studies will be performed to assess the extent of the disease. Blood studies include a complete **blood count**, **liver function tests**, and a CEA. Imaging studies will include a **chest x ray** and a CAT scan (computed tomography scan) of the abdomen. The chest x ray will determine if there is spread to the lung, and the CAT scan will evaluate potential spread to the liver as well as any local invasive characteristics of the primary tumor. If the patient has any neurologic symptoms, a CAT scan of the brain will be performed, and if the

KEY TERMS

Adenocarcinoma—Type of cancer beginning in glandular epithelium.

Adjuvant therapy—Treatment involving radiation, chemotherapy (drug treatment), or hormone therapy, or a combination of all three given after the primary treatment for the possibility of residual microscopic disease.

Anastomosis—Surgical reconnection of the ends of the bowel after removal of a portion of the bowel.

Anemia—The condition caused by too few circulating red blood cells, often manifested in part by fatigue.

Carcinogens—Substances in the environment that cause cancer, presumably by inducing mutations, with prolonged exposure.

Electrolytes—Salts, such as sodium and chloride.

Epithelium—Cells composing the lining of an organ.

Lymphatics—Channels that are conduits for lymph.

Lymph nodes—Cellular filters through which lymphatics flow.

Malignant—Cells that have been altered such that they have lost normal control mechanisms and are capable of local invasion and spread to other areas of the body.

Metastasis—Site of invasive tumor growth that originated from a malignancy elsewhere in the body.

Mutation—A change in the genetic makeup of a cell that may occur spontaneously or be environmentally induced.

Occult blood—Presence of blood that cannot be seen with the naked eye.

Polyps—Localized growths of the epithelium that can be benign, precancerous, or harbor malignancy.

Radical resection—Surgical resection that takes the blood supply and lymph system supplying the organ along with the organ.

Resect—To remove surgically.

Sacrum—Posterior bony wall of the pelvis.

Systemic—Referring to throughout the body.

patient is experiencing bone **pain**, a bone scan will also be performed.

Treatment

Once the diagnosis has been confirmed by biopsy, the clinical stage of the cancer is assigned. Using the characteristics of the primary tumor, its depth of penetration through the bowel, and the presence or absence of regional or distant metastases, the stage of the cancer is derived. Often, the depth of penetration through the bowel or the presence of regional lymph nodes can't be assigned before surgery.

Colon cancer is assigned stages I through IV based on the following general criteria:

- Stage I: the tumor is confined to the epithelium or has not penetrated through the first layer of muscle in the bowel wall.
- Stage II: the tumor has penetrated through to the outer wall of the colon or has gone through it, possibly invading other local tissue.
- Stage III: any depth or size of tumor associated with regional lymph node involvement.
- Stage IV: any of previous criteria associated with distant metastasis.

With many cancers other than colon cancer, staging plays an important pre-treatment role to best determine treatment options. In colon cancer, almost all colon cancers are treated with surgery first, regardless of stage. Colon cancers through stage III, and even some stage IV colon cancers, are treated with surgery first before any other treatments are considered.

Surgery

Surgical removal of the involved anatomic segment of colon (colectomy) along with its blood supply and regional lymph nodes is the primary therapy for colon cancer. Usually, on the basis of the blood supply, the partial colectomies are separated into right, left, transverse, or sigmoid. The removal of the blood supply at its origin along with the regional lymph nodes that accompany it assures an adequate margin of normal colon on either side of the primary tumor. When the cancer lies in a position such that the blood supply and lymph drainage lies between two of the major vessels, both vessels are taken to assure complete radical resection or removal (extend-

ed radical right or left colectomy). If the primary tumor penetrates through the bowel wall, any tissue adjacent to the tumor extension is also taken if feasible.

Surgery is used as primary therapy for stages I through III colon cancer unless there are signs that local invasion will not permit complete removal of the tumor, as may occur in advanced stage III tumors. However, this circumstance is very rare, and occurs in less than 2% of all colon cancer cases.

After the resection is completed, the ends of the remaining colon are reconstructed; the hook-up is called an anastomosis. Once healing has occurred, there may be a slight increase in the frequency of bowel movements. This effect usually lasts only for several weeks. Most patients go on to develop completely normal bowel function.

Occasionally, the anastomosis would be risky and cannot be performed. (Most commonly, this occurs when the bowel could not be adequately evacuated in an emergency circumstance due to bowel obstruction.) When the anastomosis cannot be performed, a **colostomy** is performed instead. A colostomy is performed by bringing the end of the colon through the abdominal wall and sewing it to the skin. The patient will have to wear an appliance (a bag) to manage the stool. The colostomy may be temporary and the patient may undergo a hook-up at a later, safer date, or the colostomy may be permanent. In most cases, emergent colostomies are not reversed and are permanent.

Radiation

Radiation therapy is used as an adjunct to surgery if there is concern about potential for local recurrence post-operatively and the area of concern will tolerate the radiation. For instance, if the tumor invaded muscle of the abdominal wall but was not completely removed, this area would be considered for radiation. Radiation has significant dose limits when residual bowel is exposed to it because the small and large intestine do not tolerate radiation well.

Radiation is also used in the treatment of patients who present with or progress to having metastatic disease. It is particularly useful in shrinking metastatic colon cancer to the brain.

Chemotherapy

Chemotherapy is useful for patients who have had all identifiable tumor removed and are at risk for recurrence (adjuvant chemotherapy). Chemotherapy may also be used when the cancer is stage IV and is beyond the scope of regional therapy, but this use is rare.

Adjuvant therapy is considered in stage II disease with deep penetration or in stage III patients. Standard therapy is treatment with 5-fluorouracil, (5FU) combined with leucovorin for a period of six to 12 months. 5FU is an antimetabolite and leukovorin improves the response rate. (A response is a temporary regression of the cancer in response to the chemotherapy.) Another agent, levamisole, (which seems to stimulate the immune system), may be substituted for leucovorin. These protocols reduce rate of recurrence by about 15% and reduce mortality by about 10%. The regimens do have some toxicity, but usually are tolerated fairly well.

Similar chemotherapy may be administered for stage IV disease or if a patient progresses and develops metastases. Results show response rates of about 20%. Unfortunately, these patients eventually succumb to the disease, and this chemotherapy may not prolong survival or improve quality of life in Stage IV patients. Clinical trials have now shown that the results can be improved with the addition of another agent to this regimen. Irinotecan does not seem to increase toxicity but it improved response rates to 39%, added two to three months to disease-free survival, and prolonged overall survival by a little over two months.

Alternative treatment

Alternative therapies have not been studied in a large-scale, scientific way. Large doses of **vitamins**, fiber, and green tea are among therapies tried. Avoiding cigarettes and alcohol may be helpful. Before initiating any alternative therapies, the patient is wise to consult his/her physician to be sure that these therapies do not complicate or interfere with the established therapy.

Prognosis

Prognosis is the long-term outlook or survival after therapy. Overall, about 50% of patients treated for colon cancer survive the disease. As expected, the survival rates are dependent upon the stage of the cancer at the time of diagnosis, making early detection a very worthwhile endeavor.

About 15% of patients present with stage I disease and 85–90% survive. Stage II represents 20–30% of cases and 65–75% survive. Thirt to forty percent comprise the stage III presentation of which 55% survive. The remaining 20–25% present with stage IV disease and are very rarely cured.

Prevention

There is not an absolute way of preventing colon cancer. Still, there are steps an individual can take to dramatically lessen the risk or to identify the precursors of colon cancer so that it does not manifest itself. The patient with a familial history can enter screening and

surveillance programs earlier than the general population. High-fiber diets and vitamins, avoiding **obesity**, and staying active lessen the risk. Avoiding cigarettes and alcohol may be helpful. By controlling these environmental factors, an individual can lessen risk and to this degree prevent the disease.

By undergoing appropriate screening when uncontrollable genetic risk factors have been identified, an individual may be rewarded by the identification of benign polyps that can be treated as opposed to having these growths degenerate into a malignancy.

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Colon therapy *see* **Colonic irrigation**

Colonic irrigation

Definition

Colonic irrigation is also known as **hydrotherapy** of the colon, high colonic, entero-lavage, or simply colonic. It is the process of cleansing the colon by passing several gallons of water through it with the use of special equipment. It is similar to an enema but treats the whole colon, not just the lower bowel. This has the effect of flushing out impacted fecal matter, toxins, mucous, and even parasites that often build up over the passage of time. It is a procedure that should only be undertaken by a qualified practitioner.

Purpose

Anyone suffering from gas, bloating, cramping pains, **acne** and other skin complaints, arthritis, and a list of bowel complaints such as diverticulitis and irritable bowel etc., may benefit from colonic irrigation. In particular, **cancer** patients are often advised to undertake a course of colonic irrigation sessions as an essential part of their treatment. When a biological cancer therapy begins to enable the body to breakdown a cancerous mass, it is essential that speedy and effective elimination of the resulting toxins is achieved.

Colon and bowel cancer is one of the leading causes of **death** in the United States, and alternative practitioners insist that it can be prevented by efficient hygiene procedures. Providing that care is taken to replace the natural organisms that flourish in the bowel, many health benefits can be expected from colonic irrigation. In general, alternative practitioners maintain that an ill-functioning bowel is the source of all disease, and therefore keeping it clean will be an effective protection against this.

Removing large amounts of toxic matter relieves the patient and can lead to the alleviation of symptoms such as arthritis, **chronic fatigue syndrome**, **candidiasis**, and a host of other illnesses. Properly executed, colonic irrigation can help restore normal peristaltic action to a sluggish bowel, thus reducing the need for more hydrotherapy treatments over time. In addition, removing the layer of fecal matter which coats the intestines in many individuals allows improved assimilation of the nutrients from foods and can alleviate symptoms of vitamin and other nutrient deficiencies. Many alternative health practitioners consider some form of hydrotherapy for the bowel to be essential in the treatment of degenerative diseases.

Description

Origins

Cleansing the colon with the use of hydrotherapy is not a new concept. Forms of colonic irrigation have been used successfully for decades to relieve chronic toxicity and even acute cases of toxemia.

Over time, many people develop a thick layer of fecal matter that coats their colon. It hardens and becomes impacted, reducing the efficiency of the bowel,

and in some cases, completely obstructing normal elimination of waste matter from the body. It is quite common for people to only have one bowel movement per day, and some as few as one or two per week.

Alternative practitioners advise that we probably should have one bowel movement for every meal that we eat. If not, then we are not eliminating wastes completely, and if input exceeds output, then we will surely suffer the consequences at some point.

Incomplete elimination of body wastes may result in the following, depending on where the deposits end up:

- sluggish system
- joint **pain** and arthritis
- irritable bowel syndrome
- diverticulitis
- **Crohn's disease**
- leaky gut syndrome
- heart problem
- migraine
- **allergies**
- bad breath
- acne and other skin problems such as psoriasis
- asthma
- early senility and **Alzheimer's disease**
- chronic **fatigue** syndrome
- cancer, particularly of the bowel
- multiple sclerosis

During colonic irrigation, a small speculum is passed into the patient's bowel through the rectum. This is attached to a tube, which leads to a machine that pumps temperature-controlled water into the colon at a controlled rate (to be controlled by either the practitioner or the patient). The temperature of the water should ideally be kept as close to body temperature as possible.

The patient will temporarily be filled with water up to the level of the entire colon. Patients say they can feel the water up under their ribs but that the process, although sometimes uncomfortable, is not painful. The amount of water will vary but will generally be in the region of between two and six liters (or quarts) at any one time. This triggers peristaltic action and the patient will begin to expel the water along with fecal matter back through the tube and into the machine.

The fecal matter is flushed out through a viewing tube, so that what is eliminated may be monitored. Quite often, unsuspected parasites are expelled, along with very old fecal material, very dark in color, which may have been in the colon for years. Some therapists comment that it looks like aging rubber.

KEY TERMS

Dysbiosis—The condition that results when the natural flora of the gut are thrown out of balance, such as when antibiotics are taken.

Peristalsis—The natural wave-like action of a healthy bowel that transports matter from one end of the bowel to the other.

Probiotics—Supplements of beneficial microorganisms that normally colonize the gut.

Toxemia—Poisoning of the blood.

During the treatment, the therapist will gently massage the patient's abdomen to help dislodge impacted fecal matter. In addition to massage, sometimes **acupressure**, **reflexology**, or lymphatic drainage techniques may be used to loosen deposits and stimulate the bowel. It is important that the right amount of water is used, as too much will cause discomfort and too little will be ineffective. If correctly done, colonic irrigation is not painful at all and some patients claim to sleep through their treatment.

Sanitation is vital to this process. The tubes and speculums used are generally disposable, but other parts of the machine, such as the viewing tube, must be sterilized after each patient.

Normally, a series of treatments will be required to achieve desired results regarding the elimination of impacted, decaying matter, and restoration of bowel regularity. Initially, only gas and recent fecal matter may be expelled. The residue attached to the colon wall is usually the result of years of neglect, and therapists say that one cannot expect complete relief in only one session.

Impacted fecal matter can cause an imbalance of the natural organisms that normally populate the bowel, causing what is known as dysbiosis. Under ideal conditions, the bowel is populated by a variety of naturally occurring organisms. It seems that the enzymes occurring in fresh fruit and vegetables encourage these beneficial organisms. One of the results of eating processed denatured foods is that this natural balance is upset, and food may begin to rot in the bowel instead of being processed.

Decomposing matter can cause a toxic condition and may lead to many health problems, as **constipation** causes backed up pollution of the body cells. The process of repair and elimination of wastes enters a downward spiral which at best will cause fatigue, lack of energy and

premature aging, and, at worst, can cause degenerative diseases, among them allergies, and even cancer and Alzheimer's disease.

The cost of colonic irrigation treatments varies, but is generally between $35–70 per session, which may last from 45 minutes to one hour. The cost of the machine itself ranges from $4,000–12,000, but again, it should be noted that only qualified therapists should conduct sessions.

Preparations

Most practitioners prefer that distilled or purified water is used for colonic irrigation, but others use sterilized tap water.

Precautions

It may be advisable to use a probiotic pessary after colonic irrigation, to ensure replacement of desirable natural flora. There are certain conditions that either partly or completely preclude the use of colonic irrigation, such as an active attack of Crohn's disease, bleeding ulcers, and hyperacidosis. If in doubt, a qualified practitioner should be consulted. Anyone suffering from these conditions should always notify the practitioner when receiving colonic irrigation treatments.

Side effects

Some allopathic practitioners claim that colonic irrigation flushes out essential electrolytes and friendly bacteria from the bowel and that it can be dangerous. Practitioners counter that this can easily be remedied with the use of probiotics, and that in any case, these possible disadvantages are easily offset by the benefits of having large amounts of putrefying matter, harmful organisms, and parasites removed from the system.

Research and general acceptance

Although many alternative health care practitioners swear by colonic irrigation, there is a large allopathic lobby that claims that there are no benefits to be had, and that there are dangers involved. However, there are many decades of records and research from the alternative health care community that indicate that this therapy may have a valuable place in the treatment of degenerative diseases and toxic conditions.

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Intestinal Health Institute. 4427 East Fifth St., Tucson, AZ 85711. (520) 325-9686. info@sheilas.com. <http://www.sheilas.com>.

Patricia Skinner

Colonoscopy

Definition

Colonoscopy is a medical procedure where a long, flexible, tubular instrument called the colonoscope is used to view the entire inner lining of the colon (large intestine) and the rectum.

Purpose

A colonoscopy is generally recommended when the patient complains of rectal bleeding or has a change in bowel habits and other unexplained abdominal symptoms. The test is frequently used to test for colorectal **cancer**, especially when polyps or tumor-like growths have been detected using the **barium enema** and other diagnostic tests. Polyps can be removed through the colonoscope and samples of tissue (biopsies) can be taken to test for the presence of cancerous cells.

The test also enables the physician to check for bowel diseases such as **ulcerative colitis** and **Crohn's disease**. It is a necessary tool in monitoring patients who have a past history of polyps or **colon cancer**.

Description

The procedure can be done either in the doctor's office or in a special procedure room of a local hospital. An intravenous (IV) line will be started in a vein in the arm. The patient is generally given a sedative and a painkiller through the IV line.

During the colonoscopy, the patient will be asked to lie on his/her left side with his/her knees drawn up towards the abdomen. The doctor begins the procedure by inserting a lubricated, gloved finger into the anus to check for any abnormal masses or blockage. A thin, well-lubricated colonoscope will then be inserted into the anus and it will be gently advanced through the colon. The lining of the intestine will be examined through the scope. Occasionally air may be pumped through the colonoscope to help clear the path or open the colon. If there are

Colonoscopy is a procedure where a long and flexible tubular instrument called a colonoscope is inserted into the patient's anus in order to view the lining of the colon and rectum. It is performed to test for colorectal cancer and other bowel diseases, and enables the physician to collect tissue samples for laboratory analysis. *(Illustration by Electronic Illustrators Group.)*

excessive secretions, stool, or blood that obstruct the viewing, they will be suctioned out through the scope. The doctor may press on the abdomen or ask the patient to change his/her position in order to advance the scope through the colon.

The entire length of the large intestine can be examined in this manner. If suspicious growths are observed, tiny biopsy forceps or brushes can be inserted through the colon and tissue samples can be obtained. Small polyps can also be removed through the colonoscope. After the procedure, the colonoscope is slowly withdrawn and the instilled air is allowed to escape. The anal area is then cleansed with tissues.

The procedure may take anywhere from 30 minutes to two hours depending on how easy it is to advance the scope through the colon. Colonoscopy can be a long and uncomfortable procedure, and the bowel cleaning preparation may be tiring and can produce **diarrhea** and cramping. During the colonoscopy, the sedative and the **pain** medications will keep the patient very drowsy and relaxed. Most patients complain of minor discomfort and pressure from the colonoscope moving inside. However, the procedure is not painful.

Preparation

The doctor should be notified if the patient has **allergies** to any medications or anesthetics; any bleeding problems; or if the woman is pregnant. The doctor should also be informed of all the medications that the person is currently on and if he or she has had a barium x-ray examination recently. If the patient has had heart valves replaced, the doctor should be informed so that appropriate **antibiotics** can be administered to prevent any chance of infection. The risks of the procedure will be

KEY TERMS

Barium enema—An x-ray test of the bowel after giving the patient an enema of a white chalky substance that outlines the colon and the rectum.

Biopsy—Removal of a tissue sample for examination under the microscope to check for cancer cells.

Colonoscope—A thin, flexible, hollow, lighted tube that in inserted through the rectum into the colon to enable the doctor to view the entire lining of the colon.

Crohn's disease—A chronic inflammatory disease where the immune system starts attacking one's own body. The disease generally starts in the gastrointestinal tract.

Diverticulosis—A pouchlike section that bulges through the large intestine's muscular walls but is not inflamed. It may cause bleeding, stomach distress and excess gas.

Pathologist—A doctor who specializes in the diagnosis of disease by studying cells and tissues under a microscope.

Polyps—An abnormal growth that develops on the inside of a hollow organ such as the colon.

Ulcerative colitis—A chronic condition where recurrent ulcers are found in the colon. It is manifested clinically by abdominal cramping, and rectal bleeding.

explained to the patient before performing the procedure and the patient will be asked to sign a consent form.

It is important that the colon be thoroughly cleaned before performing the examination. Hence, before the examination, considerable preparation is necessary to clear the colon of all stool. The patient will be asked to refrain from eating any solid food for 24–48 hours before the test. Only clear liquids such as juices, broth, and Jello are recommended. The patient is advised to drink plenty of water to avoid **dehydration**. The evening before the test, the patient will have to take a strong laxative that the doctor has prescribed. Several 1 qt **enemas** of warm tap water may have to be taken on the morning of the exam. Commercial enemas (e.g., Fleet) may be used.

The patient will be given specific instructions on how to use the enema and how many such enemas are necessary. Generally, the procedure has to be repeated until the return from the enema is clear of stool particles. On the morning of the examination, the patient is instructed not to eat or drink anything. The preparatory procedures are extremely important since, if the colon is not thoroughly clean, the exam cannot be done.

Aftercare

After the procedure, the patient is kept under observation until the effects of the medications wear off. The patient will have to be driven home by somebody and can generally resume a normal diet and usual activities unless otherwise instructed. The patient will be advised to drink lots of fluids to replace those lost by **laxatives** and **fasting**.

For a few hours after the procedure, the patient may feel groggy. There may be some abdominal cramping and considerable amount of gas may be passed. If a biopsy was performed or a polyp was removed, there may be small amounts of blood in the stool for a few days. If the patient experiences severe abdominal pain or has persistent and heavy bleeding, it should be brought to the doctor's attention immediately.

Risks

The procedure is virtually free of any complications and risks. Very rarely (two in 1000 cases) there may be a perforation (a hole) in the intestinal wall. Heavy bleeding due to the removal of the polyp or from the biopsy site occurs very infrequently (one in 1000 cases). Infections due to a colonoscopy are also extremely rare. Patients with artificial or abnormal heart valves are usually given antibiotics before and after the procedure to prevent an infection.

Normal results

The results are said to be normal if the lining of the colon is a pale reddish pink and there are no abnormal looking masses that are found in the lining of the colon.

Abnormal results

Abnormal results would imply that polyps or other suspicious-looking masses were detected in the lining of the intestine. Polyps can be removed during the procedure and tissue samples can be biopsied. If cancerous cells are detected in the tissue samples, then a diagnosis of colon cancer is made. The pathologist analyzes the tumor cells further to estimate the aggressiveness of the tumor and the extent of spread of the disease. This is crucial before deciding on the mode of treatment for the disease. Abnormal findings could also be due to inflam-

matory bowel diseases such as ulcerative colitis or Crohn's disease. A condition called diverticulosis, where many small fingerlike pouches protrude from the colon wall, may also contribute to an abnormal result in the colonoscopy.

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National Cancer Institute. Building 31, Room 10A31, 31 Center Drive, MSC 2580, Bethesda, MD 20892-2580. (800) 422-6237. <http://www.nci.nih.gov>.

United Ostomy Association, Inc. (UOA). 19772 MacArthur Blvd., Suite 200, Irvine, CA 92612-2405. (800) 826-0826. <http://www.uoa.org>.

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Color blindness

Definition

Color blindness is an abnormal condition characterized by the inability to clearly distinguish different colors of the spectrum. The difficulties can be mild to severe. It is a misleading term because people with color blindness are not blind. Rather, they tend to see colors in a limited range of hues; a rare few may not see colors at all.

Description

Normal color vision requires the use of specialized receptor cells called cones, which are located in the retina of the eye. There are three types of cones, termed red, blue, and green, which enable people to see a wide spectrum of colors. An abnormality, or deficiency, of any of the types of cones will result in abnormal color vision.

There are three basic variants of color blindness. Red/green color blindness (deuteranopia) is the most common deficiency, affecting 8% of Caucasian males and 0.5% of Caucasian females. The prevalence varies with culture.

Blue color blindness (protanopia) is an inability to distinguish both blue and yellow, which are seen as white or gray. Protanopia is quite rare and has equal prevalence in males and females. It is common for young children to have blue/green confusion that becomes less pronounced in adulthood. Blue color deficiency often appears in people who have physical disorders such as liver disease or **diabetes mellitus**.

A total inability to distinguish colors (achromatopsia) is exceedingly rare. These affected individuals view the world in shades of gray. They frequently have poor visual acuity and are extremely sensitive to light (photophobia), which causes them to squint in ordinary light.

Researchers studying red/green color blindness in the United Kingdom reported an average prevalence of only 4.7% in one group. Only 1% of Eskimo males are color blind. Approximately 2.9% of boys from Saudi Arabia and 3.7% from India were found to have deficient color vision. Red/green color blindness may slightly increase an affected person's chances of contracting **leprosy**. Pre-term infants exhibit an increased prevalence of blue color blindness. Achromatopsia has a prevalence of about 1 in 33,000 in the United States and affects males and females equally.

Causes and symptoms

Red/green and blue color blindness appear to be located on at least two different gene locations. The majority of affected individuals are males. Females are carriers, but are not normally affected. This indicates that the X chromosome is one of the locations for color blindness. Male offspring of females who carry the altered gene have a 50-50 chance of being color-blind. The rare female that has red/green color blindness, or rarer still, blue color blindness, indicates there is an involvement of another gene. As of 2001, the location of this gene has not been identified.

Achromatopsia, the complete inability to distinguish color, is an autosomal recessive disease of the retina. This means that both parents have one copy of the altered gene but do not have the disease. Each of their children has a 25% chance of not having the gene, a 50% chance of having one altered gene (and, like the parents, being unaffected), and a 25% risk of having both the altered gene and the condition. In 1997, the achromatopsia gene was located on chromosome 2.

The inability to correctly identify colors is the only sign of color blindness. It is important to note that people with red/green or blue varieties of color blindness use other cues such as color saturation and object shape or location to distinguish colors. They can often distinguish

KEY TERMS

Achromatopsia—The inability to distinguish any colors.

Cones—Receptor cells that allow the perception of colors.

Deuteranopia—The inability or difficulty in distinguishing red/green colors.

Photophobia—An extreme sensitivity to light.

Protanopia—The inability of difficulty in distinguishing blue and yellow colors.

Retina—The light-sensitive layer of tissue in the back of the eye that receives and transmits visual signals to the brain through the optic nerve.

Rod—Photoreceptor that is highly sensitive to low levels of light and transmits images in shades of gray.

red or green if they can visually compare the colors. However, most have difficulty accurately identifying colors without any other references. Most people with any impairment in color vision learn colors, as do other young children. These individuals often reach adolescence before their visual deficiency is identified.

Color blindness is sometimes acquired. Chronic illnesses that can lead to color blindness include **Alzheimer's disease**, diabetes mellitus, **glaucoma**, leukemia, liver disease, chronic **alcoholism**, **macular degeneration**, **multiple sclerosis**, **Parkinson's disease**, sickle cell anemia, and **retinitis pigmentosa**. Accidents or strokes that damage the retina or affect particular areas of the brain eye can lead to color blindness. Some medications such as **antibiotics**, **barbiturates**, anti-tuberculosis drugs, high blood pressure medications, and several medications used to treat nervous disorders and psychological problems may cause color blindness. Industrial or environmental chemicals such as carbon monoxide, carbon disulfide, fertilizers, styrene, and some containing lead can cause loss of color vision. Occasionally, changes can occur in the affected person's capacity to see colors after age 60.

Diagnosis

There are several tests available to identify problems associated with color vision. The most commonly used is the American Optical/Hardy, Rand, and Ritter Pseudoisochromatic test. It is composed of several discs filled with colored dots of different sizes and colors. A person with normal color vision looking at a test item sees a number that is clearly located somewhere in the center of a circle of variously colored dots. A color-blind person is not able to distinguish the number.

The Ishihara test is comprised of eight plates that are similar to the American Optical Pseudoisochromatic test plates. The individual being tested looks for numbers among the various colored dots on each test plate. Some plates distinguish between red/green and blue color blindness. Individuals with normal color vision perceive one number. Those with red/green color deficiency see a different number. Those with blue color vision see yet a different number.

A third analytical tool is the Titmus II Vision Tester Color Perception test. The subject looks into a stereoscopic machine. The test stimulus most often used in professional offices contains six different designs or numbers on a black background, framed in a yellow border. Titmus II can test one eye at a time. However, its value is limited because it can only identify red/green deficiencies and is not highly accurate.

Treatment

There is no treatment or cure for color blindness. Most color vision deficient persons compensate well for their abnormality and usually rely on color cues and details that are not consciously evident to persons with typical color vision.

Inherited color blindness cannot be prevented. In the case of some types of acquired color deficiency, if the cause of the problem is removed, the condition may improve with time. But for most people with acquired color blindness, the damage is usually permanent.

Prognosis

Color blindness that is inherited is present in both eyes and remains constant over an individual's entire life. Some cases of acquired color vision loss are not severe, may appear in only one eye, and last for only a short time. Other cases tend to be progressive, becoming worse with time.

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American Academy of Ophthalmology. PO Box 7424, San Francisco, CA 94120-7424. (415) 561-8500. <http://www.eyenet.org>.

International Colour Vision Society: Forschungsstelle fuer Experimentelle Ophthalmologie. Roentgenweg 11, Tuebingen, D-72076. Germany <http://orlab.optom.unsw.edu.au/ICVS>.

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Colorectal cancer *see* **Colon cancer; Rectal cancer**

Colostomy

Definition

Ostomy is a surgical procedure used to create an opening for urine and feces to be released from the body. Colostomy refers to a surgical procedure where a portion of the large intestine is brought through the abdominal wall to carry stool out of the body.

Purpose

A colostomy is created as a means to treat various disorders of the large intestine, including **cancer**, obstruction, inflammatory bowel disease, ruptured diverticulum, **ischemia** (compromised blood supply), or traumatic injury. Temporary colostomies are created to divert stool from injured or diseased portions of the large intestine, allowing rest and healing. Permanent colostomies are performed when the distal bowel (bowel at the farthest distance) must be removed or is blocked and inoperable. Although colorectal cancer is the most common indication for a permanent colostomy, only about 10–15% of patients with this diagnosis require a colostomy.

Description

Surgery will result in one of three types of colostomies:

- End colostomy. The functioning end of the intestine (the section of bowel that remains connected to the upper gastrointestinal tract) is brought out onto the surface of the abdomen, forming the stoma by cuffing the intestine back on itself and suturing the end to the skin. A stoma is an artificial opening created to the surface of the body. The surface of the stoma is actually the lining of the intestine, usually appearing moist and pink. The distal portion of bowel (now connected only to the rectum) may be removed, or sutured closed and left in the abdomen. An end colostomy is usually a permanent ostomy, resulting from trauma, cancer or another pathological condition.
- Double–barrel colostomy. This colsotomy involves the creation of two separate stomas on the abdominal wall. The proximal (nearest) stoma is the functional end that is connected to the upper gastrointestinal tract and will drain stool. The distal stoma, connected to the rectum and also called a mucous fistula, drains small amounts of mucus material. This is most often a temporary colostomy performed to rest an area of bowel, and to be later closed.
- Loop colostomy. This colostomy is created by bringing a loop of bowel through an incision in the abdominal wall. The loop is held in place outside the abdomen by a plastic rod slipped beneath it. An incision is made in the bowel to allow the passage of stool through the loop colostomy. The supporting rod is removed approximately 7-10 days after surgery, when healing has occurred that will prevent the loop of bowel from

A colostomy is a surgical procedure in which a portion of the large intestine, or colon, is brought through the abdominal wall to carry feces out of the body. There are three types of colostomies: end colostomy, double-barrel colostomy, and loop colostomy. The loop colostomy is featured in the illustration above. *(Illustration by Electronic Illustrators Group.)*

retracting into the abdomen. A loop colostomy is most often performed for creation of a temporary stoma to divert stool away from an area of intestine that has been blocked or ruptured.

Preparation

As with any surgical procedure, the patient will be required to sign a consent form after the procedure is explained thoroughly. Blood and urine studies, along with various x rays and an electrocardiograph (EKG), may be ordered as the doctor deems necessary. If possible, the patient should visit an enterostomal therapist, who will mark an appropriate place on the abdomen for the stoma, and offer pre-operative education on ostomy management.

In order to empty and cleanse the bowel, the patient may be placed on a low residue diet for several days prior to surgery. A liquid diet may be ordered for at least the day before surgery, with nothing by mouth after midnight. A series of **enemas** and/or oral preparations (GoLytely or Colyte) may be ordered to empty the bowel of stool. Oral anti-infectives (neomycin, erythromycin, or kanamycin sulfate) may be ordered to decrease bacteria in the intestine and help prevent post-operative infection. A nasogastric tube is inserted from the nose to the stomach on the day of surgery or during surgery to remove gastric secretions and prevent **nausea and vomiting**. A urinary catheter (a thin plastic tube) may also be inserted to keep the bladder empty during surgery, giving more space in the surgical field and decreasing chances of accidental injury.

Aftercare

Post-operative care for the patient with a new colostomy, as with those who have had any major surgery, involves monitoring of blood pressure, pulse, respirations, and temperature. Breathing tends to be shallow because of the effect of anesthesia and the patient's reluctance to breathe deeply and experience **pain** that is caused by the abdominal incision. The patient is instructed how to support the operative site during deep breathing and coughing, and given pain medication as necessary. Fluid intake and output is measured, and the operative site is observed

for color and amount of wound drainage. The nasogastric tube will remain in place, attached to low intermittent suction until bowel activity resumes. For the first 24–48 hours after surgery, the colostomy will drain bloody mucus. Fluids and electrolytes are infused intravenously until the patient's diet is can gradually be resumed, beginning with liquids. Usually within 72 hours, passage of gas and stool through the stoma begins. Initially the stool is liquid, gradually thickening as the patient begins to take solid foods. The patient is usually out of bed in 8–24 hours after surgery and discharged in 2–4 days.

A colostomy pouch will generally have been placed on the patient's abdomen, around the stoma, during surgery. During the hospital stay, the patient and his or her caregivers will be educated on how to care for the colostomy. Determination of appropriate pouching supplies and a schedule of how often to change the pouch should be established. Regular assessment and meticulous care of the skin surrounding the stoma is important to maintain an adequate surface on which to apply the pouch. Some patients with colostomies are able to routinely irrigate the stoma, resulting in regulation of bowel function; rather than needing to wear a pouch, these patients may need only a dressing or cap over their stoma. Often, an enterostomal therapist will visit the patient at home after discharge to help with the patient's resumption of normal daily activities.

KEY TERMS

Diverticulum—Pouches that project off the wall of the intestine, visible as opaque on an x ray after the patient has swallowed a contrast (dye) substance.

Embolism—Blockage of a blood vessel by any small piece of material traveling in the blood. The emboli may be caused by germs, air, blood clots, or fat.

Enema—Insertion of a tube into the rectum to infuse fluid into the bowel and encourage a bowel movement. Ordinary enemas contain tap water, mixtures of soap and water, glycerine and water, or other materials.

Intestine—Commonly called the bowels, divided into the small and large intestine. They extend from the stomach to the anus. The small intestine is about 20 ft (6 m) long. The large intestine is about 5 ft (1.5 m) long.

Ischemia—A compromise in blood supply delivered to body tissues that causes tissue damage or death.

Ostomy—A surgically created opening in the abdomen for elimination of waste products (urine or stool).

Risks

Potential complications of colostomy surgery include:

- excessive bleeding
- surgical wound infection
- thrombophlebitis (inflammation and blood clot to veins in the legs)
- pneumonia
- pulmonary **embolism** (blood clot or air bubble in the lungs' blood supply)

Normal results

Complete healing is expected without complications. The period of time required for recovery from the surgery may vary depending of the patient's overall health prior to surgery. The colostomy patient without other medical complications should be able to resume all daily activities once recovered from the surgery.

Abnormal results

The doctor should be made aware of any of the following problems after surgery:

- increased pain, swelling, redness, drainage, or bleeding in the surgical area
- headache, muscle aches, **dizziness,** or **fever**
- increased abdominal pain or swelling, **constipation**, nausea or vomiting or black, tarry stools

Stomal complications to be monitored include:

- Death (necrosis) of stomal tissue. Caused by inadequate blood supply, this complication is usually visible 12–24 hours after the operation and may require additional surgery.
- Retraction (stoma is flush with the abdomen surface or has moved below it). Caused by insufficient stomal length, this complication may be managed by use of special pouching supplies. Elective revision of the stoma is also an option.
- Prolapse (stoma increases length above the surface of the abdomen). Most often results from an overly large opening in the abdominal wall or inadequate fixation of the bowel to the abdominal wall. Surgical correction is required when blood supply is compromised.
- Stenosis (narrowing at the opening of the stoma). Often associated with infection around the stoma or scarring. Mild stenosis can be removed under local anesthesia.

Severe stenosis may require surgery for reshaping the stoma.

- Parastomal **hernia** (bowel causing bulge in the abdominal wall next to the stoma). This is due to placement of the stoma where the abdominal wall is weak or creation of an overly large opening in the abdominal wall. The use of an ostomy support belt and special pouching supplies may be adequate. If severe, the defect in the abdominal wall should be repaired and the stoma moved to another location.

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Colposcopy

Definition

Colposcopy is a procedure that allows a physician to take a closer look at a woman's cervix and vagina using a special instrument called a colposcope. It is used to check for precancerous or abnormal areas. The colposcope can magnify the area between 10 and 40 times; some devices also can take photographs.

Purpose

The colposcope helps to identify abnormal areas of the cervix or vagina so that small pieces of tissue (biopsies) can be taken for further analysis.

Colposcopy is used to identify or rule out the existence of any precancerous conditions in the cervical tissue. If a **PAP test** shows abnormal cell growth, further testing, such as colposcopy, often is required. A PAP test is a screening test that involves scraping cells from the outside of the cervix. If abnormal cells are found, the physician will attempt to find the area that produced the abnormal cells and remove it for further study (biopsy). Only then can a diagnosis be made.

A colposcopy makes it possible for a physician to view this healthy cervix without surgery. *(Photograph by Dr. P. Marazzi, Custom Medical Stock Photo. Reproduced by permission.)*

Colposcopy may also be performed if the cervix looks abnormal during a routine examination. It may also be suggested for women with **genital warts** and for diethylstilbestrol (DES) daughters (women whose mothers took DES when pregnant with them).

Precautions

Women who are pregnant, or who suspect that they are pregnant, must tell their doctor before the procedure begins. Pregnant women can, and should, have a colposcopy if they have an abnormal PAP test. However, special precautions must be taken during biopsy of the cervix.

Description

A colposcopy is performed in a physician's office and is similar to a regular gynecologic exam. An instrument called a speculum is used to hold the vagina open, and the gynecologist looks at the cervix and vagina through the colposcope instead simply by eye, as in a routine examination.

The colposcope is placed outside the patient's body and never touches the skin. The cervix and vagina are swabbed with dilute acetic acid (vinegar). The solution highlights abnormal areas by turning them white (instead of a normal pink color). Abnormal areas can also be identified by looking for a characteristic pattern made by abnormal blood vessels.

This colposcopic view of the cervix reveals CIN 2 dysplasia, or abnormal growth of cells. This is the second stage in the development of cervical cancer. *(Custom Medical Stock Photo. Reproduced by permission.)*

If any abnormal areas are seen, the doctor will take a biopsy of the tissue, a common procedure that takes about 15 minutes. Several samples might be taken, depending on the size of the abnormal area. A biopsy may cause temporary discomfort and cramping, which usually go away within a few minutes. If the abnormal area appears to extend inside the cervical canal, a scraping of the canal may be done. The biopsy results are usually available within a week.

If the tissue sample indicates abnormal growth (dysplasia) or precancer, and if the entire abnormal area can be seen, the doctor can destroy the tissue using one of several procedures, including ones that use high heat (diathermy), extreme cold (cryosurgery), or lasers. Another procedure, called a loop electrosurgical excision (LEEP), uses low-voltage high-frequency radio waves to excise tissue. If any of the abnormal tissue is within the cervical canal, a cone biopsy (removal of a conical section of the cervix for inspection) will be needed.

Preparation

Colposcopy is a painless procedure that does not require any anesthetic medication. If a biopsy is done, there may be mild cramps or a sharp pinching when the tissue is removed. To lessen this **pain**, your doctor may recommend 800 mg of ibuprofen (Motrin) taken the night before and the morning of the procedure (no later than 30 minutes before the appointment). Patients who are pregnant or allergic to **aspirin** or ibuprofen can take two tablets of **acetaminophen** (Tylenol) instead.

Aftercare

If a biopsy was done, there may be a dark vaginal discharge afterwards. After the sample is removed, the doctor applies Monsel's solution to the area to stop the bleeding. When this mixes with blood it creates a black fluid that looks like coffee grounds for a couple of days after the procedure. It is also normal to have some spotting after a colposcopy.

Patients should not use tampons or put anything else in the vagina for at least a week after the procedure, or until the doctor says it's safe. In addition, women should

KEY TERMS

Biopsy—Removal of sample of abnormal tissue for more extensive examination under a microscope.

Cervix—The neck of the uterus.

Cryosurgery—Freezing and destroying abnormal cells.

DES—The abbreviation for diethylstilbestrol, a synthetic form of estrogen that was widely prescribed to women from 1940 to 1970 to prevent complications. It was linked to several serious birth defects and disorders of the reproductive system in daughters of women who took DES. In 1971, the FDA suggested it not be used during pregnancy and banned its use in 1979 as a growth promoter in livestock.

Diathermy—Also called electrocautery, this is a procedure that heats and destroys abnormal cells. It is gradually being replaced by cryosurgery, lasers, or LEEP.

Human papilloma virus—A virus that causes common warts of the hands and feet, as well as lesions in the genital and vaginal area. More than 50 types of HPV have been identified, some of which are linked to cancerous and precancerous conditions, including cancer of the cervix.

Loop electrosurgical excision (LEEP)—A procedure that can help diagnose and treat cervical abnormalities, using a thin wire loop that emits a low-voltage high-frequency radio wave that can excise tissue. It is considered better than either lasers or electrocautery because it can both diagnose and treat precancerous cells or early stage cancer at the same time.

PAP test—The common term for the Papanicolaou test, a simple smear method of examining stained cells to detect cancer of the cervix.

Speculum—A retractor used to separate the walls of the vagina to make visual examination easier.

not have sex or douche for at least a week after the procedure because of the risk of infection.

Risks

Occasionally, patients may have bleeding or infection after biopsy. Bleeding is usually controlled with a topical medication.

A patient should call her doctor right away if she notices any of the following symptoms:

- heavy vaginal bleeding (more than one sanitary pad an hour)
- fever, chills, or an unpleasant vaginal odor
- lower abdominal pain.

Normal results

If visual inspection shows that the surface of the cervix is smooth and pink, this is considered normal. If abnormal areas are found and biopsied and the results show no indication of **cancer**, a precancerous condition, or other disease, this also is considered normal.

Abnormal results

Abnormal conditions that can be detected using colposcopy and biopsy include precancerous tissue changes (cervical dysplasia), cancer, and cervical **warts** (human papilloma virus).

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American Society for Colposcopy and Cervical Pathology. 20 W. Washington St., Ste. #1, Hagerstown, MD 21740. (800) 787-7227. <http://www.asccp.org>.

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Coma

Definition

Coma, from the Greek word "koma," meaning deep sleep, is a state of extreme unresponsiveness, in which an individual exhibits no voluntary movement or behavior. Furthermore, in a deep coma, even painful stimuli (actions which, when performed on a healthy individual, result in reactions) are unable to affect any response, and normal reflexes may be lost.

Description

Coma lies on a spectrum with other alterations in consciousness. The level of consciousness required by, for example, someone reading this passage lies at one extreme end of the spectrum, while complete brain **death** lies at the other end of the spectrum. In between are such states as obtundation, drowsiness, and stupor. All of these are conditions which, unlike coma, still allow the individual to respond to stimuli, although such a response may be brief and require stimulus of greater than normal intensity.

In order to understand the loss of function suffered by a comatose individual, it is necessary to first understand the important characteristics of the conscious state. Consciousness is defined by two fundamental elements: awareness and arousal.

Awareness allows one to receive and process all the information communicated by the five senses, and thus relate to oneself and to the outside world. Awareness has both psychological and physiological components. The psychological component is governed by an individual's mind and mental processes. The physiological component refers to the functioning of an individual's brain, and therefore that brain's physical and chemical condition. Awareness is regulated by cortical areas within the cerebral hemispheres, the outermost layer of the brain that separates humans from other animals by allowing for greater intellectual functioning.

Arousal is regulated solely by physiological functioning and consists of more primitive responsiveness to the world, as demonstrated by predictable reflex (involuntary) responses to stimuli. Arousal is maintained by the reticular activating system (RAS). This is not an anatomical area of the brain, but rather a network of structures (including the brainstem, the medulla, and the thalamus) and nerve pathways, which function together to produce and maintain arousal.

Causes and symptoms

Coma, then, is the result of something that interferes with the functioning of the cerebral cortex and/or the functioning of the structures which make up the RAS. In fact, a huge and varied number of conditions can result in coma. A good way of categorizing these conditions is to consider the anatomic and the metabolic causes of coma. Anatomic causes of coma are those conditions that disrupt the normal physical architecture of the brain structures responsible for consciousness, either at the level of

A side-view of the brain, showing movement of the reticular activating substance (RAS) essential to consciousness

Diffuse and bilateral damage to the cerebral cortex (relative preservation of brain-stem reflexes)

Possible causes
- Damage due to lack of oxygen or restricted blood flow, perhaps resulting from cardiac arrest, an anaesthetic accident, or shock
- Damage incurred from metabolic processes associated with kidney or liver failure, or with hypoglycemia
- Trauma damage
- Damage due to a bout with meningitis, encephalomyelitis, or a severe systemic infection

Mass lesions in this region resulting in compression of the brain-stem and damage to the reticular activating substance (RAS)

Structural lesions within this region also resulting in compression of the brain-stem and damage to the reticular activating substance (RAS)

Possible causes • Cerebellar tumors, abscesses, or hemorrhages

Lesions within the brain-stem directly suppressing the reticular activating substance (RAS)

Possible causes • Drug overdosage

The four brain conditions that result in coma. *(Illustration by Hans & Cassady.)*

KEY TERMS

Anatomic—Related to the physical structure of an organ or organism.

Metabolic—Refers to the chemical processes of an organ or organism.

Neuron—The cells within the body which make up the nervous system, specifically those along which information travels.

Physiological—Pertaining to the functioning of an organ, as governed by the interactions between its physical and chemical conditions.

Psychological—Pertaining to the mind, its mental processes, and its emotional makeup.

Stimulus/stimuli—Action or actions performed on an individual which predictably provoke(s) a reaction.

the cerebal cortex or the brainstem, while metabolic causes of coma consist of those conditions that change the chemical environment of the brain, thereby adversely affecting function.

There are many metabolic causes of coma, including:

- A decrease in the delivery to the brain of substances necessary for appropriate brain functioning, such as oxygen, glucose (sugar), and sodium.
- The presence of certain substances that disrupt the functioning of neurons. Drugs or alcohol in toxic quantities can result in neuronal dysfunction, as can substances normally found in the body, but that, due to some diseased state, accumulate at toxic levels. Accumulated substances that might cause coma include ammonia due to liver disease, ketones due to uncontrolled diabetes, or carbon dioxide due to a severe **asthma** attack.
- The changes in chemical levels in the brain due to the electrical derangements caused by seizures.

Diagnosis

As in any neurologic condition, history and examination form the cornerstone of diagnosis when the patient is in a coma; however, history must be obtained from family, friends, or EMS. The Glasgow Coma Scale is a system of examining a comatose patient. It is helpful for evaluating the depth of the coma, tracking the patient's progress, and predicting (somewhat) the ultimate outcome of the coma. The Glasgow Coma Scale assigns a different number of points for exam results in three different categories: opening the eyes, verbal response (using words or voice to respond), and motor response (moving a part of the body). Fifteen is the largest possible number of total points, indicating the highest level of functioning. The highest level of functioning would be demonstrated by an individual who spontaneously opens his/her eyes, gives appropriate answers to questions about his/her situation, and can carry out a command (such as "move your leg" or "nod your head"). Three is the least possible number of total points and would be given to a patient for whom not even a painful stimulus is sufficient to provoke a response. In the middle are those patients who may be able to respond, but who require an intense or painful stimulus, and whose response may demonstrate some degree of brain malfunctioning (such as a person whose only response to **pain** in a limb is to bend that limb in toward the body). When performed as part of the admission examination, a Glasgow score of three to five points often suggests that the patient has likely suffered fatal brain damage, while eight or more points indicates that the patient's chances for recovery are good. Expansion of the pupils and respiratory pattern are also important. Metabolic causes of coma are diagnosed from blood work and **urinalysis** to evaluate blood chemistry, drug screen, and blood cell abnormalities that may indicate infection. Anatomic causes of coma are diagnosed from **computed tomography scans** (CT) or **magnetic resonance imaging** (MRI) scans.

Treatment

Coma is a medical emergency, and attention must first be directed to maintaining the patient's respiration and circulation, using intubation aand ventilation, administration of intravenous fluids or blood as needed, and other supportive care. If head trama has not been excluded, the neck should be stablized in the event of fracture. It is obviously extremely important for a physician to determine quickly the cause of a coma, so that potentially reversible conditions are treated immediately. For example, an infection may be treated with **antibiotics**; a **brain tumor** may be removed; and brain swelling from an injury can be reduced with certain medications. Various metabolic disorders can be addressed by supplying the individual with the correct amount of oxygen, glucose, or sodium; by treating the underlying disease in liver disease, asthma, or diabetes; and by halting seizures with medication. Because of their low incidence of side effects and potential for prompt reversal of coma in certain conditions, glucose, the B-vitamin thiamine, and Narcan (to counteract any narcotic-type drugs) are routinely given.

Prognosis

Some conditions that cause coma can be completely reversed, restoring the individual to his or her original level of functioning. However, if areas of the brain have been sufficiently damaged due to the severity or duration of the condition which led to the coma, the individual may recover from the coma with permanent disabilities, or may even never regain consciousness. Take, for example, the situation of someone whose coma was caused by brain injury in a car accident. Such an injury can result in one of three outcomes. In the event of a less severe brain injury, with minimal swelling, an individual may indeed recover consciousness and regain all of his or her original abilities. In the event of a more severe brain injury, with swelling that resulted in further pressure on areas of the brain, an individual may regain consciousness, but may have some degree of impairment. The impairment may be physical (such as **paralysis** of a leg) or may even result in a change in the individual's intellectual functioning and/or personality. The most severe types of brain injury, short of death, result in states in which the individual loses all ability to function and remains deeply unresponsive. An individual who has suffered such a severe brain injury may remain in a coma indefinitely. This condition is termed persistent **vegetative state**.

Outcome from a coma is therefore quite variable and depends a great deal on the cause and duration of the coma. In the case of drug poisonings, extremely high rates of recovery can be expected following prompt medical attention. Patients who have suffered head injuries tend to do better than do patients whose coma was caused by other types of medical illnesses. Leaving out those people whose coma followed drug **poisoning**, only about 15% of patients who remain in a coma for more than just a few hours make a good recovery. Those adult patients who remain in a coma for greater than four weeks have almost no chance of eventually regaining their previous level of functioning. On the other hand, children and young adults have regained functioning even after two months in a coma.

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American Academy of Neurology. 1080 Montreal Ave., St. Paul, MN 55116. (612) 695-1940. <http://www.aan.com>.

Coma Recovery Association, Inc. 570 Elmont Rd., Suite 104, Elmont, NY 11003. (516) 355-0951.

Rosalyn Carson-DeWitt, MD

Combat neurosis *see* **Post-traumatic stress disorder**

Common cold

Definition

The common cold is a viral infection of the upper respiratory system, including the nose, throat, sinuses, eustachian tubes, trachea, larynx, and bronchial tubes. Although over 200 different viruses can cause a cold, 30–50% are caused by a group known as rhinoviruses. Almost all colds clear up in less than two weeks without complications.

Description

Colds, sometimes called rhinovirus or coronavirus infections, are the most common illness to strike any part of the body. It is estimated that the average person has more than 50 colds during a lifetime. Anyone can get a cold, although pre-school and grade school children catch them more frequently than adolescents and adults. Repeated exposure to viruses causing colds creates partial immunity.

Although most colds resolve on their own without complications, they are a leading cause of visits to the doctor and of time lost from work and school. Treating symptoms of the common cold has given rise to a multi-million dollar industry in over-the-counter medications.

Cold season in the United States begins in early autumn and extends through early spring. Although it is not true that getting wet or being in a draft causes a cold (a person has to come in contact with the virus to catch a cold), certain conditions may lead to increased susceptibility. These include:

- fatigue and overwork
- emotional **stress**
- poor **nutrition**
- **smoking**
- living or working in crowded conditions

Colds make the upper respiratory system less resistant to bacterial infection. Secondary bacterial infection may lead to middle ear infection, **bronchitis**, **pneumonia**, sinus infection, or **strep throat**. People with chronic lung disease, **asthma**, diabetes, or a weakened immune system are more likely to develop these complications.

Causes and symptoms

Colds are caused by more than 200 different viruses. The most common groups are rhinoviruses and coronaviruses. Different groups of viruses are more infectious at different seasons of the year, but knowing the exact virus causing the cold is not important in treatment.

People with colds are contagious during the first two to four days of the infection. Colds pass from person to person in several ways. When an infected person coughs, sneezes, or speaks, tiny fluid droplets containing the virus are expelled. If these are breathed in by other people, the virus may establish itself in their noses and airways.

Colds may also be passed through direct contact. If a person with a cold touches his runny nose or watery eyes, then shakes hands with another person some of the virus is transferred to the uninfected person. If that person then touches his mouth, nose, or eyes, the virus is transferred to an environment where it can reproduce and cause a cold.

Finally, cold viruses can be spread through inanimate objects (door knobs, telephones, toys) that become contaminated with the virus. This is a common method of transmission in child care centers. If a child with a cold touches his runny nose, then plays with a toy, some of the virus may be transferred to the toy. When another child plays with the toy a short time later, he may pick up some of the virus on his hands. The second child then touches his contaminated hands to his eyes, nose, or mouth and transfers some of the cold virus to himself.

Once acquired, the cold virus attaches itself to the lining of the nasal passages and sinuses. This causes the infected cells to release a chemical called histamine. Histamine increases the blood flow to the infected cells, causing swelling, congestion, and increased mucus production. Within one to three days the infected person begins to show cold symptoms.

The first cold symptoms are a tickle in the throat, runny nose, and sneezing. The initial discharge from the nose is clear and thin. Later it changes to a thick yellow or greenish discharge. Most adults do not develop a **fever** when they catch a cold. Young children may develop a low fever of up to 102°F (38.9°C).

In addition to a runny nose and fever, signs of a cold include coughing, sneezing, nasal congestion, **headache**, muscle ache, chills, **sore throat**, hoarseness, watery eyes, tiredness, and lack of appetite. The **cough** that accompanies a cold is usually intermittent and dry.

Most people begin to feel better four to five days after their cold symptoms become noticeable. All symptoms are generally gone within ten days, except for a dry cough that may linger for up to three weeks.

Colds make people more susceptible to bacterial infections such as strep throat, middle ear infections, and sinus infections. A person whose cold does not begin to improve within a week; or who experiences chest **pain**, fever for more than a few days, difficulty breathing, bluish lips or fingernails, a cough that brings up greenish-yellow or grayish sputum, skin rash, swollen glands, or whitish spots on the tonsils or throat should consult a doctor to see if they have acquired a secondary bacterial infection that needs to be treated with an antibiotic.

People who have **emphysema**, chronic lung disease, diabetes, or a weakened immune system—either from diseases such as **AIDS** or leukemia, or as the result of medications, (**corticosteroids**, **chemotherapy** drugs)—should consult their doctor if they get a cold. People with these health problems are more likely to get a secondary infection.

Diagnosis

Colds are diagnosed by observing a person's symptoms. There are no laboratory tests readily available to detect the cold virus. However, a doctor may do a **throat culture** or blood test to rule out a secondary infection.

Influenza is sometimes confused with a cold, but flu causes much more severe symptoms and generally a fever. **Allergies** to molds or pollens also can make the nose run. Allergies are usually more persistent than the common cold. An allergist can do tests to determine if the cold-like symptoms are being caused by an allergic reaction. Also, some people get a runny nose when they go outside in winter and breathe cold air. This type of runny nose is not a symptom of a cold.

Treatment

There are no medicines that will cure the common cold. Given time, the body's immune system will make antibodies to fight the infection, and the cold will be resolved without any intervention. **Antibiotics** are useless against a cold. However, a great deal of money is spent by pharmaceutical companies in the United States promoting products designed to relieve cold symptoms. These products usually contain **antihistamines**, **decongestants**, and/or pain relievers.

Antihistamines block the action of the chemical histamine that is produced when the cold virus invades the

cells lining the nasal passages. Histamine increases blood flow and causes the cells to swell. Antihistamines are taken to relieve the symptoms of sneezing, runny nose, itchy eyes, and congestion. Side effects are **dry mouth** and drowsiness, especially with the first few doses. Antihistamines should not be taken by people who are driving or operating dangerous equipment. Some people have allergic reactions to antihistamines. Common over-the-counter antihistamines include Chlor-Trimeton, Dimetapp, Tavist, and Actifed. The generic name for two common antihistamines are chlorpheniramine and diphenhydramine.

Decongestants work to constrict the blood flow to the vessels in the nose. This can shrink the tissue, reduce congestion, and open inflamed nasal passages, making breathing easier. Decongestants can make people feel jittery or keep them from sleeping. They should not be used by people with heart disease, high blood pressure, or **glaucoma**. Some common decongestants are Neo-Synepherine, Novafed, and Sudafed. The generic names of common decongestants include phenylephrine, phenylpropanolamine, pseudoephedrine, and in nasal sprays naphazoline, oxymetazoline and xylometazoline.

Many over the counter medications are combinations of both antihistamines and decongestants; an ache and pain reliever, such as **acetaminophen** (Datril, Tylenol, Panadol) or ibuprofen (Advil, Nuprin, Motrin, Medipren); and a cough suppressant (dextromethorphan). Common combination medications include Tylenol Cold and Flu, Triaminic, Sudafed Plus, and Tavist D. **Aspirin** should not be given to children with a cold because of its association with a risk of **Reye's syndrome**, a serious disease.

Nasal sprays and nose drops are other products promoted for reducing nasal congestion. These usually contain a decongestant, but the decongestant can act more quickly and strongly than ones found in pills or liquids because it is applied directly in the nose. Congestion returns after a few hours.

People can become dependent on nasal sprays and nose drops. If used for a long time, users may suffer withdrawal symptoms when these products are discontinued. Nasal sprays and nose drops should not be used for more than a few days. Check the label for recommendations on length and frequency of use.

People react differently to different cold medications and may find some more helpful than others. A medication may be effective initially, then lose some of its effectiveness. Children sometimes react differently than adults. Over-the-counter cold remedies should not be given to infants without consulting a doctor first.

Cold Remedies

	Symptoms	Side effects
Antihistamines	Congestion Itchy eyes Runny nose Sneezing Stuffy nose	Drowsiness Dry mouth and eyes
Decongestants	Congestion Stuffy nose	Insomnia Rapid heart beat Stimulation

Care should be taken not to exceed the recommended dosages, especially when combination medications or nasal sprays are taken. Individuals should determine whether they wish to use any of these drugs. None of them shorten or cure a cold. At best they help a person feel more comfortable. People who are confused about the drugs in any over-the-counter cold remedies should ask their pharmacist for an explanation.

In addition to the optional use of over the counter cold remedies, there are some self-care steps that people can take to ease their discomfort. These include:

- drinking plenty of fluids, but avoiding acidic juices, which may irritate the throat
- gargling with warm salt water—made by adding one teaspoon of salt to 8 oz of water—for a sore throat
- not smoking
- getting plenty of rest
- using a cool-mist room humidifier to ease congestion and sore throat
- rubbing Vaseline or other lubricant under the nose to prevent irritation from frequent nose blowing
- for babies too young to blow their noses, the mucus should be suctioned gently with an infant nasal aspirator, it may be necessary to soften the mucus first with a few drops of salt water

Alternative treatment

Alternative practitioners emphasize that people get colds because their immune systems are weak. They point out that everyone is exposed to cold viruses, but not everyone gets every cold. The difference seems to be in the ability of the immune system to fight infection. Prevention focuses on strengthening the immune system by eating a healthy diet low in sugars and high in fresh fruits and vegetables, practicing **meditation** to reduce stress, and getting regular moderate **exercise**.

Once cold symptoms appear, some naturopathic practitioners believe the symptoms should be allowed to

KEY TERMS

Bronchial tubes—The major airways to the lungs and their main branches.

Coronavirus—a genus of viruses that cause respiratory disease and gastroenteritis.

Corticosteroids—A group of hormones produced naturally by the adrenal gland or manufactured synthetically. They are often used to treat inflammation. Examples include cortisone and prednisone.

Eustachian tube—A thin tube between the middle ear and the pharnyx. Its purpose is to equalize pressure on either side of the ear drum.

Rhinovirus—A virus that infects the upper respiratory system and causes the common cold.

run their course without interference. Others suggest the following:

- Inhaling a steaming mixture of lemon oil, thyme oil, eucalyptus, and tea tree oil (*Melaleuca* spp.). (**Aromatherapy**)
- Gargling with a mixture of water, salt, and turmeric powder or astringents such as alum, sumac, sage, and bayberry to ease a sore throat. (**Ayurvedic medicine**)
- Taking coneflower (*Echinacea* spp.) or goldenseal (*Hydrastis canadensis*). Other useful herbs to reduce symptoms include yarrow (*Achillea millefolium*), eyebright (*Euphrasia officinalis*), garlic (*Allium sativum*), and onions (*Allium cepa*). (Herbal)
- Microdoses of *Viscue album*, *Natrum muriaticum*, *Allium cepa*, or *Nux vomica*. (**Homeopathy**)
- Taking yin chiao (sometimes transliterated as yinquiao) tablets that contain honeysuckle and forsythia when symptoms appear. Natural herb loquat syrup for cough and sinus congestion and Chinese ephedra (*ma-huang*) for runny nose. (Chinese traditional medicine)
- The use of zinc lozenges every two hours along with high doses of vitamin C is suggested. Some practitioners also suggest eliminating dairy products for the duration of the cold. (Nutritional therapy).

The use of zinc lozenges may be moving toward acceptance by practitioners of traditional medicine. In 1996 the Cleveland Clinic tested zinc gluconate lozenges and found using zinc in the first 24 hours after cold symptoms occurred shortened the duration of symptoms. The mechanism by which zinc worked was not clear, but additional studies are underway.

Prognosis

Given time, the body will make antibodies to cure itself of a cold. Most colds last a week to 10 days. Most people start feeling better within four or five days. Occasionally a cold will lead to a secondary bacterial infection that causes strep throat, bronchitis, pneumonia, sinus infection, or a middle ear infection. These conditions usually clear up rapidly when treated with an antibiotic.

Prevention

It is not possible to prevent colds because the viruses that cause colds are common and highly infectious. However, there are some steps individuals can take to reduce their spread. These include:

- washing hands well and frequently, especially after touching the nose or before handling food
- covering the mouth and nose when sneezing
- disposing of used tissues properly
- avoiding close contact with someone who has a cold during the first two to four days of their infection
- not sharing food, eating utensils, or cups with anyone
- avoiding crowded places where cold germs can spread
- eating a healthy diet and getting adequate sleep

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Tish Davidson

Common variable immunodeficiency

Definition

Common variable **immunodeficiency** is an immunodeficiency disorder characterized by a low level of antibodies. Patients with this disease are subject to recurring infections.

Description

Immunodeficiency means that the immune system is deficient in one or more of its components and is unable to respond effectively. Common variable immunodeficiency is the most common of the immunodeficiency disorders. Patients with this disease have frequent infections, especially those caused by the same microorganism. Recurring infections are an indication that the immune system is not responding normally and developing immunity to reinfection. Patients with common variable immunodeficiency have a normal number of B cells, the lymphocytes that make antibodies. In approximately one-third of these patients, the number of B cells in the blood that have IgG antibodies on their surface is lower than normal, but there are normal numbers of B cells in their bone marrow. B cells with IgG antibodies on their surface are capable of responding to microorganisms. The lack of IgG on the surface of the B cells means that they are not prepared to fight infection. The T-cell lymphocytes, those cells responsible for cellular immunity, are usually normal, although some cell signal components may be lacking.

Causes and symptoms

The cause of common variable immunodeficiency is not known, although some forms seem to be hereditary. The main symptom is recurring infections that tend to be chronic rather than acute. Patients may also develop **diarrhea** and, as a consequence of the diarrhea, do not absorb food efficiently. This can lead to malnourishment that can aggravate the disorder. Common variable immunodeficiency normally appears in children after the age of 10. **Autoimmune disorders** such as **rheumatoid arthritis**, **thyroiditis**, and **systemic lupus erythematosus** and certain cancers such as lymphomas and leukemias may be associated with common variable immunodeficiency.

Diagnosis

As is true of most immunodeficiency disorders, one of the first signs that the patient has the condition is recurrent infections. Patients with common variable immunodeficiency are subject to recurrent infections, especially those caused by microbes that don't normally cause disease in normal persons. The main diagnostic test that distinguishes common variable immunodeficiency from other immunodeficiency diseases is the low antibody level despite the normal number of B cells. Antibody levels are tested in the serum by a procedure called electrophoresis. This procedure both quantifies the amount of antibody present and identifies the various classes of antibodies. The main class of antibody for fighting infectious diseases is IgG.

Treatment

There is no treatment that will cure the disorder. Treatment for common variable immunodeficiency aims at boosting the body's immune response and preventing or controlling infections. Immune serum, obtained from donated blood, is given as a source of antibodies to boost the immune response. Immune serum is obtained from donated blood. It contains whatever antibodies the donors had in their blood. Consequently, it may not contain all the antibodies that the patient needs and may lack antibodies specific for some of the recurring infections that these patients suffer. **Antibiotics** are used routinely at the first sign of an infection to help the patient eliminate infectious microorganisms.

Prognosis

With good medical care, people with common variable immunodeficiency usually have a normal life span.

Prevention

The disease itself cannot be prevented, but patients and their families can take precautions to prevent the recurrent infections commonly associated with it. For example, good hygiene and **nutrition** are important, as is avoiding crowds or other people who have active infections.

Resources

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John T. Lohr, PhD

Complement deficiencies

Definition

Complement deficiencies are a group of disorders in which there is a reduced level of specific proteins, complement, involved in proper immune functioning.

Description

Complement plays several functions in immunity. It can poke holes in bacteria, kill bacteria that are first targeted by antibodies, or, working with antibodies, point

KEY TERMS

Autoimmune diseases—A group of diseases, like rheumatoid arthritis and systemic lupus erythematosus, in which immune cells turn on the body, attacking various tissues and organs.

Hereditary angioedema—A complement deficiency characterized by lymphatic vessel blockages that cause temporary swelling (edema) of areas of the skin, mucous membranes, and, sometimes, internal organs.

Leucocyte adhesion deficiency syndrome—A complement deficiency syndrome characterized by recurrent infections of the skin, mucous membranes, and gastrointestinal tract and the absence of pus formation. This disorder is sometimes apparent at birth when separation of the umbilical cord takes longer than normal.

Meningitis—An inflammation of the lining surrounding the brain and spinal cord.

Paroxysmal nocturnal hemoglobinuria (PNH)—A rare complement disorder characterized by episodes of red blood cell destruction (hemolysis) and blood in the urine (hemoglobinuria) that is worse at night.

Systemic lupus erythematosus—An autoimmune disease in which the immune system attacks the body's connective tissue. A butterfly-shaped facial rash is characteristic.

White blood cells—Cells that are key in immune defense. There are various types, including those that engulf and kill invading bacteria.

out which bacteria need to be engulfed by white blood cells. Without sufficient complement, the body is prone to frequent infections, like **pneumonia** or **meningitis**, or other illnesses, including autoimmune diseases, like **systemic lupus erythematosus**. Since there are more than 20 different types of complement, the disease that results depends on the specific complement that is lacking.

Cause and symptoms

A defect in the complement system can be genetic, but a secondary complement deficiency can also result from ailments that involve a lot of protein loss, including serious **burns**, liver or kidney disease, and autoimmune diseases, like lupus. Symptoms vary depending on the specific complement deficiency and the disease that results. Some people remain healthy with no symptoms at all. Others, who suffer from frequent infections, may develop a high **fever**, **diarrhea**, headaches with a stiff neck, or a **cough** with chest **pain**. If an autoimmune disease develops, like lupus, the person may lose weight, suffer from a rash, and have joint pain. Other symptoms of complement deficiency diseases (like hereditary angioedema, paroxysmal nocturnal hemoglobinuria, or leukocyte adhesion deficiency syndrome) include abdominal and back pain, skin infections, **edema** or swelling of the face and red bumps on the skin.

Diagnosis

There are blood tests that determine the activity of the complement system. The two most common screening tests, CH50 and APH50, tell the physician which group of complement components have a defect. More specific blood tests for the individual complement components (e.g., C3 or C4 complement) are then performed. Other specialized blood tests, including C1 esterase level, Ham test, and a white **blood count**, may also be performed.

Treatment

There is no way to treat the actual complement deficiency. However, **antibiotics** are used to treat infections and vaccinations are given to reduce the risk of disease. Often, the person is vaccinated against infections that include **influenza**, pneumonia, and meningitis. In some cases, (e.g., a specific disease called paroxysmal nocturnal hemoglobinuria [PNH]), a bone marrow transplant may be recommended.

Alternative treatment

There is no alternative treatment for complement problems.

Prognosis

Since complement deficiencies include a wide range of disorders, the prognoses can also vary widely. Some patients remain healthy their entire life. Others are hospitalized frequently because of infections which, if not properly treated, can be fatal. Those with autoimmune diseases could have a normal life expectancy. There are some complement deficiencies, that have a high mortality rate. In those cases, **death** may occur within 10 years after diagnosis.

Prevention

There is currently no way to prevent complement deficiencies.

Resources

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Jeanine Barone, Physiologist

Complete blood count *see* **Blood count**

Computed tomography scans

Definition

Computed tomography (CT) scans are completed with the use of a 360-degree x-ray beam and computer production of images. These scans allow for cross-sectional views of body organs and tissues.

Purpose

CT scans are used to image a wide variety of body structures and internal organs. Since the 1990s, CT equipment has become more affordable and available. In some diagnoses, CT scans have become the first imaging exam of choice. Because the computerized image is so sharp, focused, and three-dimensional, many tissues can be better differentiated than on standard x rays. Common CT indications include:

- Sinus studies. The CT scan can show details of **sinusitis** and bone **fractures**. Physicians may order a CT of the sinuses to provide an accurate map for surgery.
- Brain studies. Brain scans can detect hematomas, tumors, and strokes. The introduction of CT scanning, especially spiral CT, has helped reduce the need for more invasive procedures such as cerebral **angiography**.
- Body scans. CT scans of the body will often be used to observe abdominal organs, such as the liver, kidneys, adrenal glands, spleen, and lymph nodes, and extremities.
- Aorta scans. CT scans can focus on the thoracic or abdominal aorta to locate aneurysms and other possible aortic diseases.
- Chest scans. CT scans of the chest are useful in distinguishing tumors and in detailing accumulation of fluid in chest infections.

Precautions

Pregnant women or those who could possibly be pregnant should not have a CT scan unless the diagnostic benefits outweigh the risks. Pregnant patients should particularly avoid full body or abdominal scans. If the exam is necessary for obstetrics purposes, technologists are instructed not to repeat films if there are errors. Pregnant patients receiving CT or any x-ray exam away from the abdominal area may be protected by a lead apron; most radiation, known as scatter, travels through the body and is not blocked by the apron.

Contrast agents are often used in CT exams and the use of these agents should be discussed with the medical professional prior to the procedure. Patients should be asked to sign a consent form concerning the administration of contrast. One of the common contrast agents, iodine, can cause allergic reactions. Patients who are known to be allergic to iodine (or shellfish) should inform the physician prior to the CT scan.

Description

Computed tomography, also called CT scan, CAT scan, or computerized axial tomography, is a combination of focused x-ray beams and computerized production of an image. Introduced in the early 1970s, this radiologic procedure has advanced rapidly and is now widely used, sometimes in the place of standard x rays.

CT equipment

A CT scan may be performed in a hospital or outpatient imaging center. Although the equipment looks large and intimidating, it is very sophisticated and fairly comfortable. The patient is asked to lie on a gantry, or narrow table, that slides into the center of the scanner. The scanner looks like a doughnut and is round in the middle, which allows the x-ray beam to rotate around the patient. The scanner section may also be tilted slightly to allow for certain cross-sectional angles.

CT procedure

The patient will feel the gantry move very slightly as the precise adjustments for each sectional image are

Colorized CT scan of human abdomen—aorta is dead center/red *(Photo Researchers. Reproduced by permission.)*

made. A technologist watches the procedure from a window and views the images on a computer screen.

It is essential that the patient lie very still during the procedure to prevent motion blurring. In some studies, such as chest CTs, the patient will be asked to hold his or her breath during image capture.

Following the procedure, films of the images are usually printed for the radiologist and referring physician to review. A radiologist can also interpret CT exams on a special computer screen. The procedure time will vary in length depending on the area being imaged. Average study times are from 30 to 60 minutes. Some patients may be concerned about claustrophobia, but the width of the "doughnut" portion of the scanner is such that many patients can be reassured of openness.

The CT image

While traditional x rays image organs in two dimensions, with the possibility that organs in the front of the body are superimposed over those in the back, CT scans allow for a more three-dimensional effect. Some have compared CT images to slices in a loaf of bread. Precise sections of the body can be located and imaged as cross-sectional views. The screen before the technologist shows a computer's analysis of each section detected by the x-ray beam. Thus, various densities of tissue can be easily distinguished.

Contrast agents

Contrast agents are often used in CT exams and in other radiology procedures to illuminate certain details of anatomy which may not be easily seen. Some contrasts are natural, such as air or water. Other times, a water-based contrast agent is administered for specific diagnostic purposes. Barium sulfate is commonly used in gastroenterology procedures. The patient may drink this contrast, or receive it in an enema. Oral and rectal contrast are usually given when examining the abdomen or cells, and not given when scanning the brain or chest. Iodine is the most widely used intravenous contrast agent and is given through an intravenous needle.

If contrast agents are used in the CT exam, these will be administered several minutes before the study begins. Abdominal CT patients may be asked to drink a contrast medium. Some patients may experience a salty taste, flushing of the face, warmth or slight nausea, or **hives** from an intravenous contrast injection. Technologists and radiologists have equipment and training to help patients through these minor reactions and to handle more severe reactions. Severe reactions to contrast are rare, but do occur.

Spiral CT

Spiral CT, also called helical CT, is a newer version of CT scanning which is continuous in motion and allows for three-dimensional recreation of images. For example, traditional CT allows the technologist to take slices at very small and precise intervals one after the other. Spiral CT allows for a continuous flow of images, without stopping the scanner to move to the next image slice. A major advantage of spiral CT is the ability to reconstruct images anywhere along the length of the study area. The procedure also speeds up the imaging process, meaning less time for the patient to lie still. The ability to image contrast more rapidly after it is injected, when it is at its highest level, is another advantage of spiral CT's high speed.

Some facilities will have both spiral and conventional CT available. Although spiral is more advantageous for many applications, conventional CT is still a superior and precise method for imaging many tissues and structures. The physician will evaluate which type of CT works best for the specific exam purpose.

Preparation

If a contrast medium is administered, the patient may be asked to fast from about four to six hours prior to the procedure. Patients will usually be given a gown (like a typical hospital gown) to be worn during the procedure. All metal and jewelry should be removed to avoid artifacts on the film.

Aftercare

No aftercare is generally required following a CT scan. Immediately following the exam, the technologist will continue to watch the patient for possible adverse contrast reactions. Patients are instructed to advise the

technologist of any symptoms, particularly respiratory difficulty. The site of contrast injection will be bandaged and may feel tender following the exam. Hives may develop later and usually do not require treatment.

Risks

Radiation exposure from a CT scan is similar to, though higher than, that of a conventional x ray. Although this is a risk to pregnant women, the exposure to other adults is minimal and should produce no effects. Although severe contrast reactions are rare, they are a risk of many CT procedures.

Normal results

Normal findings on a CT exam show bone, the most dense tissue, as white areas. Tissues and fat will show as various shades of gray, and fluids will be gray or black. Air will also look black. Intravenous, oral, and rectal contrast appear as white areas. The radiologist can determine if tissues and organs appear normal by the sensitivity of the gray shadows. In CT, the images that can cut through a section of tissue or organ provide three-dimensional viewing for the radiologist and referring physician.

Abnormal results

Abnormal results may show different characteristics of tissues within organs. Accumulations of blood or other fluids where they do not belong may be detected. Radiologists can differentiate among types of tumors throughout the body by viewing details of their makeup.

Sinus studies

The increasing availability and lowered cost of CT scanning has led to its increased use in sinus studies, either as a replacement for a sinus x ray or as a follow-up to an abnormal sinus radiograph. The sensitivity of CT allows for location of areas of sinus infection, particularly chronic infection. CT scans can show the extent and location of tiny fractures to the sinus and nasal bones. Foreign bodies in the sinus and nasal area are also easily detected by CT. CT imaging of the sinuses is important in evaluating trauma or disease of the sphenoid bone (the wedge shaped bone at the base of the skull). Sinus tumors will show as shades of gray indicating the difference in their density from that of normal tissues in the area.

Brain studies

The precise differences in density allowed by CT scan can clearly show tumors, strokes, or lesions in the brain area as altered densities. These lighter or darker areas on the image may indicate a tumor or hematoma within the brain and skull area. Different types of tumors can be identified by the presence of **edema**, by the tissue's density, or by studying blood vessel location and activity. The speed and convenience of CT often allows for detection of hemorrhage before symptoms even occur. Congenital abnormalities in children, such as **hydrocephalus**, may also be confirmed with CT. Hydrocephalus is suggested by enlargement of the fluid structures called ventricles of the brain.

Computerized CT scan of facial sinuses. *(Pascal Goetgheluck. Photo Researchers. Reproduced by permission.)*

Body scans

The body scan can identify abnormal body structures and organs. Throughout the body, a CT may indicate tumors or cysts, enlarged lymph nodes, abnormal collections of fluids, blood or fat, and metastasis of **cancer**. Tumors resulting from metastasis are different in makeup than primary tumors, or those that originate in the location of study. Fractures or damage to soft tissues and ligaments will be more easily seen on the sensitive images produced by CT scanning, though CT is not usually done for these. Liver conditions, such as **cirrhosis** or abscessed or **fatty liver**, may be observed on the body scan.

CT of the aorta

CT provides the ability to see and measure the thickness of the aortal wall, which is very helpful in diagnosing aortic aneurysms. The use of contrast will help see details within the aorta. In addition, density can identify calcification, and this helps differentiate between acute and chronic problems. An abnormal CT scan may indicate signs of aortic clots. Aortic rupture is suggested by signs such as a hematoma around the aorta or the escape of blood from its cavity.

KEY TERMS

Aneurysm—The bulging of the blood vessel wall. Aortic aneurysms are the most dangerous. Aneurysms can break and cause bleeding.

Contrast (agent, medium)—A substance injected into the body that illuminates certain structures that would otherwise be hard to see on the radiograph (film).

Gantry—A name for the couch or table used in a CT scan. The patient lies on the gantry while it slides into the x-ray scanner portion.

Hematoma—A collection of blood that has escaped from the vessels. It may clot and harden, causing pain to the patient.

Hydrocephalus—A collection of fluid on or around the brain. The pressure from the spinal fluid causes the ventricles to widen.

Metastasis—Secondary cancer, or cancer that has spread from one body organ or tissue to another.

Radiologist—A medical doctor specially trained in radiology (x ray) interpretation and its use in the diagnosis of disease and injury.

Spiral CT—Also referred to as helical CT, this method allows for continuous 360-degree x-ray image capture.

Thoracic—Refers to the chest area. The thorax runs between the abdomen and neck and is encased in the ribs.

Chest scans

In addition to those findings that may indicate aortic aneurysms, chest CT studies can show other problems in the heart and lungs, and distinguish between an **aortic aneurysm** and a tumor adjacent to the aorta. The computer will not only show differences between air, water, tissues, and bone, but will also assign numerical values to the various densities. Coin-sized lesions in the lungs may be indicative of **tuberculosis** or tumors. CT will help distinguish among the two. Enlarged lymph nodes in the chest area may indicate **Hodgkin's disease**. Spiral CT is particularly effective at identifying pulmonary emboli (clots in the lung's blood vessels).

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ORGANIZATIONS

American College of Radiology. 1891 Preston White Drive, Reston, VA 22091. (800) 227-5463. <http://www.acr.org>.

Teresa Norris, RN

Computerized axial tomography *see* **Computed tomography scans**

Concussion

Definition

Concussion is a trauma-induced change in mental status, with confusion and **amnesia**, and with or without a brief loss of consciousness.

Description

A concussion occurs when the head hits or is hit by an object, or when the brain is jarred against the skull, with sufficient force to cause temporary loss of function in the higher centers of the brain. The injured person may remain conscious or lose consciousness briefly, and is disoriented for some minutes after the blow. According to the Centers for Disease Control and Prevention, approximately 300,000 people sustain mild to moderate sports-related brain injuries each year, most of them young men between 16 and 25.

While concussion usually resolves on its own without lasting effect, it can set the stage for a much more serious condition. "Second impact syndrome" occurs when a person with a concussion, even a very mild one, suffers a second blow before fully recovering from the first. The brain swelling and increased intracranial pressure that can result is potentially fatal. More than 20 such cases have been reported since the syndrome was first described in 1984.

Causes and symptoms

Causes

Most concussions are caused by motor vehicle accidents and **sports injuries**. In motor vehicle accidents, concussion can occur without an actual blow to the head. Instead, concussion occurs because the skull suddenly decelerates or stops, which causes the brain to be jarred against the skull. Contact sports, especially football,

hockey, and boxing, are among those most likely to lead to concussion. Other significant causes include falls, collisions, or blows due to bicycling, horseback riding, skiing, and soccer.

The risk of concussion from football is extremely high, especially at the high school level. Studies show that approximately one in five players suffer concussion or more serious brain injury during their brief high-school careers. The rate at the collegiate level is approximately 1 in 20. Rates for hockey players are not known as certainly, but are believed to be similar.

Concussion and lasting brain damage is an especially significant risk for boxers, since the goal of the sport is, in fact, to deliver a concussion to the opponent. For this reason, the American Academy of Neurology has called for a ban on boxing. Repeated concussions over months or years can cause cumulative **head injury**. The cumulative brain injuries suffered by most boxers can lead to permanent brain damage. Multiple blows to the head can cause "punch-drunk" syndrome or **dementia** pugilistica, as evidenced by Muhammed Ali, whose parkinsonism is a result of his career in the ring.

Young children are likely to suffer concussions from falls or collisions on the playground or around the home. **Child abuse** is, unfortunately, another common cause of concussion.

Symptoms

Symptoms of concussion include:

- headache
- disorientation as to time, date, or place
- confusion
- dizziness
- vacant stare or confused expression
- incoherent or incomprehensible speech
- incoordination or weakness
- amnesia for the events immediately preceding the blow
- nausea or vomiting
- double vision
- ringing in the ears

These symptoms may last from several minutes to several hours. More severe or longer-lasting symptoms may indicate more severe brain injury. The person with a concussion may or may not lose consciousness from the blow; if so, it will be for several minutes at the most. More prolonged unconsciousness indicates more severe brain injury.

The severity of concussion is graded on a three-point scale, used as a basis for treatment decisions.

KEY TERMS

Amnesia—A loss of memory that may be caused by brain injury, such as concussion.

Parkinsonism—A neurological disorder that includes a fine tremor, muscular weakness and rigidity, and an altered way of walking.

- Grade 1: no loss of consciousness, transient confusion, and other symptoms that resolve within 15 minutes.
- Grade 2: no loss of consciousness, transient confusion, and other symptoms that require more than 15 minutes to resolve.
- Grade 3: loss of consciousness for any period.

Days or weeks after the accident, the person may show signs of:

- headache
- poor attention and concentration
- memory difficulties
- anxiety
- depression
- sleep disturbances
- light and noise intolerance

The occurrence of such symptoms is called "post-concussion syndrome."

Diagnosis

It is very important for those attending a person with concussion to pay close attention to the person's symptoms and progression immediately after the accident. The duration of unconsciousness and degree of confusion are very important indicators of the severity of the injury and help guide the diagnostic process and treatment decisions.

A doctor, nurse, or emergency medical technician may make an immediate assessment based on the severity of the symptoms; a **neurologic exam** of the pupils, coordination, and sensation; and brief tests of orientation, memory, and concentration. Those with very mild concussions may not need to be hospitalized or have expensive diagnostic tests. Questionable or more severe cases may require **computed tomography scan** (CT) or **magnetic resonance imaging** (MRI) scans to look for brain injury.

Treatment

The symptoms of concussion usually clear quickly and without lasting effect, if no further injury is sus-

tained during the healing process. Guidelines for returning to sports activities are based on the severity of the concussion.

A grade 1 concussion can usually be treated with rest and continued observation alone. The person may return to sports activities that same day, but only after examination by a trained professional, and after all symptoms have completely resolved. If the person sustains a second concussion of any severity that same day, he or she should not be allowed to continue contact sports until he or she has been symptom-free, during both rest and activity, for one week.

A person with a grade 2 concussion must discontinue sports activity for the day, should be evaluated by a trained professional, and should be observed closely throughout the day to make sure that all symptoms have completely cleared. Worsening of symptoms, or continuation of any symptoms beyond one week, indicates the need for a CT or MRI scan. Return to contact sports should only occur after one week with no symptoms, both at rest and during activity, and following examination by a physician. Following a second grade 2 concussion, the person should remain symptom-free for two weeks before resuming contact sports.

A person with a grade 3 concussion (involving any loss of consciousness, no matter how brief) should be examined by a medical professional either on the scene or in an emergency room. More severe symptoms may warrant a CT or MRI scan, along with a thorough neurological and physical exam. The person should be hospitalized if any abnormalities are found or if confusion persists. Prolonged unconsciousness and worsening symptoms require urgent neurosurgical evaluation or transfer to a trauma center. Following discharge from professional care, the patient is closely monitored for neurological symptoms which may arise or worsen. If headaches or other symptoms worsen or last longer than one week, a CT or MRI scan should be performed. Contact sports are avoided for one week following unconsciousness of only seconds, and for two weeks for unconsciousness of a minute or more. A person receiving a second grade 3 concussion should avoid contact sports for at least a month after all symptoms have cleared, and then only with the approval of a physician. If signs of brain swelling or bleeding are seen on a CT or MRI scan, the athlete should not return to the sport for the rest of the season, or even indefinitely.

For someone who has sustained a concussion of any severity, it is critically important that he or she avoid the possibility of another blow to the head until well after all symptoms have cleared to prevent second-impact syndrome. The guidelines above are designed to minimize the risk of this syndrome.

Prognosis

Concussion usually leaves no lasting neurological problems. Nonetheless, symptoms of **post-concussion syndrome** may last for weeks or even months.

Studies of concussion in contact sports have shown that the risk of sustaining a second concussion is even greater than it was for the first if the person continues to engage in the sport.

Prevention

Many cases of concussion can be prevented by using appropriate protective equipment. This includes seat belts and air bags in automobiles, and helmets in all contact sports. Helmets should also be worn when bicycling, skiing, or horseback riding. Soccer players should avoid heading the ball when it is kicked at high velocity from close range. Playground equipment should be underlaid with soft material, either sand or special matting.

The value of high-contact sports such as boxing, football, or hockey should be weighed against the high risk of brain injury during a young person's participation in the sport. Steering a child's general enthusiasm for sports into activities less apt to produce head impacts may reduce the likelihood of brain injury.

Resources

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ORGANIZATIONS

American Academy of Neurology. 1080 Montreal Ave., St. Paul, MN 55116. (612) 695-1940. <http://www.aan.com>.

Richard Robinson

Condom

Definition

Male condoms are thin sheaths of latex (rubber), polyurethane (plastic), or animal tissue that are rolled onto an erect penis immediately prior to intercourse. They are commonly called "safes" or "rubbers." Female condoms are made of polyurethane and are inserted into the vaginal

A condom is most effective when it is placed on the penis correctly without trapping air between the penis and the condom. *(Illustration by Argosy, Inc.)*

canal before sexual relations. The open end covers the outside of the vagina, and the closed ring fits over the cervix (opening into the uterus). Both types of condoms collect the male semen at ejaculation, acting as a barrier to fertilization. Condoms also perform as barriers to the exchange of bodily fluids and are subsequently an important tool in the prevention of **sexually transmitted diseases** (STDs).

Purpose

Both male and female condoms are used to prevent **pregnancy** and to protect against STDs such as human **immunodeficiency** virus (HIV), **gonorrhea**, chlamydia, and **syphilis**. To accomplish these goals, the condom must be applied and removed correctly.

Precautions

Male and female condoms should not be used together as there is a risk that one of them may come off. The male condom should not be snug on the tip of the penis. A space of about 0.5 in should be left at the end to avoid the possibility of it breaking during sexual intercourse. The penis must be withdrawn quickly after ejaculation to prevent the condom from falling off as the penis softens. The condom should therefore always be removed while the penis is still erect to prevent the sperm from spilling into the vagina.

Description

Male condoms made from animal tissue and linen have been in use for centuries. Latex condoms were introduced in the late 1800s and gained immediate popularity because they were inexpensive and effective. At that time, they were primarily used to protect against STDs. A common complaint made by many consumers is that condoms reduce penis sensitivity and impair orgasm. Both men and women may develop **allergies** to

KEY TERMS

Ejaculate—To expel semen.

Semen—The thick whitish liquid released from the penis during sexual intercourse. It contains sperm and other secretions.

Sperm or spermatozoa—The part of the semen that is generative—can cause fertilization of the female ovum.

Spermicide—An agent that is destructive to sperm.

Vagina—The genital canal in the female, leading from the vulva to the uterus.

the latex. Consumer interest in female condoms has been slight.

Male condoms may be purchased lubricated, ribbed, or treated with spermicide (a chemical that kills sperm). To be effective, condoms must be removed carefully so as not to "spill" the contents into the vaginal canal. Condoms that leak or break do not provide protection against pregnancy or disease.

If used correctly, male condoms have an effectiveness rate of about 90% for preventing pregnancy, but this rate can be increased to about 99% if used with a spermicide. (Several types of spermicides are available; they can be purchased in the form of contraceptive creams and jellies, foams, or films.) Benefits associated with this type of contraceptive device include easy availability (no prescription is required), convenience of use, and lack of serious side effects. The primary disadvantage is that sexual activity must be interrupted in order to put the condom on.

Female condoms, when used correctly and at every instance of intercourse, were shown to prevent pregnancy in over 95% of women surveyed over the course of six months. When used inconsistently, the female condom was shown to have a failure rate of 21% in the same study. One benefit of the female condom is that it may be inserted immediately before sexual intercourse or up to eight hours prior, so that sexual activity does not need to be interrupted for its insertion. One study performed by a manufacturer of the female condom indicated that 50–75% of couples in numerous countries found the barrier acceptable for use.

Condoms provide better protection against STDs than any other contraceptive method. One study conducted in the 1990s indicated that out of 123 couples with one HIV-positive partner, not one healthy individual contracted the disease when condoms were used with every instance of sexual intercourse. A similar 1993 study showed that out of 171 couples with one HIV-positive partner, all but two individuals were protected against HIV transmission with condom use. In addition to HIV, condoms provide effective transmission against gonorrhea, chlamydia, syphilis, **chancroid**, and **trichomoniasis**. A measure of protection is also provided against **hepatitis B** virus (HBV), human papillomavirus (HPV), and herpes simplex virus (HSV).

Before purchasing a condom, check the expiration date. Prior to use, examine the condom for holes. If a lubricant is going to be used, it should be water soluble because petroleum jellies, such as Vaseline, and other oil based lubricants can weaken latex. It is also important to note that condoms made from animal tissue or plastic are not recommended as a protection against STDs.

Resources

OTHER

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Stephanie Dionne

Conduct disorder

Definition

Conduct disorder (CD) is a behavioral and emotional disorder of childhood and adolescence. Children with conduct disorder act inappropriately, infringe on the rights of others, and violate the behavioral expectations of others.

Description

CD is present in approximately 9% of boys and 2–9% of girls under the age of 18. Children with conduct disorder act out aggressively and express anger inappropriately. They engage in a variety of antisocial and destructive acts, including violence towards people and animals, destruction of property, lying, stealing,

truancy, and running away from home. They often begin using and abusing drugs and alcohol, and having sex at an early age. Irritability, temper tantrums, and low self-esteem are common personality traits of children with CD.

Causes and symptoms

There are two sub-types of CD, one beginning in childhood and the other in adolescence. There is no known cause. Researchers and physicians suggest that this disease may be caused by the following:

- poor parent-child relationships
- dysfunctional families
- drug abuse
- physical abuse
- poor relationships with other children
- cognitive problems leading to school failures
- brain damage
- biological defects

Difficulty in school is an early sign of potential conduct disorder problems. While the patient's IQ tends to be in the normal range, they can have trouble with verbal and abstract reasoning skills and may lag behind their classmates, and consequently, feel as if they don't "fit in." The frustration and loss of self-esteem resulting from this academic and social inadequacy can trigger the development of CD.

A dysfunctional home environment can be another major contributor to CD. An emotionally, physically, or sexually abusive home environment, a family history of antisocial personality disorder, or parental substance abuse can damage a child's perceptions of himself and put him on a path toward negative behavior. Other less obvious environmental factors can also play a part in the development of conduct disorder. Long-term studies have shown that maternal **smoking** during **pregnancy** may be linked to the development of CD in boys. Animal and human studies point out that nicotine can have undesirable effects on babies. These include altered structure and function of their nervous systems, learning deficits, and behavioral problems. In a study of 177 boys ages seven-12 years, those with mothers who smoked over one half a package of cigarettes daily while pregnant were more apt to have a CD than those with mothers who did not smoke.

Other conditions that may cause or co-exist with CD include **head injury**, substance abuse disorder, major depressive disorder, and attention deficit hyperactivity disorder (**ADHD**). Thirty to fifty percent of children diagnosed with ADHD, a disorder characterized by a persistent pattern of inattention and/or hyperactivity, also have CD.

CD is defined as a repetitive behavioral pattern of violating the rights of others or societal norms. Three of the following criteria, or symptoms, are required over the previous 12 months for a diagnosis of CD (one of the three must have occurred in the past six months):

- bullies, threatens, or intimidates others
- picks fights
- has used a dangerous weapon
- has been physically cruel to people
- has been physically cruel to animals
- has stolen while confronting a victim (for example, mugging or extortion)
- has forced someone into sexual activity
- has deliberately set a fire with the intention of causing damage
- has deliberately destroyed property of others
- has broken into someone else's house or car
- frequently lies to get something or to avoid obligations
- has stolen without confronting a victim or breaking and entering (e.g., shoplifting or forgery)
- stays out at night; breaks curfew (beginning before 13 years of age)
- has run away from home overnight at least twice (or once for a lengthy period)
- is often truant from school (beginning before 13 years of age).

Diagnosis

CD is diagnosed and treated by a number of social workers, school counselors, psychiatrists, and psychologists. Genuine diagnosis may require psychiatric expertise to rule out such conditions as **bipolar disorder** or ADHD. A comprehensive evaluation of the child should ideally include interviews with the child and parents, a full social and medical history, a cognitive evaluation, and a psychiatric exam. One or more clinical inventories or scales may be used to assess the child for conduct disorder—including the Youth Self-Report, the Overt Aggression Scale (OAS), Behavioral Assessment System for Children (BASC), Child Behavior Checklist (CBCL), and Diagnostic Interview Schedule for Children (DISC). The tests are verbal and/or written and are administered in both hospital and outpatient settings.

KEY TERMS

ADHD—Attention deficit hyperactivity disorder; a disorder characterized by a persistent pattern of inattention and/or hyperactivity.

Major depressive disorder—A mood disorder characterized by profound feelings of sadness or despair.

Treatment

Treating conduct disorder requires an approach that addresses both the child and his environment. Behavioral therapy and psychotherapy can help a child with CD to control his anger and develop new coping skills. Family **group therapy** may also be effective in some cases. Parents should be counseled on how to set appropriate limits with their child and be consistent and realistic when disciplining. If an abusive home life is at the root of the conduct problem, every effort should be made to move the child into a more supportive environment. Parent training programs are increasing in number.

For children with coexisting ADHD, substance abuse, depression, or **learning disorders**, treating these conditions first is preferred, and may result in a significant improvement to the CD condition. In all cases of CD, treatment should begin when symptoms first appear. Recent studies have shown Ritalin to be a useful drug for both ADHD and CD.

When aggressive behavior is severe, mood stabilizing medication, including lithium (Cibalith-S, Eskalith, Lithane, Lithobid, Lithonate, Lithotabs), carbamazepine (Tegretol, Atretol), and propranolol (Inderal), may be an appropriate option for treating the aggressive symptoms. However, placing the child into a structured setting or treatment program such as a psychiatric hospital may be just as beneficial for easing aggression as medication.

Prognosis

The prognosis for children with CD is not bright. Follow-up studies of conduct disordered children have shown a high incidence of antisocial personality disorder, affective illnesses, and chronic criminal behavior later in life. However, proper treatment of co-existing disorders, early identification and intervention, and long-term support may improve the outlook significantly.

Prevention

A supportive, nurturing, and structured home environment is believed to be the best defense against CD. Children with learning disabilities and/or difficulties in school should get immediate and appropriate academic assistance. Addressing these problems when they first appear helps to prevent the frustration and low self-esteem that may lead to CD later on.

Resources

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ORGANIZATIONS

American Academy of Child and Adolescent Psychiatry (AACAP). 3615 Wisconsin Ave. NW, Washington, DC 20016. (202) 966-7300. <http://www.aacap.org>.

Children and Adults with Attention Deficit Disorder (CH.A.D.D.). 8181 Professional Place, Suite 201

Paula Anne Ford-Martin

Conductive hearing loss *see* **Hearing loss**

Condylomata acuminata *see* **Genital warts**

Cone biopsy *see* **Cervical conization**

Congenital adrenal hyperplasia

Definition

Congenital adrenal hyperplasia is (CAH) a genetic disorder characterized by a deficiency in the hormones cortisol and aldosterone and an over-production of the

hormone androgen, which is present at birth and affects sexual development.

Description

CAH is a form of adrenal insufficiency in which the enzyme that produces two important adrenal steroid hormones, cortisol and aldosterone, is deficient. Because cortisol production is impeded, the adrenal gland instead overproduces androgens (male steroid hormones). Females with CAH are born with an enlarged clitoris and normal internal reproductive tract structures. Males have normal genitals at birth. CAH causes abnormal growth for both sexes; patients will be tall as children and short as adults. Females develop male characteristics, and males experience premature sexual development.

In its most severe form, called salt-wasting CAH, a life-threatening adrenal crisis can occur if the disorder is untreated. Adrenal crisis can cause **dehydration**, **shock**, and **death** within 14 days of birth. There is also a mild form of CAH that occurs later in childhood or young adult life in which patients have partial enzyme deficiency.

CAH, a genetic disorder, is the most common adrenal gland disorder in infants and children, occurring in one in 10,000 total births worldwide. It affects both females and males. It is also called adrenogenital syndrome.

Causes and symptoms

CAH is an inherited disorder. It is a recessive disease, which means that a child must inherit one copy of the defective gene from each parent who is a carrier; when two carriers have children, each **pregnancy** carries a 25% risk of producing an affected child.

In females, CAH produces an enlarged clitoris at birth and masculinization of features as the child grows, such as deepening of the voice, facial hair, and failure to menstruate or abnormal periods at **puberty**. Females with severe CAH may be mistaken for males at birth. In males, the genitals are normal at birth, but the child becomes muscular, the penis enlarges, pubic hair appears, and the voice deepens long before normal puberty, sometimes as early as two to three years of age.

In the severe salt-wasting form of CAH, newborns may develop symptoms shortly after birth, including vomiting, dehydration, electrolyte (a compound such as sodium or calcium that separates to form ions when dissolved in water) changes, and cardiac arrhythmia.

In the mild form of CAH, which occurs in late childhood or early adulthood, symptoms include premature development of pubic hair, irregular menstrual periods, unwanted body hair, or severe **acne**. However, sometimes there are no symptoms.

Adrenal cortical hyperplasia. The adrenal on the right is normal, that on the left shows hyperplasia. *(Photo Researchers, Inc. Reproduced by permission.)*

Diagnosis

CAH is diagnosed by a careful examination of the genitals and blood and urine tests that measure the hormones produced by the adrenal gland. A number of states in the United States perform a hormonal test (a heel prick blood test) for CAH and other inherited diseases within a few days of birth. In questionable cases, **genetic testing** can provide a definitive diagnosis. For some forms of CAH, prenatal diagnosis is possible through chronic villus sampling in the first trimester and by measuring certain hormones in the amniotic fluid during the second trimester.

Treatment

The goal of treatment for CAH is to return the androgen levels to normal. This is usually accomplished through drug therapy, although surgery is an alternative. Lifelong treatment is required.

Drug therapy consists of a cortisol-like steroid medication called a glucocorticoid. Oral hydrocortisone is prescribed for children, and prednisone or dexamethasone is prescribed for older patients. For patients with salt-wasting CAH, fludrocortisone, which acts like aldosterone (the missing hormone), is also prescribed. Infants and small children may also receive salt tablets, while older patients are told to eat salty foods. Medical therapy achieves hormonal balance most of the time, but CAH patients can have periods of fluctuating hormonal control that lead to increases in the dose of steroids prescribed. Side effects of steroids include stunted growth. Steroid therapy should not be suddenly stopped, since adrenal insufficiency results.

Patients with CAH should see a pediatric endocrinologist frequently. The endocrinologist will assess height,

KEY TERMS

Adrenal glands—The two endocrine glands located above the kidney that secrete hormones and epinephrine.

Aldosterone—A hormone secreted by the adrenal glands that is important for maintaining salt and water balance in the body.

Androgens—Steroid hormones that cause masculinization.

Congenital—Present at birth.

Cortisol—A steroid hormone secreted by the adrenal cortex that is important for maintenance of body fluids, electrolytes, and blood sugar levels.

Hormone—A chemical messenger produced by the endocrine glands or certain other cells. Hormones are usually carried in the blood stream and regulate some metabolic activities.

Steroids—Hormones, including aldosterone, cortisol, and androgens, derived from cholesterol that share a four-ring structure.

weight, and blood pressure, and order an annual x ray of the wrist (to assess bone age), as well as assess blood hormone levels. CAH patients with the milder form of the disorder are usually effectively treated with hydrocortisone or prednisone, if they need medical treatment at all.

Females with CAH who have masculine external genitalia require surgery to reconstruct the clitoris and/or vagina. This is usually performed between the ages of one and three.

An experimental type of drug therapy—a three-drug combination, with an androgen blocking agent (flutamide), an aromatase inhibitor (testolactone), and low dose hydrocortisone—is currently being studied by physicians at the National Institutes of Health. Preliminary results are encouraging, but it will be many years before the safety and effectiveness of this therapy is fully known.

Adrenalectomy, a surgical procedure to remove the adrenal glands, is a more radical treatment for CAH. It was widely used before the advent of steroids. Today, it is recommended for CAH patients with little or no enzyme activity and can be accomplished by **laparoscopy**. This is a minimally invasive type of surgery done through one or more small 1 in (2.5 cm) incisions and a laparoscope, an instrument with a fiber-optic light containing a tube with openings for surgical instruments. Adrenalectomy is followed by hormone therapy, but in lower doses than CAH patients not treated surgically receive.

Prognosis

CAH can be controlled and successfully treated in most patients as long as they remain on drug therapy.

Prevention

Prenatal therapy, in which a pregnant woman at risk for a second CAH child is given dexamethasone to decrease secretion of androgens by the adrenal glands of the female fetus, has been in use for about 10 years. This therapy is started in the first trimester when fetal adrenal production of androgens begins, but before prenatal diagnosis is done that would provide definitive information about the sex of the fetus and its disease status. This means that a number of fetuses are exposed to unnecessary steroid treatment in order to prevent the development of male-like genitals in female fetuses with CAH. Several hundred children have undergone this treatment with no major adverse effects, but its long-term risks are unknown. Since there is very little data on the effectiveness and safety of prenatal therapy, it should only be offered to patients who clearly understand the risks and benefits and who are capable of complying with strict monitoring and follow-up throughout pregnancy and after the child is born.

Parents with a family history of CAH, including a child who has CAH, should seek **genetic counseling**. Genetic testing during pregnancy can provide information on the risk of having a child with CAH.

Resources

BOOKS

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Jennifer Sisk

Congenital amputation

Definition

Congenital **amputation** is the absence of a fetal limb or fetal part at birth. This condition may be the result of the constriction of fibrous bands within the membrane that surrounds the developing fetus (amniotic band syndrome) or the exposure to substances known to cause **birth defects** (teratogenic agents). Other factors, including genetics, may also play a role.

Description

An estimated one in 2,000 babies are born with all or part of a limb missing, ranging from a missing part of a finger to the absence of both arms and both legs. Congenital amputation is the least common reason for amputation. However, there are occasional periods in history where the number of congenital amputations increased. For example, the thalidomide tragedy of the early 1960s occurred after pregnant mothers in western Europe were given a tranquilizer containing the drug. The result was a drastic increase in the number of babies born with deformed limbs. In this example, the birth defect usually presented itself as very small, deformed versions of normal limbs. More recently, birth defects as a result of radiation exposure near the site of the Chernobyl disaster in Russia have left numerous children with malformed or absent limbs.

Causes and symptoms

The exact cause of congenital amputations is unknown. However, according to the March of Dimes, most birth defects have one or more genetic factors and one or more environmental factors. It is also known that most birth defects occur in the first three months of **pregnancy**, when the organs of the fetus are forming. Within these crucial first weeks, frequently prior to when a woman is aware of the pregnancy, the developing fetus is most susceptible to substances that can cause birth defects (teratogens). Exposure to teratogens can cause congenital amputation. In other cases, tight amniotic bands may constrict the developing fetus, preventing a limb from forming properly, if at all. It is estimated that this amniotic band syndrome occurs in between one in 12,000 and one in 15,000 live births.

An infant with congenital amputation may be missing an entire limb or just a portion of a limb. Congenital amputation resulting in the complete absence of a limb beyond a certain point (and leaving a stump) is called transverse deficiency or amelia. Longitudinal deficiencies occur when a specific part of a limb is missing; for example, when the fibula bone in the lower leg is missing, but the rest of the leg is intact. Phocomelia is the condition in which only a mid-portion of a limb is missing, as when the hands or feet are attached directly to the trunk.

Diagnosis

Many cases of congenital amputation are not diagnosed until the baby is born. Ultrasound examinations may reveal the absence of a limb in some developing fetuses, but routine ultrasounds may not pick up signs of more subtle defects. However, if a doctor suspects that the fetus is at risk for developing a limb deficiency (for example, if the mother has been exposed to radiation), a more detailed ultrasound examination may be performed.

Treatment

Successful treatment of a child with congenital amputation involves an entire medical team, including a pediatrician, an orthopedist, a psychiatrist or psychologist, a prosthetist (an expert in making prosthetics, or artificial limbs), a social worker, and occupational and physical therapists. The accepted method of treatment is to fit the child early with a functional prosthesis because this leads to normal development and less wasting away (atrophy) of the muscles of the limbs present. However, some parents and physicians believe that the child should be allowed to learn to play and perform tasks without a prosthesis, if possible. When the child is older, he or she can be involved in the decision of whether or not to be fitted for a prosthesis.

Recently, there have been cases in which physicians have detected amniotic band constriction interfering with limb development fairly early in its course. In 1997, doctors at the Florida Institute for Fetal Diagnosis and Therapy reported two cases in which minimally invasive surgery freed constricting amniotic bands and preserved the affected limbs.

Alternative treatment

Prevention of birth defects begins with building the well-being of the mother before pregnancy. Prenatal care

KEY TERMS

Prosthesis—An artificial replacement for a missing part of the body.

Teratogen—Any substance, agent, or process that interferes with normal prenatal development, causing the formation of one or more developmental abnormalities of the fetus.

should be strong and educational so that the mother understands both her genetic risks and her environmental risks. Several disciplines in alternative therapy also recommend various supplements and **vitamins** that may reduce the chances of birth defects. If a surgical procedure is planned, naturopathic and homeopathic pre- and post-surgical therapies can speed recovery.

Prognosis

A congenital limb deficiency has a profound effect on the life of the child and parents. However, occupational therapy can help the child learn to accomplish many tasks. In addition, some experts believe that early fitting of a prosthesis will enhance acceptance of the prosthesis by the child and parents.

Prevention

Studies have suggested that a multivitamin including **folic acid** may reduce birth defects, including congenital abnormalities. **Smoking**, drinking alcohol, and eating a poor diet while pregnant may increase the risk of congenital abnormalities. Daily, heavy exposure to chemicals may be dangerous while pregnant.

Resources

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Jeffrey P. Larson, RPT

Congenital bladder diverticulum *see* **Congenital bladder anomalies**

Congenital bladder anomalies

Definition

The two most common congenital bladder abnormalities are exstrophy and congenital diverticula. An exstrophic bladder is one that is open to the outside and turned inside-out, so that its inside is visible at birth, protruding from the lower abdomen. A diverticulum is an extension of a hollow organ, usually shaped like a pouch with a narrow opening.

Description

During fetal development, folds enclose tissues and organs and eventually fuse at the edges to form sealed compartments. Both in the front and the back, folds eventually become major body structures. In the back, the entire spinal column folds in like a pipe wrapped in a pillow. In the front, the entire lower urinary system is folded in.

- Exstrophy of the bladder represents a failure of this folding process to complete itself, so the organs form with more or less of their front side missing and open to the outside. At the same time, the front of the pelvic bone is widely separated. The abdominal wall is open, too. In fact, the defect often extends all the way to the penis in the male or splits the clitoris in the female.
- A congenital bladder diverticulum represent an area of weakness in the bladder wall through which extrudes some of the lining of the bladder. (A small balloon squeezed in a fist will create diverticula-like effect between the fingers.) Bladder diverticula may be multiple, and they often occur at the ureterovesical junction—the entrance of the upper urinary system into the bladder. In this location, they may cause urine to reflux into the ureter and kidney, leading to infection and possible kidney damage.

Causes and symptoms

As with many **birth defects**, the causes are not well known. Lack of prenatal care and **nutrition** has been linked to many birth defects; however, beyond the avoidance of known teratogens (anything that can cause a birth defect), there is little prevention possible. Exstrophy is rare, occurring in about one in 40,000 births. Diverticula are more common, but less serious.

If left untreated, the patient with bladder exstrophy will have no control over urination and is more likely to develop **bladder cancer**. Diverticula, particularly if it causes urine reflux, may lead to chronic infection and its subsequent consequences.

Diagnosis

A major consideration with congenital abnormalities is that they tend to be multiple. Further, each one is unique in its extent and severity. Exstrophy can involve the rectum and large bowel and coexist with hernias. The obvious bladder exstrophy seen at birth will prompt immediate action and a search for other anomalies.

Diverticula are not visible and will be detected only if they cause trouble. They are usually found in an examination for the cause of recurring urinary infections. X rays of the urinary system or a **cystoscopy** (examination with a telescope-like instrument) will identify them. Often, the two procedures are done together: a urologist will perform the cystoscopy, then a radiologist will instill a contrast agent into the bladder and take x rays.

Treatment

Surgery is necessary and can usually produce successful results. If possible, the surgery must be done within 48 hours of birth. Prior to surgery, the exposed organs must be protected and all related defects identified and managed. Delay in the surgery leads to the frequent need to divert the urine into the bowel because the partially repaired bladder cannot control the flow. After surgery, the likelihood of infection requires monitoring.

Alternative treatment

After surgery ongoing precautions to reduce frequency of infection may need to be used. Cranberry juice has the ability to keep bacteria from adhering to the membranes and can help prevent infection whenever there is increased risk. There are botanical and homeopathic treatments available, however consultation by a trained practitioner is recommended before treatment.

Prognosis

With immediate surgery, three-quarters of patients can be successfully repaired. They will have control of their urine and no long-term consequences. The rate of infection is greater for those with congenital bladder anomalies, since any abnormality in the urinary system predisposes it to invasion by bacteria.

Prevention

Birth defects often have no precisely identified cause, therefore prevention is limited to general measures such as early and continuous prenatal care, appropriate nutrition, and a healthy lifestyle.

KEY TERMS

Congenital—Present at birth.

Cystoscopy—Examination of the urinary bladder with a thin telescope-like instrument.

Exstrophy—Being turned inside out combined with being outside the body.

Diverticulum—A pouch extending from a hollow organ.

Radiologist—A physician who specializes in creating images of the internal organs of the body.

Teratogen—Any agent that can cause birth defects.

Ureter—The tube that transports urine from the kidney to the bladder.

Ureterovesical junction—The joining of the ureter to the bladder.

Urologist—A surgeon who specializes in diseases of the urinary system.

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J. Ricker Polsdorfer, MD

Congenital brain defects

Definition

Congenital brain defects are a group of disorders of brain development.

Description

Brain development begins shortly after conception and continues throughout the growth of a fetus. A com-

plex genetic program coordinates the formation, growth, and migration of billions of neurons, or nerve cells, and their development into discrete, interacting brain regions. Interruption of this program, especially early in development, can cause structural defects in the brain. In addition, normal brain formation requires proper development of the surrounding skull, and skull defects may lead to brain malformation. Congenital brain defects may be caused by inherited genetic defects, spontaneous mutations within the genes of the embryo, or effects on the embryo due to the mother's infection, trauma, or drug use.

Early on in development, a flat strip of tissue along the back of the fetus rolls up to form a tube. This so-called "neural tube" develops into the spinal cord, and at one end, the brain. Closure of the tube is required for subsequent development of the tissue within. Anencephaly (literally "without brain"), results when the topmost portion of the tube fails to close. Anencephaly is the most common severe malformation seen in stillborn births. It is about four times more common in females than males. Anencephaly is sometimes seen to run in families, and for parents who have conceived one anencephalic fetus, the risk of a second is as high as 5%. Fewer than half of babies with anencephaly are born alive, and survival beyond the first month is rare.

Encephalocele is a protrusion of part of the brain through a defect in the skull. The most common site for encephalocele is along the front-to-back midline of the skull, usually at the rear, although frontal encephaloceles are more common among Asians. Pressure within the skull pushes out cranial tissue. The protective layer over the brain, the meninges, grows to cover the protrusion, as does skin in some cases. Defects in skull closure are thought to cause some cases of encephalocele, while defects in neural tube closure may cause others. Encephaloceles may be small and contain little or no brain tissue, or may be quite large and contain a significant fraction of the brain.

Failure of neural-tube closure below the level of the brain prevents full development of the surrounding vertebral bones and leads to **spina bifida**, or a divided spinal column. Incomplete closure causes protrusion of the spinal cord and meninges, called meningomyelocele. Some cases of spina bifida are accompanied by another defect at the base of the brain, known as the Arnold-Chiari malformation or Chiari II malformation. For reasons that are unclear, part of the cerebellum is displaced downward into the spinal column. Symptoms may be present at birth or delayed until early childhood.

The Dandy-Walker malformation is marked by incomplete formation, or absence of, the central section of the cerebellum, and the growth of cysts within the lowest of the brain's ventricles. The ventricles are fluid-filled cavities within the brain, through which cerebrospinal fluid (CSF) normally circulates. The cysts may block the exit of the fluid, causing **hydrocephalus**. Symptoms may be present at birth or delayed until early childhood.

Soon after closure of the neural tube, the brain divides into two halves, or hemispheres. Failure of division is termed holoprosencephaly (literally "whole forebrain"). Holoprosencephaly is almost always accompanied by facial and cranial deformities along the midline, including cleft lip, cleft palate, fused eye sockets and a single eye (cyclopia), and deformities of the limbs, heart, gastrointestinal tract, and other internal organs. Most infants are either stillborn or die soon after birth. Survivors suffer from severe neurological impairments.

The normal ridges and valleys of the mature brain are formed after cells from the inside of the developing brain migrate to the outside and multiply. When these cells fail to migrate, the surface remains smooth, a condition called lissencephaly ("smooth brain"). Lissencephaly is often associated with facial abnormalities including a small jaw, a high forehead, a short nose, and low-set ears.

If damaged during growth, especially within the first 20 weeks, brain tissue may stop growing, while tissue around it continues to form. This causes an abnormal cleft or groove to appear on the surface of the brain, called schizencephaly (literally "split brain"). This cleft should not be confused with the normal wrinkled brain surface, nor should the name be mistaken for **schizophrenia**, a mental disorder. Generalized destruction of tissue or lack of brain development may lead to hydranencephaly, in which cerebrospinal fluid fills much of the space normally occupied by the brain. Hydranencephaly is distinct from hydrocephalus, in which CSF accumulates within a normally-formed brain, putting pressure on it and possibly causing skull expansion.

Excessive brain size is termed megalencephaly (literally "big brain"). Megalencephaly is defined as any brain size above the 98th percentile within the population. Some cases are familial, and may be entirely benign. Others are due to metabolic or neurologic disease. The opposite condition, microcephaly, may be caused by failure of the brain to develop, or by intrauterine infection, drug toxicity, or brain trauma.

Causes and symptoms

Causes

Congenital brain defects may have genetic, infectious, toxic, or traumatic causes. In most cases, no certain cause can be identified.

GENETIC CAUSES. Some brain defects are caused by trisomy, the inclusion of a third copy of a chromosome normally occurring in pairs. Most trisomies occur because of improper division of the chromosomes during formation of eggs or sperm. Trisomy of chromosome 9 can cause some cases of Dandy-Walker and Chiari II malformation. Some cases of holoprosencephaly are caused by trisomy of chromosome 13, while others are due to abnormalities in chromosomes 7 or 18. Individual gene defects, either inherited or spontaneous, are responsible for other cases of congenital brain malformations.

DRUGS. Drugs known to cause congenital brain defects when used by the mother during critical developmental periods include:

- anticonvulsant drugs
- retinoic acid and tretinoin
- warfarin
- alcohol
- cocaine

OTHER. Other causes of congenital brain defects include:

- intrauterine infections, including cytomegalovirus, **rubella**, herpes simplex, and varicella zoster
- maternal **diabetes mellitus**
- maternal **phenylketonuria**
- fetal trauma

Symptoms

Besides the features listed above, symptoms of congenital brain defects may include:

- Chiari II malformation: impaired swallowing and gag reflex, loss of the breathing reflex, facial **paralysis**, uncontrolled eye movements (**nystagmus**), impaired balance and gait.
- Dandy-Walker malformation: symptoms of hydrocephalus, lack of muscle tone or "floppiness," seizures, spasticity, deafness, irritability, **visual impairment**, deterioration of consciousness, paralysis.
- Lissencephaly: lack of muscle tone, seizures, developmental delay, spasticity, **cerebral palsy**.
- Hydranencephaly: irritability, spasticity, seizures, temperature oscillations.
- megalencephaly due to neurological or metabolic disease: **mental retardation**, seizures.

KEY TERMS

Amniocentesis—Removal of fluid from the sac surrounding a fetus for purposes of diagnosis.

Cerebrospinal fluid—Fluid produced within the brain for nutrient transport and structural purposes. CSF circulates through the ventricles, open spaces within the brain, and drains through the membranes surrounding the brain.

Congenital—Defect present at birth.

Fetus—The unborn human, developing in a woman's uterus, from the eighth week after fertilization to birth.

Diagnosis

Congenital brain defects are diagnosed either from direct **physical examination** or imaging studies including **computed tomography scans** (CT) and **magnetic resonance imaging** (MRI) scans. **Electroencephalography** (EEG) may be used to reveal characteristic abnormalities.

Prenatal diagnosis of neural tube defects causing anencephaly or meningomyelocele is possible through ultrasound examination and maternal blood testing for alpha-fetoprotein, which is almost always elevated. Ultrasound can also be used to diagnose Dandy-Walker and Chiari II malformations. **Amniocentesis** may reveal trisomies or other chromosomal abnormalities.

Treatment

Meningomyelocele may be treated with surgery to close the open portion of the spinal cord. Surgery for encephalocele is possible only if there is a minimal amount of brain tissue protruding. Malformations associated with hydrocephalus (Dandy-Walker, Chiari II, and some cases of hydranencephaly) may be treated by installation of a drainage shunt for cerebrospinal fluid. Drugs may be used to treat some symptoms of brain defects, including seizures and spasticity.

Prognosis

Most congenital brain defects carry a very poor prognosis. Surgical treatment of meningomyelocele and encephalocele may be successful, with lasting neurologi-

cal deficiencies that vary in severity. Early treatment of hydrocephalus may prevent more severe brain damage.

Prevention

Some cases of congenital brain defects can be prevented with good maternal **nutrition**, including **folic acid** supplements. Folic acid is a vitamin that has been shown to reduce the incidence of neural tube defects. Pregnant women should avoid exposure to infection, especially during the first trimester. Abstention from drugs and alcohol during **pregnancy** may reduce risk. **Genetic counseling** is advisable for parents who have had one child with anencephaly, since the likelihood of having another is increased.

Resources

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Richard Robinson

Congenital defects *see* **Birth defects**

Congenital hip dysplasia

Definition

A condition of abnormal development of the hip, resulting in hip joint instability and potential dislocation of the thigh bone from the socket in the pelvis. This condition has been more recently termed developmental hip dysplasia, as it often develops over the first few weeks, months, or years of life.

Description

Congenital hip dysplasia is a disorder in children that is either present at birth or shortly thereafter. During gestation, the infant's hip should be developing with the head of the thigh bone (femur) sitting perfectly centered in its shallow socket (acetabulum). The acetabulum should cover the head of the femur as if it were a ball sitting inside of a cup. In the event of congenital hip dysplasia, the development of the acetabulum in an infant allows the femoral head to ride upward out of the joint socket, especially when weight bearing begins.

Causes and symptoms

Clinical studies show a familial tendency toward hip dysplasia, with more females affected than males. This disorder is found in many cultures around the world. However, statistics show that the Native American population has a high incidence of hip dislocation. This has been documented to be due to the common practice of swaddling and using cradleboards for restraining the infants. This places the infant's hips into extreme adduction (brought together). The incidence of congenital hip dysplasia is also higher in infants born by caesarian and breech position births. Evidence also shows a greater chance of this hip abnormality in the first born compared to the second or third child. Hormonal changes within the mother during **pregnancy**, resulting in increased ligament laxity, is thought to possibly cross over to the placenta and cause the baby to have lax ligaments while still in the womb. Other symptoms of complete dislocation include a shortening of the leg and limited ability to abduct the leg.

Diagnosis

Because the abnormalities of this hip problem often vary, a thorough **physical examination** is necessary for an accurate diagnosis of congenital hip dysplasia. The hip disorder can be diagnosed by moving the hip to determine if the head of the femur is moving in and out of the hip joint. One specific method, called the Ortolani test, begins with each of the examiners' hands around the infant's knees, with the second and third fingers pointing down the child's thigh. With the legs abducted (moved apart), the examiner may be able to discern a distinct clicking sound with motion. If symptoms are present with a noted increase in abduction, the test is considered positive for hip joint instability. It is important to note this test is only valid a few weeks after birth.

The Barlow method is another test performed with the infant's hip brought together with knees in full bent position. The examiner's middle finger is placed over the outside of the hipbone while the thumb is placed on the inner side of the knee. The hip is abducted to where it can be felt if the hip is sliding out and then back in the joint. In older babies, if there is a lack of range of motion in one hip or even both hips, it is possible that the movement is blocked because the hip has dislocated and the muscles have contracted in that position. Also in older infants, hip dislocation is evident if one leg looks shorter than the other.

X-ray films can be helpful in detecting abnormal findings of the hip joint. X rays may also be helpful in finding the proper positioning of the hip joint for treatments of

casting. Ultrasound has been noted as a safe and effective tool for the diagnosis of congenital hip dysplasia. Ultrasound has advantages over x rays, as several positions are noted during the ultrasound procedure. This is in contrast to only one position observed during the x ray.

Treatment

The objective of treatment is to replace the head of the femur into the acetabulum and, by applying constant pressure, to enlarge and deepen the socket. In the past, stabilization was achieved by placing rolled cotton diapers or a pillow between the thighs, thereby keeping the knees in a frog like position. More recently, the Pavlik harness and von Rosen splint are commonly used in infants up to the age of six months. A stiff shell cast may be used, which achieves the same purpose, spreading the legs apart and forcing the head of the femur into the acetabulum. In some cases, in older children between six to 18 months, surgery may be necessary to reposition the joint. Also at this age, the use of closed manipulation may be applied successfully, by moving the leg around manually to replace joint. Operations are not only performed to reduce the dislocation of the hip, but also to repair a defect in the acetabulum. A cast is applied after the operation to hold the head of the femur in the correct position. The use of a home **traction** program is now more common. However, after the age of eight years, surgical procedures are primarily done for **pain** reduction measures only. Total hip surgeries may be inevitable later in adulthood.

Alternative treatment

Nonsurgical treatments include **exercise** programs, orthosis (a force system, often involving braces), and medications. A physical therapist may develop a program that includes strengthening, range-of-motion exercises, pain control, and functional activities. **Chiropractic** medicine may be helpful, especially the procedures of closed manipulations, to reduce the dislocated hip joint.

Prognosis

Unless corrected soon after birth, abnormal stresses cause malformation of the developing femur, with a characteristic limp or waddling gait. If cases of congenital hip dysplasia go untreated, the child will have difficulty walking, which could result in life-long pain. In addition, if this condition goes untreated, the abnormal hip positioning will force the acetabulum to locate to another position to accommodate the displaced femur.

Prevention

Prevention includes proper prenatal care to determine the position of the baby in the womb. This may be helpful in preparing for possible breech births associated with hip problems. Avoiding excessive and prolonged infant hip adduction may help prevent strain on the hip joints. Early diagnosis remains an important part of prevention of congenital hip dysplasia.

KEY TERMS

Acetabulum—The large cup-shaped cavity at the junction of pelvis and femur or thigh bone.

Orthosis—A force system designed to control or correct or compensate for a bone deformity, deforming forces, or forces absent from the body.

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ORGANIZATIONS

March of Dimes Birth Defects Foundation. 1275 Mamaroneck Ave., White Plains, NY 10605. (914) 428-7100. <http://www.modimes.org>.

Jeffrey P. Larson, RPT

Congenital lobar emphysema

Definition

Congenital lobar **emphysema** is a chronic disease that causes respiratory distress in infants.

Description

Congenital lobar emphysema, also called infantile lobar emphysema, is a respiratory disease that occurs in infants when air enters the lungs but cannot leave easily. The lungs become over-inflated, causing respiratory function to decrease and air to leak out into the space around the lungs.

KEY TERMS

Congenital—A disease or condition that is present at birth.

Emphysema—A condition in which the air sacs in the lungs become overinflated, causing a decrease in respiratory function.

Lobar—Relating to a lobe, a rounded projecting part of the lungs.

Half of the cases of congenital lobar emphysema occur in the first four weeks of life, and three-quarters occur in infants less than six months old. Congenital lobar emphysema is more common in boys than in girls.

Each person has two lungs, right and left. The right lung is divided into three sections, called lobes, and the left lung into two lobes. Congenital lobar emphysema usually affects only one lobe, and this is usually an upper lobe. It occurs most frequently in the left upper lobe, followed by the right middle lobe.

Causes and symptoms

The cause of congenital lobar emphysema often cannot be identified. The airway may be obstructed or the infant's lungs may not have developed properly. Congenital lobar emphysema is almost never of genetic origin.

Symptoms of congenital lobar emphysema include:

- shortness of breath
- wheezing
- lips and fingernail beds that have a bluish tinge

Diagnosis

Congenital lobar emphysema is usually identified within the first two weeks of the infant's life. It is diagnosed by respiratory symptoms and a **chest x ray**, which shows the over-inflation of the affected lobe and may show a blocked air passage.

Treatment

For infants with no, mild, or intermittent symptoms, no treatment is necessary. For more serious cases of congenital lobar emphysema, surgery is necessary, usually a lobectomy to remove the affected lung lobe.

Alternative treatment

Alternative treatments that may be helpful for congenital lobar emphysema are aimed at supporting and strengthening the patient's respiratory function. Vitamin and mineral supplementation may be recommended as may herbal remedies such as lobelia (*Lobelia inflata*) that strengthen the lungs and enhance their elasticity. Homeopathic constitutional care may also be beneficial for this condition.

Prognosis

Surgery for congenital lobar emphysema has excellent results.

Prevention

Congenital lobar emphysema cannot be prevented.

Resources

BOOKS

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ORGANIZATIONS

American Lung Association. 1740 Broadway, New York, NY 10019. (800) 586-4872. <http://www.lungusa.org>.

National Heart, Lung and Blood Institute. P.O. Box 30105, Bethesda, MD 20824-0105. (301) 251-1222. <http://www.nhlbi.nih.gov>.

National Jewish Center for Immunology and Respiratory Medicine. 1400 Jackson St., Denver, CO 80206. (800) 222-5864. <http://www.nationaljewish.org/main.html>.

Lori De Milto

Congenital megacolon *see* **Hirschsprung's disease**

Congenital thymic hypoplasia *see* **DiGeorge syndrome**

Congenital ureter anomalies

Definition

The ureter drains urine from the kidney into the bladder. It is not simply a tube but an active organ that propels urine forward by muscular action. It has a valve at its bottom end that prevents urine from flowing backward into the kidney. Normally, there is one ureter on each side of the body for each kidney. However, among the many abnormalities of ureteral development, duplication is quite common. Ureters may also be malformed in a variety of ways—some harmful, others not.

Description

The urogenital system, for some reason, is more likely than any other to have **birth defects**, and they can occur in endless variety. Ureters can be duplicated completely or partially, they can be in the wrong place, they can be deformed, and they can end in the wrong place. The trouble these abnormalities bring is directly related to their effect on the flow of urine. As long as urine flows normally through them, and only in one direction, no harm is done.

- Duplication of ureters is quite common, either in part or completely. Kidneys are sometimes duplicated as well. Someone may have four kidneys and four ureters or two kidneys, half of each drained by a separate ureter, or a single kidney with two, three, or four ureters attached. As long as urine can flow easily in the correct direction, such malformations may never be detected. If, however, one of the ureters has a dead end, a stricture or stenosis (narrowing), or a leaky ureterovesical valve (valve between the ureter and bladder), infection is the likely result.
- Stricture or stenosis of a ureter prevents urine from flowing freely. Whenever flow is obstructed in the body—urine, bile, mucus, or any other liquid—infection follows. Ureters can be obstructed anywhere along their course, though the ureterovesical valve is the most common place.
- A ureter may have an ectopic (out of place) orifice (opening)—it may enter the bladder, or even another structure, where it does not belong and therefore without an adequate valve to control reflux.
- The primary ureter, or a duplicate, may not even reach the bladder, but rather terminate in a dead end. Urine will stagnate there and eventually cause infection.
- A ureter can be perfectly normal but in the wrong place, such as behind the vena cava (the large vein in the middle of the abdomen). A so-called retrocaval ureter may be pinched by the vena cava so that flow is hindered. Other aberrant locations may also lead to compression and impaired flow.

Besides infection, urine that backs up will cause the ureter and the kidney to dilate. Eventually, the kidney will stop functioning because of the back pressure. This condition is called hydronephrosis—a kidney swollen with urine.

Causes and symptoms

The causes of birth defects are multiple and often unknown. Furthermore, the precise cause of specific birth defects has only rarely been identified. Such is the case with congenital ureteral anomalies.

KEY TERMS

Congenital—Present at birth.

Contrast agent—A chemical or other substance placed in the body to show structures that would not otherwise be visible on x ray or other imaging studies.

Cystoscopy—Looking into the urinary bladder with a thin telescope-like instrument.

Ectopic—Out of place.

Septicemia—A serious whole body infection spreading through the blood stream.

Uretreovesical valve—A sphincter (an opening controlled by a circular muscle), located where the ureter enters the bladder, that keeps urine from flowing backward toward the kidney.

Urogenital—Both the urinary system and the sexual organs, which form together in the developing embryo.

Practically the only symptom generated by ureteral abnormalities is urinary tract infection. A lower tract infection—in the bladder—is called **cystitis**. In children, it may cause **fever** and systemic symptoms, but in adults it causes only cloudy, burning, and frequent urine. Upper tract infections, on the other hand, can be serious for both adults and children, causing high fevers, back **pain**, severe generalized discomfort, and even leading to kidney failure or septicemia (infection spreading throughout the body by way of the blood stream).

In rare cases, urine from an ectopic ureter will bypass the bladder and dribble out of the bottom somewhere, through a natural orifice like the vagina or a completely separate unnatural opening.

Diagnosis

Serious or recurrent urinary infections will prompt a search for underlying abnormalities. **Cystoscopy** (looking into the bladder with a thin telescope-like instrument) and x rays with a contrast agent to illuminate the urinary system will usually identify the defect. **Computed tomography scans** (CT) and **magnetic resonance imaging** (MRI) scans may provide additional information. Urine cultures to identify the infecting germs will be repeated frequently until the problem is corrected.

Treatment

Sometimes the recurring infections caused by flow abnormalities can be treated with repeated and changing

courses of **antibiotics**. Over time, the infecting germs develop resistance to most treatments, especially the safer ones. If it can be done with acceptable risk, it is better to repair the defect surgically. Urologists have an arsenal of approaches to urine drainage that range from simply reimplanting a ureter into the bladder, in such a way that an effective valve is created, to building a new bladder out of a piece of bowel.

Alternative treatment

There are botanical and homeopathic treatments available for urinary tract infection. None can take the place of correcting a problem that is occurring because of a malformed or dysfunctional organ system. Once correction of the cause is addressed and there is unimpeded flow of urine, adequate fluid intake can contribute to prevention of future infections.

Prognosis

As long as damage to the kidneys from infection or back pressure has not become significant, the surgical repair of troublesome ureteral defects produces excellent long-term results in the great majority of cases. Monitoring for recurrent infections is always a good idea, and occasional checking of kidney function will detect hidden ongoing damage.

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J. Ricker Polsdorfer, MD

Congestive cardiomyopathy

Definition

Cardiomyopathy is an ongoing disease process that damages the muscle wall of the lower chambers of the heart. Congestive cardiomyopathy is the most common form of cardiomyopathy. In congestive cardiomyopathy, also called dilated cardiomyopathy, the walls of the heart chambers stretch (dilate) to hold a greater volume of blood than normal. Congestive cardiomyopathy is the final stage of many heart diseases and the most common condition resulting in congestive **heart failure**.

Description

About 50,000 Americans develop cardiomyopathy each year. Of those, 87% have congestive cardiomyopathy. Primary cardiomyopathy accounts for only 1% of all deaths from heart disease.

When the heart muscle is damaged by a disease process, it cannot pump enough blood to meet the body's needs. Uninjured areas of the walls of the two lower heart chambers (called ventricles) stretch to make up for the lost pumping action. At first, the enlarged chambers allow more blood to be pumped with less force. The stretched muscle can also contract more forcefully. Over time, the heart muscle continues to stretch, ultimately becoming weaker. The heart is forced to work harder to pump blood by beating faster. Eventually it cannot keep up, and blood backs up into the veins, legs, and lungs. When this happens, the condition is called congestive heart failure.

Congestive cardiomyopathy usually affects both ventricles. Blood backed up into the lungs from the left ventricle causes fluid to congest the lung tissue. This is called **pulmonary edema**. When the right ventricle fails to pump enough blood, blood backs up into the veins causing **edema** in the legs, feet, ankles, and abdomen.

Causes and symptoms

Congestive cardiomyopathy may be caused by a number of conditions. Cardiomyopathy with a known cause is called secondary cardiomyopathy. When no cause can be identified, it is called primary cardiomyopathy or idiopathic cardiomyopathy. About 80% of all cases of cardiomyopathy do not have a known cause. Many heart specialists think that many cases of idiopathic congestive cardiomyopathy may be caused by a viral infection. Because cardiomyopathy may occur many years after a viral infection and viruses sometimes go undetected in laboratory tests, it is difficult to know if a virus is the cause. Some people have a weak heart from advanced **coronary artery disease** that causes heart muscle damage. This is sometimes called ischemic cardiomyopathy.

Conditions that can cause congestive cardiomyopathy are:

- Coronary artery disease
- Infections

KEY TERMS

Angiotensin-converting enzyme (ACE) inhibitor—A drug that relaxes blood vessel walls and lowers blood pressure.

Atherosclerosis—Buildup of a fatty substance called a plaque inside blood vessels.

Cardiac catheterization—A diagnostic test for evaluating heart disease; a catheter is inserted into an artery and passed into the heart.

Cardiomyopathy—Disease of the heart muscle.

Congestive cardiomyopathy—Also called dilated cardiomyopathy; cardiomyopathy in which the walls of the heart chambers stretch, enlarging the heart ventricles so they can hold a greater volume of blood than normal.

Coxsackievirus B—A type of virus in the group Enterovirus that causes an infection similar to polio, but without paralysis.

Digitalis—A drug that helps the heart muscle to have stronger pumping action.

Dilated cardiomyopathy—Also called congestive cardiomyopathy; cardiomyopathy in which the walls of the heart chambers stretch, enlarging the heart ventricles so they can hold a greater volume of blood than normal.

Diuretic—A type of drug that helps the kidneys eliminate excess salt and water.

Edema—Swelling caused by fluid buildup in tissues.

Granulomatous myocarditis—Also called giant cell myocarditis, this noninfectious inflammation of the heart causes large areas of tissue death in the heart muscle, ventricular enlargement, and clots inside the heart chambers.

Idiopathic cardiomyopathy—Cardiomyopathy without a known cause.

Sarcoidosis—A chronic disease that causes formation of abnormal areas containing inflammatory cells, called granulomas, in any organ or tissue; in the heart, large areas of the heart muscle can be involved, causing cardiomyopathy.

Vasodilator—Any drug that relaxes blood vessel walls.

Ventricle—One of the two lower chambers of the heart.

Wegener's granulomatosis—A disease usually affecting males that causes the infiltration of inflammatory cells and tissue death in the lungs, kidneys, blood vessels, heart, and other tissues.

- noninfectious inflammatory conditions
- alcohol and other drugs or toxins
- **hypertension**
- nutritional and metabolic disorders
- **pregnancy**.

Coronary artery disease is one of the most common causes of congestive cardiomyopathy. In coronary artery disease, the arteries supplying blood to the heart become narrowed or blocked. When blood flow to an area of the heart is completely blocked, the person has a **heart attack**. The heart muscle suffers damage when its blood supply is reduced or blocked. Significant recurrent muscle damage can occur silently. This damage can lead to congestive cardiomyopathy.

Infections caused by bacteria, viruses, and other microorganisms can involve the heart, causing inflammation of the heart muscle (**myocarditis**). The inflammation may damage the heart muscle and cause congestive cardiomyopathy. In the United States, the coxsackievirus B is the most common cause of viral congestive cardiomyopathy.

Myocarditis can also be caused by noninfectious disorders. For example, the conditions **sarcoidosis**, granulomatous myocarditis, and **Wegener's granulomatosis** cause inflammation and tissue **death** in the heart muscle.

Years of drinking excessive amounts of alcohol can weaken the heart muscle, leading to congestive cardiomyopathy. Other drugs and toxins, such as **cocaine**, pesticides, and other chemicals, may have the same effect.

High blood pressure (hypertension) puts extra pressure on blood vessels and the heart. This increased pressure makes the heart work harder to pump blood, which may thicken and damage the chamber walls.

Severe nutritional deficiencies can weaken the heart muscle and affect its pumping ability. Certain disorders of metabolism, including **diabetes mellitus** and thyroid disorders, can also lead to congestive cardiomyopathy.

Occasionally, inflammation of the heart muscle and congestive cardiomyopathy may develop late in pregnan-

cy or shortly after a woman gives birth. This type of congestive cardiomyopathy is called peripartum cardiomyopathy. The cause of congestive cardiomyopathy in pregnancy is not known.

Congestive cardiomyopathy usually is a chronic condition, developing gradually over time. Patients with early congestive cardiomyopathy may not have symptoms. The most common symptoms are **fatigue** and **shortness of breath** on exertion. Unfortunately, **sudden cardiac death** is not uncommon with this condition. It stems from irregular heart rhythms in the ventricles (ventricular **arrhythmias**).

Patients with more advanced congestive cardiomyopathy may also have chest or abdominal pains, extreme tiredness, **dizziness**, and swelling of the legs and ankles.

Diagnosis

Diagnosis of congestive cardiomyopathy is based on:

- symptoms
- medical history
- **physical examination**
- **chest x ray**
- electrocardiogram (ECG; also called EKG)
- echocardiogram
- **cardiac catheterization**

The diagnosis is based on the patient's symptoms, a complete physical examination, and tests that detect abnormalities of the heart chambers. The physician listens to the heart with a stethoscope to detect abnormal heart rhythms and heart sounds. A heart murmur might mean that the heart valves are not closing properly due to the ventricles being enlarged.

A chest x ray can show if the heart is enlarged and if there is fluid in the lungs. Abnormalities of heart valves and other structures may also be seen on a chest x ray.

An electrocardiogram provides a record of electrical changes in the heart muscle during the heartbeat. It gives information on the heart rhythm and can show if the heart chamber is enlarged. An ECG can detect damage to the heart muscle and the amount of damage.

Echocardiography uses sound waves to make images of the heart. These images can show if the heart wall or chambers are enlarged and if there are any abnormalities of the heart valves. Echocardiography can also evaluate the pumping efficiency of the ventricles.

Cardiac catheterization usually is only used if a diagnosis cannot be made with other methods. In cardiac catheterization, a small tube (called a catheter) is inserted into an artery and passed into the heart. It is used to measure pressure in the heart and the amount of blood pumped by the heart. A small tissue sample of the heart muscle can be removed through the catheter for examination under a microscope (biopsy). This biopsy can show the type and amount of damage to the heart muscle.

Treatment

When a patient is diagnosed with congestive cardiomyopathy, physicians try to find out the cause. If coronary artery disease is not the culprit, in most other cases a cause is not identified. When a condition responsible for the congestive cardiomyopathy is diagnosed, treatment is aimed at correcting the underlying condition. Congestive cardiomyopathy caused by drinking excess alcohol or by drugs or toxins can be treated by eliminating the alcohol or toxin completely. In some cases, the heart may recover after the toxic substance is removed from the body. Bacterial myocarditis is treated with an antibiotic to eliminate the bacteria.

There is no cure for idiopathic congestive cardiomyopathy. Medicines are given to reduce the workload of the heart and to relieve the symptoms.

One or more of the following types of medicines may be prescribed for congestive cardiomyopathy:

- digitalis
- **diuretics**
- **vasodilators**
- **beta blockers**
- angiotensin converting enzyme inhibitors (ACE inhibitors)
- angiotensin receptor blockers

Digitalis helps the heart muscle to have stronger pumping action. Diuretics help eliminate excess salt and water from the kidneys by making patients urinate more often. This helps reduce the swelling caused by fluid buildup in the tissues. Vasodilators, beta blockers, and ACE inhibitors lower blood pressure and expand the blood vessels so blood can move more easily through them. This action makes it easier for the heart to pump blood through the vessels.

Patients may also be given anticoagulant medications to prevent clots from forming due to pooling of blood in the heart chambers. Medicines to prevent abnormal heart rhythms (arrhythmias) may be given, but some of these drugs can also reduce the force of heart contractions. Automatic implantable cardioverter defibrillators (AICDs) can treat life-threatening arrhythmias, which are relatively common in severe cardiomyopathy.

Certain lifestyle changes may help reduce the workload on the heart and relieve symptoms. Some patients may need to change their diet, stop drinking alcohol, begin a physician-supervised **exercise** program, and/or stop **smoking**.

Severe congestive cardiomyopathy usually causes heart failure. When the heart muscle is damaged so severely that medicines cannot help, a heart transplant may be the only remaining treatment to be considered.

Prognosis

The outlook for a patient with congestive cardiomyopathy depends on the severity of the disease and the person's health. Generally, congestive cardiomyopathy worsens over time and the prognosis is not good. About 50% of patients with congestive cardiomyopathy live for five years after the diagnosis. Twenty five percent of patients are alive 10 years after diagnosis. Women with congestive cardiomyopathy live twice as long as men with the disease. Many of the deaths are caused by sudden abnormal heart rhythms.

Prevention

Because idiopathic congestive cardiomyopathy does not have a known cause, there is no sure way to prevent it. The best way to prevent congestive cardiomyopathy is to avoid known causes such as drinking excess alcohol or taking toxic drugs. Eating a nutritious diet and getting regular exercise to improve overall fitness also can help the heart to stay healthy.

Congestive cardiomyopathy may also be prevented by identifying and treating any conditions that might damage the heart muscle. These include high blood pressure and coronary artery disease. Regular blood pressure checks and obtaining immediate medical care for hypertension and symptoms of coronary artery disease, such as chest **pain**, are important to keep the heart functioning properly.

Finally, diagnosing and treating congestive cardiomyopathy before the heart becomes severely damaged may improve the outlook.

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Toni Rizzo

Congestive heart failure *see* **Heart failure**

Congenital heart disease

Definition

Congenital heart disease, also called congenital heart defect, includes a variety of malformations of the heart or its major blood vessels that are present at birth.

Description

Congenital heart disease occurs when the heart or blood vessels near the heart do not develop properly before birth. Some infants are born with mild types of congenital heart disease, but most need surgery in order to survive. Patients who have had surgery are likely to experience other cardiac problems later in life.

Most types of congenital heart disease obstruct the flow of blood in the heart or the nearby vessels, or cause an abnormal flow of blood through the heart. Rarer types of congenital heart disease occur when the newborn has only one ventricle, or when the pulmonary artery and the aorta come out of the same ventricle, or when one side of the heart is not completely formed.

Patent ductus arteriosus

Patent ductus arteriosus refers to the opening of a passageway—or temporary blood vessel (ductus)—to carry the blood from the heart to the aorta before birth, allowing blood to bypass the lungs, which are not yet functional. The ductus should close spontaneously in the first few hours or days after birth. When it does not close in the newborn, some of the blood that should flow through the aorta then returns to the lungs. Patent ductus arteriosus is common in premature babies, but rare in full-term babies. It has also been associated with mothers who had German **measles** (**rubella**) while pregnant.

Hypoplastic left heart syndrome

Hypoplastic left heart syndrome, a condition in which the left side of the heart is underdeveloped, is rare, but it is the most serious type of congenital heart disease.

With this syndrome, blood reaches the aorta, which pumps blood to the entire body, only from the ductus, which then normally closes within a few days of birth. In hypoplastic left heart syndrome, the baby seems normal at birth, but as the ductus closes, blood cannot reach the aorta and circulation fails.

Obstruction defects

When heart valves, arteries, or veins are narrowed, they partly or completely block the flow of blood. The most common obstruction defects are **pulmonary valve stenosis**, **aortic valve stenosis**, and **coarctation of the aorta**. Bicuspid aortic valve and subaortic stenosis are less common.

Stenosis is a narrowing of the valves or arteries. In pulmonary stenosis, the pulmonary valve does not open properly, forcing the right ventricle to work harder. In aortic stenosis, the improperly formed aortic valve is narrowed. As the left ventricle works harder to pump blood through the body, it becomes enlarged. In coarctation of the aorta, the aorta is constricted, reducing the flow of blood to the lower part of the body and increasing blood pressure in the upper body.

A bicuspid aortic valve has only two flaps instead of three, which can lead to stenosis in adulthood. Subaortic stenosis is a narrowing of the left ventricle below the aortic valve, that limits the flow of blood from the left ventricle.

Septal defects

When a baby is born with a hole in the septum (the wall separating the right and left sides of the heart), blood leaks from the left side of the heart to the right, or from a higher pressure zone to a lower pressure zone. A major leakage can lead to enlargement of the heart and failing circulation. The most common types of septal defects are **atrial septal defect**, an opening between the two upper heart chambers, and **ventricular septal defect**, an opening between the two lower heart chambers. Ventricular septal defect accounts for about 15% of all cases of congenital heart disease in the United States.

Cyanotic defects

Heart disorders that cause a decreased, inadequate amount of oxygen in blood pumped to the body are called cyanotic defects. Cyanotic defects, including truncus arteriosus, total anomalous pulmonary venous return, **tetralogy of Fallot**, **transposition of the great arteries**, and tricuspid atresia, result in a blue discoloration of the skin due to low oxygen levels. About 10% of cases of congenital heart disease in the United States are tetralogy of Fallot, which includes four defects. The major defects are a large hole between the ventricles, which allows oxygen-poor blood to mix with oxygen-rich blood, and narrowing at or beneath the pulmonary valve. The other defects are an overly muscular right ventricle and an aorta that lies over the ventricular hole.

In transposition (reversal of position) of the great arteries, the pulmonary artery and the aorta are reversed, causing oxygen-rich blood to re-circulate to the lungs while oxygen-poor blood goes to the rest of the body. In tricuspid atresia, the baby lacks a triscupid valve and blood cannot flow properly from the right atrium to the right ventricle.

Other defects

Ebstein's anomaly is a rare congenital syndrome that causes malformed tricuspid valve leaflets, which allow blood to leak between the right ventricle and the right atrium. It also may cause a hole in the wall between the left and right atrium. Treatment often involves repairing the tricuspid valve. Ebstein's anomaly may be associated with maternal use of the psychiatric drug lithium during **pregnancy**.

Brugada syndrome is another rare congenital heart defect that appears in adulthood and may cause sudden **death** if untreated. Symptoms, which include rapid, uneven heart beat, often appear at night. Scientists believe that Brugada syndrome is caused by mutations in the gene SCN5A, which involves cardiac sodium channels.

Infants born with DiGeorge sequence can have heart defects such as a malformed aortic arch and tetralogy of Fallot. Researchers believe DiGeorge sequence is most often caused by mutations in genes in the region 22q11.

Marfan syndrome is a connective tissue disorder that causes tears in the aorta. Since the disease also causes excessive bone growth, most Marfan syndrome patients are over six feet tall. In athletes, and others, it can lead to sudden death. Researchers believe the defect responsible for Marfan's syndrome is found in gene FBN1, on chromosome 15.

About 32,000 infants are born every year with congenital heart disease, which is the most common birth defect. About half of these cases require medical treatment. More than one million people with heart defects are currently living in the United States.

Causes and symptoms

In most cases, the causes of congenital heart disease are unknown. Genetic and environmental factors and lifestyle habits can all be involved. The likelihood of hav-

ing a child with a congenital heart disease increases if the mother or father, another child, or another relative had congenital heart disease or a family history of sudden death. Viral infections, such as German measles, can produce congenital heart disease. Women with diabetes and **phenylketonuria** also are at higher risk of having children with congenital heart defects. Many cases of congenital heart disease result from the mother's excessive use of alcohol or taking illegal drugs, such as **cocaine**, while pregnant. The mother's exposure to certain anticonvulsant and dermatologic drugs during pregnancy can also cause congenital heart disease. There are many genetic conditions, such as **Down syndrome**, which affect multiple organs and can cause congenital heart disease.

Symptoms of congenital heart disease in general include: **shortness of breath**, difficulty feeding in infancy, sweating, **cyanosis** (bluish discoloration of the skin), heart murmur, respiratory infections that recur excessively, stunted growth, and limbs and muscles that are underdeveloped.

Symptoms of specific types of congenital heart disease are as follows:

- Patent ductus arteriosus: quick tiring, slow growth, susceptibility to **pneumonia**, rapid breathing. If the ductus is small, there are no symptoms.
- Hypoplastic left heart syndrome: ashen color, rapid and difficult breathing, inability to eat.
- Obstruction defects: cyanosis (skin that is discolored blue), chest **pain**, tiring easily, **dizziness** or **fainting**, congestive **heart failure**, and high blood pressure.
- Septal defects: difficulty breathing, stunted growth. Sometimes there are no symptoms.
- Cyanotic defects: cyanosis, sudden rapid breathing or unconsciousness, and shortness of breath and fainting during **exercise**.

KEY TERMS

Aorta—The main artery located above the heart that pumps oxygenated blood out into the body. Many congenital heart defects affect the aorta.

Congenital—Refers to a disorder that is present at birth.

Cyanotic—Marked by bluish discoloration of the skin due to a lack of oxygen in the blood. It is one of the types of congenital heart disease.

Ductus—The blood vessel that joins the pulmonary artery and the aorta. When the ductus does not close at birth, it causes a type of congenital heart disease called patent ductus arteriosus.

Electrocardiograph (ECG, EKG)—A test used to measure electrical impulses coming from the heart in order to gain information about its structure or function.

Hypoplastic—Incomplete or underdevelopment of a tissue or organ. Hypoplastic left heart syndrome is the most serious type of congenital heart disease.

Neuchal translucency—A pocket of fluid at the back of an embryo's neck visible via ultrasound that, when thickened, may indicate the infant will be born with a congenital heart defect.

Septal—Relating to the septum, the thin muscle wall dividing the right and left sides of the heart. Holes in the septum are called septal defects.

Stenosis—The constricting or narrowing of an opening or passageway.

Diagnosis

Echocardiography and cardiac **magnetic resonance imaging** (MRI) are used to confirm congenital heart disease when it is suggested by the symptoms and **physical examination**. An echocardiograph will display an image of the heart that is formed by sound waves. It detects valve and other heart problems. Fetal echocardiography is used to diagnose congenital heart disease in utero, usually after 20 weeks of pregnancy. Between 10 and 14 weeks of pregnancy, physicians also may use an ultrasound to look for a thickness at the nuchal translucency, a pocket of fluid in back of the embryo's neck, which may indicate a cardiac defect in 55% of cases. Cardiac MRI, a scanning method that uses magnetic fields and radio waves, can help physicians evaluate congenital heart disease, but is not always necessary. Physicians also may use a chest x ray to look at the size and location of the heart and lungs, or an electrocardiograph (ECG), which measures electrical impulses to create a graph of the heart beat.

Treatment

Congenital heart disease is treated with drugs and/or surgery. Drugs used include **diuretics**, which aid the baby in excreting water and salts, and digoxin, which strengthens the contraction of the heart, slows the heartbeat, and removes fluid from tissues.

Surgical procedures seek to repair the defect as much as possible and restore circulation to as close to

normal as possible. Sometimes, multiple surgical procedures are necessary. Surgical procedures include: arterial switch, balloon atrial septostomy, **balloon valvuloplasty**, Damus-Kaye-Stansel procedure, Fontan procedure, pulmonary artery banding, Ross procedure, shunt procedure, and venous switch or intra-atrial baffle.

Arterial switch, to correct transposition of the great arteries, involves connecting the aorta to the left ventricle and connecting the pulmonary artery to the right ventricle. Balloon atrial septostomy, also done to correct transposition of the great arteries, enlarges the atrial opening during heart catheterization. Balloon valvuloplasty uses a balloon-tipped catheter to open a narrowed heart valve, improving the flow of blood in pulmonary stenosis. It is sometimes used in aortic stenosis. Transposition of the great arteries can also be corrected by the Damus-Kaye-Stansel procedure, in which the pulmonary artery is cut in two and connected to the ascending aorta and the farthest section of the right ventricle.

For tricuspid atresia and pulmonary atresia, the Fontan procedure connects the right atrium to the pulmonary artery directly or with a conduit, and the atrial defect is closed. Pulmonary artery banding, narrowing the pulmonary artery with a band to reduce blood flow and pressure in the lungs, is used for ventricular septal defect, atrioventricular canal defect, and tricuspid atresia. Later, the band can be removed and the defect corrected with open-heart surgery.

To correct aortic stenosis, the Ross procedure grafts the pulmonary artery to the aorta. For tetralogy of Fallot, tricuspid atresia, or pulmonary atresia, the shunt procedure creates a passage between blood vessels, sending blood into parts of the body that need it. For transposition of the great arteries, venous switch creates a tunnel inside the atria to re-direct oxygen-rich blood to the right ventricle and aorta and venous blood to the left ventricle and pulmonary artery.

When all other options fail, some patients may need a heart transplant. Children with congenital heart disease require lifelong monitoring, even after successful surgery. The American Heart Association recommends regular dental check-ups and the preventive use of **antibiotics** to protect patients from heart infections, or **endocarditis**. Since children with congenital heart disease have slower growth, **nutrition** is important. Physicians may also limit their athletic activity.

Prognosis

The outlook for children with congenital heart disease has improved markedly in the past two decades. Many types of congenital heart disease that would have been fatal can now be treated successfully. Research on diagnosing heart defects when the fetus is in the womb may lead to future treatment to correct defects before birth. Promising new prevention methods and treatments include genetic screening and the cultivation of cardiac tissue in the laboratory that could be used to repair congenital heart defects.

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Congenital Heart Disease Information and Resources. 1561 Clark Dr., Yardley, PA 19067. <http://www.tchin.org>.

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Melissa Knopper

Conjunctivitis

Definition

Conjuctivitis is an inflammation or redness of the lining of the white part of the eye and the underside of the eyelid (conjunctiva) that can be caused by infection, allergic reaction, or physical agents like infrared or ultraviolet light.

Description

Conjunctivitis is the inflammation of the conjunctiva, a thin, delicate membrane that covers the eyeball and lines the eyelid. Conjunctivitis is an extremely common eye problem because the conjunctiva is continually

exposed to microorganisms and environmental agents that can cause infections or allergic reactions. Conjunctivitis can be acute or chronic depending upon how long the condition lasts, the severity of symptoms, and the type of organism or agent involved. It can also affect one or both eyes and, if caused by infection, can be very easily transmitted to others during close physical contact, particularly among children in a daycare center. Other names for conjunctivitis include pink eye and red eye.

Causes and symptoms

Conjunctivitis may be caused by a viral infection, such as a cold, acute respiratory infection, or disease such as **measles**, herpes simplex, or herpes zoster. Symptoms include mild to severe discomfort in one or both eyes, redness, swelling of the eyelids, and watery, yellow, or green discharge. Symptoms may last anywhere from several days to two weeks. Infection with an adenovirus, however, may also cause a significant amount of pus-like discharge and a scratchy, foreign body-type of sensation in the eye. This may also be accompanied by swelling and tenderness of the lymph nodes near the ear.

Bacterial conjunctivitis can occur in adults and children and is caused by organisms such as *Staphylococcus*, *Streptococcus*, and *Hemophilus*. Symptoms of bacterial conjunctivitis include a pus-like discharge and crusty eyelids after awakening. Redness of the conjunctiva can be mild to severe and may be accompanied by swelling. Persons with symptoms of conjunctivitis who are sexually active may possibly be infected with the bacteria that cause either **gonorrhea** or chlamydia. There may be large amounts of pus-like discharge, and symptoms may include intolerance to light (photophobia), watery mucous discharge, and tenderness in the lymph nodes near the ear that may persist for up to three months.

Conjunctivitis may also be caused by environmental hazards, such as wind, smoke, dust, and allergic reactions caused by pollen, dust, or grass. Symptoms range from **itching** and redness to a mucous discharge. Persons who wear contact lenses may develop allergic conjunctivitis caused by the various eye solutions and foreign proteins contained in them.

Other less common causes of conjunctivitis include exposure to sun lamps or the electrical arcs used during welding, and problems with inadequate drainage of the tear ducts.

Diagnosis

An accurate diagnosis of conjunctivitis centers on taking a patient history to learn when symptoms began, how long the condition has been going on, the symptoms experienced, and other predisposing factors, such as upper respiratory complaints, **allergies**, **sexually transmitted diseases**, herpes simplex infections, and exposure to persons with pink eye. It may be helpful to learn whether an aspect of an individual's occupation may be the cause, for example, welding. Diagnostic tests are usually not indicated unless initial treatment fails or an infection with gonorrhea or chlamydia is suspected. In such cases, the discharge may be cultured and Gram stained to determine the organism responsible for causing the condition. Cultures and smears are relatively painless.

This person has severe conjunctivitis, most likely caused by an allergic reaction. *(Custom Medical Stock Photo. Reproduced by permission.)*

Treatment

The treatment of conjunctivitis depends on what caused the condition. In all cases, warm compresses applied to the affected eye several times a day may help to reduce discomfort.

Conjunctivitis due to a viral infection, particularly those due to adenoviruses, are usually treated by applying warm compresses to the eye(s) and applying topical antibiotic ointments to prevent secondary bacterial infections.

Viral conjunctivitis caused by herpes simplex should be referred to an ophthalmologist. Topical steroids are commonly prescribed in combination with antiviral therapy.

In cases of bacterial conjunctivitis, a physician may prescribe an antibiotic eye ointment or eye drops containing sodium sulfacetamide (Sulamyd) to be applied daily for seven to 14 days. If, after 72 hours, the condition does not improve, a physician or primary care provider should be notified because the bacteria involved may be resistant to the antibiotic used or the cause may not be bacterial.

For cases of conjunctivitis caused by a gonococcal organism, a physician may prescribe an intramuscular injection of ceftriaxone (Rocephin) and a topical antibi-

Conjunctivitis is the inflammation of the conjunctiva, a thin, delicate membrane that covers the eyeball and lines the eyelid. It may be caused by a viral infection, such as a cold or acute respiratory infection, or by such diseases as measles, herpes simplex, or herpes zoster. *(Illustration by Electronic Illustrators Group.)*

otic ointment containing erythromycin or bactracin to be applied four times daily for two to three weeks. Sexual partners should also be treated.

With accompanying chlamydia infection, a topical antibiotic ointment containing erythromycin (Ilotycin) may be prescribed to be applied 1-2 times daily. In addition, oral erythromycin or tetracycline therapy may be indicated for three to four weeks. Here again, sexual partners should also be treated.

Allergic conjunctivitis can be treated by removing the allergic substance from a person's environment, if possible; by applying cool compresses to the eye; and by administering eye drops four to six times daily for four days. Also, the antihistamine diphenhydramine hydrochloride (Benadryl) may help to relieve itchy eyes.

Alternative treatment

Conjunctivitis caused by gonococcal and chlamydial infection usually requires conventional medical treatment. With bacterial, viral, and allergic conjunctivitis, however, alternative options can be helpful. Internal immune enhancement with supplementation can aid in the resolution of bacterial and viral conjunctivitis. Removal of the allergic agent is an essential step in treating allergic conjunctivitis. As with any of the recommended treatments, however, if no improvement is seen within 48–72 hours, a physician should be consulted.

Homeopathically, there are a number of acute remedies designed to treat conjunctivitis. These include *Pulsatilla* (windflower, *Pulsatilla nigricans*), *Belladonna*, and eyebright (*Euphrasia officinalis*). Eye drops, prepared with homeopathic remedies and/or herbs, can be a good substitute for pharmaceutical eye drops. Eye washes can also be made. Herbal eyewashes made with eyebright (1 tsp. dried herb steeped in 1 pint of boiling water) or chamomile (*Matricaria recutita*; 2–3 tsp in 1 pt of boiling water) may be helpful. Eyewashes should be strained and cooled before use, and close attention should be paid to make sure that any solution put into the eye is sterile.

Other simple home remedies may help relieve the discomfort associated with conjunctivitis. A boric acid eyewash can be used to clean and soothe the eyes. A warm compress applied to the eyes for five to 10 minutes three times a day can help relieve the discomfort of bacterial and viral conjunctivitis. A cool compress or cool, damp tea bags placed on the eyes can ease the discomfort of allergic conjunctivitis.

Prognosis

If treated properly, the prognosis for conjunctivitis is good. Conjunctivitis caused by an allergic reaction should clear up once the allergen is removed. However, allergic conjunctivitis will likely recur if the individual again comes into contact with the particular allergen. Conjunctivitis caused by bacteria or a virus, if treated properly, is usually resolved in 10–14 days. If there is no relief of symptoms in 48–72 hours, or there is moderate to severe eye **pain**, changes in vision, or the conjunctivitis is suspected to be caused by herpes simplex, a physician should be notified immediately. If untreated or if treatment fails and is not corrected, conjunctivitis may cause **visual impairment** by spreading to other parts of the eye, such as the cornea.

Prevention

Conjunctivitis can, in many cases, be prevented, or at least the course of the disease can be shortened by following some simple practices.

- Frequently wash hands using antiseptic soap, and use single-use towels during the disease to prevent spreading the infection.
- Avoid chemical irritants and known allergens.
- If in an area where welding occurs, use the proper protective eye wear and screens to prevent damaging the eyes.
- Use a clean tissue to remove discharge from eyes, and wash hands to prevent the spread of infection.

KEY TERMS

Adenovirus—A virus that affects the upper respiratory tract.

Chlamydia—The most common bacterial sexually transmitted disease in the United States that often accompanies gonorrhea and is known for its lack of evident symptoms in the majority of women.

Gonococcal—The bacteria *Neisseria gonorrheae* that causes gonorrhea, a sexually transmitted infection of the genitals and urinary tract. The gonococcal organism may occasionally affect the eye, causing blindness if not treated.

Herpes simplex virus—A virus that can cause fever and blistering on the skin, mucous membranes, or genitalia.

Herpes zoster virus—Acute inflammatory virus that attacks the nerve cells on the root of each spinal nerve with skin eruptions along a sensory nerve ending.

Staphylococcus—A bacterial organism, looking much like a cluster of grapes, that can infect various body systems.

Streptococcus—An organism that causes infections of either the upper respiratory or gastrointestinal tract.

- If medication is prescribed, finish the course of **antibiotics**, as directed, to make sure that the infection is cleared up and does not recur.
- Avoid contact, such as vigorous physical activities, with other persons until symptoms resolve.

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Consciousness disorders *see* **Coma**

Constipation

Definition

Constipation is an acute or chronic condition in which bowel movements occur less often than usual or consist of hard, dry stools that are painful or difficult to pass. Bowel habits vary, but an adult who has not had a bowel movement in three days or a child who has not had a bowel movement in four days is considered constipated.

Description

Constipation is one of the most common medical complaints in the United States. Constipation can occur at any age, and is more common among individuals who resist the urge to move their bowels at their body's signal. This often happens when children start school or enter daycare and feel shy about asking permission to use the bathroom.

Constipation is more common in women than in men and is especially apt to occur during **pregnancy**. Age alone does not increase the frequency of constipation, but elderly people (especially women) are more likely to suffer from constipation.

Although this condition is rarely serious, it can lead to:

- bowel obstruction
- chronic constipation
- hemorrhoids (a mass of dilated veins in swollen tissue around the anus)
- hernia (a protrusion of an organ through a tear in the muscle wall)
- spastic colitis (**irritable bowel syndrome**, a condition characterized by alternating periods of **diarrhea** and constipation)
- laxative dependency

Chronic constipation may be a symptom of colorectal **cancer**, depression, diabetes, diverticulosis (small pouches in the muscles of the large intestine), **lead poisoning**, or **Parkinson's disease**.

In someone who is elderly or disabled, constipation may be a symptom of bowel impaction, a more serious condition in which feces are trapped in the lower part of the large intestine. A doctor should be called if an elderly or disabled person is constipated for a week or more or if a child seems to be constipated.

A doctor should be notified whenever constipation occurs after starting a new prescription, vitamin, or mineral supplement or is accompanied by blood in the stools, changes in bowel patterns, or **fever** and abdominal **pain**.

Causes and symptoms

Constipation usually results from not getting enough **exercise**, not drinking enough water, or from a diet that does not include an adequate amount of fiber-rich foods like beans, bran cereals, fruits, raw vegetables, rice, and whole-grain breads.

Other causes of constipation include anal fissure (a tear or crack in the lining of the anus); **chronic kidney failure**; colon or **rectal cancer**; depression; **hypercalcemia** (abnormally high levels of calcium in the blood); **hypothyroidism** (underactive thyroid gland); illness requiring complete bed rest; irritable bowel syndrome; and **stress**.

Constipation can also be a side effect of:

- aluminum salts in **antacids**
- antihistamines
- antipsychotic drugs
- aspirin
- belladonna (*Atopa belladonna,* source of atropine, a medication used to relieve spasms and dilate the pupils of the eye)
- beta blockers (medications used to stabilize irregular heartbeat, lower high blood pressure, reduce chest pain)
- blood pressure medications
- calcium channel blockers (medication prescribed to treat high blood pressure, chest pain, some types of irregular heartbeat and **stroke**, and some non-cardiac diseases)
- diuretics (drugs that promote the formation and secretion of urine)
- iron or calcium supplements
- narcotics (potentially addictive drugs that relieve pain and cause mood changes)
- tricyclic antidepressants (medications prescribed to treat chronic pain, depression, headaches, and other illnesses)

An adult who is constipated may feel bloated, have a **headache**, swollen abdomen, or pass rock-like feces; or strain, bleed, or feel pain during bowel movements. A constipated baby may strain, cry, draw the legs toward the abdomen, or arch the back when having a bowel movement.

Diagnosis

Everyone becomes constipated once in a while, but a doctor should be notified if significant changes in bowel patterns last for more than a week or if symptoms continue more than three weeks after increasing activity and fiber and fluid intake.

The patient's observations and medical history help a primary care physician diagnose constipation. The doctor uses his fingers to see if there is a hardened mass in the abdomen, and may perform a **rectal examination**. Other diagnostic procedures include a **barium enema**, which reveals blockage inside the intestine; laboratory analysis of blood and stool samples for internal bleeding or other symptoms of systemic disease; and a **sigmoidoscopy** (examination of the sigmoid area of the colon with a flexible tube equipped with a magnifying lens).

Physical and psychological assessments and a detailed history of bowel habits are especially important when an elderly person complains of constipation.

Treatment

If changes in diet and activity fail to relieve occasional constipation, an over-the-counter laxative may be used for a few days. Preparations that soften stools or add bulk (bran, psyllium) work more slowly but are safer than Epsom salts and other harsh **laxatives** or herbal laxatives containing senna (*Cassia senna*) or buckthorn (*Rhamnus purshianna*), which can harm the nerves and lining of the colon.

A woman who is pregnant should never use a laxative. Neither should anyone who is experiencing abdominal pain, nausea, or vomiting.

A warm-water or mineral oil enema can relieve constipation, and a non-digestible sugar (lactulose) or special electrolyte solution is recommended for adults and older children with stubborn symptoms.

If a patient has an impacted bowel, the doctor inserts a gloved finger into the rectum and gently dislodges the hardened feces.

Alternative treatment

Initially, alternative practitioners will suggest that the patient drink an adequate amount of water each day (six to eight glasses), exercise on a regular basis, and eat a diet high in soluble and insoluble fibers. Soluble fibers include pectin, flax, and gums; insoluble fibers include psyllium and brans from grains like wheat and oats. Fresh fruits and vegetables contain both soluble and insoluble fibers. Castor oil, applied topically to the abdomen and covered by a heat source (a heating pad or hot water bottle), can help relieve constipation when used nightly for 20–30 minutes.

Acupressure

This needleless form of **acupuncture** is said to relax the abdomen, ease discomfort, and stimulate regular bowel movements when diet and exercise fail to do so. After lying down, the patient closes his eyes and takes a deep breath. For two minutes, he applies gentle fingertip pressure to a point about two and one-half inches below the navel.

Accupressure can also be applied to the outer edges of one elbow crease and maintained for 30 seconds before pressing the crease of the other elbow. This should be done three times a day to relieve constipation.

Aromatherapy

Six drops of rosemary (*Rosmarinus officinalis*) and six drops of thyme (*Thymus* spp.) diluted by 1 oz of almond oil, olive oil, or another carrier oil can relieve constipation when used to massage the abdomen.

Herbal therapy

A variety of herbal therapies can be useful in the treatment of constipation. Several herbs, including chamomile (*Matricaria recutita*), dandelion (*Taraxacum mongolicum*), and burdock (*Arctium lappa*), act as bitters, stimulating the movement of the digestive and excretory systems. There are also "laxative" herbs that assist with bowel movement. Two of these are senna (*Cassia senna*) and buckthorn (*Rhamnus purshiana*). These "laxative" herbs are stronger acting on elimination than bitters and can sometimes cause cramping (mixing them with a calming herb like fennel or caraway can help reduce cramping). Both senna and buckthorn are powerful herbs that are best used with direction from an experienced practitioner, since they can have adverse side effects and the patient may become dependent on them.

Homeopathy

Homeopathy also can offer assistance with constipation. There are acute remedies for constipation that can be found in one of the many home remedy books on homeopathic medicine. A constitutional prescription also can help rebalance someone who is struggling with constipation.

Constipation is an acute or chronic condition in which bowel movements occur less often than usual or consist of hard, dry stools that are painful or difficult to pass. *(Illustration by Electronic Illustrators Group).*

Massage

Massaging the leg from knee to hip in the morning, at night, and before trying to move the bowels is said to relieve constipation. There is also a specific Swedish massage technique that can help relieve constipation.

Yoga

The knee-chest position, said to relieve gas and stimulate abdominal organs, involves:

- standing straight with arms at the sides
- lifting the right knee toward the chest
- grasping the right ankle with the left hand
- pulling the leg as close to the chest as possible
- holding the position for about eight seconds
- repeating these steps with the left leg

The cobra position, which can be repeated as many as four time a day, involves:

- lying on the stomach with legs together
- placing the palms just below the shoulders, holding elbows close to the body
- inhaling, then lifting the head (face forward) and chest off the floor

- keeping the navel in contact with the floor
- looking as far upward as possible
- holding this position for three to six seconds
- exhaling and lowering the chest

Prognosis

Changes in diet and exercise usually eliminate the problem.

Prevention

Most Americans consume between 11–18 g of fiber a day. Consumption of 30 grams of fiber and between six and eight glasses of water each day can generally prevent constipation.

Thirty-five grams of fiber a day (an amount equal to five servings of fruits and vegetables, and a large bowl of high-fiber cereal) can relieve constipation.

Daily use of 500 mg vitamin C and 400 mg magnesium can prevent constipation. If symptoms do occur, each dosage can be increased by 100 mg a day, up to a maximum of 5,000 mg vitamin C and 1,000 mg magnesium. Use of preventive doses should be resumed after relief occurs, and vitamin C should be decreased to the pre-diarrhea dosage if the patient develops diarrhea.

Sitting on the toilet for 10 minutes at the same time every day, preferably after a meal, can induce regular bowel movements. This may not become effective for a few months, and it is important to defecate whenever necessary.

Fiber supplements containing psyllium (*Plantago psyllium*) usually become effective within about 48 hours and can be used every day without causing dependency. Powdered flaxseed (*Linium usitatissimum*) works the same way. Insoluble fiber, like wheat or oat bran, is as effective as psyllium but may give the patient gas at first.

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Maureen Haggerty

Constitutional homeopathic remedies *see* **Homeopathic remedies, constitutional prescribing**

Consumption *see* **Tuberculosis**

Contact dermatitis

Definition

Contact **dermatitis** is the name for any skin inflammation that occurs when the skin's surface comes in contact with a substance originating outside the body. There are two kinds of contact dermatitis, irritant and allergic.

Description

Thousands of natural and man-made substances can cause contact dermatitis, which is the most common skin condition requiring medical attention and the foremost source of work-related disease. Florists, domestic workers, hairdressers, food preparers, and employees in industry, construction, and health care are the people most at risk of contracting work-related contact dermatitis. Americans spend roughly $300 million a year in their quest for relief from contact dermatitis, not counting the considerable sums devoted by governments and businesses to regulating and policing the use of skin-threatening chemicals in the workplace. But exactly how many people suffer from contact dermatitis remains unclear; a 1997 article in the *Journal of the American Medical Association* notes that figures ranging from 1% to 15% have been put forward for Western industrial nations.

Causes and symptoms

Irritant contact dermatitis (ICD) is the more commonly reported of the two kinds of contact dermatitis, and is seen in about 80% of cases. It can be caused by soaps, detergents, solvents, adhesives, fiberglass, and other substances that are able to directly injure the skin. Most attacks are slight and confined to the hands and forearms, but can affect any part of the body that comes

in contact with an irritating substance. The symptoms can take many forms: redness, **itching**, crusting, swelling, blistering, oozing, dryness, scaliness, thickening of the skin, and a feeling of warmth at the site of contact. In extreme cases, severe blistering can occur and open sores can form. Jobs that require frequent skin exposure to water, such as hairdressing and food preparation, can make the skin more susceptible to ICD.

Allergic contact dermatitis (ACD) results when repeated exposure to an allergen (an allergy-causing substance) triggers an immune response that inflames the skin. Tens of thousands of drugs, pesticides, cosmetics, food additives, commercial chemicals, and other substances have been identified as potential allergens. Fewer than 30, however, are responsible the majority of ACD cases. Common culprits include poison ivy, poison oak, and poison sumac; fragrances and preservatives in cosmetics and personal care products; latex items such as gloves and condoms; and formaldehyde. Many people find that they are allergic to the nickel in inexpensive jewelry. ACD is usually confined to the area of skin that comes in contact with the allergen, typically the hands or face. Symptoms range from mild to severe and resemble those of ICD; a patch test may be needed to determine which kind of contact dermatitis a person is suffering from.

The abdomen of a male patient afflicted with contact dermatitis, triggered by an allergic reaction to a nickel belt buckle. *(Photograph by Dr. P. Marazzi, Custom Medical Stock Photo. Reproduced by permission.)*

Diagnosis

Diagnosis begins with a **physical examination** and asking the patient questions about his or her health and daily activities. When contact dermatitis is suspected, the doctor attempts to learn as much as possible about the patient's hobbies, workplace duties, use of medications and cosmetics, etc.—anything that might shed light on the source of the disease. In some cases, an examination of the home or workplace is undertaken. If the dermatitis is mild, responds well to treatment, and does not recur, ordinarily the investigation is at an end. More difficult cases require patch testing to identify the allergen.

Two methods of patch testing are currently used. The most widely used method, the Finn chamber method, employs a multiwell, aluminum patch. Each well is filled with a small amount of the allergen being tested and the patch is taped to normal skin on the patient's upper back. After 48 hours, the patch is removed and an initial reading is taken. A second reading is made a few days later. The second method of patch testing involves applying a small amount of the test substance to directly to normal skin and covering it with a dressing that keeps air out and keeps the test substance in (occlusive dressing). After 48 hours, the dressing is taken off to see if a reaction has occurred. Identifying the allergen may require repeated testing, can take weeks or months, and is not always successful. Moreover, patch testing works only with ACD, though it is considered an essential step in ruling out ICD.

Treatment

The best treatment for contact dermatitis is to identify the allergen or irritating substance and avoid further contact with it. If the culprit is, for instance, a cosmetic, avoidance is a simple matter, but in some situations, such as an allergy to an essential workplace chemical for which no substitute can be found, avoidance may be impossible or force the sufferer to find new work or make other drastic changes in his or her life. Barrier creams and protective clothing such as gloves, masks, and long-sleeved shirts are ways of coping with contact dermatitis when avoidance is impossible, though they are not always effective.

For the symptoms themselves, treatments in mild cases include cool compresses and nonprescription lotions and ointments. When the symptoms are severe, **corticosteroids** applied to the skin or taken orally are used. Contact dermatitis that leads to a bacterial skin infection is treated with **antibiotics**.

Alternative treatment

Herbal remedies have been used for centuries to treat skin disorders including contact dermatitis. An experienced herbalist can recommend the remedies that

KEY TERMS

Antibiotics—Substances used against microorganisms that cause infection.

Corticosteroids—A group of anti-inflammatory substances often used to treat skin conditions.

Immune response—The protective reaction by the immune system against foreign antigens (substances that the body perceives as potentially dangerous). The immune system combats disease by neutralizing or destroying antigens.

will be most effective for an individual's condition. Among the herbs often recommended are:

- Burdock (*Arctium lappa*) minimizes inflammation and boosts the immune system. It is taken internally as a tea or tincture (a concentrated herbal extract prepared with alcohol).
- Calendula (*Calendula officinalis*) is a natural antiseptic and anti-inflammatory agent. It is applied topically in a lotion, ointment, or oil to the affected area.
- Aloe (*Aloe barbadensis*) soothes skin irritations. The gel is applied topically to the affected area.

A homeopath treating a patient with contact dermatitis will do a thorough investigation of the individual's history and exposures before prescribing a remedy. One homeopathic remedy commonly prescribed to relieve the itching associated with contact dermatitis is *Rhus toxicodendron* taken internally three to four times daily.

Poison ivy, poison oak, and poison sumac are common culprits in cases of allergic contact dermatitis. Following exposure to these plants, rash development may be prevented by washing the area with soap and water within 15 minutes of exposure. The leaves of jewelweed (*Impatiens* spp.), which often grows near poison ivy, may neutralize the poison-ivy allergen if rubbed on the skin right after contact. Several topical remedies may help relieve the itching associated with allergic contact dermatitis, including the juice of plantain leaves (*Plantago major*); a paste made of equal parts of green clay and goldenseal root (*Hydrastis canadensis*); a paste made of salt, water, clay, and peppermint (*Mentha piperita*) oil; and calamine lotion.

Prognosis

If the offending substance is promptly identified and avoided, the chances of a quick and complete recovery are excellent. Otherwise, symptom management—not cure—is the best doctors can offer. For some people, contact dermatitis becomes a chronic and disabling condition that can have a profound effect on employability and quality of life.

Prevention

Avoidance of known or suspected allergens or irritating substances is the best prevention. If avoidance is difficult, barrier creams and protective clothing can be tried. Skin that comes in contact with an offending substance should be thoroughly washed as soon as possible.

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Howard Baker

Contact lenses *see* **Eye glasses and contact lenses**

Continent urinary diversion *see* **Urinary diversion surgery**

Continuous ambulatory electrocardiography *see* **Holter monitoring**

Continuous positive airway *see* **Inhalation therapies**

Contraception

Definition

Contraception (birth control) prevents **pregnancy** by interfering with the normal process of ovulation, fer-

Various types of contraception. *(Photo Researchers, Inc. Reproduced by permission.)*

Types Of Contraceptives

Effectiveness	Predicted (%)	Actual (%)
Birth control pills	99.9	97
Condoms	98	88
Depo Provera	99.7	99.7
Diaphragm	94	82
IUDs	99.2	97
Norplant	99.7	99.7
Tubal sterilization	99.8	99.6
Spermicides	97	79
Vasectomy	99.9	99.9

tilization, and implantation. There are different kinds of birth control that act at different points in the process.

Purpose

Every month, a woman's body begins the process that can potentially lead to pregnancy. An egg (ovum) matures, the mucus that is secreted by the cervix (a cylindrical-shaped organ at the lower end of the uterus) changes to be more inviting to sperm, and the lining of the uterus grows in preparation for receiving a fertilized egg. Any woman who wants to prevent pregnancy must use a reliable form of birth control.

Birth control (contraception) is designed to interfere with the normal process and prevent the pregnancy that could result. There are different kinds of birth control that act at different points in the process, from ovulation, through fertilization, to implantation. Each method has its own side effects and risks. Some methods are more reliable than others.

Although there are many different types of birth control, they can be divided into a few groups based on how they work. These groups include:

- Hormonal methods—These use medications (hormones) to prevent ovulation. Hormonal methods include birth control pills (**oral contraceptives**), Depo Provera injections and Norplant.
- Barrier methods—These methods work by preventing the sperm from getting to and fertilizing the egg. Barrier methods include the **condom**, diaphragm, and cervical cap. The condom is the only form of birth control that also protects against **sexually transmitted diseases**, including HIV (the virus that causes **AIDS**).
- Spermicides—These medications kill sperm on contact. Most spermicides contain nonoxynyl-9. Spermicides come in many different forms such as jelly, foam, tablets, and even a transparent film. All are placed in the vagina. Spermicides work best when they are used at the same time as a barrier method.
- Intrauterine devices—Intrauterine contraceptive devices (IUDs) are inserted into the uterus, where they stay from one to 10 years. An **IUD** prevents the fertilized egg from implanting in the lining of the uterus, and may have other effects as well.
- Tubal sterilization—Tubal sterilization is a permanent form of contraception for women. Each fallopian tube is either tied or burned closed. The sperm cannot reach the egg, and the egg cannot travel to the uterus.
- Vasectomy—is the male form of sterilization, and should also be considered permanent. In **vasectomy**, the vas defrens, the tiny tubes that carry the sperm into the semen, are cut and tied off. Thus, no sperm can get into the semen.

Unfortunately, there is no perfect form of birth control. Only abstinence (not having sexual intercourse) can protect against unwanted pregnancy with 100% reliability. The failure rates, which means the rates of pregnancy, for most forms of birth control are quite low. However, some forms of birth control are more difficult or inconvenient to use than others. In actual practice, the birth control methods that are more difficult or inconvenient have much higher failure rates because they are not used faithfully.

Description

All the different forms of birth control have one thing in common. They are only effective if used faithfully. Birth control pills will work only if taken every day; the

A variety of intrauterine contraceptive devices. The probability of a pregnancy for year of use is about 2 to 3%. IUDs made with copper coils should be replaced every 3 to 5 years. *(Photo Researchers, Inc. Reproduced by permission.)*

diaphragm is effective only if used during every episode of sexual intercourse. The same is true for condoms and the cervical cap. Some methods are automatically working every day, no matter what. These methods include Depo Provera, Norplant, the IUD, and tubal sterilization.

There are many different ways to use birth control. They can be divided into several groups:

- By mouth (oral)—Birth control pills must be taken by mouth every day.
- Injected—Depo Provera is a hormonal medication that is given by injection every three months.
- Implanted—Norplant is a long-acting hormonal form of birth control that is implanted under the skin of the upper arm.
- Vaginal—Spermicides and barrier methods work in the vagina.
- Intra-uterine—The IUD is inserted into the uterus.
- Surgical—Tubal sterilization is a form of surgery. A doctor must perform the procedure in a hospital or surgical clinic. Many women need general anesthesia.

The methods of birth control differ from each other in the timing of when they are used. Some methods of birth control must be used specifically at the time of sexual intercourse (condoms, diaphragm, cervical cap, spermicides). All other methods of birth control must be working all the time to provide protection (hormonal methods, IUDs, tubal sterilization).

Precautions

There are risks associated with some forms of birth control. Some of the risks of each method are listed below:

- Birth control pills—The hormone (estrogen) in birth control pills can increase the risk of **heart attack** in women over 40 who smoke.
- IUD—The IUD can increase the risk of serious pelvic infection. The IUD can also injure the uterus by poking into or through the uterine wall. Surgery might be needed to fix this.
- Tubal sterilization—"Tying the tubes" is a surgical procedure and has all the risks of any other surgery, including the risks of anesthesia, infection, and bleeding.

Preparation

No specific preparation is needed before using contraception. However, a woman must be sure that she is not already pregnant before using a hormonal method or having an IUD placed.

Aftercare

No aftercare is needed.

Risks

Many methods of birth control have side effects. Knowing the side effects can help a woman to determine which method of birth control is right for her.

- Hormonal methods—The hormones in birth control pills, Depo Provera, and Norplant can cause changes in menstrual periods, changes in mood, weight gain, **acne**, and headaches. In addition, it may take many months to begin ovulating again once a woman stops using Depo Provera or Norplant.
- Barrier methods—A woman must insert the diaphragm in just the right way to be sure that it works properly. Some women get more urinary tract infections if they use a diaphragm. This is because the diaphragm can press against the urethra, the tube that connects the bladder to the outside.
- Spermicides—Some women and men are allergic to spermicides or find them irritating to the skin.
- IUD—The IUD is a foreign body that stays inside the uterus, and the uterus tries to get it out. A woman may have heavier menstrual periods and more menstrual cramping with an IUD in place.

KEY TERMS

Fallopian tubes—The thin tubes that connect the ovary to the uterus. Ova (eggs) travel from the ovary to the uterus. If the egg has been fertilized, it can implant in the uterus.

Fertilization—The joining of the sperm and the egg; conception.

Implantation—The process in which the fertilized egg embeds itself in the wall of the uterus.

Ovulation—The release of an egg (ovum) from the ovary.

- Tubal sterilization—Some women report increased menstrual discomfort after **tubal ligation**. It is not known if this is related to the tubal ligation itself.

There is no perfect form of birth control. Every method has a small failure rate and side effects. Some methods carry additional risks. However, every method of birth control can be effective if used properly.

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Contractures

Definition

Contractures are the chronic loss of joint motion due to structural changes in non-bony tissue. These non-bony tissues include muscles, ligaments, and tendons.

Description

Contractures can occur at any joint of the body. This joint dysfunction may be a result of **immobilization** from injury or disease; nerve injury, such as spinal cord damage and **stroke**; or muscle, tendon, or ligament disease.

Causes and symptoms

There are a number of pathologies and diseases that can lead to joint contractures. The primary causes resulting in a joint contraction are muscle imbalance, **pain**, prolonged bed rest, and immobilization. Because of the frequency of **fractures** and surgery, immobilization is the most frequent cause of joint contractures. Symptoms include a significant loss of motion to any specific joint that results in immobility. If the contracture is of a significant degree, pain can result even without any voluntary joint movement.

Diagnosis

Manual testing of joint mobility by a healthcare professional skilled in joint mobilization techniques (e.g. a physical therapist) will identify indications of restricted structures within the joint. Measuring the motion of the joint with a device termed a "goniometer" can be useful if the decrease of motion can be shown to be a proven result of a joint contracture. X rays can be of some benefit in the diagnosis of contractures, because a visible decrease in joint space may indicate a tight, contracted joint. Most physicians will make the diagnosis after a thorough **physical examination** involving physical and manual testing of the joint motion.

Treatment

Manual techniques

Joint mobilization and stretching of soft tissues is a common technique used to increase joint elasticity. Structures are stretched in similar directions to those which take place upon normal joint motion. Some healthcare professionals may use some form of heat prior to the stretching and mobilization. If appropriate, **exercise** may follow manual techniques to help maintain the additional motion achieved.

Mechanical techniques

Devices known as continuous passive motion machines are very popular, especially following surgery of joints. Continuous passive motion machines (CPM) are specifically adjusted to each individual's need. This method is administered within the first 24–72 hours after the injury or surgery. The joint is mechanically moved through the patient's tolerable motion. CPM machines have been proved to accelerate the return motion process, allowing patients more function in less time.

KEY TERMS

Mobilization—Making movable, restoring the power of motion in a joint. Movement which increases joint mobility.

Muscle tone—Also termed tonus; the normal state of balanced tension in the tissues of the body, especially the muscles.

Casting or splinting

Casting or splinting techniques are used to provide a constant stretch to the soft tissues surrounding a joint. It is most effective when used to increase motion of a joint from prolonged immobilization. It is also popular for treating contractures resulting from an increase in muscle tone from nerve injury. After an initial holding cast is applied for seven to 10 days, a series of positional casts are applied at weekly intervals. Before the application of each new cast, the joint is moved as much as can be tolerated by the patient, and measured by a goniometer. When as much motion as possible is obtained after stretching, another final cast is applied to maintain the newly acquired motion.

Surgery

In some cases the contracture may be severe and not respond to conservative treatment. In this event, manipulation of the joint under a general anesthesia may be necessary.

Alternative treatment

In some areas of the body, **chiropractic** techniques have been found to be useful to improve motion. **Massage therapy** can be beneficial by promoting additional circulation to joint structures, causing better elasticity. **Yoga** can help prevent as well as rehabilitate a contracture and can facilitate the return of joint mobility.

Prognosis

Prognosis of contractures will depend upon the cause of the contracture. In general, the earlier the treatment for the contracture begins, the better the prognosis.

Prevention

Prevention of contractures and deformities from **spinal cord injury**, fracture, and immobilization is achieved through a program of positioning, splinting if appropriate, and range-of-motion exercises either manually or mechanically aided. These activities should be started as early as possible for optimal results.

Resources

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The American College of Rheumatology. 1800 Century Place, Suite 250, Atlanta, GA 30345. (404) 633-3777. <http://www.rheumatology.org>.

American Physical Therapy Association. 1111 North Fairfax St., Alexandria, Virginia 22314. (800) 999-2782. <https://www.apta.org>.

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Conversion disorder *see* **Somatoform disorders**

Cooley's anemia *see* **Thalassemia**

Cooling treatments

Definition

Cooling treatments lower body temperature in order to relieve **pain**, swelling, constriction of blood vessels, and to decrease the liklihood of cellular damage by slowing the metabolism. Sponge baths, cold compresses, and cold packs are all wet cooling treatments. Dry treatments, such as ice bags and chemical cold packs, are also used to lower body temperature.

Purpose

The most common reason for cooling a body is **fever** or hyperthermia (extremely high fever). The body can sustain temperatures up to 104°F (40°C) with relative safety; however, when temperatures rise above 104°F (40°C), damage to the brain, muscles, blood, and kidneys is increasingly likely. Cooling treatments are also applied immediately following sprains, **bruises**, **burns**, eye injuries, and muscle spasms to help alleviate the resulting swelling, pain, and discoloration of the skin.

Cooling treatments slow chemical reactions within the body. For this reason, cooling tissues below normal temperature (98.6°F/37°C) can prevent injury from inadequate oxygen or **nutrition**. Cold water drowning victims suffering from **hypothermia** (cooling of the body below its normal temperature) have been successfully resuscitated after long periods underwater without medical complications because of this effect. For the past 40 years, heart surgeons have been experimenting with hypothermia to protect tissues from lack of blood circulation during an operation. Neurosurgeons are also working with hypothermia to protect the very sensitive brain tissues during periods of absent or reduced blood flow.

Description

Depending on the medical need, various cooling methods are used.

- Cold packs and ice bags are placed on a localized site and provide topical relief. These compresses should be covered with a waterproof material to protect the skin. Repeated treatments produce the desired pain and swelling relief.
- Cold treatments are placed on the groin and under the arms to treat hyperthermia. Treatments are refreshed periodically until the appropriate temperature is attained.
- A tepid sponge bath relieves fever without cooling the body too fast. Eighty degrees Farenheit is still 20°F below body temperature and yet warm enough not to drive blood from the skin, thereby preventing the cooling from getting to the body's core. Limbs are bathed first and then the chest, abdomen, back, and buttocks.
- Perfusion of isolated regions like the brain by using cooled blood is an experimental treatment, offering promising results for the treatment of stroke.

Preparation

Topical treatments are prepared with ice, cold water (59°F/15°C), and chemical cold packs. Tepid baths should be 80–93°F (26.7–34°C).

Risks

Small children, adults with circulation problems, and the elderly are all at risk of tissue damage. Rapid cooling causes chills, which in effect raise the body's temperature by raising its metabolism. Blood clots may form from thickened blood caused by the temperature change.

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Coombs' tests

Definition

Coombs' tests are blood tests that identify the causes of anemia.

Purpose

Anemia, which literally means no blood, refers to blood with abnormally low oxygen-carrying capacity. The hemoglobin in red blood cells carries oxygen. One of the many causes of anemia is destruction of red blood cells, a process called hemolysis (*hemo* means blood and *lysis* means disintegration). A simple **blood count** detects anemia. Even the test done before a blood donation can identify anemia. To detect hemolysis requires other tests. The Coombs' tests are conducted in order to determine the cause of anemia.

One characteristic of hemolysis is the autoimmune response against the body's red blood cells. Instead of protecting the body from outside agents, the immune system attacks parts of its own body with a deluge of antibodies. Autoimmunity is thought to be the cause of many collagen-vascular diseases, including **rheumatoid arthritis** and **systemic lupus erythematosus**. It is also the cause of the autoimmune hemolytic **anemias**. The Coombs' tests detect the antibodies responsible for the destruction of the red blood cells.

Causes of autoimmune **hemolytic anemia** include:

- drugs such as penicillin, methyldopa (lowers blood pressure), and quinidine (treats heart rhythm disturbances)
- cancers of the lymph system—Hodgkin's disease and lymphomas
- virus infections
- collagen-vascular diseases
- mismatched blood transfusions
- Rh incompatibility between a mother and fetus. This disease is called erythroblastosis fetalis

KEY TERMS

Antibody—A protein made by the immune system and used as a weapon against foreign invaders in the body.

Antigen—The chemical that stimulates an immune response.

Anemia—Reduced oxygen-carrying capacity of the blood, due to too little hemoglobin or too few red blood cells.

Collagen-vascular disease—Various diseases inflaming and destroying connective tissue.

Hematologist—Physician who specializes in diseases of the blood.

Hemoglobin—The red pigment in blood that carries oxygen.

Hemolysis—Breaking apart red blood cells.

Rh—A blood typing group, like the ABO system. When a mother is Rh negative and her baby is Rh positive, she may develop antibodies to the baby's blood that will cause it to hemolyze.

Many times the cause cannot be identified.

Description

There are two Coombs' tests. A direct Coombs' test detects the two different antigens that might induce hemolysis in the patient's red blood cells. An indirect Coombs' test looks for antibodies to someone else's red blood cells in the patient's serum (the blood without the cells). Combining the two tests gives clues to the origin of the hemolysis.

Preparation

No preparation is needed for this test. It will probably be among the second or third set of blood tests done after anemia is diagnosed and there is a suspicion that its cause is hemolysis.

Aftercare

Coombs' tests are done on blood that is drawn from the arm.

Risks

Taking blood for testing is the most common medical procedure performed. The worst complication is a bruise at the site of the puncture or punctures. It is extremely rare for the needle to injure an important structure such as an artery or a nerve.

Normal results

If the Coombs' tests are negative, the anemia is unlikely to be autoimmune, and the hematologist will have to search elsewhere for a cause.

Abnormal results

If the test is positive, the antigens that react will narrow the search for a cause. Coombs' tests are also done for blood **transfusion** reactions to determine why the transfused blood did not match, and when there is a chance a newborn may have an Rh problem.

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Coordination tests *see* **Balance and coordination tests**

COPD *see* **Emphysema; Chronic obstructive lung disease**

Copper deficiency *see* **Mineral deficiency**

Copper excess *see* **Wilson's disease**

Cor pulmonale

Definition

Cor pulmonale is an increase in bulk of the right ventricle of the heart, generally caused by chronic diseases or malfunction of the lungs. This condition can lead to **heart failure**.

Description

Cor pulmonale, or pulmonary heart disease, occurs in 25% of patients with chronic obstructive pulmonary dis-

ease (COPD). In fact, about 85% of patients diagnosed with cor pulmonale have COPD. Chronic **bronchitis** and **emphysema** are types of COPD. High blood pressure in the blood vessels of the lungs (**pulmonary hypertension**) causes the enlargement of the right ventricle. In addition to COPD, cor pulmonale may also be caused by lung diseases, such as **cystic fibrosis**, **pulmonary embolism,** and pneumoconiosis. Loss of lung tissue after **lung surgery** or certain chest-wall disturbances can produce cor pulmonale, as can neuromuscular diseases, such as **muscular dystrophy**. A large pulmonary thromboembolism (blood clot) may lead to acute cor pulmonale.

Causes and symptoms

Any respiratory disease or malfunction that affects the circulatory system of the lungs may lead to cor pulmonale. These circulatory changes cause the right ventricle to compensate for the extra work required to pump blood through the lungs. The right ventricle has thin walls and is crescent-shaped. The resulting pressure causes the right ventricle to dilate and bulge, eventually leading to its failure.

Cor pulmonale should be expected in any patient with COPD and other respiratory or neuromuscular diseases. Initial symptoms of cor pulmonale may actually reflect those of the underlying disease. These may include chronic coughing, **wheezing**, weakness, **fatigue**, and **shortness of breath**. **Edema** (abnormal buildup of fluid), weakness, and discomfort in the upper chest may be evident in cor pulmonale.

Diagnosis

An electrocardiograph (EKG) will show signs such as frequent premature contractions in the atria or ventricles. Chest x rays may show enlargement of the right descending pulmonary artery. This sign, along with an enlarged main pulmonary artery, indicates pulmonary artery **hypertension** in patients with COPD. **Magnetic resonance imaging** (MRI) is often the preferred method of diagnosis for cor pulmonale because it can clearly show and measure volume of the pulmonary arteries. Other tests used to support a diagnosis of cor pulmonale may include arterial **blood gas analysis**, pulmonary function tests, and **hematocrit**.

Treatment

Treatment of cor pulmonale is aimed at increasing a patient's **exercise** tolerance and improving oxygen levels of the arterial blood. Treatment is also aimed at the underlying condition that is producing cor pulmonale. Common treatments include **antibiotics** for respiratory infection; anticoagulants to reduce the risk of thromboembolism; and digitalis, oxygen, and **phlebotomy** to reduce red blood cell count. A low-salt diet and restricted fluids are often prescribed.

KEY TERMS

Ventricle—A cavity, as in the brain or heart. The right ventricle of the heart drives blood from the heart into the pulmonary artery, which supplies blood to the lungs.

Alternative treatment

Co-management of the patient with cor pulmonale should be coordinated between the medical doctor and the alternative practitioner. The first step in treatment is to determine the cause of the condition and to evaluate all organ systems of the body. Dietary considerations, for example, a low-salt diet and reduced fluid intake aimed at reducing the edema associated with cor pulmonale, can be supportive aspects of treatment.

Prognosis

The prognosis for cor pulmonale is poor, particularly because it occurs late in the process of serious disease.

Prevention

Cor pulmonale is best prevented by prevention of COPD and other irreversible diseases that lead to heart failure. **Smoking** cessation is critically important. Carefully following the recommended course of treatment for the underlying disease may help prevent cor pulmonale.

Resources

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ORGANIZATIONS

American Heart Association. 7320 Greenville Ave. Dallas, TX 75231. (214) 373-6300. <http://www.americanheart.org>.

National Heart, Lung and Blood Institute. P.O. Box 30105, Bethesda, MD 20824-0105. (301) 251-1222. <http://www.nhlbi.nih.gov>.

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Cori's disease *see* **Glycogen storage diseases**

Corkscrew esophagus *see* **Diffuse esophageal spasm**

Corneal abrasion

Definition

A corneal abrasion is a worn or scraped-off area of the outer, clear layer of the eye (cornea).

Description

The cornea is the clear, dome-shaped outer area of the eye. It lies in front of the colored part of the eye (iris) and the black hole in the iris (pupil). The outermost layer of the eyeball consists of the cornea and the white part of the eye (sclera). A corneal abrasion is basically a superficial cut or scrape on the cornea. A corneal abrasion is not as serious as a corneal ulcer, which is generally deeper and more severe than an abrasion.

Causes and symptoms

A corneal abrasion is usually the result of direct injury to the eye, often from a fingernail scratch, makeup brushes, contact lenses, foreign body, or even twigs. Patients often complain of feeling a foreign body in their eye, and they may have **pain**, sensitivity to light, or tearing.

Diagnosis

Ophthalmologists and optometrists, who treat eye disorders, are well qualified to diagnose corneal abrasions. The doctor will check the patient's vision (visual acuity) in both eyes with an eye chart. A patient history will also be taken, which may help to determine the cause of the abrasion. A slit lamp, which is basically a microscope and light source, will allow the doctor to see the abrasion. Fluorescein, a yellow dye, may be placed into the eye to determine the extent of the abrasion. The fluorescein will temporarily stain the affected area.

Treatment

The cornea has a remarkable ability to heal itself, so treatment is designed to minimize complications. If the abrasion is very small, the doctor might just suggest an eye lubricant and a follow-up visit the next day. A very small abrasion should heal in one to two days; others usually in one week. However, to avoid a possible infection, an antibiotic eye drop may be prescribed. Sometimes additional eye drops may make the eye feel more comfortable. Depending upon the extent of the abrasion, some doctors may patch the affected eye. It is very important to go for the follow-up checkup to make sure an infection does not occur. Use of contact lenses should not be resumed without the doctor's approval.

A close-up view of an abrasion on patient's cornea. *(Photograph by Dennis R. Cain, CRA, Custom Medical Stock Photo. Reproduced by permission.)*

Prognosis

In typical cases, the prognosis is good. The cornea will heal itself, usually within several days. A very deep abrasion may lead to scarring. If the abrasion does not heal properly, a recurrent corneal erosion (RCE) may result months or even years later. The symptoms are the same as for an abrasion (e.g., tearing, foreign body sensation, and blurred vision), but it will keep occurring. Similar or additional treatment for the RCE may be necessary.

Prevention

Everyone should wear eye protection whenever this is recommended. This should be standard practice when using power tools and playing certain sports. Goggles should even be worn when mowing the lawn, because a twig can be thrown upward toward the face. Contact lens wearers should be careful to follow their doctors' instructions on caring for and wearing their lenses. Ill-fitting or dirty lenses could lead to an abrasion, so patients should go for their prescribed checkups.

Resources

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ORGANIZATIONS

American Academy of Family Physicians. 8880 Ward Parkway, Kansas City, MO 64114. (816) 333-9700. <http://www.aafp.org>.

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Corneal infection *see* **Keratitis**

Corneal keratoplasty *see* **Corneal transplantation**

Corneal transplantation

Definition

In corneal transplant, also known as keratoplasty, a patient's damaged cornea is replaced by the cornea from the eye of a human cadaver. This is the single most common type of human transplant surgery and has the highest success rate. Eye banks acquire and store eyes from donor individuals largely to supply the need for transplant corneas.

Purpose

Corneal transplant is used when vision is lost in an eye because the cornea has been damaged by disease or traumatic injury. Some of the disease conditions that might require corneal transplant include the bulging outward of the cornea (keratoconus), a malfunction of the inner layer of the cornea (Fuchs' dystrophy), and painful swelling of the cornea (pseudophakic bullous keratopathy). Some of these conditions cause cloudiness of the cornea; others alter its natural curvature, which can also reduce the quality of vision.

Injury to the cornea can occur because of chemical **burns**, mechanical trauma, or infection by viruses, bacteria, fungi, or protozoa. The herpes virus produces one of the more common infections leading to corneal transplant.

Surgery would only be used when damage to the cornea is too severe to be treated with corrective lenses. Occasionally, corneal transplant is combined with other types of eye surgery (such as **cataract surgery**) to solve multiple eye problems in one procedure.

A corneal transplant in progress. *(Photograph by Chet Szymecki, Phototake NYC. Reproduced by permission.)*

Precautions

Corneal transplant is a very safe procedure that can be performed on almost any patient who would benefit from it. Any active infection or inflammation of the eye usually needs to be brought under control before surgery can be performed.

Description

The cornea is the transparent layer of tissue at the very front of the eye. It is composed almost entirely of a special type of collagen. It normally contains no blood vessels, but because it contains nerve endings, damage to the cornea can be very painful.

In a corneal transplant, a disc of tissue is removed from the center of the eye and replaced by a corresponding disc from a donor eye. The circular incision is made using an instrument called a trephine. In one form of corneal transplant (penetrating keratoplasty), the disc removed is the entire thickness of the cornea and so is the replacement disc. Over 90% of all corneal transplants in the United States are of this type. In lamellar keratoplasty, on the other hand, only the outer layer of the cornea is removed and replaced.

The donor cornea is attached with extremely fine sutures. Surgery can be performed under anesthesia that is confined to one area of the body while the patient is awake (local anesthesia) or under anesthesia that places the entire body of the patient in a state of unconsciousness (general anesthesia.) Surgery requires 30–90 minutes.

Over 40,000 corneal transplants are performed in the United States each year. Medicare reimbursement for a corneal transplant in one eye was about $1,200 in 1997.

A less common but related procedure called epikeratophakia involves suturing the donor cornea directly

KEY TERMS

Cadaver—The human body after death.

Cataract—A condition of cloudiness of the lens of the eye.

Cornea—The transparent layer of tissue at the very front of the eye.

Corticosteroids—Synthetic hormones widely used to fight inflammation.

Epikeratophakia—A procedure in which the donor cornea is attached directly onto the host cornea.

Epithelial cells—Cells that form a thin surface coating on the outside of a body structure.

Fibrous connective tissue—Dense tissue found in various parts of the body containing very few living cells.

Fuchs' dystrophy—A hereditary disease of the inner layer of the cornea. Treatment requires penetrating keratoplasty. The lens of the eye may also be affected and require surgical replacement at the same time as the cornea.

Glaucoma—A vision defect caused when excessive fluid pressure within the eye damages the optic nerve.

Histocompatibility antigens—Proteins scattered throughout body tissues that are unique for almost every individual.

Keratoconus—An eye condition in which the cornea bulges outward, interfering with normal vision. Usually both eyes are affected.

Pseudophakic bullous keratopathy—Painful swelling of the cornea occasionally occurring after surgery to implant an artificial lens in place of a lens affected by cataract.

Retinal detachment—A serious vision disorder in which the light-detecting layer of cells inside the eye (retina) is separated from its normal support tissue and no longer functions properly.

Trephine—A small surgical instrument that is rotated to cut a circular incision.

onto the surface of the existing host cornea. The only tissue removed from the host is the extremely thin epithelial cell layer on the outside of the host cornea. There is no permanent damage to the host cornea, and this procedure can be reversed. It is usually employed in children. In adults, the use of contact lenses can usually achieve the same goals.

Preparation

No special preparation for corneal transplant is needed. Some eye surgeons may request the patient have a complete **physical examination** before surgery. The patient may also be asked to skip breakfast on the day of surgery.

Aftercare

Corneal transplant is often performed on an outpatient basis, although some patients need brief hospitalization after surgery. The patient will wear an eye patch at least overnight. An eye shield or glasses must be worn to protect the eye until the surgical wound has healed. Eye drops will be prescribed for the patient to use for several weeks after surgery. These drops include **antibiotics** to prevent infection as well as **corticosteroids** to reduce inflammation and prevent graft rejection.

For the first few days after surgery, the eye may feel scratchy and irritated. Vision will be somewhat blurry for as long as several months.

Sutures are often left in place for six months, and occasionally for as long as two years.

Risks

Corneal transplants are highly successful, with over 90% of operations in United States achieving restoration of sight. However, there is always some risk associated with any surgery. Complications that can occur include infection, **glaucoma**, **retinal detachment**, cataract formation, and rejection of the donor cornea.

Graft rejection occurs in 5–30% of patients, a complication possible with any procedure involving tissue transplantation from another person (allograft). Allograft rejection results from a reaction of the patient's immune system to the donor tissue. Cell surface proteins called histocompatibility antigens trigger this reaction. These antigens are often associated with vascular tissue (blood vessels) within the graft tissue. Since the cornea normally contains no blood vessels, it experiences a very low rate of rejection. Generally, blood typing and **tissue typing** are not needed in corneal transplants, and no close match between donor and recipient is required. Symp-

toms of rejection include persistent discomfort, sensitivity to light, redness, or a change in vision.

If a rejection reaction does occur, it can usually be blocked by steroid treatment. Rejection reactions may become noticeable within weeks after surgery, but may not occur until 10 or even 20 years after the transplant. When full rejection does occur, the surgery will usually need to be repeated.

Although the cornea is not normally vascular, some corneal diseases cause vascularization (the growth of blood vessels) into the cornea. In patients with these conditions, careful testing of both donor and recipient is performed just as in transplantation of other organs and tissues such as hearts, kidneys, and bone marrow. In such patients, repeated surgery is sometimes necessary in order to achieve a successful transplant.

Cornea donors are carefully screened. Individuals with infectious diseases are not accepted as donors.

Resources

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ORGANIZATIONS

American Academy of Ophthalmology. 655 Beach Street, P.O. Box 7424, San Francisco, CA 94120-7424. <http://www.eyenet.org>.

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Corneal ulcers

Definition

The cornea, the clear front part of the eye through which light passes, is subject to many infections and to injury from exposure and from **foreign objects**. Infection and injury cause inflammation of the cornea—a condition called **keratitis**. Tissue loss because of inflammation produces an ulcer. The ulcer can either be centrally located, thus greatly affecting vision, or peripherally located. There are about 30,000 cases of bacterial corneal ulcers in the United States each year.

A close-up view of an ulcer on cornea. *(Custom Medical Stock Photo. Reproduced by permission.)*

Description

The most common cause of corneal ulcers is germs, but most of them cannot invade a healthy cornea with adequate tears and a functioning eyelid. They gain access because injury has impaired these defense mechanisms. A direct injury from a foreign object inoculates germs directly through the outer layer of the cornea, just as it does to the skin. A caustic chemical can inflame the cornea by itself or so damage it that germs can invade. Improper use of contact lenses has become a common cause of corneal injury. Eyelid or tear function failure is the other way to make the eye vulnerable to infection. Tears and the eyelid together wash the eye and prevent foreign material from settling in. Tears contain enzymes and other substances to help protect against infection. Certain diseases dry up tear production, leaving the cornea dry and defenseless. Other diseases paralyze or weaken the eyelids so that they cannot effectively protect and cleanse the eyes.

Causes and symptoms

Viruses, bacteria, fungi, and a protozoan called *Acanthamoeba* can all invade the cornea and damage it under suitable conditions.

- Bacteria from a common **conjunctivitis** (pink eye) rarely spread to the cornea, but can if untreated.

KEY TERMS

Fluorescein—A fluorescent chemical used to examine the cornea.

Germ—A disease-causing microorganism.

Inflammation—The body's reaction to irritation.

Topical corticosteroids—Cortisone and related drugs used on the skin and in the eye, usually for allergic conditions.

- Fecal bacteria are more likely to be able to infect the cornea.
- A bacterium called *Pseudomonas aeruginosa*, which can contaminate eyedrops, is particularly able to cause corneal infection.
- A group of incomplete bacteria known as *Chlamydia* can be transmitted to the eye directly by flies or dirty hands. One form of chlamydial infection is the leading cause of blindness in developing countries and is known as Egyptian ophthalmia or **trachoma**. Another type of *Chlamydia* causes a sexually transmitted disease.
- Other sexually transmitted diseases—for example, syphilis—can affect the cornea.

The most common viruses to damage the cornea are adenoviruses and herpes viruses. Viral and fungal infections are often caused by improper use of topical **corticosteroids**. If topical corticosteroids are used in a patient with herpes simplex keratitis, the ulcer can get much worse and blindness could result.

Symptoms are obvious. The cornea is intensely sensitive, so corneal ulcers normally produce severe **pain**. If the corneal ulcer is centrally located, vision is impaired or completely absent. Tearing is present and the eye is red. It hurts to look at bright lights.

Diagnosis

The doctor will take a case history to try to determine the cause of the ulcer. This can include improper use of contact lenses; injury, such as a scratch from a twig; or severe dry eye. An instrument called a slit lamp will be used to examine the cornea. The slit lamp is a microscope with a light source that magnifies the cornea, allowing the extent of the ulcer to be seen. Fluorescein, a yellow dye, may be used to illuminate further detail. If a germ is responsible for the ulcer, identification may require scraping samples directly from the cornea, conjunctiva, and lids, and sending them to the laboratory.

Treatment

A corneal ulcer needs to be treated aggressively, as it can result in loss of vision. The first step is to eliminate infection. Broad spectrum **antibiotics** will be used before the lab results come back. Medications may then be changed to more specifically target the cause of the infection. A combination of medications may be necessary. Patients should return for their follow-up visits so that the doctor can monitor the healing process. The cornea can heal from many insults, but if it remains scarred, **corneal transplantation** may be necessary to restore vision. If the corneal ulcer is large, hospitalization may be necessary.

Prognosis

Treated early enough, corneal infections will usually resolve, perhaps even without the formation of an ulcer. However, left untreated, infections can lead to ulcers and the corneal ulcer can result in scarring or perforation of the cornea. Other problems may occur as well, including **glaucoma**. Patients with certain systemic diseases that impede healing (such as **diabetes mellitus** or **rheumatoid arthritis**) may need more aggressive treatment. The later the treatment, the more damage will be done and the more scarring will result. Corneal transplant is standard treatment with a high probability of success.

Prevention

Attentive care of contact lenses will greatly reduce the incidence of corneal damage and ulceration. Germs that cause no problems in the mouth or on the hands can damage the eye, so contact lens wearers must wash their hands before touching their lenses and must not use saliva to moisten them. Tap water should not be used to rinse the lenses. Contacts should be removed whenever there is irritation and left out until the eyes are back to normal. It is not advisable to wear contact lenses while swimming or in hot tubs. Daily wear contact lenses have been found to be less of a risk than contacts for overnight wear (extended wear). Organisms have been cultured from contact lens cases, so the cases should be rinsed in hot water and allowed to air dry. Cases should be replaced every three months. Patients should follow their doctors' schedules for replacement of the contacts.

Eye protection in the workplace, or wherever tiny particles are flying around, is essential. Ultraviolet (UV) coatings on glasses or sunglasses can help protect the eyes from the sun's rays. Goggles with UV protection should be worn when skiing or in suntanning salons to protect against UV rays. Prompt attention to any red eye should prevent progressive damage.

For people with inadequate tears, use of artificial tears eyedrops will prevent damage from drying. Eyelids that do not close adequately may temporarily have to be sewn shut to protect the eye until more lasting treatment can be instituted.

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American Optometric Association. 243 North Lindbergh Blvd., St. Louis, MO 63141. (314) 991-4100. <http://www.aoanet.org>.

Prevent Blindness America. 500 East Remington Road, Schaumburg, IL 60173. (800) 331-2020. <http://www.preventblindness.org>.

J. Ricker Polsdorfer, MD

Corns and calluses

Definition

A corn is a small, painful, raised bump on the outer skin layer. A callus is a rough, thickened patch of skin.

Description

Corns and calluses are one of the three major foot problems in the United States. The other two are foot infections and toenail problems. Corns and calluses affect about 5% of the population.

Corns usually appear on non-weight-bearing areas like the outside of the little toe or the tops of other toes. Women have corns more often than men, probably because women wear high-heeled shoes and other shoes that do not fit properly. Corns have hard cores shaped like inverted pyramids. Sharp **pain** occurs whenever downward pressure is applied, and a dull ache may be felt at other times.

Calluses occur most often on the heels and balls of the feet, the knees, and the palms of the hands. However, they can develop on any part of the body that is subject to repeated pressure or irritation. Calluses are usually more than an inch wide—larger than corns. They generally don't hurt unless pressure is applied.

Corns on toes. *(Custom Medical Stock Photo. Reproduced by permission.)*

Types of corns

A hard corn is a compact lump with a thick core. Hard corns usually form on the tops of the toes, on the outside of the little toe, or on the sole of the foot.

A soft corn is a small, inflamed patch of skin with a smooth center. Soft corns usually appear between the toes.

A seed corn is the least common type of corn. Occurring only on the heel or ball of the foot, a seed corn consists of a circle of stiff skin surrounding a plug of cholesterol.

Types of calluses

A plantar callus, a callus that occurs on the sole of the foot, has a white center. Hereditary calluses develop where there is no apparent friction, run in families, and occur most often in children.

Causes and symptoms

Corns and calluses form to prevent injury to skin that is repeatedly pinched, rubbed, or irritated. The most common causes are:

- shoes that are too tight or too loose, or have very high heels
- tight socks or stockings
- deformed toes

KEY TERMS

Ayurveda—Ayurveda is a system of wholistic medicine from India that aims to bring the individual into harmony with nature. It provides guidance regarding food and lifestyle, so that healthy people can stay healthy and people with health challenges can improve their health.

Bursitis—Inflammation of a bursa, a fluid-filled cavity or sac. In the body, bursae are located at places where friction might otherwise develop.

- walking down a long hill, or standing or walking on a hard surface for a long time

Jobs or hobbies that cause steady or recurring pressure on the same spot can also cause calluses.

Symptoms include hard growths on the skin in response to direct pressure. Corns may be extremely sore and surrounded by inflamed, swollen skin.

Diagnosis

Corns can be recognized on sight. A family physician or podiatrist may scrape skin off what seems to be a callus, but may actually be a wart. If the lesion is a wart, it will bleed. A callus will not bleed, but will reveal another layer of dead skin.

Treatment

Corns and calluses do not usually require medical attention unless the person who has them has **diabetes mellitus**, poor circulation, or other problems that make self-care difficult.

Treatment should begin as soon as an abnormality appears. The first step is to identify and eliminate the source of pressure. Placing moleskin pads over corns can relieve pressure, and large wads of cotton, lamb's wool, or moleskin can cushion calluses.

Using hydrocortisone creams or soaking feet in a solution of Epsom salts and very warm water for at least five minutes a day before rubbing the area with a pumice stone will remove part or all of some calluses. Rubbing corns just makes them hurt more.

Applying petroleum jelly or lanolin-enriched hand lotion helps keep skin soft, but corn-removing ointments that contain acid can damage healthy skin. They should never be used by pregnant women or by people who are diabetic or who have poor circulation.

It is important to see a doctor if the skin of a corn or callus is cut, because it may become infected. If a corn discharges pus or clear fluid, it is infected. A family physician, podiatrist, or orthopedist may:

- remove (debride) affected layers of skin
- prescribe oral **antibiotics** to eliminate infection
- drain pus from infected corns
- inject cortisone into the affected area to decrease pain or inflammation
- perform surgery to correct toe deformities or remove bits of bone

Alternative treatment

Standing and walking correctly can sometimes eliminate excess foot pressure. Several types of bodywork can help correct body imbalances. Bodywork is a term used for any of a number of systems, including **Aston-Patterning**, the **Feldenkrais method**, and **rolfing**, that manipulate the body through massage, movement education, or meditational techniques.

Aloe (*Aloe barbadensis*) cream is an effective skin softener, and two or three daily applications of calendula (*Calendula officinalis*) salve can soften skin and prevent inflammation. One teaspoon of lemon juice mixed with one teaspoon of dried chamomile (*Martricaria recutita*) tea and one crushed garlic clove dissolves thickened skin.

An ayurvedic practitioner may recommend the following treatment:

- apply each day a paste made by combining one teaspoon of aloe vera gel with half that amount of turmeric (*Circuma longa*)
- bandage overnight
- soak in warm water for 10 minutes every morning
- massage gently with mustard (*Brassica cruciferae*) oil

Prognosis

Most corns and calluses disappear about three weeks after the pressure that caused them is eliminated. They are apt to recur if the pressure returns.

Extreme pain can change the way a person stands or walks. Such changes can, in turn, cause pain in the ankle, back, hip, or knee.

Bursitis, a painful, inflamed fluid-filled sac, can develop beneath a corn. An ulcer or broken area within a corn can reach to the bone. Infection can have serious consequences for people who have diabetes or poor circulation.

Prevention

Corns and calluses can usually be prevented by avoiding friction-causing activities and wearing shoes that fit properly, are activity-appropriate, and are kept in good repair. Soles and heels that wear unevenly may indicate a need for corrective footwear or special insoles. Socks and stockings should not cramp the toes. Gloves, kneepads, and other protective gear should also be worn as needed.

Feet should be measured, while standing, whenever buying new shoes. It is best to shop for shoes late in the day, when feet are likely to be swollen. It is also important to buy shoes with toe-wiggling room and to try new shoes on both feet.

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Maureen Haggerty

Coronary artery bypass graft surgery

Definition

Coronary artery bypass graft surgery is a surgical procedure in which one or more blocked coronary arteries are bypassed by a blood vessel graft to restore normal blood flow to the heart. These grafts usually come from the patient's own arteries and veins located in the leg, arm, or chest.

Purpose

Coronary artery bypass graft surgery (also called coronary artery bypass surgery, CABG, and bypass operation) is performed to restore blood flow to the heart. This relieves chest **pain** and **ischemia**, improves the patient's quality of life, and in some cases, prolongs the patient's life. The goals of the procedure are to enable the patient to resume a normal lifestyle and to lower the risk of a **heart attack**.

The decision to perform coronary artery bypass graft surgery is a complex one, and there is some disagreement among experts as to when it is indicated. Many experts feel that it has been performed too frequently in the United States. According to the American Heart Association, appropriate candidates for coronary artery bypass graft surgery include patients with blockages in at least three major coronary arteries, especially if the blockages are in arteries that feed the heart's left ventricle; patients with **angina** so severe that even mild exertion causes chest pain; and patients who cannot tolerate percutaneous transluminal coronary **angioplasty** and do not respond well to drug therapy. It is well accepted that coronary artery bypass graft surgery is the treatment of choice for patients with severe **coronary artery disease** (three or more diseased arteries with impaired function in the left ventricle).

Precautions

Coronary artery bypass graft surgery should ideally be postponed for three months after a heart attack. Patients should be medically stable before the surgery, if possible.

Description

Coronary artery bypass graft surgery builds a detour around one or more blocked coronary arteries with a graft from a healthy vein or artery. The graft goes around the clogged artery (or arteries) to create new pathways for oxygen-rich blood to flow to the heart.

Coronary artery bypass graft surgery is major surgery performed in a hospital. The length of the procedure depends upon the number of arteries being bypassed, but it generally takes from four to six hours—sometimes longer. The average hospital stay is four to seven days. Full recovery from coronary artery bypass graft surgery takes three to four months. Within four to six weeks, people with sedentary office jobs can return to work; people with physical jobs must wait longer and sometimes change careers.

Coronary artery bypass graft surgery is widely performed in the United States. The American Heart Association estimates that 573,000 coronary artery bypass graft surgeries were performed on 363,000 patients in 1995. Seventy-four percent of these procedures were performed on men and 44% on men and women under the age of 65 (1995 data). The estimated average cost of this procedure in 1995 was $44,820.

Coronary artery bypass graft surgery builds a detour around one or more blocked coronary arteries with a graft from a healthy vein or artery. The graft goes around the clogged artery (or arteries) to create new pathways for oxygen-rich blood to flow to the heart. *(Illustration by Electronic Illustrators Group.)*

Procedure

The surgery team for coronary artery bypass graft surgery includes the cardiovascular surgeon, assisting surgeons, a cardiovascular anesthesiologist, a perfusion technologist (who operates the heart-lung machine), and specially trained nurses. After general anesthesia is administered, the surgeon removes the veins or prepares the arteries for grafting. If the saphenous vein is to be used, a series of incisions are made in the patient's thigh or calf. More commonly, a segment of the internal mammary artery will be used and the incisions are made in the chest wall. The surgeon then makes an incision from the patient's neck to navel, saws through the breastbone, and retracts the rib cage open to expose the heart. The patient is connected to a heart-lung machine, also called a cardiopulmonary bypass pump, that cools the body to reduce the need for oxygen and takes over for the heart and lungs during the procedure. The heart is then stopped and a cold solution of potassium-enriched normal saline is injected into the aortic root and the coronary arteries to lower the temperature of the heart, which prevents damage to the tissue.

Next, a small opening is made just below the blockage in the diseased coronary artery. Blood will be redirected through this opening once the graft is sewn in place. If a leg vein is used, one end is connected to the coronary artery and the other to the aorta. If a mammary artery is used, one end is connected to the coronary artery while the other remains attached to the aorta. The procedure is repeated on as many coronary arteries as necessary. Most patients who have coronary artery bypass graft surgery have at least three grafts done during the procedure.

Electric shocks start the heart pumping again after the grafts have been completed. The heart-lung machine is turned off and the blood slowly returns to normal body temperature. After implanting pacing electrodes (if needed) and inserting a chest tube, the surgeon closes the chest cavity.

Success rate of coronary artery bypass graft surgery

About 90% of patients experience significant improvements after coronary artery bypass graft surgery. Patients experience full relief from chest pain and resume their normal activities in about 70% of the cases; the remaining 20% experience partial relief. In 5–10% of coronary artery bypass graft surgeries, the bypass graft stops supplying blood to the bypassed artery within one year. Younger peo-

ple who are healthy except for the heart disease do well with bypass surgery. Patients who have poorer results from coronary artery bypass graft surgery include those over the age of 70, those who have poor left ventricular function, or are undergoing a repeat surgery or other procedures concurrently, and those who continue **smoking**, do not treat **high cholesterol** or other coronary risk factors, or have another debilitating disease.

Long term, symptoms recur in only about 3–4% of patients per year. Five years after coronary artery bypass graft surgery, survival expectancy is 90%, at 10 years it is about 80%, at 15 years it is about 55%, and at 20 years it is about 40%.

Angina recurs in about 40% of patients after about 10 years. In most cases, it is less severe than before the surgery and can be controlled by drug therapy. In patients who have had vein grafts, 40% of the grafts are severely obstructed 10 years after the procedure. Repeat coronary artery bypass graft surgery may be necessary, and is usually less successful than the first surgery.

Minimally invasive coronary artery bypass graft surgery

There are two new types of minimally invasive coronary artery bypass graft surgery: port-access coronary artery bypass (also called PACAB or PortCAB) and minimally invasive coronary artery bypass (also called MIDCAB). These procedures are minimally invasive because they do not require the neck-to-navel incision, sawing through the breastbone, or opening the rib cage to expose the heart. Both procedures enable surgeons to work on the coronary arteries through small chest holes called ports and other small incisions. Port-access coronary artery bypass requires the use of a heart-lung machine but minimally invasive coronary artery bypass does not. Advantages of these procedures over standard coronary artery bypass graft surgery include a shorter hospital stay, a shorter recovery period, and lower costs.

Port-access coronary artery bypass enables surgeons to perform bypasses through smaller incisions. Using a video monitor to view the procedure, the surgeon passes instruments through ports in the patient's chest to perform the bypass. Mammary arteries or leg veins are used for the grafts. Minimally invasive coronary artery bypass is performed on a beating heart and is appropriate only for bypasses of one or two arteries. Small ports are made in the patient's chest, along with a small incision directly over the coronary artery to be bypassed. Generally, the surgeon uses a mammary artery for the bypass.

Early data on outcomes for port-access coronary artery bypass and minimally invasive coronary artery bypass are favorable. Mortality rates with port-access coronary artery bypass and minimally invasive coronary artery bypass are both less than 3%—about the same as in standard coronary artery bypass graft surgery. One clinical trial indicated that survival at seven years was the same in minimally invasive coronary artery bypass and standard coronary artery bypass graft surgery, but that another intervention was necessary five times more often with minimally invasive coronary artery bypass than with standard coronary artery bypass graft surgery. The American Heart Association Council on Cardio-Thoracic and Vascular Surgery feels that both procedures appear promising but that further study is needed. More data covering longer term outcomes are necessary in order to fully assess these procedures.

Preparation

The patient is usually admitted to the hospital the day before the coronary artery bypass graft surgery is scheduled. Coronary **angiography** has been previously performed to show the surgeon where the arteries are blocked and where the grafts might best be positioned. The patient is given a blood-thinning drug—usually heparin—that helps to prevent blood clots. The evening before the surgery, the patient showers with antiseptic soap and is shaved from chin to toes. After midnight, food and fluids are restricted. A sedative is prescribed on the morning of surgery and sometimes the night before. Heart monitoring begins.

Aftercare

The patient recovers in a surgical intensive care unit for at least the first two days after the surgery. He or she is connected to chest and breathing tubes, a mechanical ventilator, a heart monitor and other monitoring equipment, and a urinary catheter. The breathing tube and ventilator are usually removed within six hours of surgery, but the other tubes remain in place as long as the patient is in the intensive care unit. Drugs are prescribed to control pain and to prevent unwanted blood clotting. The patient is closely monitored. Vital signs and other parameters, such as heart sounds and oxygen and carbon dioxide levels in arterial blood, are checked frequently. The chest tube is checked to ensure that it is draining properly. The patient is fed intravenously for the first day or two. Daily doses of **aspirin** are started within six to 24 hours after the procedure. Chest physiotherapy is started after the ventilator and breathing tube are removed. The therapy includes coughing, turning frequently, and taking deep breaths. Other exercises will be encouraged to improve the patient's circulation and prevent complications due to prolonged bed rest.

If there are no complications, the patient begins to resume a normal routine around the second day. This includes eating regular food, sitting up, and walking

KEY TERMS

Aorta—The main artery which carries blood from the heart to the rest of the body The aorta is the largest artery in the body.

Graft—To implant living tissue surgically. In coronary artery bypass graft surgery, healthy veins or arteries are grafted to coronary arteries.

Mammary artery—A chest wall artery that descends from the aorta and is commonly used for bypass grafts.

Saphenous vein—A long vein in the thigh or calf commonly used for bypass grafts.

Ventricles—The left and right ventricles are the large chambers of the heart. The ventricles propel blood to the lungs and the rest of the body.

around a little bit. Before being released from the hospital, the patient usually spends a few days under observation in a non-surgical unit. During this time, counseling is usually provided on eating right and starting a light **exercise** program to keep the heart healthy. Patients should eat a lot of fruits, vegetables, grains, and non-fat or low-fat dairy products, and reduce fats to less than 30% of all calories. An exercise program will usually be tailored for the patient, who will be encouraged to participate in a **cardiac rehabilitation** program where exercise will be supervised by professionals. Cardiac **rehabilitation** programs, offered by hospitals and other organizations, may also include classes on heart-healthy living.

Full recovery from coronary artery bypass graft surgery takes three to four months and is a gradual process. Upon release from the hospital, the patient will feel weak because of the extended bed rest in the hospital. Within a few weeks, the patient should begin to feel stronger.

While the incision scar from coronary artery bypass graft surgery heals, which takes one to two months, it may be sore. The scar should not be bumped, scratched, or otherwise disturbed. An exercise test is often conducted after the patient leaves the hospital to determine how effective the surgery was and to confirm that progressive exercise is safe.

Risks

Coronary artery bypass graft surgery is major surgery and patients may experience any of the complications associated with major surgery. The risk of **death** during coronary artery bypass graft surgery is two to three percent. Possible complications include graft closure and development of blockages in other arteries, long-term development of atherosclerotic disease of saphenous vein grafts, abnormal heart rhythms, high or low blood pressure, blood clots that can lead to a **stroke** or heart attack, infections, and depression. There is a higher risk for complications in patients who are heavy smokers, patients who have serious lung, kidney, or metabolic problems, or patients who have a reduced supply of blood to the brain.

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Texas Heart Institute. Heart Information Service. P.O. Box 20345, Houston, TX 77225-0345. <http://www.tmc.edu/thi>.

Lori De Milto

Coronary artery disease

Definition

Coronary artery disease is a narrowing or blockage of the arteries and vessels that provide oxygen and nutri-

ents to the heart. It is caused by **atherosclerosis**, an accumulation of fatty materials on the inner linings of arteries. The resulting blockage restricts blood flow to the heart. When the blood flow is completely cut off, the result is a **heart attack**.

Description

Coronary artery disease, also called coronary heart disease or heart disease, is the leading cause of **death** for both men and women in the United States. According to the American Heart Association, in 1995 one in every 4.8 deaths in the United States was caused by coronary artery disease. About every 29 seconds, one American will have a heart attack; about every minute, one American will die from a heart attack. Fourteen million Americans have active symptoms of coronary artery disease (heart attack or chest pains). Many millions more have silent coronary disease, the first indication of which can be sudden death.

Coronary artery disease occurs when the coronary arteries become partially blocked or clogged. This blockage limits the flow of blood from the coronary arteries, which are the major arteries supplying oxygen-rich blood to the heart. The coronary arteries expand when the heart is working harder and needs more oxygen. Arteries would expand, for example, when a person is climbing stairs, exercising, or having sex. If the arteries are unable to expand, the heart is deprived of oxygen (myocardial **ischemia**). When the blockage is limited, chest **pain** or pressure, called **angina,** may occur. When the blockage cuts off the flow of blood, the result is heart attack (myocardial infarction or heart muscle death).

Healthy coronary arteries are clean, smooth, and slick. The artery walls are flexible and can expand to let more blood through when the heart needs to work harder. The disease process in arteries is thought to begin with an injury to the linings and walls of the arteries. This injury makes them susceptible to atherosclerosis and blood clots (thrombosis).

Causes and symptoms

Coronary artery disease is usually caused by atherosclerosis. Cholesterol and other fatty substances accumulate on the inner wall of the arteries. They attract fibrous tissue, blood components, and calcium and harden into artery-clogging plaques. Atherosclerotic plaques often form blood clots that can also block the coronary arteries (coronary thrombosis). Congenital defects and muscle spasms can also block blood flow. Recent research indicates that infection from organisms such as chlamydia bacteria may be responsible for some cases of coronary artery disease.

A number of major contributing factors increase the risk of developing coronary artery disease. Some of these can be changed and some cannot. People with more risk factors are more likely to develop coronary artery disease.

Major risk factors

Major risk factors significantly increase the chance of developing coronary artery disease. Those that cannot be changed are:

- Heredity—People whose parents have coronary artery disease are more likely to develop it. African-Americans are also at increased risk because they experience a higher rate of severe **hypertension** than whites do.
- Sex—Men are more likely to have heart attacks than women are and to have them at a younger age. Over age 60, however, women have coronary artery disease at a rate equal to that of men.
- Age—Men who are 45 years of age and older and women who are 55 years of age and older are more likely to have coronary artery disease. Occasionally, coronary disease may strike a person in the 30s. Older people (those over 65) are more likely to die of a heart attack. Older women are twice as likely as older men to die within a few weeks of a heart attack.

Major risk factors that can be changed are:

- Smoking—Smoking increases both the chance of developing coronary artery disease and the chance of dying from it. Smokers are two to four times more likely than are non-smokers to die of sudden heart attack. They are more than twice as likely as non-smokers to have a heart attack. They are also more likely to die within an hour of a heart attack. Second hand smoke may also increase risk.
- High cholesterol—Dietary sources of cholesterol are meat, eggs, and other animal products. The body also produces it. Age, sex, heredity, and diet affect one's blood cholesterol. Total blood cholesterol is considered high at levels above 240 mg/dL and borderline at 200-239 mg/dL. High-risk levels of low-density lipoprotein (LDL cholesterol) begin at 130–159 mg/dL, depending on other risk factors. Risk of developing coronary artery disease increases steadily as blood cholesterol levels increase above 160 mg/dL. When a person has other risk factors, the risk multiplies.
- High blood pressure—High blood pressure makes the heart work harder and weakens it over time. It increases the risk of heart attack, **stroke**, kidney failure, and congestive **heart failure**. A blood pressure of 140 over 90 or above is considered high. As the numbers rise, high blood pressure goes from Stage 1 (mild) to Stage 4 (very severe). In combination with **obesity**, **smoking**,

high cholesterol, or diabetes, high blood pressure raises the risk of heart attack or stroke several times.

- Lack of physical activity—Lack of **exercise** increases the risk of coronary artery disease. Even modest physical activity, like walking, is beneficial if done regularly.
- Diabetes mellitus—The risk of developing coronary artery disease is seriously increased for diabetics. More than 80% of diabetics die of some type of heart or blood vessel disease.

Contributing risk factors

Contributing risk factors have been linked to coronary artery disease, but their significance is not known yet. Contributing risk factors are:

- Obesity—Excess weight increases the strain on the heart and increases the risk of developing coronary artery disease even if no other risk factors are present. Obesity increases blood pressure and blood cholesterol and can lead to diabetes.
- **Stress** and anger—Some scientists believe that stress and anger can contribute to the development of coronary artery disease and increase the blood's tendency to form clots (thrombosis). Stress, the mental and physical reaction to life's irritations and challenges, increases the heart rate and blood pressure and can injure the lining of the arteries. Evidence shows that anger increases the risk of dying from heart disease. The risk of heart attack is more than double after an episode of anger.

Chest pain (angina) is the main symptom of coronary heart disease but it is not always present. Other symptoms include **shortness of breath**, chest heaviness, tightness, pain, a burning sensation, squeezing, or pressure either behind the breastbone or in the arms, neck, or jaws. Many people have no symptoms of coronary artery disease before having a heart attack; 63% of women and 48% of men who died suddenly of coronary artery disease had no previous symptoms of the disease, according to the American Heart Association.

Diagnosis

Diagnosis begins with a visit to the physician, who will take a medical history, discuss symptoms, listen to the heart, and perform basic screening tests. These tests will measure weight, blood pressure, blood lipid levels, and **fasting** blood glucose levels. Other diagnostic tests include resting and exercise electrocardiogram, **echocardiography**, radionuclide scans, and coronary **angiography**. The treadmill exercise (stress) test is an appropriate screening test for those with high risk factors even when they feel well.

An electrocardiogram (ECG) shows the heart's activity and may reveal a lack of oxygen (ischemia). Electrodes covered with conducting jelly are placed on the patient's chest, arms, and legs. They send impulses of the heart's activity through an oscilloscope (a monitor) to a recorder that traces them on paper. The test takes about 10 minutes and is performed in a physician's office. A definite diagnosis cannot be made from **electrocardiography**. About 50% of patients with significant coronary artery disease have normal resting electrocardiograms. Another type of electrocardiogram, known as the exercise **stress test**, measures how the heart and blood vessels respond to exertion when the patient is exercising on a treadmill or a stationary bike. This test is performed in a physician's office or an exercise laboratory. It takes 15–30 minutes. It is not perfectly accurate. It sometimes gives a normal reading when the patient has a heart problem or an abnormal reading when the patient does not.

If the electrocardiogram reveals a problem or is inconclusive, the next step is exercise echocardiography or nuclear scanning (angiography). Echocardiography, cardiac ultrasound, uses sound waves to create an image of the heart's chambers and valves. A technician applies gel to a hand-held transducer, then presses it against the patient's chest. The heart's sound waves are converted into an image that can be displayed on a monitor. It does not reveal the coronary arteries themselves, but can detect abnormalities in heart wall motion caused by coronary disease. Performed in a cardiology outpatient diagnostic laboratory, the test takes 30–60 minutes.

Radionuclide angiography enables physicians to see the blood flow of the coronary arteries. Nuclear scans are performed by injecting a small amount of radiopharmaceutical such as thallium into the bloodstream. A device that uses gamma rays to produce an image of the radioactive material (gamma camera) records pictures of the heart. Radionuclide scans are not dangerous. The radiation exposure is about the same as that in a **chest x ray**. The tiny amount of radioactive material used disappears from the body in a few days. Radionuclide scans cost about four times as much as exercise stress tests but provide more information.

In radionuclide angiography, a scanning camera passes back and forth over the patient who lies on a table. Radionuclide angiography is usually performed in a hospital's nuclear medicine department and takes 30–60 minutes. Thallium scanning is usually done in conjunction with an exercise stress test. When the stress test is finished, thallium or sestamibi is injected. The patient resumes exercise for one minute to absorb the thallium. For patients who cannot exercise, cardiac blood flow and heart rate may be increased by intravenous dipyridamole (Persantine) or adenosine. Thallium scanning is done

twice, immediately after injecting the radiopharmaceutical and again four hours (and maybe 24 hours) later. It is usually performed in a hospital's nuclear medicine department. Each scan takes 30–60 minutes.

Coronary angiography is the most accurate method for making a diagnosis of coronary artery disease, but it is also the most invasive. It is a form of **cardiac catheterization** that shows the heart's chambers, great vessels, and coronary arteries using x-ray technology. During coronary angiography the patient is awake but sedated. ECG electrodes are placed on the patient's chest and an intravenous line is inserted. A local anesthetic is injected into the site where the catheter will be inserted. The cardiologist inserts a catheter into a blood vessel and guides it into the heart. A contrast dye is injected to make the heart visible on x-ray cinematography. Coronary angiography is performed in a cardiac catheterization laboratory either in an outpatient or inpatient surgery unit. It takes from 30 minutes to two hours.

Treatment

Coronary artery disease can be treated many ways. The choice of treatment depends on the severity of the disease. Treatments include lifestyle changes and drug therapy, percutaneous transluminal coronary **angioplasty**, and coronary artery bypass surgery. Coronary artery disease is a chronic disease requiring lifelong care. Angioplasty or bypass surgery is not a "cure."

People with less severe coronary artery disease may gain adequate control through lifestyle changes and drug therapy. Many of the lifestyle changes that prevent disease progression—a low-fat, low-cholesterol diet, weight loss if needed, exercise, and not smoking—also help prevent the disease from developing. These lifestyle changes are discussed in more detail under prevention.

Drugs such as nitrates, beta-blockers, and calcium-channel blockers relieve chest pain and complications of coronary artery disease, but they cannot clear blocked arteries. Nitrates (nitroglycerin) improve blood flow to the heart. Beta-blockers (acebutelol, propranolol) reduce the amount of oxygen required by the heart during stress. One type of calcium-channel blocker (verapamil, diltiazem hydrochloride) helps keep the arteries open and reduces blood pressure. **Aspirin** helps prevent blood clots from forming on plaques, reducing the likelihood of a heart attack. Cholesterol-lowering medications are also indicated in most cases.

Percutaneous transluminal coronary angioplasty and bypass surgery are procedures that enter the body (invasive procedures) to improve blood flow in the coronary arteries. Percutaneous transluminal coronary angioplasty, usually called coronary angioplasty, is a non-surgical procedure. A catheter tipped with a balloon is threaded from a blood vessel in the thigh into the blocked artery. The balloon is inflated, compressing the plaque to enlarge the blood vessel and open the blocked artery. The balloon is deflated, and the catheter is removed. Coronary angioplasty is performed by a cardiologist in a hospital and generally requires a stay of one or two days. Coronary angioplasty is successful about 90% of the

KEY TERMS

Atherosclerosis—A process in which the walls of the coronary arteries thicken due to the accumulation of plaque in the blood vessels. Atherosclerosis is the cause of coronary artery disease.

Angina—Chest pain that happens when diseased blood vessels restrict the flow of blood to the heart. Angina is often the first symptom of coronary artery disease.

Beta-blocker—A drug that blocks some of the effects of fight-or-flight hormone adrenaline (epinephrine and norepinephrine), slowing the heart rate and lowering the blood pressure.

Calcium-channel blocker—A drug that blocks the entry of calcium into the muscle cells of small blood vessels (arterioles) and keeps them from narrowing.

Coronary arteries—The main arteries that provide blood to the heart. The coronary arteries surround the heart like a crown, coming out of the aorta, arching down over the top of the heart, and dividing into two branches. These are the arteries in which coronary artery disease occurs.

HDL cholesterol—High-density lipoprotein cholesterol is a component of cholesterol that helps protect against heart disease. HDL is nicknamed "good" cholesterol

LDL Cholesterol—Low-density lipoprotein cholesterol is the primary cholesterol molecule. High levels of LDL increase the risk of coronary heart disease. LDL is nicknamed "bad" cholesterol.

Plaque—A deposit of fatty and other substances that accumulate in the lining of the artery wall.

Triglyceride—A fat that comes from food or is made from other energy sources in the body. Elevated triglyceride levels contribute to the development of atherosclerosis.

time, but for one-third of patients the artery narrows again within six months. The procedure can be repeated. It is less invasive and less expensive than coronary artery bypass surgery.

In coronary artery bypass surgery, a healthy artery or vein from an arm, leg, or chest wall is used to build a detour around the coronary artery blockage. The healthy vessel then supplies oxygen-rich blood to the heart. Bypass surgery is major surgery. It is appropriate for those patients with blockages in two or three major coronary arteries, those with severely narrowed left main coronary arteries, and those who have not responded to other treatments. It is performed in a hospital under general anesthesia. A heart-lung machine is used to support the patient while the healthy vein or artery is attached past the blockage to the coronary artery. About 70% of patients who have bypass surgery experience full relief from angina; about 20% experience partial relief. Only about 3–4% of patients per year experience a return of symptoms. Survival rates after bypass surgery decrease over time. At five years after surgery, survival expectancy is 90%; at 10 years about 80%, at 15 years about 55%, and at 20 years about 40%.

Three semi-experimental surgical procedures for unblocking coronary arteries are currently being studied. **Atherectomy** is a procedure in which the cardiologist shaves off and removes strips of plaque from the blocked artery. In laser angioplasty, a catheter with a laser tip is inserted into the affected artery to burn or break down the plaque. A metal coil called a stent can be implanted permanently to keep a blocked artery open. Stenting is becoming more common.

Alternative treatment

Natural therapies may reduce the risk of certain types of heart disease, but once symptoms appear, conventional medical attention is necessary. A healthy diet (including cold-water fish as a source of essential fatty acids) and exercise, important components of conventional prevention and treatment strategies, also are emphasized in alternative approaches to coronary artery disease. Herbal medicine has a variety of remedies that may have a beneficial effect on coronary artery disease. For example, ginger (*Zingiber officinale*) may help reduce cholesterol. Garlic (*Allium sativum*), ginger, and hot red or chili peppers are all circulatory enhancers that can help prevent blood clots. **Yoga** and other bodywork, massage, relaxation therapies, and talking therapies may also help prevent coronary artery disease and stop, or even reverse, the progression of atherosclerosis. Vitamin and mineral therapy to reduce, reverse, or protect against coronary artery disease includes chromium; calcium and magnesium; B-complex **vitamins**; the anti-oxidant vitamins C and E; selenium; and zinc. **Traditional Chinese medicine** may recommend herbal remedies, massage, **acupuncture**, and dietary modification.

Prognosis

In many cases, coronary artery disease can be successfully treated. Advances in medicine and healthier lifestyles have caused a substantial decline in death rates from coronary artery disease since the mid-1980s. New diagnostic techniques enable doctors to identify and treat coronary artery disease in its earliest stages. New technologies and surgical procedures have extended the lives of many patients who would otherwise have died. Research on coronary artery disease continues.

Prevention

A healthy lifestyle can help prevent coronary artery disease and help keep it from progressing. A heart-healthy lifestyle includes eating right, regular exercise, maintaining a healthy weight, no smoking, moderate drinking, no recreational drugs, controlling hypertension, and managing stress. **Cardiac rehabilitation** programs are excellent to help prevent recurring coronary problems for people who are at risk and who have had coronary events and procedures.

Eat right

A healthy diet includes a variety of foods that are low in fat, especially saturated fat, low in cholesterol, and high in fiber. It includes plenty of fruits and vegetables and limited sodium. Some foods are low in fat but high in cholesterol and some are low in cholesterol but high in fat. Saturated fat raises cholesterol and, in excessive amounts, increases the amount of the clot-forming proteins in blood. Polyunsaturated and monounsaturated fats are good for the heart. Fat should comprise no more than 30% of total daily calories.

Cholesterol, a waxy substance containing fats, is found in foods such as meat, eggs, and other animal products. It is also produced in the liver. Soluble fiber can help lower cholesterol. Dietary cholesterol should be limited to about 300 milligrams per day. Many popular lipid-lowering drugs can reduce LDL cholesterol by an average of 25–30% when used with a low-fat, low-cholesterol diet.

Fruits and vegetables are rich in fiber, vitamins, and **minerals**. They are low-calorie and nearly fat free. Vitamin C and beta-carotene, found in many fruits and vegetables, keep LDL-cholesterol from turning into a form that damages coronary arteries.

Excess sodium can increase the risk of high blood pressure. Many processed foods contain large amounts of sodium. Limit daily intake to about 2,400 milligrams, about the amount in a teaspoon of salt.

The "Food Guide" Pyramid developed by the U.S. Departments of Agriculture and Health and Human Services provides easy-to-follow guidelines for daily heart-healthy eating. It recommends six to 11 servings of bread, cereal, rice, and pasta; three to five servings of vegetables; two to four servings of fruit; two to three servings of milk, yogurt, and cheese; and two to three servings of meat, poultry, fish, dry beans, eggs, and nuts. Fats, oils, and sweets should be used sparingly. Canola and olive oil are better for the heart than other cooking oils. Coronary patients should be on a strict diet.

Exercise regularly

Aerobic exercise can lower blood pressure, help control weight, and increase HDL ("good") cholesterol. It may keep the blood vessels more flexible. The Centers for Disease Control and Prevention and the American College of Sports Medicine recommend moderate to intense aerobic exercise lasting about 30 minutes four or more times per week for maximum heart health. Three 10-minute exercise periods are also beneficial. Aerobic exercise—activities such as walking, jogging, and cycling—uses the large muscle groups and forces the body to use oxygen more efficiently. It can also include everyday activities such as active gardening, climbing stairs, or brisk housework. People with coronary artery disease or risk factors should consult a doctor before beginning an exercise program.

Maintain a desirable body weight

About one quarter of all Americans are overweight and nearly one-tenth are obese, according to the Surgeon General's Report on **Nutrition** and Health. People who are 20% or more over their ideal body weight have an increased risk of developing coronary artery disease. Losing weight can help reduce total and LDL cholesterol, reduce triglycerides, and boost HDL cholesterol. It may also reduce blood pressure. Eating right and exercising are two key components of losing weight.

Avoid recreational drugs

Do not smoke or use tobacco. Smoking has many adverse effects on the heart. It increases the heart rate, constricts major arteries, and can create irregular heartbeats. It raises blood pressure, contributes to the development of plaque, increases the formation of blood clots, and causes blood platelets to cluster and impede blood flow. Heart damage caused by smoking can be repaired by quitting. Even heavy smokers can return to heart health. Several studies have shown that ex-smokers face the same risk of heart disease as non-smokers within five to 10 years after they quit.

Drink in moderation. Modest consumption of alcohol may actually protect against coronary artery disease because alcohol appears to raise levels of HDL ("good") cholesterol. The American Heart Association defines moderate consumption as one ounce of alcohol per day, roughly one cocktail, one 8-ounce glass of wine, or two 12-ounce glasses of beer. However, even moderate drinking can increase risk factors for heart disease for some people (by raising blood pressure, for example). Excessive drinking is always bad for the heart. It usually raises blood pressure and can poison the heart and cause abnormal heart rhythms or even heart failure.

Do not use other recreational drugs. Commonly used recreational drugs, particularly **cocaine** and "crack," can seriously harm the heart and should never be used.

Seek treatment for hypertension

High blood pressure, one of the most common and serious risk factors for coronary artery disease, can be completely controlled through lifestyle changes and medication. Moderate hypertension can be controlled by reducing dietary intake of sodium and fat, exercising regularly, managing stress, abstaining from smoking, and drinking alcohol in moderation. People for whom these changes do not work or people with severe hypertension may be helped by many categories of medication.

Manage stress

Everyone experiences stress, the mental and physical reaction to life's irritations and challenges. Stress can sometimes be avoided and when it is inevitable, it can be controlled. Techniques for controlling stress include: taking life more slowly, spending more time with family and friends, thinking positively, getting enough sleep, exercising, and practicing relaxation techniques.

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American Heart Association. 7320 Greenville Ave. Dallas, TX 75231. (214) 373-6300. <http://www.americanheart.org>.
National Heart, Lung and Blood Institute. P.O. Box 30105, Bethesda, MD 20824-0105. (301) 251-1222. <http://www.nhlbi.nih.gov>.
Texas Heart Institute. Heart Information Service. P.O. Box 20345, Houston, TX 77225-0345. <http://www.tmc.edu/thi>.

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Lori De Milto

Coronary disease *see* **Coronary artery disease**

Coronary heart disease *see* **Coronary artery disease**

Coronary stenting

Definition

A coronary stent is an artificial support device used in the coronary artery to keep the vessel open.

Purpose

The coronary stent is a relatively new tool used to keep coronary arteries expanded, usually following a balloon **angioplasty**. Balloon angioplasty is used in patients with **coronary artery disease**. In this disease, the blood vessels on the heart become narrow. When this happens, the oxygen supply is reduced to the heart muscle. The primary cause of coronary artery disease is fat deposits blocking the arteries (**atherosclerosis**). In many cases, balloon angioplasty is unsuccessful and the vessel closes after the procedure (restenosis). By forming a rigid support, the stent can prevent restenosis and reduce the need for coronary bypass surgery. The stent is usually a stainless steel mesh tube. Since the stent will be placed inside an artery, the device comes in various sizes to match the size of the artery.

Precautions

Any foreign object in the body, like a stent, will increase the risk of thrombosis. Anticlotting medication is given to prevent this complication.

Description

Coronary stenting usually follows balloon angioplasty, which requires inserting a balloon catheter into the femoral artery in the upper thigh. When this catheter is positioned at the location of the blockage in the coronary artery, it is slowly inflated to widen that artery, and is then removed. The stent catheter is then threaded into the artery and the stent is placed around a deflated balloon. When this is correctly positioned in the coronary artery, the balloon is inflated, expanding the stent against the walls of the coronary artery. The balloon catheter is removed, leaving the stent in place to hold the coronary artery open. A cardiac **angiography** will follow to insure that the stent is keeping the artery open.

Alternative procedures

Balloon angioplasty and coronary stenting are performed to relieve the symptoms of coronary artery disease. By the time coronary artery disease progresses and requires balloon angioplasty, there is no alternative to balloon angioplasty other than coronary bypass surgery. Coronary bypass surgery carries greater risks. However, since coronary artery disease can be related to high fat **diets**, **smoking**, and lack of **exercise**, changes in lifestyle may reduce the risk of developing the disease. Various medications for cholesterol, high blood pressure, and diabetes also can help treat or prevent coronary artery disease.

Preparation

Before the stent is inserted, the patient will probably be instructed to take **aspirin** for several days. Aspirin can help decrease the possibility of blood clots forming at the

KEY TERMS

Balloon angioplasty—The use of a balloon attached to a catheter to widen an artery that has become narrowed. As the balloon is inflated, it opens the artery.

Cardiac angiography—A procedure used to visualize blood vessels of the heart. A catheter is used to inject a dye into the vessels; the vessels can then be seen by x ray.

Catheter—A long thin flexible tube that can be inserted into the body; in this case, it is threaded to the heart.

Restenosis—The narrowing of a blood vessel after it has been opened, usually by balloon angioplasty.

Thrombosis—The development of a blood clot in the vessels. This thrombosis may clog a blood vessel and stop the flow of blood.

stent. Because anesthesia will be used during the procedure, the patient should not eat or drink after midnight of the previous day.

Aftercare

Following the procedure, blood thinners (anticoagulants) will be given through a needle in a vein for about 24 hours. The patient should remain flat and still for awhile to allow the femoral artery to heal from the insertion of the catheter. Medication to control blood clotting should be taken after the patient is discharged from the hospital. A special diet may also be recommended that is low in vitamin K and cholesterol. With time, the patient should begin light exercise, like walking. It is important that no **magnetic resonance imaging** (MRI) tests are given for six months because the magnetic field may move the stent.

Risks

Although coronary stents greatly reduce the risk of restenosis following balloon angioplasty, there is still some risk that the stented artery may close. Thrombosis, bleeding, and artery damage are also risks.

Resources

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ORGANIZATIONS

American Heart Association. 7320 Greenville Ave. Dallas, TX 75231. (214) 373-6300. <http://www.americanheart.org>.

OTHER

AdvocateHealthCare. <http://www.advocatehealth.com>.

Cindy L. A. Jones, PhD

Coronary thrombosis *see* **Heart attack**

Coronavirus infection *see* **Common cold**

Corticosteroids

Definition

Corticosteriods are a group of natural and synthetic analogues of the hormones secreted by the hypothalamic-anterior pituitary-adrenocortical (HPA) axis, more commonly referred to as the pituitary gland. These include glucocorticoids, which are anti-inflammatory agents with a large number of other functions; mineralocorticoids, which control salt and water balance primarily through action on the kidneys; and corticotropins, which control secretion of hormones by the pituitary gland.

Purpose

Glucocorticoids have multiple effects, and are used for a large number of conditions. They affect glucose utilization, fat metabolism, and bone development, and are potent anti-inflammatory agents. They may be used for replacement of natural hormones in patients with pituitary deficiency (**Addison's disease**), as well as for a wide number of other conditions including, but not limited to, arthritis, **asthma**, anemia, various cancers, and skin inflammations. Additional uses include inhibition of **nausea and vomiting** after **chemotherapy**, treatment of **septic shock**, treatment of spinal cord injuries, and treatment of hirisutism (excessive hair growth). The choice of drug will vary with the condition. Cortisone and hydrocortisone, which have both glucocorticoid and mineralocorticoid effects, are the drugs of choice for replacement therapy of natural hormone deficiency. Synthetic compounds, which have greater anti-inflammatory effects and less effect on salt and water balance, are usually preferred for other purposes. These compounds include dexamethasone, which is almost exclusively glucocorticoid in its actions, as well as prednisone, prednisolone,

KEY TERMS

Hallucination—A false or distorted perception of objects, sounds, or events that seems real. Hallucinations usually result from drugs or mental disorders.

Hormone—A substance that is produced in one part of the body, then travels through the bloodstream to another part of the body where it has its effect.

Inflammation—Pain, redness, swelling, and heat that usually develop in response to injury or illness.

Ointment—A thick, spreadable substance that contains medicine and is meant to be used on the outside of the body.

Pregnancy category—A system of classifying drugs according to their established risks for use during pregnancy. Category A: controlled human studies have demonstrated no fetal risk. Category B: animal studies indicate no fetal risk, but no human studies; or adverse effects in animals, but not in well-controlled human studies. Category C: no adequate human or animal studies; or adverse fetal effects in animal studies, but no available human data. Category D: evidence of fetal risk, but benefits outweigh risks. Category X: evidence of fetal risk. Risks outweigh any benefits.

betamethasone, trimacinolone, and others. Glucocorticoids are formulated in oral dosage forms, topical creams and ointments, oral and nasal inhalations, rectal foams, and ear and eye drops.

Mineralocorticoids control the retention of sodium in the kidneys. In mineralocorticoid deficiency, there is excessive loss of sodium through the kidneys, with resulting water loss. Fludrocortisone (Florinef) is the only drug available for treatment of mineralocorticoid deficiency, and is available only in an oral dosage form.

Corticotropin (ACTH, adrenocorticotropic hormone) stimulates the pituitary gland to release cortisone. A deficiency of corticotropic hormone will have the same effects as a deficiency of cortisone. The hormone, which is available under the brand names Acthar and Actrel, is used for diagnostic testing, to determine the cause of a glucocorticoid deficiency, but is rarely used for replacement therapy since direct administration of glucocorticoids may be easier and offers better control over dosages.

Recommended dosage

The dosage of glucocorticoids varies with the drug, route of administration, condition being treated, and patient. Consult specific references.

Fludrocortisone, for use in replacement therapy, is normally dosed at 0.1 mg/day. Some patients require higher doses. It should normally be administered in conjunction with cortisone or hydrocortisone.

ACTH, when used for diagnostic purposes, is given as 10–25 units dissolved in 500 ml of 5% dextrose injection-infused IV over eight hours. A long-acting form, which may be used for replacement therapy, is given by subcutaneous (SC) or intramuscular (IM) injection at a dose of 40 to 80 units every 24–72 hours.

Precautions

Glucocorticoids

The most significant risk associated with administration of glucocorticoids is suppression of natural corticosteroid secretion. When the hormones are administered, they suppress the secretion of ACTH, which in turn reduces the secretion of the natural hormones. The extent of suppression varies with dose, drug potency, duration of treatment, and individual patient response. While suppression is seen primarily with drugs administered systemically, it can also occur with topical drugs such as creams and ointments, or drugs administered by inhalation. Abrupt cessation of corticosteroids may result in acute adrenal crisis (Addisonian crisis) that is marked by **dehydration** with severe vomiting and **diarrhea**, **hypotension**, and loss of consciousness. Acute adrenal crisis is potentially fatal.

Chronic overdose of glucocorticoids leads to Cushingoid syndrome, which is clinically identical to **Cushing's syndrome** and differs only in that in Cushingoid, the excessive steroids are from drug therapy rather than excessive glandular secretion. Symptoms vary, but most people have upper body **obesity**, rounded face, increased fat around the neck, and thinning arms and legs. In its later stages, this condition leads to weakening of bones and muscles with rib and spinal column **fractures**.

The short term adverse effects of corticosteroids are generally mild, and include **indigestion**, increased appetite, **insomnia**, and nervousness. There are also a very large number of infrequent adverse reactions, the most significant of which is drug induced-paranoia. Delerium, depression, menstrual irregularity, and increased hair growth are also possible. Consult detailed reviews for further information.

Long-term use of topical glucocorticoids can result in thinning of the skin. Oral steroid inhalations may cause

fungal overgrowth in the oral cavity. Patients must be instructed to rinse their mouths carefully after each dose. Corticosteroids are **pregnancy** category C. The drugs have caused congenital malformations in animal studies, including cleft palate. Breastfeeding should be avoided.

Mineralocorticoids

Because fludrocortisone has glucocorticoid activity as well as mineralocorticoid action, the same hazards and precautions apply to fludrocortisone as to the glucocorticoids. Overdose of fludrocortisone may also cause **edema**, **hypertension,** and congestive **heart failure**.

Corticotropins

Corticotropin has all the same risks as the glucocorticoids. Prolonged use may cause reduced response to the stimulatory effects of corticotropin.

Warnings and contraindications

Use corticosteroids with caution in patients with the following conditions:

- osteoporosis or any other bone disease
- current or past tuberculosis
- glaucoma or cataracts
- infections of any type (virus, bacteria, fungus, amoeba)
- sores in the nose or recent nose surgery (if using nasal spray forms of corticosteroids)
- underactive or overactive thyroid
- liver disease
- stomach or intestine problems
- diabetes
- heart disease
- high blood pressure
- high cholesterol
- kidney disease or kidney stones
- myasthenia gravis
- systemic lupus erythematosus (SLE)
- emotional problems
- skin conditions that cause the skin to be thinner to bruise more easily

Interactions

Corticosteroids have many drug interactions. Consult specific references.

Resources

ORGANIZATIONS

American Academy of Allergy, Asthma and Immunology. 611 East Wells Street, Milwaukee, WI 53202. (414) 272-6071. <http://www.aaaai.org>.

Asthma and Allergy Foundation of America. 1125 15th Street NW, Suite 502, Washington, DC 20005. (800) 727-8462. <http://www.aafa.org>.

National Heart, Lung and Blood Institute. National Institutes of Health. P.O. Box 30105, Bethesda, MD 20824-0105. (301) 251-1222. <http://www.nhlbi.nih.gov/nhlbi/nhlbi.htm>.

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Corticotropin test *see* **Adrenocorticotropic hormone test**

Cortisol tests

Definition

This test is a measure of serum cortisol (also known as hydrocortisone), or urine cortisol (also known as urinary free cortisol), an important hormone produced by a pair of endocrine glands called the adrenal glands.

Purpose

This test is performed on patients who may have malfunctioning adrenal glands. Blood and urine cortisol, together with the determination of adrenocorticotropic hormone (ACTH), are the three most important tests in the investigation of **Cushing's syndrome** (caused by an overproduction of cortisol) and **Addison's disease** (caused by the underproduction of cortisol).

Precautions

Increased levels of cortisol are associated with **pregnancy**. Physical and emotional **stress** can also elevate cortisol levels. Drugs that may cause increased levels of cortisol include estrogen, **oral contraceptives**, amphetamines, cortisone, and spironolactone (Aldactone). Drugs that may cause decreased levels include androgens, aminoglutethimide, betamethasone, and other steroid medications, danazol, lithium, levodopa, metyrapone and phenytoin (Dilantin).

Description

Cortisol is a potent hormone known as a glucocorticoid that affects the metabolism of carbohydrates, proteins, and fats, but especially glucose. Cortisol increases blood sugar levels by stimulating the release of glucose from glucose stores in cells. It also acts to inhibit insulin, thus affecting glucose transport into cells.

The hypothalamus (an area of the brain), the pituitary gland (sometimes called the "master gland"), and

KEY TERMS

Addison's disease—A rare disorder in which symptoms are caused by a deficiency of hydrocortisone (cortisol) and aldosterone, two corticosteroid hormones normally produced by a part of the adrenal glands called the adrenal cortex. Symptoms include weakness, tiredness, vague abdominal pain, weight loss, skin pigmentation and low blood pressure.

Adrenal glands—A pair of endocrine glands (glands that secrete hormones directly into the bloodstream) that are located on top of the kidneys.

Adrenocorticotropic hormone (ACTH)—Also called corticotropin, this hormone is produced by the pituitary gland to stimulate the adrenal cortex to release various corticosteroid hormones.

Cushing's syndrome—A hormonal disorder caused by an abnormally high level of corticosteroid hormones that are produced by the adrenal glands. Corticosteroid hormones control the body's use of nutrients and the excretion of salts and water in the urine. Symptoms include high blood sugar levels, a moon face, weight gain, and increased blood pressure

the adrenal glands coordinate the production of cortisol. After corticotropin-releasing hormone (CRH) is made in the hypothalamus, CRH stimulates the pituitary to produce adrenocorticotropic hormone (ACTH). The production of ACTH in turn stimulates a part of the adrenal glands known as the adrenal cortex to produce cortisol. Rising levels of cortisol act as a negative feedback to curtail further production of CRH and ACTH, thus completing an elaborate feedback mechanism.

There are two methods for evaluating cortisol: blood and urine. The most reliable index of cortisol secretion is the 24-hour urine sample collection, but when blood levels are required or requested by the physician, plasma cortisol should be measured in the morning and again in the afternoon. Cortisol levels normally rise and fall during the day in what is called a diurnal variation, so that cortisol is at its highest level between 6–8 A.M. and gradually falls, reaching its lowest point around midnight. One reason for ordering blood cortisol levels versus a 24-hour urine collection is that sometimes the earliest sign of adrenal malfunction is the loss of this diurnal variation, even though the cortisol levels are not yet elevated. For example, individuals with Cushing's syndrome often have upper normal plasma cortisol levels in the morning and exhibit no decline as the day progresses.

Preparation

When testing for cortisol levels through the blood, a blood specimen is usually collected at 8 A.M. and again at 4 P.M. It should be noted that normal values may be transposed in individuals who have worked during the night and slept during the day for long periods of time.

When testing for cortisol level through the urine, a 24-hour urine sample is collected, refrigerated, and sent to the reference laboratory for examination.

Risks

Risks for the blood test are minimal, but may include slight bleeding from the blood-drawing site, **fainting** or feeling lightheaded after venipuncture, or hematoma (blood accumulating under the puncture site).

Normal results

Reference ranges for cortisol vary from laboratory to laboratory but are usually within the following ranges for blood:

- adults (8 A.M.): 6–28 mg/dL; adults (4 P.M.): 2–12 mg/dL
- child one to six years (8 A.M.): 3–21 mg/dL; child one to six years (4 P.M.): 3–10 mg/dL
- newborn: 1/24 mg/dL

Reference ranges for cortisol vary from laboratory to laboratory, but are usually within the following ranges for 24-hour urine collection:

- adult: 10–100 mg/24 hours
- adolescent: 5–55 mg/24 hours
- child: 2–27 mg/24 hours

Abnormal results

Increased levels of cortisol are found in Cushing's syndrome, excess thyroid (**hyperthyroidism**), **obesity**, ACTH-producing tumors, and high levels of stress.

Decreased levels of cortisol are found in Addison's disease, conditions of low thyroid, and **hypopituitarism**, in which pituitary activity is diminished.

Resources

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Janis O. Flores

Cosmetic dentistry

Definition

Cosmetic dentistry includes a variety of dental treatments aimed at improving the appearance of the teeth.

Purpose

The purpose of cosmetic dentistry is to improve the appearance of the teeth using bleaching, bonding, veneers, reshaping, orthodontics, or implants.

KEY TERMS

Bleaching—Technique used to brighten stained teeth.

Bonding—Rebuilding, reshaping, and covering tooth defects using tooth-colored materials.

Composite resin—Plastic material matching natural tooth color used to replace missing parts of a tooth.

Description

Bleaching is done to lighten teeth that are stained or discolored. It entails the use of a bleaching solution applied by a dentist or a gel in a tray that fits over the teeth used at home under a dentist's supervision. Bonding involves applying tooth-colored plastic putty, called composite resin, to the surface of chipped or broken teeth. This resin is also used to fill cavities in front teeth (giving a more natural-looking result) and to fill gaps between teeth. Veneers are thin, porcelain shells that cover the front of the teeth. They can improve the appearance of damaged, discolored, misshapen, or misaligned teeth. Reshaping involves the removal of enamel from a misshapen tooth so that it matches other teeth. Orthodontics uses braces to correct the position of crowded or misaligned teeth. Implants are artificial teeth which are attached directly to the jaw to replace missing teeth.

Preparation

Bleaching involves having a custom-made bleaching tray made by the dentist. This tray is worn at home for several hours each day or night. Teeth slowly become white over a period of one to six weeks. Bleaching can also be done in a dentist's office. A heat- or light-activated bleaching solution is applied to six to eight teeth per visit.

Bonding involves etching the surface of the tooth so composite resin can adhere. The dentist then contours the resin to the right shape, and smooths and polishes the resin after it is hard and dry.

To prepare for the application of a veneer, a thin layer of enamel is removed from the tooth (so that the finished tooth will be flush with surrounding teeth) and an impression of the tooth is taken from which the veneer will be created. Before a veneer is applied, the tooth is etched with an acid solution and an adhesive resin is painted on the tooth. The veneer is then applied, the resin is hardened with a bonding light, and the dentist polishes the veneer.

During cosmetic reshaping, some enamel is removed from the uneven tooth so it more closely matches other teeth.

Orthodontics involves applying braces to the teeth, and wires are threaded through the braces. These wires are adjusted to gradually move the teeth to the desired new positions. Over time, crowded or misaligned teeth are straightened.

Implants are more secure and natural looking than dentures or bridgework, but are much more expensive. First an anchor for the implant is attached to the jaw bone. This surgery can take several hours. About six months later, after the bone around the anchor has healed, a post is attached to the anchor, and an artificial tooth is attached to the post. The whole process may take about nine months to complete.

Aftercare

Periodic touch-up may be needed to keep the teeth white if the teeth have been bleached or bonded. Also, the resin used in bonded teeth can be chipped by ice, popcorn kernels, or hard candy, requiring repair. Veneered teeth may need to be reveneered after five to 12 years. Once orthodontic braces are removed, regular visits to the orthodontist are advised because teeth can shift position. Implanted teeth require regular dental checkups to ensure that the anchor and post are stable.

Risks

After teeth are bleached, they may darken faster if exposed to staining products such as coffee or tobacco. Some patients experience increased sensitivity to cold while teeth are being bleached, but the sensitivity usually disappears shortly after completion of the treatment.

Bonded teeth, like bleached teeth, may also stain more easily than natural teeth. Bonding materials also chip easily.

Because cosmetic reshaping involves the removal of enamel, the process is irreversible because enamel cannot be replaced once it is removed.

The anchors of implanted teeth can loosen and cause **pain**; regular dental checkups are recommended.

Normal results

Cosmetic dentistry can improve the appearance of stained, chipped, misshapen, or crowded teeth.

Resources

ORGANIZATIONS

American Dental Association. 211 E. Chicago Ave., Chicago, IL 60611. (312) 440-2500. <http://www.ada.org>.

Joseph Knight, PA

Cosmetic surgery *see* **Plastic, cosmetic, and reconstructive surgery**

Costochondritis

Definition

Costochondritis is an inflammation and associated tenderness of the cartilage (i.e., the costochondral joints) that attaches the front of the ribs to the breastbone.

Description

Costochondritis causes **pain** in the lower rib area or upper breastbone. Some patients fear they are having a **heart attack**. The most severe pain is usually between the breast and the upper abdomen. The pain may be greater when in sitting or reclining positions. **Stress** may aggravate this condition. Generally the third or fourth ribs are affected. However, any of the seven costochondral junctions may be affected, and more often than not more than one site is involved. The inflammation can involve cartilage areas on both sides of the sternum, but usually is on one side only. Costochondritis should be distinguished from Tietze Syndrome, which is an inflammation involving the same area of the chest, but also includes swelling.

Causes and symptoms

The causes of costochondritis are not well-understood and may be difficult to establish. The most likely causes include injury, repetitive minor trauma, and unusual excessive physical activity.

KEY TERMS

Inflammation—Process whereby the immune system reacts to infection or other stimulus, characterized by pain, swelling, redness, and warmth of the affected part

The primary symptom of costochondritis is severe chest wall pain, which may vary in intensity. The pain becomes worse with trunk movement, deep breathing, and/or exertion, and better with decreased movement, quiet breathing, or changing of position. It is usually localized but may radiate extensively from the chest area. The pain has been described as sharp, nagging, aching, or pressure-like.

Diagnosis

Diagnosis is based on pain upon palpation (gentle pressing) of the affected joints. Swelling is not associated with costochondritis. Diagnosis is also dependent on the exclusion of other causes, including heart attack or bacterial or fungal infections found in IV drug users or postoperative **thoracic surgery** patients.

Treatment

The goals of treatment are to reduce inflammation and to control pain. To accomplish these goals, nonsteroidal anti-inflammatory agents (NSAIDs) are used, with ibuprofen usually selected as the drug of choice. Other NSAIDS options are flurbiprofen, mefenamic acid, ketoprofen, and naproxen. Additional treatment recommendations include the use of local heat, **biofeedback**, and gentle stretching of the pectoralis muscles two to three times a day.

For more difficult cases, where the patient continues to exhibit pain and discomfort, cortisone injections are used as therapy.

Alternative treatment

Supplements that are used to reduce inflammation have been used to treat costochondritis. Examples of such supplements include ginger root, evening primrose oil, bromelain, vitamin E, omega-3 oils, and white willow bark. Glucosamine/chondroitin sulfate, which may aid in the healing of cartilage, has also been used. Other alternative therapies include **acupuncture** and massages.

Prognosis

The prognosis for recovery from costochondritis is good. For most patients, the condition lessens in six

months to a year. However, after one year, about one-half of patients continue with some discomfort, while about one-third still report tenderness with palpation.

Prevention

Though the causes of costochondritis are not well known, avoidance of activities that may strain (e.g., the repetitive misuse of muscles) or cause trauma to the rib cage is recommended to prevent the occurrence of costochondritis. Modification of improper posture or ergonomics of the home or work place may also deter the development of this condition.

Resources

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Judith Sims

Cotrel-Dubousset spinal instrumentation *see* **Spinal instrumentation**

Cough

Definition

A cough is a forceful release of air from the lungs that can be heard. Coughing protects the respiratory system by clearing it of irritants and secretions.

Description

While people can generally cough voluntarily, a cough is usually a reflex triggered when an irritant stimulates one or more of the cough receptors found at different points in the respiratory system. These receptors then send a message to the cough center in the brain, which in turn tells the body to cough. A cough begins with a deep breath in, at which point the opening between the vocal cords at the upper part of the larynx (glottis) shuts, trapping the air in the lungs. As the diaphragm and other muscles involved in breathing press against the lungs, the glottis suddenly opens, producing an explosive outflow of air at speeds greater than 100 mi (160 km) per hour.

In normal situations, most people cough once or twice an hour during the day to clear the airway of irritants. However, when the level of irritants in the air is high or when the respiratory system becomes infected, coughing may become frequent and prolonged. It may interfere with **exercise** or sleep, and it may also cause distress if accompanied by **dizziness**, chest **pain**, or breathlessness. In the majority cases, frequent coughing lasts one to two weeks and tapers off as the irritant or infection subsides. If a cough lasts more than three weeks it is considered a chronic cough, and physicians will try to determine a cause beyond an acute infection or irritant.

Coughs are generally described as either dry or productive. A dry cough does not bring up a mixture of mucus, irritants, and other substances from the lungs (sputum), while a productive cough does. In the case of a bacterial infection, the sputum brought up in a productive cough may be greenish, gray, or brown. In the case of an allergy or viral infection it may be clear or white. In the most serious conditions, the sputum may contain blood.

Causes and symptoms

In the majority of cases, coughs are caused by respiratory infections, including:

- colds or **influenza**, the most common causes of coughs
- **bronchitis**, an inflammation of the mucous membranes of the bronchial tubes
- croup, a viral inflammation of the larynx, windpipe, and bronchial passages that produces a bark-like cough in children
- whooping cough, a bacterial infection accompanied by the high-pitched cough for which it is named
- **pneumonia**, a potentially serious bacterial infection that produces discolored or bloody mucus
- **tuberculosis**, another serious bacterial infection that produces bloody sputum
- fungal infections, such as **aspergillosis**, **histoplasmosis**, and cryptococcoses

Environmental pollutants, such as cigarette smoke, dust, or smog, can also cause a cough. In the case of cigarette smokers, the nicotine present in the smoke paralyzes the hairs (cilia) that regularly flush mucus from the respiratory system. The mucus then builds up, forcing the body to removed it by coughing. Post-nasal drip, the irritating trickle of mucus from the nasal passages into the throat caused by **allergies** or **sinusitis**, can also result in a cough. Some chronic conditions, such as **asthma**, chronic bronchitis, **emphysema**, and **cystic fibrosis**, are characterized in part by a cough. A condition in which stomach acid backs up into the esophagus (gastroe-

KEY TERMS

Antitussives—Drugs used to suppress coughing.

Expectorant—Drug used to thin mucus.

Gastroesophageal reflux—Condition in which stomach acid backs up into the esophagus.

Glottis—The opening between the vocal cords at the upper part of the larynx.

Larynx—A part of the respiratory tract between the pharynx and the trachea, having walls of cartilage and muscle and containing the vocal cords.

Sputum—The mixture of mucus, irritants, and other substances expelled from the lungs by coughing.

sophageal reflux) can cause coughing, especially when a person is lying down. A cough can also be a side-effect of medications that are administered via an inhaler. It can also be a side-effect of beta-blockers and ACE inhibitors, which are drugs used for treating high blood pressure.

Diagnosis

To determine the cause of a cough, a physician should take an exact medical history and perform an exam. Information regarding the duration of the cough, what other symptoms may accompany it, and what environmental factors may influence it aid the doctor in his or her diagnosis. The appearance of the sputum will also help determine what type of infection, if any, may be involved. The doctor may even observe the sputum microscopically for the presence of bacteria and white blood cells. Chest x rays may help indicate the presence and extent of such infections as pneumonia or tuberculosis. If these actions are not enough to determine the cause of the cough, a **bronchoscopy** or **laryngoscopy** may be ordered. These tests use slender tubular instruments to inspect the interior of the bronchi and larynx.

Treatment

Treatment of a cough generally involves addressing the condition causing it. An acute infection such as pneumonia may require **antibiotics**, an asthma-induced cough may be treated with the use of bronchodialators, or an antihistamine may be administered in the case of an allergy. Physicians prefer not to suppress a productive cough, since it aids the body in clearing respiratory system of infective agents and irritants. However, cough medicines may be given if the patient cannot rest because of the cough or if the cough is not productive, as is the case with most coughs associated with colds or flu. The two types of drugs used to treat coughs are antitussives and **expectorants**.

Antitussives

Antitussives are drugs that suppress a cough. Narcotics—primarily codeine—are used as antitussives and work by depressing the cough center in the brain. However, they can cause such side effects as drowsiness, nausea, and **constipation**. Dextromethorphan, the primary ingredient in many over-the-counter cough remedies, also depresses the brain's cough center, but without the side effects associated with narcotics. Demulcents relieve coughing by coating irritated passageways.

Expectorants

Expectorants are drugs that make mucus easier to cough up by thinning it. Guaifenesin and terpin hydrate are the primary ingredients in most over-the-counter expectorants. However, some studies have shown that in acute infections, simply increasing fluid intake has the same thinning effect as taking expectorants.

Alternative treatment

Coughs due to bacterial or viral upper respiratory infections may be effectively treated with botanical and homeopathic therapies. The choice of remedy will vary and be specific to the type of cough the patient has. Some combination over-the-counter herbal and homeopathic cough formulas can be very effective for cough relief. Lingering coughs or coughing up blood should be treated by a trained practitioner.

Many health practitioners advise increasing fluids and breathing in warm, humidified air as ways of loosening chest congestion. Others recommend hot tea flavored with honey as a temporary home remedy for coughs caused by colds or flu. Various **vitamins**, such as vitamin C, may be helpful in preventing or treating conditions (including colds and flu) that lead to coughs. Avoiding of mucous-producing foods can be effective in healing a cough condition. These mucous-producing foods can vary, based on individual intolerance, but dairy products are a major mucous-producing food for most people.

Prognosis

Because the majority of coughs are related to the **common cold** or influenza, most will end in seven to 21 days. The outcome of coughs due to a more serious underlying disease depends on the pathology of that disease.

Prevention

It is important to identify and treat the underlying disease and origin of the cough. Avoid **smoking** and coming in direct contact with people experiencing cold or flu symptoms. Wash hands frequently during episodes of upper-respiratory illnesses.

Resources

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ORGANIZATIONS

National Heart, Lung and Blood Institute. PO Box 30105, Bethesda, MD 20824-0105. (301) 251-1222. <http://www.nhlbi.nih.gov>.

Jeffrey P. Larson, RPT

KEY TERMS

Asthma—A disease in which the air passages of the lungs become inflamed and narrowed.

Bronchitis—Inflammation of the air passages of the lungs.

Chronic—A word used to describe a long-lasting condition. Chronic conditions often develop gradually and involve slow changes.

Emphysema—An irreversible lung disease in which breathing becomes increasingly difficult.

Mucus—Thick fluid produced by the moist membranes that line many body cavities and structures.

Phenylketonuria (PKU)—A genetic disorder in which the body lacks an important enzyme. If untreated, the disorder can lead to brain damage and mental retardation.

Cough suppressants

Definition

Cough suppressants are medicines that prevent or stop coughing.

Purpose

Cough suppressants act on the center in the brain that controls the cough reflex. They are meant to be used only to relieve dry, hacking coughs associated with colds and flu. They should not be used to treat coughs that bring up mucus or the chronic coughs associated with **smoking**, **asthma**, **emphysema** or other lung problems.

Many cough medicines contain cough suppressants along with other ingredients. Some combinations of ingredients may cancel each other's effects. One example is the combination of cough suppressant with an expectorant—a medicine that loosens and clears mucus from the airways. The cough suppressant interferes with the ability to cough up the mucus that the expectorant loosens.

Description

The cough suppressant described here, dextromethorphan, is an ingredient in many cough medicines, such as Vicks Formula 44, Drixoral Cough Liquid Caps, Sucrets Cough Control, Benylin DM and some Robitussin products. These medicines come in capsule, tablet, lozenge, and liquid forms and are available without a physician's prescription.

Recommended dosage

Regular (short-acting) capsules, lozenges, syrups, or tablets:

ADULTS AND CHILDREN OVER 12. 10-30 mg every 4-8 hours, as needed.

CHILDREN 6-12. 5-15 mg every 4-8 hours, as needed.

CHILDREN 2-6. 2.5-7.5 mg every 4-8 hours, as needed.

Children under 6 should not be given lozenges containing dextromethorphan because of the high dose of dextromethorphan in each lozenge.

CHILDREN UNDER 2. Check with child's physician.

Children under 6 should not be given lozenges containing dextromethorphan.

For extended-release oral suspension

ADULTS AND CHILDREN OVER 12. 60 mg every 12 hours, as needed.

CHILDREN 6-12. 30 mg every 12 hours, as needed.

CHILDREN 2-6. 15 mg every 12 hours, as needed.

CHILDREN UNDER 2. Check with child's physician.

Precautions

Do not take more than the recommended daily dosage of dextromethorphan.

Dextromethorphan is not meant to be used for coughs associated with smoking, asthma, emphysema, chronic **bronchitis**, or other lung conditions. It also should not be used for coughs that produce mucus.

A lingering cough could be a sign of a serious medical condition. Coughs that last more than seven days or are associated with **fever**, rash, **sore throat**, or lasting **headache** should have medical attention. Call a physician as soon as possible.

People with **phenylketonuria** should be aware that some products with dextromethorphan also contain the artificial sweetener aspartame, which breaks down in the body to phenylalanine.

Anyone who has asthma or liver disease should check with a physician before taking dextromethorphan.

Women who are pregnant or breastfeeding or who plan to become pregnant should check with their physicians before taking dextromethorphan.

The dye tartrazine is an ingredient in some cough suppressant products. This dye causes allergic reactions in some people, especially those who are allergic to **aspirin**.

Side effects

Side effects are rare, but may include nausea, vomiting, stomach upset, slight drowsiness, and **dizziness**.

Interactions

Patients who take **monoamine oxidase inhibitors** (MAO inhibitors) should be aware that the co-administration of products containing dextromethorphan can cause dizziness, **fainting**, fever, nausea, and possibly **coma**. Do not take dextromethorphan unless a physician permits the use of the two drugs together.

When dextromethorphan is taken with medicines that cause drowsiness, this effect may be enhanced.

Nancy Ross-Flanigan

Coughing and deep-breathing exercises *see* **Chest physical therapy**

Coxsackievirus infections *see* **Enterovirus infections**

CPK test *see* **Creatine kinase test**

CPR *see* **Cardiopulmonary resuscitation**

Crab lice *see* **Lice infestation**

Cradle cap *see* **Seborrheic dermatitis**

Cramps *see* **Dysmenorrhea**

Cranial arteritis *see* **Temporal arteritis**

Cranial manipulation *see* **Craniosacral therapy**

Craniopharyngioma *see* **Pituitary tumors**

Craniosacral therapy

Definition

Craniosacral therapy is a holistic healing practice that uses very light touching to balance the craniosacral system in the body, which includes the bones, nerves, fluids, and connective tissues of the cranium and spinal area.

Purpose

According to Upledger, craniosacral therapy is ideally suited for **attention-deficit hyperactivity disorder** (ADHD), headaches, chronic middle ear infection, **pain**, and general health maintenance. It is recommended for **autism**, **fibromyalgia**, heart disease, **osteoarthritis**, **pneumonia**, **rheumatoid arthritis**, chronic sinus infections, and **gastroenteritis** (inflammation of the lining of the stomach or small intestine). It is also used with other therapies to treat **chronic fatigue syndrome**, back pain, and menstrual irregularity. In addition, other craniosacral practitioners have reported benefits for eye dysfunction, **dyslexia**, depression, motor coordination difficulties, temporomandibular joint dysfunction (TMD), hyperactivity, **colic**, **asthma** in babies, floppy baby syndrome, **whiplash**, **cerebral palsy**, certain **birth defects**, and other central nervous system disorders.

Description

Origins

The first written reference to the movement of the spinal nerves and its importance in life, clarity, and "bringing quiet to the heart" is found in a 4,000-year-old text from China. Craniosacral work was referred to as "the art of listening." Bone setters in the Middle Ages also sensed the subtle movements of the body. They used these movements to help reset **fractures** and dislocations and to treat headaches.

In the early 1900s, the research of Dr. William Sutherland, an American osteopathic physician, detailed the movement of the cranium and pelvis. Before his research it was believed that the cranium was a solid immovable mass. Sutherland reported that the skull is actually made up of 22 separate and movable bones that are connected by layers of tissue. He called his work cranial **osteopathy**. Nephi Cotton, an American chiropractor and contemporary of Sutherland, called this approach craniology. The graduates of these two disciplines have refined and enhanced these original approaches and renamed their work as sacro-occipital technique, cranial **movement therapy**, or craniosacral therapy.

Dr. John Upledger, an osteopathic physician, and others at the Department of Biomechanics at Michigan State University, College of Osteopathic Medicine learned of Sutherland's research and developed it further. He researched the clinical observations of various osteopathic physicians. This research provided the basis for Upledger's work that he named craniosacral therapy.

Craniosacral therapy addresses the craniosacral system. This system includes the cranium, spine, and sacrum that are connected by a continuous membrane of connective tissue deep inside the body, called the dura mater. The dura mater also encloses the brain and the central nervous system. Sutherland noticed that cerebral spinal fluid rises and falls within the compartment of the dura mata. He called this movement the primary respiratory impulse; today it is known as the craniosacral rhythm (CSR) or the cranial wave.

Craniosacral therapists can most easily feel the CSR in the body by lightly touching the base of the skull or the sacrum. During a session, they feel for disturbances in the rate, amplitude, symmetry, and quality of flow of the CSR. A therapist uses very gentle touch to balance the flow of the CSR. Once the cerebrospinal fluid moves freely, the body's natural healing responses can function.

A craniosacral session generally lasts 30–90 minutes. The client remains fully clothed and lays down on a massage table while the therapist gently assesses the flow of the CSR. Upledger describes several techniques which may be used in a craniosacral therapy session. The first is energy cyst release. "This technique is a hands-on method of releasing foreign or disruptive energies from the patient's body. Energy cysts may cause the disruption of the tissues and organs were they are located." The therapist feels these cysts in the client's body and gently releases the blockage of energy.

Sutherland first wrote about a second practice called direction of energy. In this technique the therapist intends energy to pass from one of his hands, through the patient, into the other hand.

WILLIAM SUTHERLAND (1873–1954)

William Garner Sutherland studied osteopathy under its founder, Andrew Taylor Still. Dr. Sutherland made his own important discovery while examining the sutures of cranial bones the skull bones that protect the brain. What he noticed is that the sutures were designed for motion. Sutherland termed this motion the *Breath of Life*. Through his experiments and research he determined that primary respiration was essential to all other physiological functions.

When Sutherland developed his techniques for craniosacral therapy, he wanted it to serve as a vehicle for listening to the body's rhythmic motions and treat the patterns of inertia when those motions become congested. He believed that the stresses—any physical or emotional trauma—created an imbalance in the body that needed correction to restore it to full health. The therapy is a hands-on method so that the therapist can feel the subtleties of the patterns of movement and inertia. Sutherland felt that this was the way to encourage self-healing and restoration of the body's own mechanisms, taking a holistic approach to creating optimal health.

The Craniosacral Therapy Educational Trust, based on Sutherland's pioneering work, is located at 10 Normington Close, Leigham Court Road, London SW16 2QS, United Kingdom. The phone number is 07000 785778.

The third technique is called myofascial release. This is a manipulative form of bodywork that releases tension in the fascia or connective tissue of the body. This form of bodywork uses stronger touch.

Upledger's fourth technique is position of release. This involves following the client's body into the positions in which an injury occurred and holding it there. When the rhythm of the CSR suddenly stops the therapist knows that the trauma has been released.

The last technique is somatoemotional release. This technique was developed by Upledger and is an offshoot of craniosacral therapy. It is used to release the mind and body of the residual effects of trauma and injury that are "locked in the tissues."

The cost of a session varies due to the length of time needed and the qualifications of the therapist. The cost may be covered by insurance when the therapy is performed or prescribed by a licensed health care provider.

Precautions

This gentle approach is extremely safe in most cases. However, craniosacral therapy is not recommended in

cases of acute systemic infections, recent skull fracture, intracranial hemorrhage or aneurysm, or herniation of the medulla oblongata (brain stem). Craniosacral therapy does not preclude the use of other medical approaches.

Side effects

Some people may experience mild discomfort after a treatment. This may be due to re-experiencing a trauma or injury or a previously numb area may come back to life and be more sensitive. These side effects are temporary.

Research and general acceptance

More than 40 scientific papers have been published that document the various effects of craniosacral therapy. There are also 10 authoritative textbooks on this therapy. The most notable scientific papers include Viola M. Fryman's work documenting the successful treatment of 1,250 newborn children with birth defects. Edna Lay and Stephen Blood showed the effects on TMD, and John Wood documented results with psychiatric disorders. The American Dental Association has found craniosacral therapy to be an effective adjunct to orthodontic work. However, the conventional medical community has not endorsed these techniques.

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ORGANIZATIONS

Milne Institute Inc. P.O. Box 2716, Monterey, CA 93942-2716. (831) 649-1825. Fax: (831) 649-1826. <milneinst@aol.com>. <http://www.milne institute.com>.

Upledger Institute. 11211 Prosperity Farms Road, Palm Beach Gardens, FL 33410. (800) 233-5880. Fax: (561) 622-4771. <http://www.upledger.com>.

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Linda Chrisman

Craniotomy

Definition

Surgical removal of part of the skull to expose the brain.

Purpose

A craniotomy is the most commonly performed surgery for brain **tumor removal**. It may also be done to remove a blood clot and control hemorrhage, inspect the brain, perform a biopsy, or relieve pressure inside the skull.

Precautions

Before the operation, the patient will have undergone diagnostic procedures such as **computed tomography scans** (CT) or **magnetic resonance imaging** (MRI) scans to determine the underlying problem that required the craniotomy and to get a better look at the brain's structure. Cerebral **angiography** may be used to study the blood supply to the tumor, aneurysm, or other brain lesion.

Description

There are two basic ways to open the skull:

- a curving incision from behind the hairline, in front of the ear, arching above the eye
- at the nape of the neck around the occipital lobe

The surgeon marks with a felt tip pen a large square flap on the scalp that covers the surgical area. Following this mark, the surgeon makes an incision into the skin as far as the thin membrane covering the skull bone. Because the scalp is well supplied with blood, the surgeon will have to seal many small arteries. The surgeon then folds back a skin flap to expose the bone.

Using a high speed hand drill or an automatic craniotome, the surgeon makes a circle of holes in the skull, and pushes a soft metal guide under the bone from one hole to the next. A fine wire saw is then moved along the guide channel under the bone between adjacent holes. The surgeon saws through the bone until the bone flap can be removed to expose the brain.

After the surgery for the underlying cause is completed, the piece of skull is replaced and secured with pieces of fine, soft wire. Finally, the surgeon sutures the membrane, muscle, and skin of the scalp.

Preparation

Before the surgery, patients are usually given drugs to ease **anxiety**, and other medications to reduce the risk

A craniotomy is the most commonly performed surgery for brain tumor removal. There are two basic ways to open the skull: a curving incision from behind the hairline in front of the ear and at the nape of the neck (figure A). To reach the brain, the surgeon uses a hand drill to make holes in the skull, pushing a soft metal guide under the bone. The bone is sawed through until the bone flap can be removed to expose the brain (figure B). *(Illustration by Electronic Illustrators Group.)*

of swelling, seizures, and infection after the operation. Fluids may be restricted, and a diuretic may be given before and during surgery if the patient has a tendency to retain water. A catheter is inserted before the patient goes to the operating room.

The scalp is shaved in the operating room right before surgery; this is done so that any small nicks in the skin won't have a chance to become infected before the operation.

Aftercare

Oxygen, painkillers, and drugs to control swelling and seizures are given after the operation. Codeine may be given to relieve the **headache** that may occur as a result of stretching or irritation of the nerves of the scalp that happens during the craniotomy. Some type of drainage from the head may be in place, depending on the reason for the surgery.

Patients are usually out of bed within a day and out of the hospital within a week. Headache and **pain** from the scalp wound can be controlled with medications.

The bandage on the skull should be changed regularly. Sutures closing the scalp will be removed, but soft wires used to reattach the skull are permanent and require no further attention. The patient should avoid getting the scalp wet until all the sutures have been removed. A clean cap or scarf can be worn until the hair grows back.

Risks

Accessing the area of the brain that needs repair may damage other brain tissue. Therefore, the procedure carries with it some risk of brain damage that could leave the patient with some loss of brain function. The surgeon performing the operation can give the patient an assessment of the risk of his or her particular procedure.

Normal results

While every patient's experience is different depending on the reason for the surgery, age, and overall health, if the surgery has been successful, recovery is usually rapid because of the good supply of blood to the area.

Abnormal results

Possible complications after craniotomy include:

KEY TERMS

Craniotome—A type of surgical drill used to operate on the skull. It has a self-controlled system that stops the drill when the bone is penetrated.

- swelling of the brain
- excessive intracranial pressure
- infection
- seizures

Resources

BOOKS

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Carol A. Turkington

Creatine kinase test

Definition

The creatine kinase test measures the blood levels of certain muscle and brain enzyme proteins.

Purpose

Creatine kinase (CK or CPK) is an enzyme (a type of protein) found in muscle and brain. Normally, very little CK is found circulating in the blood. Elevated levels indicate damage to either muscle or brain; possibly from a myocardial infarction (**heart attack**), muscle disease, or **stroke**.

There are three types, or isoforms, of CK:

- CK-I, or BB, is produced primarily by brain and smooth muscle.
- CK-II, or MB, is produced primarily by heart muscle.
- CK-III, or MM, is produced primarily by skeletal muscle.

Precautions

No special precautions are necessary, except in patients with a bleeding disorder.

Description

A small amount of blood is drawn and used for laboratory analysis.

Preparation

Physical activity may cause a rise in CK levels, especially the CK-III fraction. Therefore, patients should not engage in strenuous physical activity the day of the test. The patient should report any recent injections, falls, or **bruises** that have occurred, as these may elevate CK levels as well.

Aftercare

No aftercare is required, except to keep the puncture site clean while it heals.

Risks

There are no risks to this test beyond the very slight risk of infection at the puncture site.

Normal results

In females, total CK should be 10–79 units per liter (U/L). In males, total CK should be 17–148 U/L. CK levels are reduced in the first half of **pregnancy**, and increased in the second half. CK levels are elevated in newborns.

The distribution of isoenzymes should be:

- CK-I: 0%
- CK-II: 0–5%
- CK-III: 95–100%

Abnormal results

Elevation of CK-I may be seen in stroke, extreme **shock**, or **brain tumor**.

Elevation of CK-II is seen after a myocardial infarction. It begins to rise three to six hours after the heart attack, and may peak within 24 hours. It should then return to normal. For this reason, it is a useful marker for recent myocardial infarction, but not for one which occurred more than a day before the test.

Elevation of CK-III indicates skeletal muscle damage. This may occur from normal **exercise**, trauma, or muscle disease. CK levels may be very high early on in **muscular dystrophy**, but may fall to normal later as muscle tissue is lost. Elevated CK is also seen in myositis, myoglobinuria, **toxoplasmosis**, and **trichinosis**. **Hypothyroidism** may also cause elevated CK.

KEY TERMS

Skeletal muscles—Muscles which move the skeleton. All of the muscles under voluntary control are skeletal muscles.

Smooth muscles—Muscles that surround the linings of the digestive system, airways, and circulatory system.

Resources

BOOKS

Corbett, Jane Vincent. *Laboratory Tests and Diagnostic Procedures with Nursing Diagnoses*. 2nd ed. Los Altos, CA: Appleton & Lange, 1987.

Richard Robinson

Creatine phosphkinase test *see* **Creatine kinase test**

Creatinine test

Definition

Creatine is an important compound produced by the body. It combines with phosphorus to make a high-energy phosphate compound in the body. Creatine phosphate is used in skeletal muscle contraction.

Purpose

The creatinine test is used to diagnose impaired kidney function and to determine renal (kidney) damage.

Precautions

A diet high in meat content can cause transient elevations of serum creatinine. Some drugs that may increase creatinine values include gentamicin, cimetidine, heavy-metal chemotherapeutic agents (e.g., cisplatin), and other drugs toxic to the kidneys, such as the **cephalosporins**.

Description

The creatinine test is used to measure the amount of creatinine in the blood. Because creatinine is a nonprotein end-product of creatine phosphate, which is used in skeletal muscle contraction, the daily production of creatine, and the following product, creatinine, depends on muscle mass, which fluctuates very little.

Creatinine is excreted entirely by the kidneys, and therefore is directly related to renal function. When the kidneys are functioning normally, the serum creatinine level should remain constant and normal. Slight increases in creatine levels can appear after meals, especially after ingestion of large quantities of meat, and some diurnal variation may occur, with a low point at 7 A.M. and a peak at 7 P.M. Serious renal disorders, such as **glomerulonephritis**, **pyelonephritis**, and urinary obstruction, will cause abnormal elevations.

The creatinine level is interpreted in conjunction with another kidney function test called the Blood Urea Nitrogen (BUN). The serum creatinine level has much the same significance as the BUN but tends to rise later. Because of this, determinations of creatinine help to chronicle a disease process. Generally, a doubling of creatinine suggests a 50% reduction in kidney filtration rate.

Preparation

The creatinine test requires a blood sample. It is recommended that the patient be **fasting** (nothing to eat or drink) for at least eight hours before the test. The physician may also require that ascorbic acid (vitamin C), **barbiturates**, and **diuretics** be withheld for 24 hours.

Risks

Risks for this test are minimal, but may include slight bleeding from the blood-drawing site, **fainting** or feeling lightheaded after venipuncture, or hematoma (blood accumulating under the puncture site).

Normal results

Normal values can vary from laboratory to laboratory, but are generally in the following ranges:

- Adult female: 0.5–1.1 mg/dL
- Adult male: 0.6–1.2 mg/dL
- Adolescent: 0.5–1.0 mg/dL
- Child: 0.3–0.7 mg/dL
- Infant: 0.2–0.4 mg/dL
- Newborn: 0.3–1.2 mg/dL

Note that variations between sources for serum creatinine normal ranges are greater than for other important tests. For example, due to the greater amount of muscle mass generally present, males normally demonstrate higher creatinine levels than females. Also, because the kidney filtration rate normally increases in **pregnancy**, serum creatinine should be slightly less during such peri-

KEY TERMS

Glomerulonephritis—Glomerulonephritis is an inflammation of the filtering units of the kidney (glomeruli). The condition hinders removal of waste products, salt, and water from the bloodstream, leading to serious complications. It is the most common cause of renal failure.

Pyelonephritis—Pyelonephritis is an inflammation of the kidney itself, usually caused by a bacterial infection. In its most serious form, complications can include high blood pressure (hypertension) and renal failure.

ods. In older patients, creatinine is reduced because of decreased muscle mass. Similarly, other patients may have creatinine levels in which muscle abnormalities must be taken into consideration, such as long-term corticosteroid therapy, high thyroid (**hyperthyroidism**), **muscular dystrophy**, or **paralysis**.

Abnormal results

Two to 4 mg/dL indicate the presence of impairment of renal function. Greater than 4 mg/dL indicates serious impairment in renal function.

Resources

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Janis O. Flores

Creeping eruption *see* **Cutaneous larva migrans**

CREST syndrome *see* **Scleroderma**

Cretinism *see* **Hypothyroidism**

Creutzfeldt-Jakob disease

Definition

Creutzfeldt-Jakob disease (CJD) is a transmissible, rapidly progressing, fatal neurodegenerative disorder called a spongioform degeneration that seems to be related to "mad cow disease."

Description

Before 1995, Creutzfeldt-Jakob disease was little-known outside of the medical profession; even within it, many practitioners did not know much about it. Most doctors had never seen a case. With the recognition of a so-called "new variant" or simply variant form of CJD with the strong possibility that those with it became infected simply by eating contaminated beef, CJD has become one of the most talked-about diseases in the world. Additionally, the radical theory that the infectious agent is a normal protein that has been changed in its form has also sparked much interest.

First described in the first part of the twentieth century independently by Cretzfeldt and Jakob, CJD is a neurodegenerative disease causing a rapidly progressing **dementia** ending in **death**, usually within eight months of the onset of symptoms. It is also a very rare disease, affecting only about one in every million in the population through out the world. In the United States, CJD is thought to affect about 250 people each year. CJD affects adults primarily between ages 50 and 75.

Spongiform encephalopathies

The most obvious pathologic feature of CJD is the formation of numerous fluid-filled spaces in the brain (vacuoles) resulting in a sponge-like appearance. CJD is one of several human "spongiform encephalopathies," diseases that produce this characteristic change in brain tissue. Others are kuru; Gerstmann-Straussler-Scheinker disease, a genetic predominantly characterized by cerebellar ataxia (a kind of movement disorder); and fatal familial **insomnia**, associated with progressive insomnia, autonomic system disfunction, and weakness caused by motor system dysfunction.

Kuru was prevalent among the Fore people in Papua, New Guinea, and spread from infected individuals after their deaths through the practice of ritual cannibalism, in which the relatives of the dead person honored him by consuming his organs, including the brain. Discovery of the infectious nature of kuru won the Nobel Prize for Carleton Gadjusek in 1976. The incubation period for kuru was between four to 30 years or more. While kuru has virtually disappeared following the cessation of these cannibalistic practices, several new cases continue to arise each year.

Cases of CJD have been grouped into three types: familial, iatrogenic, and sporadic.

- Familial CJD, representing 5–15% of cases, is inherited in an autosomal dominant manner, meaning that either parent may pass along the disease to a child, who may then develop CJD later in life.
- Iatrogenic CJD occurs when a person is infected during a medical procedure, such as organ donation, blood **transfusion**, or brain surgery. The rise in organ donation has increased this route of transmission; grafts of infected corneas and dura mater (the tissue covering the brain) have been shown to transmit CJD. Another source is hormones concentrated from the pituitary glands of cadavers, some of whom carried CJD, for use in people with growth hormone deficiencies. Iatrogenic infection from exposure to nerve-containing tissue represents a small fraction of all cases. The incubation period between exposure to the infectious agent is very long and is estimated to be from less than 10 to more than 30 years. It remains unlikely, but not impossible, that blood from patients with CJD is infectious to others by transfusion.
- Sporadic CJD represents at least 85% of all cases. Sporadic cases have no identifiable source of infection. Death usually follows first symptoms within eight months.

Animal forms and "mad cow disease"

Six forms of spongiform encephalopathies are known to occur in other mammals: scrapie in sheep, recognized for more than 200 years; chronic wasting disease in elk and mule deer in Wyoming and Colorado; transmissible mink encephalopathy; exotic ungulate encephalopathy in some types of zoo animals; feline spongiform encephalopathy in domestic cats; and bovine spongiform encephalopathy (BSE) in cows.

BSE was first recognized in Britain in 1986. Besides the spongiform changes in the brain, BSE causes dementia-like behavioral changes—hence the name "mad cow disease." BSE was thought to be an altered form of scrapie, transmitted to cows when they were fed sheep offal (slaughterhouse waste) as part of their feed, but it is now thought to be more likely to be a primary cattle disease spread by contaminated feed.

The use of slaughterhouse offal in animal feed has been common in many countries and has been practiced for at least 50 years. The trigger for the BSE epidemic in Great Britain seems to have come in the early 1980s, when the use of organic solvents for preparation of offal was altered there. It is possible that these solvents had been destroying the agent called a prion, thereby preventing infection, and that the change in preparation procedure opened the way for the agent to "jump species" and cause BSE in cows that consumed scrapie-infected meal. The slaughter of infected (but not yet visibly sick) cows at the end of their useful farm lives, and the use of their carcasses for feed, spread the infection rapidly and widely. For at least a year after BSE was first recognized in British herds, infected bovine remains continued to be incorporated into feed, spreading the disease still further. Although milk from infected cows has never been shown to pass the infectious agent, passage from infected mother to calf may have occurred through unknown means.

Beginning in 1988, the British government took steps to stop the spread of BSE, banning the use of bovine offal in feed and other products and ordering the slaughter of infected cows. By then, the slow-acting agent had become epidemic in British herds. In 1992, it was diagnosed in over 25,000 animals (1% of the British herd). By mid-1997, the cumulative number of BSE cases in the United Kingdom had risen to more than 170,000. The feeding ban did stem the tide of the epidemic; however, the number of new cases each week fell from a peak of 1,000 in 1993 to less than 300 two years later.

The export of British feed and beef to member countries was banned by the European Union, but cases of BSE had developed in Europe by then as well; however, by mid-1997, only about 1,000 cases had been identified. In 1989, the United States banned import of British beef and began monitoring United States herds in 1990. To date, no BSE has been detected in the United States, and only one case has been reported in North America in a cow imported to Canada from Great Britain.

Variant CJD: The human equivalent of mad cow disease?

From the beginning of the BSE epidemic, scientists and others in Britain feared that BSE might jump species again to infect humans who had consumed infected beef. This, however, had never occurred in scrapie from sheep, a disease known from hundreds of years. In 1996, the first report of this possibility occurred and this fear seemed to be realized with the first cases of a new variant of Creutzfeldt-Jacob disease, termed nvCJD, now just vCJD. Its victims are much younger than the 60–65 year old average for CJD, and the time from symptom onset to death has averaged 12 months or more instead of eight. The disease appears to cause more psychiatric symptoms early on. EEG abnormalities characteristic of CJD are not typically seen in vCJD.

As of July 2001, the total number of human cases of vCJD is 102. It is of major concern that the number of cases per year seems to be increasing by a factor of 1.35 each year. Almost all the cases have been found in Great Britain with three in France, one in Ireland, and one suspected in Hong Kong (who spent time in Great Britain).

Evidence is growing stronger that vCJD is in fact caused by BSE:

- almost all of the cases so far have occurred in Great Britain, the location of the BSE epidemic.
- BSE injected into monkeys produces a disease very similar to vCJD
- BSE and vCJD produce the same brain lesions after the same incubation period when injected into laboratory mice
- brain proteins isolated from vCJD victims, but not from the other forms of CJD, share similar molecular characteristics with brain proteins of animals that died from BSE

Many researchers now treat the BSE-vCJD connection as solidly established.

Assuming that BSE is the source, the question that has loomed from the beginning has been is how many people will eventually be affected. Epidemiological models of infectious disease produce estimates ranging from less than one hundred (a level already broken) to tens of thousands or more, depending on the assumptions used by the modelers. The incubation period of vCJD in humans is not known, nor are the genetic and environmental risk factors that influence susceptibility, nor the quantity of infectious agent needed to cause the disease. It is estimated that between one and two million infected cattle have been eaten by humans, most in the earliest stages of the epidemic. Estimates cannot be based on the very few cases that have developed so far. These cases could represent the very few people with the right combination of exposure and susceptibility to a relatively fast-developing infection, or they could be the first few victims of a slower-acting, more highly infectious agent.

Causes and symptoms

Causes

It is clear that Creutzfeldt-Jakob disease is caused by an infectious agent, but it is not yet clear what type of agent that is. Originally assumed to be a virus, evidence is accumulating that, instead, CJD is caused by a protein called a prion (PREE-on, for "proteinaceous infectious particle") transmitted from victim to victim. The other spongiform encephalopathies are also hypothesized to be due to prion infection.

If this hypothesis is proved true, it would represent one of the most radical new ideas in biology since the discovery of deoxyribonucleic acid (DNA). All infectious diseases, in fact all life, uses nucleic acids—DNA or ribonucleic acid (RNA)—to code the instructions needed for reproduction. Inactivation of the nucleic acids destroys the capacity to reproduce. However, when these same measures are applied to infected tissue from spongiform encephalopathy victims, infectivity is not destroyed. Furthermore, purification of infected tissue to concentrate the infectious fraction yields protein, not nucleic acid. While it remains possible that some highly stable nucleic acid remains hidden within the purified protein, this is seemingly less and less likely as further experiments are done. The "prion hypothesis," as it is called, is now widely accepted, at least provisionally, by most researchers in the field. The most vocal proponent of the hypothesis, Stanley Prusiner, was awarded the Nobel Prize in 1997 for his work in the prion diseases.

A prion is an altered form of a normal brain protein. The normal protein has a helical shape along part of its length. In the prion form, a sheet structure replaces the helix. According to the hypothesis, when the normal form interacts with the prion form, some of its helical part is converted to a sheet, thus creating a new prion capable of transforming other normal forms. In this way, the disease process resembles crystallization more than typical viral infection, in which the virus commands the host's cellular machinery to reproduce more of the virus. Build-up of the sheet form causes accumulation of abnormal protein clumps and degeneration of brain cells, which is thought to cause the disease.

The brain protein affected by the prion, called PrP, is part of the membrane of brain cells, but its exact function is unknown. It is composed of about 250 subunits, called amino acids, coded for by a gene on chromosome 20. Slight genetic differences, called polymorphisms, give rise to two slightly different normal protein forms: subunit 129 is a "methionine" in one form, but is "valine" in the other. A person may have all of one, all of the other, or a mixture of the two, depending on their genetic inheritance. Both forms have the normal helical structure, and function normally. However, susceptibility to prion conversion is influenced by subunit 129: a person with a mixture of forms is more resistant to conversion. All the cases of vCJD tested have had just methionine at 129. Exposure to the infectious agent is, of course, still required for disease development. Prion diseases are not contagious in the usual sense, and transmission from an infected person to another person requires direct inoculation of infectious material.

Familial CJD, on the other hand, does not require exposure, but develops through the inheritance of other, more disruptive mutations in the gene for the normal PrP protein. Researchers believe these mutations increase the likelihood that the protein may more spontaneously "flip" to the sheet form; once created, these can then convert other normal-form molecules. The other two inherited human prion diseases, Gerstmann-Straussler-

Scheinker disease and fatal familial insomnia, involve different mutations in the same gene.

The large majority of CJD cases are sporadic, meaning they have no known route of infection or genetic link. Causes of sporadic CJD are likely to be diverse and may include spontaneous genetic mutation, spontaneous protein changes, or unrecognized exposure to infectious agents. It is highly likely that future research will identify more risk factors associated with sporadic CJD.

Symptoms

About one in four people with CJD begin their illness with weakness, changes in sleep patterns, weight loss, or loss of appetite or sexual drive. A person with CJD may first complain of visual disturbances, including double vision, blurry vision, or partial loss of vision. Some visual symptoms are secondary to cortical blindness related to death of nerve cells in the occipital lobe of the brain responsible for vision. This form of visual loss is unusual in that patients may be unaware that they are unable to see. These symptoms may appear weeks to months before the onset of dementia.

The most characteristic symptom of CJD is rapidly progressing dementia, or loss of mental function. Dementia is marked by:

- memory losses
- impaired abstraction and planning
- language and comprehension disturbances
- poor judgment
- disorientation
- decreased attention and increased restlessness
- personality changes and psychosis
- hallucinations

Muscle spasms and jerking movements, called myoclonus, are also a prominent symptom of CJD. Balance and coordination disturbance (ataxia), is common in CJD, and is more pronounced in nvCJD. Stiffness, difficulty moving, and other features representing **Parkinson's disease** are seen and can progress to akinetic **mutism**, which is a state of being unable to speak or move.

Diagnosis

CJD is diagnosed by a clinical neurological exam and **electroencephalography** (EEG), which shows characteristic spikes called triphasic sharp waves. **Magnetic resonance imaging** (MRI) or **computed tomography scans** (CT) should be done to exclude other forms of dementia, and in CJD typically shows atrophy or loss of brain tissue. Lumbar puncture, or spinal tap, may be done to rule out other causes of dementia (as cell count, chemical analysis, and other routine tests are normal in CJD) and to identify elevated levels of marker proteins known as 14-3-3. Another marker, neuron-specific enolase, may also be increased in CJD. CJD is conclusively diagnosed after death by brain **autopsy**. Scientists are investigating whether testing lymphatic tissue such as the tonsil may be an early tool in vCJD diagnosis. Additionally, recent studies have suggested that other blood tests may be useful as well.

Treatment

There is no cure for CJD, and no treatment that slows the progression of the disease. Drug therapy and nursing care are aimed at minimizing psychiatric symptoms and increasing patient comfort. However, the rapid progression of CJD frustrates most attempts at treatment, since decreasing cognitive function and more prominent behavioral symptoms develop so quickly. Despite the generally grim prognosis, a few CJD patients progress more slowly and live longer than the average; for these patients, treatment will be more satisfactory. Scientists are investigating whether some medicines that can "break" the abnormal protein form may be useful and whether a vaccine could help.

Prognosis

Creutzfeldt-Jakob disease is invariably fatal, with death following symptom onset by an average of eight months. About 5% of patients live longer than two years. Death from vCJD has averaged approximately 12 months after onset.

Prevention

There is no known way to prevent sporadic CJD, by far the most common type. Not everyone who inherits the gene mutation for familial CJD will develop the disease, but at present, there is no known way to predict who will and who won't succumb. The incidence of iatrogenic CJD has fallen with recognition of its sources, the development of better screening techniques for infected tissue, and the use of sterilization techniques for surgical instruments that inactivate prion proteins.

Strategies for prevention of vCJD are a controversial matter, as they involve a significant sector of the agricultural industry and a central feature of the diet in many countries. The infectious potential of contaminated meat is unknown, because the ability to detect prions within meat is limited. Surveillance of North American herds strongly suggests there is no BSE here, and strict regulations on imports of European livestock make future outbreaks highly unlikely. Therefore, avoidance of all meat

KEY TERMS

Autosomal dominant inheritance—A pattern of inheritance in which a trait will be expressed if the gene is inherited from either parent.

Encephalopathy—Brain disorder characterized by memory impairment and other symptoms.

Iatrogenic—Caused by a medical procedure.

Nucleic acids—The cellular molecules DNA and RNA that act as coded instructions for the production of proteins and are copied for transmission of inherited traits.

originating in North America, simply on grounds of BSE risk, is a personal choice unsupported by current data. The ban on the export of British beef continues in countries of the European Union, although some herds in these countries have developed low levels of infection as well.

Resources

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ORGANIZATION

Creutzfeldt-Jakob Disease Foundation. P.O. Box 611625, North Miami, FL 33261-1625. <http://members.aol.com/crjakob/contact.html>.

The UK Creutzfeldt-Jakob Disease Surveillance Unit. <http://www.cjd.ed.ac.uk/index.htm>.

Larry I. Lutwick, MD

Cri du chat syndrome

Definition

Cri du chat syndrome occurs when a piece of chromosomal material is missing from a particular region on chromosome 5. Individuals with this syndrome have unusual facial features, poor muscle tone(hypotonia), small head size (microcephaly), and **mental retardation**. A classic feature of the syndrome is the cat-like cry made by infants with this disorder.

Description

Dr. Jerome Lejeune first described cri du chat syndrome in 1963. The syndrome is named for the cat-like cry made by infants with this genetic disorder. *Cri du chat* means "cry of the cat" in French. This unusual cry is caused by abnormal development of the larynx (organ in the throat responsible for voice production). Cri du chat syndrome is also called "5p minus syndrome" because it is caused by a deletion, or removal, of genetic material from chromosome 5. The deletion that causes cri du chat syndrome occurs on the short or "p" arm of chromosome 5. This deleted genetic material is vital for normal development. Absence of this material results in the features associated with cri du chat syndrome.

A high-pitched mewing cry during infancy is a classic feature of cri du chat. Infants with cri du chat also typically have low birth weight, slow growth, a small head (microcephaly) and poor muscle tone (hypotonia). Infants with cri du chat may have congenital heart defects. Individuals with cri du chat syndrome have language difficulties, delayed motor skill development, and mental retardation. Behavioral problems may also develop as the child matures.

It has been estimated that cri du chat syndrome occurs in one of every 50,000 live births. According to the 5p minus Society, approximately 50–60 children are born with cri du chat syndrome in the United States each year. It can occur in all races and in both sexes.

Causes and symptoms

Cri du chat is the result of a chromosome abnormality—a deleted piece of chromosomal material on chromosome 5. In 90% of patients with cri du chat syndrome, the deletion is sporadic. This means that it happens randomly and is not hereditary. If a child has cri du chat due to a sporadic deletion, the chance the parents could have another child with cri du chat is 1%. In approximately 10% of patients with cri du chat, there is a hereditary chromosomal rearrangement that causes the deletion. If a parent has this rearrangement, the risk for them to have a child with cri du chat is greater than 1%.

An abnormal larynx causes the unusual cat-like cry made by infants that is a hallmark feature of the syndrome. As children with cri du chat get older, the cat-like cry becomes less noticeable. This can make the diagnosis more difficult in older patients. In addition to the cat-like

KEY TERMS

Aminocentesis—A procedure performed at 16–18 weeks of pregnancy in which a needle is inserted through a woman's abdomen into her uterus to draw out a small sample of the amniotic fluid from around the baby. Either the fluid itself or cells from the fluid can be used for a variety of tests to obtain information about genetic disorders and other medical conditions in the fetus.

Centromere—The centromere is the constricted region of a chromosome. It performs certain functions during cell division.

Chorionic villus sampling (CVS)—A procedure used for prenatal diagnosis at 10–12 weeks gestation. Under ultrasound guidance a needle is inserted either through the mother's vagina or abdominal wall and a sample of cells is collected from around the early embryo. These cells are then tested for chromosome abnormalities or other genetic diseases.

Chromosome—A microscopic thread-like structure found within each cell of the body and consists of a complex of proteins and DNA. Humans have 46 chromosomes arranged into 23 pairs. Changes in either the total number of chromosomes or their shape and size (structure) may lead to physical or mental abnormalities.

Congenital—Refers to a disorder that is present at birth.

Deletion—The absence of genetic material that is normally found in a chromosome. Often, the genetic material is missing due to an error in replication of an egg or sperm cell.

Hypotonia—Reduced or diminished muscle tone.

Karyotyping—A laboratory procedure in which chromosomes are separated from cells, stained and arranged so that their structure can be studied under the microscope.

Microcephaly—An abnormally small head.

cry, individuals with cri du chat also have unusual facial features. These facial differences can be very subtle or more obvious. Microcephaly (small head size) is common. During infancy many patients with cri du chat do not gain weight or grow normally. Approximately 30% of infants with cri du chat have a congenital heart defect. Hypotonia (poor muscle tone) is also common, leading to problems with eating and slow, but normal, development. Mental retardation is present in all patients with cri du chat, but the degree of mental retardation varies between patients.

Diagnosis

During infancy, the diagnosis of cri du chat syndrome is strongly suspected if the characteristic cat-like cry is heard. If a child has this unusual cry or other features seen in cri du chat syndrome, chromosome testing should be performed. Chromosome analysis provides the definitive diagnosis of cri du chat syndrome and can be performed from a blood test. Chromosome analysis, also called "karyotyping," involves staining the chromosomes and examining them under a microscope. In some cases the deletion of material from chromosome 5 can be easily seen. In other cases, further testing must be performed. FISH (fluorescence in-situ hybridization) is a special technique that detects very small deletions. The majority of the deletions that cause cri du chat syndrome can be identified using the FISH technique.

Cri du chat syndrome can be detected before birth if the mother undergoes **amniocentesis** testing or chorionic villus sampling(CVS). This testing would only be recommended if the mother or father is known to have a chromosome rearrangement, or if they already have a child with cri du chat syndrome.

Treatment

Currently, there is no cure for cri du chat syndrome. Treatment consists of supportive care and developmental therapy.

Prognosis

Individuals with cri du chat have a 10% mortality during infancy due to complications associated with congenital heart defects, hypotonia, and feeding difficulties. Once these problems are controlled, most individuals with cri du chat syndrome have a normal lifespan. The degree of mental retardation can be severe. However, a recent study suggested that the severity is somewhat affected by the amount of therapy received.

Resources

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ORGANIZATIONS

5p- Society. 7108 Katella Ave. #502, Stanton, CA 90680. (888) 970-0777. <http://www.fivepminus.org>.

Alliance of Genetic Support Groups. 4301 Connecticut Ave. NW, Suite 404, Washington, DC 20008. (202) 966-5557. Fax: (202) 966-8553. <http://www.geneticalliance.org>.

Cri du Chat Society. Dept. of Human Genetics, Box 33, MCV Station, Richmond VA 23298. (804) 786-9632.

Cri du Chat Syndrome Support Group. <http://www.cridchat.u-net.com>.

National Organization for Rare Disorders (NORD). P.O. Box 8923, New Fairfield, CT 06812-8923. (203) 746-6518 or (800) 999-6673. Fax: (203) 746-6481. <http://www.rarediseases.org>.

OTHER

OMIM—Online Mendelian Inheritance in Man. <http://www.ncbi.nlm.nih.gov/Omim/>.

Holly Ann Ishmael, MS

Crib death *see* **Sudden infant death syndrome**

Crohn's disease

Definition

Crohn's disease is a type of inflammatory bowel disease (IBD), resulting in swelling and dysfunction of the intestinal tract.

Description

Crohn's disease involves inflammation of the intestine, especially the small intestine. Inflammation refers to swelling, redness, and loss of normal function. There is evidence that the inflammation is caused by various products of the immune system that attack the body itself instead of helpfully attacking a foreign invader (a virus or bacteria, for example). The inflammation of Crohn's disease most commonly affects the last part of the ileum (a section of the small intestine), and often includes the large intestine (the colon). However, inflammation may also occur in other areas of the gastrointestinal tract, affecting the mouth, esophagus, or stomach. Crohn's disease differs from **ulcerative colitis**, the other major type of IBD, in two important ways:

- The inflammation of Crohn's disease may be discontinuous, meaning that areas of involvement in the intestine may be separated by normal, unaffected segments of intestine. The affected areas are called "regional enteritis," while the normal areas are called "skip areas."
- The inflammation of Crohn's disease affects all the layers of the intestinal wall, while ulcerative colitis affects only the lining of the intestine.

Also, ulcerative colitis does not usually involve the small intestine; in rare cases it involves the terminal ileum (so-called "backwash" ileitis).

In addition to inflammation, Crohn's disease causes ulcerations, or irritated pits in the intestinal wall. These pits occur because the inflammation has made areas of tissue shed.

Crohn's disease may be diagnosed at any age, although most diagnoses are made between the ages of 15–35. About 0.02–0.04% of the population suffers from this disorder, with men and women having an equal chance of being stricken. Whites are more frequently affected than other racial groups, and people of Jewish origin are between three and six times more likely to suffer from IBD. IBD runs in families; an IBD patient has a 20% chance of having other relatives who are fellow sufferers.

Crohn's disease is a chronic disorder. While the symptoms can be improved, a patient will not be completely cured of the underlying disease.

Causes and symptoms

The cause of Crohn's disease is unknown. No infectious agent (virus, bacteria, or fungi) has been identified as the cause of Crohn's disease. Still, some researchers have theorized that some type of infection may have originally been responsible for triggering the immune system, resulting in the continuing and out-of-control cycle of inflammation that occurs in Crohn's disease. Other evidence for a disorder of the immune system includes the high incidence of other immune disorders that may occur along with Crohn's disease.

The first symptoms of Crohn's disease include **diarrhea**, **fever**, abdominal **pain**, inability to eat, weight loss, and **fatigue**. Some patients have severe pain that mimics **appendicitis**. It is rare, however, for patients to notice blood in their bowel movements. Because Crohn's disease severely limits the ability of the affected intestine to absorb

the nutrients from food, a patient with Crohn's disease can have signs of **malnutrition**, depending on the amount of intestine affected and the duration of the disease.

The combination of severe inflammation, ulceration, and scarring that occurs in Crohn's disease can result in serious complications, including obstruction, **abscess** formation, and fistula formation.

An obstruction is a blockage in the intestine. This obstruction prevents the intestinal contents from passing beyond the point of the blockage. The intestinal contents "back up," resulting in **constipation**, vomiting, and intense pain. Although rare in Crohn's disease (because of the increased thickness of the intestinal wall due to swelling and scarring), a severe bowel obstruction can result in an intestinal wall perforation (a hole in the intestine). Such a hole in the intestinal wall would allow the intestinal contents, usually containing bacteria, to enter the abdomen. This complication could result in a severe, life-threatening infection.

Abcess formation is the development of a walled-off pocket of infection. A patient with an abscess will have bouts of fever, increased abdominal pain, and may have a lump or mass that can be felt through the wall of the abdomen.

Fistula formation is the formation of abnormal channels. These channels may connect one area of the intestine to another neighboring section of intestine. Fistuals may join an area of the intestine to the vagina or bladder, or they may drain an area of the intestine through the skin. Abscesses and fistulas commonly affect the area around the anus and rectum (the very last portions of the colon allowing waste to leave the body). These abnormal connections allow the bacteria that normally live in the intestine to enter other areas of the body, causing potentially serious infections.

Patients suffering from Crohn's disease also have a significant chance of experiencing other disorders. Some of these may relate specifically to the intestinal disease, and others appear to have some relationship to the imbalanced immune system. The faulty absorption state of the bowel can result in **gallstones** and **kidney stones**. Inflamed areas in the abdomen may press on the tube that drains urine from the kidney to the bladder (the ureter). Ureter compression can make urine back up into the kidney, enlarge the ureter and kidney, and can potentially lead to kidney damage. Patients with Crohn's disease also frequently suffer from:

- arthritis (inflammation of the joints)
- spondylitis (inflammation of the vertebrae, the bones of the spine)
- ulcers of the mouth and skin

A barium x-ray showing the colon of a patient with Crohn's disease where the large and small intestines join (bottom left). *(Custom Medical Stock Photo. Reproduced by permission.)*

- painful, red bumps on the skin
- inflammation of several eye areas
- inflammation of the liver, gallbladder, and/or the channels (ducts) that carry bile between and within the liver, gallbladder, and intestine

The chance of developing **cancer** of the intestine is greater than normal among patients with Crohn's disease, although this chance is not as high as among those patients with ulcerative colitis

Diagnosis

Diagnosis is first suspected based on a patient's symptoms. Blood tests may reveal an increase in certain types of white blood cells, an indication that some type of inflammation is occurring in the body. The blood tests may also reveal anemia and other signs of malnutrition due to malabsorption (low blood protein; variations in

KEY TERMS

Abscess—A walled-off pocket of pus caused by infection.

Endoscope—A medical instrument that can be passed into an area of the body (the bladder or intestine, for example) to allow examination of that area. The endoscope usually has a fiber-optic camera that allows a greatly magnified image to be shown on a television screen viewed by the operator. Many endoscopes also allow the operator to retrieve a small sample (biopsy) of the area being examined to more closely view the tissue under a microscope.

Fistule—An abnormal channel that creates an open passageway between two structures that do not normally connect.

Gastrointestinal tract—The entire length of the digestive system, running from the stomach, through the small intestine, large intestine, and out the rectum and anus.

Immune system—The body system responsible for producing various cells and chemicals that fight infection by viruses, bacteria, fungi, and other foreign invaders. In autoimmune disease, these cells and chemicals turn against the body itself.

Inflammation—The result of the body's attempts to fight off and wall off an area that is infected. Inflammation results in the classic signs of redness, heat, swelling, and loss of function.

Obstruction—A blockage.

Ulceration—A pitted area or break in the continuity of a surface such as skin or mucous membrane.

the amount of calcium, potassium, and magnesium present in the blood; changes in certain markers of liver function). Stool samples may be examined to make sure that no infectious agent is causing the diarrhea, and to see if the waste contains blood.

During an endoscopic exam, a doctor passes a flexible tube with a tiny, fiber-optic camera device through the rectum and into the colon. The doctor can then carefully examine the lining of the intestine for signs of inflammation and ulceration that might suggest Crohn's disease. A tiny sample (a biopsy) of the intestine can also be taken through the endoscope, and the tissue will be examined under a microscope for evidence of Crohn's disease.

X rays can be helpful for diagnosis, and also for determining how much of the intestine is involved in the disease. For these x rays, the patient must either drink a chalky solution containing barium, or receive a **barium enema** (a solution that is administered through the rectum). Barium helps to "light up" the intestine, allowing more detail to be seen on the resulting x rays.

While Crohn's disease and ulcerative colitis are similar, they are also very different. Although it can be difficult to determine whether a patient has Crohn's disease or ulcerative colitis, it is important to make every effort to distinguish between these two diseases. Because the long-term complications of the diseases are different, treatment will depend on careful diagnosis of the specific IBD present.

Treatment

Treatments for Crohn's disease try to reduce the underlying inflammation, the resulting malabsorption/malnutrition, the uncomfortable symptoms of crampy abdominal pain and diarrhea, and the possible complications (obstructions, abscesses, and fistulas).

Inflammation can be treated with a drug called sulfasalazine. Sulfasalazine is made up of two parts. One part is related to the sulfa **antibiotics**; the other part is a form of the anti-inflammatory chemical, salicylic acid (related to **aspirin**). Sulfasalazine is not well absorbed from the intestine, so it stays mostly within the intestine, where it is broken down into its components. It is believed that the salicylic acid component actively treats Crohn's disease by fighting inflammation. Some patients do not respond to sulfasalazine, and require steroid medications (such as prednisone). Steroids, however, must be used carefully to avoid the complications of these drugs, including increased risk of infection and weakening of bones (**osteoporosis**). Some very potent immunosuppressive drugs, which interfere with the products of the immune system and can hopefully decrease inflammation, may be used for those patients who do not improve on steroids.

A new drug called infliximab (Remicade) appears to be a powerful treatment for Crohn's disease, particularly for patients who have not responded well to other forms of treatment. Infliximab is administered through infusion, and consists of a monoclonal antibody that interferes with the inflammatory process mediated by tumor necrosis factor-alpha (TNF-a). Patients taking infliximab seem to be able to decrease their use of steroid medications, and require fewer surgical interventions. Furthermore, infliximab is the first medication approved for treating fistulas. Unfortunately, infliximab can only be used on a short-term basis, because its interference with TNF-a activity can also predispose patients to serious infection. More

research is needed to try to harness the benefits of infliximab, while avoiding the potential complications.

Serious cases of malabsorption/malnutrition may need to be treated by providing nutritional supplements. These supplements must be in a form that can be absorbed from the damaged, inflamed intestine. Some patients find that certain foods are hard to digest, including milk, large quantities of fiber, and spicy foods. When patients are suffering from an obstruction, or during periods of time when symptoms of the disease are at their worst, they may need to drink specially formulated, high-calorie liquid supplements. Those patients who are severely ill may need to receive their **nutrition** through a needle inserted in a vein (intravenously), or even by a tiny tube (a catheter) inserted directly into a major vein in the chest.

A number of medications are available to help decrease the cramping and pain associated with Crohn's disease. These include loperamide, tincture of opium, and codeine. Some fiber preparations (methylcellulose or psyllium) may be helpful, although some patients do not tolerate them well.

The first step in treating an obstruction involves general attempts to decrease inflammation with sulfasalazine, steroids, or immunosuppressive drugs. A patient with a severe obstruction will have to stop taking all food and drink by mouth, allowing the bowel to "rest." Abscesses and other infections will require antibiotics. Surgery may be required to repair an obstruction that does not resolve on its own, to remove an abscess, or to repair a fistula. Such surgery may involve the removal of a section of the intestine. In extremely severe cases of Crohn's disease that do not respond to treatment, a patient may need to have the entire large intestine removed (an operation called a colectomy). In this case, a piece of the remaining small intestine is pulled through an opening in the abdomen. This bit of intestine is fashioned surgically to allow a special bag to be placed over it. This bag catches the body's waste, which no longer can be passed through the large intestine and out of the anus. This opening, which will remain in place for life, is called an ileostomy.

Prognosis

Crohn's disease is a life-long illness. The severity of the disease can vary, and a patient can experience periods of time when the disease is not active and he or she is symptom-free. However, the complications and risks of Crohn's disease tend to increase over time. Well over 60% of all patients with Crohn's disease will require surgery, and about half of these patients will require more than one operation over time. About 5–10% of all Crohn's patients will die of their disease, primarily due to massive infection.

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Crohn's & Colitis Foundation of America, Inc. 386 Park Avenue South, 17th Floor, New York, NY 10016-8804. (800) 932-2423.

Rosalyn S. Carson-DeWitt

Cromolyn *see* **Antiasthmatic drugs**

Cross-eye *see* **Strabismus**

Cross-gender identification *see* **Gender identity disorder**

Croup

Definition

Croup is a common childhood ailment. Typically, it arises from a viral infection of the larynx (voice box) and is associated with mild upper respiratory symptoms such as a runny nose and **cough**. The key symptom is a harsh barking cough. Croup is usually not serious, and most children recover within a few days. In a small percentage of cases, a child develops breathing difficulties and may need medical attention.

Description

At one time, the term croup was primarily associated with **diphtheria**, a life-threatening respiratory infection. Owing to widespread vaccinations, diphtheria has become rare in the United States, and croup currently

refers to a mild viral infection of the larynx. Croup is also known as laryngotracheitis, a medical term that describes the inflammation of the trachea (windpipe) and larynx.

Parainfluenza viruses are the typical root cause of the infection, but **influenza** (flu) and cold viruses may sometimes be responsible. All of these viruses are highly contagious and easily transmitted between individuals via sneezing and coughing. Children between the ages of three months and six years are usually affected, with the greatest incidence at one to two years of age. Croup can occur at any time of the year, but it is most typical during early autumn and winter. The characteristic harsh barking of a croupy cough can be very distressing, but it rarely indicates a serious problem. Most children with croup can be treated very effectively at home; however, 1–5% may require medical treatment.

Croup may sometimes be confused with more serious conditions, such as **epiglottitis** or bacterial tracheitis. These ailments arise from bacterial infection and must receive medical treatment.

Causes and symptoms

Owing to an upper respiratory viral infection, the larynx and trachea may become inflamed or swollen. The hallmark sign of croup is a harsh, barking cough. This cough may be preceded by one to three days of symptoms that resemble a slight cold. A croupy cough is often accompanied by a runny nose, hoarseness, and a low **fever**. When the child inhales, there may be a raspy or high-pitched noise, called **stridor**, owing to the narrowed airway and accumulated mucus. In the presence of stridor, medical attention is required.

However, the airway rarely narrows so much that breathing is impeded. Symptoms usually abate completely within a few days. Medical treatment may be sought if the child's symptoms do not respond to home treatment.

Emergency medical treatment is required immediately if the child has difficulty breathing, swallowing, or talking; develops a high fever (103°F/39.4°C or more); seems unalert or confused; or has pale or blue-tinged skin.

Diagnosis

Croup is diagnosed based on the symptoms. If symptoms are particularly severe, or do not respond to treatment, an x ray of the throat area is done to assess the possibility of epiglottitis or other blockage of the airway.

Treatment

Home treatment is the usual method of managing croup symptoms. It is important that the child is kept comfortable and calm to the best degree possible, because crying can make symptoms seem worse. Humid air can help a child with croup feel more comfortable. Recommended methods include sitting in a steamy bathroom with the hot water running or using a cool-water vaporizer or humidifier. Breathing may also be eased by going outside into cooler air. The child should drink frequently in order to stay well hydrated. To treat any fever, the child may be given an appropriate dose of **acetaminophen** (like Tylenol). **Antihistamines** and **decongestants** are ineffective in treating croup. Children under the age of 18 should not be given aspirin, as it may cause **Reye's syndrome**, a life-threatening disease of the brain.

If the child does not respond to home treatment, medical treatment at a doctor's office or an emergency room could be necessary. Based on the severity of symptoms and the response to treatment, the child may need to be admitted to a hospital.

For immediate symptom relief, epinephrine may be administered as an inhaled aerosol. Effects last for up to two hours, but there is a possibility that symptoms may return. For that reason, the child is kept under supervision for three or more hours. Another effective drug is a glucocorticoid, dexamethasone. This drug requires more time to take effect, but is longer lasting. It can be administered orally or as an injection. Another glucocorticoid, budesonide, has been used outside the United States for treating croup. It is administered as an inhaled aerosol and has been shown to be effective; however, it is not available as a treatment option in the United States.

Of the 1–5% of children requiring medical treatment, approximately 1% need respiratory support. Such support involves intubation (inserting a tube into the trachea) and oxygen administration.

Alternative treatment

Botanical/herbal medicines can be helpful in healing the cough that is commonly associated with croup. Several herbs to consider for cough treatment include aniseed (*Pimpinella anisum*), sundew (*Drosera rotundifolia*), thyme (*Thymus vulgaris*), and wild cherry bark (*Prunus serotina*). Homeopathic medicine can be very effective in treating cases of croup. Choosing the correct remedy (a common choice is aconite or monkshood, *Aconitum napellus*) is always the key to the success of this type of treatment.

Prognosis

Croup is a temporary condition and children typically recover completely within three to six days. Children can experience one or more episodes of croup during early childhood; however, croup is rarely a dangerous condition.

KEY TERMS

Diphtheria—A serious, frequently fatal, bacterial infection that affects the respiratory tract. Vaccinations given in childhood have made diphtheria very rare in the United States.

Epiglottitis—A bacterial infection that affects the epiglottis. The epiglottis is a flap of tissue that prevents food and fluid from entering the trachea. The infection causes it to become swollen, potentially blocking the airway. Other symptoms include a high fever, nonbarking cough, muffled voice, and an inability to swallow properly (possibly indicated by drooling).

Glucocorticoid—A hormone that helps in digestion of carbohydrates and reduces inflammation.

Larynx—Commonly called the voice box, it is the area of the trachea that contains the vocal cords.

Stridor—The medical term used to describe the high-pitched or rasping noise made when air is inhaled.

Trachea—Commonly called the windpipe, it is the air pathway that connects the nose and mouth to the lungs.

Prevention

Croup is caused by highly transmissible viruses. Similar to other common childhood ailments, prevention is not applicable.

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Julia Barrett

Cryoglobulin test

Definition

Cryoglobulin is an abnormal blood protein associated with several diseases. Testing for cryoglobulin is done when a person has symptoms of this protein or is being evaluated for one of the associated diseases.

Purpose

Cryoglobulin clumps in cold temperatures. This physical characteristic causes people with cryoglobulin to have symptoms during cold weather: blanching, numbness, and **pain** in their fingers or toes (Raynaud's phenomenon); bleeding into the skin (purpura); and pain in joints (arthralgia). People with these symptoms or any other symptoms that appear in cold weather should be tested for cryoglobulin.

Diseases that cause the body to make extra or abnormal proteins are often associated with cryoglobulin. These diseases include cancers involving white blood cells, infections, **autoimmune disorders**, and rheumatoid diseases.

This test provides information about the cause of symptoms in a person who already has a disease process. It doesn't diagnose a specific disease or monitor the course of a disease.

Precautions

This test is not a screening test for disease in a person without symptoms.

Description

Laboratory testing for cryoglobulin is based on the fact that cryoglobulin clumps when cooled and dissolves when warmed. The test is done on a person's serum (the yellow liquid part of blood that separates from the cells after the blood clots). The serum is kept warm from the time drawn until the cells and the serum are separated in the laboratory. The serum is placed at 33.8°F (1°C) for one to seven days. If there is clumping, cryoglobulins are present. The amount of cryoglobulins is determined by measuring the amount of clumping. Negative tests are checked through seven days.

Additional testing is done to find out what kind of cryoglobulin protein is present. There are three kinds of cryoglobulin, each associated with different diseases.

The test, also called the cold sensitivity antibodies test, is covered by insurance when medically necessary. Results are usually available the following day.

Preparation

This test requires 15–20 mL of blood. A healthcare worker ties a tourniquet on the person's upper arm, locates a vein in the inner elbow region, and inserts a

KEY TERMS

Cryoglobulin—An abnormal blood protein associated with several diseases. It is characterized by its tendency to clump in cold temperatures.

needle into that vein. Vacuum action draws the blood through the needle into an attached tube. Collection of the sample takes only a few minutes. The blood must be kept warm, at body temperature, until the laboratory can separate the cells from the serum.

Aftercare

Discomfort or bruising may occur at the puncture site or the person may feel dizzy or faint. Pressure to the puncture site until the bleeding stops reduces bruising. Warm packs to the puncture site relieve discomfort.

Normal results

Negative or absent.

Abnormal results

If the person has cryoglobulin, the amount is reported. Larger amounts of cryoglobulin are associated with cancers or abnormalities involving white blood cells, moderate amounts are associated with autoimmune disorders and rheumatoid diseases, and smaller amounts are associated with infections.

The type of cryoglobulin is also reported. Type I cryoglobulin, also called monoclonal cryoglobulinemia, is found in cancers or abnormalities of white blood cells. Type II, also called mixed cryoglobulinemia, is associated with autoimmune disorders, rheumatoid diseases, and infections, particularly chronic **hepatitis B**.

The physician must interpret the cryoglobulin result along with other test results and the patient's clinical condition and medical history.

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Nancy J. Nordenson

Cryosurgery *see* **Cryotherapy**

Cryotherapy

Definition

Cryotherapy is a technique that uses an extremely cold liquid or instrument to freeze and destroy abnormal skin cells that require removal. The technique has been in use since the turn of the century, but modern techniques have made it widely available to dermatologists and primary care doctors. The technique is also called cryosurgery.

Purpose

Cryotherapy can be employed to destroy a variety of benign skin growths, such as **warts**, pre-cancerous lesions (such as actinic keratoses), and malignant lesions (such as basal cell and squamous cell cancers). The goal of cryotherapy is to freeze and destroy targeted skin growths while preserving the surrounding skin from injury.

Precautions

Cryotherapy is not recommended for certain areas of the body because of the danger of destruction of tissue or unacceptable scarring. These areas include: skin that overlies nerves, the corners of the eyes, the fold of skin between the nose and lip, the skin surrounding the nostrils, and the border between the lips and the rest of the face. Lesions that are suspected or known to be **malignant melanoma** should not be treated with cryotherapy, but should instead be removed surgically. Similarly, basal cell or squamous cell carcinomas that have reappeared at the site of a previously treated tumor should also be removed surgically. If it remains unclear whether a growth is benign or malignant, a sample of tissue should be removed for analysis (biopsy) by a pathologist before any attempts to destroy the lesion with cryotherapy. Care should be taken in people with diabetes or certain circulation problems when cryotherapy is considered for growths located on their lower legs, ankles, and feet. In these patients, healing can be poor and the risk of infection can be higher than for other patients.

Description

There are three main techniques to performing cryotherapy. In the simplest technique, usually reserved for warts and other benign skin growths, the physician

will dip a cotton swab or other applicator into a cup containing a "cryogen," such as liquid nitrogen, and apply it directly to the skin growth to freeze it. At a temperature of -320°F (-196°C), liquid nitrogen is the coldest cryogen available. The goal is to freeze the skin growth as quickly as possible, and then let it thaw slowly to cause maximum destruction of the skin cells. A second application may be necessary depending on the size of the growth. In another cryotherapy technique, a device is used to direct a small spray of liquid nitrogen or other cryogen directly onto the skin growth. Freezing may last from five to 20 seconds, depending on the size of the lesion. A second freeze-thaw cycle may be required. Sometimes, the physician will insert a small needle connected to a thermometer into the lesion to make certain the lesion is cooled to a low enough temperature to guarantee maximum destruction. In a third option, liquid nitrogen or another cryogen is circulated through a probe to cool it to low temperatures. The probe is then brought into direct contact with the skin lesion to freeze it. The freeze time can take two to three times longer than with the spray technique.

KEY TERMS

Actinic keratosis—A crusty, scaly pre-cancerous skin lesion caused by damage from the sun. Frequently treated with cryotherapy.

Basal cell cancer—The most common form of skin cancer; it usually appears as one or several nodules having a central depression. It rarely spreads (metasticizes), but is locally invasive.

Cryogen—A substance with a very low boiling point, such as liquid nitrogen, used in cryotherapy treatment.

Melanoma—The most dangerous form of skin cancer. It should not be treated with cryotherapy, but should be removed surgically instead.

Squamous cell cancer—A form of skin cancer that usually originates in sun-damaged areas or pre-existing lesions; at first local and superficial, it may later spread to other areas of the body.

Preparation

Extensive preparation prior to cryotherapy is not required. The area to be treated should be clean and dry, but sterile preparation is not necessary. Patients should know that they will experience some **pain** at the time of the freezing, but local anesthesia is usually not required. The physician may want to reduce the size of certain growths, such as warts, prior to the cryotherapy procedure, and may have patients apply salicylic acid preparations to the growth over several weeks. Sometimes, the physician will pare away some of the tissue using a device called a curette or a scalpel.

Aftercare

Redness, swelling, and the formation of a blister at the site of cryotherapy are all expected results of the treatment. A gauze dressing is applied and patients should wash the site three or four times daily while fluid continues to ooze from the wound, usually for five to 14 days. A dry crust then forms that falls off by itself. **Wounds** on the head and neck may take four to six weeks to heal, but those on the body, arms, and legs can take longer. Some patients experience pain at the site following the treatment. This can usually be eased with **acetaminophen** (Tylenol), though in some cases a stronger pain reliever may be required.

Risks

Cryotherapy poses little risk and can be well-tolerated by elderly and other patients who are not good candidates for other surgical procedures. As with other surgical procedures, there is some risk of scarring, infection, and damage to underlying skin and tissue. These risks are generally minimal in the hands of experienced users of cryotherapy.

Normal results

Some redness, swelling, blistering and oozing of fluid are all common results of cryotherapy. Healing time can vary by the site treated and the cryotherapy technique used. When cryogen is applied directly to the growth, healing may occur in three weeks. Growths treated on the head and neck with the spray technique may take four to six weeks to heal; growths treated on other areas of the body may take considerably longer. Cryotherapy boasts high success rates in permanently removing skin growths; even for malignant lesions such as squamous cell and basal cell cancers, studies have shown a cure rate of up to 98%. For certain types of growths, such as some forms of warts, repeat treatments over several weeks are necessary to prevent the growth's return.

Abnormal results

Although cryotherapy is a relatively low risk procedure, some side effects may occur as a result of the treatment. They include:

- Infection. Though uncommon, infection is more likely on the lower legs where healing can take several months.

- Pigmentary changes. Both hypopigmentation (lightening of the skin) and **hyperpigmentation** (darkening of the skin) are possible after cryotherapy. Both generally last a few months, but can be longer lasting.
- Nerve damage. Though rare, damage to nerves is possible, particularly in areas where they lie closer to the surface of the skin, such as the fingers, the wrist, and the area behind the ear. Reports suggest this will disappear within several months.

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ORGANIZATIONS

American Academy of Dermatology. 930 N. Meacham Road, P.O. Box 4014, Schaumburg, IL 60168-4014. (847) 330-0230. <http://www.aad.org>.

American Society for Dermatologic Surgery. 930 N. Meacham Road, P.O. Box 4014, Schaumburg, IL 60168-4014. (847) 330-9830. <http://www.asds-net.org>.

Richard H. Camer

Cryptococcosis

Definition

Cryptococcosis is an infection caused by inhaling the fungus *Cryptococcus neoformans*. It is one of the diseases most often affecting **AIDS** patients. Cryptococcosis may be limited to the lungs, but frequently spreads throughout the body. Although almost any organ can be infected, the fungus is often fatal if it infects the nervous system where it causes an inflammation of the membranes covering the brain and spinal cord (**meningitis**).

Description

The fungus causing cryptococcus, *C. neoformans*, is found worldwide in soil contaminated with pigeon or other bird droppings. It has also been found on unwashed raw fruit. Cryptococcosis is a rare disease in healthy individuals, but is the most common fungal infection affecting people with AIDS.

People with **Hodgkin's disease** or who are taking large doses of drugs that suppress the functioning of the immune system (**corticosteroids**, **chemotherapy** drugs) are also more susceptible to cryptococcal infection. Cryptococcosis is also called cryptococcal meningitis (when the brain is infected), Busse-Buschke disease, European **blastomycosis**, torular meningitis, or torulosis.

Causes and symptoms

Once the cryptococcal fungus reaches the lungs, three things can happen. The immune system can heal the body without medical intervention, the disease can stay localized in the lungs, or it can spread throughout the body. In healthy people with normally functioning immune systems, the body usually heals itself, and the infected person notices no symptoms and has no complications (asymptomatic). The disease does not spread from one person to another.

Cryptococcosis is an opportunistic infection that puts people with immune system diseases at higher risk of developing more serious forms of the disease. In the United States, 6–10% of all patients with AIDS get cryptococcosis.

If the body does not heal itself, the fungus begins to grow in the lungs and form nodules that can be seen on chest x rays. In the early stages of infection, an individual usually only exhibits symptoms of a respiratory infection, such as a dry **cough**, so the disease is rarely diagnosed.

The fungus can remain dormant in the lungs and produce an active infection later if the immune system is weakened. If the disease becomes active, it can cause cryptococcal **pneumonia** in the lungs. Unfortunately, however, cryptococcal pneumonia has symptoms similar to other pneumonias (cough, chest **pain**, difficulty breathing), making it difficult to accurately diagnose. The infection can spread to other parts of the body, particularly the brain and central nervous system.

Most patients are not diagnosed as having cryptococcosis until they show signs of cryptococcal meningitis, or infection of the membranes surrounding the brain and spinal cord. Symptoms appear gradually over a period of two to four weeks. **Fever** and **headache** are the most common symptoms, occurring in about 85% of patients. Nausea, vomiting, unwanted weight loss, and **fatigue** are also common. Other symptoms seen in 25–30% of patients are blurred vision, stiff neck, aversion to light, and seizures. Since the symptoms of classic

meningitis, such as stiff neck and aversion to light, do not occur in many patients, diagnosis is often delayed. In addition to meningitis, inflammation of the brain (**encephalitis**) and brain lesions called cryptococcomas or tortulomas can also develop.

In addition to the brain, the cryptococcal infection can spread to the kidneys, bone marrow, heart, adrenal glands, lymph nodes, urinary tract, blood, and skin. Often times preceding the development of cryptococcal meningitis, painless **rashes** and lesions that mimic other skin diseases, such as *molluscum contagiosum*, may develop. A small percentage of patients with brain infections show infections in other organs as well.

Diagnosis

Physicians who regularly work with AIDS patients have the most experience in diagnosing cryptococcosis. The preferred methods of diagnosis use simple and very accurate blood and cerebrospinal fluid (CSF) tests that detect the presence of an antigen produced by the fungus. The cerebrospinal fluid test is generally more sensitive to detecting the meningitis form of the infection. CSF is collected during a procedure called a lumbar puncture, during which an anesthetic is applied to a small area of the back near the spine and a needle is used to withdraw a sample of cerebrospinal fluid from the space between the vertebrae and the spinal cord. Once obtained, a small amount of ink (called India ink) is added to a sample of CSF or a sample prepared from **skin lesions**. If the fungus is present, it will become visible when the ink binds to the capsule or covering that surrounds the fungus. Faster results are obtained with the India ink test, but it is less accurate than the blood test (75–85% accuracy compared to 99% accuracy with the blood test) because some strains are not visible using this method. Antigen tests are routinely recommended for non-symptomatic patients with advanced AIDS.

Another way to diagnose cryptococcosis is to culture a sample of sputum, tissue from a **lung biopsy**, or CSF in the laboratory to isolate the fungus. Cultures are also done to assess the effectiveness of treatment.

Chest x rays are useful in assessing lung damage and may reveal a single mass or multiple distinct nodules, but the x ray alone does not lead to a definitive diagnosis of cryptococcosis.

Treatment

Once cryptococcosis is diagnosed, treatment begins with amphotericin B (Fungizone), sometimes in combination with 5-flucytosine (Ancobon). Amphotericin B is a powerful fungistatic drug with potentially toxic side effects, such as kidney toxicity and lower concentrations of an important blood component called hemoglobin. This medication can also cause fever, chills, **nausea and vomiting**, **diarrhea**, headache, and muscle aches. Treatment is generally given intravenously during a hospital stay and continues until the patient is stable or improving (no more than two to three weeks). 5-flucytosine is given orally. Patients may also receive other medication to minimize the side effects from these drugs.

This lesion appearing on this person's body is due to exposure of the *C. neoformans* fungus. *(Photo Researchers, Inc. Reproduced by permission.)*

Amphotericin B, with or without 5-flucytosine, is given for several weeks until the patient is stable, after which the patient receives oral fluconazole (Diflucan). Fluconazole is a broad-spectrum antifungal drug with few serious side effects. Patient with AIDS must continue taking fluconazole for the rest of their lives to prevent a relapse of cryptococcosis. Sometimes fluconazole is given to patients with advanced AIDS as a preventative (prophylactic) measure.

Because of the high cost of fluconazole, the manufacturer of the drug, Pfizer, has established a financial assistance plan to make the drug available at lower cost to those who meet certain criteria. Patients needing this drug should ask their doctors about this program.

Prognosis

Untreated cryptococcosis is always fatal. The acute mortality rate for patients with AIDS is 10–25%. Most deaths are attributable to cryptococcal meningitis and occur within two weeks after diagnosis. For AIDS patients who do not receive continued suppressive therapy (fluconazole), the relapse rate is 50–60% within six months and a shortened life expectancy. Once the cryptococcosis infection has been successfully treated, individuals may be left with a variety of neurologic symptoms,

KEY TERMS

Adrenal gland—A pair of organs located above the kidneys. The outer tissue of the gland produces the hormones epinephrine (adrenaline) and norepinephrine, while the inner tissue produces several steroid hormones.

Amphotericin B (Fengizone)—An antifungal medication, prescribed for topical or systemic use in treating fungal infections.

Antibody—A specific protein produced by the immune system in response to a specific foreign protein or particle called an antigen.

Antigen—A foreign protein or particle capable of eliciting an immune response.

Asymptomatic—Persons who carry a disease but who do not exhibit symptoms of the disease are said to be asymptomatic.

Biopsy—The removal of a tissue sample for diagnostic purposes.

Cerebrospinal fluid (CSF)—The clear fluid that surrounds the spinal cord and brain and acts as a shock absorber.

Corticosteroids—A group of hormones produced naturally by the adrenal gland or manufactured synthetically. They are often used to treat inflammation. Examples include cortisone and prednisone.

Encephalitis—Inflammation of the brain.

Hodgkin's disease—A disease that causes chronic inflammation of the lymph nodes, spleen, liver and kidneys. It is also called malignant lymphoma.

Hydrocephalus—Build-up of fluid around the brain.

Immunocompromised—A state in which the immune system is suppressed or not functioning properly.

India ink test—A diagnostic test used to detect the cyptococcal organism *C. neoformans*. A dye, called India ink, is added to a sample of CSF fluid, and if the fungi is present, they will become visible as the dye binds to the capsule surrounding the fungus.

Lumbar puncture—Also called a spinal tap, a procedure in which a thin needle is used to withdraw a sample of cerebrospinal fluid for diagnostic purposes from the area surrounding the spine.

Meningitis—Inflammation of the membranes covering the brain and spinal cord called the meninges.

Molluscum contagiosum—A disease of the skin and mucuous membranes, caused by a poxvirus and found all over the world.

Opportunistic infection—An infection that is normally mild in a healthy individual, but which takes advantage of an ill person's weakened immune system to move into the body, grow, spread, and cause serious illness.

Pneumonia—Inflammation of the lungs, typically caused by a virus, bacteria, or other organism.

such as weakness, headache, and hearing or visual loss. In addition, fluid may accumulate around the brain (**hydrocephalus**).

Prevention

The best way to prevent cryptococcosis is to stay free of HIV infection. People with suppressed immune systems should try to stay away from areas contaminated with pigeon or other bird droppings, such as the attics of old buildings, barns, and areas under bridges where pigeons roost.

Resources

ORGANIZATIONS

Centers for Disease Control and Prevention. 1600 Clifton Rd., NE, Atlanta, GA 30333. (800) 311-3435, (404) 639-3311. <http://www.cdc.gov>.

National Aids Clearinghouse. 800-458-5231.

National Aids Hotline. 800-342-AIDS.

Project Inform. 205 13th Street, #2001, San Francisco, CA 94103. (800) 822-7422. <http://www.projinf.org>.

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Tish Davidson

Cryptococcus neoformans infection *see* **Cryptococcosis**

Cryptorchidism *see* **Undescended testes**

Cryptosporidiosis

Definition

Cryptosporidiosis refers to infection by the spore-forming protozoan known as *Cryptosporidia*. Protozoa are a group of parasites that infect the human intestine, and include the better known *Giardia*. *Cryptosporidia* was first identified in 1976 as a cause of disease in humans.

Description

Cryptosporidia are normally passed in the feces of infected persons and animals in the form of cysts. The cysts can remain in the ground and water for months, and when ingested produce symptoms after maturing in the intestine and the bile ducts. When viewed under the microscope, they appear as small bluish-staining round bodies. Most common sources of infection are other humans, water supplies, or reservoirs. These are contaminated by animals that defecate in these areas. An outbreak in Milwaukee in 1993 in which over 400,000 persons were affected was traced to the city's water supply. Cysts of *Cryptosporidia* are extremely resistant to the disinfectants that are commonly used in most water treatment plants and are incompletely removed by filtration.

Most persons who experience significant symptoms have an altered immune system, and suffer from diseases such as **AIDS** and **cancer**. However, as shown in the Milwaukee outbreak, even those with normal immunity can experience symptoms.

Causes and symptoms

Cysts of *Cryptosporidia* mature in the intestine and bile ducts within three to five days of ingestion. As noted, large-scale infections from contaminated water supplies has been documented. However, human to human transmission (such as occurs in day care centers or through sexual behavior) is also an important cause.

Many individuals can be infected without any illness, but the major symptom is **diarrhea**, which is often watery and incapacitating. **Dehydration**, low-grade **fever**, nausea, and abdominal cramps are frequent.

In those with a normal immune system, the disease usually lasts about 10 days. For patients with altered immunity (immunocompromised), the story is quite different, with diarrhea becoming chronic, debilitating, and even fatal.

Complications

Dehydration and **malnutrition** are the most common effects of infection. In about 20% of AIDS patients, bile duct infection also occurs and causes symptoms similar to gallbladder attacks. Eighty percent or more of those with infection of the bile ducts die from the disease. The lungs and pancreas are also sometimes involved. *Cryptosporidia* are just one cause of the diarrhea wasting syndrome in AIDS, which results in severe weight loss and malnutrition.

Diagnosis

This is based on either finding the characteristic cysts in stool specimens, or on biopsy of an infected organ, such as the intestine.

Treatment

The first aim of treatment is to avoid dehydration. Oral Rehydration Solution (ORS) or intravenous fluids may be needed. Medications used to treat diarrhea by decreasing intestinal motility (Anti-Motility Agents), such as loperamide or diphenoxylate, are also useful, but should only be used with the advice of a physician.

Treatment aimed directly at *Cryptosporidia* is only partially effective, and rarely eliminates the organism. The medication most commonly used is paromomycin (Humatin), but others are presently under evaluation.

Prognosis

Cryptosporidia rarely cause a serious disease in persons with normal immune systems. Replacement of fluids is all that is usually needed. On the other hand, those with altered immune systems often suffer for months to years. Paramomycin and other drugs have been able to improve symptoms in over half of those treated. Unfortunately, many organisms are resistant, and recurrence is frequent.

Prevention

The best way to prevent cryptosporidiosis is to minimize exposure to cysts from infected humans and animals. Proper hand washing technique, especially in day care centers, is recommended.

Resources

BOOKS

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KEY TERMS

Anti-motility medications—Medications such as loperamide (sold as Imodium), dephenoxylate (sold as Lomotil), or medications containing codeine or narcotics that decrease the ability of the intestine to contract. This can worsen the condition of a patient with dysentery or colitis.

Cyst—A protective sac that includes either fluid or the cell of an organism. The cyst enables many organisms to survive in the environment for long periods of time without need for food or water.

Immunocompromised—A change or alteration of the immune system that normally serves to fight off infections and other illnesses. This can involve changes in antibodies that the body produces (hygogammaglobulinemia), or defect in the cells that partake in the immune response. Diseases such as AIDS and cancer exhibit changes in the body's natural immunity.

Oral Rehydration Solution (ORS)—A liquid preparation developed by the World Health Organization that can decrease fluid loss in persons with diarrhea. Originally developed to be prepared with materials available in the home, commercial preparations have recently come into use.

Parasite—An organism that lives on or in another and takes nourishment (food and fluids) from that organism.

Protozoa—Group of extremely small single cell (unicellular) or acellular organisms that are found in moist soil or water. They tend to exist as parasites, living off other life forms.

Spore—A resistant form of certain species of bacteria, protozoa, and other organisms.

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C-section *see* **Cesarean section**

CSF analysis *see* **Cerebrospinal fluid (CSF) analysis**

CT-guided biopsy

Definition

Computed tomography (CT) is a process that images anatomic information from a cross-sectional plane of the body. Biopsy is the process of taking a sample of tissue from the body for analysis. CT is commonly used in biopsies to provide images that help guide the tools or equipment necessary to perform the biopsy to the appropriate area of the body.

Purpose

CT is used in the process of performing a biopsy, such as a needle biopsy, in order to guide the needle to the site of the biopsy and to provide rapid and precise localization of the needle. CT enables imaging of areas that are normally beyond visible boundaries. This enables the physician to see the target area clearly and help to ensure that the tissue being removed is from the target lesion.

Precautions

The patient that suffers from claustrophobia will want to discuss this with their physician. This procedure

KEY TERMS

Lesion—A pathologic change in tissues.

Malignancy—A locally invasive and destructive growth.

involves the patient being placed into the CT scanner, typically a small, enclosed area. Depending on the specific type of biopsies being performed, certain anesthetics will be used, so discuss drug **allergies** with your physician.

Description

CT can assist in providing more enhanced images of a suspicious lesion. It helps to determine whether a tumor is truly solitary or not. CT can characterize the tumor and aid in the estimation of malignancy.

Preparation

Since there are many different types of biopsies, you should follow the instructions from your physician to prepare for your CT-guided biopsy. Patients who suffer from claustrophobia should discuss their concerns with the physician. In some cases, medicine can be given that will relax the patient during the procedure.

Risks

CT-guided biopsy does not increase the risk of the biopsy any more than any other radiologic imaging such as x ray.

Normal results

Because the area being biopsied, as well as the specific type of biopsy procedure can vary, results will vary. Before undergoing the procedure, notification procedure should be clearly defined.

Resources

BOOKS

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CT-myelogram *see* **Myelography**

CT scan *see* **Computed tomography scans**

Culture-fair test

Definition

A culture-fair test is a test designed to be free of cultural bias, as far as possible, so that no one culture has an advantage over another. The test is designed to not be influenced by verbal ability, cultural climate, or educational level.

Purpose

The purpose of a culture-fair test is to eliminate any social or cultural advantages, or disadvantages, that a person may have due to their upbringing. The test can be administered to anyone, from any nation, speaking any language. A culture-fair test may help identify learning or emotional problems. The duration of the test varies for the individual types of tests available, but the time is approximately between 12–18 minutes per section (a test usually has two to four sections).

A culture-fair test is often administered by employers in order to determine the best location for new employees in a large company. The wide variety of culture-fair tests availiable allows the administrator to select which area is most vital, whether it be general intelligence, knowledge of a specific area, or emotional stability.

Precautions

There is doubt as to whether any test can truly be culturally unbiased or can ever be made completely fair to all persons independent of culture. There are no other precautions.

Description

A culture-fair test is a non-verbal paper-pencil test that can be administered to patients as young as four

years old. The patient only needs the ability to recognize shapes and figures and perceive their respective relationships. Some examples of tasks in the test may include:

- completing series
- classifying
- solving matrices
- evaluating conditions

The culture-fair test is also often referred to as a culture-free test or unbiased test. There are many variations of the test including class, economic, and intelligence tests. The threading theme among the various tests is their design to be culturally unbiased.

Preparation

The only preparation necessary to administer the test is pre-ordered materials and a quiet and secluded location for the duration of the test.

Aftercare

Post-test treatment depends on the results of the test and the specifics of the individual patient. Any further treatment is best prescribed by the doctor.

Risks

There are no risks associated with the culture-fair test.

Normal results

The results can be compared to the key that comes with the purchase of a culture-fair test. All results should be compared to the included key.

Abnormal results

The results can be compared to the key that comes with the purchase of a culture-fair test. All results should be compared to the included key.

Resources

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Michael Sherwin Walston
Ronald Watson, PhD

Cultures for sexually transmitted diseases
see **Sexually transmitted diseases cultures**

Cushing's syndrome

Definition

Cushing's syndrome is a relatively rare endocrine (hormonal) disorder resulting from excessive exposure to the hormone cortisol. The disorder, which leads to a variety of symptoms and physical abnormalities, is most commonly caused by taking medications containing the hormone over a long period of time. A more rare form of the disorder occurs when the body itself produces an excessive amount of cortisol.

Description

The adrenals are two glands, each of which is perched on the upper part of the two kidneys. The outer part of the gland is known as the cortex; the inner part is known as the medulla. Each of these parts of the adrenal gland is responsible for producing different types of hormones. Regulation of hormone production and release from the adrenal cortex involves the pituitary gland, a small gland located at the base of the brain. After the hypothalamus (the part of the brain containing secretions important to metabolic activities) sends "releasing hormones" to the pituitary gland, the pituitary secretes a hormone called adrenocorticotropic hormone (ACTH). The ACTH then travels through the bloodstream to the adrenal cortex, where it encourages the production and release of cortisol (sometimes called the "stress" hormone) and other adrenocortical hormones.

Cortisol, a very potent glucocorticoid—a group of adrenocortical hormones that protects the body from **stress** and affect protein and carbohydrate metabolism—is involved in regulating the functioning of nearly every type of organ and tissue in the body, and is considered to be one of the few hormones absolutely necessary for life. Cortisol is involved in:

- complex processing and utilization of many nutrients, including sugars (carbohydrates), fats, and proteins
- normal functioning of the circulatory system and the heart
- functioning of muscles
- normal kidney function
- production of blood cells
- normal processes involved in maintaining the skeletal system
- proper functioning of the brain and nerves
- normal responses of the immune system

Cushing's syndrome, also called hypercortisolism, has an adverse effect on all of the processes described

above. The syndrome occurs in approximately 10 to 15 out of every one million people per year, usually striking adults between the ages of 20 and 50.

Causes and symptoms

The most common cause of Cushing's syndrome is the long-term use of glucocorticoid hormones in medications. Medications such as prednisone are used in a number of inflammatory conditions. Such conditions include **rheumatoid arthritis**, **asthma**, **vasculitis**, lupus, and a variety of other **autoimmune disorders** in which the body's immune cells accidentally attack some part of the body itself. In these disorders, the glucocorticoids are used to dampen the immune response, thereby decreasing damage to the body.

Cushing's syndrome can also be caused by three different categories of disease:

- a pituitary tumor producing abnormally large quantities of ACTH
- the abnormal production of ACTH by some source other than the pituitary
- a tumor within the adrenal gland overproducing cortisol

Although it is rare, about two-thirds of endogenous (occurring within the body rather than from a source outside the body, like a medication) Cushing's syndrome is a result of Cushing's disease. The term "Cushing's disease" refers to Cushing's syndrome, which is caused by excessive secretion of ACTH by a pituitary tumor, usually an adenoma (noncancerous tumor). The pituitary tumor causes increased growth of the adrenal cortex (hyperplasia) and increased cortisol production. Cushing's disease affects women more often than men.

Tumors in locations other than the pituitary can also produce ACTH. This is called ectopic ACTH syndrome ("ectopic" refers to something existing out of its normal place). Tumors in the lung account for more than half of all cases of ectopic ACTH syndrome. Other types of tumors that may produce ACTH include tumors of the thymus, the pancreas, the thyroid, and the adrenal gland. Nearly all adrenal gland tumors are benign (noncancerous), although in rare instances a tumor may actually be cancerous.

Symptoms of cortisol excess (resulting from medication or from the body's excess production of the hormone) include:

- weight gain
- an abnormal accumulation of fatty pads in the face (creating the distinctive "moon face" of Cushing's syndrome); in the trunk (termed "truncal obesity"); and over the upper back and the back of the neck (giving the individual what has been called a "buffalo hump")
- purple and pink stretch marks across the abdomen and flanks
- high blood pressure
- weak, thinning bones (osteoporosis)
- weak muscles
- low energy
- thin, fragile skin, with a tendency toward both bruising and slow healing
- abnormalities in the processing of sugars (glucose), with occasional development of actual diabetes
- kidney stones
- increased risk of infections
- emotional disturbances, including mood swings, depression, irritability, confusion, or even a complete break with reality (psychosis)

Woman with Cushing's syndrome. *(Photo Researchers, Inc. Reproduced by permission.)*

KEY TERMS

Adenoma—A type of noncancerous (benign) tumor that often involves the overgrowth of certain cells of the type normally found within glands.

Adrenocorticotropic hormone (ACTH)—A pituitary hormone that stimulates the cortex of the adrenal glands to produce adrenal cortical hormones.

Cortisol—A hormone secreted by the cortex of the adrenal gland. Cortisol regulates the function of nearly every organ and tissue in the body.

Ectopic—In an abnormal position.

Endocrine—Pertaining to a gland that secretes directly into the bloodstream.

Gland—A collection of cells whose function is to release certain chemicals (hormones) that are important to the functioning of other, sometimes distantly located, organs or body systems.

Glucocorticoids—General class of adrenal cortical hormones that are mainly active in protecting against stress and in protein and carbohydrate metabolism.

Hormone—A chemical produced in one part of the body that travels to another part of the body in order to exert its effect.

Hypothalamus—the part of the brain containing secretions important to metabolic activities.

Pituitary—A gland located at the base of the brain, the pituitary produces a number of hormones, including hormones that regulate growth and reproductive function.

- irregular menstrual periods in women
- decreased sex drive in men and difficulty maintaining an erection
- abormal hair growth in women (in a male pattern, such as in the beard and mustache area), as well as loss of hair from the head (receding hair line)

Diagnosis

Diagnosing Cushing's syndrome can be complex. Diagnosis must not only identify the cortisol excess, but also locate its source. Many of the symptoms listed above can be attributed to numerous other diseases. Although a number of these symptoms seen together would certainly suggest Cushing's syndrome, the symptoms are still not specific to Cushing's syndrome. Following a review of the patient's medical history, **physical examination**, and routine blood tests, a series of more sophisticated tests is available to achieve a diagnosis.

24-hour free cortisol test

This is the most specific diagnostic test for identifying Cushing's syndrome. It involves measuring the amount of cortisol present in the urine over a 24-hour period. When excess cortisol is present in the bloodstream, it is processed by the kidneys and removed as waste in the urine. This 24-hour free cortisol test requires that an individual collect exactly 24-hours' worth of urine in a single container. The urine is then analyzed in a laboratory to determine the quantity of cortisol present. This technique can also be paired with the administration of dexamethasone, which in a normal individual would cause urine cortisol to be very low. Once a diagnosis has been made using the 24-hour free cortisol test, other tests are used to find the exact location of the abnormality causing excess cortisol production.

Dexamethasone suppression test

This test is useful in distinguishing individuals with excess ACTH production due to a pituitary adenoma from those with ectopic ACTH-producing tumors. Patients are given dexamethasone (a synthetic glucocorticoid) orally every six hours for four days. Low doses of dexamethasone are given during the first two days; for the last two days, higher doses are administered. Before dexamethasone is administered, as well as on each day of the test, 24-hour urine collections are obtained.

Because cortisol and other glucocorticoids signal the pituitary to decrease ACTH, the normal response after taking dexamethasone is a drop in blood and urine cortisol levels. Thus, the cortisol response to dexamethasone differs depending on whether the cause of Cushing's syndrome is a pituitary adenoma or an ectopic ACTH-producing tumor.

However, the dexamethasone suppression test may produce false-positive results in patients with conditions such as depression, alcohol abuse, high estrogen levels, acute illness, and stress. On the other hand, drugs such as phenytoin and phenobarbital may produce false-negative results. Thus, patients are usually advised to stop taking these drugs at least one week prior to the test.

Corticotropin-releasing hormone (CRH) stimulation test

The CRH stimulation test is given to help distinguish between patients with pituitary adenomas and

those with either ectopic ACTH syndrome or cortisol-secreting adrenal tumors. In this test, patients are given an injection of CRH, the corticotropin-releasing hormone that causes the pituitary to secrete ACTH. In patients with pituitary adenomas, blood levels of ACTH and cortisol usually rise. However, in patients with ectopic ACTH syndrome, this rise is rarely seen. In patients with cortisol-secreting adrenal tumors, this rise almost never occurs.

Petrosal sinus sampling

Although this test is not always necessary, it may be used to distinguish between a pituitary adenoma and an ectopic source of ACTH. Petrosal sinus sampling involves drawing blood directly from veins that drain the pituitary. This test, which is usually performed with local anesthesia and mild **sedation**, requires inserting tiny, flexible tubes (catheters) through a vein in the upper thigh or groin area. The catheters are then threaded up slowly until they reach veins in an area of the skull known as the petrosal sinuses. X rays are typically used to confirm the correct position of the catheters. Often CRH is also given during the test to increase the accuracy of results.

When blood tested from the petrosal sinuses reveals a higher ACTH level than blood drawn from a vein in the forearm, the likely diagnosis is a pituitary adenoma. When the two samples show similar levels of ACTH, the diagnosis indicates ectopic ACTH syndrome.

Radiologic imaging tests

Imaging tests such as **computed tomography scans** (CT) and **magnetic resonance imaging** (MRI) are only used to look at the pituitary and adrenal glands after a firm diagnosis has already been made. The presence of a pituitary or adrenal tumor does not necessarily guarantee that it is the source of increased ACTH production. Many healthy people with no symptoms or disease whatsoever have noncancerous tumors in the pituitary and adrenal glands. Thus, CT and MRI is often used to image the pituitary and adrenal glands in preparation for surgery.

Treatment

The choice of a specific treatment depends on the type of problem causing the cortisol excess. Pituitary and adrenal adenomas are usually removed surgically. Malignant adrenal tumors always require surgical removal.

Treatment of ectopic ACTH syndrome also involves removing all of the cancerous cells that are producing ACTH. This may be done through surgery, **chemotherapy** (using combinations of cancer-killing drugs), or **radiation therapy** (using x rays to kill **cancer** cells), depending on the type of cancer and how far it has spread. Radiation therapy may also be used on the pituitary (with or without surgery) for patients who cannot undergo surgery, or for patients whose surgery did not successfully decrease pituitary release of ACTH.

There are a number of drugs that are effective in decreasing adrenal production of cortisol. These medications include mitotane, ketoconazole, metyrapone, trilostane, aminoglutethimide, and **mifepristone**. These drugs are sometimes given prior to surgery in an effort to reverse the problems brought on by cortisol excess. However, the drugs may also need to be administered after surgery (sometimes along with radiation treatments) in patients who continue to have excess pituitary production of ACTH.

Because pituitary surgery can cause ACTH levels to drop too low, some patients require short-term treatment with a cortisol-like medication after surgery. Patients who need adrenal surgery may also require glucocorticoid replacement. If the entire adrenal gland has been removed, the patient must take oral glucocorticoids for the rest of his or her life.

Prognosis

Prognosis depends on the source of the problem. When pituitary adenomas are identified as the source of increased ACTH leading to cortisol excess, about 80% of patients are cured by surgery. When cortisol excess is due to some other form of cancer, the prognosis depends on the type of cancer and the extent of its spread.

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ORGANIZATION

Cushing's Support and Research Foundation, Inc. 65 East India Row, Suite 22B, Boston, MA 02110. (617) 723-3674. <http://www.world.std.com>.
National Adrenal Disease Foundation. 505 Northern Boulevard, Suite 200, Great Neck, NY 11021. (516) 487-4992. <http://www.medhelp.org>.
National Institute of Neurological Disorders and Stroke (NINDS). National Institutes of Health, Bethesda, MD 20892-2560. <http://www.ninds.nih.gov>.
Pituitary Network Association. 16350 Ventura Boulevard, #231, Encino, CA 91436. (805)499-9973. <http://www.pituitary.org>.

Rosalyn Carson-DeWitt

Cutaneous larva migrans

Definition

Cutaneous larvae migrans is a parasitic skin disease caused by a hookworm larvae that usually infests dogs, cats, and other animals. Humans can pick up the infection by walking barefoot on soil or beaches contaminated with animal feces.

Description

Cutaneous larvae migrans (also called "creeping eruption" or "ground itch") is found in southeastern and Gulf states, and in tropical developing countries.

The hookworms that cause the condition are small, round blood-sucking worms that infest about 700 million people around the world. Cutaneous larvae migrans occurs most often among children, those who crawl beneath raised buildings, and sunbathers who lie down on wet sand contaminated with hookworm larvae.

Causes and symptoms

After an animal passes feces that are infested with hookworm eggs, the eggs hatch into infective larvae that are able to penetrate human skin (even through solid material, such as a beach towel). The larvae are commonly found in shaded, moist, or sandy areas (such as beaches, a child's sandbox, or areas underneath a house), where they are easily picked up by bare feet or buttocks.

Linear red rashes around a patient's knee caused by burrowing larvae of the dog hookworm *Ancylostoma braziliensis.* *(Photograph by Dr. P. Marazzi, Custom Medical Stock Photo. Reproduced by permission.)*

In minor infestations, there may be no symptoms at all. In more severe cases, a red elevation of the skin (papule) appears within a few hours after the larvae have penetrated the skin. This usually arises first in areas that are in contact with the soil, such as the feet, hands, and buttocks.

Between a few days and a few months after infection, the larvae begin to migrate beneath the skin, leaving extremely itchy red lines that may be accompanied by blisters. These red lines usually appear at the top of the sole of the foot or on the buttocks.

Tyically, the larvae travel through the bloodstream, to the lungs, and then migrate into the mouth where they are swallowed and attach to the small intestine lining. There they mature into adult worms. In cases where the larvae migrate through the lungs, they can produce anemia, **cough**, and **pneumonia**, in addition to the itchy rash.

Diagnosis

The condition can be diagnosed by microscopic inspection of feces which can reveal hookworm eggs. In addition visual inspection of the skin would reveal telltale itchy red lines and blisters.

Treatment

People without intestinal symptoms do not need treatment, since the worms will eventually die or be

KEY TERMS

Larvae—Immature forms of certain worms.

excreted. Thiabendazole or albendazole are used to treat the infestation. Mild infections can be treated by applying one of the drugs to the skin along the tracks and the normal skin surrounding the area. Thiabendazole also can be given internally, but taken this way it can cause side effects including **dizziness**, nausea, and vomiting

Prognosis

No matter how severe an infestation, with adequate treatment patients recover completely. However, if the patient scratches the lesions open, the areas can become vulnerable to bacterial infection.

Prevention

In the United States, the prevalence of dogs and cats with hookworms is the reason why the infective larvae are found so commonly in soil and sand. The play habits of children, together with their attraction to pets, puts them at high risk for hookworm infection and cutaneous larvae migrans.

Human hookworm infestation can be prevented by practicing good personal hygiene, deworming pets, and not allowing children to play in potentially contaminated environments.

Resources

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Carol A. Turkington

Cutaneous T-cell lymphoma

Definition

Cutaneous T-cell lymphoma (CTCL) is a malignancy of the T-helper (CD4+) cells of the immune system.

Description

CTCL, also known as mycosis fungoides, is a **cancer** of the white blood cells that primarily affects the skin and only secondarily affects other sites. This disease involves the uncontrollable proliferation of T-lymphocytes known as T-helper cells, so named because of their role in the immune response. T-helper cells are characterized by the presence of a protein receptor on its surface called CD4. Accordingly, T-helper cells are said to be CD4+.

The proliferation of T-helper cells results in the penetration, or infiltration, of these abnormal cells into the epidermal layer of the skin. The skin reacts with slightly scaling lesions that itch, although the sites of greatest infiltration do not necessarily correspond to the sites of the lesions. The lesions are most often located on the trunk, but can be present on any part of the body. In the most common course of the disease, the patchy lesions progress to palpable plaques that are deeper red and have more defined edges. As the disease worsens, skin tumors develop that are often mushroom-shaped, hence the name mycosis fungoides. Finally, the cancer progresses to extracutanous involvement, often in the lymph nodes or the viscera.

CTCL is a rare disease, with an annual incidence of about 0.29 cases per 100,000 persons in the United States. It is about half as common in Eastern Europe. However, this discrepancy may be attributed to a differing physician awareness of the disease rather than a true difference in occurrence. In the Unites States, there are about 500 to 600 new cases a year and about 100 to 200 deaths. Usually seen in older adults, the median age at diagnosis is 55 to 60 years, and it strikes twice as many men as women.

Causes and symptoms

The cause of CTCL is unknown. Exposure to chemicals or pesticides has been suggested but the most recent study on the subject failed to show a connection between exposure and development of the disease. The ability to isolate various viruses from cell lines grown from cells of CTCL patients raises the question of a viral cause, but studies have been unable to confirm these suspicions.

The symptoms of CTCL are seen primarily in the skin, with itchy red patches or plaques and, usually over time, mushroom-shaped skin tumors. Any part of the skin can be involved and the extent and distribution of the rash or tumors vary greatly from patient to patient. The only really universal symptom of the disease is the itch and this symptom is usually what brings the patient to the doctor for treatment. If the disease spreads outside of the skin, the symptoms include swelling of the lymph

nodes, usually most severe in those draining the areas with skin involvement. Spread to the viscera is most often manifested as disorders of the lungs, upper digestive tract, central nervous system, or liver but virtually any organ can be shown to be involved at **autopsy**.

Diagnosis

Diagnosis of CTCL is often difficult in the early stages because of its slow progression and ability to mimic many other benign skin conditions. The early patches of CTCL resemble eczema, **psoriasis**, and **contact dermatitis**. In a further complication, the early manifestations of the disease can respond favorably to the topical corticosteroid treatments prescribed for these skin disorders. This has the unfortunate result of the disease being missed and the patient remaining untreated for years. CTCL is most likely discovered when a physician maintains a suspicion about the disease, performs multiple skin biopsies, and provides close follow-up after the initial presentation.

Skin biopsies showing penetration of abnormal cells into the epidermal tissue are necessary to make a firm diagnosis of CTCL. Several molecular studies can also help support the diagnosis. The first looks at the cellular proteins seen on the surface of the abnormal cells. Many cases of CTCL show the retention of the CD4+ protein, but the loss of other proteins usually seen on the surface of mature CD4+ cells, such as Leu-8 or Leu-9. The abnormal cells also show unusual rearrangements at the genetic level for the gene that encodes the T-cell receptors. These rearrangements can be identified using Southern blot analysis. The information from the molecular tests, combined with the presence of abnormal cells in the epidermis, strongly supports the CTCL diagnosis.

Treatment

Treatment of CTCL depends on the stage of the disease. The current staging of this disease was first presented at the International Consensus Conference on CTCL in 1997. The staging attempts to show the complex interaction between the various outward symptoms of the disease and prognosis. The system has seven clinical stages based on skin involvement (tumor = T), lymph node involvement (LN), and presence of visceral metastases (M).

The first stage, IA, is characterized by plaques covering less than 10% of the body (T1) and no visceral involvement (M0). Lymph node condition at this stage can be uninvolved, reactive to the skin disease, or dermatopathic (biopsies showing CTCL involvement) but not enlarged (LN0-2). The shorthand expression of this stage is therefore T1, LN0-2, M0. The next stage, IB, differs from IA in that greater than 10% of the body is covered by plaques (T2, LN0-2, M0). Stage IIA occurs with any amount of plaques in addition to the ability to palpate the lymph node and the lymph uninvolved, reactive, or dermatopathic (T1-2, LN0-2, M0).

Treatments applied to the skin are preferred for patients having these preliminary stages of the disease, commonly topical **chemotherapy** with mechlorethamine hydrochloride (nitrogen mustard) or **phototherapy** of psoralen plus ultraviolet A (PUVA). Topical chemotherapy involves application to the skin of nitrogen mustard, an alkylating agent, in a concentration of 10–20 mg/dL in an aqueous or ointment base. Treatment of affected skin is suggested at a minimum and application over the entire skin surface is often recommended. Care needs to be taken that coverage of involved skin is adequate, as patients who self-apply the drug often cannot reach all affected areas. The most common side effect is skin hypersensitivity to the drug. Nearly all patients respond favorably to this treatment, with a 32–61% complete response rate, based on amount of skin involvement. Unfortunately, only 10–15% of patients maintain a complete response rate after discontinuing the treatment.

Phototherapy involves treatment with an orally administered drug, 8-methyloxypsoralen, that renders the skin sensitive to long-wave ultraviolet light (UVA), followed by controlled exposure to the radiation. During the initial treatment period, which may last as long as six months, patients are treated two to three times weekly. This is reduced to about once monthly after initial clearing of the lesions. Redness of the skin and blistering are the most common side effects of the treatment and are much more common in patients presenting with overall skin redness, or erythroderma, so lower intensities of light are usually used in this case. About 50% of all patients experience complete clearance with this treatment. Some patients with very fair skin and limited skin involvement can successfully treat themselves at home with special lamps and no psoralen.

The next stage, IIB, involves one or more cutaneous tumors, in combination with absent or present palpable lymph nodes, lymph uninvolved, reactive, or dermatopathic, and no visceral involvement (T3, LN0-2, M0). Stage III is characterized by erythroderma, an abnormal redness over widespread areas of the skin (T4, LN0-2, M0).

For more extensive disease, **radiation therapy** is an effective treatment option. It is generally used after the topical treatments have proven ineffective. Individual plaques or tumors can be treated using electrons, orthovoltage x rays, or megavoltage photons with exposure in the range of 15 to 25 Gy. Photon therapy has proven particularly useful once the lymph nodes are involved. Anoth-

er possibility is total-skin electron beam therapy (TSEB), although the availability of this treatment method is limited. It involves irradiation of the entire body with energized electrons. Side effects of this treatment include loss of finger and toe nails, acute redness of the skin, and inability to sweat for about six to 12 months after therapy. Almost all patients respond favorably to radiation treatment and any reoccurrence is usually much less severe.

Combinations of different types of treatments is a very common approach to the management of CTCL. Topical nitrogen mustard or PUVA is often used after completion of radiation treatment to prolong the effects. The addition of genetically engineered interferon to PUVA therapy significantly increases the percentage of patients showing a complete response. Furthermore, although treatments using chemotherapy drugs alone, such as deoxycofomycin or etretinate, have been disappointing for CTCL, combining these drugs with interferon has shown promising results. Interferon has also been combined with retinoid treatments, although the mechanism of action of retinoids (Vitamin A analogues) against CTCL is unknown.

The final two stages of the disease are IVA and IVB. IVA presents as any amount of skin involvement, absent or present palpable lymph nodes, no visceral involvement, and lymph that contains large clusters of convoluted cells or obliterated nodes (T1-4, LN3-4). IVB differs in the addition of palpable lymph nodes and visceral involvement (T1-4, LN3-4, M1). All of the treatment methods described above are appropriate for the final two stages of the disease.

Alternative treatment

Itching of the skin is one of the most troublesome symptoms of CTCL. One alternative treatment for itchiness is the application of a brewed solution of chickweed that is applied to the skin using cloth compresses. Another suggested topical application is a mixture of vitamin E, vitamin A, unflavored yogurt, honey, and zinc oxide. Evening primrose oil applied topically is also claimed to reduce itch and promote healing.

Prognosis

The prognosis for CTCL is dependent on the stage of the disease. Prognosis is very good if the disease has only progressed to Stage IA, with a mean survival of 20 or more years. At this point, the disease is a very low mortality risk to the patient, with most deaths occurring to persons in this group unrelated to CTCL. For patients diagnosed at stages IB and IIA, the median survival is about 12 years. The disease in both of these stages involves intermediate risk to the patient. Patients in stage III and IVA have a mean life expectancy of about five years. At these later stages, the disease is high risk, with most deaths occurring by infection due to the depleted immune system of the later-stage patient. Once a patient has reached stage IVB, the mean life expectancy is one year.

KEY TERMS

Alkylating agent—A chemical that alters the composition of the genetic material of rapidly dividing cells, such as cancer cells, causing selective cell death; used as a topical chemotherapeutic agent to treat CTCL.

Erythroderma—An abnormal reddening of the entire skin surface.

T-helper cells—A cellular component of the immune system that plays a major role in ridding the body of bacteria and viruses, characterized by the presence of the CD4 protein on its surface; the type of cell that divides uncontrollable with CTCL.

Total-skin electron beam therapy—A method of radiation therapy used to treat CTCL that involves bombarding the entire body surface with high-energy electrons.

Prevention

Studies have been unable to link CTCL to any environmental or genetic factors, so prevention at this time is not possible.

Resources

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ORGANIZATIONS

National Cancer Institute. Building 31 Room 10A31 31 Center Drive MSC 2580 Bethesda, MD 20892-2580. (800)422-6237. <http://cancernet.nci.nih.gov>.

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Cutis laxa

Definition

Cutis laxa (Latin for loose or lax skin) is a connective tissue disorder in which the skin lacks elasticity and hangs in loose folds.

Description

Cutis laxa is extremely rare; less than a few hundred cases worldwide have been described.

The several forms of cutis laxa are divided into primary cutis laxa, which is present from birth and is hereditary, secondary cutis laxa, which arises later in life and may be either hereditary, and acquired cutis laxa, which arises later in life and is not hereditary. Loose skin, the primary and most obvious symptom of these diseases, is caused by underlying defects in connective tissue structure, which also cause more serious internal problems in vocal cords, bones, cartilage, blood vessels, bladder, kidney, digestive system, and lungs. The loose skin is particularly obvious on the face, and children with the disorder look sad or mournful.

There are four genetic forms of the disease: sex-linked, autosomal dominant, and two types of autosomal recessive inheritance. The recessive forms are the most common and are usually more severe than the other forms.

Causes and Symptoms

Sex-linked cutis laxa is caused by a defective gene on the X chromosome. In addition to loose skin, its symptoms are mild **mental retardation**, loose joints, bone abnormalities (like hooked nose, pigeon breast, and funnel breast), frequent loose stools, urinary tract blockages, and deficiencies in lysyl oxidase, an enzyme required for the formation of properly functioning connective tissue. (But the defective gene does not code for lysyl oxidase.)

Autosomal dominant cutis laxa is caused by a defective gene carried on an autosomal (not sex-linked) chromosome. Its symptoms are loose, hanging skin, missing elastic fibers, premature **aging**, and pulmonary **emphysema**. Only a few families are known with cutis laxa inherited as a dominant trait.

Autosomal recessive cutis laxa type 1 is caused by a defective gene on chromosome 5. Symptoms include emphysema; diverticula in the esophagus, duodenum, and bladder; lax and dislocated joints; tortuous arteries; hernias; lysyl oxidase deficiencies; and retarded growth.

Autosomal recessive cutis laxa type 2 is also inherited as a recessive trait. In addition to the loose skin, this form of the disease is characterized by bone abnormalities, the delayed joining of the cranial (skull) bones, hip dislocation, curvature of the spine, flat feet, and excessive **tooth decay**.

Acquired cutis laxa tends to follow (and may be caused by) severe illness characterized by **fever**, inflammation, and a severe skin rash (**erythema multiforme**); an injury to the nerves that control blood vessel dilation and contraction; or an autoimmune condition.

Diagnosis

The signs of cutis laxa are very obvious, and it is usually easy to diagnose by examining the skin. The determination of which form of cutis laxa is present is aided by information about the associated symptoms and by family histories.

Treatment

There is no effective cure for any of these disorders. Complications are treated by appropriate specialists, for example, cardiologists, gastroenterologists, rheumatologists, and dermatologists. Plastic surgery can be helpful for cosmetic purposes, but the skin may become loose again.

Prognosis

The prognosis for cutis laxa varies with the form of the disorder. The effects may be relatively mild with individuals living a fairly normal, full life, or the disease may be fatal.

Prevention

The inherited forms of cutis laxa are genetically determined and are not currently preventable. **Genetic counseling** can be helpful for anyone with a family history of cutis laxa. The cause of acquired cutis laxa is not known, so no preventive measures can be taken.

Resources

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ORGANIZATIONS

British Coalition of Heritable Disorders of Connective Tissue. Rochester House, 5 Aldershot Road, Fleet, Hampshire GU13 9NG, United Kingdom. (012) 52-810472.

National Arthritis and Musculoskeletal and Skin Diseases Information Clearinghouse, National Institutes of Health. 1 AMS Circle, Bethesda, Maryland 20892-3675. (877) 226-4267. <http://www.nih.gov/niams/healthinfo/info.htm>.

KEY TERMS

Autosomal—Refers to the 22 pairs (in humans) of chromosomes not involved with sex determination.

Connective tissue—Tissue that supports and binds other tissue; much of it occurs outside of cells (extra-cellular) and consists of fibrous webs of the polymers, elastin and collagen. Cutis laxa is associated with defects in these fibers.

Diverticula—Pouches in the walls of organs.

Dominant trait—A genetic trait where one copy of the gene is sufficient to yield an outward display of the trait; dominant genes mask the presence of recessive genes; dominant traits can be inherited from only one parent.

Duodenum—The uppermost part of the small intestine, about 10 in (25 cm) long.

Esophagus—The tube connecting the throat to the stomach, about 10 in (25 cm) long.

Funnel breast (also known as pectus excavatum)—A condition where there is a hollow depression in the lower part of the chest.

Gene—A portion of a DNA molecule that either codes for a protein or RNA molecule or has a regulatory function.

Lysyl oxidase—An enzyme required for the crosslinking of elastin and collagen molecules to form properly functioning connective tissue; present in relatively low levels in at least some forms of cutis laxa.

Pigeon breast (also known as pectus carinatum)—A chest shape with a central projection resembling the keel of a boat.

Recessive trait—An inherited trait that is outwardly obvious only when two copies of the gene for that trait are present; an individual displaying a recessive trait must have inherited one copy of the defective gene from each parent.

Sex-linked—Refers to genes or traits carried on one of the sex chromosomes, usually the X.

Tortuous arteries—Arteries with many bends and twists.

X chromosome—One of the two types of sex chromosomes; females have two X chromosomes, while males have one X chromosome and one Y chromosome.

OTHER

OMIM Homepage, Online Mendelian Inheritance in Man. <http://www.ncbi.nlm.nih.gov/Omim>.

Lorraine Lica, PhD

Cuts *see* **Wounds**

CVA *see* **Stroke**

CVS *see* **Chorionic villus sampling**

Cyanosis

Definition

Cyanosis is a physical sign causing bluish discoloration of the skin and mucous membranes. Cyanosis is caused by a lack of oxygen in the blood. Cyanosis is associated with cold temperatures, **heart failure**, lung diseases, and smothering. It is seen in infants at birth as a result of heart defects, **respiratory distress syndrome**, or lung and breathing problems.

This elderly woman's lips turned purple due to central cyanosis, a condition most commonly due to slow blood circulation, leading to a bluish skin coloration. *(Photo Researchers, Inc. Reproduced by permission.)*

Description

Blood contains a red pigment (hemoglobin) in its red blood cells. Hemoglobin picks up oxygen from the lungs, then circulates it through arteries and releases it to cells through tiny capillaries. After giving up its oxygen, blood cir-

KEY TERMS

Hemoglobin—A colored substance (pigment) in the blood that carries oxygen to tissues and gives blood its red color.

Respiratory distress syndrome—Also known as hyaline membrane disease, this is a condition of premature infants in which the lungs are imperfectly expanded due to a lack of a substance on the lungs that reduces tension.

culates back to the lungs through capillaries and veins. Hemoglobin, as well as blood, is bright red when it contains oxygen, but appears dark or "bluish" after it gives up oxygen.

The blue discoloration of cyanosis is seen most readily in the beds of the fingernails and toenails, and on the lips and tongue. It often appears transiently as a result of slowed blood flow through the skin due to the cold. As such, it is not a serious symptom. However, in other cases, cyanosis is a serious symptom of underlying disease.

Causes and symptoms

The blue color of the skin and mucous membranes is caused by a lack of oxygen in the blood. Low blood oxygen may be caused by poor blood circulation, or heart or breathing problems. It can also be caused by being in a low-oxygen environment or by **carbon monoxide poisoning**. More rarely, cyanosis can be present at birth as a sign of **congenital heart disease**, in which some of the blood is not pumped to the lungs where oxygen would make the blood a bright red color. Instead, the blood goes to the rest of the body and remains unoxygenated. Cyanosis also may be caused by **poisoning** from chemicals, drugs, or contaminated food and water.

Other signs of low blood oxygen may accompany cyanosis, including feeling lightheaded or **fainting**.

Treatment

Treatment of the underlying disease can restore proper color to the skin.

Prognosis

If the underlying condition (such as heart or lung disease) can be properly treated, the skin will return to its normal shade.

Resources

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Carol A. Turkington

Cyclic vomiting syndrome

Definition

Cyclic vomiting syndrome (CVS) is a rare disorder characterized by recurring periods of vomiting in an otherwise normal child.

Description

Children in the pre-school or early school years are most susceptible to CVS, although it can appear anywhere from infancy to adulthood. This disorder was identified a century ago, but its cause is still unknown. Episodes can be triggered by emotional **stress** or infections, can last hours or days, and can return at any time. Abdominal **pain** is a frequent feature.

Causes and symptoms

The cause of CVS is still a mystery. Similarities to migraine suggest a common cause, but as yet no firm evidence has surfaced. Patients can usually identify some factor that precedes an attack. Vomiting can be protracted and lead to complications such as **dehydration**, chemical imbalances, tearing and burning, and bleeding of the esophagus (swallowing tube). Between attacks, there is no sign of any illness.

Diagnosis

The most important and difficult aspect of CVS is to be sure there is not an acute and life-threatening event in progress. So many diseases can cause vomiting—from bowel obstruction to epilepsy—that an accurate and timely diagnosis is critical. Because there is no way to prove the diagnosis of CVS, the physician must instead disprove every other diagnosis. This can be tedious, expensive, exhausting, and involve almost every system in the body. The first episode may be diagnosed as a stomach flu when nothing more serious turns up. Only after several episodes and several fruitless searches for a cause will a physician normally consider the diagnosis of CVS.

Treatment

Several different medications have given good results in small trials. The **antimigraine drugs** amitriptyline and cyproheptadine performed well for one study group. Propanolol is sometimes effective, and erythromycin helped several patients in one study, not because it is an antibiotic but because it irritates the stomach and encourages it to move its contents forward instead of in reverse.

Alternative treatment

Constitutional homeopathic medicine can work well in treating CVS because it addresses rebalancing the whole person, not just the symptoms.

Prognosis

The disease may go on for many years without a change in pattern. If the acute complications of prolonged vomiting can be successfully prevented or managed, most patients can lead normal lives between episodes. Medications may ease the symptoms during attacks.

Resources

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Cyclobenzaprine *see* **Muscle relaxants**

Cyclophospha *see* **Anticancer drugs**

Cyclospora infection *see* **Cyclosporiasis**

Cyclosporiasis

Definition

Cyclosporiasis refers to infection by the spore-forming protozoan known as *Cyclospora*. Protozoa are a group of parasites that infect the human intestine. Parasites are organisms that live in another body, called the host, and get food and liquids from that host. This parasite is a member of the group of protozoa known as coccidia, to which *Cryptosporidia* also belongs. This group of parasites infects the human intestine, and causes chronic recurrent infections in those with altered immunity or **AIDS**. Even in people with normal immune function, *Cyclopsora* can cause prolonged bouts of **diarrhea** and other gastrointestinal symptoms.

Description

Until recently, *Cyclospora* was considered to be a form of algae. The parasite causes a common form of waterborne infectious diarrhea throughout the world. Just how the parasite gets into water sources is not yet clear. It is known that ingestion of small cysts in contaminated water leads to disease.

Causes and symptoms

Symptoms begin after an incubation period of about a day or so following ingestion of cysts. A brief period of flu-like illness characterized by weakness and low-grade **fever** is followed by watery diarrhea, nausea, loss of appetite, and muscle aches. In some patients, symptoms may wax and wane for weeks, and there are those in whom nausea and burping may predominate. It is also believed that infection can occur without any symptoms at all.

In patients with abnormal immunity (immunocompromised patients), such as those with AIDS and **cancer**, prolonged diarrhea and severe weight loss often become a major problem. The bile ducts are also susceptible to infection in AIDS patients.

Diagnosis

The disease should be suspected in anyone with a history of prolonged or recurrent diarrhea. The parasite is identified either by staining stool specimens or by apply-

KEY TERMS

Anti-motility medications—Medications such as loperamide (sold as Imodium), dephenoxylate (sold as Lomotil), or medications containing codeine or narcotics that decrease the ability of the intestine to contract. This can worsen the condition of a patient with dysentery or colitis.

Cyst—A protective sac that includes either fluid or the cell of an organism. The cyst enables many organisms to survive in the environment for long periods of time without need for food or water.

Immunocompromised—A change or alteration of the immune system that normally serves to fight off infections other illnesses. This can involve changes in antibodies that the body produces (hygogammaglobulinemia), or a defect in the cells that partake in the immune response. Diseases such as AIDS and cancer exhibit changes in the body's natural immunity.

Oral Rehydration Solution (ORS)—A liquid preparation developed by the World Health Organization that can decrease fluid loss in persons with diarrhea. Originally developed to be prepared with materials available in the home, commercial preparations have recently come into use.

Parasite—An organism that lives on or in another and takes nourishment (food and fluids) from that organism.

Protozoa—Group of extremely small single cell (unicellular) or acellular organisms that are found in moist soil or water. They tend to exist as parasites, living off other life forms.

Spore—A resistant form of certain species of bacteria, protozoa, and other organisms.

ing certain fluorescent ultraviolet techniques to find the characteristic cysts. Biopsy of an infected organ such as the intestine through an endoscope is another way to make the diagnosis.

Treatment

The first aim of treatment as with any severe diarrheal illness is to avoid **dehydration** and **malnutrition**. Oral Rehydration Solution (ORS) or intravenous fluids are sometimes needed. Medications used to treat diarrhea by decreasing intestinal motility, such as loperamide or diphenoxylate are also useful, but should only be used with the advice of a physician.

The use of the medication, trimethoprim-sulfamethoxazole (Bactrim) for one week can be successful in treating intestinal infections and prevents relapse in those with a normal immune system. The same medicine can be prescribed to treat infections of both the intestine or bile ducts in immunocompromised individuals, but maintenance or continuous treatment is often needed.

Prognosis

The outlook is quite good for individuals in whom a diagnosis is made. Even without treatment, symptoms usually do not last much more than a month or so except in cases with altered immunity. Fortunately, treatment is usually successful even in those patients.

Prevention

Aside from a waterborne source as the origin of infection, little else is known about how the parasite is transmitted. Therefore, little can be done regarding prevention, except to maintain proper hand washing techniques and hygiene.

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OTHER

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David Kaminstein, MD

Cyclosporine *see* **Immunosuppressant drugs**

Cystectomy

Definition

Cystectomy is a surgical procedure to remove the bladder.

Purpose

Cystectomy is performed to treat **cancer** of the bladder. Radiation and **chemotherapy** are also used to treat **bladder cancer**. Surgery is used to remove cancer when it is in the muscle of the bladder.

Precautions

Cystectomy is an aggressive treatment that may not be appropriate for patients with superficial tumors that respond to more conservative treatment.

Description

Cystectomy is a major surgical operation. The patient is placed under general anesthesia. An incision is made across the lower abdomen. The ureters are located, tied and cut. The ureters connect the kidneys to the bladder. Cutting them frees the bladder for removal. The bladder and associated organs are removed. In men, the prostate is removed with the bladder. In women, the uterus, fallopian tubes, ovaries, and part of the vagina are removed with the bladder. The bladder collects urine from the kidneys for excretion at a later time. Since the bladder is removed, a new method must be created to remove the urine. A small piece of the small intestine is removed, cleaned, and tied at one end to form a tube. The other end is used to form a stoma, an opening through the abdominal wall to the outside. The ureters are then connected to the tube. Urine produced by the kidneys now flows down the ureters, into the tube, and through the stoma. The patient wears a bag to collect the urine.

Preparation

The medical team will discuss the procedure and tell the patient where the stoma will appear and what it will look like. The patient receives instruction on caring for a stoma and bag. Counseling may be initiated. A period of **fasting** and an enema may be required.

KEY TERMS

Ureters—Tubes that connect the kidneys to the bladder. Urine produced by the kidneys passes through the ureters to the bladder.

Aftercare

After the operation, the patient is given fluid-based **nutrition** until the intestines being to function normally again. **Antibiotics** are given to prevent infection of the incision sites. The nature of the organs removed mean that there will be major lifestyle changes for the person undergoing the operation. Men will become impotent because nerves controlling penile erection are cut during removal of the bladder. In women, **infertility** is a consequence because the ovaries and uterus are removed. However, most women who undergo cystectomy are postmenopausal and past their childbearing years.

Both men and women are fitted with an external bag that connects to the stoma and collects the urine. The bag is generally worn around the waist under the clothing. It takes a period of adjustment to get used to wearing the bag. Because there is no bladder, urine is excreted as it is produced, essentially continuously. The stoma must be treated properly to ensure that it does not become infected or blocked. Patients must be trained to care for their stoma. Often there is a period of psychological adjustment to the major change in life style created by the stoma and bag. Patients should be prepared for this by discussion with their physician.

Risks

As with any major surgery, there is a risk of infection; in this case, infection of the intestine is especially dangerous as it can lead to **peritonitis** (inflammation of the membrane lining the abdomen).

Normal results

The bladder is successfully removed and a stoma created. Intestinal function returns to normal and the patient learns proper care of the stoma and bag. He or she adjusts to lifestyle changes and returns to a normal routine of work and recreation, some sports excluded.

Abnormal results

The patient develops an infection at the incision site. The patient does not make a successful psychological adjustment to the long term consequences of **impotence**

and urinary diversion. In some women, the vagina is constricted, which may require a secondary procedure.

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John T. Lohr, PhD

Cystic fibrosis

Definition

Cystic fibrosis (CF) is an inherited disease that affects the lungs, digestive system, sweat glands, and male fertility. Its name derives from the fibrous scar tissue that develops in the pancreas, one of the principal organs affected by the disease.

Description

Cystic fibrosis affects the body's ability to move salt and water in and out of cells. This defect causes the lungs and pancreas to secrete thick mucus, blocking passageways and preventing proper function.

CF affects approximately 30,000 children and young adults in the United States, and about 3,000 babies are born with CF every year. CF primarily affects people of white northern-European descent; rates are much lower in non-white populations.

Many of the symptoms of CF can be treated with drugs or nutritional supplements. Close attention to and prompt treatment of respiratory and digestive complications have dramatically increased the expected life span of a person with CF. While several decades ago most children with CF died by age two, today about half of all people with CF live past age 31. That median age is expected to grow as new treatments are developed, and it is estimated that a person born in 1998 with CF has a median expected life span of 40 years.

Causes and symptoms

Causes

Cystic fibrosis is a genetic disease, meaning it is caused by a defect in the person's genes. Genes, found in the nucleus of all the body's cells, control cell function by serving as the blueprint for the production of proteins. Proteins carry out a wide variety of functions within cells. The gene that, when defective, causes CF, is called the CFTR gene, which stands for cystic fibrosis transmembrane conductance regulator. A simple defect in this gene leads to all the consequences of CF. There are over 500 known defects in the CFTR gene that can cause CF. However, 70% of all people with a defective CFTR gene have the same defect, known as delta-F508.

Much as sentences are composed of long strings of words, each made of letters; genes can be thought of as long strings of chemical words, each made of chemical letters, called nucleotides. Just as a sentence can be changed by rearranging its letters, genes can be mutated, or changed, by changes in the sequence of their nucleotide letters. The gene defects in CF are called point mutations, meaning that the gene is mutated only at one small spot along its length. In other words, the delta-F508 mutation is a loss of one "letter" out of thousands within the CFTR gene. As a result, the CFTR protein made from its blueprint is made incorrectly, and cannot perform its function properly.

The CFTR protein helps to produce mucus. Mucus is a complex mixture of salts, water, sugars, and proteins that cleanses, lubricates, and protects many passageways in the body, including those in the lungs and pancreas. The role of the CFTR protein is to allow chloride ions to exit the mucus-producing cells. When the chloride ions leave these cells, water follows, thinning the mucus. In this way, the CFTR protein helps to keep mucus from becoming thick and sluggish, thus allowing the mucus to be moved steadily along the passageways to aid in cleansing.

In CF, the CFTR protein cannot allow chloride ions out of the mucus-producing cells. With less chloride leaving, less water leaves, and the mucus becomes thick and sticky. It can no longer move freely through the passageways, so they become clogged. In the pancreas, clogged passageways prevent secretion of digestive enzymes into the intestine, causing serious impairment of digestion—especially of fat—which may lead to **malnutrition**. Mucus in the lungs may plug the airways, preventing good air exchange and, ultimately, leading to **emphysema**. The mucus is also a rich source of nutrients for bacteria, leading to frequent infections.

INHERITANCE OF CYSTIC FIBROSIS. To understand the inheritance pattern of CF, it is important to realize that genes actually have two functions. First, as noted above, they serve as the blueprint for the production of proteins. Second, they are the material of inheritance: parents pass on characteristics to their children by combining the genes in egg and sperm to make a new individual.

DOROTHY ANDERSEN, MD (1901–1963)

(Library of Congress)

Dorothy Andersen was born on May 15, 1901, in Asheville, North Carolina. She was the only child of Hans Peter Andersen and the former Mary Louise Mason. Orphaned as a young adult, Andersen put herself through Saint Johnsbury Academy and Mount Holyoke College before enrolling in the Johns Hopkins School of Medicine, from which she received her M.D. in 1926.

Andersen turned instead to medical research as a pathologist at Babies Hospital of the Columbia-Presbyterian Medical Center in New York City, where she stayed for more than 20 years, eventually becoming chief of pathology in 1952. Andersen is probably best known for discovery of cystic fibrosis in 1935. That discovery came about during the postmortem examination of a child who had supposedly died of celiac disease, a nutritional disorder. She searched for similar cases in the autopsy files and in medical literature, eventually realizing that she had found a disease that had never been described and to which she gave the name cystic fibrosis.

Each person actually has two copies of each gene, including the CFTR gene, in each of their body cells. During sperm and egg production, however, these two copies separate, so that each sperm or egg contains only one copy of each gene. When sperm and egg unite, the newly created cell once again has two copies of each gene.

The two gene copies may be the same or they may be slightly different. For the CFTR gene, for instance, a person may have two normal copies, or one normal and one mutated copy, or two mutated copies. A person with two mutated copies will develop cystic fibrosis. A person with one mutated copy is said to be a carrier. A carrier will not have symptoms of CF, but can pass on the mutated CFTR gene to his/her children.

When two carriers have children, they have a one in four chance of having a child with CF each time they conceive. They have a two in four chance of having a child who is a carrier, and a one in four chance of having a child with two normal CFTR genes.

Approximately one in every 25 Americans of northern-European descent is a carrier of the mutated CF gene, while only one in 17,000 African Americans and one in 30,000 Asian Americans are carriers. Since carriers are symptom-free, very few people will know whether or not they are carriers unless there is a family history of the disease. Two white Americans with no family history of CF have a one in 2,500 chance of having a child with CF.

It may seem puzzling that a mutated gene with such harmful consequences would remain so common; one might guess that the high mortality of CF would quickly lead to loss of the mutated gene from the population. Some researchers now believe the reason for the persistence of the CF gene is that carriers, those with only one copy of the gene, are protected from the full effects of **cholera**, a microorganism that infects the intestine, causing intense **diarrhea** and eventual **death** by **dehydration**. It is believed that having one copy of the CF gene is enough to prevent the full effects of cholera infection, while not enough to cause the symptoms of CF. This so-called "heterozygote advantage" is seen in some other genetic disorders, including sickle-cell anemia.

Symptoms

The most severe effects of cystic fibrosis are seen in two body systems: the gastrointestinal (digestive) system, and the respiratory tract, from the nose to the lungs. CF also affects the sweat glands and male fertility. Symptoms develop gradually, with gastrointestinal symptoms often the first to appear.

GASTROINTESTINAL SYSTEM. Ten to fifteen percent of babies who inherit CF have meconium **ileus** at birth.

Meconium is the first dark stool that a baby passes after birth; ileus is an obstruction of the digestive tract. The meconium of a newborn with meconium ileus is thickened and sticky, due to the presence of thickened mucus from the intestinal glands. Meconium ileus causes abdominal swelling and vomiting, and often requires surgery immediately after birth. Presence of meconium ileus is considered highly indicative of CF. Borderline cases may be misdiagnosed, however, and attributed instead to "milk allergy."

Other abdominal symptoms are caused by the inability of the pancreas to supply digestive enzymes to the intestine. During normal digestion, as food passes from the stomach into the small intestine, it is mixed with pancreatic secretions which help to break down the nutrients for absorption. While the intestines themselves also provide some digestive enzymes, the pancreas is the major source of enzymes for the digestion of all types of foods, especially fats and proteins.

In CF, thick mucus blocks the pancreatic duct, which is eventually closed off completely by scar tissue formation, leading to a condition known as pancreatic insufficiency. Without pancreatic enzymes, large amounts of undigested food pass into the large intestine. Bacterial action on this rich food source can cause gas and abdominal swelling. The large amount of fat remaining in the feces makes it bulky, oily, and foul-smelling.

Because nutrients are only poorly digested and absorbed, the person with CF is often ravenously hungry, underweight, and shorter than expected for his age. When CF is not treated for a longer period, a child may develop symptoms of malnutrition, including anemia, bloating, and, paradoxically, appetite loss.

Diabetes becomes increasingly likely as a person with CF ages. Scarring of the pancreas slowly destroys those pancreatic cells which produce insulin, producing type I, or insulin-dependent diabetes.

Gall stones affect approximately 10% of adults with CF. Liver problems are less common, but can be caused by the buildup of fat within the liver. Complications of liver enlargement may include internal hemorrhaging, abdominal fluid (**ascites**), spleen enlargement, and liver failure.

Other gastrointestinal symptoms can include a prolapsed rectum, in which part of the rectal lining protrudes through the anus; intestinal obstruction; and rarely, **intussusception**, in which part of the intestinal tube slips over an adjoining part, cutting off blood supply.

Somewhat less than 10% of people with CF do not have gastrointestinal symptoms. Most of these people do not have the delta-F508 mutation, but rather a different one, which presumably allows at least some of their CFTR proteins to function normally in the pancreas.

RESPIRATORY TRACT. The respiratory tract includes the nose, the throat, the trachea (or windpipe), the bronchi (which branch off from the trachea within each lung), the smaller bronchioles, and the blind sacs called alveoli, in which gas exchange takes place between air and blood.

Swelling of the sinuses within the nose is common in people with CF. This usually shows up on x-ray, and may aid the diagnosis of CF. However, this swelling, called pansinusitis, rarely causes problems, and does not usually require treatment.

Nasal polyps, or growths, affect about one in five people with CF. These growths are not cancerous, and do not require removal unless they become annoying. While nasal polyps appear in older people without CF, especially those with **allergies**, they are rare in children without CF.

The lungs are the site of the most life-threatening effects of CF. The production of a thick, sticky mucus increases the likelihood of infection, decreases the ability to protect against infection, causes inflammation and swelling, decreases the functional capacity of the lungs, and may lead to emphysema. People with CF will live with chronic populations of bacteria in their lungs, and lung infection is the major cause of death for those with CF.

The bronchioles and bronchi normally produce a thin, clear mucus that traps foreign particles including bacteria and viruses. Tiny hair-like projections on the surface of these passageways slowly sweep the mucus along, out of the lungs and up the trachea to the back of the throat, where it may be swallowed or coughed up. This "mucociliary escalator" is one of the principal defenses against lung infection.

The thickened mucus of CF prevents easy movement out of the lungs, and increases the irritation and inflammation of lung tissue. This inflammation swells the passageways, partially closing them down, further hampering the movement of mucus. A person with CF is likely to **cough** more frequently and more vigorously as the lungs attempt to clean themselves out.

At the same time, infection becomes more likely since the mucus is a rich source of nutrients. **Bronchitis**, bronchiolitis, and **pneumonia** are frequent in CF. The most common infecting organisms are the bacteria *Staphylococcus aureus*, *Haemophilus influenzae*, and *Pseudomonas aeruginosa*. A small percentage of people with CF have infections caused by *Burkholderia cepacia*, a bacterium which is resistant to most current **antibiotics** (*Burkholderia cepacia* was formerly known as

Pseudomonas cepacia.) The fungus *Aspergillus fumigatus* may infect older children and adults.

The body's response to infection is to increase mucus production; white blood cells fighting the infection thicken the mucus even further as they break down and release their cell contents. These white blood cells also provoke more inflammation, continuing the downward spiral that marks untreated CF.

As mucus accumulates, it can plug up the smaller passageways in the lungs, decreasing functional lung volume. Getting enough air can become difficult; tiredness, **shortness of breath**, and intolerance of **exercise** become more common. Because air passes obstructions more easily during inhalation than during exhalation, over time, air becomes trapped in the smallest chambers of the lungs, the alveoli. As millions of alveoli gradually expand, the chest takes on the enlarged, barrel-shaped appearance typical of emphysema.

For unknown reasons, recurrent respiratory infections lead to "digital clubbing," in which the last joint of the fingers and toes becomes slightly enlarged.

SWEAT GLANDS. The CFTR protein helps to regulate the amount of salt in sweat. People with CF have sweat that is much saltier than normal, and measuring the saltiness of a person's sweat is the most important diagnostic test for CF. Parents may notice that their infants taste salty when they kiss them. Excess salt loss is not usually a problem except during prolonged exercise or heat. While most older children and adults with CF compensate for this extra salt loss by eating more salty foods, infants and young children are in danger of suffering its effects (such as heat prostration), especially during summer. Heat prostration is marked by lethargy, weakness, and loss of appetite, and should be treated as an emergency condition.

FERTILITY. Ninety-eight percent of men with CF are sterile, due to complete obstruction or absence of the vas deferens, the tube carrying sperm out of the testes. While boys and men with CF form normal sperm and have normal levels of sex hormones, sperm are unable to leave the testes, and fertilization is not possible. Most women with CF are fertile, though they often have more trouble getting pregnant than women without CF. In both boys and girls, **puberty** is often delayed, most likely due to the effects of poor **nutrition** or chronic lung infection. Women with good lung health usually have no problems with **pregnancy**, while those with ongoing lung infection often do poorly.

KEY TERMS

Carrier—A person with one copy of a defective gene, who does not have the disease it causes, but can pass along the defective gene to offspring.

CFTR—Cystic fibrosis transmembrane conductance regulator, the protein responsible for regulating chloride movement across cells in some tissues. When a person has two defective copies of the CFTR gene, cystic fibrosis is the result.

Emphysema—A pathological accumulation of air in organs or tissues; term especially applied to the condition when in the lungs.

Mucociliary escalator—The coordinated action of tiny projections on the surfaces of cells lining the respiratory tract, which moves mucus up and out of the lungs.

Mucolytic—An agent that dissolves or destroys mucin, the chief component of mucus.

Pancreatic insufficiency—Reduction or absence of pancreatic secretions into the digestive system due to scarring and blockage of the pancreatic duct.

Diagnosis

The decision to test a child for cystic fibrosis may be triggered by concerns about recurring gastrointestinal or respiratory symptoms, or salty sweat. A child born with meconium ileus will be tested before leaving the hospital. Families with a history of CF may wish to have all children tested, especially if there is a child who already has the disease. Some hospitals now require routine screening of newborns for CF.

Sweat test

The sweat test is both the easiest and most accurate test for CF. In this test, a small amount of the drug pilocarpine is placed on the skin. A very small electrical current is then applied to the area, which drives the pilocarpine into the skin. The drug stimulates sweating in the treated area. The sweat is absorbed onto a piece of filter paper, and is then analyzed for its salt content. A person with CF will have salt concentrations that are one-and-one-half to two times greater than normal. The test can be done on persons of any age, including newborns, and its results can be determined within an hour. Virtually every person who has CF will test positively on it, and virtually everyone who does not will test negatively.

Genetic testing

The discovery of the CFTR gene in 1989 allowed the development of an accurate genetic test for CF.

Genes from a small blood or tissue sample are analyzed for specific mutations; presence of two copies of the mutated gene confirms the diagnosis of CF in all but a very few cases. However, since there are so many different possible mutations, and since testing for all of them would be too expensive and time-consuming, a negative gene test cannot rule out the possibility of CF.

Couples planning a family may decide to have themselves tested if one or both have a family history of CF. Prenatal **genetic testing** is possible through **amniocentesis**. Many couples who already have one child with CF decide to undergo prenatal screening in subsequent pregnancies, and use the results to determine whether to terminate the pregnancy. Siblings in these families are also usually tested, both to determine if they will develop CF, and to determine if they are carriers, to aid in their own family planning. If the sibling has no symptoms, determining his carrier status is often delayed until his teen years or later, when he is closer to needing the information to make decisions.

Newborn screening

Some states now require screening of newborns for CF, using a test known as the IRT test. This is a blood test which measures the level of immunoreactive trypsinogen, which is generally higher in babies with CF than those without it. This test gives many false positive results immediately after birth, and so requires a second test several weeks later. A second positive result is usually followed by a sweat test.

Treatment

There is no cure for CF. Treatment has advanced considerably in the past several decades, increasing both the life span and the quality of life for most people affected by CF. Early diagnosis is important to prevent malnutrition and infection from weakening the young child. With proper management, many people with CF engage in the full range of school and sports activities.

Nutrition

People with CF usually require high-calorie **diets** and vitamin supplements. Height, weight, and growth of a person with CF are monitored regularly. Most people with CF need to take pancreatic enzymes to supplement or replace the inadequate secretions of the pancreas. Tablets containing pancreatic enzymes are taken with every meal; depending on the size of the tablet and the meal, as many as 20 tablets may be needed. Because of incomplete absorption even with pancreatic enzymes, a person with CF needs to take in about 30% more food than a person without CF. Low-fat diets are *not* recommended except in special circumstances, since fat is a source of both essential fatty acids and abundant calories.

Some people with CF cannot absorb enough nutrients from the foods they eat, even with specialized diets and enzymes. For these people, tube feeding is an option. Nutrients can be introduced directly into the stomach through a tube inserted either through the nose (a nasogastric tube) or through the abdominal wall (a **gastrostomy** tube). A jejunostomy tube, inserted into the small intestine, is also an option. Tube feeding can provide nutrition at any time, including at night while the person is sleeping, allowing constant intake of high-quality nutrients. The feeding tube may be removed during the day, allowing normal meals to be taken.

Respiratory health

The key to maintaining respiratory health in a person with CF is regular monitoring and early treatment. Lung function tests are done frequently to track changes in functional lung volume and respiratory effort. Sputum samples are analyzed to determine the types of bacteria present in the lungs. Chest x rays are usually taken at least once a year. Lung scans, using a radioactive gas, can show closed off areas not seen on the x ray. Circulation in the lungs may be monitored by injection of a radioactive substance into the bloodstream.

People with CF live with chronic bacterial colonization; that is, their lungs are constantly host to several species of bacteria. Good general health, especially good nutrition, can keep the immune system healthy, which decreases the frequency with which these colonies begin an infection, or attack on the lung tissue. Exercise is another important way to maintain health, and people with CF are encouraged to maintain a program of regular exercise.

In addition, clearing mucus from the lungs helps to prevent infection; and mucus control is an important aspect of CF management. Postural drainage is used to allow gravity to aid the mucociliary escalator. For this technique, the person with CF lies on a tilted surface with head downward, alternately on the stomach, back, or side, depending on the section of lung to be drained. An assistant thumps the rib cage to help loosen the secretions. A device called a "flutter" offers another way to loosen secretions: it consists of a stainless steel ball in a tube. When a person exhales through it, the ball vibrates, sending vibrations back through the air in the lungs. Some special breathing techniques may also help clear the lungs.

Several drugs are available to prevent the airways from becoming clogged with mucus. **Bronchodilators** and theophyllines open up the airways; steroids reduce inflammation; and mucolytics loosen secretions. Acetyl-

cysteine (Mucomyst) has been used as a mucolytic for many years but is not prescribe frequently now, while DNase (Pulmozyme) is a newer product gaining in popularity. DNase breaks down the DNA from dead white blood cells and bacteria found in thick mucus.

People with CF may pick up bacteria from other CF patients. This is especially true of *Burkholderia cepacia*, which is not usually found in people without CF. While the ideal recommendation from a health standpoint might be to avoid contact with others who have CF, this is not usually practical (since CF clinics are a major site of care), nor does it meet the psychological and social needs of many people with CF. At a minimum, CF centers recommend avoiding prolonged close contact between people with CF, and scrupulous hygiene, including frequent hand washing. Some CF clinics schedule appointments on different days for those with and without *B. cepacia* colonies.

Some doctors choose to prescribe antibiotics only during infection, while others prefer long-term antibiotic treatment against *S. aureus*. The choice of antibiotic depends on the particular organism or organisms found. Some antibiotics are given as aerosols directly into the lungs. Antibiotic treatment may be prolonged and aggressive.

Supplemental oxygen may be needed as lung disease progresses. **Respiratory failure** may develop, requiring temporary use of a ventilator to perform the work of breathing.

Lung transplantation has become increasingly common for people with CF, although the number of people who receive them is still much lower than those who want them. Transplantation is not a cure, however, and has been likened to trading one disease for another. Long-term immunosuppression is required, increasing the likelihood of other types of infection. About 50% of adults and more than 80% of children who receive lung transplants live longer than two years. Liver transplants are also done for CF patients whose livers have been damaged by fibrosis.

Long-term use of ibuprofen has been shown to help some people with CF, presumably by reducing inflammation in the lungs. Close medical supervision is necessary, however, since the effective dose is high and not everyone benefits. Ibuprofen at the required doses interferes with kidney function, and together with aminoglycoside antibiotics, may cause kidney failure.

A number of experimental treatments are currently the subject of much research. Some evidence indicates that aminoglycoside antibiotics may help overcome the genetic defect in some CF mutations, allowing the protein to be made normally. While promising, these results would apply to only about 5% of those with CF.

Gene therapy is currently the most ambitious approach to curing CF. In this set of techniques, non-defective copies of the CFTR gene are delivered to affected cells, where they are taken up and used to create the CFTR protein. While elegant and simple in theory, gene therapy has met with a large number of difficulties in trials so far, including immune resistance, very short duration of the introduced gene, and inadequately widespread delivery.

Alternative treatment

In homeopathic medicine, the symptoms of the disease would be addressed to enhance the quality of life for the person with cystic fibrosis. Treating the cause of CF, because of the genetic basis for the disease, is not possible. Homeopathic medicine seeks to treat the whole person, however, and in CF, this approach might include:

- mucolytics to help thin mucous
- supplementation of pancreatic enzymes to assist in digestion
- respiratory symptoms can be addressed to open lung passages
- hydrotherapy techniques to help ease the respiratory symptoms and help the body eliminate
- immune enhancements can help revent the development of secondary infections
- dietary enhancements and adjustments are used to treat digestive and nutritional problems

Prognosis

People with CF may lead relatively normal lives with the control of symptoms. The possible effect of pregnancy on the health of a woman with CF requires careful consideration before beginning a family as do issues of longevity and their children's status as carriers. Although most men with CF are functionally sterile, new procedures for removing sperm from the testes are being tried, and may offer more men the chance to become fathers.

Approximately half of people with CF live past the age of 30. Because of better and earlier treatment, a person born today with CF is expected, on average, to live to age 40.

Prevention

Adults with a family history of cystic fibrosis may obtain a genetic test of their carrier status for purposes of family planning. Prenatal testing is also available. There is currently no known way to prevent development of CF in a person with two defective gene copies.

Resources

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OTHER

CysticFibrosis.com. <http://www.cysticfibrosis.com>.

Richard Robinson

Cystinuria

Definition

Cystinuria is an inborn error of amino acid transport that results in the defective absorption by the kidneys of the amino acid called cystine. The name means "cystine in the urine."

Description

Cystine is an amino acid. Amino acids are organic compounds needed by the body to make proteins and for many normal functions. When the kidneys don't absorb cystine, this compound builds up in the urine. When the amount of cystine in the urine exceeds its solubility (the greatest amount that can be dissolved), crystals form. As the amount of cystine continues to increase in the urine, the number of crystals also increases. When very large numbers of cystine crystals form, they clump together into what is called a stone.

Causes and symptoms

Cystinuria is a rare disease that occurs when people inherit an abnormal gene from their parents. This disease occurs in differing degrees of severity in people who have inherited either one or two abnormal genes. Humans have two copies of each gene. When both are abnormal, the condition is called homozygous for the disease. When one copy is normal and the other is abnormal, the condition is called heterozygous for the disease. Persons with one abnormal gene can have a milder form of cystinuria that rarely results in the formation of stones.

Severe cystinuria occurs when people are homozygous for the disease. For these individuals, the kidneys may excrete as much as 30 times the normal amount of cystine. Research has shown that this condition is caused by mutations on chromosome number two (humans have 23 pairs of chromosomes).

A person who has inherited cystinuria may have other abnormal bodily functions. In addition to excess levels of the amino acid cystine, high amounts of the amino acids lysine, arginine, and ornithine are found in the urine. This condition indicates that these amino acids are not being reabsorbed by the body.

When excess cystine crystals clump together to form a stone, the stone can block portions of the interior of the kidney or the tube (the ureter) that connects the kidney to the urinary bladder. These cystine stones can be painful, and depending upon where the stone becomes trapped, the **pain** can be felt in the lower back or the abdomen. **Nausea and vomiting** can also occur, and patients may sometimes feel the need to urinate often. Cystine stones can also cause blood in the urine. When the urinary tract is blocked by a stone, urinary tract infections or kidney failure may result.

Diagnosis

Small stones (called "silent") often do not cause any symptoms, although they can be detected by an x ray. Large stones are often painful and easily noticed by the patient. Blood in the urine can also mean that a stone has formed.

When the urine contains extremely high amounts of cystine, yellow-brown hexagonal crystals are visible when a sample is examined under the microscope. Urine samples can also be mixed with chemicals that change color when high levels of cystine are present. When the compound nitroprusside is added to urine that has been made alkaline by the addition of ammonia, the urine specimen turns red if it contains excess cystine.

Treatment

No treatment can decrease cystine excretion. The best treatment for cystinuria is to prevent stones from forming. Stones can be prevented by drinking enough liquid each day (about 5–7 qts) to produce at least 8 pts of urine, thus keeping the concentration of cystine in the urine low. Because a person doesn't drink throughout the night, less urine is produced, and the likelihood of stone formation increases. This risk can be minimized by drinking water or other liquids just before going to bed.

Drug treatments

In addition to drinking large amounts of fluids, it is helpful to make the urine more alkaline. Cystine dis-

solves more easily in alkaline urine. To increase urine alkalinity, a person may take sodium bicarbonate and acetazolamide. Penicillamine, a drug that increases the solubility of cystine, may be prescribed for patients who do not respond well to other therapies. This drug must be used with caution, however, because it can cause serious side effects or allergic reactions. For those unable to take penicillamine, another drug, alpha-mercaptopropionylglycine (Thiola), may be prescribed.

Surgical treatments

Most stones can be removed from the body by normal urination, helped by drinking large amounts of water. Large stones that cannot be passed this way must be removed by surgical procedures.

Large stones can be surgically removed by having a device called a uretoscope placed into the urethra, up through the bladder and into the ureter, where the trapped stone can be seen and removed. Another method involves using sound-wave energy aimed from outside the body to break the large stone into small pieces that can be passed by urination. This external technique is called extracorporeal shock-wave **lithotripsy** (ESWL).

For large stones in the kidney, a procedure called percutaneous nephrolithomy may be used. In this procedure, the surgeon makes a small incision in the back over the kidney. An instrument called a nephroscope is inserted through the incision into the kidney. The surgeon uses the nephroscope to locate and remove the stone. If the stone is very large, it may be broken up into smaller pieces by an ultrasonic or other kind of probe before removal.

Prognosis

As many as 50% of patients who have had surgical treatment for a kidney stone will have another stone within five years if no medicines are used to treat this condition.

Prevention

Cystinuria is a genetic disorder that currently cannot be prevented.

Resources

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National Kidney Foundation. 30 East 33rd St., New York, NY 10016. (800) 622-9010. <http://www.kidney.org>.

Dominic De Bellis, PhD

KEY TERMS

Alkaline—A solution is considered alkaline if it contains fewer hydrogen atoms than pure water.

Amino acid—An organic compound made of an amino group (containing nitrogen and hydrogen) and a carbolic acid group. Amino acids are an essential part of protein molecules.

Nephroscope—An instrument made of a light source in a tube. The tube is inserted into the kidney through an incision in the back and used to locate kidney stones. The stones are broken up with high frequency sound waves and removed by suction through the scope.

Nitroprusside—A compound that is used in laboratory tests to identify large amounts of cystine in urine samples.

Uretoscope—A tube-shaped device inserted into the body through the urinary system that allows objects to be both seen and grasped for removal.

Cystitis

Definition

Cystitis is defined as inflammation of the urinary bladder. **Urethritis** is an inflammation of the urethra, which is the passageway that connects the bladder with the exterior of the body. Sometimes cystitis and urethritis are referred to collectively as a lower urinary tract infection, or UTI. Infection of the upper urinary tract involves the spread of bacteria to the kidney and is called **pyelonephritis**.

Description

The frequency of bladder infections in humans varies significantly according to age and sex. The male/female

ratio of UTIs in children younger than 12 months is 4:1 because of the high rate of **birth defects** in the urinary tract of male infants. In adult life, the male/female ratio of UTIs is 1:50. After age 50, however, the incidence among males increases due to prostate disorders.

Cystitis in women

Cystitis is a common female problem. It is estimated that 50% of adult women experience at least one episode of dysuria (painful urination); half of these patients have a bacterial UTI. Between 2–5% of women's visits to primary care doctors are for UTI symptoms. About 90% of UTIs in women are uncomplicated but recurrent.

Cystitis in men

UTIs are uncommon in younger and middle-aged men, but may occur as complications of bacterial infections of the kidney or prostate gland.

Cystitis in children

In children, cystitis is often caused by congenital abnormalities (present at birth) of the urinary tract. **Vesicoureteral reflux** is a condition in which the child cannot completely empty the bladder. It allows urine to remain in or flow backward (reflux) into the partially empty bladder.

Causes and symptoms

The causes of cystitis vary according to sex because of the differences in anatomical structure of the urinary tract.

Females

Most bladder infections in women are so-called ascending infections, which means that they are caused by disease agents traveling upward through the urethra to the bladder. The relative shortness of the female urethra (1.2–2 in in length) makes it easy for bacteria to gain entry to the bladder and multiply. The most common bacteria associated with UTIs in women include ***Escherichia coli*** (about 80% of cases), *Staphylococcus saprophyticus*, *Klebsiella*, *Enterobacter*, and *Proteus* species. Risk factors for UTIs in women include:

- Sexual intercourse. The risk of infection increases if the woman has multiple partners.
- Use of a diaphragm for **contraception**
- An abnormally short urethra
- Diabetes or chronic **dehydration**
- The absence of a specific enzyme (fucosyltransferase) in vaginal secretions. The lack of this enzyme makes it easier for the vagina to harbor bacteria that cause UTIs.
- Inadequate personal hygiene. Bacteria from fecal matter or vaginal discharges can enter the female urethra because its opening is very close to the vagina and anus.
- History of previous UTIs. About 80% of women with cystitis develop recurrences within two years.

The early symptoms of cystitis in women are dysuria, or **pain** on urination; urgency, or a sudden strong desire to urinate; and increased frequency of urination. About 50% of female patients experience **fever**, pain in the lower back or flanks, **nausea and vomiting**, or shaking chills. These symptoms indicate pyelonephritis, or spread of the infection to the upper urinary tract.

Males

Most UTIs in adult males are complications of kidney or prostate infections. They are usually associated with a tumor or **kidney stones** that block the flow of urine and are often persistent infections caused by drug-resistant organisms. UTIs in men are most likely to be caused by *E. coli* or another gram-negative bacterium. *S. saprophyticus*, which is the second most common cause of UTIs in women, rarely causes infections in men. Risk factors for UTIs in men include:

- Lack of **circumcision**. The foreskin can harbor bacteria that cause UTIs.
- Urinary catheterization. The longer the period of catheterization, the higher the risk of UTIs.

The symptoms of cystitis and pyelonephritis in men are the same as in women.

Hemorrhagic cystitis

Hemorrhagic cystitis, which is marked by large quantities of blood in the urine, is caused by an acute bacterial infection of the bladder. In some cases, hemorrhagic cystitis is a side effect of **radiation therapy** or treatment with cyclophosphamide. Hemorrhagic cystitis in children is associated with adenovirus type 11.

Diagnosis

When cystitis is suspected, the doctor will first examine the patient's abdomen and lower back, to evaluate unusual enlargements of the kidneys or swelling of the bladder. In small children, the doctor will check for fever, abdominal masses, and a swollen bladder.

The next step in diagnosis is collection of a urine sample. The procedure differs somewhat for women and men. Laboratory testing of urine samples can now be performed with dipsticks that indicate immune system responses to infection, as well as with microscopic analysis of samples. Normal human urine is sterile. The

presence of bacteria or pus in the urine usually indicates infection. The presence of hematuria, or blood in the urine, may indicate acute UTIs, kidney disease, kidney stones, inflammation of the prostate (in men), **endometriosis** (in women), or **cancer** of the urinary tract. In some cases, blood in the urine results from athletic training, particularly in runners.

Females

Female patients require a pelvic examination as part of the procedure to obtain urine specimens. The patient lies on an obstetrical table with legs in the stirrups. The doctor first takes a vaginal culture smear. The patient is then asked to void while lying on the table. The first 5–10 ml are collected to test for urethral infection. A midstream urine sample of 200 ml is then collected to test for bladder infection.

In women, a vaginal bacterial count that is higher than those of the two urine samples indicates vaginitis. A high bacterial count in the first urine sample indicates urethritis. A count of more than 104 bacteria CFU/ml (colony forming units per milliliter) in the midstream sample indicates a bladder or kidney infection. A colony is a large number of microorganisms that grow from a single cell within a substance called a culture. A bacterial count can be given in CFU (colony forming units).

Males

In male patients, the doctor will cleanse the opening to the urethra with an antiseptic before collecting the urine sample. The first 10 ml of specimen are collected separately. The patient then voids a midstream sample of 200 ml. Following the second sample, the doctor will massage the patient's prostate and collect several drops of prostatic fluid. The patient then voids a third urine specimen for prostatic culture.

A high bacterial count in the first urine specimen or the prostatic specimens indicates urethritis or prostate infections respectively. A bacterial count greater than 100,000 bacteria CFU/ml in the midstream sample suggests a bladder or kidney infection.

Other tests

Women with recurrent UTIs can be given ultrasound tests of the kidneys and bladder together with a voiding cystourethrogram to test for structural abnormalities. (A cystourethrogram is an x-ray test in which an iodine dye is used to better view the urinary bladder and urethra.) Voiding cystourethrograms are also used to evaluate children with UTIs. In some cases, **computed tomography scans** (CT scans) can be used to evaluate patients for possible cancers in the urinary tract.

KEY TERMS

Bacteriuria—The presence of bacteria in the urine.

Dysuria—Painful or difficult urination.

Hematuria—The presence of blood in the urine.

Pyelonephritis—Bacterial inflammation of the upper urinary tract.

Urethritis—Inflammation of the urethra, which is the passage through which the urine moves from the bladder to the outside of the body.

Treatment

Medications

Uncomplicated cystitis is treated with **antibiotics**. These include penicillin, ampicillin, and amoxicillin; sulfisoxazole or sulfamethoxazole; trimethoprim; nitrofurantoin; **cephalosporins**; or **fluoroquinolones**. (Flouroquinolones are generally not used in children under 18 years of age.) Treatment for women is short-term; most patients respond within three days. Men do not respond as well to short-term treatment and require seven to 10 days of oral antibiotics for uncomplicated UTIs.

Patients of either sex may be given phenazopyridine or flavoxate to relieve painful urination.

Trimethoprim and nitrofurantoin are preferred for treating recurrent UTIs in women.

Over 50% of older men with UTIs also suffer from infection of the prostate gland. Some antibiotics, including amoxicillin and the cephalosporins, do not affect the prostate gland. Fluoroquinolone antibiotics or trimethoprim are the drugs of choice for these patients.

Patients with pyelonephritis can be treated with oral antibiotics or intramuscular doses of cephalosporins. Medications are given for 10–14 days, and sometimes longer. If the patient requires hospitalization because of high fever and dehydration caused by vomiting, antibiotics can be given intravenously.

Surgery

A minority of women with complicated UTIs may require surgical treatment to prevent recurrent infections. Surgery is also used to treat reflux problems (movement of the urine backwards) or other structural abnormalities in children and anatomical abnormalities in adult males.

Alternative treatment

Alternative treatment for cystitis may emphasize eliminating all sugar from the diet and drinking lots of water. Drinking unsweetened cranberry juice not only adds fluid, but is also thought to help prevent cystitis by making it more difficult for bacteria to cling to the bladder wall. A variety of herbal therapies are also recommended. Generally, the recommended herbs are antimicrobials, such as garlic (*Allium sativum*), goldenseal (*Hydrastis canadensis*), and bearberry (*Arctostaphylos uva-ursi*), and/or demulcents that soothe and coat the urinary tract, including corn silk and marsh mallow (*Althaea officinalis*).

Homeopathic medicine can also be effective in treating cystitis. Choosing the correct remedy based on the individual's symptoms is always key to the success of this type of treatment. **Acupuncture** and Chinese traditional herbal medicine can also be helpful in treating acute and chronic cases of cystitis.

Prognosis

Females

The prognosis for recovery from uncomplicated cystitis is excellent.

Males

The prognosis for recovery from uncomplicated UTIs is excellent; however, complicated UTIs in males are difficult to treat because they often involve bacteria that are resistant to commonly used antibiotics.

Prevention

Females

Women with two or more UTIs within a six-month period are sometimes given prophylactic treatment, usually nitrofurantoin or trimethoprim for three to six months. In some cases the patient is advised to take an antibiotic tablet following sexual intercourse.

Other preventive measures for women include:

- drinking large amounts of fluid
- voiding frequently, particularly after intercourse
- proper cleansing of the area around the urethra

Males

The primary preventive measure for males is prompt treatment of prostate infections. Chronic **prostatitis** may go unnoticed, but can trigger recurrent UTIs. In addition, males who require temporary catheterization following surgery can be given antibiotics to lower the risk of UTIs.

Resources

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Cystometry

Definition

Cystometry is a test of bladder function in which pressure and volume of fluid in the bladder is measured during filling, storage, and voiding.

Purpose

The urinary bladder stores urine produced by the kidneys. The main muscle of the bladder wall, the detrusor, relaxes to allow expansion of the bladder during filling. The urethra, the tube through which urine exits, is held closed by a ring of muscle, known as the urethral sphincter. As volume increases, stretching of the detrusor and pressure on the sphincter sends signals to the brain, indicating the need for urination, or voiding. Voluntary relaxation of the sphincter and automatic contractions of the detrusor allow successful and virtually complete voiding.

A cystometry study is performed to diagnose problems with urination, including incontinence, urinary retention, and recurrent urinary tract infections. Urinary difficulties may occur because of weak or hyperactive sphincter or detrusor, or incoordination of their two

activities. Infection of the bladder or urethra may cause incontinence, as can obstruction of the urethra from scar tissue, prostate enlargement, or other benign or cancerous growths. Loss of sensation due to nerve damage can lead to chronic overfilling.

Precautions

The mild irritation of the urinary tract necessary for insertion of the catheter may occasionally cause flushing, sweating, and nausea.

Description

The patient begins by emptying the bladder as much as possible. A thin plastic catheter is then slowly inserted into the urethra until it reaches the bladder. Measurements are taken of the residual urine volume and bladder pressure. Pressure measurements may require a rectal probe to account for the contribution of the abdominal muscles to the pressure recording.

The bladder is then gradually filled with either warm water, room temperature water, saline solution, carbon dioxide gas, or a contrast solution for x-ray analysis, depending on the type of study being done. The patient is asked to describe sensations during filling, including temperature sensations and when the first feeling of bladder fullness occurs. Once the bladder is completely full, the patient is asked to begin voiding, and measurements are again made of pressure and volume, as well as flow rate and pressure.

Preparation

There is no special preparation needed for this test. The patient may be asked to stop taking certain medications in advance of the test, including sedatives, cholinergics, and anticholinergics.

Aftercare

Cystometry can be somewhat uncomfortable. The patient may wish to reserve an hour or so afterward to recover. Urinary frequency or urgency, and some reddening of the urine, may last for a day. Increasing fluid intake helps to flush out the bladder, but caffeinated, carbonated, or alcoholic beverages are discouraged, because they may irritate the bladder lining. Signs of infection, such as **fever**, chills, **low back pain**, or persistent blood in the urine, should be reported to the examining physician.

Risks

There is a slight risk of infection due to tearing of the urethral lining.

KEY TERMS

Detrusor—Muscle of the bladder wall.

Sphincter—Ring of muscle between the bladder and the urethra that functions to close off the urethra.

Urethra—Tube that empties urine from the bladder to the exterior of the body.

Normal results

The normal bladder should not begin contractions during filling and should initially expand without resistance. A feeling of fullness occurs with a volume of 100–200 ml. The adult bladder capacity is 300–500 ml. The sphincter should relax and open when the patient wills it, accompanied by detrusor contractions. During voiding, detrusor contraction should be smooth and lead to a steady urine stream.

Abnormal results

Inability of the bladder to relax during filling, or low bladder volume, may indicate interstitial **cystitis**, prostate enlargement, or **bladder cancer**. Contraction of the bladder during filling may be due to irritation from infection or cysts, obstruction of the bladder outlet, or neurological disease such as **stroke**, **multiple sclerosis**, or **spinal cord injury**. Diminished sensation may occur with nerve lesions, **peripheral neuropathy**, or chronic overfilling.

Resources

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Cystoscopy

Definition

Cystoscopy (cystourethroscopy) is a diagnostic procedure that is used to look at the bladder (lower urinary

Cystoscopy is a diagnostic procedure which is used to view the bladder, collect urine samples, and examine the prostate gland. This procedure also enables biopsies to be taken. The primary instrument used in cystoscopy is the cystoscope, a tube which is inserted through the penis into the urethra, and ultimately into the bladder. *(Illustration by Electronic Illustrators Group.)*

tract), collect urine samples, and examine the prostate gland. Performed with an optic instrument known as a cystoscope (urethroscope), this instrument uses a lighted tip for guidance to aid in diagnosing urinary tract disease and prostate disease. Performed by a urologist, this surgical test also enables biopsies to be taken or small stones to be removed by way of a hollow channel in the cystoscope.

Purpose

Categorized as an endoscopic procedure, cystoscopy is used by urologists to examine the entire bladder lining and take biopsies of any areas that look questionable. This test is not used on a routine basis, but may benefit the urologist who is needing further information about a patient who displays the following symptoms or diagnosis:

- blood in the urine (also known as hematuria)
- incontinence or the inabililty to control urination
- a urinary tract infection
- a urinary tract which display signs of congenital abnormalities
- tumors located in the bladder
- the presence of bladder or **kidney stones**
- a stiffness or strained feeling of the urethra or ureters
- symptoms of an **enlarged prostate**

Blood and urine studies, in addition to x rays of the kidneys, ureters, and bladder, may all occur before a cystoscopy. At the time of surgery, a retrograde pyelogram may also be performed. Additional blood studies may be needed immediately following surgery.

Precautions

While the cystoscopy procedure is commonly relied upon to gather additional diagnostic information, it is an invasive surgical technique that may involve risks for certain patients. Those who are extremely overweight (obese), smoke, are recovering from a recent illness, or are treating a chronic condition may face additional risks from surgery.

Surgical risk also increases in patients who are currently using certain drugs including antihypertensives; **muscle relaxants**; tranquilizers; sleep inducers; insulin; sedatives; **beta blockers**; or cortisone. Those who use mind-altering drugs also put themselves at increased risk of complications during surgery. The following mind-altering drugs should be avoided: narcotics; psychedelics; hallucinogens; marijuana; sedatives; hypnotics; or **cocaine**.

Description

Depending on the type of information needed from a cystoscopy, the procedure typically takes 10–40 minutes to complete. The patient will be asked to urinate before surgery which allows an accurate measurement of the remaining urine in the bladder. A well lubricated cystoscope is inserted through the urethra into the bladder where a urine sample is taken. Fluid is then pushed in to inflate the bladder and allow the urologist to examine the entire bladder wall.

During an examination, the urologist may take the following steps: remove either bladder or kidney stones; gather tissue samples; and treat any suspicious lesions. In order to perform x-ray studies (retrograde pyelogram), a harmless dye is injected into the ureters by way of a catheter that is passed through the previously placed cystoscope. After completion of all needed tests, the cystoscope is removed.

Preparation

As a procedure that can be completed in a hospital, doctor's office, or outpatient surgical facility, an injection

A cystoscope helps the doctor examine the urethra, bladder, and prostate. *(Illustration by Argosy Inc.)*

of spinal or general anesthesia may be used prior to a cystoscopy. While this test is typically performed on an outpatient basis, a patient may require up to three days of recovery in the hospital.

Aftercare

Patients who have undergone a cystoscopy will be instructed to follow these steps to ensure a quick recovery:

- due to soreness or discomfort that may occur in the urethra, especially while urinating, several warm baths a day are recommended to relieve any **pain**
- allow four days for recovery
- blood may appear in the urine—this is common, and soon clears up in one to two days following the procedure
- avoid strenuous **exercise** for a minimum of two weeks following surgery
- sexual relations may continue when the urologist determines that healing is complete
- wait at least two days after surgery before driving

Patients may also be prescribed pain relievers and **antibiotics** following surgery. Minor pain may also be treated with over-the-counter, non-prescription drugs such as **acetaminophen**.

Risks

As with any surgical procedure, there are some risks involved with a cystoscopy. Complications may include: profuse bleeding; a damaged urethra; a perforated bladder; a urinary tract infection; or an injured penis.

Patients should also contact their physician if they experience any of the following symptoms following surgery: pain, redness, swelling, drainage, or bleeding from the surgical site; signs of infection that may include **headache**, muscle aches, **dizziness** or an overall ill feeling and **fever**; nausea or vomiting; strenuous or painful urination; or symptoms that may result as side-effects from the medication.

Normal results

A successful cystoscopy includes a thorough examination of the bladder and collection of urine samples for cultures. If no abnormalities are seen, the results are indicated as normal.

Abnormal results

Cystoscopy allows the urologist to detect inflammation of the bladder lining, prostatic enlargement, or tumors. If these are seen, further evaluation or biopsies may be needed in addition to the removal of some tumors.

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KEY TERMS

Endoscopy—Examination of body organs or cavities through the use of an endoscope (a lighted optical instrument used to see inside body cavities), such as a cystoscope used to complete a cystoscopy.

Retrograde pyelogram—A pyelography or x-ray technique where radiopaque dye is injected into the kidneys from below, by way of the ureters, allowing further examination of the kidneys.

Ureter—The tube that carries urine from the kidney to the bladder, with each kidney having one ureter.

Urethra—A passageway from the bladder to the outside for the discharge of urine. In the female, this canal lies between the vagina and clitoris; in the male, the urethra travels through the penis, opening at the tip.

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American Cancer Society. 1599 Clifton Rd., NE, Atlanta, GA 30329-4251. (800) 227-2345. <http://www.cancer.org>.

Beth A. Kapes

Cystourethroscopy *see* **Cystoscopy**

Cytomegalic inclusion disease *see* **Cytomegalovirus infection**

Cytomegalovirus antibody screening test

Definition

Cytomegalovirus (CMV) is a common human virus. Antibodies to CMV are evidence of a current or past infection.

Purpose

Consequences of a CMV infection can be devastating in a pregnant woman, a transplant patient, or a person with human **immunodeficiency** virus (HIV). Antibody screening helps control the infection risk for these groups.

In a healthy, nonpregnant person, CMV infection is almost never serious. Symptoms, if present, are mild, often resembling **infectious mononucleosis** due to Epstein-Barr virus. Antibody screening distinguishes between these two infections.

Description

When first exposed to CMV, a person's immune system is triggered and quickly makes antibodies to fight the virus. Antibodies are special proteins designed to attack and destroy foreign material, in this case, the cytomegalovirus.

The test combines a person's serum with a substance to which CMV antibodies attach. This antibody-antigen complex is measured and the amount of original antibody determined. If positive for antibodies, the serum is diluted, or titered, and the test repeated until the serum is so dilute it no longer gives a positive result. The last dilution that gives a positive result is the titer reported.

A test positive for CMV antibodies means the person has been infected with the virus, either currently or in the past; it doesn't mean the person has lifetime immunity. After an infection, this virus, like all members of the herpes virus group, can stay hidden inside a person and cause infection if the person's immune system later weakens and antibody protection decreases. In fact, reactivation of such hidden (or latent) infection is not at all uncommon and usually occurs without symptoms.

Transplant patients and people with weakened immune systems, including those with HIV, are vulnerable to infection from several routes, including from another person, from a donated organ or transfused blood, or from reactivation of a past infection. Before transplant, both the recipient and donor are usually tested for antibodies. A recipient who has never had CMV (negative for antibodies), should not receive an organ from a donor who has had CMV (positive for antibodies). CVM infection can be associated with organ rejection, or can cause illness such as **pneumonia**, hepatitis, or **death**. Similarly, blood is usually screened for CMV antibodies before being transfused into a person with a weakened immune system.

CMV infection is the most common congenital infection (existing at birth). The infection, passed from mother to baby, can cause permanent mental or physical damage, or death. The antibody screening test tells a

woman whether or not she has antibody protection against the virus in case she is exposed during **pregnancy**.

Tests that measure a specific type of antibody help tell the difference between a current and a past infection. Immunoglobulin M (IgM) antibodies appear at the beginning of an infection and last only weeks. Immunoglobulin G (IgG) antibodies appear 10–14 days later and can last a lifetime. A person suspected of having a current infection should be tested at the beginning of the infection and again 10–14 days later.

The CMV antibody screening test is also called the transplant reaction screening test. Results are usually available the following day.

Preparation

This test requires 5 mL of blood. Collection of the sample takes only a few minutes.

Aftercare

Discomfort or bruising may occur at the puncture site or the person may feel dizzy or faint. Pressure to the puncture site until the bleeding stops reduces bruising. Warm packs to the puncture site relieve discomfort.

Normal results

A person without previous exposure to CMV will test negative.

Abnormal results

The presence of antibodies means the person has been infected with CMV, either now or in the past. An antibody titer at least four times higher at the end of the illness than at the beginning, or the presence of IgM antibodies, indicates a recent or current first time infection.

People with weak immune systems may not generate antibodies against CMV. A current infection in a transplant patient or a person with HIV is confirmed with other tests, such as viral culture.

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KEY TERMS

Antibody—A special protein built by the body as a defense against foreign material entering the body.

Cytomegalovirus (CMV)—A common human virus causing mild or no symptoms in healthy people, but permanent damage or death to an infected fetus, a transplant patient, or a person with HIV.

Titer—A dilution of a substance with an exact known amount of fluid. For example, one part of serum diluted with four parts of saline is a titer of 1:4.

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Cytomegalovirus infection

Definition

Cytomegalovirus (CMV) is a virus related to the group of herpes viruses. Infection with CMV can cause no symptoms, or can be the source of serious illness in people with weak immune systems. CMV infection is also an important cause of **birth defects**.

Description

CMV is an extremely common organism worldwide. It is believed that about 85% of the adult population in the United States have been infected by CMV at some point in their lives. CMV is found in almost all of the body's organs. It is also found in body fluids, including semen, saliva, urine, feces, breast milk, blood, and secretions of the cervix (the narrow, lower section of the uterus).

CMV is also able to cross the placenta (the organ that provides oxygen and nutrients to the unborn baby in the uterus). Because CMV can cross the placental barrier, initial infection in a pregnant woman can lead to infection of the developing baby.

Causes and symptoms

CMV is passed between people through contact with body fluids. CMV can also be passed on through sexual

An infected retina of an AIDS patient. Cytomegaloviruses are herpes viruses that can, among other problems, act as opportunistic infectious agents in suppressed immune systems, a common problem with AIDS sufferers. *(Custom Medical Stock Photo. Reproduced by permission.)*

contact. Babies can be born infected with CMV, either becoming infected in the uterus (congenital infection) or during birth (from infected cervical secretions).

Like other herpes viruses, CMV remains inactive (dormant) within the body for life after the initial infection. Some of the more serious types of CMV infections occur in people who have been harboring the dormant virus, only to have it reactivate when their immune system is stressed. Immune systems may be weakened because of **cancer chemotherapy**, medications given after organ transplantation, or diseases that significantly lower immune resistance like acquired **immunodeficiency** syndrome (**AIDS**).

In a healthy person, initial CMV infection often occurs without symptoms and is rarely noticed. Occasionally, a first-time infection with CMV may cause a mild illness called mononucleosis. Symptoms include swollen glands, liver, and spleen; **fever**; increased white blood cells; **headache**; **fatigue**; and **sore throat**. About 8% of all mononucleosis cases are due to CMV infection. A similar infection, though slightly more serious, may occur two to four weeks after receiving a blood **transfusion** containing CMV.

In people with weakened immune systems, CMV infection can cause more serious and potentially life-threatening illnesses. These illnesses include **pneumonia**, and inflammations of the liver (hepatitis), brain (**encephalitis**), esophagus (esophagitis), large intestine (colitis), and retina of the eye (retinitis).

Babies who contract CMV from their mothers during birth rarely develop any illness from these infections. Infants born prematurely who become CMV infected during birth have a greater chance of complications, including pneumonia, hepatitis, and decreased blood platelets.

However, an unborn baby is at great risk for serious problems when the mother becomes infected with CMV for the first time while pregnant. About 10% of these babies will be born with obvious problems, including **prematurity**, lung problems, an enlarged liver and spleen, **jaundice**, anemia, low birth weight, small head size, and inflammation of the retina. About 90% of these babies may appear perfectly normal at birth. Unfortunately, about 20% of these babies will later develop severe hearing impairments and **mental retardation**.

Diagnosis

Body fluids or tissues can be tested to reveal CMV infection. However, this information is not always particularly helpful because CMV stays dormant in the cells for life. Tests to look for special immune cells (antibodies) directed specifically against CMV are useful in proving that a person has been infected with CMV. However, these tests do not give any information regarding when the CMV infection first occurred.

Treatment

Ganciclovir and foscarnet are both antiviral medications that have been used to treat patients with weak immune systems who develop a serious illness from CMV (including retinitis). As of 1998, research is still being done to try to find useful drugs to treat newborn babies suffering from congenital infection with CMV. **Antiviral drugs** are not used to treat CMV infection in otherwise healthy patients because the drugs have significant side effects that outweigh their benefits.

Prognosis

Prognosis in healthy people with CMV infection is excellent. About 0.1% of all newborn babies will have serious damage from CMV infection occurring while they were developing in the uterus. About 50% of all transplant patients will develop severe illnesses due to reactivation of dormant CMV infection. These illnesses have a high rate of serious complications and **death**.

Prevention

Prevention of CMV infection in the normal, healthy person involves good handwashing. Blood products can be screened or treated to insure that they do not contain CMV.

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Centers for Disease Control and Prevention. 1600 Clifton Rd., NE, Atlanta, GA 30333. (800) 311-3435, (404) 639-3311. <http://www.cdc.gov>.

March of Dimes Birth Defects Foundation. 1275 Mamaroneck Ave., White Plains, NY 10605. (914) 428-7100. <http://www.modimes.org>.

Rosalyn Carson-DeWitt, MD

D

D & C *see* **Dilatation and curettage**

Dacryocystitis

Definition

Dacryocystitis is an inflammation of the tear sac (lacrimal sac) at the inner corner of the eye.

Description

Tears drain into little openings (puncta) in the inner corners of the eyelids. From there, the tears travel through little tube-like structures (canaliculi) to the lacrimal sac. The nasolacrimal ducts then take the tears from the lacrimal sac to the nose. That's why people need to blow their nose when they cry a lot.

Dacryocystitis is usually caused by a blockage of the nasolacrimal duct, which allows fluid to drain into the nasal passages. When the lacrimal sac does not drain, bacteria can grow in the trapped fluid. This condition is most common in infants and people over 40 years old.

Causes and symptoms

In newborn infants, the nasolacrimal duct may fail to form an opening—a condition called dacryostenosis. The cause of dacryocystitis in adults is usually associated with inflammation and infection in the nasal region. Dacryocystitis can be acute, having a sudden onset, or it can be chronic, with symptoms occurring over the course of weeks or months. Symptoms of acute dacryocystitis can include **pain**, redness, tearing, and swelling at the inner corner of the eye by the nose. In chronic dacryocystitis, the eye area may be swollen, watery or teary, and, when pressure is applied to the area, there may be a discharge of pus or mucus through the punctum.

Dacryocystitis of the right eye. The inner corner of the lower lid is bulging from an inflamed tear sac. Blockage of the tear duct causes fluid to be trapped in the tear sac, which becomes infected. *(Custom Medical Stock Photo. Reproduced by permission.)*

Diagnosis

Dacryocystitis usually occurs in only one eye. As mentioned, the symptoms can range from watery eyes, pain, swelling, and redness to a discharge of pus when pressure is applied to the area between the bridge of the nose and the inner eyelids. A sample of the pus may be collected on a swab or in a tube for laboratory analysis. The type of antibiotic and treatment may depend on which bacteria is present. In the acute form, a blood test may reveal an elevated white blood cell (WBC) count; with a chronic infection, the WBC count is usually normal. To identify the exact location of the blockage, an x ray can be taken after a dye is injected into the duct in a procedure called dacryocystography.

KEY TERMS

Canaliculi—Also known as lacrimal ducts, these tube-like structures carry the tears from the eyes to the lacrimal sac.

Cannula— A narrow tube that can be inserted into a duct.

Dacryocystography—An x ray of the tear duct after injection of a dye that is used to help locate a blockage in the duct.

Dacryocystorhinostomy—A surgical procedure to drain the tear sac into the nasal passage.

Dacryostenosis—Obstruction or narrowing of the nasolacrimal duct. May be present at birth.

Nasoacrimal duct—The tube that carries the tears from the lacrimal sac to the nose.

Punctum—Tiny opening at the inner corners of the upper and lower lids. The area for the beginning of tear drainage.

Treatment

A warm compress applied to the area can help relieve pain and promote drainage. Topical and oral **antibiotics** may be prescribed if an infection is present. Intravenous antibiotics may be needed if the infection is severe. In some cases, a tiny tube (cannula) is inserted into the tear duct which is then flushed with a sterile salt water solution (sterile saline). If other treatments fail to clear up the symptoms, surgery (dacryocystorhinostomy) to drain the lacrimal sac into the nasal cavity can be performed. In extreme cases, the lacrimal sac will be removed completely.

In infants, gentle massage of the lacrimal sac four times daily for up to nine months can drain the sac and sometimes clear a blockage. As the infant grows, the duct may open by itself. If the duct does not open, it may need to be dilated with a minor surgical procedure.

Prognosis

Treatment of dacryocystitis with antibiotics is usually successful in clearing the infection that is present. If there is a permanent blockage that prevents drainage, infection may recur and surgery may be required to open the duct. If left untreated, the infected sac can rupture, forming an open, draining sore.

Prevention

There are no specific recommendations for the prevention of dacryocystitis; however, good hygiene may decrease the chances of infection.

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Altha Roberts Edgren

Dandruff *see* **Seborrheic dermatitis**

Death

Definition

Death is defined as the cessation of all vital functions of the body including the heartbeat, brain activity (including the brain stem), and breathing.

Description

Death comes in many forms, whether it be expected after a diagnosis of terminal illness or an unexpected accident or medical condition.

Terminal illness

When a terminal illness is diagnosed, a person, family, friends, and physicians are all able to prepare for the impending death. A terminally ill individual goes through several levels of emotional acceptance while in the process of dying. First, there is denial and **isolation**. This is followed by anger and resentment. Thirdly, a person tries to escape the inevitable. With the realization that death is eminent, most people suffer from depression. Lastly, the reality of death is realized and accepted.

Causes and symptoms

As of 2001, the two leading causes of death for both men and women in the United States were heart disease and **cancer**. Accidental death was a distant third followed by such problems as **stroke**, chronic lung disorders, **pneumonia**, suicide, **cirrhosis**, **diabetes mellitus**, and murder. The order of these causes of death varies among persons of different age, ethnicity, and gender.

Diagnosis

In an age of organ transplantation, identifying the moment of death may now involve another life. It thereby takes on supreme legal importance. It is largely due to the need for transplant organs that death has been so precisely defined.

The official signs of death include the following:

- no pupil reaction to light
- no response of the eyes to caloric (warm or cold) stimulation
- no jaw reflex (the jaw will react like the knee if hit with a reflex hammer)
- no gag reflex (touching the back of the throat induces vomiting)
- no response to **pain**
- no breathing
- a body temperature above 86°F (30°C), which eliminates the possibility of resuscitation following cold-water drowning
- no other cause for the above, such as a **head injury**
- no drugs present in the body that could cause apparent death
- all of the above for 12 hours
- all of the above for six hours and a flat-line electroencephalogram (brain wave study)
- no blood circulating to the brain, as demonstrated by **angiography**

Current ability to resuscitate people who have "died" has produced some remarkable stories. Drowning in cold water (under 50°F/10°C) so effectively slows metabolism that some persons have been revived after a half hour under water.

Treatment

Only recently has there been concerted public effort to address the care of the dying in an effort to improve their comfort and lessen their alienation from those still living. Hospice care represents one of the greatest advances made in this direction. There has also been a liberalization of the use of narcotics and other drugs for symptomatic relief and improvement in the quality of life for the dying.

Living will

One of the most difficult issues surrounding death in the era of technology is that there is now a choice, not of the event itself, but of its timing. When to die, and more often, when to let a loved one die, is coming within people's power to determine. This is both a blessing and a dilemma. Insofar as the decision can be made

ELISABETH KÜBLER-ROSS (1926–)

Contemporary physician who has become a world authority on the subject of death and after-death states. Born in Switzerland on July 8, 1926, she worked as a country doctor before moving to the United States. During World War II she spent weekends at the Kantonspital (Cantonai Hospital) in Zürich, where she volunteered to assist escaped refugees. After the war she visited Majdanek concentration camp, where the horrors of the death chambers stimulated in her a desire to help people facing death and to understand the human impulses of love and destruction. She extended her medical background by becoming a practicing psychiatrist. Her formal work with dying patients began in 1965 when she was a faculty member at the University of Chicago. She also conducted research on basic questions concerning life after death at the Manhattan State Hospital, New York. Her studies of death and dying have involved accounts by patients who reported out-of-the-body travel. Her research tends to show that while dying can be painful, death itself is a peaceful condition. Her 1969 text, *On Death and Dying*, was hailed by her colleagues and also became a popular best-seller.

In 1978 Kübler-Ross helped to found Shanti Nilaya (Final Home of Peace), a healing and growth center in Escondido, California. This was an extension of her well-known "Life-Death and Transition" workshops conducted in various parts of the United States and Canada, involving physicians, nurses, social workers, laypeople, and terminally ill patients. Much of Kübler-Ross's later research was directed toward proving the existence of life after death. Her publication *To Live Until We Say Good-bye* (1979) was both praised as a "celebration of life" and criticized as "prettifying" the real situation. She has also dealt with issues such as AIDS and "near death" experiences. In the mid-1980s Shanti Nilaya moved from San Diego County, California, to Head Waters, Virginia, where it continues to offer courses and short- and long-term therapeutic sessions.

KEY TERMS

Angiography—X rays of blood vessels filled with a contrast agent.

Caloric testing—Flushing warm and cold water into the ear stimulates the labyrinth and causes vertigo and nystagmus if all the nerve pathways are intact.

Electroencephalogram —Recording of electrical activity in the brain.

Hospice—Systematized care of dying persons.

Living will—A legal document detailing a person's wishes during the end of life, to be carried out by designated decision makers.

Stroke—Interruption of blood flow to a part of the brain with consequent brain damage, also known as a cerebrovascular accident (CVA).

ahead of time, a living will is an attempt to address this dilemma. By outlining the conditions under which one would rather be allowed to die, a person can contribute significantly to that final decision, even if not competent to do so at the time of actual death. The problem is that there are uncertainties surrounding every severely ill person. Each instance presents a greater or lesser chance of survival. The chance is often greater than zero. The best living will follows an intimate discussion with decision makers covering the many possible scenarios surrounding the end of life. This discussion is difficult, for few people like to contemplate their own demise. However, the benefits of a living will are substantial, both to physicians and to loved ones who are faced with making final decisions. Most states have passed living will laws, honoring instructions on artificial **life support** that were made while a person was still mentally competent.

Euthanasia

Another issue that has received much attention is assisted suicide (euthanasia). In 1997, the State of Oregon placed the issue on the ballot, amid much consternation and dispute. Perhaps the main reason euthanasia has become front page news is because Dr. Jack Kevorkian, a pathologist from Michigan, is one of its most vocal advocates. The issue highlights the many new problems generated by increasing ability to intervene effectively in the final moments of life and unnaturally prolong the process of dying. The public appearance of euthanasia has also stimulated discussion about more compassionate care of the dying.

Prevention

Autopsy after death is a way to precisely determine a cause of death. The word autopsy is derived from Greek meaning to see with one's own eyes. A pathologist extensively examines a body and submits a detailed report to an attending physician. Although an autopsy can do nothing for an individual after death, it can benefit the family and, in some cases, medical science. Hereditary disorders and disease may be found. This knowledge could be used to prevent illness in other family members. Information culled from an autopsy can be used to further medical research. The link between **smoking** and lung cancer was confirmed from data gathered through autopsy. Early information about **AIDS** was also compiled through autopsy reports.

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American Academy of Family Physicians. 11400 Tomahawk Creek Parkway, Leawood, KS 66211-2672. (913) 906-6000. <http://www.aafp.org>.

American Medical Association. 515 N. State Street, Chicago, IL 60610. (312) 464-5000. <http://www.ama-assn.org>.

American Society of Clinical Pathologists. 2100 West Harrison Street, Chicago, IL 60612. (312) 738-1336. <http://www.ascp.org/index.asp>.
College of American Pathologists. 325 Waukegan Road, Northfield, IL 60093. (800) 323-4040. <http://www.cap.org>.
Hospice Foundation of America. 2001 S St. NW Suite 300, Washington, DC 20009. (800) 854-3402. <http://www.hospicefoundation.org>.

OTHER

American Association of Retired Persons. <http://www.aarp.org>.
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National Center for Health Statistics. <http://www.cdc.gov/nchs>.

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Debridement

Definition

Debridement is the process of removing non-living tissue from pressure ulcers, **burns**, and other **wounds**.

Purpose

Debridement speeds the healing of pressure ulcers, burns, and other wounds. Wounds that contain non-living (necrotic) tissue take longer to heal. The necrotic tissue may become colonized with bacteria, producing an unpleasant odor. Though the wound is not necessarily infected, the bacteria can cause inflammation and strain the body's ability to fight infection. Necrotic tissue may also hide pockets of pus called abscesses. Abscesses can develop into a general infection that may lead to **amputation** or **death**.

Precautions

Not all wounds need debridement. Sometimes it is better to leave a hardened crust of dead tissue, called an eschar, than to remove it and create an open wound, particularly if the crust is stable and the wound is not inflamed. Before performing debridement, the physician will take a medical history with attention to factors that might complicate healing, such as medications being taken and **smoking**. The physician will also note the cause of the wound and the ways it has been treated. Some ulcers and other wounds occur in places where blood flow is impaired, for example, the foot ulcers that can accompany **diabetes mellitus**. In such cases, the physician or nurse may decide not to debride the wound because blood flow may be insufficient for proper healing.

Description

In debridement, dead tissue is removed so that the remaining living tissue can adequately heal. Dead tissue exposed to the air will form a hard black crust, called an eschar. Deeper tissue will remain moist and may appear white, or yellow and soft, or flimsy. The four major debridement techniques are surgical, mechanical, chemical, and autolytic.

Surgical debridement

Surgical debridement (also known as sharp debridement) uses a scalpel, scissors, or other instrument to cut dead tissue from a wound. It is the quickest and most efficient method of debridement. It is the preferred method if there is rapidly developing inflammation of the body's connective tissues (**cellulitis**) or a more generalized infection (**sepsis**) that has entered the bloodstream. The procedure can be performed at a patient's bedside. If the target tissue is deep or close to another organ, however, or if the patient is experiencing extreme **pain**, the procedure may be done in an operating room. Surgical debridement is generally performed by a physician, but in some areas of the country an advance practice nurse or physician assistant may perform the procedure.

The physician will begin by flushing the area with a saline (salt water) solution, and then will apply a topical anesthetic gel to the edges of the wound to minimize pain. Using a forceps to grip the dead tissue, the physician will cut it away bit by bit with a scalpel or scissors. Sometimes it is necessary to leave some dead tissue behind rather than disturb living tissue. The physician may repeat the process again at another session.

Mechanical debridement

In mechanical debridement, a saline-moistened dressing is allowed to dry overnight and adhere to the dead tissue. When the dressing is removed, the dead tissue is pulled away too. This process is one of the oldest methods of debridement. It can be very painful because the dressing can adhere to living as well as nonliving tissue. Because mechanical debridement cannot select between good and bad tissue, it is an unacceptable debridement method for clean wounds where a new layer of healing cells is already developing.

Chemical debridement

Chemical debridement makes use of certain enzymes and other compounds to dissolve necrotic tissue. It is more

KEY TERMS

Eschar—A hardened black crust of dead tissue that may form over a wound.

Pressure ulcer—Also known as a decubitus ulcer, pressure ulcers are open wounds that form whenever prolonged pressure is applied to skin covering bony outcrops of the body. Patients who are bedridden are at risk of developing pressure ulcers. Pressure ulcers are commonly known as bedsores.

Sepsis—A severe systemic infection in which bacteria have entered the blood stream.

selective than mechanical debridement. In fact, the body makes its own enzyme, collagenase, to break down collagen, one of the major building blocks of skin. A pharmaceutical version of collagenase is available and is highly effective as a debridement agent. As with other debridement techniques, the area first is flushed with saline. Any crust of dead tissue is etched in a cross-hatched pattern to allow the enzyme to penetrate. A topical antibiotic is also applied to prevent introducing infection into the bloodstream. A moist dressing is then placed over the wound.

Autolytic debridement

Autolytic debridement takes advantage of the body's own ability to dissolve dead tissue. The key to the technique is keeping the wound moist, which can be accomplished with a variety of dressings. These dressings help to trap wound fluid that contains growth factors, enzymes, and immune cells that promote wound healing. Autolytic debridement is more selective than any other debridement method, but it also takes the longest to work. It is inappropriate for wounds that have become infected.

Preparation

The physician or nurse will begin by assessing the need for debridement. The wound will be examined, frequently by inserting a gloved finger into the wound to estimate the depth of dead tissue and evaluate whether it lies close to other organs, bone, or important body features. The area may be flushed with a saline solution before debridement begins, and a topical anesthetic gel or injection may be applied if surgical or mechanical debridement is being performed.

Aftercare

After surgical debridement, the wound will be packed with a dry dressing for a day to control bleeding. Afterward, moist dressings are applied to promote wound healing. Moist dressings are also used after mechanical, chemical, and autolytic debridement. Many factors contribute to wound healing, which frequently can take considerable time. Debridement may need to be repeated.

Risks

It is possible that underlying tendons, blood vessels or other structures will be damaged during the examination of the wound and during surgical debridement. Surface bacteria may also be introduced deeper into the body, causing infection.

Normal results

Removal of dead tissue from pressure ulcers and other wounds speeds healing. Although these procedures cause some pain, they are generally well tolerated by patients and can be managed more aggressively. It is not uncommon to debride a wound again in a subsequent session.

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American Academy of Wound Management. 1255 23rd St., NW, Washington, DC 20037. (202) 521-0368. <http://www.aawm.org>.

Wound Care Institute. 1100 N.E. 163rd Street, Suite #101, North Miami Beach, FL 33162. (305) 919-9192. <http://woundcare.org>.

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Decompression sickness

Definition

Decompression sickness (DCS) is a dangerous and occasionally lethal condition caused by nitrogen bubbles that form in the blood and other tissues of scuba divers who surface too quickly.

Description

According to the Divers Alert Network (DAN), a worldwide organization devoted to safe-diving research and promotion, less than 1% of divers fall victim to DCS or the rarer bubble problem called **gas embolism**, air **embolism**, or arterial gas embolism (AGE). A study of the United States military community in Okinawa, where tens of thousands of sport and military dives are made each year, identified 84 DCS and 10 AGE cases in 1989–95, including nine deaths. This translated into estimates of one case in every 7,400 dives and one **death** in every 76,900 dives. DCS symptoms can be quite mild, however, and many cases certainly go unnoticed by divers.

At times the terminology adopted by writers on DCS can be confusing. Some substitute the term decompression illness (DCI) for DCS. Others treat DCI as a label encompassing both DCS and AGE. An older term for DCS is caisson disease, coined in the nineteenth century when it was discovered that bridge construction crews working at the bottom of lakes and rivers in large pressurized enclosures (caissons) were experiencing joint **pain** (a typical DCS symptom) on returning to the surface.

Causes and symptoms

The air we breathe is mostly a mixture of two gases, nitrogen (78%) and oxygen (21%). Unlike oxygen, nitrogen is a biologically inert gas, meaning that it is not metabolized (converted into other substances) by the body. For this reason, most of the nitrogen we inhale is expelled when we exhale, but some is dissolved into the blood and other tissues. During a dive, however, the lungs take in more nitrogen than usual. This happens because the surrounding water pressure is greater than the air pressure at sea level (twice as great at 33 ft [10 m], for instance). As the water pressure increases, so does the pressure of the nitrogen in the compressed air inhaled by the diver. Because increased pressure causes an increase in gas density, the diver takes in more nitrogen with each breath than he or she would at sea level. Instead of being exhaled, however, the extra nitrogen safely dissolves into the tissues, where it remains until the diver begins his or her return to the surface (under some circumstances the extra nitrogen can cause **nitrogen narcosis**, but that condition is distinct from DCS). On the way up, decompression occurs (in other words, the water pressure drops), and with the change in pressure, the extra nitrogen gradually diffuses out of the tissues and is delivered by the bloodstream to the lungs, which expel it from the body. If the diver surfaces too quickly, however, potentially dangerous nitrogen bubbles can form in the tissues and cause DCS. These bubbles can compress nerves, obstruct arteries, veins, and lymphatic vessels, and trigger harmful chemical reactions in the blood. The precise reasons for bubble formation remain unclear.

How much extra nitrogen enters the tissues varies with the dive's depth and duration. Dive tables prepared by the U.S. Navy and other organizations specify how long most divers can safely remain at a particular depth. If the dive table limits are exceeded, the diver must pause on the way up to allow the nitrogen to diffuse into the bloodstream without forming bubbles; these pauses are called decompression stops, and are carefully calibrated. DCS can occur, however, even when a diver obeys safe diving rules. In such cases, the predisposing factors include **fatigue**, **obesity**, **dehydration**, **hypothermia**, and recent alcohol use. As well, people who fly or travel to high-altitude locations without letting 12–24 hours pass after their last dive are at risk for DCS as well because their bodies undergo further decompression. This is true even when flying in commercial aircraft. Many travelers are unaware that to save money on fuel the cabin pressure in commercial aircraft is set much lower than the pressure at sea level. At 30,000 ft (9,144 m), for instance, cabin pressure is usually equivalent to the pressure at 7,000–8,000 ft (2,133–2,438 m) above sea level, a safe setting for everyone but recent divers. Exactly how long a diver should wait before flying or traveling to a high-altitude location depends on how much diving he or she has done and other considerations. If there is uncertainty about the appropriate waiting period, the sensible course of action is to let the full 24 hours pass.

Because the nitrogen bubbles that cause DCS can affect any of the body's tissues, including the blood, bones, nerves, and muscles, many kinds of symptoms are possible. Symptoms can appear minutes after a diver surfaces, and in about 80% of cases do so within eight hours. Pain is often the only symptom; this is sometimes called the bends, although many people incorrectly use that term as a synonym for DCS itself. The pain, which ranges from mild to severe, is usually limited to the joints, but can be felt anywhere. Severe **itching** (pruritis), skin **rashes**, and skin mottling (cutis marmorata) are other possible symptoms. All of these are sometimes classified as manifestations of type 1 or "mild" DCS. type 2 or "serious" DCS can lead, among other things, to **paralysis**, brain damage, heart attacks, and death. Many DCS victims, however, experience both type 1 and type 2 symptoms.

Diagnosis

Diagnosis requires taking a medical history (questioning the patient about his or her health and recent activities) and conducting a **physical examination**.

KEY TERMS

Gas embolism—The presence of a gas bubble in the bloodstream that obstructs circulation.

Hyperbaric chamber—A sealed compartment in which air pressure is gradually increased and then gradually decreased, allowing nitrogen bubbles to shrink and the nitrogen to safely diffuse out of body tissue.

Lymphatic vessels—Vessels that carry a fluid called lymph from the tissues to the bloodstream.

Nitrogen narcosis—Also called "rapture of the deep," the condition is caused by increased nitrogen pressure at depth and is characterized by symptoms similar to alcohol intoxication.

Treatment

DCS is treated by giving the patient oxygen and placing him or her in a hyperbaric chamber, an enclosure in which the air pressure is first gradually increased and then gradually decreased. This shrinks the bubbles and allows the nitrogen to safely diffuse out of the tissues. Hyperbaric chamber facilities exist throughout the United States. No matter how mild one's symptoms may appear, immediate transportation to a facility is essential. Treatment is necessary even if the symptoms clear up before the facility is reached, because bubbles may still be in the bloodstream and pose a threat. DAN maintains a list of facilities and a 24-hour hotline that can provide advice on handling DCS and other diving emergencies.

Prognosis

DCS sufferers who undergo chamber treatment within a few hours of symptom onset usually enjoy a full recovery. If treatment is delayed the consequences are less predictable, although many people have been helped even after several days have passed. A 1992 DAN report on diving accidents indicated that full recovery following chamber treatment was immediate for about 50% of divers. Some people, however, suffer numbness, tingling, or other symptoms that last weeks, months, or even a lifetime. In the Okinawa study, six of the 94 patients experienced "long-lasting" symptoms even after repeated chamber treatments.

Prevention

The obvious way to minimize the risk of falling victim to DCS is to follow the rules on safe diving and air travel after a dive. People who are obese, suffer from lung or heart problems, or are otherwise in poor health should not dive. And because the effect of nitrogen diffusion on the fetus remains unknown, diving while pregnant is not recommended.

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Divers Alert Network. The Peter B. Bennett Center, 6 West Colony Place, Durham, NC 27705. (800) 446-2671. <http://www.diversalertnetwork.org>.

Undersea and Hyperbaric Medical Society. 10531 Metropolitan Ave., Kensington, MD 20895. (301) 942-2980. <http://www.uhms.org>.

Howard Baker

Decongestants

Definition

Decongestants are medicines used to relieve nasal congestion (stuffy nose).

Purpose

A congested or stuffy nose is a common symptom of colds and **allergies**. This congestion results when membranes lining the nose become swollen. Decongestants relieve the swelling by narrowing the blood vessels that supply the nose. This reduces the blood supply to the swollen membranes, causing the membranes to shrink.

These medicines do not cure colds or reverse the effects of histamines—chemicals released as part of the

allergic reaction. They will not relieve all of the symptoms associated with colds and allergies, only the stuffiness.

When considering whether to use a decongestant for cold symptoms, keep in mind that most colds go away with or without treatment and that taking medicine is not the only way to relieve a stuffy nose. Drinking hot tea or broth or eating chicken soup may help. There are also adhesive strips can be placed on the nose to help widen the nasal passages, making breathing through the nasal passages a bit easier when congestion is present.

Precautions

Decongestant nasal sprays and nose drops may cause a problem called rebound congestion if used repeatedly over several days. When this happens, the nose remains stuffy or gets worse with every dose. The only way to stop the cycle is to stop using the drug. The stuffiness should then go away within about a week. Anyone who shows signs of severe rebound congestion should also contact his or her physician.

Do not use decongestant nasal sprays for more than three days. Decongestants taken by mouth should not be used for more than seven days. If the congestion has not gone away in this time, or if the symptoms are accompanied by **fever**, call a physician.

Do not use a decongestant nasal spray after the product's expiration date. If the product has become cloudy or discolored, throw it away and do not use it. Do not share droppers or spray bottles with anyone else, as this could spread infection. Do not let droppers and bottle tips touch countertops or other surfaces.

Some decongestants cause drowsiness. People who takes these drugs should not drive, use machines or do anything else that might be dangerous until they have found out how the drugs affect them.

In general, older people may be more sensitive to the effects of decongestants and may need to take lower doses to avoid side effects. People in this age group should not take long-acting (extended release) forms of decongestants unless they have previously taken a short-acting form with no ill effects.

Children may also be more sensitive to the effects of decongestants. Before giving any decongestant to a child, check the package label carefully. Some of these medicines are too strong for use in children. Serious side effects are possible if they are given large amounts of these drugs or if they swallow nose drops, nasal spray or eye drops. If this happens, call a physician or poison center immediately.

Special conditions

People with certain medical conditions or who are taking certain other medicines can have problems if they take decongestants. Before taking these drugs, be sure to let the physician know about any of these conditions:

ALLERGIES. Anyone who has had unusual reactions to decongestants in the past should let his or her physician know before these drugs or any similar drugs are prescribed. The physician should also be told about any allergies to foods, dyes, preservatives, or other substances.

PREGNANCY. In studies of laboratory animals, some decongestants have had unwanted effects on fetuses. However, it is not known whether such effects also occur in people. Women who are pregnant or who plan to become pregnant should check with their physicians before taking decongestants.

BREASTFEEDING. Some decongestants pass into breast milk and may have unwanted effects on nursing babies whose mothers take the drugs. Women who are breastfeeding should check with their physicians before using decongestants. If they need to take the medicine, it may be necessary to bottle feed the baby with formula while taking it.

OTHER MEDICAL CONDITIONS. Anyone with heart or blood vessel disease, high blood pressure, diabetes, **enlarged prostate**, or overactive thyroid should not take decongestants unless under a physician's supervision. The medicine can increase blood sugar in people with diabetes. It can be especially dangerous in people with high blood pressure, as it may increase blood pressure.

Before using decongestants, people with any of these medical problems should make sure their physicians are aware of their conditions:

- glaucoma
- history of mental illness

Decongestants may have a variety of side effects, and may also interact with other medications the patient is taking.

Side effects

DECONGESTANT NASAL SPRAYS AND NOSE DROPS. The most common side effects from decongestant nasal sprays and nose drops are sneezing and temporary burning, stinging, or dryness. These effects are usually temporary and do not need medical attention. If any of the following side effects occur after using a decongestant nasal spray or nose drops, stop using the medicine immediately and call the physician:

- increased blood pressure
- **headache**
- fast, slow, or fluttery heartbeat
- nervousness
- **dizziness**
- nausea
- sleep problems

DECONGESTANTS TAKEN BY MOUTH. The most common side effects of decongestants taken by mouth are nervousness, restlessness, excitability, dizziness, drowsiness, headache, nausea, weakness, and sleep problems. Anyone who has these symptoms while taking decongestants should stop taking them immediately.

Patients who have these symptoms while taking decongestants should call the physician immediately:

- increased blood pressure
- fast, irregular, or fluttery heartbeat
- severe headache
- tightness or discomfort in the chest
- breathing problems
- fear or anxiety
- **hallucinations**
- trembling or shaking
- convulsions (seizures)
- pale skin
- painful or difficult urination

Other side effects may occur. Anyone who has unusual symptoms after taking a decongestant should get in touch with his or her physician.

Interactions with other medicines

Decongestants may interact with a variety of other medicines. When this happens, the effects of one or both of the drugs may change or the risk of side effects may be greater. Do not take decongestants at the same time as these drugs:

- Monoamine oxidase inhibitors (MAO inhibitors) such as phenzeline (Nardil) or tranylcypromine (Parnate), used to treat conditions including depression and **Parkinson's disease**. Do not take decongestants at the same time as a MAO inhibitor or within two weeks of stopping treatment with an MAO inhibitor unless a physician approves.
- Other products containing the same or other decongestants.
- Caffeine.

In addition, anyone who takes decongestants should let the physician know all other medicines he or she is taking. Among the drugs that may interact with decongestants are:

- tricyclic antidepressants such as imipramine (Tofranil) or desipramine (Norpramin)
- the antidepressant maprotiline (Ludiomil)
- amantadine (Symmetrel)
- amphetamines
- medicine to relieve **asthma** or other breathing problems
- methylphenidate (Ritalin)
- appetite suppressants
- other medicine for colds, sinus problems, hay fever or other allergies
- beta-blockers such as atenolol (Tenormin) and propranolol (Inderal)
- digitalis glycosides, used to treat heart conditions

The list above does not include every drug that may interact with decongestants. Be sure to check with a physician or pharmacist before combining decongestants with any other prescription or nonprescription (over-the-counter) medicine.

Description

Decongestants are sold in many forms, including tablets, capsules, caplets, gelcaps, liqui-caps, liquids, nasal sprays, and nose drops. These drugs are sometimes combined with other medicines in cold and allergy products designed to relieve several symptoms. Some decongestant products require a physician's prescription, but there are also many nonprescription (over-the-counter) products. Ask a physician or pharmacist about choosing an appropriate decongestant.

Commonly used decongestants include oxymetazoline (Afrin and other brands) and pseudoephedrine (Sudafed, Actifed, and other brands). The decongestant oxymetazoline is also used in some eye drops to relieve redness and **itching**.

The recommended dosage depends on the drug. Check with the physician who prescribed the drug or the pharmacist who filled the prescription for the correct dosage, and always take the medicine exactly as directed. If using nonprescription (over-the-counter) types, follow the directions on the package label or ask a pharmacist for assistance. Never take larger or more frequent doses, and do not take the drug for longer than directed.

KEY TERMS

Fetus—A developing baby inside the womb.

Hallucination—A false or distorted perception of objects, sounds, or events that seems real. Hallucinations usually result from drugs or mental disorders.

Risks

Anyone considering taking a decongestant should take a close look at the labels of any already in their medicine cabinet. In 2000, the Food and Drug Administration prohibited over-the-counter sales of medicines containing the decongestant phenylpropanolamine. The medicine is associated with an increased risk of **stroke** in people ages 18 to 49, especially women. Many cold remedies contained this medicine. Contact a pharmacist if there is any question about the ingredients in a medication. Over-the-counter remedies containing phenylpropanolamine should be discarded.

Normal results

The desired result when taking decongestants is the short-term relief of nasal congestion.

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Decubitus ulcers *see* **Bedsores**

Deep vein thrombosis

Definition

Deep vein thrombosis (DVT) is a blood clot in a major vein, usually in the legs and/or pelvis.

Description

Deep vein thrombosis is a common but difficult to detect illness that can be fatal if not treated effectively. According to the American Heart Association, more than two million Americans develop deep vein thrombosis annually. An estimated 600,000 of these develop **pulmonary embolism**, a potentially fatal complication where the blood clots break off and form pulmonary emboli, plugs that block the lung arteries. Sixty thousand people die of pulmonary **embolism** each year. Deep vein thrombosis is also called venous thromboembolism, **thrombophlebitis** or phlebothrombosis.

Deep vein thrombosis is a major complication in patients who have had **orthopedic surgery** or pelvic, abdominal, or **thoracic surgery**. Patients with **cancer** and other chronic illnesses (including congestive **heart failure**), as well as those who have suffered a recent myocardial infarction, are also at high risk for developing DVT. Deep vein thrombosis can be chronic, with recurrent episodes.

Causes and symptoms

Deep vein thrombosis is caused by blood clots in blood vessels that form in veins where blood flow is sluggish or has been disturbed, in pockets in the calf's deep veins, or in veins that have been traumatized. Symptoms include swelling and tenderness of the calf or thigh, and possibly warmth. Only 23–50% of patients experience symptoms, so it's often "silent." Some individuals and families have underlying clotting tendencies that can be tested for.

Diagnosis

Deep vein thrombosis can be detected through **venography** and radionuclide venography, **Doppler ultrasonography**, and impedance plethysmography. Venography is the most accurate test, but it is not used much, because it is often painful, expensive, exposes the patient to radiation, and can cause reactions and complications. Venography identifies the location, extent, and degree of attachment of the blood clots, and enables the condition of the deep leg veins to be assessed. A contrast solution is injected into a foot vein through a catheter. The physician observes the movement of the solution through the vein with a fluoroscope while a series of x rays are taken. Venography takes 30–45 minutes and can be done in a physician's office, a laboratory, or a hospital. Radionuclide venography, in which a radioactive isotope is injected, is occasionally used, especially if a patient has had reactions to contrast solutions.

This illustration features a dissected human lower leg showing clot formation (thrombosis) along the length of a vein. *(Custom Medical Stock Photo. Reproduced by permission.)*

Doppler ultrasonography is usually the preferred procedure for detecting deep vein thrombosis. This technique uses sound waves to measure blood flow through leg veins and arteries. A blood pressure cuff is wrapped around the patient's ankle and a transducer with gel on it is placed over pulse points of the foot and lower leg. High-frequency sounds bounce off the soft tissue, and the echoes are converted into images on a monitor. It is very accurate in detecting clots above the knee that can become pulmonary embolisms. Usually performed in a physician's office or hospital outpatient diagnostic center, Doppler ultrasound usually takes 30–45 minutes.

Impedance plethysmography records changes in blood volume and vessel resistance. A blood pressure cuff is wrapped around the leg above the knee, four electrodes are placed near the knee and the ankle, and the cuff is inflated. How efficiently the veins return to normal is measured. Performed in a physician's office, it takes about 15 minutes.

KEY TERMS

Pulmonary embolism —An obstruction of a blood vessel in the lungs, usually caused by a blood clot that blocks a coronary artery. Pulmonary embolism can be very serious and, in some cases, fatal.

Thrombosis—The development of a blood clot inside a blood vessel.

Treatment

Deep vein thrombosis can be treated with drug therapy, bed rest, and gradient elastic stockings. Medications include anticoagulants that "thin" blood to prevent further growth of blood clots, as well as clot-dissolving drugs. Heparin is a common injectable anticoagulant, and is usually followed by coumadin tablets for at least three months. Bed rest with the patient's legs elevated is necessary until the condition improves. Gradient elastic stockings should then be worn, and standing for long periods of time avoided. In some cases, a filter is placed in the major vein (the inferior vena cava) to trap emboli or clots before they get to the heart and lungs.

Alternative treatment

Deep vein thrombosis can be life-threatening and must be treated with conventional medical therapies. However, there are alternative therapies that can be used in conjunction with emergency treatments to dissolve the clot that help support the body and prevent recurrence. A trained alternative health care practitioner should be consulted due to the severity of this condition.

Prognosis

In many cases, deep vein thrombosis can be successfully treated if diagnosed early.

Prevention

Deep vein thrombosis can be prevented through prophylactic anticoagulant drugs and venous stasis prevention with gradient elastic stockings and intermittent pneumatic compression of the legs. High-risk patients often need to remain on anticoagulants like Coumadin indefinitely.

Resources

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Lori De Milto

Deer-fly fever *see* **Tularemia**

Defibrillation

Definition

Defibrillation is a process in which an electronic device sends an electric shock to the heart to stop an extremely rapid, irregular heartbeat, and restore the normal heart rhythm.

Purpose

Defibrillation is performed to correct life-threatening fibrillations of the heart, which could result in cardiac arrest. It should be performed immediately after identifying that the patient is experiencing a cardiac emergency, has no pulse, and is unresponsive.

Precautions

Defibrillation should not be performed on a patient who has a pulse or is alert, as this could cause a lethal heart rhythm disturbance or cardiac arrest. The paddles used in the procedure should not be placed on a woman's breasts or over a pacemaker.

Description

Fibrillations cause the heart to stop pumping blood, leading to brain damage and/or cardiac arrest. About 10% of the ability to restart the heart is lost with every minute that the heart stays in fibrillation. **Death** can occur in minutes unless the normal heart rhythm is restored through defibrillation. Because immediate defibrillation is crucial to the patient's survival, the American Heart Association has called for the integration of defibrillation into an effective emergency cardiac care system. The system should include early access, early **cardiopulmonary resuscitation**, early defibrillation, and early advanced cardiac care.

Defibrillation by paddles. *(Photograph by Patricia Barber, RBP, Custom Medical Stock Photo. Reproduced by permission.)*

Defibrillators deliver a brief electric shock to the heart, which enables the heart's natural pacemaker to regain control and establish a normal heart rhythm. The defibrillator is an electronic device with electrocardiogram leads and paddles. During defibrillation, the paddles are placed on the patient's chest, caregivers stand back, and the electric shock is delivered. The patient's pulse and heart rhythm are continually monitored. Medications to treat possible causes of the abnormal heart rhythm may be administered. Defibrillation continues until the patient's condition stabilizes or the procedure is ordered to be discontinued.

Early defibrillators, about the size and weight of a car battery, were used primarily in ambulances and hospitals. The American Heart Association now advocates public access defibrillation; this calls for placing automated external defibrillators (AEDS) in police vehicles, airplanes, and at public events, etc. The AEDS are smaller, lighter, less expensive, and easier to use than the early defibrillators. They are computerized to provide simple, verbal instructions to the operator and to make it impossible to deliver a shock to a patient whose heart is not fibrillating. The placement of AEDs is likely to expand to many public locations.

Preparation

After help is called for, cardiopulmonary resuscitation (**CPR**) is begun and continued until the caregivers arrive and set up the defibrillator. Electrocardiogram

KEY TERMS

Cardiac arrest—A condition in which the heart stops functioning. Fibrillation can lead to cardiac arrest if not corrected quickly.

Fibrillation—Very rapid contractions or twitching of small muscle fibers in the heart.

Pacemaker—A surgically implanted electronic device that sends out electrical impulses to regulate a slow or erratic heartbeat.

leads are attached to the patient's chest. Gel or paste is applied to the defibrillator paddles, or two gel pads are placed on the patient's chest. The caregivers verify lack of a pulse, and select a charge.

Aftercare

After defibrillation, the patient's cardiac status, breathing, and vital signs are monitored until he or she is stable. Typically, this monitoring takes place after the patient has been removed to an intensive care or cardiac care unit in a hospital. An electrocardiogram and **chest x ray** are taken. The patient's skin is cleansed to remove gel or paste, and, if necessary, ointment is applied to **burns**. An intravenous line provides additional medication, as needed.

Risks

Skin burns from the defibrillator paddles are the most common complication of defibrillation. Other risks include injury to the heart muscle, abnormal heart rhythms, and blood clots.

Resources

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Lori De Milto

Definitive cancer therapy *see* **Cancer therapy, definitive**

Degenerative arthritis *see* **Osteoarthritis**

Dehydration

Definition

Dehydration is the loss of water and salts essential for normal body function.

Description

Dehydration occurs when the body loses more fluid than it takes in. This condition can result from illness; a hot, dry climate; prolonged exposure to sun or high temperatures; not drinking enough water; and overuse of **diuretics** or other medications that increase urination. Dehydration can upset the delicate fluid-salt balance needed to maintain healthy cells and tissues.

Water accounts for about 60% of a man's body weight. It represents about 50% of a woman's weight. Young and middle-aged adults who drink when they're thirsty do not generally have to do anything more to maintain their body's fluid balance. Children need more water because they expend more energy, but most children who drink when they are thirsty get as much water as their systems require.

Age and dehydration

Adults over the age of 60 who drink only when they are thirsty probably get only about 90% of the fluid they need. Developing a habit of drinking only in response to the body's thirst signals raises an older person's risk of becoming dehydrated. Seniors who have relocated to areas where the weather is warmer or dryer than the climate they are accustomed to are even likelier to become dehydrated unless they make it a practice to drink even when they are not thirsty.

Dehydration in children usually results from losing large amounts of fluid and not drinking enough water to replace the loss. This condition generally occurs in children who have stomach flu characterized by vomiting and **diarrhea**, or who can not or will not take enough fluids to compensate for excessive losses associated with **fever** and sweating of acute illness. An infant can become dehydrated only hours after becoming ill. Dehydration is a major cause of infant illness and **death** throughout the world.

Types of dehydration

Mild dehydration is the loss of no more than 5% of the body's fluid. Loss of 5–10% is considered moderate dehydration. Severe dehydration (loss of 10–15% of body fluids) is a life-threatening condition that requires immediate medical care.

Complications of dehydration

When the body's fluid supply is severely depleted, hypovolemic **shock** is likely to occur. This condition, which is also called physical collapse, is characterized by pale, cool, clammy skin; rapid heartbeat; and shallow breathing.

Blood pressure sometimes drops so low it can not be measured, and skin at the knees and elbows may become blotchy. **Anxiety**, restlessness, and thirst increase. After the patient's temperature reaches 107°F (41.7°C) damage to the brain and other vital organs occurs quickly.

Causes and symptoms

Strenuous activity, excessive sweating, high fever, and prolonged vomiting or diarrhea are common causes of dehydration. So are staying in the sun too long, not drinking enough fluids, and visiting or moving to a warm region where it doesn't often rain. Alcohol, **caffeine**, and diuretics or other medications that increase the amount of fluid excreted can cause dehydration.

Reduced fluid intake can be a result of:

- appetite loss associated with acute illness
- excessive urination (polyuria)
- nausea
- bacterial or viral infection or inflammation of the pharynx (pharyngitis)
- inflammation of the mouth caused by illness, infection, irritation, or vitamin deficiency (**stomatitis**)

Other conditions that can lead to dehydration include:

- disease of the adrenal glands, which regulate the body's water and salt balance and the function of many organ systems
- diabetes mellitus
- eating disorders
- kidney disease
- chronic lung disease

An infant who does not wet a diaper in an eight-hour period is dehydrated. The soft spot on the baby's head (fontanel) may be depressed. Symptoms of dehydration at any age include cracked lips, dry or sticky mouth, lethargy, and sunken eyes. A person who is dehydrated cries without shedding tears and does not urinate very often. The skin is less elastic than it should be and is slow to return to its normal position after being pinched.

Dehydration can cause confusion, **constipation**, discomfort, drowsiness, fever, and thirst. The skin turns pale and cold, the mucous membranes lining the mouth and nose lose their natural moisture. The pulse sometimes races and breathing becomes rapid. Significant fluid loss can cause serious neurological problems.

Diagnosis

The patient's symptoms and medical history usually suggest dehydration. **Physical examination** may reveal shock, rapid heart rate, and/or low blood pressure. Laboratory tests, including blood tests (to check electrolyte levels) and urine tests (e.g., urine specific gravity and creatinine), are used to evaluate the severity of the problem. Other laboratory tests may be ordered to determine the underlying condition (such as diabetes or an adrenal gland disorder) causing the dehydration.

Treatment

Increased fluid intake and replacement of lost electrolytes are usually sufficient to restore fluid balances in patients who are mildly or moderately dehydrated. For individuals who are mildly dehydrated, just drinking plain water may be all the treatment that is needed. Adults who need to replace lost electrolytes may drink sports beverages (e.g., Gatorade or Recharge) or consume a little additional salt. Parents should follow label instructions when giving children Pedialyte or other commercial products recommended to relieve dehydration. Children who are dehydrated should receive only clear fluids for the first 24 hours.

A child who is vomiting should sip one or two teaspoons of liquid every 10 minutes. A child who is less

than a year old and who is not vomiting should be given one tablespoon of liquid every 20 minutes. A child who is more than one year old and who is not vomiting should take two tablespoons of liquid every 30 minutes. A baby who is being breast-fed should be given clear liquids for two consecutive feedings before breastfeeding is resumed. A bottle-fed baby should be given formula diluted to half its strength for the first 24 hours after developing symptoms of dehydration.

In order to accurately calculate fluid loss, it's important to chart weight changes every day and keep a record of how many times a patient vomits or has diarrhea. Parents should note how many times a baby's diaper must be changed.

Children and adults can gradually return to their normal diet after they have stopped vomiting and no longer have diarrhea. Bland foods should be reintroduced first, with other foods added as the digestive system is able to tolerate them. Milk, ice cream, cheese, and butter should not be eaten until 72 hours after symptoms have disappeared.

Medical care

Severe dehydration can require hospitalization and intravenous fluid replacement. If an individual's blood pressure drops enough to cause or threaten the development of shock, medical treatment is usually required. A doctor should be notified whenever an infant or child exhibits signs of dehydration or a parent is concerned that a stomach virus or other acute illness may lead to dehydration.

A doctor should also be notified if:

- a child less than three months old develops a fever higher than 100°F (37.8°C)
- a child more than three months old develops a fever higher than 102°F (38.9°C)
- symptoms of dehydration worsen
- an individual urinates very sparingly or does not urinate at all during a six-hour period
- dizziness, listlessness, or excessive thirst occur
- a person who is dieting and using diuretics loses more than 3 lb (1.3 kg) in a day or more than 5 lb (2.3 kg) a week

When treating dehydration, the underlying cause must also be addressed. For example, if dehydration is caused by vomiting or diarrhea, medications may be prescribed to resolve these symptoms. Patients who are dehydrated due to diabetes, kidney disease, or adrenal gland disorders must receive treatment for these conditions as well as for the resulting dehydration.

KEY TERMS

Electrolytes—Mineral salts, such as sodium and potassium, dissolved in body fluid.

Alternative treatment

Gelatin water can be substituted for electrolyte-replacement solutions. It is made by diluting a 3-oz package in a quart of water or by adding one-quarter teaspoon of salt and a tablespoon of sugar to a pint of water.

Prognosis

Mild dehydration rarely results in complications. If the cause is eliminated and lost fluid is replaced, mild dehydration can usually be cured in 24–48 hours.

Vomiting and diarrhea that continue for several days without adequate fluid replacement can be fatal. The risk of life-threatening complications is greater for young children and the elderly. However, dehydration that is rapidly recognized and treated has a good outcome.

Prevention

Patients who are vomiting or who have diarrhea can prevent dehydration by drinking enough fluid for their urine to remain the color of pale straw. Ensuring that patients always drink adequate fluids during an illness will help prevent dehydration. Infants and young children with diarrhea and vomiting can be given electrolyte solutions such as Pedialyte to help prevent dehydration. People who are not ill can maintain proper fluid balance by drinking several glasses of water before going outside on a hot day. It is also a good idea to avoid coffee and tea, which increase body temperature and water loss.

Patients should know whether any medication they are taking can cause dehydration and should get prompt medical care to correct any underlying condition that increases the risk of dehydration.

Other methods of preventing dehydration and ensuring adequate fluid intake include:

- eating more soup at mealtime
- drinking plenty of water and juice at mealtime and between meals
- keeping a glass of water nearby when working or relaxing

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Maureen Haggerty

Delavirdine *see* **Non-nucleoside reverse transcriptase inhibitors**

Delayed hypersensitivity skin test

Definition

A delayed hypersensitivity test (DHT) is an immune function test measuring the presence of activated T cells that recognize a certain substance.

Purpose

The immune system protects against infection by viruses, bacteria, fungi, and parasites. After initial exposure to a foreign substance, or antigen, the immune system creates both antibodies and sensitized T cells. Both these immune agents respond when the body is reexposed to the antigen. Antibodies, which are circulating proteins, respond within minutes, to give what is termed an immediate hypersensitivity reaction. T cells' responses occur over several days, and are thus called delayed hypersensitivity reactions. The cascade of events initiated by the T cells leads to hardening (induration) and redness (erythema) at the injection site.

A DHT is performed for one of three reasons:

- To test for exposure to specific diseases, such as **tuberculosis** (TB). Tuberculosis testing is done by injecting into the skin a small volume of TB antigen, which contains no organisms (live or dead) but can still provoke an immune response.
- To test for allergic sensitivity to potential skin irritants, such as poison ivy. Skin allergy testing is usually done by placing a series of adhesive patches on the skin containing potential allergens, or allergy-causing substances.
- To assess the vitality of the T cell response as part of the evaluation of immune system health in infection, **cancer**, immune disorders, pre-transplantation screening, **aging**, and **malnutrition**. DHT can help predict survival in immunocompromised patients, and evaluate the success of restorative therapy. Antigens used for these tests must be ones the patient has been exposed to before, and, therefore, include inactivated antigens from common infectious agents to which the patient might have been exposed, such as **mumps**, *Candida albicans*, **tetanus** toxoid, and trichophyton (a skin fungus).

Precautions

No special precautions are necessary for most patients. Those with known hypersensitivity to certain skin irritants should alert the clinician performing the test. Some commercial preparations of fungal antigens contain mercury, a source of irritation to some patients.

Description

The most accurate TB test is the Mantoux test, in which a small amount of TB antigen is injected into the skin. The area is examined 48–72 hours after the injection.

In the patch test, 20–30 adhesive patches are usually placed on the upper back. The patches are kept in place and the area is kept dry for 48 hours. The patches are then removed, and the skin is examined 24 hours afterward, and possibly again a day or more following that. Patch testing is usually performed following a patient complaint of skin irritation from an unknown substance. Testing may suggest several candidates; identifying the right one requires careful review of the patient's possible exposure.

The test of overall T cell responsiveness is performed with several injections. Each area injected is circled and marked. Results are read 48 hours after the injection.

Preparation

No special preparation is necessary.

KEY TERMS

Allergen—A foreign substance that provokes an immune reaction in some sensitive people but not in most others.

Anaphylaxis—An exaggerated, life-threatening hypersensitivity reaction to a previously encountered antigen.

Antibody—An immune system protein made to fight infection.

Antigen—A foreign substance detected that provokes an immune reaction.

Aftercare

Patches should be kept dry. Injection sites may be washed, but excessive rubbing should be avoided. Patches and injection sites may become reddened or irritated. If a patch causes severe **itching** or discomfort, the patient should remove it immediately.

Risks

DHT is quite safe for virtually all people. There is no risk of infection from the agents injected, since they are purified antigens, not whole organisms. Life threatening, hypersensitive reactions (**anaphylaxis**) are a very small risk; patients should notify the administering physician immediately if signs of **wheezing**, swelling, or diffuse redness of the skin develops.

Normal results

Absence of exposure to TB is indicated by absent or very little skin reaction; redness or hardness smaller than 5 mm (about 0.25 in) is considered normal for a person not exposed or infected with TB.

Patch test sites should be normal or only slightly red.

T cell responsiveness tests should be positive; that is, the injected areas should be reddened and hard. Two affected areas of 2 mm or more is considered a positive result.

Abnormal results

TB exposure is indicated by a reaction of 10 mm or more. The degree of redness is not important. A 5–10 mm area could indicate exposure if there is an underlying risk to TB.

Patch test areas that become reddened and irritated indicate reaction to the substance in the patch.

Absence of any reaction to injected areas indicates lack of T cell responsiveness, a condition called anergy. T cell anergy is seen in immune deficiency diseases including **AIDS**, some cases of infectious diseases, malignancies, immunosuppressive therapy (including corticosteroid treatment), some autoimmune diseases, malnutrition, major surgery, and some viral immunizations.

Resources

BOOKS

Davies, R., and S. Ollier. *Allergy: The Facts*. Oxford University Press, 1989.

Lawlor Jr., G. J., et. al. *Manual of Allergy and Immunology.* Little, Brown and Co., 1995.

Richard Robinson

Delirium

Definition

Delirium is a state of mental confusion that develops quickly and usually fluctuates in intensity.

Description

Delirium is a syndrome, or group of symptoms, caused by a disturbance in the normal functioning of the brain. The delirious patient has a reduced awareness of and responsiveness to the environment, which may be manifested as disorientation, incoherence, and memory disturbance. Delirium is often marked by **hallucinations**, **delusions**, and a dream-like state.

Delirium affects at least one in 10 hospitalized patients, and is a common part of many terminal illnesses. Delirium is more common in the elderly than in the general population. While it is not a specific disease itself, patients with delirium usually fare worse than those with the same illness who do not have delirium.

Causes and symptoms

Causes

There are a large number of possible causes of delirium. Metabolic disorders are the single most common cause, accounting for 20–40% of all cases. This type of delirium, termed "metabolic encephalopathy," may result from organ failure, including liver or kidney failure. Other metabolic causes include **diabetes mellitus**, **hyperthyroidism** and **hypothyroidism**, vitamin defi-

ciencies, and imbalances of fluids and electrolytes in the blood. Severe **dehydration** can also cause delirium.

Drug intoxication ("intoxication confusional state") is responsible for up to 20% of delirium cases, either from side effects, overdose, or deliberate ingestion of a mind-altering substance. Medicinal drugs with delirium as a possible side effect or result of overdose include:

- anticholinergics, including atropine, scopolamine, chlorpromazine (an antipsychotic), and diphenhydramine (an antihistamine)
- sedatives, including **barbiturates**, **benzodiazepines**, and ethanol (drinking alcohol)
- antidepressant drugs
- anticonvulsant drugs
- nonsteroidal anti-inflammatory drugs (NSAIDs), including ibuprofen and **acetaminophen**
- corticosteroids, including prednisone
- anticancer drugs, including methotrexate and procarbazine
- lithium
- cimetidine
- antibiotics
- L-dopa

Delirium may result from ingestion of legal or illegal psychoactive drugs, including:

- ethanol (drinking alcohol)
- marijuana
- LSD (**lysergic acid diethylamide**) and other hallucinogens
- amphetamines
- cocaine
- opiates, including heroin and morphine
- PCP (phencyclidine)
- inhalants

Drug withdrawal may also cause delirium. Delirium tremens, or "DTs," may occur during alcohol withdrawal after prolonged or intense consumption. Withdrawal symptoms are also possible from many of the psychoactive prescription drugs.

Poisons may cause delirium ("toxic encephalopathy"), including:

- solvents, such as gasoline, kerosene, turpentine, benzene, and alcohols
- carbon monoxide
- refrigerants (Freon)
- heavy metals, such as lead, mercury, and arsenic
- insecticides, such as Parathion and Sevin
- mushrooms, such as *Amanita* species
- plants such as jimsonweed (*Datura stramonium*) and morning glory (*Ipomoea* spp.)
- animal venoms

Other causes of delirium include:

- infection
- fever
- head trauma
- epilepsy
- brain hemorrhage or infarction
- brain tumor
- low blood oxygen (hypoxemia)
- high blood carbon dioxide (hypercapnia)
- post-surgical complication.

KEY TERMS

Dementia—A loss of mental ability severe enough to interfere with functioning. While dementia and delirium have some of the same symptoms, dementia has a much slower onset.

Electroencephalogram (EEG)— A chart of the brain wave patterns picked up by electrodes placed on the scalp. This is useful for diagnosing central nervous system disorders.

Encephalopathy—A brain dysfunction or disorder.

Symptoms

The symptoms of delirium come on quickly, in hours or days, in contrast to those of **dementia**, which develop much more slowly. Delirium symptoms typically fluctuate through the day, with periods of relative calm and lucidity alternating with periods of florid delirium. The hallmark of delirium is a fluctuating level of consciousness. Symptoms may include:

- decreased awareness of the environment
- confusion or disorientation, especially of time
- memory impairment, especially of recent events
- hallucinations
- illusions and misinterpreted stimuli
- increased or decreased activity level

- mood disturbance, possibly including **anxiety**, euphoria or depression
- language or speech impairment

Diagnosis

Delirium is diagnosed through the medical history and recognition of symptoms during **mental status examination**. The most important part of diagnosis is determining the cause of the delirium. Tests may include blood and urine analysis for levels of drugs, fluids, electrolytes, and blood gases, and to test for infection; lumbar puncture ("spinal tap") to test for central nervous system infection; x ray, **computed tomography scans** (CT), or **magnetic resonance imaging** (MRI) scans to look for tumors, hemorrhage, or other brain abnormality; thyroid tests; **electroencephalography** (EEG); **electrocardiography** (ECG); and possibly others as dictated by the likely cause.

Treatment

Treatment of delirium begins with recognizing and treating the underlying cause. Delirium itself is managed by reducing disturbing stimuli, or providing soothing ones; use of simple, clear language in communication; and reassurance, especially from family members. Physical restraints may be needed if the patient is a danger to himself or others, or if he insists on removing necessary medical equipment such as intravenous lines or monitors. Sedatives or **antipsychotic drugs** may be used to reduce anxiety, hallucinations, and delusions.

Prognosis

Persons with delirium usually have a worse prognosis for the underlying disease than the person without delirium. Nonetheless, those without terminal illness usually recover from delirium. They may not, however, regain all their original cognitive abilities, and may be left with some permanent impairments, including **fatigue**, irritability, difficulty concentrating, or mood changes.

Prevention

Prevention of delirium is focused on treating or avoiding its underlying causes. The most preventable forms are those induced by drugs. Strategies for reducing delirium include following prescriptions, consulting the prescribing physician immediately if symptoms occur, and consulting the physician before discontinuing the drug, even if it has been ineffective; avoiding intoxication with legal or illegal drugs, and seeking professional assistance before suddenly discontinuing an addictive drug such as alcohol or heroin; maintaining good **nutrition**, which promotes general health and can minimize the likelihood of delirium from alcohol intoxication and withdrawal; and avoiding exposure to solvents, insecticides, heavy metals, or biological poisons in the home or workplace.

Resources

BOOKS

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Richard Robinson

Delta virus hepatitis *see* **Hepatitis D**

Delusions

Definition

A delusion is an unshakable belief in something untrue. These irrational beliefs defy normal reasoning, and remain firm even when overwhelming proof is presented to dispute them. Delusions are often accompanied by **hallucinations** and/or feelings of **paranoia**, which act to strengthen confidence in the delusion. Delusions are distinct from culturally or religiously based beliefs that may be seen as untrue by outsiders.

Description

Delusions are a common symptom of several mood and personality-related mental illnesses, including **schizoaffective disorder**, **schizophrenia**, shared psychotic disorder, major depressive disorder, and **bipolar disorder**. They are also the major feature of delusional disorder. Individuals with delusional disorder suffer from long-term, complex delusions that fall into one of six categories: persecutory, grandiose, jealousy, erotomanic, somatic, or mixed. There are also delusional disorders such as **dementia** that clearly have organic or physical causes.

Persecutory

Individuals with persecutory delusional disorder are plagued by feelings of paranoia and an irrational yet unshakable belief that someone is plotting against them, or out to harm them.

Grandiose

Individuals with grandiose delusional disorder have an over-inflated sense of self-worth. Their delusions center on their own importance, such as believing that they have done or created something of extreme value or have a "special mission."

Jealousy

Jealous delusions are unjustified and irrational beliefs that an individual's spouse or significant other has been unfaithful.

Erotomanic

Individuals with erotomanic delusional disorder believe that another person, often a stranger, is in love with them. The object of their affection is typically of a higher social status, sometimes a celebrity. This type of delusional disorder may lead to stalking or other potentially dangerous behavior.

Somatic

Somatic delusions involve the belief that something is physically wrong with the individual. The delusion may involve a medical condition or illness or a perceived deformity. This condition differs from **hypochondriasis** in that the deformity is perceived as a fixed condition not a temporary illness.

Mixed

Mixed delusions are those characterized by two or more of persecutory, grandiose, jealousy, erotomanic, or somatic themes.

Causes and symptoms

Some studies have indicated that delusions may be generated by abnormalities in the limbic system, the portion of the brain on the inner edge of the cerebral cortex that is believed to regulate emotions. The exact source of delusions has not been conclusively found, but potential causes include genetics, neurological abnormalities, and changes in brain chemistry. Delusions are also a known possible side effect of drug use and abuse (e.g., amphetamines, **cocaine**, PCP).

Diagnosis

Patients with delusional symptoms should undergo a thorough **physical examination** and patient history to rule out possible organic causes (such as dementia). If a psychological cause is suspected, a mental health professional will typically conduct an interview with the patient and administer one of several clinical inventories, or tests, to evaluate mental status.

KEY TERMS

Hallucinations—False or distorted sensory experiences that appear to be real perceptions.

Paranoia—An unfounded or exaggerated distrust of others.

Shared psychotic disorder—Also known as folie à deux; shared psychotic disorder is an uncommon disorder in which the same delusion is shared by two or more individuals.

Treatment

Delusions that are symptomatic of delusional disorder should be treated by a psychologist and/or psychiatrist. Though **antipsychotic drugs** are often not effective, antipsychotic medication such as thioridazine (Mellaril), haloperidol (Haldol), chlorpromazine (Thorazine), clozapine (Clozaril), or risperidone (Risperdal) may be prescribed, and cognitive therapy or psychotherapy may be attempted.

If an underlying condition such as schizophrenia, depression, or drug abuse is found to be triggering the delusions, an appropriate course of medication and/or psychosocial therapy is employed to treat the primary disorder. The medication, typically, will include an antipsychotic agent.

Prognosis

Delusional disorder is typically a chronic condition, but with appropriate treatment, a remission of delusional symptoms occurs in up to 50% of patients. However, because of their strong belief in the reality of their delusions and a lack of insight into their condition, individuals with this disorder may never seek treatment, or may be resistant to exploring their condition in psychotherapy.

Resources

BOOKS

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4th ed. Washington, DC: American Psychiatric Press, Inc., 1994.

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Siegel, Ronald K. *Whispers: The Voices of Paranoia*. New York: Crown, 1994.

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Manschreck, Theo C. "Delusional Disorder: The Recognition and Management of Paranoia." *Journal of Clinical Psychiatry* 57, supplement 3 (1996): 32-38.

ORGANIZATIONS

American Psychiatric Association. 1400 K Street NW, Washington DC 20005. (888) 357-7924. <http://www.psych.org>.

American Psychological Association (APA). 750 First St. NE, Washington, DC 20002-4242. (202) 336-5700. <ttp://www.apa.org>.

National Alliance for the Mentally Ill (NAMI). Colonial Place Three, 2107 Wilson Blvd., Ste. 300, Arlington, VA 22201-3042. (800) 950-6264. <http://www.nami.org>.

National Institutes of Mental Health (NIMH). 6001 Executive Boulevard, Rm. 8184, MSC 9663

Paula Anne Ford-Martin

Dementia

Definition

Dementia is a loss of mental ability severe enough to interfere with normal activities of daily living, lasting more than six months, not present since birth, and not associated with a loss or alteration of consciousness.

Description

Dementia is a group of symptoms caused by gradual **death** of brain cells. The loss of cognitive abilities that occurs with dementia leads to impairments in memory, reasoning, planning, and personality. While the overwhelming number of people with dementia are elderly, it is not an inevitable part of **aging**. Instead, dementia is caused by specific brain diseases. **Alzheimer's disease** (AD) is the most common cause, followed by vascular or multi-infarct dementia.

The prevalence of dementia has been difficult to determine, partly because of differences in definition among different studies, and partly because there is some normal decline in functional ability with age. Dementia affects 5–8% of all people between ages 65 and 74, and up to 20% of those between 75 and 84. Estimates for dementia in those 85 and over range from 30–47%. Between two and four million Americans have AD; that number is expected to grow to as many as 14 million by the middle of the twenty-first century as the population as a whole ages.

The cost of dementia can be considerable. While most people with dementia are retired and do not suffer income losses from their disease, the cost of care is often enormous. Financial burdens include lost wages for family caregivers, medical supplies and drugs, and home modifications to ensure safety. Nursing home care may cost several thousand dollars a month or more. The psychological cost is not as easily quantifiable but can be even more profound. The person with dementia loses control of many of the essential features of his life and personality, and loved ones lose a family member even as they continue to cope with the burdens of increasing dependence and unpredictability.

Causes and symptoms

Causes

Dementia is usually caused by degeneration in the cerebral cortex, the part of the brain responsible for thoughts, memories, actions and personality. Death of brain cells in this region leads to the cognitive impairment which characterizes dementia.

The most common cause of dementia is AD, accounting for half to three quarters of all cases. The brain of a person with AD becomes clogged with two abnormal structures, called neurofibrillary tangles and senile plaques. Neurofibrillary tangles are twisted masses of protein fibers inside nerve cells, or neurons. Senile plaques are composed of parts of neurons surrounding a group of proteins called beta-amyloid deposits. Why these structures develop is unknown. Current research indicates possible roles for inflammation, blood flow restriction, and toxic molecular fragments known as free radicals. Several genes have been associated with higher incidences of AD, although the exact role of these genes is still unknown.

Vascular dementia is estimated to cause from 5–30% of all dementias. It occurs from decrease in blood flow to the brain, most commonly due to a series of small strokes (multi-infarct dementia). Other cerebrovascular causes include: **vasculitis** from **syphilis**, **Lyme disease**, or **systemic lupus erythematosus**; **subdural hematoma**; and **subarachnoid hemorrhage**. Because of the usually sudden nature of its cause, the symptoms of vascular dementia tend to begin more abruptly than those of Alzheimer's dementia. Symptoms may progress stepwise with the occurrence of new strokes. Unlike AD, the incidence of vascular dementia is lower after age 75.

Other conditions which may cause dementia include:

- AIDS
- Parkinson's disease
- Lewy body disease
- Pick's disease

- Huntington's disease
- Creutzfeldt-Jakob disease
- brain tumor
- **hydrocephalus**
- head trauma
- multiple sclerosis
- prolonged abuse of alcohol or other drugs
- vitamin deficiency: thiamin, niacin, or B_{12}
- hypothyroidism
- hypercalcemia

Symptoms

Dementia is marked by a gradual impoverishment of thought and other mental activities. Losses eventually affect virtually every aspect of mental life. The slow progression of dementia is in contrast with **delirium**, which involves some of the same symptoms, but has a very rapid onset and fluctuating course with alteration in the level of consciousness. However, delirium may occur with dementia, especially since the person with dementia is more susceptible to the delirium-inducing effects of may types of drugs.

Symptoms include*:*

- Memory losses. Memory loss is usually the first symptom noticed. It may begin with misplacing valuables such as a wallet or car keys, then progress to forgetting appointments, where the car was left, and the route home, for instance. More profound losses follow, such as forgetting the names and faces of family members.
- Impaired abstraction and planning. The person with dementia may lose the ability to perform familiar tasks, to plan activities, and to draw simple conclusions from facts.
- Language and comprehension disturbances. The person may be unable to understand instructions, or follow the logic of moderately complex sentences. Later, he or she may not understand his or her own sentences, and have difficulty forming thoughts into words.
- Poor judgment. The person may not recognize the consequences of his or her actions or be able to evaluate the appropriateness of behavior. Behavior may become ribald, overly-friendly, or aggressive. Personal hygiene may be ignored.
- Impaired orientation ability. The person may not be able to identify the time of day, even from obvious visual clues; or may not recognize his or her location, even if familiar. This disability may stem partly from losses of memory and partly from impaired abstraction.
- Decreased attention and increased restlessness. This may cause the person with dementia to begin an activity and quickly lose interest, and to wander frequently. Wandering may cause significant safety problems, when combined with disorientation and memory losses. The person may begin to cook something on the stove, then become distracted and wander away while it is cooking.
- Personality changes and **psychosis**. The person may lose interest in once-pleasurable activities, and become more passive, depressed, or anxious. **Delusions**, suspicion, **paranoia**, and **hallucinations** may occur later in the disease. Sleep disturbances may occur, including **insomnia** and sleep interruptions.

Diagnosis

Since dementia usually progresses slowly, diagnosing it in its early stages can be difficult. Several office visits over several months or more may be needed. Diagnosis begins with a thorough physical exam and complete medical history, usually including comments from family members or caregivers. A family history of either AD or cerebrovascular disease may provide clues to the cause of symptoms. Simple tests of mental function, including word recall, object naming, and number-symbol matching, are used to track changes in the person's cognitive ability.

Depression is common in the elderly and can be mistaken for dementia; therefore, ruling out depression is an important part of the diagnosis. Distinguishing dementia from the mild normal cognitive decline of advanced age is also critical. The medical history includes a complete listing of drugs being taken, since a number of drugs can cause dementia-like symptoms.

Determining the cause of dementia may require a variety of medical tests, chosen to match the most likely etiology. Cerebrovascular disease, hydrocephalus, and tumors may be diagnosed with x-rays, CT or MRI scans, and vascular imaging studies. Blood tests may reveal nutritional deficiencies or hormone imbalances.

Treatment

Treatment of dementia begins with treatment of the underlying disease, where possible. The underlying causes of nutritional, hormonal, tumor-caused and drug-related dementias may be reversible to some extent. Treatment for stroke-related dementia begins by minimizing the risk of further strokes, through **smoking** cessation, **aspirin** therapy, and treatment of **hypertension**, for instance. There are no therapies that can reverse the progression of AD. Aspirin, estrogen,

vitamin E, and selegiline are currently being evaluated for their ability to slow the rate of progression.

Care for a person with dementia can be difficult and complex. The patient must learn to cope with functional and cognitive limitations, while family members or other caregivers assume increasing responsibility for the person's physical needs. In progressive dementias such as AD, the person may ultimately become completely dependent. Education of the patient and family early on in the disease progression can help them anticipate and plan for inevitable changes.

Symptoms of dementia may be treated with a combination of psychotherapy, environmental modifications, and medication. Drug therapy can be complicated by forgetfulness, especially if the prescribed drug must be taken several times daily.

Behavioral approaches may be used to reduce the frequency or severity of problem behaviors, such as aggression or socially inappropriate conduct. Problem behavior may be a reaction to frustration or overstimulation; understanding and modifying the situations that trigger it can be effective. Strategies may include breaking down complex tasks, such as dressing or feeding, into simpler steps, or reducing the amount of activity in the environment to avoid confusion and agitation. Pleasurable activities, such as crafts, games, and music, can provide therapeutic stimulation and improve mood.

Modifying the environment can increase safety and comfort while decreasing agitation. Home modifications for safety include removal or lock-up of hazards such as sharp knives, dangerous chemicals, and tools. Childproof latches or Dutch doors may be used to limit access as well. Lowering the hot water temperature to 120°F (48.9°C) or less reduces the risk of scalding. Bed rails and bathroom safety rails can be important safety measures, as well. Confusion may be reduced with simpler decorative schemes and presence of familiar objects. Covering or disguising doors (with a mural, for example) may reduce the tendency to wander. Positioning the bed in view of the bathroom can decrease incontinence.

Two drugs, tacrine (Cognex) and donepezil (Aricept), are commonly prescribed for AD. These drugs inhibit the breakdown of acetylcholine in the brain, prolonging its ability to conduct chemical messages between brain cells. They provide temporary improvement in cognitive functions for about 40% of patients with mild to moderate AD. Hydergine is sometimes prescribed as well, though it is of questionable benefit for most patients.

Psychotic symptoms, including paranoia, delusions, and hallucinations, may be treated with **antipsychotic drugs**, such as haloperidol, chlorpromazine, risperidone, and clozapine. Side effects of these drugs can be significant. **Antianxiety drugs** such as Valium may improve behavioral symptoms, especially agitation and **anxiety**, although BuSpar has fewer side effects. The anticonvulsant carbamazepine is also sometimes prescribed for agitation. Depression is treated with antidepressants, usually beginning with **selective serotonin reuptake inhibitors** (SSRIs) such as Prozac or Paxil, followed by **monoamine oxidase inhibitors** or tricyclic antidepressants. **Electroconvulsive therapy** may be appropriate for some patients with severe depression who are unresponsive to drug therapy. In general, medications should be administered very cautiously to demented patients, in the lowest possible effective doses, to minimize side effects. Supervision of taking medications is generally required.

Long-term institutional care may be needed for the person with dementia, as profound cognitive losses often precede death by a number of years. Early planning for the financial burden of nursing home care is critical. Useful information about financial planning for long-term care is available through the Alzheimer's Association.

Family members or others caring for a person with dementia are often subject to extreme **stress**, and may develop feelings of anger, resentment, guilt, and hopelessness, in addition to the sorrow they feel for their loved one and for themselves. Depression is an extremely common consequence of being a full-time caregiver for a person with dementia. Support groups can be an important way to deal with the stress of caregiving. The location and contact numbers for caregiver support groups are available from the Alzheimer's Association; they may also be available through a local social service agency or the patient's physician. Medical treatment for depression may be an important adjunct to group support.

Alternative treatment

Several drugs are currently being tested for their ability to slow the progress of AD. These include acetyl-l-carnitine, which acts on the cellular energy structures known as mitochondria; propentofylline, which may aid circulation; milameline, which acts similarly to tacrine and donezepil; and ginkgo extract.

Ginkgo extract, derived from the leaves of the *Ginkgo biloba* tree, interferes with a circulatory protein called platelet activating factor. It also increases circulation and oxygenation to the brain. Ginkgo extract has been used for many years in China and is widely prescribed in Europe for treatment of circulatory problems. A 1997 study of patients with dementia seemed to show that gingko extract could improve their symptoms, though the study was criticized for certain flaws in its method.

KEY TERMS

Donepezil—A drug commonly prescribed for Alzheimer's disease that provides temporary improvement in cognitive functions for some patients with mild-to-moderate forms of the disease.

Ginkgo extract—Made from the leaves of the *Ginkgo biloba* tree, this extract, used in other countries to treat circulatory problems, may improve the symptoms of patients with dementia.

Neurofibrillary tangles—Abnormal structures, composed of twisted masses of protein fibers within nerve cells, found in the brains of persons with Alzheimer's disease.

Senile plaques—Abnormal structures, composed of parts of nerve cells surrounding protein deposits, found in the brains of persons with Alzheimer's disease.

Tacrine—A drug commonly prescribed for Alzheimer's disease that provides temporary improvement in cognitive functions for some patients with mild-to-moderate forms of the disease.

Prognosis

The prognosis for dementia depends on the underlying disease. On average, people with Alzheimer's disease live eight years past their diagnosis, with a range from one to 20 years. Vascular dementia is usually progressive, with death from **stroke**, infection, or heart disease.

Prevention

There is no known way to prevent Alzheimer's disease, although several of the drugs under investigation may reduce its risk or slow its progression. The risk of developing multi-infarct dementia may be reduced by reducing the risk of stroke.

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Alzheimer's Association. 919 North Michigan Ave., Suite 1000, Chicago, IL 60611. (800) 272-3900. <http://www. alz.org>.

Richard Robinson

Demyelinating disease *see* **Multiple sclerosis**

Dengue fever

Definition

Dengue fever is a disease caused by one of a number of viruses that are carried by mosquitoes. These mosquitoes then transmit the virus to humans.

Description

The virus that causes dengue fever is called an arbovirus, which stands for arthropod-borne virus. Mosquitoes are a type of arthropod. In a number of regions, mosquitoes carry this virus and are responsible for passing it along to humans. These regions include the Middle East, the far East, Africa, and the Caribbean Islands. In these locations, the dengue fever arbovirus is endemic, meaning that the virus naturally and consistently lives in that location. The disease only shows up in the United States sporadically.

In order to understand how dengue fever is transmitted, several terms need to be defined. The word "host" means an animal (including a human) that can be infected with a particular disease. The word "vector" means an organism that can carry a particular disease-causing agent (like a virus or bacteria) without actually developing the disease. The vector can then pass the virus or bacteria on to a new host.

Many of the common illnesses in the United States (including the **common cold**, many viral causes of **diarrhea**, and **influenza** or "flu") are spread because the viruses that cause these illness can be passed directly from person to person. However, dengue fever cannot be passed directly from one infected person to another. Instead, the virus responsible for dengue fever requires an intermediate vector, a mosquito, that carries the virus from one host to another. The mosquito that carries the arbovirus responsible for dengue fever is the same type of mosquito that can transmit other diseases, including **yellow fever**. This mosquito is called *Aedes egypti*. The most common victims are children younger than 10 years of age.

Causes and symptoms

Dengue fever can occur when a mosquito carrying the arbovirus bites a human, passing the virus on to the new host. Once in the body, the virus travels to various glands where it multiplies. The virus can then enter the

bloodstream. The presence of the virus within the blood vessels, especially those feeding the skin, causes changes to these blood vessels. The vessels swell and leak. The spleen and lymph nodes become enlarged, and patches of liver tissue die. A process called disseminated intravascular coagulation (DIC) occurs, where chemicals responsible for clotting are used up and lead to a risk of severe bleeding (hemorrhage).

After the virus has been transmitted to the human host, a period of incubation occurs. During this time (lasting about five to eight days) the virus multiplies. Symptoms of the disease appear suddenly and include high **fever**, chills, **headache**, eye **pain**, red eyes, enlarged lymph nodes, a red flush to the face, lower back pain, extreme weakness, and severe aches in the legs and joints.

This initial period of illness lasts about two–three days. After this time, the fever drops rapidly and the patient sweats heavily. After about a day of feeling relatively well, the patient's temperature increases again, although not as much as the first time. A rash of small red bumps begins on the arms and legs, spreading to the chest, abdomen, and back. It rarely affects the face. The palms of the hands and the soles of the feet become swollen and turn bright red. The characteristic combination of fever, rash, and headache are called the "dengue triad." Most people recover fully from dengue fever, although weakness and **fatigue** may last for several weeks. Once a person has been infected with dengue fever, his or her immune system keeps producing cells that prevent reinfection for about a year.

More severe illness may occur in some people. These people may be experiencing dengue fever for the first time. However, in some cases a person may have already had dengue fever at one time, recovered, and then is reinfected with the virus. In these cases, the first infection teaches the immune system to recognize the presence of the arbovirus. When the immune cells encounter the virus during later infections, the immune system over-reacts. These types of illnesses, called dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS), involve more severe symptoms. Fever and headache are the first symptoms, but the other initial symptoms of dengue fever are absent. The patient develops a **cough**, followed by the appearance of small purplish spots (petechiae) on the skin. These petechiae are areas where blood is leaking out of the vessels. Large bruised areas appear as the bleeding worsens and abdominal pain may be severe. The patient may begin to vomit a substance that looks like coffee grounds. This is actually a sign of bleeding into the stomach. As the blood vessels become more damaged, they leak more and continue to increase in diameter (dilate), causing a decrease in blood flow to all tissues of the body. This state of low blood flow is called shock. Shock can result in damage to the body's organs (especially the heart and kidneys) because low blood flow deprives them of oxygen.

Diagnosis

Diagnosis should be suspected in endemic areas whenever a high fever goes on for two to seven days, especially if accompanied by a bleeding tendency. Symptoms of shock should suggest the progression of the disease to DSS.

The arbovirus causing dengue fever is one of the few types of arbovirus that can be isolated from the serum of the blood. The serum is the fluid in which blood cells are suspended. Serum can be tested because the phase in which the virus travels throughout the bloodstream is longer in dengue fever than in other arboviral infections. A number of tests are used to look for reactions between the patient's serum and laboratory-produced antibodies. Antibodies are special cells that recognize the markers (or antigens) present on invading organisms. During these tests, antibodies are added to a sample of the patient's serum. Healthcare workers then look for reactions that would only occur if viral antigens were present in that serum.

Treatment

There is no treatment available to shorten the course of dengue fever, DHF, or DSS. Medications can be given to lower the fever and to decrease the pain of muscle aches and headaches. Fluids are given through a needle in a vein to prevent **dehydration**. Blood transfusions may be necessary if severe hemorrhaging occurs. Oxygen should be administered to patients in shock.

Prognosis

The prognosis for uncomplicated dengue fever is very good, and almost 100% of patients fully recover. However, as many as 6–30% of all patients die when DHF occurs. The **death** rate is especially high among the youngest patients (under one year old). In places where excellent medical care is available, very close monitoring and immediate treatment of complications lowers the death rate among DHF and DSS patients to about 1%.

Prevention

Prevention of dengue fever means decreasing the mosquito population. Any sources of standing water (buckets, vases, etc.) where the mosquitoes can breed must be eliminated. Mosquito repellant is recommended for those areas where dengue fever is endemic. To help break the cycle of transmission, sick patients should be

KEY TERMS

Endemic—Naturally and consistently present in a certain geographical region.

Host—The organism (such as a monkey or human) in which another organism (such as a virus or bacteria) is living.

Vector—A carrier organism (such as a fly or mosquito) that delivers a virus (or other agent of infection) to a host.

placed in bed nets so that mosquitoes cannot bite them and become arboviral vectors.

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Rosalyn Carson-DeWitt, MD

Dental caries *see* **Tooth decay**

Dental cavity *see* **Tooth decay**

Dental hygiene *see* **Oral hygiene**

Dental injuries *see* **Dental trauma**

Dental trauma

Definition

Dental trauma is injury to the mouth, including teeth, lips, gums, tongue, and jawbones. The most common dental trauma is a broken or lost tooth.

Description

Dental trauma may be inflicted in a number of ways: contact sports, motor vehicle accidents, fights, falls, eating hard foods, drinking hot liquids, and other such mishaps. As oral tissues are highly sensitive, injuries to the mouth are typically very painful. Dental trauma should receive prompt treatment from a dentist.

Causes and symptoms

Soft tissue injuries, such as a "fat lip," a burned tongue, or a cut inside the cheek, are characterized by **pain**, redness, and swelling with or without bleeding. A broken tooth often has a sharp edge that may cut the tongue and cheek. Depending on the position of the fracture, the tooth may or may not cause **toothache** pain. When a tooth is knocked out (evulsed), the socket is swollen, painful, and bloody. A jawbone may be broken if the upper and lower teeth no longer fit together properly (**malocclusion**), or if the jaws have pain with limited ability to open and close (mobility), especially around the temporomandibular joint (TMJ).

Diagnosis

Dental trauma is readily apparent upon examination. Dental x rays may be taken to determine the extent of the damage to broken teeth. More comprehensive x rays are needed to diagnose a broken jaw.

Treatment

Soft tissue injuries may require only cold compresses to reduce swelling. Bleeding may be controlled with direct pressure applied with clean gauze. Deep lacerations and punctures may require stitches. Pain may be managed with **aspirin** or **acetaminophen** (Tylenol, Aspirin Free Excedrin) or ibuprofen (Motrin, Advil).

Treatment of a broken tooth will vary depending on the severity of the fracture. For immediate first aid, the injured tooth and surrounding area should be rinsed gently with warm water to remove dirt, then covered with a cold compress to reduce swelling and ease pain. A dentist should examine the injury as soon as possible. Any pieces from the broken tooth should be saved and brought along.

If a piece of the outer tooth has chipped off, but the inner core (pulp) is undisturbed, the dentist may simply smooth the rough edges or replace the missing section with a small composite filling. In some cases, a fragment of broken tooth may be bonded back into place. If enough tooth is missing to compromise the entire tooth structure, but the pulp is not permanently damaged, the tooth will require a protective coverage with a gold or

porcelain crown. If the pulp has been seriously damaged, the tooth will require **root canal treatment** before it receives a crown. A tooth that is vertically fractured or fractured below the gumline will require root canal treatment and protective restoration. A tooth which no longer has enough remaining structure to retain a crown may have to be extracted (surgically removed).

When a permanent tooth has been knocked out, it may be saved with prompt action. The tooth must be found immediately after it has been lost. It should be picked up by the natural crown (the top part covered by hard enamel). It must not be handled by the root. If the tooth is dirty, it may be gently rinsed under running water. It should never be scrubbed, and it should never be washed with soap, toothpaste, mouthwash, or other chemicals. The tooth should not be dried or wrapped in a tissue or cloth. It must be kept moist at all times.

The tooth may be placed in a clean container of milk, cool water with or without a pinch of salt, or in saliva. If possible, the patient and the tooth should be brought to the dentist within 30 minutes of the tooth loss. Rapid action improves the chances of successful re-implantation; however, it is possible to save a tooth after 30 minutes, if the tooth has been kept moist and handled properly.

The body usually rejects re-implantation of a primary (baby) tooth. In this case, the empty socket is treated as a soft tissue injury and monitored until the permanent tooth erupts.

A broken jaw must be set back into its proper position and stabilized with wires while it heals. Healing may take six weeks or longer, depending on the patient's age and the severity of the fracture.

Alternative treatment

There is no substitute for treatment by a dentist or other medical professional. There are, however, homeopathic remedies and herbs that can be used simultaneously with dental care and throughout the healing process. Homeopathic arnica (*Arnica montana*) should be taken as soon as possible after the injury to help the body deal with the trauma. Repeating a dose several times daily for the duration of healing is also useful. Homeopathic hypericum (*Hypericum perforatum*) can be taken if nerve pain is involved, especially with a **tooth extraction** or root canal. Homeopathic comfrey (*Symphytum officinale)* may be helpful in treating pain due to broken jaw bones, but should only be used after the bones have been reset. Calendula (*Calendula officinalis*) and plantain (*Plantago major*) can be used as a mouth rinse to enhance tissue healing. These herbs should not be used with deep lacerations that need to heal from the inside first.

KEY TERMS

Crown—1 The natural part of the tooth covered by enamel. 2 A restorative crown is a protective shell that fits over a tooth.

Eruption—The process of a tooth breaking through the gum tissue to grow into place in the mouth.

Evulsion—The forceful, and usually accidental, removal of a tooth from its socket in the bone.

Extraction—The surgical removal of a tooth from its socket in the bone.

Malocclusion—A problem in the way the upper and lower teeth fit together in biting or chewing.

Pulp—The soft innermost layer of a tooth containing blood vessels and nerves.

Root canal treatment—The process of removing diseased or damaged pulp from a tooth, then filling and sealing the pulp chamber and root canals.

Temporomandibular joint (TMJ)—The jaw joint formed by the mandible (lower jaw bone) moving against the temporal (temple and side) bone of the skull.

Prognosis

When dental trauma receives timely attention and proper treatment, the prognosis for healing is good. As with other types of trauma, infection may be a complication, but a course of antibiotics is generally effective.

Prevention

Most dental trauma is preventable. Car seat belts should always be worn, and young children should be secured in appropriate car seats. Homes should be monitored for potential tripping and slipping hazards. Childproofing measures should be taken, especially for toddlers. In addition to placing gates across stairs and padding sharp table edges, electrical cords should be tucked away. Young children may receive severe oral **burns** from gnawing on live power cords.

Everyone who participates in contact sports should wear a mouthguard to avoid dental trauma. Athletes in football, ice hockey, wrestling, and boxing commonly wear mouthguards. The mandatory use of mouthguards in football prevents about 200,000 oral injuries annually. Mouthguards should also be worn along with helmets in noncontact sports such as skateboarding, in-line skating,

and bicycling. An athlete who does not wear a mouthguard is 60 times more likely to sustain dental trauma than one who does. Any activity involving speed, an increased chance of falling, and potential contact with a hard piece of equipment has the likelihood of dental trauma that may be prevented or substantially reduced in severity with the use of mouthguards.

Resources

ORGANIZATIONS

American Academy of Pediatric Dentistry. 211 East Chicago Ave., Ste. 700, Chicago, IL 60611-2616. (312) 337-2169. <http://www.aapd.org>.

American Association of Endodontists. 211 East Chicago Ave., Ste. 1100, Chicago, IL 60611-2691. (800) 872-3636. <http://www.aae.org>.

American Association of Oral and Maxillofacial Surgeons. 9700 West Bryn Mawr Ave., Rosemont, IL 60018-5701. (847) 678-6200. <http://www.aaoms.org>.

American Dental Association. 211 E. Chicago Ave., Chicago, IL 60611. (312) 440-2500. <http://www.ada.org>.

Donald Gardner Barstow

Depersonalization disorder *see* **Dissociative disorders**

Depo-Provera/Norplant

Definition

Norplant is a long-acting hormone that is inserted under the skin and prevents conception for up to five years. Depo-Provera is also a hormone, but is administered by intramuscular injection and provides protection against **pregnancy** for three months. Lunelle is another injectable contraceptive that is administered monthly (every 28 to 30 days); it was approved by the Food and Drug Administration (FDA) in October 2000. The hormone in Norplant and Depo-Provera is progestin, a synthetic hormone similar to one found naturally in a woman's body; Lunelle contains the hormones progestin and estrogen.

Purpose

The purpose of these hormones is to prevent pregnancy; they are about 99% effective in achieving this goal. No hormonal contraceptive methods provide protection from **AIDS** or other **sexually transmitted diseases**.

Depo-Provera and Lunelle are given as an injection and work in several ways to prevent conception. First, the egg (ovum) is prevented from maturing and being released. The mucus in the cervix (opening into the uterus or womb) becomes thicker, making it difficult for the sperm to enter. Depo-Provera and Lunelle also cause the lining of the uterus to become thinner, making implantation of a fertilized egg unlikely.

A physician inserts a contraceptive implant under the skin of a woman's arm. *(Photo Researchers, Inc. Reproduced by permission.)*

An injection of Depo-Provera or Lunelle must be given within the first five days of a normal period. Depo-Provera provides protection against pregnancy for three months, while Lunelle provides similar protection for one month. Ovulation (release of a mature egg) typically occurs within 60 days of the last injection of Lunelle, about twice as fast after use of Depo-Provera. Also, because Lunelle is a combined hormone contraceptive as opposed to progestin-only Depo-Provera and Norplant, it is less likely to cause irregular or absent menstruation.

Norplant capsules contain a synthetic hormone that is slowly released over a period of up to five years. It functions like Depo-Provera in that it prevents the ovaries from producing ova (eggs) and also results in thicker mucus in the cervix, which prevents the sperm from passing through the cervix. Norplant can be inserted at any time.

Preparation

The woman being considered for Depo-Provera or Lunelle will have a pelvic and breast examination, a **Pap test** (a microscopic examination of cell samples taken from the cervix), blood pressure check, weight check, and a review of her medical history. Women who have **diabetes mellitus**, major depression, blood clotting problems, liver disease, or weight problems should use these methods only under strict medical supervision. Depo-Provera or Lunelle should not be used if the woman is pregnant, has unexplained vaginal bleeding,

KEY TERMS

Hormone—A chemical produced in a gland or organ and transported by the blood to another area of the body where it produces a specific effect.

Pap test—A microscopic examination of cell samples taken from the cervix.

suffers from severe liver disease, has **breast cancer**, or has a history of blood clots or **stroke**.

Individuals who select Norplant will receive the same basic **physical examination**. If approved for this method, a site of implantation will be selected (usually the inside of the upper arm), and the area prepared for minor surgery. The skin will be washed with soap and water, and an antiseptic, such as iodine solution, will be applied. The physician will use a local anesthetic to numb the area, a small incision will be made, the six Norplant capsules will be inserted, and the incision sewn up (sutured). Protection against pregnancy normally begins within 24 hours. If necessary, the implants can be removed in 15–20 minutes. Norplant should not be used by women who are pregnant, have blood clotting problems, or have unexplained vaginal bleeding. Advantages include light periods with less cramping and decreased anemia. This form of birth control may also be protective against **endometrial cancer**.

Because Depo-Provera and Norplant use only the hormone progestin, they may provide an alternative for women who can not use estrogen-containing birth control pills. One benefit of Lunelle, however, is that its effects wear off more quickly than Depo-Provera, an important factor in the event that a woman has serious side effects or wants to become pregnant.

Risks

The most common side effects associated with Depo-Provera and Lunelle are yellowing of the skin, **headache**, nervousness, **dizziness**, abdominal **pain**, hair loss, rash, increase in the number of migraine headaches, increased or decreased interest in sexual intercourse, the development of dark spots on the skin, depression, and weakness. Danger signs that need to reported immediately include weight gain, heavy vaginal bleeding, frequent urination, blurred vision, **fainting**, severe abdominal pain, and coughing up blood. Because the effects of Depo-Provera may last up to 12 weeks, it may take a longer time for women trying to conceive to become pregnant after discontinuing the injections.

The main reactions to Norplant include headache, weight gain, irregular periods or no period at all, breast tenderness, **acne**, gain or loss of facial hair, color changes of the skin over the area of insertion, and **ovarian cysts**. The doctor should be notified immediately of lumps in the breast, heavy vaginal bleeding, yellowing of the skin or eyes, or infection of the incision. Women who use Norplant are discouraged from **smoking**.

Normal results

These hormone contraceptive methods normally result in a success rate of 99%.

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Donald Gardner Barstow

Depression *see* **Bipolar disorder; Postpartum depression**

Depressive disorders

Definition

Depression or depressive disorders (unipolar depression) are mental illnesses characterized by a profound and persistent feeling of sadness or despair and/or a loss of interest in things that were once pleasurable. Disturbance in sleep, appetite, and mental processes are a common accompaniment.

Description

Everyone experiences feelings of unhappiness and sadness occasionally. But when these depressed feelings start to dominate everyday life and cause physical and mental deterioration, they become what are known as depressive disorders. Each year in the United States, depressive disorders affect an estimated 17 million people at an approximate annual direct and indirect cost of $53 billion. One in four women is likely to experience an episode of severe depression in her lifetime, with a 10–20% lifetime prevalence, compared to 5–10% for men. The average age a first depressive episode occurs is in the mid-20s, although the disorder strikes all age groups indiscriminately, from children to the elderly.

There are two main categories of depressive disorders: major depressive disorder and dysthymic disorder. Major depressive disorder is a moderate to severe episode of depression lasting two or more weeks. Individuals experiencing this major depressive episode may have trouble sleeping, lose interest in activities they once took pleasure in, experience a change in weight, have difficulty concentrating, feel worthless and hopeless, or have a preoccupation with **death** or suicide. In children, the major depression may appear as irritability.

While major depressive episodes may be acute (intense but short-lived), dysthymic disorder is an ongoing, chronic depression that lasts two or more years (one or more years in children) and has an average duration of 16 years. The mild to moderate depression of dysthymic disorder may rise and fall in intensity, and those afflicted with the disorder may experience some periods of normal, non-depressed mood of up to two months in length. Its onset is gradual, and dysthymic patients may not be able to pinpoint exactly when they started feeling depressed. Individuals with dysthymic disorder may experience a change in sleeping and eating patterns, low self-esteem, **fatigue**, trouble concentrating, and feelings of hopelessness.

Depression can also occur in **bipolar disorder**, an affective mental illness that causes radical emotional changes and mood swings, from manic highs to depressive lows. The majority of bipolar individuals experience alternating episodes of **mania** and depression.

Causes and symptoms

The causes behind depression are complex and not yet fully understood. While an imbalance of certain neurotransmitters—the chemicals in the brain that transmit messages between nerve cell— is believed to be key to depression, external factors such as upbringing (more so in dysthymia than major depression) may be as important. For example, it is speculated that, if an individual is abused and neglected throughout childhood and adolescence, a pattern of low self-esteem and negative thinking may emerge. From that, a lifelong pattern of depression may follow.

Signs Of Mental Depression

Depressed mood
Lack of interest or pleasure in daily activities
Significant weight loss (without dieting) or weight gain
Difficulty sleeping or excessive sleeping
Loss of energy
Feelings of worthlessness or guilt
Difficulty in making decisions
Restlessness
Recurrent thoughts of death

Heredity does seem to play a role in who develops depressive disorders. Individuals with major depression in their immediate family are up to three times more likely to have the disorder themselves. It would seem that biological and genetic factors may make certain individuals pre-disposed or prone to depressive disorders, but environmental circumstances may often trigger the disorder.

External stressors and significant life changes, such as chronic medical problems, death of a loved one, divorce or estrangement, **miscarriage**, or loss of a job, can also result in a form of depression known as adjustment disorder. Although periods of adjustment disorder usually resolve themselves, occasionally they may evolve into a major depressive disorder.

Major depressive episode

Individuals experiencing a major depressive episode have a depressed mood and/or a diminished interest or pleasure in activities. Children experiencing a major depressive episode may appear or feel irritable rather than depressed. In addition, five or more of the following symptoms will occur on an almost daily basis for a period of at least two weeks:

- Significant change in weight.
- **Insomnia** or hypersomnia (excessive sleep).
- Psychomotor agitation or retardation.
- Fatigue or loss of energy.
- Feelings of worthlessness or inappropriate guilt.
- Diminished ability to think or to concentrate, or indecisiveness.
- Recurrent thoughts of death or suicidal and/or suicide attempts.

Recent scientific research has indicated that the size of the subgenual prefrontal cortex of the brain (located behind the bridge of the nose) may be a determining factor in hereditary depressive disorders. *(Illustration by Electronic Illustrators Group.)*

Dysthymic disorder

Dysthymia commonly occurs in tandem with other psychiatric and physical conditions. Up to 70% of dysthymic patients have both dysthymic disorder and major depressive disorder, known as double depression. Substance abuse, panic disorders, **personality disorders**, social **phobias**, and other psychiatric conditions are also found in many dysthymic patients. Dysthymia is prevalent in patients with certain medical conditions, including **multiple sclerosis**, **AIDS**, **hypothyroidism**, **chronic fatigue syndrome**, **Parkinson's disease**, diabetes, and post-cardiac transplantation. The connection between dysthymic disorder and these medical conditions is unclear, but it may be related to the way the medical condition and/or its pharmacological treatment affects neurotransmitters. Dysthymic disorder can lengthen or complicate the recovery of patients also suffering from medical conditions.

Along with an underlying feeling of depression, people with dysthymic disorder experience two or more of the following symptoms on an almost daily basis for a period for two or more years (most suffer for five years), or one year or more for children:

- under or overeating
- insomnia or hypersomnia
- low energy or fatigue
- low self-esteem
- poor concentration or trouble making decisions
- feelings of hopelessness

Diagnosis

In addition to an interview, several clinical inventories or scales may be used to assess a patient's mental status and determine the presence of depressive symptoms. Among these tests are: the Hamilton Depression Scale (HAM-D), Child Depression Inventory (CDI), Geriatric Depression Scale (GDS), Beck Depression Inventory (BDI), and the Zung Self-Rating Scale for Depression. These tests may be administered in an outpatient or hospital setting by a general practitioner, social worker, psychiatrist, or psychologist.

Treatment

Major depressive and dysthymic disorders are typically treated with antidepressants or psychosocial therapy. Psychosocial therapy focuses on the personal and interpersonal issues behind depression, while antidepressant medication is prescribed to provide more immediate relief for the symptoms of the disorder. When used together correctly, therapy and antidepressants are a powerful treatment plan for the depressed patient.

Antidepressants

Selective serotonin reuptake inhibitors (SSRIs) such as fluoxetine (Prozac) and sertraline (Zoloft) reduce depression by increasing levels of serotonin, a neurotransmitter. Some clinicians prefer SSRIs for treatment of dysthymic disorder. **Anxiety**, **diarrhea**, drowsiness, **headache**, sweating, nausea, poor sexual functioning, and insomnia are all possible side effects of SSRIs.

Tricyclic antidepressants (TCAs) are less expensive than SSRIs, but have more severe side-effects, which may include persistent **dry mouth**, **sedation**, **dizziness**, and cardiac **arrhythmias**. Because of these side effects, caution is taken when prescribing TCAs to elderly patients. TCAs include amitriptyline (Elavil), imipramine (Tofranil), and nortriptyline (Aventyl, Pamelor). A 10-day supply of TCAs can be lethal if ingested all at once, so these

drugs may not be a preferred treatment option for patients at risk for suicide.

Monoamine oxidase inhibitors (MAOIS) such as tranylcypromine (Parnate) and phenelzine (Nardil) block the action of monoamine oxidase (MAO), an enzyme in the central nervous system. Patients taking MAOIs must cut foods high in tyramine (found in aged cheeses and meats) out of their diet to avoid potentially serious hypertensive side effects.

Heterocyclics include bupropion (Wellbutrin) and trazodone (Desyrel). Bupropion should not be prescribed to patients with a **seizure disorder**. Side effects of the drug may include agitation, anxiety, confusion, tremor, dry mouth, fast or irregular heartbeat, headache, low blood pressure, and insomnia. Because trazodone has a sedative effect, it is useful in treating depressed patients with insomnia. Other possible side effects of trazodone include dry mouth, gastrointestinal distress, dizziness, and headache.

Psychosocial therapy

Psychotherapy explores an individual's life to bring to light possible contributing causes of the present depression. During treatment, the therapist helps the patient to become self-aware of his or her thinking patterns and how they came to be. There are several different subtypes of psychotherapy, but all have the common goal of helping the patient develop healthy problem solving and coping skills.

Cognitive-behavioral therapy assumes that the patient's faulty thinking is causing the current depression and focuses on changing the depressed patient's thought patterns and perceptions. The therapist helps the patient identify negative or distorted thought patterns and the emotions and behavior that accompany them, and then retrains the depressed individual to recognize the thinking and react differently to it.

Electroconvulsant therapy

ECT, or **electroconvulsive therapy**, is usually employed after all therapy and pharmaceutical treatment options have been explored. However, it is sometimes used early in treatment when severe depression is present and the patient refuses oral medication, or when the patient is becoming dehydrated, extremely suicidal, or psychotic.

The treatment consists of a series of electrical pulses that move into the brain through electrodes on the patient's head. ECT is given under general anesthesia and patients are administered a muscle relaxant to prevent convulsions. Although the exact mechanisms behind the success of ECT therapy are not known, it is believed that the electrical current modifies the electrochemical processes of the brain, consequently relieving depression. Headaches, muscle soreness, nausea, and confusion are possible side effects immediately following an ECT procedure. Memory loss, typically transient, has also been reported in ECT patients.

Positron emission tomography (PET) scans comparing a normal brain with that of someone with a depressed mental disorder. *(Photo Researchers, Inc. Reproduced by permission.)*

Alternative treatment

St. John's wort (*Hypericum perforatum*) is used throughout Europe to treat depressive symptoms. Unlike traditional prescription antidepressants, this herbal antidepressant has few reported side effects. Some users may experience high blood pressure, headaches, stiff neck, nausea, and vomiting. As of early 1998, United States. clinical trials organized by the National Institute of Mental Health were still in the planning phase. Its efficacy in severe depression is very uncertain.

Homeopathic treatment can also be very therapuetic in treating depression. Good **nutrition**, proper sleep,

KEY TERMS

Hypersomnia— The need to sleep excessively; a symptom of dysthymic and major depressive disorder.

Neurotransmitter—A chemical in the brain that transmits messages between neurons, or nerve cells. Changes in the levels of certain neurotransmitters, such as serotonin, norepinephrine, and dopamine, are thought to be related to depressive disorders.

Psychomotor agitation—Disturbed physical and mental processes (e.g., fidgeting, wringing of hands, racing thoughts); a symptom of major depressive disorder.

Psychomotor retardation—Slowed physical and mental processes (e.g., slowed thinking, walking, and talking); a symptom of major depressive disorder.

exercise, and full engagement in life are very important to a healthy mental state.

Prognosis

Untreated or improperly treated depression is the number one cause of suicide in the United States. Proper treatment relieves symptoms in 80–90% of depressed patients. After each major depressive episode, the risk of recurrence climbs significantly—50% after one episode, 70% after two episodes, and 90% after three episodes. For this reason, patients need to be aware of the symptoms of recurring depression and may require long-term maintenance treatment of antidepressants and/or therapy.

Prevention

Patient education in the form of therapy or self-help groups is crucial for training patients with depressive disorders to recognize symptoms of depression and to take an active part in their treatment program. Extended maintenance treatment with antidepressants may be required in some patients to prevent relapse. Early intervention with children with depression is effective in arresting development of more severe problems.

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American Psychological Association (APA). 750 First St. NE, Washington, DC 20002-4242. (202) 336-5700. <http://www.apa.org>.

National Alliance for the Mentally Ill (NAMI). Colonial Place Three, 2107 Wilson Blvd., Ste. 300, Arlington, VA 22201-3042. (800) 950-6264. <http://www.nami.org>.

National Depressive and Manic-Depressive Association (NDMDA). 730 N. Franklin St., Suite 501, Chicago, IL 60610. (800) 826-3632. <http://www.ndmda.org>.

National Institute of Mental Health. Mental Health Public Inquiries, 5600 Fishers Lane, Room 15C-05, Rockville, MD 20857. (888) 826-9438. <http://www.nimh.nih.gov>.

Paula Anne Ford-Martin

Dermabrasion *see* **Skin resurfacing**

Dermatitis

Definition

Dermatitis is a general term used to describe inflammation of the skin.

Description

Most types of dermatitis are characterized by an itchy pink or red rash.

Contact dermatitis is an allergic reaction to something that irritates the skin and is manifested by one or more lines of red, swollen, blistered skin that may itch or

seep. It usually appears within 48 hours after touching or brushing against a substance to which the skin is sensitive. The condition is more common in adults than in children.

Contact dermatitis can occur on any part of the body, but it usually affects the hands, feet, and groin. Contact dermatitis usually does not spread from one person to another, nor does it spread beyond the area exposed to the irritant unless affected skin comes into contact with another part of the body. However, in the case of some irritants, such as poison ivy, contact dermatitis can be passed to another person or to another part of the body.

Stasis dermatitis is characterized by scaly, greasy looking skin on the lower legs and around the ankles. Stasis dermatitis is most apt to affect the inner side of the calf.

Nummular dermatitis, which is also called nummular eczematous dermatitis or nummular eczema, generally affects the hands, arms, legs, and buttocks of men and women older than 55 years of age. This stubborn inflamed rash forms circular, sometimes itchy, patches and is characterized by flares and periods of inactivity.

Atopic dermatitis is characterized by **itching**, scaling, swelling, and sometimes blistering. In early childhood it is called infantile eczema and is characterized by redness, oozing, and crusting. It is usually found on the face, inside the elbows, and behind the knees.

Seborrheic dermatitis may be dry or moist and is characterized by greasy scales and yellowish crusts on the scalp, eyelids, face, external surfaces of the ears, underarms, breasts, and groin. In infants it is called "cradle cap."

Causes and symptoms

Allergic reactions are genetically determined, and different substances cause contact dermatitis to develop in different people. A reaction to resin produced by poison ivy, poison oak, or poison sumac is the most common source of symptoms. It is, in fact, the most common allergy in this country, affecting one of every two people in the United States.

Flowers, herbs, and vegetables can also affect the skin of some people. **Burns** and **sunburn** increase the risk of dermatitis developing, and chemical irritants that can cause the condition include:

- chlorine
- cleansers
- detergents and soaps
- fabric softeners
- glues used on artificial nails
- perfumes
- topical medications

Dermatitis on hands and fingers. *(Custom Medical Stock Photo. Reproduced by permission.)*

Contact dermatitis can develop when the first contact occurs or after years of use or exposure.

Stasis dermatitis, a consequence of poor circulation, occurs when leg veins can no longer return blood to the heart as efficiently as they once did. When that happens, fluid collects in the lower legs and causes them to swell. Stasis dermatitis can also result in a rash that can break down into sores known as stasis ulcers.

The cause of nummular dermatitis is not known, but it usually occurs in cold weather and is most common in people who have dry skin. Hot weather and **stress** can aggravate this condition, as can the following:

- **allergies**
- fabric softeners
- soaps and detergents
- wool clothing
- bathing more than once a day

Atopic dermatitis can be caused by allergies, **asthma**, or stress, and there seems to be a genetic predisposition for atopic conditions. It is sometimes caused by an allergy to nickel in jewelry.

Seborrheic dermatitis (for which there may also be a genetic predisposition) is usually caused by overproduction of the oil glands. In adults it can be associated with **diabetes mellitus** or gold allergy. In infants and adults it may be caused by a biotin deficiency.

Diagnosis

The diagnosis of dermatitis is made on the basis of how the rash looks and its location. The doctor may scrape off a small piece of affected skin for microscopic examination or direct the patient to discontinue use of any potential irritant that has recently come into contact with

KEY TERMS

Allergic reaction—An inappropriate or exaggerated genetically determined reaction to a chemical that occurs only on the second or subsequent exposures to the offending agent, after the first contact has sensitized the body.

Corticosteriod—A group of synthetic hormones that are used to prevent or reduce inflammation. Toxic effects may result from rapid withdrawal after prolonged use or from continued use of large doses.

Patch test—A skin test that is done to identify allergens. A suspected substance is applied to the skin. After 24–48 hours, if the area is red and swollen, the test is positive for that substance. If no reaction occurs, another substance is applied. This is continued until the patient experiences an allergic reaction where the irritant was applied to the skin.

Rash—A spotted, pink or red skin eruption that may be accompanied by itching and is caused by disease, contact with an allergen, food ingestion, or drug reaction.

Ulcer—An open sore on the skin, resulting from tissue destruction, that is usually accompanied by redness, pain, or infection.

the affected area. Two weeks after the rash disappears, the patient may resume use of the substances, one at a time, until the condition recurs. Eliminating the substance most recently added should eliminate the irritation.

If the origin of the irritation has still not been identified, a dermatologist may perform one or more patch tests. This involves dabbing a small amount of a suspected irritant onto skin on the patient's back. If no irritation develops within a few days, another patch test is performed. The process continues until the patient experiences an allergic reaction at the spot where the irritant was applied.

Treatment

Treating contact dermatitis begins with eliminating or avoiding the source of irritation. Prescription or over-the-counter corticosteroid creams can lessen inflammation and relieve irritation. Creams, lotions, or ointments not specifically formulated for dermatitis can intensify the irritation. Oral **antihistamines** are sometimes recommended to alleviate itching, and **antibiotics** are prescribed if the rash becomes infected. Medications taken by mouth to relieve symptoms of dermatitis can make skin red and scaly and cause hair loss.

Patients who have a history of dermatitis should remove their rings before washing their hands. They should use bath oils or glycerine-based soaps and bathe in lukewarm saltwater.

Patting rather than rubbing the skin after bathing and thoroughly massaging lubricating lotion or nonprescription cortisone creams into still-damp skin can soothe red, irritated nummular dermatitis. Highly concentrated cortisone preparations should not be applied to the face, armpits, groin, or rectal area. Periodic medical monitoring is necessary to detect side effects in patients who use such preparations on **rashes** covering large areas of the body.

Coal-tar salves can help relieve symptoms of nummular dermatitis that have not responded to other treatments, but these ointments have an unpleasant odor and stain clothing.

Patients who have stasis dermatitis should elevate their legs as often as possible and sleep with a pillow between the lower legs.

Tar or zinc paste may also be used to treat stasis dermatitis. Because these compounds must remain in contact with the rash for as long as two weeks, the paste and bandages must be applied by a nurse or a doctor.

Coal-tar shampoos may be used for seborrheic dermatitis that occurs on the scalp. Sun exposure after the use of these shampoos should be avoided because the risk of sunburn of the scalp is increased.

Alternative treatment

Some herbal therapies can be useful for skin conditions. Among the herbs most often recommended are:

- Burdock root (*Arctium lappa*)
- Calendula (*Calendula officinalis*) ointment
- Chamomile (*Matricaria recutita*) ointment
- Cleavers (*Galium* ssp.)
- Evening primrose oil (*Oenothera biennis*)
- Nettles (*Urtica dioica*)

Contact dermatitis can be treated botanically and homeopathically. Grindelia (*Grindelia* spp.) and sassafras (*Sassafras albidum*) can help when applied topically. Determining the source of the problem and eliminating it is essential. Oatmeal baths are very helpful in relieving the itch. Bentonite clay packs or any mud pack draws the fluid out, and helps dry up the lesions. Cortisone creams are not recommended.

Stasis dermatitis should be treated by a trained practitioner. This condition responds well to topical herbal therapies, however, the cause must also be addressed.

Selenium-based shampoos, topical applications of flax oil and/or olive oil, and biotin supplementation are among the therapies recommended for seborrheic dermatitis.

Prognosis

Dermatitis is often chronic, but symptoms can generally be controlled.

Prevention

Contact dermatitis can be prevented by avoiding the source of irritation. If the irritant cannot be avoided completely, the patient should wear gloves and other protective clothing whenever exposure is likely to occur.

Immediately washing the exposed area with soap and water can stem allergic reactions to poison ivy, poison oak, or poison sumac, but because soaps can dry the skin, patients susceptible to dermatitis should use them only on the face, feet, genitals, and underarms.

Clothing should be loose fitting and 100% cotton. New clothing should be washed in dye-free, unscented detergent before being worn.

Injury to the lower leg can cause stasis dermatitis to ulcerate (form open sores). If stasis ulcers develop, a doctor should be notified immediately.

Yoga and other relaxation techniques may help prevent atopic dermatitis caused by stress.

Avoidance of sweating may aid in preventing seborrheic dermatitis.

A patient who has dermatitis should also notify a doctor if any of the following occurs:

- fever develops
- skin oozes or other signs of infection appear
- symptoms do not begin to subside after seven days' treatment
- he/she comes into contact with someone who has a wart, **cold sore**, or other viral skin infection

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Maureen Haggerty

Dermatophyte infections *see* **Ringworm**

DES exposure

Definition

DES (diethylstilbestrol) is a hormone that was prescribed for pregnant women in the 1950s and early 1960s. Many years later, doctors discovered that the daughters of the women who received DES were at high risk for a variety of problems, including **infertility**, **premature labor**, and **cancer** of the vagina and cervix.

Description

In the 1950s and early 1960s, several drug companies claimed that DES (diethylstilbestrol) could prevent miscarriages. DES is a synthetic hormone, related to estrogen. Since up to 20% of all pregnancies end in **miscarriage**, this seemed like an important breakthrough and DES was prescribed for many women who had bleeding in early **pregnancy**. Ultimately, it was found to have no effect on miscarriages and the practice of prescribing DES was stopped in the 1960s. Almost 10 years later, the daughters of women who had taken DES during pregnancy began to develop unusual symptoms.

Doctors discovered that when these young women reached their teens, they were at higher risk for a variety of problems, including:

- clear cell adenocarcinoma of the vagina and cervix
- infertility
- premature labor and other problems in pregnancy

Causes and symptoms

DES has affected a very specific group of women. These are women who were exposed to DES in utero before 18 weeks of pregnancy. In other words, their mothers must have taken DES within the first four to five months of pregnancy. It is now known that the female reproductive organs are formed during that time. DES

KEY TERMS

Cervix—The opening at the bottom of the uterus.

Colposcopy—A special examination of the cervix using a magnifying scope. This is a procedure that can be done in the doctor's office.

Fallopian tubes—The tubes that carry the ovum (egg) from the ovary to the uterus.

Pap smear—A screening test for precancerous and cancerous cells on the cervix. This simple test is done during a routine pelvic exam and involves scraping cells from the cervix.

appears to interfere with proper growth and development of the uterus, cervix, vagina, and fallopian tubes.

In the early 1970s, there was an increase in a rare form of cancer, clear cell adenocarcinoma of the vagina and cervix. Up until that time, doctors had seen these cancers only in elderly women. Suddenly, young women who had the disease appeared.

This was so unusual that researchers studied these women to see if they had anything in common. After a great deal of questioning and examination, it was found that they all had one factor in common. All of the young women had been exposed to DES in utero in the early weeks of pregnancy.

Today, it is difficult to imagine how shocking this discovery was. Doctors had only recently recognized that medications and exposure to chemicals during pregnancy could cause **birth defects**. This was a birth defect that had gone undetected for almost two decades.

Since then, doctors have studied DES daughters very carefully. Fortunately, the risk of clear cell adenocarcinoma is actually quite low. In fact, it appears that if a DES daughter has not developed this cancer by age 30, she will not develop it. Since all DES daughters are now over age 30, there should be no further cases related to DES exposure. However, there are a number of other symptoms and problems associated with DES exposure.

- Cervix and vagina. DES daughters often have distinctive changes of the cervix and vagina that can be seen during a **pelvic exam**. These changes include a cervical hood (a vaginal fold draped over the cervix), cockscomb cervix (an abnormally shaped cervix), and adenosis (glandular cells normally located within the cervix that appear on the outside of the cervix and in the vagina).
- Fallopian tubes. Some DES daughters have fallopian tube abnormalities that lead to infertility.
- Uterus. Many DES daughters have a uterus that is abnormal in size and shape. The classic sign is the T-shaped uterus. In the normal uterus, the cavity (hollow space inside) is rounded. In a T-shaped uterus, the cavity is reduced to a thin T. The abnormal shape of the inside of the uterus makes it harder for a woman to get pregnant and leads to a higher risk of premature labor and birth.

Diagnosis

Women who have been exposed to DES should have a pelvic exam at least once a year. In addition to the usual pelvic exam and Pap smear, DES daughters should also have Pap smears of the vagina and, if possible, **colposcopy**. During colposcopy, the doctor looks at the cervix and vagina through a special magnifying scope. In this way, tiny areas of abnormal cells can be seen. This procedure is easily performed in the doctor's office.

When DES daughters get pregnant, they may be at high risk for premature labor and birth and should be monitored very carefully.

Not all women who were exposed to DES develop problems in pregnancy. However, if problems like infertility or miscarriage do occur, the doctor may recommend a special x-ray test to check the woman's fallopian tubes and uterus. This special test is called a hysterosalpingogram.

Treatment

There is no treatment for the abnormalities of the fallopian tubes and uterus caused by DES exposure. Fortunately, there are treatments that can help with infertility and premature labor. Clear cell adenocarcinoma of the vagina or cervix must be treated with surgery and, possibly, **chemotherapy**.

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Detached retina *see* **Retinal detachment**

Detoxification

Definition

Detoxification is one of the more widely used treatments and concepts in alternative medicine. It is based on the principle that illnesses can be caused by the accumulation of toxic substances (toxins) in the body. Eliminating existing toxins and avoiding new toxins are essential parts of the healing process. Detoxification utilizes a variety of tests and techniques.

Purpose

Detoxification is helpful for those patients suffering from many chronic diseases and conditions, including **allergies**, **anxiety**, arthritis, **asthma**, chronic infections, depression, diabetes, headaches, heart disease, **high cholesterol**, low blood sugar levels, digestive disorders, mental illness, and **obesity**. It is helpful for those with conditions that are influenced by environmental factors, such as **cancer**, as well as for those who have been exposed to high levels of toxic materials due to accident or occupation. Detoxification therapy is useful for those suffering from allergies or immune system problems that conventional medicine is unable to diagnose or treat, including **chronic fatigue syndrome**, environmental illness/multiple chemical sensitivity, and **fibromyalgia**. Symptoms for those suffering these conditions may include unexplained **fatigue**, increased allergies, hypersensitivity to common materials, intolerance to certain foods and **indigestion**, aches and pains, low grade **fever**, headaches, **insomnia**, depression, sore throats, sudden weight loss or gain, lowered resistance to infection, general malaise, and disability. Detoxification can be used as a beneficial preventative measure and as a tool to increase overall health, vitality, and resistance to disease.

Description

Origins

Detoxification methods of healing have been used for thousands of years. **Fasting**, is one of the oldest therapeutic practices in medicine. Hippocrates, the ancient Greek known as the "Father of Western medicine," recommended fasting as a means for improving health. **Ayurvedic medicine**, a traditional healing system that has developed over thousands of years, utilizes detoxification methods to treat many chronic conditions and to prevent illness.

Detoxification treatment has become one of the cornerstones of alternative medicine. Conventional medicine notes that environmental factors can play a significant role in many illnesses. Environmental medicine is a field that studies exactly how those environmental factors influence disease. Conditions such as asthma, cancer, chronic fatigue syndrome, **multiple chemical sensitivity**, and many others are strongly influenced by exposure to toxic or allergenic substances in the environment. The United States Centers for Disease Control estimate that over 80% of all illnesses have environmental and lifestyle causes.

Detoxification has also become a prominent treatment as people have become more aware of environmental pollution. It is estimated that one in every four Americans suffers from some level of **heavy metal poisoning**. Heavy metals, such as lead, mercury, cadmium, and arsenic, are by-products of industry. Synthetic agriculture chemicals, many of which are known to cause health problems, are also found in food, air, and water. American agriculture uses nearly 10 lb (4.5 kg) of pesticides per person on the food supply each year. These toxins have become almost unavoidable. Pesticides that are used only on crops in the southern United States have been found in the tissue of animals in the far north of Canada. DDT, a cancer-causing insecticide that has been banned for decades, is still regularly found in the fatty tissue of animals, birds, and fish, even in extremely remote regions such as the North Pole.

The problem of toxins in the environment is compounded because humans are at the top of the food chain and are more likely to be exposed to an accumulation of toxic substances in the food supply. For instance, pesticides and herbicides are sprayed on grains that are then fed to farm animals. Toxic substances are stored in the fatty tissue of those animals. In addition, those animals are often injected with synthetic hormones, **antibiotics**, and other chemicals. When people eat meat products, they are exposed to the full range of chemicals and additives used along the entire agricultural chain. Detoxification specialists call this build up of toxins *bioaccumulation*. They assert that the bioaccumulation of toxic substances over time is responsible for many physical and mental disorders, especially ones that are increasing rapidly (like asthma, cancer, and mental illness). As a result, detoxification therapies are increasing in importance and popularity.

Toxins in the body include heavy metals and various chemicals such as pesticides, pollutants, and food additives. Drugs and alcohol have toxic effects in the body. Toxins are produced as normal by-products in the intestines by the bacteria that break down food. The digestion of protein also creates toxic by-products in the body.

The body has natural methods of detoxification. Individual cells get detoxified in the lymph and circulatory system. The liver is the principle organ of detoxifi-

cation, assisted by the kidneys and intestines. Toxins can be excreted from the body by the kidneys, bowels, skin, and lungs. Detoxification treatments become necessary when the body's natural detoxification systems become overwhelmed. This can be caused by long-term effects of improper diet, **stress**, overeating, sedentary lifestyles, illness, and poor health habits in general. When a build up of toxic substances in the body creates illness, it's called toxemia. Some people's digestive tracts become unable to digest food properly, due to years of overeating and **diets** that are high in fat and processed foods and low in fiber (the average American diet). When this happens, food cannot pass through the digestive tract efficiently. Instead of being digested properly or eliminated from the bowel, food can literally rot inside the digestive tract and produce toxic by-products. This state is known as toxic colon syndrome or intestinal toxemia.

Detoxification therapies try to activate and assist the body's own detoxification processes. They also try to eliminate additional exposure to toxins and strengthen the body and immune system so that toxic imbalances won't occur in the future.

Testing for toxic substances

Detoxification specialists use a variety of tests to determine the causes contributing to toxic conditions. These causes include infections, allergies, addictions, toxic chemicals, and digestive and organ dysfunction. Blood, urine, stool, and hair analyses, as well as **allergy tests**, are used to measure a variety of bodily functions that may indicate problems. Detoxification therapists usually have access to laboratories that specialize in sophisticated diagnostic tests for toxic conditions.

People who have toxemia are often susceptible to infection because their immune systems are weakened. Infections can be caused by parasites, bacteria, viruses, and a common yeast. Therapists will screen patients for underlying infections that may be contributing to illness.

Liver function is studied closely with blood and urine tests because the liver is the principle organ in the body responsible for removing toxic compounds. When the liver detoxifies a substance from the body, it does so in two phases. Tests are performed that indicate where problems may be occurring in these phases, which may point to specific types of toxins. Blood and urine tests can also be completed that screen for toxic chemicals such as PCBs (environmental poisons), formaldehyde (a common preservative), pesticides, and heavy metals. Another useful blood test is a test for zinc deficiency, which may reveal heavy metal **poisoning**. Hair analysis is used to test for heavy metal levels in the body. Blood and urine tests check immune system activity, and hormone levels can also indicate specific toxic compounds. A 24-hour urine analysis, where samples are taken around the clock, allows therapists to determine the efficiency of the digestive tract and kidneys. Together with stool analysis, these tests may indicate toxic bowel syndrome and digestive system disorders. Certain blood and urine tests may point to nutritional deficiencies and proper recovery diets can be designed for patients as well.

Detoxification therapists may also perform extensive allergy and hypersensitivity tests. Intradermal (between layers of the skin) and sublingual (under the tongue) allergy tests are used to determine a patient's sensitivity to a variety of common substances, including formaldehyde, auto exhaust, perfume, tobacco, chlorine, jet fuel, and other chemicals.

Food allergies require additional tests because these allergies often cause reactions that are delayed for several days after the food is eaten. The RAST (radioallergosorbent test) is a blood test that determines the level of antibodies (immunoglobulins) in the blood after specific foods are eaten. The cytotoxic test is a blood test that determines if certain substances affect blood cells, including foods and chemicals. The ELISA-ACT (enzyme-linked immunoserological assay activated cell test) is considered to be one of the most accurate tests for allergies and hypersensitivity to foods, chemicals, and other agents. Other tests for food allergies are the elimination and rotation diets, in which foods are systematically evaluated to determine the ones that are causing problems.

Detoxification therapists usually interview and counsel patients closely to determine and correct lifestyle, occupational, psychological, and emotional factors that may also be contributing to illness.

Detoxification therapies

Detoxification therapists use a variety of healing techniques after a diagnosis is made. The first step is to eliminate a patient's exposure to all toxic or allergenic substances. These include heavy metals, chemicals, radiation (from x rays, power lines, cell phones, computer screens, and microwaves), smog, polluted water, foods, drugs, **caffeine**, alcohol, perfume, excess noise, and stress. If mercury poisoning has been determined, the patient will be advised to have mercury fillings from the teeth removed, preferably by a holistic dentist.

Specific treatments are used to stimulate and assist the body's detoxification process. Dietary change is immediately enacted, eliminating allergic and unhealthy foods, and emphasizing foods that assist detoxification and support healing. Detoxification diets are generally low in fat, high in fiber, and vegetarian with a raw food emphasis. Processed foods, alcohol, and caffeine are

Common Herbs Used For Detoxification

Antibiotics	Anticatarrhals (Help Eliminate Mucus)	Blood Cleaners
Clove	Boneset	Burdock root
Echinacea	Echinacea	Dandelion root
Eucalyptus	Garlic	Echinacea
Garlic	Goldenseal root	Oregon grape root
Myrrh	Hyssop	Red clover blossoms
Prickly ash bark	Sage	Yellow dock root
Propolis	Yarrow	
Wormwood		

Diaphoretics/Skin Cleaners	Diuretics	Laxatives
Boneset	Cleavers	Buckthorn
Burdock root	Corn silk	Cascara sagrada
Cayenne pepper	Horsetail	Dandelion root
Elder flowers	Juniper berries	Licorice root
Ginger root	Parsley leaf	Rhubarb root
Goldenseal root	Uva ursi	Senna leaf
Peppermint	Yarrow dock	Yellow dock
Oregon grape root		
Yellow dock		

avoided. Nutritional supplements such as **vitamins**, **minerals**, antioxidants, amino acids, and essential fatty acids are often prescribed. Spirulina is a sea algae that is frequently given to assist in eliminating heavy metals. Lipotropic agents are certain vitamins and nutrients that promote the flow of bile and fat from the liver.

Many herbal supplements are used in detoxification therapies as well. Milk thistle extract, called silymarin, is one of the more potent herbs for detoxifying the liver. Naturopathy, Ayurvedic medicine, and **traditional Chinese medicine** (TCM) recommend numerous herbal formulas for detoxification and immune strengthening. If infections or parasites have been found, these are treated with herbal formulas and, in difficult cases, antibiotics.

For toxic bowel syndrome and digestive tract disorders, herbal **laxatives** and high fiber foods such as psyllium seeds may be given to cleanse the digestive tract and promote elimination. Colonics are used to cleanse the lower intestines. Digestive enzymes are prescribed to improve digestion, and acidophilus and other friendly bacteria are reintroduced into the system with nutritional supplements.

Fasting is another major therapy in detoxification. Fasting is one of the quickest ways to promote the elimination of stored toxins in the body and to prompt the healing process. People with severe toxic conditions are supervised closely during fasting because the number of toxins in the body temporarily increases as they are being released.

Chelation therapy is used by detoxification specialists to rid the body of heavy metals. Chelates are particular substances that bind to heavy metals and speed their elimination. Homeopathic remedies have also been shown to be effective for removing heavy metals.

Sweating therapies can also detoxify the body because the skin is a major organ of elimination. Sweating helps release those toxins that are stored in the subcutaneous (under the skin) fat cells. Saunas, therapeutic baths, and **exercise** are some of these treatments. Body therapies may also be prescribed, including **massage therapy**, **acupressure**, **shiatsu**, manual lymph drainage, and **polarity therapy**. These body therapies seek to improve circulatory and structural problems, reduce stress, and promote healing responses in the body. Mind/body therapies such as psychotherapy, counseling, and stress management techniques may be used to heal the psychological components of illness and to help patients overcome their negative patterns contributing to illness.

Practitioners and treatment costs

The costs of detoxification therapies can vary widely, depending on the number of tests and treatments required. Detoxification treatments can be lengthy and involved since illnesses associated with toxic conditions usually develop over many years and may not clear up quickly. Detoxification treatments may be lengthy because they often strive for the holistic healing of the body, mind, and emotions.

Practitioners may be conventionally trained medical doctors with specialties in environmental medicine or interests in alternative treatment. The majority of detoxification therapists are alternative practitioners, such as naturopaths, homeopaths, ayurvedic doctors, or traditional Chinese doctors. Insurance coverage varies, depending

KEY TERMS

Allergen—A foreign substance, such as mites in house dust or animal dander, that when inhaled,causes the airways to narrow and produces symptoms of asthma.

Antibody—A protein, also called immunoglobulin, produced by immune system cells to remove antigens (the foreign substances that trigger the immune response).

Fibromyalgia—A condition of debilitating pain, among other symptoms, in the muscles and the myofascia (the thin connective tissue that surrounds muscles, bones, and organs).

Hypersensitivity—The state where even a tiny amount of allergen can cause severe allergic reactions.

Multiple chemical sensitivity—A condition characterized by severe and crippling allergic reactions to commonly used substances, particularly chemicals. Also called environmental illness.

on the practitioner and the treatment involved. Consumers should review their individual insurance policies regarding treatment coverage.

Preparations

Patients can assist diagnosis and treatment by keeping detailed diaries of their activities, symptoms, and contact with environmental factors that may be affecting their health. Reducing exposure to environmental toxins and making immediate dietary and lifestyle changes may speed the detoxification process.

Side effects

During the detoxification process, patients may experience side effects of fatigue, malaise, aches and pains, emotional duress, **acne**, headaches, allergies, and symptoms of colds and flu. Detoxification specialists claim that these negative side effects are part of the healing process. These reactions are sometimes called *healing crises*, which are caused by temporarily increased levels of toxins in the body due to elimination and cleansing.

Research and general acceptance

Although environmental medicine is gaining more respect within conventional medicine, detoxification treatment is scarcely mentioned by the medical establishment. The research that exists on detoxification is largely testimonial, consisting of individual personal accounts of healing without statistics or controlled scientific experiments. In the alternative medical community, detoxification is an essential and widely accepted treatment for many illnesses and chronic conditions.

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Douglas Dupler

Deviated septum

Definition

The nasal septum is a thin structure, separating the two sides of the nose. If it is not in the middle of the nose, then it is deviated.

Description

The nasal septum is composed of two parts. Toward the back of the head the nasal septum is rigid bone, but further forward the bone becomes cartilage. With one finger in each nostril this cartilage can easily be bent back and forth. If the nasal septum is sufficiently displaced to one side, it will impede the flow of air and mucus through the nose. This condition, called a deviated septum, can cause symptoms and disease.

Causes and symptoms

A deviated septum can be a simple variation in normal structure or the result of a broken nose. Any narrowing of the nasal passageway that it causes will threaten the drainage of secretions from the sinuses, which must pass through the nose. It is a general rule of medicine that when flow is obstructed, whether it is mucus from the sinuses or bile from the gall bladder, infection results. People with **allergic rhinitis** (hay fever) are at greater risk of obstruction because their nasal passageways are already narrowed by the swollen membranes lining them. The result is **sinusitis**, which can be acute and severe or chronic and lingering.

Diagnosis

It is easy to see that a septum is deviated. It is more difficult to determine if that deviation needs correction. It is common for a patient to complain that he/she can breathe through only one nostril. Then the diagnosis is easy. A deviated septum may also contribute to **snoring**, **sleep apnea**, and other breathing disorders.

Treatment

The definitive treatment is surgical repositioning of the septum, accomplished by breaking it loose and fixing it in a proper place while it heals. **Decongestants** like pseudoephedrine or phenylpropanolamine will shrink the membranes and thereby enlarge the passages. **Antihistamines**, nasal cortisone spray, and other allergy treatments may also be temporarily beneficial.

Alternative treatment

As a palliative, saline drops and sprays are very helpful in loosening mucus in the obstructed side and preventing drying in the other side, where all the air blows. Hot peppers, such as jalapenos, can produce enough tears and discharge to flush out a stopped-up nose. An even more effective treatment is called a nasal lavage, often done using a small pot with a spout. Saline solution is poured into one nostril and allowed to flow out the other nostril.

A close-up of person with a deviated septum. *(Custom Medical Stock Photo. Reproduced by permission.)*

Then, the process is repeated in reverse. These therapies are all useful to take care of symptoms, but do not correct the problem. Nasospecific, a procedure where a deflated balloon is inserted in the nostril and inflated to a large enough degree to adjust the septal deviation, can be an alternative to surgery. A trained practitioner in the nasospecific procedure is necessary.

Prognosis

Surgical repair is curative and carries little risk. Chronic infection can be painful and lead to complications until it is resolved. If there is continued obstruction, the infection will very likely return.

Prevention

Avoidance of virus colds, airborne dusts, air pollution, and known allergens will minimize the irritation and swelling of the membranes lining the nasal passages.

KEY TERMS

Allergen—Any substance that irritates people sensitive (allergic) to it.

Allergic rhinitis—Swelling and inflammation of the nasal membranes caused by sensitivity to airborne matter like pollen or cat hair.

Saline—A salt solution in water. Normal saline has the same salt concentration as the body, 0.9%.

Sinuses—The nasal sinuses, air-filled cavities surrounding the eyes and nose, like the nose itself are lined with mucus-producing membranes. They provide cleansing to the nose, resonance to the voice, and structure to the face.

Sinusitis—Infection of the sinuses.

Sleep apnea—A condition in which breathing is temporarily interrupted during sleep. It leads to high blood pressure, sleepiness, and a variety of other problems.

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J. Ricker Polsdorfer, MD

Dextromethorphan *see* **Cough suppressants**

Diabetes insipidus

Definition

Diabetes insipidus (DI) is a disorder that causes the patient to produce tremendous quantities of urine. The massively increased urine output is usually accompanied by intense thirst.

Description

The balance of fluid within the body is maintained through a number of mechanisms. One important chemical involved in fluid balance is called antidiuretic hormone (ADH). ADH is produced by the pituitary, a small gland located at the base of the brain. In a healthy person and under normal conditions, ADH is continuously released. ADH influences the amount of fluid that the kidneys reabsorb into the circulatory system and the amount of fluid that the kidneys pass out of the body in the form of urine.

Production of ADH is regulated by the osmolality of the circulating blood. Osmolality refers to the concentration of dissolved chemicals (such as sodium, potassium, and chloride; together called solute) circulating in the fluid base of the blood (plasma). When there is very little fluid compared to the concentration of solute, the pituitary will increase ADH production. This tells the kidneys to retain more water and to decrease the amount of urine produced. As fluid is retained, the concentration of solute will normalize. At other times, when the fluid content of the blood is high in comparison to the concentration of solute, ADH production will decrease. The kidneys are then free to pass an increased amount of fluid out of the body in the urine. Again, this will allow the plasma osmolality to return to normal.

Diabetes insipidus occurs when either the amount of ADH produced by the pituitary is below normal (central DI), or the kidneys' ability to respond to ADH is defective (nephrogenic DI). In either case, a person with DI will pass extraordinarily large quantities of urine, sometimes reaching 10 or more liters each day. At the same time, the patient's blood will be very highly concentrated, with low fluid volume and high concentrations of solute.

DI occurs on average when a person is about 24 years old, and occurs more frequently in males than in females.

Causes and symptoms

DI may run in families. The cause of this type of DI is unknown. Other times, central DI can be caused by:

- an injury to the head
- brain surgery
- cancers that have spread to the pituitary gland (most commonly occurring with **breast cancer**)
- sarcoidosis (or other related disorders), causing destruction of the pituitary gland
- any condition or illness that causes decreased oxygen delivery to the brain
- the use of certain medications that decrease ADH production (like the antiseizure drug phenytoin)
- the excessive use of alcohol

Central DI may also occur in women who are pregnant or have just given birth, and in patients with **AIDS** who have suffered certain types of brain infections. Nephrogenic DI sometimes occurs in patients who are

taking the medication lithium, patients who have high levels of blood calcium, and patients who are pregnant.

DI is easily confused with an entirely unrelated disorder, psychogenic polydipsia. Polydipsia refers to drinking large amounts of water. Psychogenic polydipsia is a psychiatric problem that makes a person drink huge quantities of water uncontrollably.

Symptoms of DI include extreme thirst and the production of tremendous quantities of urine. Patients with DI typically drink huge amounts of water, and usually report a specific craving for cold water. When the amount of water passed in the urine exceeds the patient's ability to drink ample replacement water, the patient may begin to suffer from symptoms of **dehydration**. These symptoms include weakness, **fatigue**, **fever**, low blood pressure, increased heart rate, **dizziness**, and confusion. If left untreated, the patient could lapse into unconsciousness and die.

Diagnosis

Diagnosis should be suspected in any patient with sudden increased thirst and urination. Laboratory examination of urine will reveal very dilute urine, made up mostly of water with no solute. Examination of the blood will reveal very concentrated blood, high in solute and low in fluid volume.

A water deprivation test may be performed. This test requires a patient to stop all fluid intake. The patient is weighed just before the test begins, and urine is collected and examined hourly. The test is stopped when:

- the patient has lost more than 5% of his or her original body weight
- the patient has reached certain limits of low blood pressure and increased heart rate
- the urine is no longer changing significantly from one sample to the next in terms of solute concentration

The next step of the test involves injecting a synthetic form of ADH, with one last urine sample examined 60 minutes later. Comparing plasma and urine osmolality allows the doctor to diagnose either central DI, nephrogenic DI, partial DI, or psychogenic polydipsia.

Treatment

A number of medications can be given to decrease the quantity of fluid passed out into the urine. These include vasopressin (Pitressin) injected and desmopressin acetate (DDAVP) inhaled through the nose. Other medications that may be given include some antidiuretic drugs (chlorpropamide, clofibrate, carbamazepine). Patients with nephrogenic DI, however, will also require special **diets** that restrict the amount of solute taken in. These patients are also treated with a type of medication called a thiazide diuretic.

KEY TERMS

Concentration—Refers to the amount of solute present in a solution, compared to the total amount of solvent.

Dilute—A solution that has comparatively more fluid in it, relative to the quantity of solute.

Osmolality—A measure of the solute-to-solvent concentration of a solution.

Solute—Solid substances that are dissolved in liquid in order to make a solution.

Prognosis

Uncomplicated diabetes insipidus is controllable with adequate intake of water and most patients can lead normal lives.

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Rosalyn Carson-DeWitt, MD

Diabetes mellitus

Definition

Diabetes mellitus is a condition in which the pancreas no longer produces enough insulin or when cells stop responding to the insulin that is produced, so that

glucose in the blood cannot be absorbed into the cells of the body. Symptoms include frequent urination, lethargy, excessive thirst, and hunger. The treatment includes changes in diet, oral medications, and in some cases, daily injections of insulin.

Description

Diabetes mellitus is a chronic disease that causes serious health complications including renal (kidney) failure, heart disease, **stroke**, and blindness. Approximately 14 million Americans (about 5% of the population) have diabetes. Unfortunately, as many as one-half are unaware that they have it.

Background

Every cell in the human body needs energy in order to function. The body's primary energy source is glucose, a simple sugar resulting from the digestion of foods containing carbohydrates (sugars and starches). Glucose from the digested food circulates in the blood as a ready energy source for any cells that need it. Insulin is a hormone or chemical produced by cells in the pancreas, an organ located behind the stomach. Insulin bonds to a receptor site on the outside of cell and acts like a key to open a doorway into the cell through which glucose can enter. Some of the glucose can be converted to concentrated energy sources like glycogen or fatty acids and saved for later use. When there is not enough insulin produced or when the doorway no longer recognizes the insulin key, glucose stays in the blood rather entering the cells.

The body will attempt to dilute the high level of glucose in the blood, a condition called hyperglycemia, by drawing water out of the cells and into the bloodstream in an effort to dilute the sugar and excrete it in the urine. It is not unusual for people with undiagnosed diabetes to be constantly thirsty, drink large quantities of water, and urinate frequently as their bodies try to get rid of the extra glucose. This creates high levels of glucose in the urine.

At the same time that the body is trying to get rid of glucose from the blood, the cells are starving for glucose and sending signals to the body to eat more food, thus making patients extremely hungry. To provide energy for the starving cells, the body also tries to convert fats and proteins to glucose. The breakdown of fats and proteins for energy causes acid compounds called ketones to form in the blood. Ketones will also be excreted in the urine. As ketones build up in the blood, a condition called ketoacidosis can occur. This condition can be life threatening if left untreated, leading to **coma** and **death**.

Types of diabetes mellitus

Type I diabetes, sometimes called juvenile diabetes, begins most commonly in childhood or adolescence. In this form of diabetes, the body produces little or no insulin. It is characterized by a sudden onset and occurs more frequently in populations descended from Northern European countries (Finland, Scotland, Scandinavia) than in those from Southern European countries, the Middle East, or Asia. In the United States, approximately three people in 1,000 develop Type I diabetes. This form is also called insulin-dependent diabetes because people who develop this type need to have daily injections of insulin.

Brittle diabetics are a subgroup of Type I where patients have frequent and rapid swings of blood sugar levels between hyperglycemia (a condition where there is too much glucose or sugar in the blood) and **hypoglycemia** (a condition where there is abnormally low levels of glucose or sugar in the blood). These patients may require several injections of different types of insulin during the day to keep the blood sugar level within a fairly normal range.

The more common form of diabetes, Type II, occurs in approximately 3–5% of Americans under 50 years of age, and increases to 10–15% in those over 50. More than 90% of the diabetics in the United States are Type II diabetics. Sometimes called age-onset or adult-onset diabetes, this form of diabetes occurs most often in people who are overweight and who do not **exercise**. It is also more common in people of Native American, Hispanic, and African-American descent. People who have migrated to Western cultures from East India, Japan, and Australian Aboriginal cultures are also more likely to develop Type II diabetes than those who remain in their original countries.

Type II is considered a milder form of diabetes because of its slow onset (sometimes developing over the course of several years) and because it can usually be controlled with diet and oral medication. The consequences of uncontrolled and untreated Type II diabetes, however, are the just as serious as those for Type I. This form is also called noninsulin-dependent diabetes, a term that is somewhat misleading. Many people with Type II diabetes can control the condition with diet and oral medications, however, insulin injections are sometimes necessary if treatment with diet and oral medication is not working.

Another form of diabetes called **gestational diabetes** can develop during **pregnancy** and generally resolves after the baby is delivered. This diabetic condition develops during the second or third trimester of pregnancy in about 2% of pregnancies. The condition is usually treated by diet, however, insulin injections may

be required. These women who have diabetes during pregnancy are at higher risk for developing Type II diabetes within 5–10 years.

Diabetes can also develop as a result of pancreatic disease, **alcoholism**, **malnutrition**, or other severe illnesses that **stress** the body.

Causes and symptoms

Causes

The causes of diabetes mellitus are unclear, however, there seem to be both hereditary (genetic factors passed on in families) and environmental factors involved. Research has shown that some people who develop diabetes have common genetic markers. In Type I diabetes, the immune system, the body's defense system against infection, is believed to be triggered by a virus or another microorganism to destroy the cells in the pancreas that produce insulin. In Type II diabetes, age, **obesity**, and family history of diabetes play a roll.

In Type II diabetes, the pancreas may produce enough insulin, however, cells have become resistant to the insulin produced and it may not work as effectively. Symptoms of Type II diabetes can begin so gradually that a person may not know that they have it. Early signs are lethargy extreme thirst, and frequent urination. Other symptoms may include sudden weight loss, slow wound healing, urinary tract infections, gum disease, or blurred vision. It is not unusual for Type II diabetes to be detected while a patient is seeing a doctor about another health concern that is actually being caused by the yet undiagnosed diabetes.

Individuals who are at high risk of developing Type II diabetes mellitus include people who:

- are obese (more than 20% above their ideal body weight)
- have a relative with diabetes mellitus
- belong to a high-risk ethnic population (African-American, Native American, Hispanic, or Native Hawaiian)
- have been diagnosed with gestational diabetes or have delivered a baby weighing more than 9 lbs (4 kg)
- have high blood pressure (140/90 mmHg or above)
- have a high density lipoprotein cholesterol level less than or equal to 35 mg/dL and/or a triglyceride level greater than or equal to 250 mg/dL
- have had impaired glucose tolerance or impaired **fasting** glucose on previous testing

Several common medications can impair the body's use of insulin, causing a condition known as secondary diabetes. These medications include treatments for high blood pressure (furosemide, clonidine, and thiazide **diuretics**), drugs with hormonal activity (**oral contraceptives**, thyroid hormone, progestins, and glucocorticorids), and the anti-inflammation drug indomethacin. Several drugs that are used to treat **mood disorders** (such as **anxiety** and depression) can also impair glucose absorption. These drugs include haloperidol, lithium carbonate, phenothiazines, tricyclic antidepressants, and adrenergic agonists. Other medications that can cause diabetes symptoms include isoniazid, nicotinic acid, cimetidine, and heparin.

Wrinkled, dehydrated skin of a person in a diabetic coma. Untreated diabetes mellitus results in elevated blood glucose levels, causing a variety of symptoms that can culminate in a diabetic coma. *(Photo Researchers, Inc. Reproduced by permission.)*

Symptoms

Symptoms of diabetes can develop suddenly (over days or weeks) in previously healthy children or adolescents, or can develop gradually (over several years) in overweight adults over the age of 40. The classic symptoms include feeling tired and sick, frequent urination, excessive thirst, excessive hunger, and weight loss.

Ketoacidosis, a condition due to **starvation** or uncontrolled diabetes, is common in Type I diabetes. Ketones are acid compounds that form in the blood when the body breaks down fats and proteins. Symptoms include abdominal **pain**, vomiting, rapid breathing, extreme lethargy and drowsiness. Patients with ketoacidosis will also have a sweet breath odor. Left untreated, this condition can lead to coma and death.

With Type II diabetes, the condition may not become evident until the patient presents for medical treatment for some other condition. A patient may have heart disease, chronic infections of the gums and urinary tract, blurred vision, numbness in the feet and legs, or slow-healing **wounds**. Women may experience genital **itching**.

KEY TERMS

Cataracts—A condition where the lens of the eye becomes cloudy.

Diabetic peripheral neuropathy—A condition where the sensitivity of nerves to pain, temperature, and pressure is dulled particularly in the legs and feet.

Diabetic retinopathy—A condition where the tiny blood vessels to the retina, the tissues that sense light at the back of the eye, are damaged, leading to blurred vision, sudden blindness, or black spots, lines, or flashing light in the field of vision.

Glaucoma—A condition where pressure within the eye causes damage to the optic nerve, which sends visual images to the brain.

Hyperglycemia—A condition where there is too much glucose or sugar in the blood.

Hypoglycemia—A condition where there is too little glucose or sugar in the blood.

Insulin—A hormone or chemical produced by the pancreas, insulin is needed by cells of the body in order to use glucose (sugar), the body's main source of energy.

Ketoacidosis—A condition due to starvation or uncontrolled Type I diabetes. Ketones are acid compounds that form in the blood when the body breaks down fats and proteins. Symptoms include abdominal pain, vomiting, rapid breathing, extreme tiredness, and drowsiness.

Kidney dialysis—A process where blood is filtered through a dialysis machine to remove waste products that would normally be removed by the kidneys. The filtered blood is then circulated back into the patient. This process is also called renal dialysis.

Pancreas—A gland located behind the stomach that produces insulin.

Diagnosis

Diabetes is suspected based on symptoms. Urine and blood tests can be used to confirm a diagnose of diabetes based on the amount of glucose. Urine tests can also detect ketones and protein in the urine that may help diagnose diabetes and assess how well the kidneys are functioning. These tests can also be used to monitor the disease once the patient is on a standardized diet, oral medications, or insulin.

Urine tests

Clinistix and Diastix are paper strips or dipsticks that change color when dipped in urine. The test strip is compared to a chart which shows the amount of glucose in the urine based on the change in color. The level of glucose in the urine lags behind the level of glucose in the blood. Testing the urine with a test stick, paper strip, or tablet that changes color when sugar is present is not as accurate as blood testing, however it can give a fast and simple reading.

Ketones in the urine can be detected using similar types of dipstick tests (Acetest or Ketostix). Ketoacidosis can be a life-threatening situation in Type I diabetics, so having a quick and simple test to detect ketones can assist in establishing a diagnosis sooner.

Another dipstick test can determine the presence of protein or albumin in the urine. Protein in the urine can indicate problems with kidney function and can be used to track the development of renal failure. A more sensitive test for urine protein uses radioactively tagged chemicals to detect microalbuminuria, small amounts of protein in the urine, that may not show up on dipstick tests.

Blood tests

FASTING GLUCOSE TEST. Blood is drawn from a vein in the patient's arm after a period at least eight hours when the patient has not eaten, usually in the morning before breakfast. The red blood cells are separated from the sample and the amount of glucose is measured in the remaining plasma. A plasma level of 7.8 mmol/L (200 mg/L) or greater can indicate diabetes. The fasting glucose test is usually repeated on another day to confirm the results.

POSTPRANDIAL GLUCOSE TEST. Blood is taken right after the patient has eaten a meal.

ORAL GLUCOSE TOLERANCE TEST. Blood samples are taken from a vein before and after a patient drinks a thick, sweet syrup of glucose and other sugars. In a non-diabetic, the level of glucose in the blood goes up immediately after the drink and then decreases gradually as insulin is used by the body to metabolize, or absorb, the sugar. In a diabetic, the glucose in the blood goes up and stays high after drinking the sweetened liquid. A plasma glucose level of 11.1 mmol/L (200 mg/dL) or higher at two hours after drinking the syrup and at one other point during the two-hour test period confirms the diagnosis of diabetes.

A diagnosis of diabetes is confirmed if there are symptoms of diabetes and a plasma glucose level of at least 11.1 mmol/L, a fasting plasma glucose level of at least 7 mmol/L; or a two-hour plasma glucose level of at least 11.1 mmol/L during an oral glucose tolerance test.

Home blood glucose monitoring kits are available so patients with diabetes can monitor their own levels. A small needle or lancet is used to prick the finger and a drop of blood is collected and analyzed by a monitoring device. Some patients may test their blood glucose levels several times during a day and use this information to adjust their doses of insulin.

Treatment

There is currently no cure for diabetes; the condition, however, can be managed so that patients can live a relatively normal life. Treatment of diabetes focuses on two goals: keeping blood glucose within normal range and preventing the development of long-term complications. Careful monitoring of diet, exercise, and blood glucose levels are as important as the use of insulin or oral medications in preventing complications of diabetes.

Dietary changes

Diet and moderate exercise are the first treatments implemented in diabetes. For many Type II diabetics, weight loss may be an important goal in helping them to control their diabetes. A well-balanced, nutritious diet provides approximately 50–60% of calories from carbohydrates, approximately 10–20% of calories from protein, and less than 30% of calories from fat. The number of calories required by an individual depends on their age, weight, and activity level. The calorie intake also needs to be distributed over the course of the entire day so surges of glucose entering the blood system are kept to a minimum.

Keeping track of the number of calories provided by different foods can become complicated, so patients are usually advised to consult a nutritionist or dietitian. An individualized, easy to manage diet plan can be set up for each patient. Both the American Diabetes Association and the American Dietetic Association recommend **diets** based on the use of food exchange lists. Each food exchange contains a known amount of calories in the form of protein, fat, or carbohydrate. A patient's diet plan will consist of a certain number of exchanges from each food category (meat or protein, fruits, breads and starches, vegetables, and fats) to be eaten at meal times and as snacks. Patients have flexibility in choosing which foods they eat as long as they stick with the number of exchanges prescribed.

For many Type II diabetics, weight loss is an important factor in controlling their condition. The food exchange system, along with a plan of moderate exercise, can help them lose excess weight and improve their overall health.

Oral medications

Oral medications are available to lower blood glucose in Type II diabetics. The drugs first prescribed for Type II diabetes are in a class of compounds called sulfonylureas and include tolbutamide, tolazamide, acetohexamide, and chlorpropamide. Newer drugs in the same class are now available and include glyburide, glimeperide, and glipizide. The way that these drugs work is not well understood, however, they seem to stimulate cells of the pancreas to produce more insulin. New medications that are available to treat diabetes include metformin, acarbose, and troglitizone. The choice of the right medication depends in part on the individual patient profile. All drugs have side effects that may make them inappropriate for particular patients. Some for example, may stimulate weight gain or cause stomach irritation, so they may not be the best treatment for someone who is already overweight or who also has stomach ulcers. While these medications are an important aspect of treatment for Type II diabetes, they are not a substitute for a well planned diet and moderate exercise. Oral medications are not effective for Type I diabetes, in which the patient produces little or no insulin.

Insulin

Patients with Type I diabetes need daily injections of insulin to help their bodies use glucose. The amount and type of insulin required depends on the height, weight, age, food intake, and activity level of the individual diabetic patient. Some patients with Type II diabetes may need to use insulin injections if their diabetes cannot be controlled with diet, exercise, and oral medication. Injections are given subcutaneously, that is, just under the skin, using a small needle and syringe. Injection sites can be anywhere on the body where there is looser skin, including the upper arm, abdomen, or upper thigh.

Purified human insulin is most commonly used, however, insulin from beef and pork sources are also available. Insulin may be given as an injection of a single dose of one type of insulin once a day. Different types of insulin can be mixed and given in one dose or split into two or more doses during a day. Patients who require multiple injections over the course of a day may be able to use an insulin pump that administers small doses of insulin on demand. The small battery-operated pump is worn outside the body and is connected to a needle that is inserted into the abdomen. Pumps can be programmed to inject small doses of insulin at various times during the day, or the patient may be able to adjust the insulin doses to coincide with meals and exercise.

Regular insulin is fast-acting and starts to work within 15–30 minutes, with its peak glucose-lowering effect about two hours after it is injected. Its effects last for about four to six hours. NPH (neutral protamine Hagedorn) and Lente insulin are intermediate-acting, starting to work within one to three hours and lasting up to 18–26 hours. Ultra-lente is a long-acting form of insulin that starts to work within four to eight hours and lasts 28–36 hours.

Hypoglycemia, or low blood sugar, can be caused by too much insulin, too little food (or eating too late to coincide with the action of the insulin), alcohol consumption, or increased exercise. A patient with symptoms of hypoglycemia may be hungry, cranky, confused, and tired. The patient may become sweaty and shaky. Left untreated, the patient can lose consciousness or have a seizure. This condition is sometimes called an insulin reaction and should be treated by giving the patient something sweet to eat or drink like a candy, sugar cubes, juice, or another high sugar snack.

Surgery

Transplantation of a healthy pancreas into a diabetic patient is a successful treatment, however, this transplant is usually done only if a kidney transplant is performed at the same time. Although a pancreas transplant is possible, it is not clear if the potential benefits outweigh the risks of the surgery and drug therapy needed.

Alternative treatment

Since diabetes can be life-threatening if not properly managed, patients should not attempt to treat this condition without medicial supervision. A variety of alternative therapies can be helpful in managing the symptoms of diabetes and supporting patients with the disease. **Acupuncture** can help relieve the pain associated with **diabetic neuropathy** by stimulation of cetain points. A qualified practitioner should be consulted. Herbal remedies may also be helpful in managing diabetes. Although there is no herbal substitute for insulin, some herbs may help adjust blood sugar levels or manage other diabetic symptoms. Some options include:

- fenugreek (*Trigonella foenum-graecum*) has been shown in some studies to reduce blood insulin and glucose levels while also lowering cholesterol
- bilberry (*Vaccinium myrtillus*) may lower blood glucose levels, as well as helping to maintain healthy blood vessels
- garlic (*Allium sativum*) may lower blood sugar and cholesterol levels
- onions (*Allium cepa*) may help lower blood glucose levels by freeing insulin to metabolize it
- cayenne pepper (*Capsicum frutescens*) can help relieve pain in the peripheral nerves (a type of diabetic neuropathy)
- ginkgo (*Gingko biloba*) may maintain blood flow to the retina, helping to prevent diabetic retinopathy

Any therapy that lowers stress levels can also be useful in treating diabetes by helping to reduce insulin requirements. Among the alternative treatments that aim to lower stress are **hypnotherapy**, **biofeedback**, and **meditation**.

Prognosis

Uncontrolled diabetes is a leading cause of blindness, end-stage renal disease, and limb amputations. It also doubles the risks of heart disease and increases the risk of stroke. Eye problems including **cataracts**, **glaucoma**, and diabetic retinopathy are also more common in diabetics.

Diabetic **peripheral neuropathy** is a condition where nerve endings, particularly in the legs and feet become less sensitive. Diabetic foot ulcers are a particular problem since the patient does not feel the pain of a blister, callous, or other minor injury. Poor blood circulation in the legs and feet contribute to delayed wound healing. The inability to sense pain along with the complications of delayed wound healing can result in minor injuries, blisters, or callouses becoming infected and difficult to treat. In cases of severe infection, the infected tissue begins to break down and rot away. The most serious consequence of this condition is the need for **amputation** of toes, feet, or legs due to severe infection.

Heart disease and kidney disease are common complications of diabetes. Long-term complications may include the need for **kidney dialysis** or a kidney transplant due to kidney failure.

Babies born to diabetic mothers have an increased risk of **birth defects** and distress at birth.

Prevention

Research continues on ways to prevent diabetes and to detect those at risk for developing diabetes. While the onset of Type I diabetes is unpredictable, the risk of developing Type II diabetes can be reduced by maintaining ideal weight and exercising regularly. The physical and emotional stress of surgery, illness, pregnancy, and alcoholism can increase the risks of diabetes, so maintaining a healthy lifestyle is critical to preventing the onset of Type II diabetes and preventing further complications of the disease.

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Altha Roberts Edgren

Diabetic control index *see* **Glycosylated hemoglobin test**

Diabetic foot infections

Definition

Diabetic foot infections are infections that can develop in the skin, muscles, or bones of the foot as a result of the nerve damage and poor circulation that is associated with diabetes.

Description

People who have diabetes have a greater-than-average chance of developing foot infections. Because a person who has diabetes may not feel foot **pain** or discomfort, problems can remain undetected until **fever**, weakness, or other signs of systemic infection appear. As a result, even minor irritations occur more often, heal more slowly, and are more likely to result in serious health problems.

With diabetes, foot infections occur more frequently because the disease causes nervous system changes and poor circulation. Because the nerves that control sweating no longer work, the skin of the feet can become very dry and cracked, and calluses tend to occur more frequently and build up faster. If not trimmed regularly, these calluses can turn into open sores or ulcers. Because diabetic nerve damage can cause a loss of sensation (neuropathy), if the feet are not regularly inspected, an ulcer can quickly become infected and, if not treated, may result in the **death** of tissue (**gangrene**) or **amputation**.

The risk of infection is greatest for people who are over the age of 60 and for those who have one or more of the following:

- poorly controlled diabetes
- foot ulcers
- laser treatment for changes in the retina
- kidney or vascular disease
- loss of sensation (neuropathy)

Causes and symptoms

Bacteria can cause an infection through small cracks (fissures) that can develop in the dry skin around the heel and on other parts of the foot or through corns, calluses, blisters, hangnails, or ulcers. If not treated, the bacterial infection can destroy skin, tissue, and bone or spread throughout the body.

Common sites of diabetic foot infections include the following:

- blisters, corns, or callouses that bleed beneath the skin
- bunions, hammertoes, or other abnormalities in the bones of the foot

Persons with diabetes often suffer from foot ulcers, as shown above. *(Custom Medical Stock Photo. Reproduced by permission.)*

- scar tissue that has grown over the site of an earlier infection
- foot ulcers caused by pressure, nerve damage, or poor circulation (Ulcers occur most often over the ball of the foot, on the bottom of the big toe, or on the sides of the foot due to poorly fitting shoes.)
- injuries that tear or puncture the skin.

Diagnosis

A physician who specializes in the treatment of the foot (podiatrist) or the doctor who normally treats the patient's diabetes will treat the infection. An x ray of the foot will be taken to determine whether the bone has become infected. A sample from the wound will be cultured to identify the organism that is causing the infection so that the appropriate antibiotic can be selected.

Treatment

From the results of the culture, the appropriate antibiotic will be prescribed. Any dead or infected tissue will be surgically removed and, if necessary, a cast and/or special shoes may be used to protect the area. In addition, the patient will be instructed to keep off their feet. If the ulcer does not heal, the physician may perform surgery to increase blood flow to the foot. It is also important for the patient to practice good diabetes control and keep blood glucose levels from getting too high.

Alternative treatment

Acupuncture and vitamin C can boost the body's infection-fighting ability. A variety of other **vitamins** and herbs may improve general health and diabetes control. Because diabetes is a potentially deadly disease, it can be dangerous to try alternative approaches without a doctor's approval or without consulting a trained practitioner of alternative medicine.

KEY TERMS

Fissure—A deep crack.

Neuropathy—An abnormality of the nerves outside the brain and spinal cord.

Ulcer—A sore or lesion.

Prognosis

Without proper treatment, diabetic foot infections can lead to serious illness, gangrene, amputation, and even death if the infection spreads throughout the body. If treated properly and the patient practices good **foot care**, the prognosis is generally optimistic

Prevention

There are many things that a diabetic individual can do to prevent the occurrence of foot infections, including the following:

- control blood glucose and do not allow it to get too high
- avoid **smoking**
- keep blood pressure and cholesterol under control
- exercise to stimulate blood flow
- keep feet clean, dry, and warm
- check your feet every day for blisters, scratches, and skin that is hard, broken, inflamed or that feels hot or cold when touched
- after bathing, carefully dry feet and apply thin coat of petroleum jelly or hand cream to prevent dry skin from cracking
- use a pumice stone and emery board to trim calluses
- do not neglect an ulcer, should one develop

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Maureen Haggerty

Diabetic ketoacidosis

Definition

Diabetic ketoacidosis is a dangerous complication of **diabetes mellitus** in which the chemical balance of the body becomes far too acidic.

Description

Diabetic ketoacidosis (DKA) always results from a severe insulin deficiency. Insulin is the hormone secreted by the body to lower the blood sugar levels when they become too high. Diabetes mellitus is the disease resulting from the inability of the body to produce or respond properly to insulin, required by the body to convert glucose to energy. In childhood diabetes, DKA complications represent the leading cause of **death**, mostly due to the accumulation of abnormally large amounts of fluid in the brain (cerebral **edema**). DKA combines three major features: hyperglycemia, meaning excessively high blood sugar kevels hyperketonemia, meaning an overproduction of ketones by the body; and acidosis, meaning that the blood has become too acidic.

Insulin deficiency is responsible for all three conditions: the body glucose goes largely unused since most cells are unable to transport glucose into the cell without the presence of insulin; this condition makes the body use stored fat as an alternative source instead of the unavailable glucose for energy, a process that produces acidic ketones, which build up because they require insulin to be broken down. The presence of excess ketones in the bloodstream in turn causes the blood to become more acidic than the body tissues, which creates a toxic condition.

Causes and symptoms

DKA is most commonly seen in individuals with type I diabetes, under 19 years of age and is usually caused by the interruption of their insulin treatment or by acute infection or trauma. A small number of people with type II diabetes also experience ketoacidosis, but this is rare given the fact that type II diabetics still produce some insulin naturally. When DKA occurs in type II patients, it is usually caused by a decrease in food intake and an increased insulin deficiency due to hyperglycemia.

Some common DKA symptoms include:

- high blood sugar levels
- frequent urination (polyuria) and thirst
- fatigue and lethargy
- nausea
- vomiting
- abdominal pain
- fruity odor to breath
- rapid, deep breathing
- muscle stiffness or aching
- **coma**

Diagnosis

Diagnosis requires the demonstration of hyperglycemia, hyperketonemia, and acidosis. DKA is established if the patient's urine or blood is strongly positive for glucose and ketones. Normal glucose levels in a nondiabetic person on average range from 80–110 mg/dl. A person with diabetes will typically fluctuate outside those parameters. DKA glucose levels exceed 250 mg/dl and can reach 400 to 800 mg/dL. A low serum bicarbonate level (usually below 15 mEq/L) is also present, indicative of acidosis.

A blood test or **urinalysis** can quickly determine the concentration of glucose in the bloodstream. Test strips are available to patients commercially can submerge in urine to detect the presence or concentration of ketones.

Treatment

Ketoacidosis is treated under medical supervision and usually in a hospital setting.

Basic treatment includes:

- administering insulin to correct the hyperglycemia and hyperketonemia

KEY TERMS

Acidosis—A condition that causes the pH of the blood to drop and become more acidic.

Diabetes mellitus—Disease characterized by the inability of the body to produce or respond properly to insulin, which is required by the body to convert glucose to energy.

Edema—The presence of abnormally large amounts of fluid in the intercellular tissue spaces of the body.

Glucose—The type of sugar found in the blood.

Hyperglycemia—Condition characterized by excessively high levels of glucose in the blood, and occurs when the body does not have enough insulin or cannot use the insulin it does have to turn glucose into energy. Hyperglycemia is often indicative of diabetes that is out of control.

Hyperketonemia—Condition characterized by an overproduction of ketones by the body.

Hypoglycemia—Lower than normal levels of glucose in the blood.

Hypokalemia—A deficiency of potassium in the blood.

Insulin—A hormone secreted by the pancreas in response to high blood sugar levels that induces hypoglycemia. Insulin regulates the body's use of glucose and the levels of glucose in the blood by acting to open the cells so that they can intake glucose.

Ketones—Poisonous acidic chemicals produced by the body when fat instead of glucose is burned for energy. Breakdown of fat occurs when not enough insulin is present to channel glucose into body cells.

Lactic acidosis—A serious condition caused by the build up of lactic acid in the blood, causing it to become excessively acidic. Lactic acid is a by-product of glucose metabolism.

Metabolism—The sum of all chemical reactions that occur in the body resulting in growth, transformation of foodstuffs into energy, waste elimination and other bodily functions.

Polyuria—Excessive secretion of urine.

Type I diabetes—Also called juvenile diabetes. Type I diabetes typically begins early in life. Affected individuals have a primary insulin deficiency and must take insulin to stay alive.

Type II diabetes—Type II diabetes is the most common form of diabetes and usually appears in middle aged adults. It is often associated with obesity and may be delayed or controlled with diet and exercise.

- Replacing fluids intravenously lost through excessive urination and vomiting
- Balancing electrolytes to re-establish the chemical equilibrium of the blood and prevent potassium deficiency (**hypokalemia**) during treatment
- Treatment for any associated bacterial infection

Prognosis

With proper medical attention, DKA is almost always successfully treated. The DKA mortality rate is about 10%. Coma on admission adversely affects the prognosis. The major causes of death are circulatory collapse, hypokalemia, infection, and cerebral edema.

Prevention

Once diabetes has been diagnosed, prevention measures to avoid DKA include regular monitoring of blood glucose, administration of insulin, and lifestyle maintenance. Glucose monitoring is especially important during periods of **stress**, infection, and trauma when glucose concentrations typically increase as a response to these situations. Ketone tests should also be performed during these periods or when glucose is elevated.

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Gary Gilles

Diabetic neuropathy

Definition

Diabetic neuropathy is a nerve disorder caused by **diabetes mellitus**. Diabetic neuropathy may be diffuse, affecting several parts of the body, or focal, affecting a specific nerve and part of the body.

Description

The nervous system consists of two major divisions: the central nervous systems (CNS) which includes the brain, the cranial nerves, and the spinal cord, and the peripheral nervous system (PNS) which includes the nerves that link the CNS with the sensory organs, muscles, blood vessels, and glands of the body. These peripheral nerves are either motor, meaning that they are involved in motor activity such as walking, or sensory, meaning that they carry sensory information back to the CNS. The PNS also works with the CNS to regulate involuntary (autonomic) processes such as breathing, heartbeat, blood pressure, etc.

There are two types of diffuse diabetic neuropathy that affect different nervous system functions. Diffuse **peripheral neuropathy** primarily affects the limbs, damaging the nerves of the feet and hands. Autonomic neuropathy is the other form of diffuse neuropathy and it affects the heart and other internal organs.

Focal—or localized—diabetic neuropathy affects specific nerves, most commonly in the torso, leg, or head.

Diabetic neuropathy can lead to muscular weakness, loss of feeling or sensation, and loss of autonomic functions such as digestion, erection, bladder control and sweating among others.

The longer a person has diabetes, the more likely the development of one or more forms of neuropathy. Approximately 60–70% of patients with diabetes have neuropathy, but only about 5% will experience painful symptoms.

Causes and symptoms

The exact cause of diabetic neuropathy is not known. Researchers believe that the process of nerve damage is related to high glucose concentrations in the blood that could cause chemical changes in nerves, disrupting their ability to effectively send messages. High blood glucose is also known to damage the blood vessels that carry oxygen and other nutrients to the nerves. In addition, some people may have a genetic predisposition to develop neuropathy.

There is a wide range of symptoms associated with diabetic neuropathy, and they depend on which nerves and parts of the body affected and also on the type of neuropathy present. Some patients have very mild symptoms, while others are severely disabled.

Common symptoms of diffuse peripheral neuropathy include:

- numbness and feelings of tingling or burning
- insensitivity to **pain**
- needle-like jabs of pain
- extreme sensitivity to touch
- loss of balance and coordination

Common symptoms of diffuse autonomic neuropathy include:

- impaired urination and sexual function
- bladder infections
- stomach disorders, due to the impaired ability of the stomach to empty (gastric stasis)
- nausea, vomiting, bloating
- dizziness, lightheadedness, **fainting** spells
- loss of appetite

Common symptoms of focal neuropathy include:

- pain in the front of a thigh
- severe pain in the lower back
- pain in the chest or stomach
- ache behind an eye
- double vision
- paralysis on one side of the face

In severe diabetic neuropathy loss of sensation can lead to injuries that are unnoticed, progressing to infections, ulceration, and possibly **amputation**.

Diagnosis

The diagnosis of neuropathy is based on the symptoms that present during a physical exam. Pain assessment is usually the first step. Patients may have more than one type of pain, and the history helps the doctor determine whether a the pain has a neuropathic cause.

The exam may include:

- a screening test for lost sensation
- nerve conduction studies to check the flow of electric current through a nerve
- electromyography (EMG) to see how well muscles respond to electrical impulses transmitted by nearby nerves.

KEY TERMS

Central nervous system (CNS)—Part of the nervous system consisting of the brain, cranial nerves, and spinal cord. The brain is the center of higher processes, such as thought and emotion, and is responsible for the coordination and control of bodily activities and the interpretation of information from the senses. The cranial nerves and spinal cord link the brain to the peripheral nervous system.

Diabetes mellitus—Disease characterized by the inability of the body to produce or respond properly to insulin, required by the body to convert glucose to energy.

Glucose—The type of sugar found in the blood.

Peripheral nervous system (PNS)—One of the two major divisions of the nervous system. PNS nerves link the central nervous system with sensory organs, muscles, blood vessels, and glands.

- ultrasound to show how the bladder and other parts of the urinary tract are functioning
- sometimes a nerve biopsy may be performed.

Specialists who treat diabetic neuropathy include:

- neurologists: specialists in nervous system disorders
- urologists: specialists in urinary tract disorder
- gastroenterologists: specialists in digestive disorders
- podiatrists: specialists in caring for the feet

Treatment

Treatment of diabetic neuropathy is usually focused on treating the symptoms associated with the neuropathy and addressing the underlying cause by improving the control of blood sugar levels, which may heal the early stages of neuropathy.

There is no cure for the permanent nerve damage caused by neuropathy. To help control pain, the choice of proven drug therapies has broadened during the past decade. Pain medication, such as the topical skin cream capsaicin, is usually no stronger than codeine because of the potential for **addiction** with long-term use of such drugs. Four main classes of drugs are available for **pain management**, alone or in combination: tricyclic antidepressants (Imipramine, Nortriptyline), narcotic **analgesics** (Morphine), anticonvulsants (Carbamazepine, Gabapentin), and antiarrhythmics.

Prognosis

Early stage diabetic neuropathy can usually be reversed with good glucose control. Once nerve damage has occurred it cannot be reversed. The prognosis is largely dependent on the management of the underlying condition, diabetes, which may halt the progression of the neuropathy and improve symptoms. Recovery, if it occurs, is slow.

Prevention

Tight glucose control and the avoidance of alcohol and cigarettes help protect nerves from damage.

Resources

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Gary Gilles

Dialysis, kidney

Definition

Dialysis treatment replaces the function of the kidneys, which normally serve as the body's natural filtration system. Through the use of a blood filter and a chemical solution known as dialysate, the treatment removes waste products and excess fluids from the bloodstream, while maintaining the proper chemical balance of the blood. There are two types of dialysis treatment : hemodialysis and peritoneal dialysis.

Purpose

Dialysis can be used in the treatment of patients suffering from **poisoning** or overdose, in order to quickly remove drugs from the bloodstream. Its most prevalent application, however, is for patients with temporary or permanent kidney failure. For patients with end-stage renal disease (ESRD), whose kidneys are no longer capable of adequately removing fluids and wastes from their body or

Hemodialysis is the most frequently prescribed type of dialysis treatment in the United States. This treatment involves circulating the patient's blood outside of the body through a dialysis circuit. The blood is filtered and cleansed inside the hemodialyzer and returned to the body. (*Illustration by Electronic Illustrators Group.*)

of maintaining the proper level of certain kidney-regulated chemicals in the bloodstream, dialysis is the only treatment option available outside of **kidney transplantation**. In 1996 in the United States, over 200,000 people underwent regular dialysis treatments to manage their ESRD.

Precautions

Blood pressure changes associated with hemodialysis may pose a risk for patients with heart problems. Peritoneal dialysis may be the preferred treatment option in these cases.

Peritoneal dialysis is not recommended for patients with abdominal adhesions or other abdominal defects, such as a **hernia**, that might compromise the efficiency of the treatment. It is also not recommended for patients who suffer frequent bouts of diverticulitis, an inflammation of small pouches in the intestinal tract.

Description

There are two types of dialysis treatment: hemodialysis and peritoneal dialysis:

Hemodialysis

Hemodialysis is the most frequently prescribed type of dialysis treatment in the United States. The treatment involves circulating the patient's blood outside of the body through an extracorporeal circuit (ECC), or dialysis circuit. Two needles are inserted into the patient's vein, or access site, and are attached to the ECC, which consists of plastic blood tubing, a filter known as a dialyzer (artificial kidney), and a dialysis machine that monitors and maintains blood flow and administers dialysate. Dialysate is a chemical bath that is used to draw waste products out of the blood.

Since the 1980s, the majority of hemodialysis treatments in the United States have been performed with hollow fiber dialyzers. A hollow fiber dialyzer is composed of thousands of tube-like hollow fiber strands encased in a clear plastic cylinder several inches in diameter. There are two compartments within the dialyzer (the blood compartment and the dialysate compartment). The membrane that separates these two compartments is semipermeable. This means that it allows the passage of certain sized molecules across it, but prevents the pas-

KEY TERMS

Access site—The vein tapped for vascular access in hemodialysis treatments. For patients with temporary treatment needs, access to the bloodstream is gained by inserting a catheter into the subclavian vein near the patient's collarbone. Patients in long-term dialysis require stronger, more durable access sites, called fistulas or grafts, that are surgically-created.

Dialysate—A chemical bath used in dialysis to draw fluids and toxins out of the bloodstream and supply electrolytes and other chemicals to the bloodstream.

Dialysis prescription—The general parameters of dialysis treatment that vary according to each patient's individual needs. Treatment length, type of dialyzer and dialysate used, and rate of ultrafiltration are all part of the dialysis prescription.

Dialyzer—An artificial kidney usually composed of hollow fiber that is used in hemodialysis to eliminate waste products from the blood and remove excess fluids from the bloodstream.

Erythropoietin—A hormone produced by the kidneys that stimulates the production of red blood cells by bone marrow.

ESRD—End-stage renal disease; chronic or permanent kidney failure.

Extracorporeal circuit (ECC)—The path the hemodialysis patient's blood takes outside of the body. It typically consists of plastic tubing, a hemodialysis machine, and a dialyzer.

Hematocrit (Hct) level—A measure of red blood cells.

Peritoneum—The abdominal cavity; the peritoneum acts as a blood filter in peritoneal dialysis.

sage of other, larger molecules. As blood is pushed through the blood compartment in one direction, suction or vacuum pressure pulls the dialysate through the dialysate compartment in a countercurrent, or opposite direction. These opposing pressures work to drain excess fluids out of the bloodstream and into the dialysate, a process called ultrafiltration.

A second process called diffusion moves waste products in the blood across the membrane into the dialysate compartment, where they are carried out of the body. At the same time, electrolytes and other chemicals in the dialysate solution cross the membrane into the blood compartment. The purified, chemically-balanced blood is then returned to the body.

Most hemodialysis patients require treatment three times a week, for an average of three to four hours per dialysis "run." Specific treatment schedules depend on the type of dialyzer used and the patient's current physical condition. While the treatment prescription and regimen is usually overseen by a nephrologist (a doctor that specializes in the kidney), dialysis treatments are typically administered by a nurse or patient care technician in outpatient clinics known as dialysis centers, or in hospital-based dialysis units. In-home hemodialysis treatment is also an option for some patients, although access to this type of treatment may be limited by financial and lifestyle factors. An investment in equipment is required and another person in the household should be available for support and assistance with treatments.

Peritoneal dialysis

In peritoneal dialysis, the patient's peritoneum, or lining of the abdomen, acts as a blood filter. A catheter is surgically inserted into the patient's abdomen. During treatment, the catheter is used to fill the abdominal cavity with dialysate. Waste products and excess fluids move from the patient's bloodstream into the dialysate solution. After a waiting period of six to 24 hours, depending on the treatment method used, the waste-filled dialysate is drained from the abdomen, and replaced with clean dialysate.

There are three types of peritoneal dialysis:

- Continuous ambulatory peritoneal dialysis (CAPD). A continuous treatment that is self-administered and requires no machine. The patient inserts fresh dialysate solution into the abdominal cavity, waits four to six hours, and removes the used solution. The solution is immediately replaced with fresh dialysate. A bag attached to the catheter is worn under clothing.
- Continuous cyclic peritoneal dialysis (CCPD). An overnight treatment that uses a machine to drain and refill the abdominal cavity, CCPD takes 10–12 hours per session.
- Intermittent peritoneal dialysis (IPD). This hospital-based treatment is performed several times a week. A machine administers and drains the dialysate solution, and sessions can take up to 24 hours.

Peritoneal dialysis is often the treatment option of choice in infants and children, whose small size can make vascular (through a vein) access difficult to maintain. Peritoneal dialysis can also be done outside of a clinical setting, which is more conducive to regular school attendance.

Preparation

Patients are weighed immediately before and after each hemodialysis treatment to assess their fluid retention. Blood pressure and temperature are taken and the patient is assessed for physical changes since their last dialysis run. Regular blood tests monitor chemical and waste levels in the blood. Prior to treatment, patients are typically administered a dose of heparin, an anticoagulant that prevents blood clotting, to ensure the free flow of blood through the dialyzer and an uninterrupted dialysis run for the patient.

Aftercare

Both hemodialysis and peritoneal dialysis patients need to be vigilant about keeping their access sites and catheters clean and infection-free during and between dialysis runs.

Dialysis is just one facet of a comprehensive treatment approach for ESRD. Although dialysis treatment is very effective in removing toxins and fluids from the body, there are several functions of the kidney it cannot mimic, such as regulating high blood pressure and red blood cell production. Patients with ESRD need to watch their diet and fluid intake carefully and take medications as prescribed to manage their disease.

Risks

Many of the risks and side effects associated with dialysis are a combined result of both the treatment and the poor physical condition of the ESRD patient. Dialysis patients should always report side effects to their healthcare provider.

Anemia

Hematocrit (Hct) levels, a measure of red blood cells, are typically low in ESRD patients. This deficiency is caused by a lack of the hormone erythropoietin, which is normally produced by the kidneys. The problem is elevated in hemodialysis patients, who may incur blood loss during hemodialysis treatments. Epoetin alfa, or EPO (sold under the trade name Epogen), a hormone therapy, and intravenous or oral iron supplements are used to manage anemia in dialysis patients.

Cramps, nausea, vomiting, and headaches

Some hemodialysis patients experience cramps and flu-like symptoms during treatment. These can be caused by a number of factors, including the type of dialysate used, composition of the dialyzer membrane, water quality in the dialysis unit, and the ultrafiltration rate of the treatment. Adjustment of the dialysis prescription often helps alleviate many symptoms.

Hypotension

Because of the **stress** placed on the cardiovascular system with regular hemodialysis treatments, patients are at risk for **hypotension**, a sudden drop in blood pressure. This can often be controlled by medication and adjustment of the patient's dialysis prescription.

Infection

Both hemodialysis and peritoneal dialysis patients are at risk for infection. Hemodialysis patients should keep their access sites clean and watch for signs of redness and warmth that could indicate infection. Peritoneal dialysis patients must follow the same precautions with their catheter. **Peritonitis**, an infection of the peritoneum, causes flu-like symptoms and can disrupt dialysis treatments if not caught early.

Infectious diseases

Because there is a great deal of blood exposure involved in dialysis treatment, a slight risk of contracting **hepatitis B** and **hepatitis C** exists. The hepatitis B **vaccination** is recommended for most hemodialysis patients. As of 1997, there has only been one documented case of HIV being transmitted in a United States dialysis unit to a staff member, and no documented cases of HIV ever being transmitted between dialysis patients in the United States. The strict standards of **infection control** practiced in modern hemodialysis units makes the chance of contracting one of these diseases very small.

Normal results

Puffiness in the patient related to **edema**, or fluid retention, may be relieved after dialysis treatment. The patient's overall sense of physical well-being may also be improved. Because dialysis is an ongoing treatment process for many patients, a baseline for normalcy can be difficult to gauge.

Resources

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Paula Anne Ford-Martin

Diaper rash

Definition

Dermatitis of the buttocks, genitals, lower abdomen, or thigh folds of an infant or toddler is commonly referred to as diaper rash.

Description

The outside layer of skin normally forms a protective barrier that prevents infection. One of the primary causes of dermatitis in the diaper area is prolonged skin contact with wetness. Under these circumstances, natural oils are stripped away, the outer layer of skin is damaged, and there is increased susceptibility to infection by bacteria or yeast.

Diaper rash is a term that covers a broad variety of skin conditions that occur on the same area of the body. Some babies are more prone to diaper rash than others.

Causes and symptoms

Frequently a flat, red rash is caused by simple chafing of the diaper against tender skin, initiating a friction rash. This type of rash is not seen in the skin folds. It may be more pronounced around the edges of the diaper, at the waist and leg bands. The baby generally doesn't appear to experience much discomfort. Sometimes the chemicals or detergents in the diaper are contributing factors and may result in **contact dermatitis**. These **rashes** should clear up easily with proper attention. Ignoring the condition may lead to a secondary infection that is more difficult to resolve.

Friction of skin against itself can cause a rash in the baby's skin folds, called intertrigo. This rash appears as reddened areas that may ooze and is often uncomfortable when the diaper is wet. Intertrigo can also be found on other areas of the body where there are deep skin folds that tend to trap moisture.

Seborrheic dermatitis is the diaper area equivalent of cradle cap. It is scaly and greasy in appearance and may be worse in the folds of the skin.

Yeast, or candidal dermatitis, is the most common infectious cause of diaper rash. The affected areas are raised and quite red with distinct borders, and satellite lesions may occur around the edges. Yeast is part of the normal skin flora, and is often an opportunistic invader when simple diaper rash is untreated. It is particularly common after treatment with **antibiotics**, which kill the good bacteria that normally keep the yeast population in check. Usual treatments for diaper rash will not clear it up. Repeated or difficult to resolve episodes of yeast infection may warrant further medical attention, since this is sometimes associated with diabetes or immune problems.

Another infectious cause of diaper rash is **impetigo**. This bacterial infection is characterized by blisters that ooze and crust.

Diagnosis

The presence of **skin lesions** in the diaper area means that the baby has diaper rash. However, there are several types of rash that may require specific treatment

in order to heal. It is useful to be able to distinguish them by appearance as described above.

A baby with a rash that does not clear up within two to three days or a rash with blisters or bleeding should be seen by a healthcare professional for further evaluation.

Treatment

Antibiotics are generally prescribed for rashes caused by bacteria, particularly impetigo. This may be a topical or oral formulation, depending on the size of the area involved and the severity of the infection.

Over-the-counter antifungal creams, such as Lotrimin, are often recommended to treat a rash resulting from yeast. If topical treatment is not effective, an oral antifungal may be prescribed.

Mild steroid creams, such as 0.5–1% hydrocortisone, can be used for seborrheic dermatitis and sometimes intertrigo. Prescription strength creams may be needed for short-term treatment of more stubborn cases.

Alternative treatment

Good diaper hygiene will prevent or clear up many simple cases of diaper rash. Diapers should be checked very frequently and changed as soon as they are wet or soiled. Good air circulation is also important for healthy skin. Babies should have some time without wearing a diaper, and a waterproof pad can be used to protect the bed or other surface. Rubber pants, or other occlusive fabrics, should not be used over the diaper area. Some cloth-like disposable diapers promote better air circulation than plastic-type diapers. It may be necessary for mothers to experiment with diaper types to see if the baby's skin reacts better to cloth or disposable ones. If disposable diapers are used, the baby's skin may react differently to various brands. If the baby is wearing cloth diapers, they should be washed in a mild detergent and double rinsed.

The diaper area should be cleaned with something mild, even plain water. Some wipes contain alcohol or chemicals that can be irritating for some babies. Plain water may be the best cleansing substance when there is a rash. Using warm water in a spray bottle (or giving a quick bath) and then lightly patting the skin dry can produce less skin trauma than using wipes. In the event of suspected yeast, a tablespoon of cider vinegar can be added to a cup of warm water and used as a cleansing solution. This is dilute enough that it should not burn, but acidifies the skin pH enough to hamper the yeast growth.

Barrier ointments can be valuable to treat rashes. Those that contain zinc oxide are especially effective. These creams and ointments protect already irritated skin from the additional insult of urine and stool, particularly if the baby has **diarrhea**. Cornstarch powder may be used on rashes that are moist, such as impetigo.

Baby with severe diaper rash. *(Custom Medical Stock Photo. Reproduced by permission.)*

Nutrition

What the baby eats can make a difference in stool frequency and acidity. Typically, breast-fed babies will have fewer problems with rashes. When adding a new food to the diet, the baby should be observed closely to see whether rashes are produced around the baby's mouth or anus. If this occurs, the new food should be discontinued.

Babies who are taking antibiotics are more likely to get rashes due to yeast. To help bring the good bacterial counts back to normal, *Lactobacillus bifidus* can be added to the diet. It is available in powder form from most health food stores.

Herbal treatment

Some herbal preparations can be useful for diaper rash. Calendula reduces inflammation, tightens tissues, and disinfects. It has been recommended for seborrheic dermatitis as well as for general inflammation of the skin. The ointment should be applied at each diaper change. Chickweed ointment can also be soothing for irritated skin and may be applied once or twice daily.

Prognosis

Treated appropriately, diaper rash will resolve fairly quickly if there is no underlying health problem or skin disease.

Prevention

Frequent diaper changes are important to keep the skin dry and healthy. Application of powders and oint-

KEY TERMS

Dermatitis—Inflammation of the skin.

ments is not necessary when there is no rash. Finding the best combination of cleansing and diapering products for the individual baby will also help to prevent diaper rash.

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Judith Turner

Diaphragm (birth control)

Definition

Diaphragms are dome-shaped barrier methods of **contraception** that block sperm from entering the uterus. They are made of latex (rubber) and formed like a shallow cup. Since vaginas vary in size, each patient will need to be fitted by a doctor or nurse with a diaphragm that conforms to the shape and contour of the vagina as well as the strength of the muscles in the vaginal walls. Diaphragms must be used with spermicidal cream or jelly. The device should cause no discomfort, and neither the woman nor her partner should feel that it is there.

Purpose

The purpose of a diaphragm is to prevent access to the womb (uterus) by the sperm and thus prevent conception. The level of effectiveness is about 95%.

Precautions

Each client will undergo a **physical examination** and a Pap smear. If these are normal, the physician will fit the patient for the device and give instructions on how to insert, remove, and clean the object. She will also be taught the signs and symptoms of potential complications.

Description

Prior to insertion, the inside of the dome and the rim are covered with a thick layer (perhaps a tablespoon) of a spermicide that is compatible with the diaphragm being used. The domed area covers the opening into the uterus (cervix) and keeps the spermicide in place. As a result, any sperm that might get under the diaphragm will be destroyed.

Diaphragms may be inserted two to three hours prior to intercourse, and must be left in place for six to eight hours following sexual relations. During this time the woman may not swim, bathe, or douche, but she may shower. If she desires to have intercourse again before the six to eight hours have passed, the diaphragm should not be removed. Instead, an applicator full of spermicide should be deposited into the vagina.

A diaphragm will last for a year or more. It should be examined weekly for holes. This can be done by holding it up to the light or filling it with water.

Preparation

Before inserting the diaphragm, the woman should empty her bladder and wash her hands with soap and water. The device should be checked for leaks by filling it with water or holding it up to the light. A spermicidal jelly is then applied to the inside and outside, and especially around the rim. While standing with one foot elevated on a chair or step, lying down, or squatting, the woman folds the diaphragm inward toward the middle and inserts it into the vagina as far as it will go.

Aftercare

When removed, the diaphragm should be washed with a mild soap and water. After being dried, it can be dusted with corn starch before being returned to its container. The diaphragm should always be stored away from sunlight and heat in a cool, dry place. It should not be washed with harsh or perfumed soaps or used with perfumed powders because either of these substances can damage the diaphragm.

Risks

Although rare, wearing the diaphragm longer than the recommended time can result in **toxic shock syndrome**. The signs and symptoms of this serious illness include sudden onset of high **fever**, vomiting, **diarrhea**, **dizziness**, faintness, weakness, aching muscles and joints, and rash. The doctor must be notified immediately if any of these conditions appear. An allergic reaction to the spermicide or the material from which the device is

KEY TERMS

Spermicide—A substance that kills sperm.

Toxic shock syndrome—An uncommon, but potentially fatal, disease that has been associated with the use of diaphragms and vaginal tampons. The symptoms include high fever, vomiting, and diarrhea.

made is also possible. Diaphragm use is also associated with an increased risk of bladder infections.

It should be noted that the diaphragm can become dislodged during intercourse, which could result in an unwanted **pregnancy**. To ensure a secure fit, a woman should be examined for a refitting if she gains or loses more than 10 lbs (4.5 kg), or after she gives birth.

Normal results

Consumers can expect an efficiency rate of about 95% in preventing pregnancy. Using a male **condom** in conjunction with the diaphragm decreases the potential for pregnancy. Diaphragms provide no protection against **AIDS** or other **sexually transmitted diseases**.

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Diaphragmatic hernia *see* **Hernia**

Diarrhea

Definition

To most individuals, diarrhea means an increased frequency or decreased consistency of bowel movements; however, the medical definition is more exact than this. In many developed countries, the average number of bowel movements is three per day. However, researchers have found that diarrhea best correlates with an increase in stool weight; stool weights above 10 oz (300 g) per day generally indicates diarrhea. This is mainly due to excess water, which normally makes up 60–85% of fecal matter. In this way, true diarrhea is distinguished from diseases that cause only an increase in the number of bowel movements (hyperdefecation), or incontinence (involuntary loss of bowel contents).

Diarrhea is also classified by physicians into acute, which lasts one to two weeks, and chronic, which continues for longer than 23 weeks. Viral and bacterial infections are the most common causes of acute diarrhea.

Description

In many cases, acute infectious diarrhea is a mild, limited annoyance. However, worldwide acute infectious diarrhea has a huge impact, causing over five million deaths per year. While most deaths are among children under five years of age in developing nations, the impact, even in developed countries, is considerable. For example, over 250,000 individuals are admitted to hospitals in the United States each year because of one of these episodes. Rapid diagnosis and proper treatment can prevent much of the suffering associated with these devastating illnesses.

Chronic diarrhea also has a considerable effect on health, as well as on social and economic well being. Patients with **celiac disease**, inflammatory bowel disease, and other prolonged diarrheal illnesses develop nutritional deficiencies that diminish growth and immunity. They affect social interaction and result in the loss of many working hours.

Causes and symptoms

Diarrhea occurs because more fluid passes through the large intestine (colon) than that organ can absorb. As a rule, the colon can absorb several times more fluid than is required on a daily basis. However, when this reserve capacity is overwhelmed, diarrhea occurs.

Diarrhea is caused by infections or illnesses that either lead to excess production of fluids or prevent absorption of fluids. Also, certain substances in the colon,

such as fats and bile acids, can interfere with water absorption and cause diarrhea. In addition, rapid passage of material through the colon can also do the same.

Symptoms related to any diarrheal illness are often those associated with any injury to the gastrointestinal tract, such as **fever**, nausea, vomiting, and abdominal **pain**. All or none of these may be present depending on the disease causing the diarrhea. The number of bowel movements can vary—up to 20 or more per day. In some patients, blood or pus is present in the stool. Bowel movements may be difficult to flush (float) or contain undigested food material.

The most common causes of acute diarrhea are infections (the cause of **traveler's diarrhea**), **food poisoning**, and medications. Medications are a frequent and often over-looked cause, especially **antibiotics** and **antacids**. Less often, various sugar free foods, which sometimes contain poorly absorbable materials, cause diarrhea.

Chronic diarrhea is frequently due to many of the same things that cause the shorter episodes (infections, medications, etc.); symptoms just last longer. Some infections can become chronic. This occurs mainly with parasitic infections (such as *Giardia*) or when patients have altered immunity (**AIDS**).

The following are the more usual causes of chronic diarrhea:

- AIDS
- colon **cancer** and other bowel tumors
- endocrine or hormonal abnormalities (thyroid, **diabetes mellitus**, etc.)
- food allergy
- inflammatory bowel disease (**Crohn's disease** and **ulcerative colitis**)
- lactose intolerance
- malabsorption syndromes (celiac and Whipple's disease)
- other (alcohol, microscopic colitis, radiation, surgery)

Complications

The major effects of diarrhea are **dehydration**, **malnutrition**, and weight loss. Signs of dehydration can be hard to notice, but increasing thirst, **dry mouth**, weakness or lightheadedness (particularly if worsening on standing), or a darkening/decrease in urination are suggestive. Severe dehydration leads to changes in the body's chemistry and could become life-threatening. Dehydration from diarrhea can result in kidney failure, neurological symptoms, arthritis, and skin problems.

Diagnosis

Most cases of acute diarrhea never need diagnosis or treatment, as many are mild and produce few problems. But patients with fever over 102°F (38.9°C), signs of dehydration, bloody bowel movements, severe abdominal pain, known immune disease, or prior use of antibiotics need prompt medical evaluation.

When diagnostic studies are needed, the most useful are **stool culture** and examination for parasites; however these are often negative and a cause cannot be found in a large number of patients. The earlier cultures are performed, the greater the chance of obtaining a positive result. For those with a history of antibiotic use in the preceding two months, stool samples need to be examined for the toxins that cause **antibiotic-associated colitis**. Tests are also available to check stool samples for microscopic amounts of blood and for cells that indicate severe inflammation of the colon. Examination with an endoscope is sometimes helpful in determining severity and extent of inflammation. Tests to check changes in blood chemistry (potassium, magnesium, etc.) and a complete **blood count** (CBC) are also often performed.

Chronic diarrhea is quite different, and most patients with this condition will receive some degree of testing. Many exams are the same as for an acute episode, as some infections and parasites cause both types of diarrhea. A careful history to evaluate medication use, dietary changes, family history of illnesses, and other symptoms is necessary. Key points in determining the seriousness of symptoms are weight loss of over 10 lb (4.5 kg), blood in the stool, and nocturnal diarrhea (symptoms that awaken the patient from sleep).

Both prescription and over-the-counter medications can contain additives, such as lactose and sorbitol, that will produce diarrhea in sensitive individuals. Review of **allergies** or skin changes may also point to a cause. Social history may indicate if **stress** is playing a role or identify activities which can be associated with diarrhea (for example, diarrhea that occurs in runners).

A combination of stool, blood, and urine tests may be needed in the evaluation of chronic diarrhea; in addition a number of endoscopic and x-ray studies are frequently required.

Treatment

Treatment is ideally directed toward correcting the cause; however, the first aim should be to prevent or treat dehydration and nutritional deficiencies. The type of fluid and nutrient replacement will depend on whether oral feedings can be taken and the severity of fluid loss-

es. Oral rehydration solution (ORS) or intravenous fluids are the choices; ORS is preferred if possible.

A physician should be notified if the patient is dehydrated, and if oral replacement is suggested then commercial (Pedialyte and others) or homemade preparations can be used. The World Health Organization (WHO) has provided this easy recipe for home preparation, which can be taken in small frequent sips:

- Table salt—3/4 tsp
- Baking powder—1 tsp
- Orange juice—1 c
- Water—1 qt (1 L)

When feasible, food intake should be continued even in those with acute diarrhea. A physician should be consulted as to what type and how much food is permitted.

Anti-motility agents (loperamide, diphenoxylate) are useful for those with chronic symptoms; their use is limited or even contraindicated in most individuals with acute diarrhea, especially in those with high fever or bloody bowel movements. They should not be taken without the advice of a physician.

Other treatments are available, depending on the cause of symptoms. For example, the bulk agent psyllium helps some patients by absorbing excess fluid and solidifying stools; cholestyramine, which binds bile acids, is effective in treating bile salt induced diarrhea. Low fat **diets** or more easily digestible fat is useful in some patients. New **antidiarrheal drugs** that decrease excessive secretion of fluid by the intestinal tract is another approach for some diseases. Avoidance of medications or other products that are known to cause diarrhea (such as lactose) is curative in some, but should be discussed with a physician.

Alternative treatment

It is especially important to find the cause of diarrhea, since stopping diarrhea when it is the body's way of eliminating something foreign is not helpful and can be harmful in the long run.

One effective alternative approach to preventing and treating diarrhea involves oral supplementation of aspects of the normal flora in the colon with the yeasts *Lactobacillus acidophilus*, *L. bifidus*, or *Saccharomyces boulardii*. In clinical settings, these "biotherapeutic" agents have repeatedly been helpful in the resolution of diarrhea, especially antibiotic-associated diarrhea. Their effectiveness is also supported by the results of a research study published in the *Journal of the American Medical Association* in 1996.

KEY TERMS

Anti-motiltiy medications—Medications such as loperamide (Imodium), diphenoxylate (Lomotil), or medications containing codeine or narcotics that decrease the ability of the intestine to contract. These can worsen the condition of a patient with dysentery or colitis.

Colitis—Inflammation of the colon.

Endoscope—An endoscope, as used in the field of gastroenterology, is a thin flexible tube that uses a lens or miniature camera to view various areas of the gastrointestinal tract. Both diagnosis, through biopsies or other means, and therapeutic procedures can be done with this instrument.

Endoscopy—The performance of an exam using an endoscope is known generally as endoscopy.

Lactose intolerance—An inability to properly digest milk and dairy products.

Oral rehydration solution (ORS)—A liquid preparation developed by the World Health Organization that can decrease fluid loss in persons with diarrhea. Originally developed to be prepared with materials available in the home, commercial preparations have recently come into use.

Steatorrhea—Excessive amounts of fat in the feces.

Nutrient replacement also plays a role in preventing and treating episodes of diarrhea. Zinc especially appears to have an effect on the immune system, and deficiency of this mineral can lead to chronic diarrhea. Also, zinc replacement improves growth in young patients. Plenty of fluids, especially water, should be taken by individuals suffering from diarrhea to prevent dehydration. The BRAT diet also can be useful in helping to resolve diarrhea. This diet limits food intake to bananas, rice, applesauce, and toast. These foods provide soluble and insoluble fiber without irritation. If the toast is slightly burnt, the charcoal can help sequester toxins and pull them from the body.

Acute homeopathic remedies can be very effective for treating diarrhea especially in infants and young children.

Prognosis

Prognosis is related to the cause of the diarrhea; for most individuals in developed countries, a bout of acute, infectious diarrhea is at best uncomfortable. However, in

both industrialized and developing areas, serious complications and **death** can occur.

For those with chronic symptoms, an extensive number of tests are usually necessary to make a proper diagnosis and begin treatment; a specific diagnosis is found in 90% of patients. In some, however, no specific cause is found and only treatment with bulk agents or antimotility agents is indicated.

Prevention

Proper hygiene and food handling techniques will prevent many cases. Traveler's diarrhea can be avoided by use of Pepto-Bismol and/or antibiotics, if necessary. The most important action is to prevent the complications of dehydration.

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Diazep *see* **Benzodiazepines**

Diclofenac *see* **Nonsteroidal anti-inflammatory drugs**

Dicyclomine *see* **Antispasmodic drugs**

Didanosine *see* **Antiretroviral drugs**

Diets

Definition

Humans may alter their usual eating habits for many reasons, including weight loss, disease prevention or treatment, removing toxins from the body, or to achieve a general improvement in physical and mental health. Others adopt special diets for religious reasons. In the case of some vegetarians and vegans, dietary changes are made out of ethical concerns for the rights of animals.

Purpose

People who are moderately to severely overweight can derive substantial health benefits from a weight-loss diet. A weight reduction of just 10–20 (4.5–9.1 kg) can result in reduced cholesterol levels and lower blood pressure. Weight-related health problems include heart disease, diabetes, high blood pressure, and high levels of blood sugar and cholesterol.

In individuals who are not overweight, dietary changes may also be useful in the prevention or treatment of a range of ailments including acquired immunodeficiency syndrome (**AIDS**), **cancer**, **osteoporosis**, inflammatory bowel disease, chronic pulmonary disease,

Suggested daily food servings. *(Illustration by Electronic Illustrators Group.)*

renal disease, **Parkinson's disease**, seizure disorders, and food **allergies** and intolerances.

Description

Origins

The practice of altering diet for special reasons has existed since antiquity. For example, Judaism has included numerous dietary restrictions for thousands of years. One ancient Jewish sect, the Essenes, is said to have developed a primitive **detoxification** diet aimed at preparing the bodies, minds, and spirits of its members for the coming of a "messiah" who would deliver them from their Roman captors. Preventative and therapeutic diets became quite popular during the late twentieth century. Books promoting the latest dietary plan continue to make the bestseller lists, although not all of the information given is considered authoritative.

The idea of a healthful diet is to provide all of the calories and nutrients needed by the body for optimal performance, at the same time ensuring that neither nutritional deficiencies nor excesses occur. Diet plans that claim to accomplish those objectives are so numerous they are virtually uncountable. These diets employ a variety of approaches, including the following:

- Fixed-menu: Offers little choice to the dieter. Specifies exactly which foods will be consumed. Easy to follow, but may be considered "boring" to some dieters.
- Formula: Replaces some or all meals with a nutritionally balanced liquid formula or powder.
- Exchange-type: Allows the dieter to choose between selected foods from each food group.
- Flexible: Doesn't concern itself with the overall diet, simply with one aspect such as fat or energy.

Diets may also be classified according to the types of foods they allow. For example, an omnivorous diet consists of both animal and plant foods, whereas a lacto-ovo-vegetarian diet permits no animal flesh, but does include eggs, milk, and dairy products. A vegan diet is a stricter form of **vegetarianism** in which eggs, cheese, and other milk products are prohibited.

A third way of classifying diets is according to their purpose: religious, weight-loss, detoxification, lifestyle-related, or aimed at prevention or treatment of a specific disease.

Precautions

Dieters should be cautious about plans that severely restrict the size of food portions, or that eliminate entire food groups from the diet. It is highly probable that they will become discouraged and drop out of such programs. The best diet is one that can be maintained indefinitely without ill effects, that offers sufficient variety and balance to provide everything needed for good health, and that is considerate of personal food preferences.

Low-fat diets are not recommended for children under the age of two. Young children need extra fat to maintain their active, growing bodies. Fat intake may be gradually reduced between the ages of two and five, after which it should be limited to a maximum of 30% of total calories through adulthood. Saturated fat should be restricted to no more than 10% of total calories.

Weight-loss dieters should be wary of the "yo-yo" effect that occurs when numerous attempts are made to reduce weight using high-risk, quick-fix diets. This continued "cycling" between weight loss and weight gain can slow the basal metabolic rate and can sometimes lead to eating disorders. The dieter may become discouraged and frustrated by this success/failure cycle. The end result of "yo-yo" dieting is that it becomes more difficult to maintain a healthy weight.

Caution should also be exercised about weight-loss diets that require continued purchases of special prepackaged foods. Not only do these tend to be costly and overprocessed, they may also prevent dieters from learning the food-selection and preparation skills essential to maintenance of weight loss. Further, dieters should consider whether they want to carry these special foods to work, restaurants, or homes of friends.

Concern has been expressed about weight-loss diet plans that do not include **exercise**, considered essential to long-term weight management. Some diets and supplements may be inadvisable for patients with special conditions or situations.

Certain fad diets purporting to be official diets of groups such as the American Heart Association and the Mayo Clinic are in no way endorsed by those institutions. Patients thinking of starting such a diet should check with the institution to ensure its name has not been misappropriated by an unscrupulous practitioner.

Side effects

A wide range of side effects (some quite serious) can result from special diets, especially those that are nutritionally unbalanced. Further problems can arise if the dieter is taking high doses of dietary supplements. Food is essential to life, and improper **nutrition** can result in serious illness or **death**.

Research and general acceptance

It is agreed among traditional and complementary practitioners that many patients could substantially benefit from improved eating habits. Specialized diets have proved effective against a wide variety of conditions and diseases. However, dozens of unproved but widely publicized "fad diets" emerge each year, prompting widespread concerns about their usefulness, cost to the consumer, and their safety.

Resources

ORGANIZATIONS

American Dietetic Association. 216 West Jackson Blvd., Chicago, IL 60606-6995. (312) 899-0040. <http://www.eatright.org>.

David Helwig

Diffuse esophageal spasm

Definition

Diffuse esophageal spasm is a term used to define an uncoordinated or spastic esophagus.

Description

The esophagus is a muscular tube that actively transports food from the throat to the stomach by rhythmic contractions known as peristalsis. The actual mechanism and anatomy are quite complex, involving three distinct segments and allowing a person to swallow even when upside-down. Diffuse esophageal spasm describes a condition where the entire esophagus is spastic—along its entire length, the muscular activity is increased and uncoordinated. The name corkscrew esophagus describes perfectly the appearance of this disorder on x rays.

X rays may reveal a slightly different appearance and result in the designation rosary bead esophagus, but the cause is still diffuse spasm, and the two entities behave in the same way.

Causes and symptoms

The cause appears to be disruption of the complex system of nerves that coordinates the muscular activity. The result is difficulty swallowing (dysphagia) and **pain** that feels like a **heart attack** and can involve the entire chest, jaw, and arms.

KEY TERMS

Contrast agent—A substance that produces shadows on x rays.

Manometry—Measurement of pressure.

Peristalsis—Slow, rhythmic contractions of the muscles in a tubular organ, such as the intestines, that propel the contents along.

Diagnosis

Swallowing problems usually call for esophagograms. In the x ray department, the patient is given a contrast agent to drink. During swallowing, x rays record the passage of the agent down the esophagus and into the stomach. Instead of a straight tube with well-coordinated waves of contraction, the resulting x rays show a writhing organ resembling a giant corkscrew.

Another test that is used in many disorders of esophageal motility is manometry. Pressures inside the esophagus are measured every inch or so using a balloon device that is passed all the way down to the stomach. The result is a precise record of its activity that yields a specific diagnosis.

Treatment

Soft and liquid foods pass more easily than solid pieces. Medications of several types are helpful—nifedipine, hydralazine, isoproterenol, and nitrates being the most successful. Several other treatments have uncertain results. For severe cases, relief is obtained two-thirds of the time by cutting the muscles along the entire length of the esophagus. This is a major surgical procedure.

Prognosis

This condition does not go away, nor is treatment entirely satisfactory. Patients need to be careful of what they eat and continue on medication if a beneficial one is found. Fortunately, the condition does not get progressively worse as time passes.

Resources

BOOKS

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J. Ricker Polsdorfer, MD

DiGeorge syndrome

Definition

DiGeorge syndrome (also called congenital thymic hypoplasia, or third and fourth pharyngeal pouch syndrome) is a birth defect that is caused by an abnormal chromosome and affects the baby's immune system. The syndrome is marked by absence or underdevelopment of the thymus and parathyroid glands. It is named for the pediatrician who first described it in 1965.

Description

The prevalence of DiGeorge syndrome is debated; the estimates range from 1:4000 to 1:6395. Because the symptoms caused by the chromosomal abnormality vary somewhat from patient to patient, the syndrome probably occurs much more often than was previously thought. DiGeorge syndrome is sometimes described as one of the "CATCH 22" disorders, so named because of their characteristics—cardiac defects, abnormal facial features, thymus underdevelopment, cleft palate, and hypocalcemia—caused by a deletion of several genes in chromosome 22. The specific facial features associated with DiGeorge syndrome include low-set ears, wide-set eyes, a small jaw, and a short groove in the upper lip. The male/female ratio is 1:1. The syndrome appears to be equally common in all racial and ethnic groups.

Causes and symptoms

DiGeorge syndrome is caused either by inheritance of a defective chromosome 22 or by a new defect in chromosome 22 in the fetus. The type of defect that is involved is called deletion. A deletion occurs when the genetic material in the chromosomes does not recombine properly during the formation of sperm or egg cells. The deletion means that several genes from chromosome 22 are missing in DiGeorge syndrome patients. According to a 1999 study, 6% of children with DiGeorge syndrome inherited the deletion from a parent, while 94% had a new deletion. Other conditions that are associated with

DiGeorge syndrome are diabetes (a condition where the pancreas no longer produces enough insulin) in the mother and **fetal alcohol syndrome** (a pattern of **birth defects** and learning and behavioral problems affecting individuals whose mothers consumed alcohol during **pregnancy**).

The loss of the genes in the deleted material means that the baby's third and fourth pharyngeal pouches fail to develop normally during the twelfth week of pregnancy. This developmental failure results in a completely or partially absent thymus gland and parathyroid glands. In addition, 74% of fetuses with DiGeorge syndrome have severe heart defects. The child is born with a defective immune system and an abnormally low level of calcium in the blood.

These defects usually become apparent within 48 hours of birth. The infant's heart defects may lead to **heart failure**, or there may be seizures and other evidence of a low level of calcium in the blood (**hypocalcemia**).

Diagnosis

Diagnosis of DiGeorge syndrome can be made by ultrasound examination around the eighteenth week of pregnancy, when abnormalities in the development of the heart or the palate can be detected. Another technique that is used to diagnose the syndrome before birth is called fluorescence in situ hybridization, or FISH. This technique uses DNA probes from the DiGeorge region on chromosome 22. FISH can be performed on cell samples obtained by **amniocentesis** as early as the fourteenth week of pregnancy. It confirms about 95% of cases of DiGeorge syndrome.

If the mother has not had prenatal testing, the diagnosis of DiGeorge syndrome is sometimes suggested by the child's facial features at birth. In other cases, the doctor makes the diagnosis during heart surgery when he or she notices the absence or abnormal location of the thymus gland. The diagnosis can be confirmed by blood tests for calcium, phosphorus, and parathyroid hormone levels, and by the sheep cell test for immune function.

Treatment

Hypocalcemia

Hypocalcemia in DiGeorge patients is unusually difficult to treat. Infants are usually given calcium and vitamin D by mouth. Severe cases have been treated by transplantation of fetal thymus tissue or bone marrow.

Heart defects

Infants with life-threatening heart defects are treated surgically.

Defective immune function

Children with DiGeorge syndrome should be kept on low-phosphorus **diets** and kept away from crowds or other sources of infection. They should not be immunized with vaccines made from live viruses or given **corticosteroids**.

Prognosis

The prognosis is variable; many infants with DiGeorge syndrome die from overwhelming infection, seizures, or heart failure within the first year. Advances in heart surgery indicate that the prognosis is most closely linked to the severity of the heart defects and the partial presence of the thymus gland. In most children who survive, the number of T cells, a type of white blood cell, in the blood rises spontaneously as they mature. Survivors are likely to be mentally retarded, however, and to have other developmental difficulties, including psychiatric problems in later life.

Prevention

Genetic counseling is recommended for parents of children with DiGeorge syndrome because the disorder can be detected prior to birth. Although most children with DiGeorge syndrome did not inherit the chromosome deletion from their parents, they have a 50% chance of passing the deletion on to their own children.

Because of the association between DiGeorge syndrome and fetal alcohol syndrome, pregnant women should avoid drinking alcoholic beverages.

Resources

BOOKS

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ORGANIZATIONS

Canadian 22q Group. 320 Cote Street Antoine, West Montreal, Quebec H3Y 2J4.

KEY TERMS

Deletion—A genetic abnormality in which a segment of a chromosome is lost. DiGeorge syndrome is caused by a deletion on human chromosome 22.

Fetal alcohol syndrome—A cluster of birth defects that includes abnormal facial features and mental retardation, caused by the mother's consumption of alcoholic beverages during pregnancy.

Fluorescence in situ hybridization (FISH)—A technique for diagnosing DiGeorge syndrome before birth by analyzing cells obtained by amniocentesis with DNA probes. FISH is about 95% accurate.

Hypocalcemia—An abnormally low level of calcium in the blood.

Hypoplasia—A deficiency or underdevelopment of a tissue or body structure.

T cells—A type of white blood cell produced in the thymus gland. T cells are an important part of the immune system. Infants born with an underdeveloped or absent thymus do not have a normal level of T cells in their blood.

Chromosome Deletion Outreach, Inc. P.O. Box 724, Boca Raton, FL 33429-0724. (888) 236-6680.

International DiGeorge/VCF Support Network, c/o Family Voices of New York. 46 1/2 Clinton Avenue, Cortland, NY 13045. (607) 753-1250.

Rebecca J. Frey, PhD

Digital rectal examination *see* **Rectal examination**

Digitalis drugs

Definition

Digitalis drugs are medicines made from a type of foxglove plant (*Digitalis purpurea*) that have a stimulating effect on the heart.

Purpose

Digitalis drugs are used to treat heart problems such as congestive **heart failure** and irregular heartbeat. These medicines help make the heart stronger and more efficient. This, in turn, improves blood circulation and helps relieve the swelling of the hands and ankles that is common in people with heart problems.

Description

Digitalis drugs, also known as digitalis glycosides, are available only with a physician's prescription. They are sold in tablet, capsule, liquid, and injectable forms. Commonly used digitalis drugs are digitoxin (Crystodigin) and digoxin (Lanoxin).

Recommended dosage

The recommended dosage is different for each patient. The physician who prescribes the medicine will determine the correct dose. Taking exactly the right amount of medicine and taking it exactly as directed are very important. Never take larger or more frequent doses. During treatment with a digitalis heart medicine, the physician will monitor blood levels of the drug and will decide whether the dose needs to be changed. Patients should never change the dose of this medicine unless told to do so by their physicians.

Precautions

Seeing a physician regularly while taking digitalis drugs is very important. The physician will check to make sure the medicine is working as it should and will make any necessary changes in dosage or in instructions for taking the medicine.

Patients taking digitalis drugs should learn to take their pulse and should check it regularly while under treatment with this medicine. Changes in pulse rate, rhythm, or force could be signs of side effects.

Do not stop taking this medicine suddenly without checking with the physician who prescribed it. This could cause a serious change in heart function.

Digitalis drugs are responsible for many accidental poisonings in children. Keep this medicine out of the reach of children.

Be alert to the signs of overdose. Overdosing is a serious concern with digitalis drugs, because the amount of medicine that most people need to help their heart problems is very close to the amount that can cause problems from overdose. If any of these signs of overdose occur, check with a physician as soon as possible:

- loss of appetite
- nausea
- vomiting

Digitalis purpurea. *(Photo Researcher, Inc. Reproduced by permission.)*

- pain in the lower stomach
- diarrhea
- extreme tiredness or weakness
- extremely slow or irregular heartbeat (or fast heartbeat in children)
- blurred vision or other vision changes
- drowsiness
- confusion or depression
- headache
- fainting

Anyone who is taking digitalis drugs should be sure to tell the health care professional in charge before having any surgical or dental procedures or receiving emergency treatment. Physicians may advise people taking digitalis drugs to wear or carry medical identification indicating that they are taking this medicine.

Patients need to be very careful not to accidentally take this medicine in place of another medicine that looks similar. Patients who are taking other medicines that look like their digitalis medicine should ask their pharmacists for suggestions on how to avoid mix-ups.

Anyone who has had unusual reactions to digitalis drugs in the past should let his or her physician know before taking the drugs again. The physician should also be told about any **allergies** to foods, dyes, preservatives, or other substances.

Women who are pregnant or breastfeeding or who may become pregnant should check with their physicians before using digitalis drugs.

Older people may be especially sensitive to the effects of digitalis drugs, which may increase the chance of overdose.

Before using digitalis drugs, people with any of the following medical problems should make sure their physicians are aware of their conditions:

- heart disease
- heart rhythm problems
- severe lung disease
- kidney disease
- liver disease
- thyroid disease

Side effects

Side effects are rare with this medicine. Check with a physician as soon as possible if a skin rash, **hives,** or any other unusual or troublesome symptoms occur. Watch for signs of overdose.

Interactions

Digitalis drugs may interact with a number of other medicines. When this happens, the effects of one or both of the drugs may change or the risk of side effects may be greater. For example:

- Taking digitalis drugs with other heart medicines, amphetamines, or diet pills could increase the risk of heart rhythm problems.
- Calcium channel blockers, used to treat high blood pressure, may cause higher than usual levels of digitalis drugs in the body that could lead to symptoms of overdose as covered in the above section.
- Diuretics (water pills) or other medicines that lower the amount of potassium in the body may increase the side effects of digitalis drugs.
- Medicines that increase the amount of potassium in the body may raise the risk of serious heart rhythm problems when taken with digitalis drugs.

- Diarrhea medicine or cholesterol-lowering drugs such as cholestyramine (Questran) and colestipol (Colestid) may keep digitalis medicines from being absorbed into the body. To prevent this problem, digitalis drugs should be taken several hours before or after taking these medicines.

The list above does not include every drug that may interact with digitalis drugs. Be sure to check with a physician or pharmacist before taking any other prescription or nonprescription (over-the-counter) medicine.

In addition, a diet high in fiber may interfere with the effects of digitalis drugs by preventing the medicine from being absorbed into the body. To avoid this problem, eat high fiber foods (such as bran products, whole wheat bread, and fresh fruits and vegetables) several hours before or after taking digitalis medicine.

Nancy Ross-Flanigan

Digoxin *see* **Digitalis drugs; Antiarrhythmic drugs**

Dilatation and curettage

Definition

Dilatation and curettage (D & C) is a gynecological procedure in which the lining of the uterus (endometrium) is scraped away.

Purpose

D & C is commonly used to obtain tissue for microscopic evaluation to rule out **cancer**. D & C may also be used to diagnose and treat heavy menstrual bleeding, and to diagnose endometrial polyps and **uterine fibroids**. A D & C can be used as a treatment as well, to remove **pregnancy** tissue after a **miscarriage**, incomplete abortion, or **childbirth**. Endometrial polyps may be removed, and sometimes benign uterine tumors (fibroids) may be scraped away. D & C can also be used as an early abortion technique up to 16 weeks.

Description

D & C is usually performed under general anesthesia, although local or epidural anesthesia can also be used. A local lessens risk and costs, but the woman will feel cramping during the procedure. The type of anesthesia used often depends upon the reason for the D & C.

In the procedure (which takes only minutes to perform), the doctor inserts an instrument to hold open the

When performing a D & C, the physician inserts a speculum to separate and hold the vaginal walls, then stretches open the cervix with a dilator. Once the cervix is dilated, the physician will insert a curette into the uterus and scrapes away small portions of the uterine lining for laboratory analysis. *(Illustration by Electronic Illustrators Group.)*

KEY TERMS

Endometrial polyps—A growth in the lining of the uterus (endometrium) that may cause bleeding and can develop into cancer.

Epidural anesthesia—A type of anesthesia that is injected into the epidural space of the spinal cord to numb the nerves leading to the lower half of the body.

Uterine fibroid—A noncancerous tumor of the uterus that can range from the size of a pea to the size of a grapefruit. Small fibroids require no treatment, but those causing serious symptoms may need to be removed.

vaginal walls, and then stretches the opening of the uterus to the vagina (the cervix) by inserting a series of tapering rods, each thicker than the previous one, or by using other specialized instruments. This process of opening the cervix is called dilation.

Once the cervix is dilated, the physician inserts a spoon-shaped surgical device called a curette into the uterus. The curette is used to scrape away the uterine lining. One or more small tissue samples from the lining of the uterus or the cervical canal are sent for analysis by microscope to check for abnormal cells.

Although simpler, less expensive techniques such as a vacuum aspiration are quickly replacing the D & C as a diagnostic method, it is still often used to diagnose and treat a number of conditions.

Preparation

Because opening the cervix can be painful, sedatives may be given before the procedure begins. Deep breathing and other relaxation techniques may help ease cramping during cervical dilation.

Aftercare

A woman who has had a D & C performed in a hospital can usually go home the same day or the next day. Many women experience backache and mild cramps after the procedure, and may pass small blood clots for a day or so. Vaginal staining or bleeding may continue for several weeks.

Most women can resume normal activities almost immediately. Patients should avoid sexual intercourse, douching, and tampon use for at least two weeks to prevent infection while the cervix is closing and to allow the endometrium to heal completely.

Risks

The primary risk after the procedure is infection. Signs of infection include:

- fever
- heavy bleeding
- severe cramps
- foul-smelling vaginal discharge

A woman should report any of these symptoms to her doctor, who can treat the infection with **antibiotics** before it becomes serious.

D & C is a surgical operation, which carries certain risks associated with general anesthesia. Rare complications include puncture of the uterus (which usually heals on its own) or puncture of the bowel or bladder (which require further surgery to repair).

Normal results

Removal of the uterine lining causes no side effects, and may be beneficial if the lining has thickened so much that it causes heavy periods. The uterine lining soon grows again normally, as part of the menstrual cycle.

Resources

BOOKS

Carlson, Karen J., Stephanie A. Eisenstat, and Terra Ziporyn. *The Harvard Guide to Women's Health*. Cambridge, MA: Harvard University Press, 1996.

Carol A. Turkington

Dilated cardiomyopathy *see* **Congestive cardiomyopathy**

Diltiazem *see* **Calcium channel blockers**

Dilution test *see* **Kidney function tests**

Diphenhydramine *see* **Antihistamines**

Diphtheria

Definition

Diphtheria is a potentially fatal, contagious disease that usually involves the nose, throat, and air passages,

but may also infect the skin. Its most striking feature is the formation of a grayish membrane covering the tonsils and upper part of the throat.

Description

Like many other upper respiratory diseases, diphtheria is most likely to break out during the winter months. At one time it was a major childhood killer, but it is now rare in developed countries because of widespread immunization. Since 1988, all confirmed cases in the United States have involved visitors or immigrants. In countries that do not have routine immunization against this infection, the mortality rate varies from 1.5–25%.

Persons who have not been immunized may get diphtheria at any age. The disease is spread most often by droplets from the coughing or sneezing of an infected person or carrier. The incubation period is two to seven days, with an average of three days. It is vital to seek medical help at once when diphtheria is suspected, because treatment requires emergency measures for adults as well as children.

Causes and symptoms

The symptoms of diphtheria are caused by toxins produced by the diphtheria bacillus, *Corynebacterium diphtheriae* (from the Greek for "rubber membrane"). In fact, toxin production is related to infections of the bacillus itself with a particular bacteria virus called a phage (from bacteriophage; a virus that infects bacteria). The intoxication destroys healthy tissue in the upper area of the throat around the tonsils, or in open **wounds** in the skin. Fluid from the dying cells then coagulates to form the telltale gray or grayish green membrane. Inside the membrane, the bacteria produce an exotoxin, which is a poisonous secretion that causes the life-threatening symptoms of diphtheria. The exotoxin is carried throughout the body in the bloodstream, destroying healthy tissue in other parts of the body.

The most serious complications caused by the exotoxin are inflammations of the heart muscle (**myocarditis**) and damage to the nervous system. The risk of serious complications is increased as the time between onset of symptoms and the administration of antitoxin increases, and as the size of the membrane formed increases. The myocarditis may cause disturbances in the heart rhythm and may culminate in **heart failure**. The symptoms of nervous system involvement can include seeing double (diplopia), painful or difficult swallowing, and slurred speech or loss of voice, which are all indications of the exotoxin's effect on nerve functions. The exotoxin may also cause severe swelling in the neck ("bull neck").

The signs and symptoms of diphtheria vary according to the location of the infection:

Nasal

Nasal diphtheria produces few symptoms other than a watery or bloody discharge. On examination, there may be a small visible membrane in the nasal passages. Nasal infection rarely causes complications by itself, but it is a public health problem because it spreads the disease more rapidly than other forms of diphtheria.

Pharyngeal

Pharyngeal diphtheria gets its name from the pharynx, which is the part of the upper throat that connects the mouth and nasal passages with the voice box. This is the most common form of diphtheria, causing the characteristic throat membrane. The membrane often bleeds if it is scraped or cut. It is important not to try to remove the membrane because the trauma may increase the body's absorption of the exotoxin. Other signs and symptoms of pharyngeal diphtheria include mild **sore throat**, **fever** of 101–102°F (38.3–38.9°C), a rapid pulse, and general body weakness.

Laryngeal

Laryngeal diphtheria, which involves the voice box or larynx, is the form most likely to produce serious complications. The fever is usually higher in this form of diphtheria (103–104°F or 39.4–40°C) and the patient is very weak. Patients may have a severe **cough**, have difficulty breathing, or lose their voice completely. The development of a "bull neck" indicates a high level of exotoxin in the bloodstream. Obstruction of the airway may result in respiratory compromise and **death**.

Skin

This form of diphtheria, which is sometimes called cutaneous diphtheria, accounts for about 33% of diphtheria cases. It is found chiefly among people with poor hygiene. Any break in the skin can become infected with diphtheria. The infected tissue develops an ulcerated area and a diphtheria membrane may form over the wound but is not always present. The wound or ulcer is slow to heal and may be numb or insensitive when touched.

Diagnosis

Because diphtheria must be treated as quickly as possible, doctors usually make the diagnosis on the basis of the visible symptoms without waiting for test results.

In making the diagnosis, the doctor examines the patient's eyes, ears, nose, and throat in order to rule out

other diseases that may cause fever and sore throat, such as **infectious mononucleosis**, a sinus infection, or **strep throat**. The most important single symptom that suggests diphtheria is the membrane. When a patient develops skin infections during an outbreak of diphtheria, the doctor will consider the possibility of cutaneous diphtheria and take a smear to confirm the diagnosis.

Laboratory tests

The diagnosis of diphtheria can be confirmed by the results of a culture obtained from the infected area. Material from the swab is put on a microscope slide and stained using a procedure called Gram's stain. The diphtheria bacillus is called Gram-positive because it holds the dye after the slide is rinsed with alcohol. Under the microscope, diphtheria bacilli look like beaded rod-shaped cells, grouped in patterns that resemble Chinese characters. Another laboratory test involves growing the diphtheria bacillus on a special material called Loeffler's medium.

Treatment

Diphtheria is a serious disease requiring hospital treatment in an intensive care unit if the patient has developed respiratory symptoms. Treatment includes a combination of medications and supportive care:

Antitoxin

The most important step is prompt administration of diphtheria antitoxin, without waiting for laboratory results. The antitoxin is made from horse serum and works by neutralizing any circulating exotoxin. The doctor must first test the patient for sensitivity to animal serum. Patients who are sensitive (about 10%) must be desensitized with diluted antitoxin, since the antitoxin is the only specific substance that will counteract diphtheria exotoxin. No human antitoxin is available for the treatment of diphtheria.

The dose ranges from 20,000–100,000 units, depending on the severity and length of time of symptoms occurring before treatment. Diphtheria antitoxin is usually given intravenously.

Antibiotics

Antibiotics are given to wipe out the bacteria, to prevent the spread of the disease, and to protect the patient from developing **pneumonia**. They are not a substitute for treatment with antitoxin. Both adults and children may be given penicillin, ampicillin, or erythromycin. Erythromycin appears to be more effective than penicillin in treating people who are carriers because of better penetration into the infected area.

Cutaneous diphtheria is usually treated by cleansing the wound thoroughly with soap and water, and giving the patient antibiotics for 10 days.

Supportive care

Diphtheria patients need bed rest with intensive nursing care, including extra fluids, oxygenation, and monitoring for possible heart problems, airway blockage, or involvement of the nervous system. Patients with laryngeal diphtheria are kept in a **croup** tent or high-humidity environment; they may also need throat suctioning or emergency surgery if their airway is blocked.

Patients recovering from diphtheria should rest at home for a minimum of two to three weeks, especially if they have heart complications. In addition, patients should be immunized against diphtheria after recovery, because having the disease does not always induce antitoxin formation and protect them from reinfection.

Prevention of complications

Diphtheria patients who develop myocarditis may be treated with oxygen and with medications to prevent irregular heart rhythms. An artificial pacemaker may be needed. Patients with difficulty swallowing can be fed through a tube inserted into the stomach through the nose. Patients who cannot breathe are usually put on mechanical respirators.

Prognosis

The prognosis depends on the size and location of the membrane and on early treatment with antitoxin; the longer the delay, the higher the death rate. The most vulnerable patients are children under age 15 and those who develop pneumonia or myocarditis. Nasal and cutaneous diphtheria are rarely fatal.

Prevention

Prevention of diphtheria has four aspects:

Immunization

Universal immunization is the most effective means of preventing diphtheria. The standard course of immunization for healthy children is three doses of DPT (diphtheria-tetanus-pertussis) preparation given between two months and six months of age, with booster doses given at 18 months and at entry into school. Adults should be immunized at 10 year intervals with Td (tetanus-diphtheria) toxoid. A toxoid is a bacterial toxin that is treated to make it harmless but still can induce immunity to the disease.

KEY TERMS

Antitoxin—An antibody against an exotoxin, usually derived from horse serum.

Bacillus—A rod-shaped bacterium, such as the diphtheria bacterium.

Carrier—A person who may harbor an organism without symptoms and may transmit it to others.

Cutaneous—Located in the skin.

Diphtheria-tetanus-pertussis (DTP)—The standard preparation used to immunize children against diphtheria, tetanus, and whooping cough. A so-called "acellular pertussis" vaccine (aP) is usually used since its release in the mid-1990s.

Exotoxin—A poisonous secretion produced by bacilli which is carried in the bloodstream to other parts of the body.

Gram's stain—A dye staining technique used in laboratory tests to determine the presence and type of bacteria.

Loeffler's medium—A special substance used to grow diphtheria bacilli to confirm the diagnosis.

Myocarditis—Inflammation of the heart tissue.

Toxoid—A preparation made from inactivated exotoxin, used in immunization.

Isolation of patients

Diphtheria patients must be isolated for one to seven days or until two successive cultures show that they are no longer contagious. Children placed in **isolation** are usually assigned a primary nurse for emotional support.

Identification and treatment of contacts

Because diphtheria is highly contagious and has a short incubation period, family members and other contacts of diphtheria patients must be watched for symptoms and tested to see if they are carriers. They are usually given antibiotics for seven days and a booster shot of diphtheria/tetanus toxoid.

Reporting cases to public health authorities

Reporting is necessary to track potential epidemics, to help doctors identify the specific strain of diphtheria, and to see if resistance to penicillin or erythromycin has developed.

Resources

BOOKS

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Rebecca J. Frey

Diplegia *see* **Paralysis**

Direct Coombs' test *see* **Coombs' tests**

Direct laryngoscopy *see* **Laryngoscopy**

Discoid lupus erythematosus

Definition

Discoid lupus erythematosus (DLE) is a disease in which coin-shaped (discoid) red bumps appear on the skin.

Description

The disease called discoid lupus erythematosus only affects the skin, although similar discoid **skin lesions** can occur in the serious disease called **systemic lupus erythematosus** (SLE). Only about 10% of all patients with DLE will go on to develop the multi-organ disease SLE.

The tendency to develop DLE seems to run in families. Although men or women of any age can develop DLE, it occurs in women three times more frequently than in men. The typical DLE patient is a woman in her 30s.

Discoloration of the hands is one characteristic of discoid lupus erythematosus. *(Custom Medical Stock Photo. Reproduced by permission.)*

Causes and symptoms

The cause of DLE is unknown. It is thought that DLE (like SLE) may be an autoimmune disorder. **Autoimmune disorders** are those that occur when cells of the immune system are misdirected against the body. Normally, immune cells work to recognize and help destroy foreign invaders like bacteria, viruses, and fungi. In autoimmune disorders, these cells mistakenly recognize various tissues of the body as foreign invaders, and attack and destroy these tissues. In SLE, the misdirected immune cells are antibodies. In DLE, the damaging cells are believed to be a type of white blood cell called a T lymphocyte. The injury to the skin results in inflammation and the characteristic discoid lesions.

In DLE, the characteristic skin lesion is circular and raised. The reddish rash is about 5–10 mm in diameter, with the center often somewhat scaly and lighter in color than the darker outer ring. The surface of these lesions is sometimes described as "warty." There is rarely any **itching** or **pain** associated with discoid lesions. They tend to appear on the face, ears, neck, scalp, chest, back, and arms. As DLE lesions heal, they leave thickened, scarred areas of skin. When the scalp is severely affected, there may be associated hair loss (**alopecia**).

People with DLE tend to be quite sensitive to the sun. They are more likely to get a **sunburn**, and the sun is likely to worsen their discoid lesions.

Diagnosis

Diagnosis of DLE usually requires a **skin biopsy**. A small sample of a discoid lesion is removed, specially prepared, and examined under a microscope. Usually, the lesion has certain microscopic characteristics that allow it to be identified as a DLE lesion. Blood tests will not reveal the type of antibodies present in SLE, and **physical examination** usually does not reveal anything other than the skin lesions. If antibodies exist in the blood, or if other symptoms or physical signs are found, it is possible that the discoid lesions are a sign of SLE rather than DLE.

Treatment

Treatment of DLE primarily involves the use of a variety of skin creams. **Sunscreens** are used for protection. Steroid creams can be applied to decrease inflammation. Occasionally, small amounts of a steroid preparation will be injected with a needle into a specific lesion. Because of their long list of side effects, steroid preparations taken by mouth are avoided. Sometimes, short-term treatment with oral steroids will be used for particularly severe DLE outbreaks. Medications used to treat the infectious disease **malaria** are often used to treat DLE.

Alternative treatment

Alternative treatments for DLE include eating a healthy diet, low in red meat and dairy products and high in fish containing omega-3 fatty acids. These types of fish include mackerel, sardines, and salmon. Following a healthy diet is thought to decrease inflammation. Dietary supplements believed to be helpful include **vitamins** B, C, E, and selenium. Vitamin A is also recommended to improve DLE lesions. Constitutional homeopathic treatment can help heal DLE as well as help prevent it developing into SLE.

Prognosis

For the most part, the prognosis for people with DLE is excellent. While the lesions may be cosmetically unsightly, they are not life threatening and usually do not cause a patient to change his or her lifestyle. Only about 10% of patients with DLE will go on to develop SLE.

Prevention

DLE cannot be prevented. Recommendations to prevent flares of DLE in patients with the disease include avoiding exposure to sun and consistently using sunscreen.

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KEY TERMS

Antibody—Specialized cells of the immune system that can recognize organisms invading the body (like bacteria, viruses, and fungi). The antibodies are then able to start a complex chain of events designed to kill these foreign invaders.

Autoimmune disorder—A disorder in which the body's antibodies mistake the body's own tissues for foreign invaders. The immune system then attacks and causes damage to these tissues.

Immune system—The system of specialized organs, lymph nodes, and blood cells throughout the body that work together to defend the body against foreign invaders (bacteria, viruses, fungi, etc.).

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ORGANIZATIONS

The American College of Rheumatology. 1800 Century Place, Suite 250, Atlanta, GA 30345. (404) 633-3777. <http://www.rheumatology.org>.

Lupus Foundation of America. 1300 Piccard Dr., Suite 200, Rockville, MD 20850. (800) 558-0121. <http://www.lupus.org>.

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Disk removal

Definition

One of the most common types of back surgery is disk removal (diskectomy), the removal of an intervertebral disk, the flexible plate that connects any two adjacent vertebrae in the spine. Intervertebral disks act as **shock** absorbers, protecting the brain and spinal cord from the impact produced by the body's movements.

Purpose

About 150,000 Americans undergo disk removal each year in the United States. Removing the invertebral disk is performed to treat back **pain** that has lasted at least six weeks as a result of an abnormal disk and that has not responded to conservative treatment. Surgery is also performed if there is pressure on the lumbosacral nerve roots that causes weakness or bowel or bladder disfunction.

As a person ages, the disks between the vertebrae degenerate and dry out, and the fibers holding them in place tear. Eventually, the disk can form a blister-like bulge, compressing nerves in the spine and causing pain. This is called a "prolapsed" (or herniated) disk. If such a disk causes muscle weakness or interferes with bladder or bowel function because it is pressing on a nerve root, immediate surgery to remove the disk may be needed.

The aim of the surgery is to try to relieve all pressure on nerve roots by removing the pulpy material from the disk, or the disk itself. If it is necessary to remove material from several nearby vertebrae, the spine may become unsteady. In this case, the surgeon will perform a spinal fusion, removing all the disks between two or more vertebrae and roughening the bones so that the vertebrae heal together. Bone strips taken from the patient's leg or hip may be used to help hold the vertebrae together. Spinal fusion decreases pain but it also decreases spinal mobility.

Precautions

The doctor will obtain x rays, neuroimaging studies, including computed tomography scan (CT scan) myelogram and **magnetic resonance imaging** (MRI), and clinical exams to determine the precise location of the affected disk.

Description

The surgery is done under general anaesthesia, which puts the patient to sleep and affects the whole body. Operating on the patient's back, the neurosurgeon or orthopedic surgeon makes an opening into the vertebral canal, and then moves the dura and the bundle of nerves called the "cauda equina" (horse's tail) aside, which exposes the disk. If a portion of the disk has moved from between the vertebrae out into the nerve canal, it is simply removed. If the disk itself has become fragmented and partially displaced, or not fragmented but bulging extensively, the surgeon will remove the bulging or displaced part of the disk and the part that lies in the space between the vertebrae.

Preparation

The patient is given an injection an hour before the surgery to dry up internal fluids and encourage drowsiness.

KEY TERMS

Diskectomy—The surgical removal of a portion of an invertebral disk.

Dura—The strongest and outermost of three membranes that protect the brain, spinal cord, and nerves of the cauda equina.

Herniated disk—A blisterlike bulging or protrusion of the contents of the disk out through the fibers that normally hold them in place. It is also called a ruptured disk, slipped disk, or displaced disk.

Intervertebral disk—Cylindrical elastic-like gel pads that separate and join each pair of vertebrae in the spine.

Laminectomy—An operation in which the surgeon cuts through the covering of a vertebra to reach a herniated disk in order to remove it.

Vertebra—The bones that make up the back bone (spine).

Aftercare

After the operation, the patient will awaken lying flat and face down, and must remain this way for several days, changing position only to avoid **bedsores**. There maybe slight pain or stiffness in the back area.

Patients should sleep on a firm mattress and avoid bending at the waist, lifting heavy weights, or sitting in one spot for a long time (such as riding in a car).

After surgery, patients can usually leave the hospital on the fourth or fifth day. They must:

- avoid sitting for more than 15–20 minutes
- use a reclined chair
- avoid bending, twisting, or lifting
- begin gentle walking (indoors or outdoors), gradually increasing
- begin stationary biking or gentle swimming after two weeks
- continue **exercise** for the next four weeks
- slow down if they experience more than minor pain in the back or leg

Risks

All surgery carries some risk due to heart and lung problems or the anesthesia itself, but this risk is generally extremely small. (The risk of **death** from general anesthesia for all types of surgery, for example, is only about 1 in 1,600.)

The most common risk of the surgery is infection, which occurs in 1–2% of cases. Rarely, the surgery can damage nerves in the lower back or major blood vessels in front of the disk. Occasionally, there may be some residual **paralysis** of a particular leg or bladder muscle after surgery, but this is the result of the disk problem that necessitated the surgery, not the operation itself.

While disk removals can relieve pain in 90% of cases, there are some people who do not get pain relief, depending on how long they had the condition requiring surgery and other factors.

Normal results

After about five days, most patients can leave the hospital. They can resume all normal activities, including work, after four to six weeks of recuperation at home.

In properly evaluated patients, there is a very good chance that disk removal will be successful in easing pain. Even in patients over age 60, disk surgery has a "good to excellent" result for 87% of patients. Disk surgery can relieve both back and leg pain, but the greatest pain relief will occur with the leg pain.

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Diskectomy *see* **Disk removal**

Dislocations and subluxations

Definition

In medicine, the terms dislocation and subluxation refer to the displacement of bones that form a joint. These conditions affecting the joint most often result from trauma that causes adjoining bones to no longer align with each other. A partial or incomplete dislocation is called a subluxation.

Description

In a healthy joint, the bones are normally held together with tough, fibrous bands called ligaments. These ligaments are attached to each bone along with a fibrous sac surrounding the joint called the articular capsule or joint capsule. The ligaments and joint capsule are relatively strong and nonelastic but permit movement within normal limits for each particular joint. In the event of a dislocation, one of the bones making up the joint is forced out of its natural alignment from excessive stretching and tearing of the joint ligaments and capsule. Muscles and tendons surrounding the joint are usually stretched and injured to some degree.

Causes and symptoms

A violent movement at the joint that exceeds normal limits usually causes a joint dislocation. Although dislocations often result from trauma, they sometimes occur as a result of disease affecting the joint structures. In the process of the dislocation, there is tearing of the ligaments and the articular capsule, which are vital structures for connecting the bone. Following a dislocation, the bones affected are often immobile and the affected limb may be locked in an abnormal position; **fractures** are also a concern with severe dislocations.

Important factors in recognizing a dislocation or subluxation include a history of experiencing a fall or receiving a blow in a particular joint followed by the sudden onset of loss of function to the involved limb. Immediately after the dislocation, the joint almost always swells significantly and feels painful when pressure is applied (point tenderness). If trauma to the joint causing the dislocation or subluxation is violent in nature, small chips of bone can be torn away with the supporting structures. Chronic recurrent dislocations may take place without severe **pain** because of the somewhat slack condition of the surrounding muscles and other supporting tissues. A first-time dislocation is considered and treated as a possible fracture. Risk factors that can increase susceptibility of joint dislocation and subluxation are shallow or abnormally formed joint surfaces present at birth (congenital) and/or other diseases of ligaments and tissue around a joint. Some infants are born with a hip dislocation. Both sexes and all ages are affected.

Diagnosis

A thorough medical history and physical exam by a physician is the first step in the correct diagnosis of dislocations and subluxations. X rays of the joint and adjacent bones can locate and help determine the extent of dislocated joints

This x ray shows the dislocation between two bones in a finger. *(Photo Researchers, Inc. Reproduced by permission.)*

Treatment

Immediately after the dislocation, the application of ice is helpful to control swelling and decrease pain. If the patient needs to be transported, it is important to prevent the joint from moving (**immobilization**). At times, a cast or splint may be used to immobilize the joint and ensure proper alignment and healing. The treatment of realigning bones following a dislocation is called reduction. This may include simple maneuvers that manipulate the joint to reposition the bones or surgical procedures to restore the joint to its normal position. A general anesthesia or muscle relaxant may be used to help make joint reduction possible by relaxing surrounding muscles in spasm. **Acetaminophen** or **aspirin** are sometimes used to control moderate pain, and narcotics may be prescribed by the physician if the pain is severe. Recurring dislocation may require surgical reconstruction or replacement of the joint. It is not recommended to attempt to reset a dislocated joint outside of a medical

Dislocations and subluxations refer to the displacement of bones that form a joint. Such conditions most often result from trauma causing adjoining bones to no longer touch each other. A partial or incomplete dislocation is called a subluxation. The illustrations above indicate dislocation of the jaw bone, shoulder blade, hip bone, and the thumb. *(Illustration by Electronic Illustrators Group.)*

environment with experienced medical personnel, because a fracture may be present.

Alternative treatment

Chiropractic care has been shown to be effective for joint subluxation and dislocation, especially in the spine. Swelling can be addressed using botanical therapies. Bromelain, a pineapple enzyme, and tumeric (*Curcuma longa*) are the most potent botanical remedies for this purpose. Acute homeopathic care with arnica (*Arnica montana*) can reduce the trauma to the body. Ligament and tendon strengthening can be assisted both botanically and homeopathically.

Prognosis

Joint ligaments have poor blood supply and, therefore, heal slowly. This healing process continues long after the symptoms of the dislocation injury have diminished. Once a joint has been either subluxated or completely dislocated, the connective tissue binding or holding it in correct alignment is stretched to such an extent that the joint becomes extremely vulnerable to repeated dislocations. However, this chance of recurrent dislocation and subluxation will decrease if a proper **rehabilitation** program is implemented to strengthen surrounding muscles of the joint. Most joint dislocations are curable with prompt treatment. After the dislocation has been corrected, the joint may require immobilization with a cast or sling for two to eight weeks.

Prevention

When an individual is involved in strenuous sports or heavy work, involved joints may be protected by elastic bandage wraps, tape wraps, knee and shoulder pads, or special support stockings. Keeping the muscles surrounding the joint strong will also help prevent dislocations. Long-term problems may also be prevented by allowing an adequate amount of time for an injured joint to rest and heal prior to resuming full activity.

KEY TERMS

Articular capsule—An envelope of tissue that surrounds a free moving joint, composed of an external layer of white fibrous tissue and an external synovial membrane that secretes a lubricant into the joint.

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Disopyramide *see* **Antiarrhythmic drugs**

Disproportionate dwarfism *see* **Achondroplasia**

Dissecting aneurysm *see* **Aortic dissection**

Dissecting hematoma *see* **Aortic dissection**

Disseminated lupus erythematosus *see* **Systemic lupus erythematosus**

Dissociative disorders

Definition

The dissociative disorders are a group of mental disorders that affect consciousness are defined as causing significant interference with the patient's general functioning, including social relationships and employment.

Description

In order to have a clear picture of these disorders, dissociation should first be understood. Dissociation is a mechanism that allows the mind to separate or compartmentalize certain memories or thoughts from normal consciousness. These split-off mental contents are not erased. They may resurface spontaneously or be triggered by objects or events in the person's environment.

Dissociation is a process that occurs along a spectrum of severity. It does not necessarily mean that a person has a dissociative disorder or other mental illness. A mild degree of dissociation occurs with some physical stressors; people who have gone without sleep for a long period of time, have had "laughing gas" for dental surgery, or have been in a minor accident often have brief dissociative experiences. Another commonplace example of dissociation is a person becoming involved in a book or movie so completely that the surroundings or the passage of time are not noticed. Another example might be driving on the highway and taking several exits without noticing or remembering. Dissociation is related to hypnosis in that hypnotic trance also involves a temporarily altered state of consciousness. Most patients with dissociative disorders are highly hypnotizable.

People in other cultures sometimes have dissociative experiences in the course of religious (in certain trance states) or other group activities. These occurrences should not be judged in terms of what is considered "normal" in the United States.

Moderate or severe forms of dissociation are caused by such traumatic experiences as childhood **abuse**, combat, criminal attacks, brainwashing in hostage situations, or involvement in a natural or transportation disaster. Patients with **acute stress disorder**, **post-traumatic stress disorder** (PTSD), or conversion disorder and somatization disorder may develop dissociative symptoms. Recent studies of trauma indicate that the human brain stores traumatic memories in a different way than normal memories. Traumatic memories are not processed or integrated into a person's ongoing life in the same fashion as normal memories. Instead they are dissociated, or "split off," and may erupt into consciousness from time to time without warning. The affected person cannot control or "edit" these memories. Over a period of time, these two sets of memories, the normal and the traumatic, may coexist as parallel sets without being combined or blended. In extreme cases, different sets of dissociated memories may alter subpersonalities of patients with dissociative identity disorder (**multiple personality disorder**).

The dissociative disorders vary in their severity and the suddenness of onset. It is difficult to give statistics

for their frequency in the United States because they are a relatively new category and are often misdiagnosed. And, criterion for diagnosis require significant impairment in social or vocational functioning.

Dissociative amnesia

Dissociative **amnesia** is a disorder in which the distinctive feature is the patient's inability to remember important personal information to a degree that cannot be explained by normal forgetfulness. In many cases, it is a reaction to a traumatic accident or witnessing a violent crime. Patients with dissociative amnesia may develop depersonalization or trance states as part of the disorder, but they do not experience a change in identity.

Dissociative fugue

Dissociative fugue is a disorder in which a person temporarily loses his or her sense of personal identity and travels to another location where he or she may assume a new identity. Again, this condition usually follows a major stressor or trauma. Apart from inability to recall their past or personal information, patients with dissociative fugue do not behave strangely or appear disturbed to others. Cases of dissociative fugue are more common in wartime or in communities disrupted by a natural disaster.

Depersonalization disorder

Depersonalization disorder is a disturbance in which the patient's primary symptom is a sense of detachment from the self. Depersonalization as a symptom (not as a disorder) is quite common in college-age populations. It is often associated with sleep deprivation or "recreational" drug use. It may be accompanied by "derealization" (where objects in an environment appear altered). Patients sometimes describe depersonalization as feeling like a robot or watching themselves from the outside. Depersonalization disorder may also involve feelings of numbness or loss of emotional "aliveness."

Dissociative identity disorder (DID)

Dissociative identity disorder (DID) is the newer name for multiple personality disorder (MPD). DID is considered the most severe dissociative disorder and involves all of the major dissociative symptoms.

Dissociative disorder not otherwise specified (DDNOS)

DDNOS is a diagnostic category ascribed to patients with dissociative symptoms that do not meet the full criteria for a specific dissociative disorder.

Causes and symptoms

The moderate to severe dissociation that occurs in patients with dissociative disorders is understood to result from a set of causes:

- an innate ability to dissociate easily
- repeated episodes of severe physical or sexual abuse in childhood
- the lack of a supportive or comforting person to counteract abusive relative(s)
- the influence of other relatives with dissociative symptoms or disorders

The relationship of dissociative disorders to childhood abuse has led to intense controversy and lawsuits concerning the accuracy of childhood memories. The brain's storage, retrieval, and interpretation of memories are still not fully understood. Controversy also exists regarding how much individuals presenting dissociative disorders have been influenced by books and movies to describe a certain set of symptoms (scripting).

The major dissociative symptoms are:

Amnesia

Amnesia in a dissociative disorder is marked by gaps in a patient's memory for long periods of time or for traumatic events. Doctors can distinguish this type of amnesia from loss of memory caused by head injuries or drug intoxication, because the amnesia is "spotty" and related to highly charged events and feelings.

Depersonalization

Depersonalization is a dissociative symptom in which the patient feels that his or her body is unreal, is changing, or is dissolving. Some patients experience depersonalization as being outside their bodies or watching a movie of themselves.

Derealization

Derealization is a dissociative symptom in which the external environment is perceived as unreal. The patient may see walls, buildings, or other objects as changing in shape, size, or color. In some cases, the patient may feel that other persons are machines or robots, though the patient is able to acknowledge the unreality of this feeling.

Identity disturbances

Patients with dissociative fugue, DDNOS, or DID often experience confusion about their identities or even assume new identities. Identity disturbances result from the patient having split off entire personality traits

or characteristics as well as memories. When a stressful or traumatic experience triggers the reemergence of these dissociated parts, the patient may act differently, answer to a different name, or appear confused by his or her surroundings.

Diagnosis

When a doctor is evaluating a patient with dissociative symptoms, he or she will first rule out physical conditions that sometimes produce amnesia, depersonalization, or derealization. These physical conditions include epilepsy, head injuries, brain disease, side effects of medications, substance abuse, intoxication, **AIDS, dementia** complex, or recent periods of extreme physical **stress** and sleeplessness. In some cases, the doctor may give the patient an electroencephalogram (EEG) to exclude epilepsy or other seizure disorders.

If the patient appears to be physically normal, the doctor will rule out psychotic disturbances, including **schizophrenia**. In addition, doctors can use some **psychological tests** to narrow the diagnosis. One is a screener, the Dissociative Experiences Scale (DES). If the patient has a high score on this test, he or she can be evaluated further with the Dissociative Disorders Interview Schedule (DDIS) or the Structured Clinical Interview for *DSM-IV* Dissociative Disorders (SCID-D). It is also possible for doctors to measure a patient's hypnotizability as part of a diagnostic evaluation.

Treatment

Treatment of the dissociative disorders often combines several methods.

Psychotherapy

Patients with dissociative disorders often require treatment by a therapist with some specialized understanding of dissociation. This background is particularly important if the patient's symptoms include identity problems. Many patients with dissociative disorders are helped by group as well as individual treatment.

Medications

Some doctors will prescribe tranquilizers or antidepressants for the **anxiety** and/or depression that often accompany dissociative disorders. Patients with dissociative disorders are, however, at risk for abusing or becoming dependent on medications. As of 2001, there is no drug that can reliably counteract dissociation itself.

Hypnosis

Hypnosis is frequently recommended as a method of treatment for dissociative disorders, partly because hypnosis is related to the process of dissociation. Hypnosis may help patients recover repressed ideas and memories. Therapists treating patients with DID sometimes use hypnosis in the process of "fusing" the patient's alternate personalities.

KEY TERMS

Amnesia—A general medical term for loss of memory that is not due to ordinary forgetfulness. Amnesia can be caused by head injuries, brain disease, or epilepsy, as well as by dissociation.

Depersonalization—A dissociative symptom in which the patient feels that his or her body is unreal, is changing, or is dissolving.

Derealization—A dissociative symptom in which the external environment is perceived as unreal.

Dissociation—A psychological mechanism that allows the mind to split off traumatic memories or disturbing ideas from conscious awareness.

Fugue—A dissociative experience during which a person travels away from home, has amnesia for their past, and may be confused about their identity but otherwise appear normal.

Hypnosis—The means by which a state of extreme relaxation and suggestibility is induced: used to treat amnesia and identity disturbances that occur in dissociative disorders.

Multiple personality disorder (MPD)—An older term for dissociative identity disorder (DID).

Trauma—A disastrous or life-threatening event that can cause severe emotional distress, including dissociative symptoms and disorders.

Prognosis

Prognoses for dissociative disorders vary. Recovery from dissociative fugue is usually rapid. Dissociative amnesia may resolve quickly, but can become a chronic disorder in some patients. Depersonalization disorder, DDNOS, and DID are usually chronic conditions. DID usually requires five or more years of treatment for recovery.

Prevention

Since the primary cause of dissociative disorders is thought to involve extended periods of humanly inflicted trauma, prevention depends on the elimination of **child**

abuse and psychological abuse of adult prisoners or hostages.

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Dissociative identity disorder *see* **Multiple personality disorder**

Diuretics

Definition

Diuretics are medicines that help reduce the amount of water in the body.

Purpose

Diuretics are used to treat the buildup of excess fluid in the body that occurs with some medical conditions such as congestive **heart failure**, liver disease, and kidney disease. Some diuretics are also prescribed to treat high blood pressure. These drugs act on the kidneys to increase urine output. This reduces the amount of fluid in the bloodstream, which in turn lowers blood pressure.

Description

There are several types of diuretics, also called water pills:

- Loop diuretics, such as bumetanide (Bumex) and furosemide (Lasix), get their name from the loop-shaped part of the kidneys where they have their effect.
- Thiazide diuretics include such commonly used diuretics as hydrochlorothiazide (HydroDIURIL, Esidrix), chlorothiazide (Diuril), and chlorthalidone (Hygroton).
- Potassium-sparing diuretics prevent the loss of potassium, which is a problem with other types of diuretics. Examples of potassium-sparing diuretics are amiloride (Midamor) and triamterene (Dyrenium).

In addition, some medicines contain combinations of two diuretics. The brands Dyazide and Maxzide, for example, contain the thiazide diuretic hydrochlorothiazide with the potassium-sparing diuretic triamterene.

Some nonprescription (over-the-counter) medicines contain diuretics. However, the medicines described here cannot be bought without a physician's prescription. They are available in tablet, capsule, liquid, and injectable forms.

Recommended dosage

The recommended dosage depends on the type of diuretic and may be different for different patients. Check with the physician who prescribed the drug or the pharmacist who filled the prescription for the correct dosage, and take the medicine exactly as directed.

Precautions

Seeing a physician regularly while taking a diuretic is important. The physician will check to make sure the medicine is working as it should and will watch for unwanted side effects.

Some people feel unusually tired when they first start taking diuretics. This effect usually becomes less noticeable over time, as the body adjusts to the medicine.

Because diuretics increase urine output, people who take this medicine may need to urinate more often, even during the night. Health care professionals can help patients schedule their doses to avoid interfering with their sleep or regular activities.

For patients taking the kinds of diuretics that rob potassium from the body, physicians may recommend adding potassium-rich foods or drinks, such as citrus fruits and juices, to the diet. Or they may suggest taking a potassium supplement or taking another medicine that keeps the body from losing too much potassium. If the physician recommends any of these measures, be sure to closely follow his or her directions. Do not make other diet changes without checking with the physician. People who are taking potassium-sparing diuretics should not add potassium to their **diets**, as too much potassium may be harmful.

People who take diuretics may lose too much water or potassium when they get sick, especially if they have severe vomiting and **diarrhea**. They should check with their physicians if they become ill.

These medicines make some people feel lightheaded, dizzy, or faint when they get up after sitting or lying down. Older people are especially likely to have this problem. Drinking alcohol, exercising, standing for long periods, or being in hot weather may make the problem worse. To lessen the problem, get up gradually and hold onto something for support if possible. Avoid drinking too much alcohol and be careful in hot weather or when exercising or standing for a long time.

Anyone who is taking a diuretic should be sure to tell the health care professional in charge before having surgical or dental procedures, medical tests or emergency treatment.

Some diuretics make the skin more sensitive to sunlight. Even brief exposure to sun can cause a severe **sunburn**, **itching**, a rash, redness, or other changes in skin color. While being treated with this medicine, avoid being in direct sunlight, especially between 10 a.m. and 3 p.m.; wear a hat and tightly woven clothing that covers the arms and legs; use a sunscreen with a skin protection factor (SPF) of at least 15; protect the lips with a sun block lipstick; and do not use tanning beds, tanning booths, or sunlamps. People with fair skin may need to use a sunscreen with a higher skin protection factor.

Special conditions

People who have certain medical conditions or who are taking certain other medicines may have problems if they take diuretics. Before taking these drugs, be sure to let the physician know about any of these conditions:

ALLERGIES. Anyone who has had unusual reactions to diuretics or **sulfonamides** (sulfa drugs) in the past should let his or her physician know before using a diuretic. The physician should also be told about any **allergies** to foods, dyes, preservatives, or other substances.

PREGNANCY. Diuretics will not help the swelling of hands and feet that some women have during **pregnancy**. In general, pregnant women should not use diuretics unless a physician recommends their use. Although studies have not been done on pregnant women, studies of laboratory animals show that some diuretics can cause harmful effects when taken during pregnancy.

BREASTFEEDING. Some diuretics pass into breast milk, but no reports exist of problems in nursing babies whose mothers use this medicine. However, thiazide diuretics may decrease the flow of breast milk. Women who are breastfeeding and need to use a diuretic should check with their physicians.

OTHER MEDICAL CONDITIONS. Side effects of some diuretics may be more likely in people who have had a recent **heart attack** or who have liver disease or severe kidney disease. Other diuretics may not work properly in people with liver disease or severe kidney disease. Diuretics may worsen certain medical conditions, such as **gout**, **kidney stones**, **pancreatitis**, lupus erythematosus, and hearing problems. In addition, people with diabetes should be aware that diuretics may increase blood sugar levels. People with heart or blood vessel disease should know that some diuretics increase cholesterol or triglyceride levels. The risk of an allergic reaction to certain diuretics is greater in people with bronchial **asthma**. Before using diuretics, people with any of these medical problems should make sure their physicians are aware of their conditions. Also, people who have trouble urinating or who have high potassium levels in their blood may not be able to take diuretics and should check with a physician before using them.

USE OF CERTAIN MEDICINES. Taking diuretics with certain other drugs may affect the way the drugs work or may increase the chance of side effects.

Side effects

Some side effects, such as loss of appetite, **nausea and vomiting**, stomach cramps, diarrhea and **dizziness**, usually lessen or go away as the body adjusts to the medicine. These problems do not need medical attention unless they continue or interfere with normal activities.

Patients taking potassium-sparing diuretics should know the signs of too much potassium and should check with a physician as soon as possible if any of these symptoms occur:

- irregular heartbeat
- breathing problems
- numbness or tingling in the hands, feet, or lips

KEY TERMS

Inflammation—Pain, redness, swelling, and heat that usually develop in response to injury or illness.

Lupus erythematosus—A chronic disease that affects the skin, joints, and certain internal organs.

Pancreas—A gland located beneath the stomach. The pancreas produces juices that help break down food.

Potassium—A mineral found in whole grains, meat, legumes, and some fruits and vegetables. Potassium is important for many body processes, including proper functioning of the nerves and muscles.

Triglyceride—A substance formed in the body from fat in the diet. Triglycerides are the main fatty materials in the blood. Together with protein, they make up high- and low-density lipoproteins (HDLs and LDLs). Triglyceride levels are important in the diagnosis and treatment of many diseases including high blood pressure, diabetes, and heart disease.

- confusion or nervousness
- unusual tiredness or weakness
- weak or heavy feeling in the legs

Patients taking diuretics that cause potassium loss should know the signs of too little potassium and should check with a physician as soon as possible if they have any of these symptoms:

- fast or irregular heartbeat
- weak pulse
- nausea or vomiting
- dry mouth
- excessive thirst
- muscle cramps or **pain**
- unusual tiredness or weakness
- mental or mood changes

Interactions

Diuretics may interact with other medicines. When this happens, the effects of one or both of the drugs may change or the risk of side effects may be greater. Anyone who takes a diuretic should let the physician know all other medicines he or she is taking and should ask whether the possible interactions can interfere with drug therapy. Among the drugs that may interact with diuretics are:

- Angiotensin-converting enzyme (ACE) inhibitors, such as benazepril (Lotensin), captopril (Capoten), and enalapril (Vasotec), used to treat high blood pressure. Taking these drugs with potassium-sparing diuretics may cause levels of potassium in the blood to be too high, increasing the chance of side effects.
- Cholesterol-lowering drugs such as cholestyramine (Questran) and colestipol (Colestid). Taking these drugs with combination diuretics such as Dyazide and Maxzide may keep the diuretic from working. Take the diuretic at least one hour before or four hours after the cholesterol-lowering drug.
- Cyclosporine (Sandimmune), a medicine that suppresses the immune system. Taking this medicine with potassium-sparing diuretics may increase the chance of side effects by causing levels of potassium in the blood to be too high.
- Potassium supplements, other medicines containing potassium, or salt substitutes that contain potassium. Taking these with potassium-sparing diuretics may lead to too much potassium in the blood, increasing the chance of side effects.
- Lithium, used to treat **bipolar disorder** (manic-depressive illness). Using this medicine with potassium-sparing diuretics may allow lithium to build up to poisonous levels in the body.
- Digitalis heart drugs, such as digoxin (Lanoxin). Using this medicine with combination diuretics such as triamterene-hydrocholorthiazide (Dyazide, Maxzide) may cause blood levels of the heart medicine to be too high, making side effects such as changes in heartbeat more likely.

The list above does not include every drug that may interact with diuretics. Check with a physician or pharmacist before combining diuretics with any other prescription or nonprescription (over-the-counter) medicine.

Nancy Ross-Flanigan

Diverticulitis *see* **Diverticulosis and diverticulitis**

Diverticulosis and diverticulitis

Definition

Diverticulosis refers to a condition in which the inner, lining layer of the large intestine (colon) bulges

out (herniates) through the outer, muscular layer. These outpouchings are called diverticula. Diverticulitis refers to the development of inflammation and infection in one or more diverticula.

Description

Diverticula tend to occur most frequently in the last segment of the large intestine, the sigmoid colon. They occur with decreasing frequency as one examines further back toward the beginning of the large intestine. The chance of developing diverticula increases with age, so that by the age of 50, about 20–50% of all people will have some diverticula. By the age of 90, virtually everyone will have developed some diverticula. Most diverticula measure about 3 mm to just over 3 cm in diameter. Larger diverticula, termed giant diverticula, are quite infrequent, but may measure as large as 15 cm in diameter.

Causes and symptoms

Diverticula are believed to be caused by overly forceful contractions of the muscular wall of the large intestine. As areas of this wall spasm, they become weaker and weaker, allowing the inner lining to bulge through. The anatomically weakest areas of the intestinal wall occur next to blood vessels which course through the wall, so diverticula commonly occur in this location.

Diverticula are most common in the developed countries of the West (North America, Great Britain, northern and western Europe). This is thought to be due to the diet of these countries, which tends to be quite low in fiber. A diet low in fiber results in the production of smaller volumes of stool. In order to move this smaller stool along the colon and out of the rectum, the colon must narrow itself significantly, and does so by contracting down forcefully. This causes an increase in pressure, which, over time, weakens the muscular wall of the intestine and allows diverticular pockets to develop.

The origin of giant diverticula development is not completely understood, although one theory involves gas repeatedly entering and becoming trapped in an already-existing diverticulum, causing stretching and expansion of that diverticulum.

The great majority of people with diverticulosis will remain symptom-free. Many diverticula are quite accidentally discovered during examinations for other conditions of the intestinal tract.

Some people with diverticulosis have symptoms such as **constipation**, cramping, and bloating. It is unclear whether these symptoms are actually caused by the diverticula themselves, or whether some other gastrointestinal condition (such as **irritable bowel syndrome**) might be responsible. A complication of diverticulosis occurs because many diverticula develop in areas very near blood vessels. Therefore, one serious risk of diverticulosis involves bleeding. Although an infrequent complication, the bleeding can be quite severe. Seventy-five percent of such bleeding episodes occur due to diverticula located on the right side of the colon. About 50% of the time, such bleeding will stop on its own.

A barium study x ray showing colonic diverticulosis. *(Custom Medical Stock Photo. Reproduced by permission.)*

One of the most common and potentially serious complications of diverticulosis is inflammation and infection of a particular diverticulum, called diverticulitis.

Diverticulitis is three times more likely to occur in the left side of the large intestine. Since most diverticula are located in the sigmoid colon (the final segment of the large intestine which empties into the rectum), most diverticulitis also takes place in the sigmoid. The elderly have the most serious complications from diverticulitis, although very severe infections can also occur in patients

under the age of 50. Men are three times as likely as women to be stricken with diverticulitis.

Diverticulitis is believed to occur when a hardened piece of stool, undigested food, and bacteria (called a fecalith) becomes lodged in a diverticulum. This blockage interferes with the blood supply to the area, and infection sets in.

An individual with diverticulitis will experience **pain** (especially in the lower left side of the abdomen) and **fever**. In response to the infection and the irritation of nearby tissues within the abdomen, the abdominal muscles may begin to spasm. About 25% of all patients with diverticulitis will have some rectal bleeding, although this rarely becomes severe. Walled-off pockets of infection, called abscesses, may appear within the wall of the intestine, or even on the exterior surface of the intestine. When a diverticulum weakens sufficiently, and is filled to bulging with infected pus, a perforation in the intestinal wall may develop. When the infected contents of the intestine spill out into the abdomen, the severe infection called **peritonitis** may occur. Peritonitis is an infection and inflammation of the lining of the abdominal cavity, the peritoneum. Other complications of diverticulitis include the formation of abnormal connections between two organs that normally do not connect (fistulas; for example, the intestine and the bladder), and scarring outside of the intestine which squeezes off a portion of the intestine, obstructing it.

Diagnosis

As mentioned, the majority of diverticula do not cause any symptoms, and are often found by coincidence during an examination being performed for some other medical condition.

When diverticula are suspected because a patient begins to have sudden rectal bleeding, the location of the bleeding can be studied by performing an **angiography**. Angiography involves inserting a tiny tube through an artery in the leg, and moving it up into one of the major arteries of the gastrointestinal system. A particular chemical (contrast medium) which will show up on x-ray films is injected, and the area of bleeding is located by looking for an area where the contrast is leaking into the interior (lumen) of the intestine.

A procedure called endoscopy provides another method for examining the colon and locating the site of bleeding. In endoscopy, a small, flexible scope (endoscope) is inserted through the rectum and into the intestine. The scope usually bears a fiber-optic camera, which allows the view through this endoscope to be projected onto a television screen. The operator can introduce the endoscope further and further through the intestine to find the location of the bleeding.

Diagnosis of diverticulitis is not difficult in patients with previously diagnosed diverticulosis. The presence of abdominal pain and fever in such an individual would make the suspicion of diverticulitis quite high. Examination of the abdomen will usually reveal tenderness to touch, with the patient's abdominal muscles contracting strongly to protect the tender area. During a rectal exam (performed by inserting a finger into the rectum), a doctor may be able to feel an abnormal mass. Touching this mass may prove painful to the patient.

When a practitioner is suspicious of diverticulitis as the cause for the patient's symptoms, he or she will most likely avoid the types of tests usually used to diagnose gastrointestinal disorders. These include **barium enema** and endoscopy. The concern is that the increased pressure exerted on the intestine during these exams may increase the likelihood of intestinal perforation. After medical treatment for the diverticulitis, these examinations may be performed in order to learn the extent of the patient's disease.

Treatment

Only about 20% of patients with diverticulosis ever have symptoms which lead them to seek medical help. Most people never know that they have diverticula. For those individuals who have cramping pain and constipation believed to be due to diverticulosis, the usual prescription involves increasing the fiber in the diet. This can be done by adding special diet supplements of bran or psyllium seed, which increase stool volume. Bleeding diverticula can usually be treated by bed rest, with blood **transfusion** needed for more severe bleeding (hemorrhaging). In cases of very heavy hemorrhaging, medications which encourage clotting can be injected during the course of a diagnostic angiography.

While there are almost no situations when uncomplicated diverticulosis requires surgery, giant diverticula always require removal. This is due to the very high chance of infection and perforation of these diverticula. When giant diverticula are diagnosed, the usual treatment involves removing that portion of the intestine.

Treatment for uncomplicated diverticulitis usually requires hospitalization. "Resting the bowel" is a mainstay of treatment, and involves keeping the patient from eating or sometimes even drinking anything by mouth. Therefore, the patient will need to receive fluids through a needle in the vein (intravenous or IV fluids). **Antibiotics** will also be administered through the IV. Some physicians will agree to try treatment at home for very mildly ill patients. These patients will be put on a liquid diet and receive oral antibiotics.

The various complications of diverticulitis need to be treated aggressively, because the **death** rate from such things as perforation and peritonitis is quite high. Abscesses can be drained of their infected contents by inserting a needle through the skin of the abdomen and into the **abscess**. When this is unsuccessful, open abdominal surgery will be required to remove the piece of the intestine containing the abscess. Fistulas require surgical repair, including the removal of the length of intestine containing the origin of the fistula, followed by immediate reconnection of the two free ends of intestine. Peritonitis requires open surgery. The entire abdominal cavity is cleaned by being irrigated (washed) with a warmed sterile saltwater solution, and the damaged piece of intestine is removed. Obstructions require immediate surgery to prevent perforation. Massive, uncontrollable bleeding, while rare, may require removal of part or all of the large intestine.

During any of these types of operations, the surgeon must make an important decision regarding the quantity of intestine which must be removed. When the amount of intestine removed is great, it may be necessary to perform a **colostomy**. A colostomy involves pulling the end of the remaining intestine through the abdominal wall, to the outside. This bit of intestine is then fashioned so that a bag can be fit over it. The patient's waste (feces) collect in the bag, because the intestine no longer connects with the rectum. This colostomy may be temporary, in which case another operation will be required to reconnect the intestine, after some months of substantial healing has occurred. Other times, the colostomy will need to be permanent, and the patient will have to adjust to living permanently with the colostomy bag. Most people with colostomies are able to go on with a very active life.

Occasionally, a patient will have such severe diverticular disease that a surgeon recommends planning ahead, and schedules removal of a portion of the colon. This is done to avoid the high risk of surgery performed after a complication has set in. Certain developments in a patient will identify those patients who are at very high risk of experiencing dangerous complications. Such elective surgery may be recommended:

- when an older individual has had several attacks of diverticulitis
- when someone under the age of 50 has had even one attack
- when treatment does not get rid of a painful mass
- when the intestine appears to be narrowing on x-ray examination (this could suggest the presence of **cancer**)
- when certain patients begin to regularly experience painful urination or urinary infections (this suggests that there may be a connection between the intestine and the bladder)
- when there is any question of cancer
- when the diverticular disease appears to be progressing rapidly

KEY TERMS

Angiography—An x-ray study of the arteries in a particular part of the body. Angiography is often performed in order to localize internal bleeding.

Bowel obstruction—A blockage in the intestine which prevents the normal flow of waste down the length of the intestine.

Colostomy—A procedure performed when a large quantity of intestine is removed. The end piece of the intestine leading to the rectum is closed.

Diverticula—Outpouchings in the large intestine caused when the inner, lining layer of the large intestine (colon) bulges out (herniates) through the outer, muscular layer.

Endoscopy—Examination of an area of the gastrointestinal tract by putting a lighted scope, usually bearing a fiber-optic camera, into the rectum, and passing it through the intestine.

Fistula—An abnormal connection formed between two organs that usually have no connection whatsoever.

Sigmoid colon—The final portion of the large intestine that empties into the rectum.

Prognosis

The prognosis for people with diverticula is excellent, with only 20% of such patients ever seeking any medical help for their condition.

While diverticulitis can be a difficult and painful disease, it is usually quite treatable. Prognosis is worse for individuals who have other medical problems, particularly those requiring the use of steroid medications, which increase the chances of developing a serious infection. Prognosis is also worse in the elderly.

Prevention

While there is no absolutely certain way to prevent the development of diverticula, it is believed that high-fiber **diets** are of help. Foods that are recommended for

their high fiber content include whole grain breads and cereals, and all types of fruits and vegetables. Most experts suggest that individuals take in about 0.71–1.23 oz (20–35 g) of fiber daily. If this is not possible to achieve through a person's diet, there are fiber products which can be mixed into 8 oz (.237 l) of water or juice, and which provide about 0.13–19 oz (4–6 g) of fiber.

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Rosalyn Carson-DeWitt, MD

Dizziness

Definition

As a disorder, dizziness is classified into three categories—vertigo, syncope, and nonsyncope nonvertigo. Each category has a characteristic set of symptoms, all related to the sense of balance. In general, syncope is defined by a brief loss of consciousness (**fainting**) or by dimmed vision and feeling uncoordinated, confused, and lightheaded. Many people experience a sensation like syncope when they stand up too fast. Vertigo is the feeling that either the individual or the surroundings are spinning. This sensation is like being on a spinning amusement park ride. Individuals with nonsyncope nonvertigo dizziness feel as though they cannot keep their balance. This feeling may become worse with movement.

Description

The brain coordinates information from the eyes, the inner ear, and the body's senses to maintain balance. If any of these information sources is disrupted, the brain may not be able to compensate. For example, people sometimes experience **motion sickness** because the information from their body tells the brain that they are sitting still, but information from the eyes indicates that they are moving. The messages don't correspond and dizziness results.

Vision and the body's senses are the most important systems for maintaining balance, but problems in the inner ear are the most frequent cause of dizziness. The inner ear, also called the vestibular system, contains fluid that helps fine tune the information the brain receives from the eyes and the body. When fluid volume or pressure in one inner ear changes, information about balance is altered. The discrepancy gives conflicting messages to the brain about balance and induces dizziness.

Certain medical conditions can cause dizziness, because they affect the systems that maintain balance. For example, the inner ear is very sensitive to changes in blood flow. Because medical conditions such as high blood pressure or low blood sugar can affect blood flow, these conditions are frequently accompanied by dizziness. Circulation disorders are the most common causes of dizziness. Other causes are **head injury**, ear infection, **allergies**, and nervous system disorders.

Dizziness often disappears without treatment or with treatment of the underlying problem, but it can be long term or chronic. According to the National Institutes of Health, 42% of Americans will seek medical help for dizziness at some point in their lives. The costs may exceed a billion dollars and account for five million doctor visits annually. Episodes of dizziness increase with age. Among people aged 75 or older, dizziness is the most frequent reason for seeing a doctor.

Causes and symptoms

Careful attention to symptoms can help determine the underlying cause of the dizziness. Underlying problems may be benign and easily treated or they may be dangerous and in need of intensive therapy. Not all cases of dizziness can be linked to a specific cause. More than one type of dizziness can be experienced at the same time and symptoms may be mixed. Episodes of dizziness may last for a few seconds or for days. The length of an episode is related to the underlying cause.

The symptoms of syncope include dimmed vision, loss of coordination, confusion, lightheadedness, and sweating. These symptoms can lead to a brief loss of con-

sciousness or fainting. They are related to a reduced flow of blood to the brain; they often occur when a person is standing up and can be relieved by sitting or lying down. Vertigo is characterized by a sensation of spinning or turning, accompanied by nausea, vomiting, ringing in the ears, **headache**, or **fatigue**. An individual may have trouble walking, remaining coordinated, or keeping balance. Nonsyncope nonvertigo dizziness is characterized by a feeling of being off balance that becomes worse if the individual tries moving or performing detail-intense tasks.

A person may experience dizziness for many reasons. Syncope is associated with low blood pressure, heart problems, and disorders in the autonomic nervous system, the system of involuntary functions such as breathing. Syncope may also arise from emotional distress, **pain**, and other reactions to outside stressors. Nonsyncope nonvertigo dizziness may be caused by rapid breathing, low blood sugar, or **migraine headache**, as well as by more serious medical conditions.

Vertigo is often associated with inner ear problems called vestibular disorders. A particularly intense vestibular disorder, Méniére's disease, interferes with the volume of fluid in the inner ear. This disease, which affects approximately one in every 1,000 people, causes intermittent vertigo over the course of weeks, months, or years. Méniére's disease is often accompanied by ringing or buzzing in the ear, **hearing loss**, and a feeling that the ear is blocked. Damage to the nerve that leads from the ear to the brain can also cause vertigo. Such damage can result from head injury or a tumor. An **acoustic neuroma**, for example, is a benign tumor that wraps around the nerve. Vertigo can also be caused by disorders of the central nervous system and the circulatory system, such as hardening of the arteries (arteriosclerosis), **stroke**, or **multiple sclerosis**.

Some medications cause changes in blood pressure or blood flow. These medications can cause dizziness in some people. Prescription medications carry warnings of such side effects, but common drugs, such as **caffeine** or nicotine can also cause dizziness. Certain **antibiotics** can damage the inner ear and cause hearing loss and dizziness.

Diet may cause dizziness. The role of diet may be direct, as through alcohol intake. It may be also be indirect, as through arteriosclerosis caused by a high-fat diet. Some people experience a slight dip in blood sugar and mild dizziness if they miss a meal, but this condition is rarely dangerous unless the person is diabetic. Food sensitivities or allergies can also be a cause of dizziness. Chronic conditions, such as heart disease, and serious acute problems, such as seizures and strokes, can cause dizziness. However, such conditions usually exhibit other characteristic symptoms.

Diagnosis

During the initial medical examination, an individual with dizziness should provide a detailed description of the type of dizziness experienced, when it occurs, and how often each episode lasts. A diary of symptoms may help track this information. Report any symptoms that accompany the dizziness, such as a ringing in the ear or nausea, any recent injury or infection, and any medication taken.

Blood pressure, pulse, respiration, and body temperature are checked, and the ear, nose, and throat are scrutinized. The sense of balance is assessed by moving the individual's head to various positions or by tilt-table testing. In tilt-table testing, the person lies on a table that can be shifted into different positions and reports any dizziness that occurs.

Further tests may be indicated by the initial examination. Hearing tests help assess ear damage. x rays, computed tomography scan (CT scan), and **magnetic resonance imaging** (MRI) can pinpoint evidence of nerve damage, tumor, or other structural problems. If a vestibular disorder is suspected, a technique called electronystagmography (ENG) may be used. ENG measures the electrical impulses generated by eye movements. Blood tests can determine diabetes, **high cholesterol**, and other diseases. In some cases, a heart evaluation may be useful. Despite thorough testing, an underlying cause cannot always be determined.

Treatment

Treatment is determined by the underlying cause. If an individual has a cold or **influenza**, a few days of bed rest is usually adequate to resolve dizziness. Other causes of dizziness, such as mild vestibular system damage, may resolve without medical treatment.

If dizziness continues, drug therapy may prove helpful. Because circulatory problems often cause dizziness, medication may be prescribed to control blood pressure or to treat arteriosclerosis. Sedatives may be useful to relieve the tension that can trigger or aggravate dizziness. Low blood sugar associated with diabetes sometimes causes dizziness and is treated by controlling blood sugar levels. An individual may be asked to avoid caffeine, nicotine, alcohol, and any substances that cause allergic reactions. A low-salt diet may also help some people.

When other measures have failed, surgery may be suggested to relieve pressure on the inner ear. If the dizziness is not treatable by drugs, surgery, or other means, physical therapy may be used and the patient may be taught coping mechanisms for the problem.

KEY TERMS

Acoustic neuroma—A benign tumor that grows on the nerve leading from the inner ear to the brain. As the tumor grows, it exerts pressure on the inner ear and causes severe vertigo.

Arteriosclerosis—Hardening of the arteries caused by high blood cholesterol and high blood pressure.

Autonomic nervous system—The part of the nervous system that controls involuntary functions such as breathing and heart beat.

Computed tomography (CT)—An imaging technique in which cross-sectional x rays of the body are compiled to create a three-dimensional image of the body's internal structures.

Electronystagmography—A method for measuring the electricity generated by eye movements. Electrodes are placed on the skin around the eye and the individual is subjected to a variety of stimuli so that the quality of eye movements can be assessed.

Magnetic resonance imaging (MRI)—An imaging technique that uses a large circular magnet and radio waves to generate signals from atoms in the body. These signals are used to construct images of internal structures.

Vestibular system—The area of the inner ear that helps maintain balance.

Alternative treatment

Because dizziness may arise from serious conditions, it is advisable to seek medical treatment. Alternative treatments can often be used alongside conventional medicine without conflict. Relaxation techniques, such as **yoga** and **massage therapy** that focus on relieving tension, are popularly recommended methods for reducing **stress**. Aromatherapists recommend a warm bath scented with essential oils of lavender, geranium, and sandalwood.

Homeopathic therapies can work very effectively for dizziness, and are especially applicable when no organic cause can be identified. An osteopath or chiropractor may suggest adjustments of the head, jaw, neck, and lower back to relieve pressure on the inner ear. Acupuncturists also offer some treatment options for acute and chronic cases of dizziness. Nutritionists may be able to offer advice and guidance in choosing dietary supplements, identifying foods to avoid, and balancing nutritional needs.

Prognosis

Outcome depends on the cause of dizziness. Controlling or curing the underlying factors usually relieves dizziness. In some cases, dizziness disappears without treatment. In a few cases, dizziness can become a permanent disabling condition and a person's options are limited.

Prevention

Most people learn through experience that certain activities will make them dizzy and they learn to avoid them. For example, if reading in a car produces motion sickness, an individual leaves reading materials for after the trip. Changes to the diet can also cut down on episodes of dizziness in susceptible people. Relaxation techniques can help ward off tension and **anxiety** that can cause dizziness.

These techniques can help minimize or even prevent dizziness for people with chronic diseases. For example, persons with Méniére's disease may avoid episodes of vertigo by leaving salt, alcohol, and caffeine out of their **diets**. Reducing blood cholesterol can help diminish arteriosclerosis and indirectly treat dizziness.

Some cases of dizziness cannot be prevented. Acoustic neuromas, for example, are not predictable or preventable. When the underlying cause of dizziness cannot be discovered, it may be difficult to recommend preventive measures. Alternative approaches designed to rebalance the body's energy flow, such as **acupuncture** and constitutional **homeopathy**, may be helpful in cases where the cause of dizziness cannot be pinpointed.

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ORGANIZATIONS

Méniére's Network. 1817 Patterson St., Nashville, TN 37203. (800) 545-4327. <http://www.earfoundation.org>.

The Vestibular Disorders Association. PO Box 4467, Portland, OR 97208-4467. (503) 229-7705. <http://www.teleport.com/~veda>.

Julia Barrett

DKA *see* **Diabetic ketoacidosis**

DLE *see* **Discoid lupus erythematosus**

Domestic violence *see* **Abuse**

Donovanosis *see* **Granuloma inguinale**

Doppler echocardiography *see* **Echocardiography**

Doppler ultrasonography

Definition

Doppler ultrasonography is a non-invasive diagnostic procedure that changes sound waves into an image that can be viewed on a monitor.

Purpose

Doppler ultrasonography can detect the direction, velocity, and turbulence of blood flow. It is frequently used to detect problems with heart valves or to measure blood flow through the arteries. Specifically, it is useful in the work up of **stroke** patients, in assessing blood flow in the abdomen or legs, and in viewing the heart to monitor carotid artery diseases.

Precautions

The test is widely used because it is noninvasive, uses no x rays, and gives excellent images. It is harmless, painless, and widely available.

Description

Doppler ultrasonography makes use of two different principles. The ultrasound principle is this: when a high-frequency sound is produced and aimed at a target, it will be reflected by its target and the reflected sound can be detected back at its origin. In addition, it is known that certain crystals (called piezoelectric crystals) produce an electrical pulse when vibrated by a returning sound.

The Doppler principle is simply that sound pitch increases as the source moves toward the listener and decreases as it moves away.

Medical science utilizes these two principles in the following way. A transducer (sometimes called a probe) containing piezoelectric crystals sends a series of short sound pulses into the body and pauses between each pulse to listen for the returning sounds. The machine then determines the direction and depth of each returning sound and coverts this into a point of light on a television monitor. Thousands of these pulses are computed and displayed every second to produce an image of the organ being studied. The image allows the doctor to see the organ functioning in real time.

Doppler ultrasonography can detect the direction, velocity, and turbulence of blood flow. Because it is non-invasive and uses no x rays, doppler ultrasongraphy is widely used for numerous diagnostic procedures. *(Illustration by Electronic Illustrators Group.)*

The newest addition to this test is the addition of color. Adding color to the image shows the direction and rate of blood flow more clearly.

During a Doppler ultrasonography procedure the technician will apply a gel to the skin, then place the transducer against the skin at various angles. The transducer sends the information it receives to a television monitor that shows a moving image of the organ being studied. The technician can save these images either on video tape, paper, or x-ray film for further study.

Preparation

There is no special preparation needed for this test. The ultrasound technician may apply a clear gel to the skin in order to help the transducer more freely over the body.

Aftercare

No aftercare is necessary.

Normal results

A Doppler ultrasonography test showing no restricted blood flow, is a normal finding.

KEY TERMS

Doppler effect—The principle that the sound of an object moving toward you has a higher pitch than the sound when it's moving away from you.

Transducer—The part of a machine that changes signals in one form into another form.

Ultrasound—Sound that is too high for the human ear to hear.

Abnormal results

Disrupted or obstructed blood flow through the neck arteries may indicate the person is a risk of having a stroke. (Narrowed arterial flow in the legs does not necessarily indicate a risk of stroke.)

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Dorothy Elinor Stonely

Down syndrome

Definition

Down syndrome is the most common cause of **mental retardation** and malformation in a newborn. It occurs because of the presence of an extra chromosome.

Description

Chromosomes are the units of genetic information that exist within every cell of the body. Twenty-three distinctive pairs, or 46 total chromosomes, are located within the nucleus (central structure) of each cell. When a baby is conceived by the combining of one sperm cell with one egg cell, the baby receives 23 chromosomes from each parent, for a total of 46 chromosomes. Sometimes, an accident in the production of a sperm or egg cell causes that cell to contain 24 chromosomes. This event is referred to as nondisjunction. When this defective cell is involved in the conception of a baby, that baby will have a total of 47 chromosomes. The extra chromosome in Down syndrome is labeled number 21. For this reason, the existence of three such chromosomes is sometimes referred to as Trisomy 21.

In a very rare number of Down syndrome cases (about 1–2%), the original egg and sperm cells are completely normal. The problem occurs sometime shortly after fertilization; during the phase where cells are dividing rapidly. One cell divides abnormally, creating a line of cells with an extra chromosome 21. This form of genetic disorder is called a mosaic. The individual with this type of Down syndrome has two types of cells: those with 46 chromosomes (the normal number), and those with 47 chromosomes (as occurs in Down syndrome). Some researchers have suggested that individuals with this type of mosaic form of Down syndrome have less severe signs and symptoms of the disorder.

Another relatively rare genetic accident which can cause Down syndrome is called translocation. During cell division, the number 21 chromosome somehow breaks. A piece of the 21 chromosome then becomes attached to another chromosome. Each cell still has 46 chromosomes, but the extra piece of chromosome 21 results in the signs and symptoms of Down syndrome. Translocations occur in about 3–4% of cases of Down syndrome.

Down syndrome occurs in about one in every 800–1,000 births. It affects an equal number of boys and girls. Less than 25% of Down syndrome cases occur due to an extra chromosome in the sperm cell. The majority of cases of Down syndrome occur due to an extra chromosome 21 within the egg cell supplied by the mother (nondisjunction). As a woman's age (maternal age) increases, the risk of having a Down syndrome baby increases significantly. For example, at younger ages, the risk is about one in 4,000. By the time the woman is age 35, the risk increases to one in 400; by age 40 the risk increases to one in 110; and by age 45 the risk becomes one in 35. There is no increased risk of either mosaicism or translocation with increased maternal age.

Causes and symptoms

While Down syndrome is a chromosomal disorder, a baby is usually identified at birth through observation of a set of common physical characteristics. Babies with Down syndrome tend to be overly quiet, less responsive, with weak, floppy muscles. Furthermore, a number of physical signs may be present. These include:

- flat appearing face
- small head

- flat bridge of the nose
- smaller than normal, low-set nose
- small mouth, which causes the tongue to stick out and to appear overly large
- upward slanting eyes
- extra folds of skin located at the inside corner of each eye, near the nose (called epicanthal folds)
- rounded cheeks
- small, misshapen ears
- small, wide hands
- an unusual, deep crease across the center of the palm (called a simian crease)
- a malformed fifth finger
- a wide space between the big and the second toes
- unusual creases on the soles of the feet
- overly-flexible joints (sometimes referred to as being double-jointed)
- ahorter than normal height

Other types of defects often accompany Down syndrome. About 30–50% of all children with Down syndrome are found to have heart defects. A number of different heart defects are common in Down syndrome, including abnormal openings (holes) in the walls that separate the heart's chambers (**atrial septal defect**, **ventricular septal defect**). These result in abnormal patterns of blood flow within the heart. The abnormal blood flow often means that less oxygen is sent into circulation throughout the body. Another heart defect that occurs in Down syndrome is called **Tetralogy of Fallot**. Tetralogy of Fallot consists of a hole in the heart, along with three other major heart defects.

Malformations of the gastrointestinal tract are present in about 5–7% of children with Down syndrome. The most common malformation is a narrowed, obstructed duodenum (the part of the intestine into which the stomach empties). This disorder, called duodenal atresia, interferes with the baby's milk or formula leaving the stomach and entering the intestine for digestion. The baby often vomits forcibly after feeding, and cannot gain weight appropriately until the defect is repaired.

Other medical conditions that occur in patients with Down syndrome include an increased chance of developing infections, especially ear infections and **pneumonia**; certain kidney disorders; thyroid disease (especially low or hypothyroid); **hearing loss**; vision impairment requiring glasses (corrective lenses); and a 20-times greater chance of developing leukemia (a blood disorder).

Development in a baby and child with Down syndrome occurs at a much slower than normal rate. Because of weak, floppy muscles (hypotonia), babies learn to sit up, crawl, and walk much later than their normal peers. Talking is also quite delayed. The level of mental retardation is considered to be mild-to-moderate in Down syndrome. The actual IQ range of Down syndrome children is quite varied, but the majority of such children are in what is sometimes known as the trainable range. This means that most people with Down syndrome can be trained to do regular self-care tasks, function in a socially appropriate manner in a normal home environment, and even hold simple jobs.

As people with Down syndrome age, they face an increased chance of developing the brain disease called Alzheimer's (sometimes referred to as **dementia** or senility). Most people have a six in 100 risk of developing Alzheimer's, but people with Down syndrome have a 25 in 100 chance of the disease. **Alzheimer's disease** causes the brain to shrink and to break down. The number of brain cells decreases, and abnormal deposits and structural arrangements occur. This process results in a loss of brain functioning. People with Alzheimer's have strikingly faulty memories. Over time, people with Alzheimer's disease will lapse into an increasingly unresponsive state. Some researchers have shown that even Down syndrome patients who do not appear to have Alzheimer's disease have the same changes occurring to the structures and cells of their brains.

As people with Down syndrome age, they also have an increased chance of developing a number of other illnesses, including **cataracts**, thyroid problems, diabetes, and seizure disorders.

Diagnosis

Diagnosis is usually suspected at birth, when the characteristic physical signs of Down syndrome are noted. Once this suspicion has been raised, **genetic testing** (chromosome analysis) can be undertaken in order to verify the presence of the disorder. This testing is usually done on a blood sample, although chromosome analysis can also be done on other types of tissue, including skin. The cells to be studied are prepared in a laboratory. Chemical stain is added to make the characteristics of the cells and the chromosomes stand out. Chemicals are added to prompt the cells to go through normal development, up to the point where the chromosomes are most visible, prior to cell division. At this point, they are examined under a microscope and photographed. The photograph is used to sort the different sizes and shapes of chromosomes into pairs. In most cases of Down syndrome, one extra chromosome 21 will be revealed. The final result of such testing, with the photographed chromosomes paired and organized by shape and size, is called the individual's karyotype.

Treatment

No treatment is available to cure Down syndrome. Treatment is directed at addressing the individual concerns of a particular patient. For example, heart defects will many times require surgical repair, as will duodenal atresia. Many Down syndrome patients will need to wear glasses to correct vision. Patients with hearing impairment benefit from **hearing aids**.

A new drug, referred to as a "smart drug," has been receiving some attention in the treatment of Down syndrome patients. This drug, piracetam, has not been proven to increase intellectual ability, despite testimonials that have been receiving attention on television and the Internet. Piracetam has not been approved for use in the United States, although it is being sold via the Internet. The National Down Syndrome Society and the National Down Syndrome Congress do not recommend the use of this drug as of 2001.

While some decades ago, all Down syndrome children were quickly placed into institutions for lifelong care. Research shows very clearly that the best outlook for children with Down syndrome is a normal family life in their own home. This requires careful support and education of the parents and the siblings. It is a life-changing event to learn that a new baby has a permanent condition that will effect essentially all aspects of his or her development. Some community groups exist to help families deal with the emotional effects of this new information, and to help plan for the baby's future. Schools are required to provide services for children with Down syndrome, sometimes in separate special education classrooms, and sometimes in regular classrooms (this is called mainstreaming or inclusion).

Prognosis

The prognosis in Down syndrome is quite variable, depending on the types of complications (heart defects, susceptibility to infections, development of leukemia) of each individual baby. The severity of the retardation can also vary significantly. Without the presence of heart defects, about 90% of children with Down syndrome live into their teens. People with Down syndrome appear to go through the normal physical changes of **aging** more rapidly, however. The average age of **death** for an individual with Down syndrome is about 50–55 years.

Still, the prognosis for a baby born with Down syndrome is better than ever before. Because of modern medical treatments, including **antibiotics** to treat infections and surgery to treat heart defects and duodenal atresia, life expectancy has greatly increased. Community and family support allows people with Down syndrome to have rich, meaningful relationships. Because of educational programs, some people with Down syndrome are able to hold jobs.

Men with Down syndrome appear to be uniformly sterile (meaning that they are unable to have offspring). Women with Down syndrome, however, are fully capable of having babies. About 50% of these babies, however, will also be born with Down syndrome.

Prevention

Efforts at prevention of Down syndrome are aimed at **genetic counseling** of couples who are preparing to have babies. A counselor needs to inform a woman that her risk of having a baby with Down syndrome increases with her increasing age. Two types of testing is available during a **pregnancy** to determine if the baby being carried has Down syndrome.

Screening tests are used to estimate the chance that an individual woman will have a baby with Down syndrome. At 14–17 weeks of pregnancy, measurements of a substance called AFP (alpha-fetoprotein) can be performed. AFP is normally found circulating in the blood of a pregnant woman, but may be unusually high or low with certain disorders. Carrying a baby with Down syndrome often causes AFP to be lower than normal. This information alone, or along with measurements of two other hormones, is considered along with the mother's age to calculate the risk of the baby being born with Down syndrome. These results are only predictions, and are only correct about 60% of the time.

The only way to definitively establish (with about 98–99% accuracy) the presence or absence of Down syndrome in a developing baby, is to test tissue from the pregnancy itself. This is usually done either by **amniocentesis** or **chorionic villus sampling** (CVS). In amniocentesis, a small amount of the fluid in which the baby is floating is withdrawn with a long, thin needle. In chorionic villus sampling, a tiny tube is inserted into the opening of the uterus to retrieve a small sample of the placenta (the organ that attaches the growing baby to the mother via the umbilical cord, and provides oxygen and **nutrition**). Both amniocentesis and CVS allow the baby's own karyotype to be determined. A couple must then decide whether to use this information in order to begin to prepare for the arrival of a baby with Down syndrome, or to terminate the pregnancy.

Once a couple has had one baby with Down syndrome, they are often concerned about the likelihood of future offspring also being born with the disorder. Most research indicates that this chance remains the same as for any woman at a similar age. However, when the baby

KEY TERMS

Chromosome—The structures that carry genetic information. Chromosomes are located within every cell, and are responsible for directing the development and functioning of all the cells in the body. The normal number is 46 (23 pairs).

Karyotype—The specific chromosomal makeup of a particular cell.

Mental retardation—A condition where an individual has a lower-than-normal IQ, and thus is developmentally delayed.

Mosaic—A term referring to a genetic situation, in which an individual's cells do not have the exact same composition of chromosomes. In Down syndrome, this may mean that some of the individual's cells have a normal 46 chromosomes, while other cells have an abnormal 47 chromosomes.

Nondisjunction—A genetic term referring to an event which takes place during cell division, in which a genetic accident causes an egg or sperm cell to have 24 chromosomes, rather than the normal 23.

Translocation—A genetic term referring to a situation during cell division in which a piece of one chromosome breaks off and sticks to another chromosome.

Trisomy—The condition of having three identical chromosomes, instead of the normal two.

with Down syndrome has the type that results from a translocation, it is possible that one of the two parents is a carrier of that defect. A carrier "carries" the genetic defect, but does not actually have the disorder. When one parent is a carrier of a translocation, the chance of future offspring having Down syndrome is greatly increased. The specific risk will have to be calculated by a genetic counselor.

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National Down Syndrome Society. 666 Broadway, 8th Floor, New York, NY 10012-2317. (800) 221-4602. <http://www.ndss.org>.

Kim A. Sharp, M.Ln.

Down's syndrome *see* **Down syndrome**

Doxazosin *see* **Alpha$_1$-adrenergic blockers**

Doxepin *see* **Antidepressants, tricyclic**

Doxycycline *see* **Tetracyclines**

Dracontiasis *see* **Guinea worm infection**

Dracunculiasis *see* **Guinea worm infection**

Drooping eyelid *see* **Ptosis**

Drowning *see* **Near-drowning**

Drug abuse *see* **Substance abuse and dependence**

Drug addiction *see* **Substance abuse and dependence**

Drug dependence *see* **Substance abuse and dependence**

Drug metabolism/interactions

Definition

Drug metabolism is the process by which the body breaks down and converts medication into active chemical substances.

Precautions

Drugs can interact with other drugs, foods, and beverages. Interactions can lessen or magnify the desired therapeutic effect of a drug, or may cause unwanted or unexpected side effects. There are thousands of possible drug-to-drug and drug-to-food interactions, and many medications and supplements are contraindicated (not recommended) under certain conditions or in patients with specific diseases and disorders. This is why it is imperative that patients always keep their physician fully informed about all drugs and dietary supplements (including herbal remedies) they are taking.

Description

The primary site of drug metabolism is the liver, the organ that plays a major role in metabolism, digestion, **detoxification,** and elimination of substances from the body. Enzymes in the liver are responsible for chemically changing drug components into substances known as metabolites. Metabolites are then bound to other substances for excretion through the lungs, or bodily fluids such as saliva, sweat, breast milk, and urine, or through reabsorption by the intestines. The primary mode of excretion is through the kidneys.

The family of liver isoenzymes known as cytochrome P-450 are crucial to drug metabolism. These enzymes (labeled CYP1A2, CYP2C9, CYP2C19, CYP2D6, and CYP3A4) have a catabolic action on substances, breaking them down into metabolites. Consequently, they also act to lower the concentration of medication in the bloodstream.

Drug interactions can occur when one drug inhibits or induces a P-450 that acts on another drug. An example is nicotine, a drug contained in tobacco, and known to induce P-450s. Individuals with liver disease (e.g., **cirrhosis**) may also have insufficient levels of P-450 enzymes. As a result, the concentration of drugs metabolized by these enzymes (e.g., amprenavir and other **protease inhibitors**) remains high and can build up to toxic levels in the bloodstream. In addition, certain medications and foods, such as grapefruit juice, can inactivate or lessen the metabolic activity of P-450s. Changing the drug dosage can alleviate the problem in some cases.

The metabolic rate can vary significantly from person to person, and drug dosages that work quickly and effectively in one individual may not work well for another. Factors such as genetics, environment, **nutrition** and age also influence drug metabolism; infants and elderly patients may have a reduced capacity to metabolize certain drugs, and may require adjustments in dosage.

Causes and symptoms

Drugs that commonly interact with other medications include:

- **Diuretics**. Diuretics such as hydrochlorothiazide can reduce serum potassium and sodium electrolyte levels when taken with digoxin and lithium, respectively.
- Monoamine oxidase inhibitors (MAOIs). MAOI antidepressants can cause convulsions and other serious side effects when used with tricyclic antidepressants (e.g., Imipramine, Nortriptyline), **selective serotonin reuptake inhibitors** (SSRIs), or sympathomimetic drugs (e.g., amphetamines).
- **Antibiotics**. Antibiotics may reduce the efficiency of oral contraceptives.
- Metals. Medications containing metals, such as **antacids** with aluminum additives and iron supplements, can reduce the absorption of **tetracyclines** and fluoroquinolones.
- Drugs that inhibit liver enzyme function. Drugs that slow drug metabolism include ciprofloxacin, erythromycin, fluoxetine, nefazodone, paroxetine, and ritonavir. The therapeutic effect of other medications taken with these drugs may be amplified. Warfarin, a blood thinner, should be used with great caution in individuals taking these drugs.

Foods and beverages that may interact with drugs include:

- Grapefruit juice. Grapefruit juice inhibits the metabolism of many medications, including cyclosporine, felodipine, nifedipine, nitrendipine, nisoldipine, carbamazepine, triazolam, and midazolam.
- Foods and beverages with tyramines. Red wine, malted beers, smoked foods (e.g., fish and meats), dried fruits, and aged cheeses may contain tyramines, and can cause a severe and dangerous elevation in blood pressure when taken with MAOI inhibitors (a class of antidepressants).
- Dairy products. Milk, cream, and other dairy products containing calcium can prevention the absorption of antibiotics such as tetracycline, doxycycline, and ciprofloxacin when they are taken with the drug. In addition, whole milk with vitamin D can cause milk-alkali syndrome in patients taking aluminum hydroxide antacids.
- Caffeinated beverages. The **caffeine** contained in coffee and colas can influence drug metabolism.
- Alcohol. Alcohol is a central nervous system depressant, and should not be taken with other CNS depressants

KEY TERMS

Catabolism—A process of metabolism that breaks down complex substances into simple ones.

Cirrhosis—Liver disease characterized by the widespread disruption of the normal liver structure and function.

CNS depressant—Anything that depresses, or slows, the sympathetic impulses of the central nervous system (i.e., respiratory rate, heart rate).

Drug interaction—A chemical or physiological reaction that can occur when two different drugs are taken together.

Enzymes—Organic substances (proteins) composed of amino acids that trigger and regulate chemical reactions in the body. There are over 700 identified human enzymes.

Liver—A solid organ located on the right in the upper abdomen. It plays a major role in metabolism, digestion, detoxification, and elimination of substances from the body.

Metabolism—The sum of all the physical and chemical processes occurring in the body to organize and maintain life.

Metabolites—Substances produced by metabolism or by a metabolic process.

Milk-alkali syndrome—Elevated blood calcium levels and alkalosis caused by excessive intake of milk and alkalis. Usually occurs in the treatment of peptic ulcer.

(e.g., antipsychotics, **antihistamines**). In addition, certain fermented beverages may contain tyramines

This list is not all-inclusive and individuals should always let their doctor and pharmacist know when they are taking other medications, herbal remedies, or dietary supplements. Anyone who experiences a serious reaction to a drug that is not consistent with its product labelling should report the event to their doctor and/or the MedWatch adverse event reporting system of the United States Food and Drug Administration (FDA).

Alternative treatment

The growing use of herbal supplements has also increased the opportunity for adverse drug and herbal interactions. In 2000, the FDA issued a warning on the popular herb **St. John's wort** (*Hypericum perforatum*). The supplement was found to inhibit the effect of indinavir, a protease inhibitor used in the treatment of HIV. It may also affect the action of cyclosporine and other protease inhibitors (e.g., amprenavir, ritonavir). Further clinical studies are still necessary to determine the full metabolic effects of the herb.

Other herbs which may interact with allopathic medications include gingko bilboa, ginseng, and garlic, which may all heighten the blood thinning effect of the anticoagulant warfarin. Because herbs are regulated by the FDA as dietary supplements, they do not require the same extensive clinical trials and premarket testing as drugs do before they are cleared for sale in the United States As such, there is still much to learn about the potential interactions and adverse effects associated with herbal supplements. Individuals who experience serious side effects from dietary supplements should report them to FDA's MedWatch program.

Diagnosis

Drug interactions can be difficult to detect. In some cases, adverse reactions may closely resemble the symptoms of the disease or condition the medication was prescribed to treat. Patients who take a number of medications or self-treat with over-the-counter drugs and/or herbal remedies may not be able to determine which drug actually triggered the interaction. A 2001 study by University of Florida researchers found that less than half of the women participating disclosed their use of herbal therapies to their healthcare providers. In cases where a serious drug or herb interaction occurs, withholding this information can delay diagnosis and put the patient at increased risk.

Treatment

Treatment of a drug interaction is dependant on a number of factors, including the medication(s) or supplements used and the medical history of the patient. A dosage adjustment may reverse the effects of some interactions. Serious or life-threatening interactions will require more aggressive therapies.

Prevention

Patients with chronic health conditions, particularly those with liver disorders, should always inform their

healthcare professional before taking any over-the-counter (OTC) medications or dietary supplements. Because of the risk for a drug-to-drug interaction, individuals should also let their doctor know if they are taking drugs prescribed by other physicians. Individuals should closely follow instructions for use and package directions on both prescription and over-the-counter drugs. Consulting with a pharmacist and/or physician may be beneficial if package directions are unclear to the patient.

As a rule, grapefruit juice should not be taken with medication unless recommended by a doctor. Patients taking MAOI inhibitors should always check food and beverage labels to ensure tyramines aren't included, and should avoid all fermented drinks.

Resources

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ORGANIZATION

United States Food and Drug Administration (FDA). MedWatch Adverse Events Reporting Program. 5600 Fishers Lane, Rockville, MD 20852-9787. 800-FDA-1088. <http://www.fda.gov/medwatch/>.

Paula Anne Ford-Martin

Drug overdose

Definition

A drug overdose is the accidental or intentional use of a drug or medicine in an amount that is higher than is normally used.

Description

All drugs have the potential to be misused, whether legally prescribed by a doctor, purchased over-the-counter at the local drug store, or bought illegally on the street. Taken in combination with other drugs or with alcohol, even drugs normally considered safe can cause **death** or serious long term consequences. Children are particularly at risk for accidental overdose, accounting for over one million poisonings each year from drugs, alcohol, and other chemicals and toxic substances. People who suffer from depression and who have suicidal thoughts are also at high risk for drug overdose.

Causes and symptoms

Accidental drug overdose may be the result of misuse of prescription medicines or commonly used medications like **pain** relievers and cold remedies. Symptoms differ depending on the drug taken. Some of the drugs commonly involved in overdoses are listed below along with symptoms and outcomes.

Acetaminophen is the generic name for the commonly used pain reliever Tylenol. Overdose of this drug causes liver damage with symptoms that include loss of appetite, tiredness, **nausea and vomiting**, paleness, and sweating. The next stage of symptoms indicates liver failure and includes abdominal pain and tenderness, swelling of the liver, and abnormal blood tests for liver enzymes. In the last stage of this **poisoning**, liver failure advances and the patient becomes jaundiced, with yellowing of the skin and whites of the eyes. They may also experience kidney failure, bleeding disorders, and encephalopathy (swelling of the brain).

Anticholinergic drugs (drugs that block the action of acetylcholine, a neurotransmitter) like atropine, scopolamine, belladonna, **antihistamines**, and antipsychotic agents cause the skin and moist tissues (like in the mouth and nose) to become dry and flushed. Dilated pupils, an inability to urinate, and mental disturbances are also symptoms. Severe toxicity can lead to seizures, abnormal heart rhythms, extremely high blood pressure, and **coma**.

Antidepressant drugs like amitriptyline, desipramine, and nortriptyline can cause irregular heart rate, vomiting, low blood pressure, confusion, and seizures. An overdose of antidepressants also causes symptoms similar to those seen with anticholinergic drug overdoses.

Cholinergic drugs (drugs that stimulate the parasympathetic nervous system) like carbamate and pilocarpine cause nausea, **diarrhea**, increased secretion of body fluids (sweat, tears, saliva, and urine), **fatigue**, and muscle weakness. Convulsions are possible. Death can occur due to **respiratory failure** and **heart failure**.

Cocaine and crack cocaine overdoses cause seizures, high blood pressure, increased heart rate, **paranoia**, and other changes in behavior. **Heart attack** or **stroke** are serious risks within three days after cocaine overdose.

Depressant drugs (tranquilizers, **antianxiety drugs**, sleeping pills) cause sleepiness, slowed or slurred speech, difficulty walking or standing, blurred vision, impaired ability to think, disorientation, and mood changes. Over-

dose symptoms can include slowed breathing, very low blood pressure, stupor, coma, **shock**, and death.

Digoxin, a drug used to regulate the heart, can cause irregular heart beats, nausea, confusion, loss of appetite, and blurred vision.

Narcotics or opiates are drugs like heroin, morphine, and codeine. Clonidine and diphenoxylate (Lomotil) are also in this category. Overdose with opiate drugs causes **sedation** (sleepiness), low blood pressure, slowed heart rate, and slowed breathing. Pinpoint pupils, where the black centers of the eyes become smaller than normal, are common in opiate overdose. However, if other drugs are taken at the same time as the opiates, they may counteract this effect on the pupils. A serious risk is that the patient will stop breathing.

Salicylates are found in **aspirin** and some creams or ointments used for muscle and joint pain (like Ben-Gay), and creams for **psoriasis**, a skin condition. Initial symptoms are gastrointestinal irritation, **fever**, and vomiting, possibly with blood in the vomit. This overdose will cause **metabolic acidosis** and **respiratory alkalosis**, conditions where the body's acid/base balance is malfunctioning. Symptoms include rapid heart beat and fast breathing. Nervous system symptoms include confusion, **hallucinations**, tiredness, and ringing in the ears. An increased tendency to bleed is also common. Serious complications include acute renal failure, coma, and heart failure. Acute salicylate poisoning can lead to death.

Diagnosis

Diagnosis of a drug overdose may be based on the symptoms that develop, however, the drug may do extensive damage to the body before significant symptoms develop. If the patient is conscious, he or she may be able to tell what drugs were taken and in what amounts. The patient's recent medical and social history may also help in a diagnosis. For example, a list of medications that the patient takes, whether or not alcohol was consumed recently, even if the patient has eaten in the last few hours before the overdose, can be valuable in determining what was taken and how fast it will be absorbed into the system.

Different drugs have varying effects on the body's acid/base balance and on certain elements in the blood like potassium and calcium. Blood tests can be used to detect changes in body chemistry that may give clues to what drugs were taken. Blood can also be screened for various drugs in the system. Once the overdose drug is identified, blood tests can be used to monitor how fast the drug is being cleared out of the body. Urine tests can also be used to screen for some drugs and to detect changes in the body's chemistry. Blood and urine tests may show if there is damage to the liver or kidneys as a result of the overdose.

Treatment

Immediate care

If a drug overdose is discovered or suspected, and the person is unconscious, having convulsions, or is not breathing, call for emergency help immediately. If the person who took the drug is not having symptoms, don't wait to see if symptoms develop; call a poison control center immediately. Providing as much information as possible to the poison control center can help determine what the next course of action should be.

The poison control center, paramedics, and emergency room staff will want to know:

- what drug(s) were taken—try to locate the drug's container.
- how much of the drug was taken
- when was the drug taken
- was the drug taken with alcohol or any other drugs or chemicals
- what is the age of the patient
- what symptoms are the patient experiencing
- is the patient conscious
- is the patient breathing

The poison control center may recommend trying to get the patient to vomit. A liquid called **ipecac** syrup, which is used to induce vomiting, is available from pharmacies without a prescription. Pediatricians may recommend that families keep ipecac syrup on hand in households with children. This medication should be used only on the advice of a medical professional. Vomiting should not be induced if the patient is unconscious.

Emergency care

Emergency medical treatment may include:

- Assessment of the patient's airway and breathing to making sure that the trachea, the passage to the lungs, is not blocked. If needed, a tube may be inserted through the mouth and into the trachea to help the patient breath. This procedure is called intubation.
- Assessment of the patient's heart rate, blood pressure, body temperature, and other physical signs that might indicate the effects of the drug.
- Blood and urine samples may be collected to test for the presence of the suspected overdose drug, and any other drugs or alcohol that might be present.

KEY TERMS

Gastric lavage—Also called a stomach pump. For this procedure, a flexible tube is inserted through the nose, down the throat, and into the stomach and the contents of the stomach are suctioned out. The inside of the stomach is rinsed with a saline (salt water) solution.

Intubation—A procedure where a tube is inserted through the mouth and into the trachea keep the airway open and to help the patient breathe.

- Elimination of the drug that has not yet been absorbed is attempted. Vomiting may be induced using ipecac syrup or other drugs that cause vomiting. Ipecac syrup should not be given to patients who overdosed with tricyclic antidepressants, theophylline, or any drug that causes a significant change in mental status. If a patient vomits while unconscious, there is a serious risk of **choking**.
- Gastric lavage, or washing out the stomach, may be attempted. For this procedure a tube flexible tube is inserted through the nose, down the throat, and into the stomach. The contents of the stomach are then suctioned out through the tube. A solution of saline (salt water) is injected into the tube to rinse out the stomach. This solution is then suctioned out. This is the process used when someone has his/her stomach pumped.
- Activated charcoal is sometimes given to absorb the drug.
- Medication to stimulate urination or defecation may be given to try to flush the excess drug out of the body faster.
- Intravenous (IV) fluids may be given. An intravenous line, a needle inserted into a vein, may be put into the arm or back of the hand. Fluids, either sterile saline (salt water solution) or dextrose (sugar water solution), can be administered through this line. Increasing fluids can help to flush the drug out of the system and to reestablish balance of fluids and **minerals** in the body. The pH (acid/base balance) of the body may need to be corrected by administering electrolytes like sodium, potassium, and bicarbonate through this IV line. If drugs need to be administered quickly, they can also be injected directly into the IV line.
- Hemodialysis is a procedure where blood is circulated out of the body, pumped through a dialysis machine, then reintroduced back into the body. This process can be used to filter some drugs out of the blood. It may also be used temporarily or long term if the kidneys are damaged due to the overdose.
- Antidotes are available for some drug overdoses. An antidote is another drug that counteracts or blocks the overdose drug. For example, acetaminophen overdose can be treated with an oral medication, N-acetylcysteine (Mucomyst), if the level of acetaminophen found in the blood is extremely high. Naloxone is an anti-narcotic drug that is given to counteract narcotic poisoning. Nalmefen or **methadone** may also be used.
- Psychiatric evaluation may be recommended if the drug overdose was taken deliberately.

Prognosis

While many victims of drug overdose recover without long term effects, there can be serious consequences. Some drug overdoses cause the failure of major organs like the kidneys or liver, or failure of whole systems like the respiratory or circulatory systems. Patients who survive drug overdose may need **kidney dialysis**, kidney or liver transplant, or ongoing care as a result of heart failure, stroke, or coma. Death can occur in almost any drug overdose situation, particularly if treatment is not started immediately.

Prevention

To protect children from accidental drug overdose, all medications should be stored in containers with child resistant caps. All drugs should be out of sight and out of reach of children, preferably in a locked cabinet. Prescription medications should be used according to directions and only by the person whose name is on the label. Threats of suicide need to be taken seriously and appropriate help sought for people with depression or other mental illness that may lead to suicide.

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Altha Roberts Edgren

Drug therapy monitoring

Definition

Drug therapy monitoring, also known as Therapeutic Drug Monitoring (TDM), is a means of monitoring drug levels in the blood.

Purpose

TDM is employed to measure blood drug levels so that the most effective dosage can be determined, with toxicity prevented. TDM is also utilized to identify non-compliant patients (those patients who, for whatever reason, either cannot or will not comply with drug dosages as prescribed by the physician).

Precautions

Because so many different factors influence blood drug levels, the following points should be taken into consideration during TDM: the age and weight of the patient; the route of administration of the drug; the drug's absorption rate, excretion rate, delivery rate, and dosage; other medications the patient is taking; other diseases the patient has; the patient's compliance regarding the drug treatment regimen; and the laboratory methods used to test for the drug.

Description

TDM is a practical tool that can help the physician provide effective and safe drug therapy in patients who need medication. Monitoring can be used to confirm a blood drug concentration level that is above or below the therapeutic range, or if the desired therapeutic effect of the drug is not as expected. If this is the case, and dosages beyond normal then have to be prescribed, TDM can minimize the time that elapses.

TDM is important for patients who have other diseases that can affect drug levels, or who take other medicines that may affect drug levels by interacting with the drug being tested. As an example, without drug monitoring, the physician cannot be sure if a patient's lack of response to an antibiotic reflects bacterial resistance, or is the result of failure to reach the proper therapeutic range of antibiotic concentration in the blood. In cases of life-threatening infections, timing of effective antibiotic therapy is critical to success. It is equally crucial to avoid toxicity in a seriously ill patient. Therefore, if toxic symptoms appear with standard dosages, TDM can be used to determine changes in dosing.

Drawn blood, used for TDM, demonstrates a drug action in the body at any specific time, whereas drug levels examined from urine samples reflect the presence of a drug over many days (depending on the rate of excretion). Therefore, blood testing is the procedure of choice when definite data are required. However, for adequate absorption and therapeutic levels to be accurate, it is important to allow for sufficient time to pass between the administration of the medication and the collection of the blood sample.

Blood specimens for drug monitoring can be taken at two different times: during the drug's highest therapeutic concentration ("peak" level), or its lowest ("trough" level). Occasionally called residual levels, trough levels show sufficient therapeutic levels; whereas peak levels show **poisoning** (toxicity). Peak and trough levels should fall within the therapeutic range.

Preparation

In preparing for this test, the following guidelines should be observed:

- Depending on the drug to be tested, the physician should decide if the patient is to be **fasting** (nothing to eat or drink for a specified period of hours) before the test.
- For patients suspected of symptoms of drug toxicity, the best time to draw the blood specimen is when the symptoms are occurring.
- If there is a question as to whether an adequate dose of the drug is being achieved, it is best to obtain trough (lowest therapeutic concentration) levels.
- Peak (highest concentration) levels are usually obtained one to two hours after oral intake, approximately one hour after intramuscular (IM) administration (a shot in the muscle), and approximately 30 minutes after intravenous (IV) administration. Residual, or trough, levels are usually obtained within 15 minutes of the next scheduled dose.

Therapeutic Drug Monitoring: Therapeutic And Toxic Range

Drug Level*	Use	Therapeutic Level*	Toxic
Aceteminophen mg/ml	Analgesic, antipyretic	Depends on use	>250
Amikacin mg/ml	Antibiotic	12–25 mg/ml**	>25
Aminophylline ng/ml	Bronchodilator	10–20 mg/ml	>20
Amitriptyline ng/ml	Antidepressant	120–150 ng/ml	>500
Carbamazepine mg/ml	Anticonvulsant	5–12 mg/ml	>12
Chloramphenicol mg/ml	Antibiotic	10–20 mg/ml	>25
Digoxin ng/ml	Cardiotonic	0.8–2.0 ng/ml	>2.4
Gentamicin	Antibiotic	4–12 mg/L	>12 mg/L
Lidocaine	Antiarrhythmic	1.5–5.0 mg/ml	>5 mg/ml
Lithium mEq/L	Antimanic	0.7–2.0 mEq/L	>2.0
Nortriptyline ng/ml	Antidepressant	50–150 ng/ml	>500
Phenobarbital mg/ml	Anticonvulsant	10–30 mg/ml	>40
Phenytoin mg/ml	Anticonvulsant	7–20 mg/ml	>30
Procainamide mg/ml	Antiarrhythmic	4–8 mg/ml	>16
Propranolol ng/ml	Antiarrhythmic	50–100 ng/ml	>150
Quinidine mg/ml	Antiarrhytmic	1–4 mg/ml	>10
Theophylline mg/ml	Bronchodilator	10–20 mg/ml	>20
Tobramycin mg/ml	Antibiotic	4–12 mg/ml**	>12
Valproic acid mg/ml	Anticonvulsant	50–100 mg/ml	>100

* Values are laboratory-specific
**Concentration obtained 30 minutes after the end of a 30–minute infusion.

Risks

Risks for this test are minimal, but may include slight bleeding from the blood-drawing site, **fainting** or feeling lightheaded after blood is drawn, or accumulation of blood under the puncture site (hematoma).

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Janis O. Flores

Drugs used in labor

Definition

These drugs are used to induce (start) or continue labor.

Purpose

The drug decribed here, oxytocin, makes the uterus (womb) contract. Physicians use it to deliberately start labor. Because there are some risks with using oxytocin, this should be done only when there are good medical reasons. Any woman who is being given oxytocin should make sure she has discussed the benefits and risks with her physician.

Oxytocin also may be used to control bleeding after delivery or to help make the milk flow in women who are breastfeeding their babies.

Description

Oxytocin is a hormone and is available only with a physician's prescription. When used to start or continue labor, it is slowly injected into a vein. A nasal spray form is used to increase milk flow in breastfeeding. Some commonly used brand names are Pitocin and Syntocinon.

Recommended dosage

The dosages given here are average doses. However, doses may be different for different patients. Follow the orders of the physician who prescribed the drug.

For increasing milk production:

One spray into one or both nostrils, two to three minutes before nursing or using a breast pump.

For starting or continuing labor:

The physician in charge will determine the appropriate dose.

Precautions

Oxytocin does not help increase or continue labor in all patients. When it does not help, the physician may deliver the baby by **cesarean section**.

KEY TERMS

Cesarean section—The delivery of a baby through a surgical procedure.

Fetus—A developing baby inside the womb.

Hormone—A substance that is produced in one part of the body, then travels through the bloodstream to another part of the body where it has its effect.

In women who are especially sensitive to oxytocin, the drug may cause contractions to become too strong. This could tear the uterus or deprive the fetus of blood and oxygen during labor.

Oxytocin does not help improve milk flow in all women who are breastfeeding. Check with a physician if the drug does not seem to be working.

Women with heart disease, high blood pressure, or kidney disease should let their physicians know about these conditions before taking oxytocin. Also, anyone who has had an unusual reaction to oxytocin in the past should inform their physician.

Side effects

Oxytocin has caused irregular heartbeat and increased bleeding in some women after delivery. It may also cause **jaundice** (yellowing of the eyes and skin) in newborns.

Other side effects are rare, but may include nausea, vomiting, confusion, **dizziness**, convulsions, breathing problems, **headache**, **hives**, skin rash, **itching**, pelvic or abdominal **pain**, and weakness. The nasal spray form may cause watery eyes or irritation of the nose.

Interactions

Anyone who takes oxytocin should let the physician know all other medicines she is taking.

Nancy Ross-Flanigan

Dry mouth

Definition

Dry mouth, known medically as xerostomia, is the abnormal reduction of saliva due to medication, disease, or medical therapy.

Description

Dry mouth due to the lack of saliva can be a serious medical problem. Decreased salivation can make swallowing difficult, can decrease taste sensation, and can promote **tooth decay**.

Causes and symptoms

Dry mouth, resulting from thickened or reduced salvia flow, can be caused by a number of factors: medications, both prescription and over-the-counter; systemic diseases, such as anemia or diabetes, manifestations of **Sjögren's syndrome** (as **rheumatoid arthritis**, lupus, chronic hardening and thickening of the skin, or chronic and progressive inflammation of sketal muscles); infections of the salivary glands; blockage of the salivary ducts caused by stones or tumors forming in the ducts through which the saliva passes; **dehydration**; medical therapies, such as local surgery or radiation; secretion reduction normally involved in the **aging** proces; and emotional **stress**.

Diagnosis

The diagnosis of dry mouth is not difficult. The patient will state that his or her saliva is very thick or non-existent. Finding the cause of the dry mouth may be more difficult and require some laboratory testing. Salivary gland biopsy for stones or tumors should be performed if indicated.

Treatment

The treatment of dry mouth involves the management of the condition causing it. If dry mouth is caused by medication, the medication should be changed. If dry mouth is caused by blockage of the salivary ducts, the cause of the blockage should be investigated. When systemic diseases, such as diabetes and anemia, are brought under control dry mouth problems may decrease.

The use of caffeine-containing beverages, alcoholic beverages, and mouthwashes containing alcohol should be minimized. The drinking of water and fruit juices will decrease dry mouth problems. Chewing gum and lemon drops can be used to stimulate saliva flow. Bitters also can initiate salivary flow as long as the salivary glands and ducts are functional. Commercial saliva substitutes are available without prescription and can be used as frequently as needed. Use of a humidifier in the bedroom reduces nighttime oral dryness.

Prognosis

The prognosis for patients with xerostomia due to medication problems is good, if the offending agent can

KEY TERMS

Salivary duct—Tube through which saliva is carried from the salivary gland to the mouth.

Salivary gland—Gland in which saliva forms.

be changed. Dry mouth due to systemic problems may be eliminated or improved once the disease causing the dry mouth is under control. Persistent xerostomia can be managed well with saliva substitutes.

Prevention

A patient needs to ask his or her health care provider if any medication to be prescribed will cause dry mouth. Patients with persistent xerostomia need to practice good **oral hygiene** and visit a dentist on a regular basis; the lack of adequate saliva can cause severe dental decay. The salivary glands are very sensitive to radiation, so any patient scheduled for **radiation therapy** of the head and neck needs to discuss with the radiation therapist ways to minimize exposure of the salivary glands to radiation.

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American Dental Association. 211 E. Chicago Ave., Chicago, IL 60611. (312) 440-2500. <http://www.ada.org>.

American Medical Association. 515 N. State St., Chicago, IL 60612. (312) 464-5000. <http://www.ama-assn.org>.

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Dry skin *see* **Ichthyosis**

Dual energy x-ray absorptiometry (DXA) scan *see* **Bone density test**

DUB *see* **Dysfunctional uterine bleeding**

Duchenne muscular dystrophy *see* **Muscular dystrophy**

Duodenal atresia *see* **Duodenal obstruction**

Duodenal obstruction

Definition

Duodenal obstruction is a failure of food to pass out of the stomach either from a complete or partial obstruction.

Description

The duodenum is the first part of the intestine, into which the stomach, the gall bladder, and the pancreas empty their contents. The pylorus connects the duodenum with the stomach and contains the valve that regulates stomach emptying. Obstruction usually occurs right at this outlet, so that the gall bladder and pancreas are unable to drain their secretions without hindrance.

Causes and symptoms

Obstruction of the duodenum occurs in adults and infants, each for a different set of reasons. In adults, the usual cause is a peptic ulcer of such antiquity that repeated cycles of injury and scarring have narrowed the passageway. Medical treatment of ulcers has progressed to the point where such obstinate ulcer disease is rarely seen any more. In infants, the conditions are congenital—either the channel is underdeveloped or the pylorus is overdeveloped. The first type is called duodenal hypoplasia and the second is termed hypertrophic **pyloric stenosis**. In rare cases, the channel may be missing altogether, a condition called duodenal atresia. To say that these anomalies are congenital is not to say their cause is understood. As with most **birth defects**, the specific cause is not known.

Food that cannot exit the stomach in the forward direction will return whence it came. Vomiting is the constant symptom of duodenal obstruction. It may be preceded by **indigestion** and nausea as the stomach attempts to squeeze its contents through an ever narrowing outlet.

Hypertrophic pyloric stenosis appears soon after birth. The infant will vomit feedings, lose weight, and be restless and irritable.

Diagnosis

X rays taken with contrast material in the stomach readily demonstrate the site of the blockage and often the ulcer that caused it. Gastroscopy is another way to evaluate the problem. In infants, x rays may not be necessary to detect pyloric stenosis. It is often possible to feel the enlarged pylorus, like an olive, deep under the ribs and see the stomach rippling as it labors to force food through.

Treatment

Bowel obstruction requires a surgeon, sometimes immediately. Newer surgical techniques constantly improve the outcome, but obstruction is a mechanical problem that needs a mechanical solution. Most adults who come to surgery for obstruction have suffered for years from peptic ulcer disease. They will usually benefit from **ulcer surgery** at the same time their obstruction is relieved. The surgeon will therefore select a procedure that combines relief of obstruction with remedy for ulcer disease. There are many choices. In fact, even without obstruction, functional considerations require ulcer surgery to include enhancement of stomach emptying.

To treat an infant with hypertrophic pyloric stenosis, some surgeons have had success with forceful balloon dilation of the pylorus done through a gastroscope, but the standard procedure is to cut across the overdeveloped circular muscle that is constricting the stomach outlet. There are reports of infant hypertrophic pyloric stenosis remitting without surgery following a very careful feeding schedule, but mortality is unacceptably high.

Prognosis

A functioning and unrestricted intestine is a prerequisite for living independent of the most advanced and continuous medical care available. Achieving this desirable goal is the rule with surgery for duodenal obstructions of all types. The bowel is so malleable that there is a rearrangement to suit every occasion. The variety of possible configurations is limited only by the surgeon's imagination.

Prevention

Prompt and effective treatment of peptic ulcers will prevent chronic scarring and narrowing. Drugs developed over the past few decades have all but eliminated the need for ulcer surgery.

Resources

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KEY TERMS

Atresia—Failure to develop; complete absence.

Contrast agent—A substance that produces shadows on an x ray so that hollow structures can be more easily seen.

Gastroscopy—Looking into the stomach with a flexible viewing instrument called a gastroscope.

Hypoplasia—Incomplete development.

Peptic ulcer—A wound in the lower stomach and duodenum caused by stomach acid and a newly discovered germ called *Helicobacter pylori*.

Duodenal stenosis *see* **Duodenal obstruction**

Duodenal ulcers *see* **Ulcers (digestive)**

Duodenum x rays *see* **Hypotonic duodenography**

Duplicated ureter *see* **Congenital ureter anomalies**

Dwarfism *see* **Achondroplasia; Pituitary dwarfism**

Dysfunctional uterine bleeding

Definition

Dysfunctional uterine bleeding is irregular, abnormal uterine bleeding that is not caused by a tumor, infection, or **pregnancy**.

Description

Dysfunctional uterine bleeding (DUB) is a disorder that occurs most frequently in women at the beginning and end of their reproductive lives. About half the cases occur in women over 45 years of age, and about one fifth occur in women under age 20.

Dysfunctional uterine bleeding is diagnosed when other causes of uterine bleeding have been eliminated. Failure of the ovary to release an egg during the menstrual cycle occurs in about 70% of women with DUB. This is probably related to a hormonal imbalance.

DUB is common in women who have **polycystic ovary syndrome** (cysts on the ovaries). Women who are on dialysis may also have heavy or prolonged periods. So do some women who use an intrauterine device (**IUD**) for birth control.

DUB is similar to several other types of uterine bleeding disorders and sometimes overlaps these conditions.

Menorrhagia

Menorrhagia, sometimes called hypermenorrhea, is another term for abnormally long, heavy periods. This type of period can be a symptom of DUB, or many other diseases or disorders. In menorrhagia, menstrual periods occur regularly, but last more than seven days, and blood loss exceeds 3 oz (88.7 ml). Passing blood clots is common. Between 15–20% of healthy women experience debilitating menorrhagia that interferes with their normal activities. Menorrhagia may or may not signify a serious underlying problem.

Metrorrhagia

Metrorrhagia is bleeding between menstrual periods. Bleeding is heavy and irregular as opposed to ovulatory spotting which is light bleeding, in mid-cycle, at the time of ovulation.

Polymenorrhea

Polymenorrhea describes the condition of having too frequent periods. Periods occur more often than every 21 days, and ovulation usually does not occur during the cycle.

Causes and symptoms

Dysfunctional uterine bleeding often occurs when the endometrium, or lining of the uterus, is stimulated to grow by the hormone estrogen. When exposure to estrogen is extended, or not balanced by the presence of progesterone, the endometrium continues to grow until it outgrows its blood supply. Then it sloughs off, causing irregular bleeding. If the bleeding is heavy enough and frequent enough, anemia can result.

Menorrhagia is representative of DUB. It is caused by many conditions including some outside the reproductive system. Causes of menorrhagia include:

- adenomyosis (a benign condition characterized by growths in the area of the uterus)
- imbalance between the hormones estrogen and progesterone
- fibroid tumors
- pelvic infection
- **endometrial cancer** (**cancer** of the inner mucous membrane of the uterus)
- endometrial polyps
- **endometriosis** (a condition in which endometrial or endrometrial-like tissue appears outside of its normal place in the uterus)
- use of an intrauterine device (IUD) for **contraception**
- hypothyroidism
- blood clotting problems (rare)
- lupus erythematosus
- pelvic inflammatory disease
- steroid therapy
- advanced liver disease
- renal (kidney) disease
- chemotherapy (cancer treatment with chemicals)

To diagnose dysfunctional uterine bleeding, many of the potential causes mentioned above must be eliminated. When all potential causes connected with pregnancy, infection, and tumors (benign or malignant) are eliminated, then menorrhagia is presumed to be caused by dysfunctional uterine bleeding.

Diagnosis

Diagnosis of any menstrual irregularity begins with the patient herself. The doctor will ask for a detailed description of the problem, and take a history of how long it has existed, and any patterns the patient has observed. A woman can assist the doctor in diagnosing the cause of abnormal uterine bleeding by keeping a record of the time, frequency, length, and quantity of bleeding. She should also tell the doctor about any illnesses, including long-standing conditions, like **diabetes mellitus**. The doctor will also inquire about sexual activity, use of contraceptives, current medications, and past surgical procedures.

Laboratory tests

After taking the woman's history, the gynecologist or family practitioner does a pelvic examination and Pap smear. To rule out specific causes of abnormal bleeding, the doctor may also do a pregnancy test and blood tests to check the level of thyroid hormone. Based on the initial test results, the doctor may want to do tests to determine the level of other hormones that play a role in reproduction. A test of blood clotting time and an adrenal function test are also commonly done.

Imaging

Imaging tests are important diagnostic tools for evaluating abnormal uterine bleeding. Ultrasound examination of the pelvic and abdominal area is used to help locate **uterine fibroids**, also called uterine leiomyoma, a type of tumor. Visual examination through hysterscopy—where a camera inside a thin tube is inserted directly into the uterus so that the doctor can see the uterine lining—is also used to assess the condition of the uterus.

Hystersalpingography can help outline endometrial polyps and fibroids and help detect endometrial cancer. In this procedure an x ray is taken after contrast media has been injected into the cervix. **Magnetic resonance imaging** (MRI) of the pelvic region can also be used to locate fibroids and tumors.

Invasive procedures

Endometrial biopsy (the removal and examination of endometrial tissue) is the most important testing procedure. It allows the doctor to sample small areas of the uterine lining, while cervical biopsy allows the cervix to be sampled. Tissues are then examined for any abnormalities.

Dilation and curettage (D & C), once common is rarely done today for diagnosis of DUB. It is done while the patient is under either general or regional anesthesia. Women over 30 are more likely to need a D & C, as part of the diagnostic procedure, than younger women.

Because DUB is diagnosed by eliminating other possible disorders, diagnosis can take a long time and involve many tests and procedures. Older women are likely to need more extensive tests than adolescents because the likelihood of reproductive cancers is greater in this age group, and therefore must be definitively eliminated before treating bleeding symptoms.

Treatment

Treatment of DUB depends on the cause of the bleeding and the age of the patient. When the underlying cause of the disorder is known, that disorder is treated. Otherwise the goal of treatment is to relieve the symptoms to a degree that uterine bleeding does not interfere with a woman's normal activities or cause anemia.

Generally the first approach to controlling DUB is to use **oral contraceptives** that provide a balance between the hormones estrogen and progesterone. Oral contraceptives are often very effective in adolescents and young women in their twenties. NSAIDs (**nonsteroidal anti-inflammatory drugs**), like Naprosyn and Motrin, are also used to treat DUB.

KEY TERMS

Dilation and curettage (D & C)—A procedure performed under anesthesia during which the cervix is dilated, and tissue lining the uterus is scraped out with a metal spoon-shaped instrument or a suction tube. The procedure can be either diagnostic, or to remove polyps.

Endometrial biopsy—The removal of tissue either by suction or scraping of samples of tissue from the uterus. The cervix is not dilated. The procedure has a lower rate of diagnostic accuracy than a D & C, but can be done as an office procedure under local anesthesia.

Endometrial cancer—Cancer of the inner mucous membrane of the uterus.

Fibroids, or fibroid tumors—Fibroid tumors are non-cancerous (benign) growths in the uterus. They occur in 30–40% of women over age 40, and do not need to be removed unless they are causing symptoms that interfere with a woman's normal activities.

Hypothyroidism—A disorder in which the thyroid gland produces too little thyroid hormone causing a decrease in the rate of metabolism with associated effects on the reproductive system.

Lupus erythematosus—A chronic inflammatory disease in which inappropriate immune system reactions cause abnormalities in the blood vessels and connective tissue.

Progesterone—A hormone naturally secreted by the ovary, or manufactured synthetically, that prepares the uterus for implantation of a fertilized egg.

Prostaglandins—A group of chemicals that mediate, or determine the actions of other chemicals in the cell or body.

When bleeding cannot be controlled by hormone treatment, surgery may be necessary. Dilation and curettage sometimes relieves the symptoms of DUB. If that fails, endometrial ablation removes the uterine lining, but preserves a woman's uterus. This procedure is sometimes be used instead of **hysterectomy**. However, as it affects the uterus, it can only be used when a woman has completed her childbearing years. The prescription of iron is also important to decrease the risk of enemia.

Until the 1980s, hysterectomy often was used to treat heavy uterine bleeding. Today hysterectomy is used less frequently to treat DUB, and then only after other methods of controlling the symptoms have failed. A hysterectomy leaves a woman unable to bear children, and, therefore, is limited largely to women who are unable to, or uninterested in, bearing children. Still, hysterectomy is a common treatment for long-standing DUB in women done with childbearing.

Alternative treatment

Alternative practitioners concentrate on good **nutrition** as a way to prevent heavy periods that are not caused by uterine fibroids, endometrial polyps, endometriosis, or cancer. Iron supplementation (100 mg per day) not only helps prevent anemia, but also appears to reduce menorrhagia in many women. Other recommended dietary supplements include **vitamins** A and C. Vitamin C improves capillary fragility and enhances iron uptake.

Vitamin E and bioflavonoid supplements are also recommended. Vitamin E can help reduce blood flow, and bioflavonoids help strengthen the capillaries. Vitamin K is known to play a role in clotting and is helpful in situations where heavy bleeding may be due to clotting abnormalities

Botanical medicines used to assist in treating abnormal bleeding include spotted cranesbill (*Geranium maculatum*), birthroot (*Trillium pendulum*), blue cohosh (*Caulophyllum thalictroides*), witch hazel (*Hamamelis virginiana*), shepherd's purse (*Capsella bursa-pastoris*), and yarrow (*Achillea millifolia*). These are all stiptic herbs that act to tighten blood vessels and tissue. Hormonal balance can also be addressed with herbal formulations containing phytoestrogens and phytoprogesterone.

Prognosis

Response to treatment for DUB is highly individual and is not easy to predict. The outcome depends largely on the woman's medical condition and her age. Many women, especially adolescents, are successfully treated with hormones (usually oral contraceptives). As a last resort, hysterectomy removes the source of the problem by removing the uterus, but this operation is not without risk, or the possibility of complications.

Prevention

Dysfunctional uterine bleeding is not a preventable disorder.

Resources

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Tish Davidson

Dyslexia

Definition

Dyslexia is a learning disability characterized by problems in reading, spelling, writing, speaking, or listening. In many cases, dyslexia appears to be inherited.

Description

The word dyslexia is derived from the Greek word, *dys* (meaning poor or inadequate) and the word *lexis* (meaning words or language).

The National Institutes of Health estimates that about 15% of the United States population is affected by learning disabilities, mostly with problems in language and reading. The condition appears in all ages, races, and income levels. Dyslexia is not a disease, but describes rather a different kind of mind that learns in a different way from other people. Many people with the condition are gifted and very productive; dyslexia is not at all linked to low intelligence. In fact, intelligence has nothing to do with dyslexia.

Dyslexic children seem to have trouble learning early reading skills, problems hearing individual sounds in words, analyzing whole words in parts, and blending sounds into words. Letters such as "d" and "b" may be confused.

A student with dyslexia has difficulty copying words. *(Photograph by Will & Deni McIntyre, Photo Researchers, Inc. Reproduced by permission.)*

When a person is dyslexic, there is often an unexpected difference between achievement and aptitude. However, each person with dyslexia has different strengths and weaknesses, although many have unusual talents in art, athletics, architecture, graphics, drama, music, or engineering. These special talents are often in areas that require the ability to integrate sight, spatial skills, and coordination.

Often, a person with dyslexia has a problem translating language into thought (such as in listening or reading), or translating thought into language (such as in writing or speaking).

Common characteristics include problems with:

- identifying single words
- understanding sounds in words, sound order, or rhymes
- spelling
- transposing letters in words
- handwriting
- reading comprehension
- delayed spoken language
- confusion with directions, or right/left handedness
- confusion with opposites (up/down, early/late, and so on)
- mathematics

Causes and symptoms

The underlying cause of dyslexia is not known, although research suggests the condition is often inherited. In 1999, The Centre for Reading Research in Norway presented the first research to study the largest family with reading problems ever known. By studying the reading and writing abilities of close to 80 family members across four generations the researchers reported, for the first time, that chromosome 2 can be involved in the inheritability of dyslexia. When a fault occurs on this gene it leads to difficulties in processing written language. Previous studies have pointed out linkages of other potential dyslexia genes to chromosome 1, chromosome 15 (DYX1 gene), and to chromosome 6 (DYX2 gene). The researchers who pinpointed the newly localized gene on chromosome 2 (DYX3) hope that this finding will lead to earlier and more precise diagnoses of dyslexia.

New research suggests a possible link with a subtle visual problem that affects the speed with which affected

KEY TERMS

Spatial skills—The ability to locate objects in three dimensional world using sight or touch.

people can read. Other experts believe that dyslexia is related to differences in the structure and function of the brain that manifests differently in different people.

Diagnosis

Anyone who is suspected to have dyslexia should have a comprehensive evaluation, including hearing, vision, and intelligence testing. The test should include all areas of learning and learning processes, not just reading.

As further research pinpoints the genes responsible for some cases of dyslexia, there is a possibility that earlier testing will be established to allow for timely interventions to prevent the onset of the condition and to treat it when it does occur.

Unfortunately, in many schools, a child is not identified as having dyslexia until after repeated failures.

Treatment

If a child is diagnosed with dyslexia, the parents should find out from the school or the diagnostician exactly what the problem is, and what method of teaching is recommended and why. No single method will work with every child, and experts often disagree as to the best method to use.

The primary focus of treatment is aimed at helping the specific learning problem of each affected person. Most often, this may include modifying teaching methods and the educational environment, since traditional educational methods will not always work with a dyslexic child.

People with dyslexia need a structured language program, with direct instruction in the letter-sound system. Teachers must give the rules governing written language. Most experts agree that the teacher should emphasize the association between simple phonetic units with letters or letter groups, rather than an approach that stresses memorizing whole words.

It is important to teach these students using all the senses: hearing, touching, writing, and speaking, provided by an instructor who is specifically trained in a program that is effective for dyslexic students.

Prognosis

Many successful and even famous people have dyslexia. How well a person with dyslexia functions in life depends on the way the disability affects that person. There is a great deal of variation among different people with dyslexia, producing different symptoms and different degrees of severity.

Prognosis is usually good if the condition is diagnosed early, and if the person has a strong self image with supportive family, friends, and teachers. It is imperative for a good outcome that the person be involved in a good remedial program.

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ORGANIZATION

International Dyslexia Association (formerly the Orton Dyslexia Society). 8600 LaSalle Rd., Chester Bldg., Ste. 382, Baltimore, MD 21286. (800) ABC-D123.

Learning Disabilities Association. 4156 Library Rd., Pittsburgh, PA 15234. (412) 341-1515.

Beth Kapes

Dyslipidemia *see* **Hyperlipoproteinemia**

Dysmenorrhea

Definition

Dysmenorrhea is the occurrance of painful cramps during menstruation.

Description

More than half of all girls and women suffer from dysmenorrhea (cramps), a dull or throbbing **pain** that

usually centers in the lower mid-abdomen, radiating toward the lower back or thighs. Menstruating women of any age can experience cramps.

While the pain may be only mild for some women, others experience severe discomfort that can significantly interfere with everyday activities for several days each month.

Causes and symptoms

Dysmenorrhea is called "primary" when there is no specific abnormality, and "secondary" when the pain is caused by an underlying gynecological problem. It is believed that primary dysmenorrhea occurs when hormone-like substances called "prostaglandins" produced by uterine tissue trigger strong muscle contractions in the uterus during menstruation. However, the level of prostaglandins doesn't seem to have anything to do with how strong a woman's cramps are. Some women have high levels of prostaglandins and no cramps, whereas other women with low levels have severe cramps. This is why experts assume that cramps must also be related to other things (such as genetics, **stress**, and different body types) in addition to prostaglandins. The first year or two of a girl's periods are not usually very painful. However, once ovulation begins, the blood levels of the prostaglandins rise, leading to stronger contractions.

Secondary dysmenorrhea may be caused by **endometriosis**, fibroid tumors, or an infection in the pelvis.

The likelihood that a woman will have cramps increases if she:

- has a family history of painful periods
- leads a stressful life
- doesn't get enough **exercise**
- uses **caffeine**
- has pelvic inflammatory disease

Symptoms include a dull, throbbing cramping in the lower abdomen that may radiate to the lower back and thighs. In addition, some women may experience **nausea and vomiting**, **diarrhea**, irritability, sweating, or **dizziness**. Cramps usually last for two or three days at the beginning of each menstrual period. Many women often notice their painful periods disappear after they have their first child, probably due to the stretching of the opening of the uterus or because the birth improves the uterine blood supply and muscle activity.

Diagnosis

A doctor should perform a thorough **pelvic exam** and take a patient history to rule out an underlying condition that could cause cramps.

KEY TERMS

Endometriosis—The growth of uterine tissue outside the uterus.

Hormone—A chemical messenger secreted by a gland and released into the blood, which allows it to travel to distant cells where it exerts an effect.

Ovary—One of the two almond-shaped glands in the female body that produces the hormones estrogen and progesterone.

Ovulation—The monthly release of an egg from an ovary.

Progesterone—The hormone produced by the ovary after ovulation that prepares the uterine lining for a fertilized egg.

Uterus—The female reproductive organ that contains and nourishes a fetus from implantation until birth.

Treatment

Secondary dysmenorrhea is controlled by treating the underlying disorder.

Several drugs can lessen or completely eliminate the pain of primary dysmenorrhea. The most popular choice are the **nonsteroidal anti-inflammatory drugs** (NSAIDs), which prevent or decrease the formation of prostaglandins. These include **aspirin**, ibuprofen (Advil), and naproxen (Aleve). For more severe pain, prescription strength ibuprofen (Motrin) is available. These drugs are usually begun at the first sign of the period and taken for a day or two. There are many different types of NSAIDs, and women may find that one works better for them than the others.

If an NSAID is not available, **acetaminophen** (Tylenol) may also help ease the pain. Heat applied to the painful area may bring relief, and a warm bath twice a day also may help. While birth control pills will ease the pain of dysmenorrhea because they lead to lower hormone levels, they are not usually prescribed just for **pain management** unless the woman also wants to use them as a birth control method. This is because these pills may carry other more significant side effects and risks.

New studies of a drug patch containing glyceryl trinitrate to treat dysmenorrhea suggest that it also may help ease pain. This drug has been used in the past to ease preterm contractions in pregnant women.

Alternative treatment

Simply changing the position of the body can help ease cramps. The simplest technique is assuming the fetal position, with knees pulled up to the chest while hugging a heating pad or pillow to the abdomen. Likewise, several **yoga** positions are popular ways to ease menstrual pain. In the "cat stretch," position, the woman rests on her hands and knees, slowly arching the back. The pelvic tilt is another popular yoga position, in which the woman lies with knees bent, and then lifts the pelvis and buttocks.

Dietary recommendations to ease cramps include increasing fiber, calcium, and complex carbohydrates, cutting fat, red meat, dairy products, caffeine, salt, and sugar. **Smoking** also has been found to worsen cramps. Recent research suggests that vitamin B supplements, primarily vitamin B_6 in a complex, magnesium, and fish oil supplements (omega-3 fatty acids) also may help relieve cramps.

Other women find relief through visualization, concentrating on the pain as a particular color and gaining control of the sensations. **Aromatherapy** and massage may ease pain for some women. Others find that imagining a white light hovering over the painful area can actually lessen the pain for brief periods.

Exercise may be a way to reduce the pain of menstrual cramps through the brain's production of endorphins, the body's own painkillers. And orgasm can make a woman feel more comfortable by releasing tension in the pelvic muscles.

Acupuncture and Chinese herbs are another popular alternative treatments for cramps.

Prognosis

Medication should lessen or eliminate pain.

Prevention

NSAIDs taken a day before the period begins should eliminate cramps for some women.

Resources

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ORGANIZATIONS

American College of Obstetricians and Gynecologists. 409 12th Street, S.W., PO Box 96920

Federation of Feminist Women's Health Centers.1469 Humboldt Rd, Suite 200, Chico, CA 96928. (530) 891-1911.

National Women's Health Network. 514 10th St. NW, Suite 400, Washington, DC 20004. (202) 628-7814. <http://www.womenshealthnetwork.org>.

Carol A. Turkington

Dysmetria *see* **Movement disorders**

Dyspepsia

Definition

Dyspepsia can be defined as painful, difficult, or disturbed digestion, which may be accompanied by symptoms such as **nausea and vomiting**, **heartburn**, bloating, and stomach discomfort.

Causes and symptoms

The digestive problems may have an identifiable cause, such as bacterial or viral infection, peptic ulcer, gallbladder, or liver disease. The bacteria *Helicobacter pylori* is often found in those individuals suffering from duodenal or gastric ulcers. Investigation of recurrent **indigestion** should rule out these possible causes.

Often, there is no organic cause for the problem, in which case dyspepsia is classified as functional or nonulcer dyspepsia. There is evidence that functional dyspepsia may be related to abnormal motility of the upper gastrointestinal tract (a state known as dysmotility in which the esophagus, stomach, and upper intestine behave abnormally). These patients may respond to a group of drugs called prokinate agents. A review of eating habits (e.g. chewing with the mouth open, gulping food, or talking while chewing) may reveal a tendency to swallow air. This may contribute to feeling bloated, or to excessive belching. **Smoking**, **caffeine**, alcohol, or carbonated beverages may contribute to the discomfort. When there is sensitivity or allergy to certain food substances, eating those foods may cause gastrointestinal distress. Some medications are associated with indigestion. Stomach problems may also be a response to **stress** or emotional unrest.

A false-color gamma scan of a human stomach with dyspepsia, or indigestion, during tests to study its rate of emptying. *(Photograph by Jean-Perrin, Custom Medical Stock Photo. Reproduced by permission.)*

KEY TERMS

Anemia—Diagnosed through laboratory study of the blood, a deficiency in hemoglobin or red blood cells, often associated with paleness or loss of energy.

Endoscopy—A diagnostic procedure using a lighted instrument to examine a body cavity or internal organ. Endoscopy permits collection of tissue and culture specimens.

Diagnosis

A **physical examination** by a health care professional may reveal mid-abdominal **pain**. A **rectal examination** may be done to rule out bleeding. If blood is found on rectal exam, laboratory studies, including a **blood count** may be ordered. Endoscopy and barium studies may be used to rule out underlying gastrointestinal disease. Upper gastrointestinal x-ray studies using barium may allow for visualization of abnormalities. Endoscopy permits collection of tissue and culture specimens which may be used to further confirm a diagnosis.

Treatment

The treatment of dyspepsia is based on assessment of symptoms and suspected causative factors. Clinical evaluation is aimed at distinguishing those patients who require immediate diagnostic work-ups from those who can safely benefit from more conservative initial treatment. Some of the latter may require only reassurance, dietary modifications, or antacid use. Medications to block production of stomach acids, prokinate agents, or antibiotic treatment may be considered. Further diagnostic investigation is indicated if there is severe abdominal pain, pain radiating to the back, unexplained weight loss, difficulty swallowing, a palpable mass, or anemia. Additional work-up is also indicated if a patient does not respond to prescribed medications.

Prognosis

Statistics show an average of 20% of patients with dyspepsia have duodenalor gastric ulcer disease, 20% have **irritable bowel syndrome**, fewer than 1% of patients had **cancer**, and the range for functional, or non-ulcer dyspepsia (**gastritis** or superficial erosions), was from 5–40%.

Resources

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Dysphasia *see* **Aphasia**

Dyspnea *see* **Shortness of breath**

Dysthymic disorder *see* **Depressive disorders**

Dystonia *see* **Movement disorders**

E

E. coli see ***Escherichia coli***

E. coli infection *see* **Enterobacterial infections**

E. coli O157:H7 infection ***see Escherichia coli***

Ear canal infection *see* **Otitis externa**

Ear exam with an otoscope

Definition

An otoscope is a hand-held instrument with a tiny light and a cone-shaped attachment called an ear speculum, which is used to examine the ear canal. An ear examination is a normal part of most physical examinations by a doctor or nurse. It is also done when an ear infection or other type of ear problem is suspected.

Purpose

An otoscope is used to look into the ear canal to see the ear drum. Redness or fluid in the eardrum can indicate an ear infection. Some otoscopes can deliver a small puff of air to the eardrum to see if the eardrum will vibrate (which is normal). This type of ear examination with an otoscope can also detect a build up of wax in the ear canal, or a rupture or puncture of the eardrum.

Precautions

No special precautions are required. However, if an ear infection is present, an ear examination may cause some discomfort or **pain**.

Description

An ear examination with an otoscope is usually done by a doctor or a nurse as part of a complete **physical examination**. The ears may also be examined if an ear infection is suspected due to **fever**, ear pain, or **hearing loss**. The patient will often be asked to tip the head slightly toward the shoulder so the ear to be examined is pointing up. The doctor or nurse may hold the ear lobe as the speculum is inserted into the ear, and may adjust the position of the otoscope to get a better view of the ear canal and eardrum. Both ears are usually examined, even if there seems to be a problem with just one ear.

Preparation

No special preparation is required prior to an ear examination with an otoscope. The ear speculum, which is inserted into the ear, is cleaned and sanitized before it is used. The speculums come in various sizes, and the doctor or nurse will select the size that will be most comfortable for the patient's ear.

Aftercare

If an ear infection is diagnosed, the patient may require treatment with **antibiotics**. If there is a buildup of wax in the ear canal, it might be rinsed or scraped out.

Risks

This type of ear examination is simple and generally harmless. Caution should always be used any time an object is inserted into the ear. This process could irritate an infected external ear canal and could rupture an eardrum if performed improperly or if the patient moves.

Normal results

The ear canal is normally skin-colored and is covered with tiny hairs. It is normal for the ear canal to have some yellowish-brown earwax. The eardrum is typically thin, shiny, and pearly-white to light gray in color. The tiny bones in the middle ear can be seen pushing on the

KEY TERMS

Ear speculum—A cone- or funnel-shaped attachment for an otoscope which is inserted into the ear canal to examine the eardrum.

Otoscope—A hand-held instrument with a tiny light and a funnel-shaped attachment called an ear speculum, which is used to examine the ear canal and eardrum.

eardrum membrane like tent poles. The light from the otoscope will reflect off of the surface of the ear drum.

Abnormal results

An ear infection will cause the eardrum to look red and swollen. In cases where the eardrum has ruptured, there may be fluid draining from the middle ear. A doctor may also see scarring, retraction of the eardrum, or bulging of the eardrum.

Resources

ORGANIZATIONS

American Academy of Otolaryngology-Head and Neck Surgery, Inc. One Prince St., Alexandria VA 22314-3357. (703) 836-4444. <http://www.entnet.org>.

Ear Foundation. 1817 Patterson St., Nashville, TN 37203. (800) 545-4327. <http://www.earfoundation.org>.

Hearing Health Information. 2100 W. 3rd St., Los Angeles, CA 90057. (213) 483-4431.

National Institute on Deafness and Other Communication Disorders. National Institutes of Health, 31 Center Drive, MSC 2320, Bethesda, MD USA 20892-2320. (800) 241-1044. <http://www.nidcd.nih.gov>.

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Altha Roberts Edgren

Ear surgery

Definition

Ear surgery is the treatment of diseases, injuries, or deformations of the ear by operation with instruments.

Purpose

Ear surgery is performed to correct certain types of **hearing loss**, and to treat diseases of, injuries to, or deformities of the ear's auditory tube, middle ear, inner ear, and auditory and vestibular systems. Ear surgery is commonly performed to treat conductive hearing loss, persistent ear infections, unhealed perforated eardrums, congenital ear defects, and tumors.

Ear surgery is performed on children and adults. In some cases, surgery is the only treatment; in others, it is used only when more conservative medical treatment fails.

Precautions

The precautions vary, depending on the type ofear surgery under consideration. For example, **stapedectomy** (removal of parts of the middle ear and insertion of prosthesis parts) should not be performed on people with external or middle ear infection or inner ear disease. For people with complete hearing loss in the other ear, it should be performed cautiously. Microsurgery for the removal of a cholesteatoma (a cyst-like mass of cells in the middle ear) should not be performed on patients who are extremely ill or have other medical conditions. Tympanoplasty (any surgical procedure on the eardrum or middle ear) should not be performed on patients with chronic sinus or nasal problems or in some patients with medical problems such as poorly controlled diabetes and heart disease. Surgery for congenital microtia and atresia (abscense of normal bodily openings, such as the outer ear canal) should not be performed if the middle ear space is totally or almost totally absent.

Description

Most ear surgery is microsurgery, performed with an operating microscope to enable the surgeon to view the very small structures of the ear. The use of minimally invasive **laser surgery** for middle ear procedures is growing. Laser surgery reduces the amount of trauma due to vibration, enhances coagulation, and enables surgeons to access hard to reach places in the middle ear. Laser surgery can be performed in an office operating suite. Types of ear surgery include stapedectomy, tympanoplasty, myringotomy and ear tube surgery, ear surgery to repair a **perforated eardrum**, **cochlear implants**, and **tumor removal**.

Stapedectomy

To restore hearing loss, which is usually due to **otosclerosis**, stapedectomy is performed. Stapedectomy is the removal of all or part of the stapes, one of the bones in the middle ear, and replacement with a tiny prosthesis. An incision is made in the middle ear, the small bones are identified, and the stapes is removed. The stainless steel wire and cellulose sponge prosthesis is inserted, blood

and fluid are drained, and the wound is closed. Performed in a hospital or outpatient surgical facility under local or general anesthetic, full recovery takes about three weeks but hearing should improve immediately.

Tympanoplasty

Tympanoplasty is performed to reconstruct the eardrum after partial or total conductive hearing loss, usually caused by chronic middle ear infections, or perforations that do not heal. This is usually a same day surgery, performed under either local or general anesthesia. After making an incision in the ear to view the perforation, the ear drum is elevated away from the ear canal and lifted forward. If the bones of hearing (ossicular chain) are functioning, tissue is taken from the ear and grafted to the eardrum to close the perforation. A thin sheet of silastic and Gelfoam hold the graft in place. The ear is stitched together, and a sterile patch is placed on the outside of the ear canal. Tympanoplasty is successful in over 90% of all cases. The need for ossicular reconstruction (reconstruction of tiny bones of the middle ear) is sometimes known before surgery and and even when identified during surgery, can usually be done while reconstructing the eardrum. If the gap between the anvil bone and the stapes is small, a small piece of bone or cartilage from the patient can be inserted; if is is large, the incus bone is removed, modelled into a prosthesis, and reinserted between the stapes and the malleus. Reconstruction could also be achieved by inserting a strut made from artificial bone. For tympanoplasty with ossicular reconstruction, the patient usually stays in the hospital overnight. The recovery period is about four weeks.

Myringotomy and ear tube surgery

Myringotomy and ear tube surgery is performed to drain ear fluid and prevent ear infections when **antibiotics** don't work or when ear infections are chronic. The process normalizes pressure in the middle ear and decreases fluid accumulation. It is most commonly performed on infants and children, in whom ear infections are most frequent, and may be done on one or both ears. The surgeon makes a small hole in the ear drum, then uses suction to remove fluid. A small ear tube of metal or plastic is inserted into the ear drum to allow continual drainage. The tube prevents infections as long as it stays in place, which varies from six months to three years. When the tube falls out, the hole grows over. As many of 25% of children under the age of two who need ear tubes may need them again. Myringotomy and ear tube surgery is performed in a hospital, using a general anesthetic for most children and a local anesthetic for older children or adults. No anesthetic may be used for infants. The procedure usually takes about two hours. Most patients can go home the same day; children under three years of age and those with chronic diseases usually stay overnight.

Microsurgery being performed in the inner ear. *(Photograph by Hans Halberstadt, Photo Researchers, Inc. Reproduced by permission.)*

Ear surgery for a perforated eardrum

Ear surgery for a perforated eardrum is only performed in rare cases where it does not heal on its own. In most cases, this is performed in a surgeon's office using a topical anesthetic. The surgeon scratches the undersurface of the eardrum, stimulating the skin to heal and the eardrum to close. A thin patch placed on the eardrum's outer surface allows the skin under the eardrum to heal.

Cochlear implants

Cochlear implants stimulate nerve ends within the inner ear, enabling deaf children to hear. The device has a microphone that remains outside the ear, a processor that selects and codes speech sounds, and a receiver/stimulator to convert the coded sounds to electric signals that stimulate the hearing nerve and are recognized by the brain as sound. During surgery, an incision is made behind and slightly above the ear. A circular hole is drilled in the bone to receive the device's internal coil. The mastoid bone leading to the middle ear is opened to receive the electrodes. The internal coil is inserted and secured, followed by the electrodes. The wound is stitched up and when it heals, an external unit comprised of a stimulator with a microphone is worn behind the ear. Performed in a hospital under general anesthesia, the operation takes about two hours and usually requires a hospital stay overnight. The patient can resume normal activities in two to three weeks.

Ear surgery for tumors

Some ear tumors can be very serious and should be removed surgically. For a tumor on the skin of the ear canal, the skin is removed surgically, the bone beneath it

KEY TERMS

Auditory—Relating to the sense of the organs of hearing.

Cholesteatoma—A cystic mass of cells in the middle ear, occurring as a congential defect or as a serious complication of a disease or traumtic condition of the ear.

Otologic—Relating to the study, diagnosis, and treatment of diseases of the ear and related structures.

is drilled away, and a skin graft is placed in the ear canal. If the tumor is near the eardrum, the skin of the ear canal and the eardrum are removed along with the bone surrounding the ear canal. A skin graft is placed on the bare bone. For basal cell cancers and low grade glandular malignancies, surgical resection of the ear canal is adequate. Squamous cell carcinoma, a serious form of **cancer**, of the external ear canal requires radical surgery, followed by **radiation therapy**. Cholesteatoma, a benign tumor caused by an infection in a perforated eardrum that did not heal properly and can destroy the bones of hearing, is removed with microsurgery. **Mastoidectomy** is performed for **mastoiditis**, an inflammation of the middle ear, if medical therapy does not work. Petrous apicectomy is performed to drain the petrous apicitis, the bone between the middle ear and the clivis.

Ear surgery for congenital ear defects

Congenital atresia, the absence of the external ear canal, and congenital microtia, abnormal growth of the external ear, often occur together, although atresia can occur without microtia. Surgery to reconstruct the ear usually takes place when the child is four or five years old and may require several operations. A facial plastic surgeon and an ear surgeon work together, repairing the microtia first and then the atresia. During surgery, a bony opening is created over the bones of hearing. The surfaces of the bony ear canal are then relined with a skin graft from the thigh or abdomen. Tissue from behind the eardrum is used to create a new eardrum. In many cases, the middle ear will also need to be reconstructed. Surgery is performed in a hospital under general anesthesia.

Other types of ear surgery

Surgery may also be appropriate to remove multiple bony overgrowths of the ear canal or in rare cases of compromised auditory tube function, to narrow the tube.

Preparation

The preparation depends upon the type of ear surgery performed. For many procedures, blood and urine studies and hearing tests are conducted.

Aftercare

The type of aftercare depends upon the type of surgery performed. In most cases, the ear(s) should be kept dry and warm. Non-prescription drugs such as **acetaminophen** can be used for **pain**.

Risks

The type of risk depends on the type of surgery performed. Total hearing loss is rare.

Resources

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ORGANIZATIONS

American Academy of Otolaryngology-Head and Neck Surgery, Inc. One Prince St., Alexandria VA 22314-3357. (703) 836-4444. <http://www.entnet.org>.

American Hearing Research Foundation. 55 E. Washington St., Suite 2022, Chicago, IL 60602. (312) 726-9670. <http://www.american-hearing.org/>.

American Speech-Language-Hearing Association. 10801 Rockville Pike, Rockville, MD 20852. (800) 638-8255. <http://www.asha.org>.

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Lori De Milto

Ear tubes *see* **Myringotomy and ear tubes**

Ear wax impaction *see* **Cerumen impaction**

Eardrum perforation *see* **Perforated eardrum**

Eastern equine encephalitis *see* **Arbovirus encephalitis**

Eating disorders *see* **Anorexia nervosa; Bulimia nervosa**

Eaton agent pneumonia *see* **Mycoplasma infections**

Ebola virus infection *see* **Hemorrhagic fevers**

Ecchymosis *see* **Bruises**

ECG *see* **Electrocardiography**

Echinacea

Definition

Echinacea, or purple coneflower, is a perennial herb of the Composite family, commonly known as the daisy family. Most often referred to as the purple coneflower, this hardy plant also known as Sampson root, Missouri snakeroot, and rudbeckia. The prominent, bristly seed head inspired the generic name of the plant, taken from the Greek word *echinos* meaning hedgehog.

Description

Echinacea is a North American prairie native, abundant in the Midwest, and cultivated widely in ornamental and medicinal gardens. The purple-pink rays of the blossom droop downward from a brassy hued center cone composed of many small, tubular florets. The conspicuous flowers bloom singly on stout, prickly stems from mid-summer to autumn. Flower heads may grow to 4 in (10.16 cm) across. The dark green leaves are opposite, entire, lanceolate, toothed, and hairy with three prominent veins. The narrow upper leaves are attached to the stem with stalks. The lower leaves are longer, emerging from the stem without a leaf stalk, and growing to 8 in (20.32 cm) in length. The plant develops deep, slender, black roots. Echinacea propagates easily from seed or by root cuttings. However, due to its increasing popularity as an herbal supplement, echinacea is numbered among the 19 medicinal plants considered at risk by the Vermont nonprofit organization, United Plant Savers.

Purpose

Three species of echinacea are useful medicinally: *Echinacea augustifolia, Echinacea purpurea*, and *Echinacea pallida*. The entire plant has numerous medicinal properties that act synergistically to good effect. Echinacea is most often used to boost the immune system and fight infection. Research has shown that echinacea increases production of interferon in the body. It is antiseptic and antimicrobial, with properties that act to increase the number of white blood cells available to destroy bacteria and slow the spread of infection. As a depurative, the herbal extract cleanses and purifies the bloodstream, and has been used effectively to treat **boils**. Echinacea is vulnerary, promoting wound healing through the action of a chemical substance in the root known as caffeic acid glycoside. As an alterative and an immunomodulator, echinacea acts gradually to promote beneficial change in the entire system. It has also been used to treat urinary infection and *Candida albicans* infections. Echinacea is a febrifuge, useful in reducing fevers. It is also useful in the treatment of **hemorrhoids**. A tincture, or a strong decoction of echinacea serves as an effective mouthwash for the treatment of pyorrhea and gingivitis.

Native American plains Indians relied on echinacea as an all-purpose antiseptic. The Sioux tribe valued the root as a remedy for snake bite, the Cheyenne tribe chewed the root to quench thirst, and another tribe washed their hands in a decoction of echinacea to increase their tolerance of heat. European settlers learned of the North American herb's many uses, and soon numerous echinacea-based remedies were commercially available from pharmaceutical companies in the United States. Echinacea was a popular remedy in the United States through the 1930s. It was among many medicinal herbs listed in the *U.S. Pharmacopoeia*, the official United States government listing of pharmaceutical raw materials and recipes. The herb fell out of popular use in the United States with the availability of **antibiotics**. In West Germany, over 200 preparations are made from the species *E. purpurea*. Commercially prepared salves, tinctures, teas, and extracts are marketed using standardized extracts. Echinacea is regaining its status in the United States as a household medicine-chest staple in many homes. It is one of the best-selling herbal supplements in United States health food stores.

Clinical studies have found that the entire plant possesses medicinal properties with varying levels of effectiveness. Echinacea is of particular benefit in the treatment of upper respiratory tract infections. Some research has shown that echinacea activates the macrophages that destroy **cancer** cells and pathogens. When taken after cancer treatments, an extract of the root has been found to increase the body's production of white blood cells. Echinacea has been shown to be most effective when taken at the first sign of illness, rather than when used as a daily preventative. Other research has demonstrated the signifi-

KEY TERMS

Alterative—A medicinal substance that acts gradually to nourish and improve the system.

Antimicrobial—A plant substance that acts to inhibit the growth of harmful microorganisms, or acts to destroy them.

Febrifuge—A plant substance that acts to prevent or reduce fever.

Glycoside—An herbal carbohydrate that exerts powerful effect on hormone-producing tissues. The glycoside breaks down into a sugar and a non-sugar component.

Lanceolate—Narrow, leaf shape that is longer than it is wide, and pointed at the end.

Macrophage—Specialized cells present throughout the lymphoid tissues of the body that circulate in the bloodstream. Macrophages have a surface marker that stimulates other cells to react to an antigen.

cant effect of *E. purpurea* root on reducing the duration and severity of colds and flu. Some herbal references list only the root as the medicinal part, others include the aerial parts of the plant, particularly the leaf. But research studies in Europe and the United States have concluded that the entire plant is medicinally effective. Most research has been done on the species *E. pallida* and *E. purpurea*. All three species of echinacea are rich in **vitamins** and **minerals**. Echinacea is an herbal source of niacin, chromium, iron, manganese, selenium, silicon, and zinc.

Preparations

The quality of any herbal supplement depends greatly on the conditions of weather and soil where the herb was grown, the timing and care in harvesting, and the manner of preparation and storage.

Decoction is the best method to extract the mineral salts and other healing components from the coarser herb materials, such as the root, bark, and stems. It is prepared by adding 1 oz (28.4 g) of the dried plant materials, or 2 oz (56.7 g) of fresh plant parts, to 1 pt (0.47 l) of pure, unchlorinated, boiled water in a non-metallic pot. Simmer for about one half hour. Strain and cover. A decoction may be refrigerated for up to two days and retain its healing qualities.

An infusion is the method used to derive benefits from the leaves, flowers, and stems in the form of an herbal tea. Use twice as much fresh, chopped herb as dried herb. Steep in 1 pt (0.47 l) of boiled, unchlorinated water for 10–15 minutes. Strain and cover. Drink warm, sweetened with honey if desired. A standard dose is three cups per day. An infusion will keep for up to two days in the refrigerator and retain its healing qualities.

A tincture is the usual method to prepare a concentrated form of the herbal remedy. Tinctures, properly prepared and stored, will retain medicinal potency for two years or more. Combine 4 oz (114 g) of finely cut fresh or powdered dry herb with 1 pt (0.47 l) of brandy, gin, or vodka in a glass container. The alcohol should be enough to cover the plant parts and have a 50/50 ratio of alcohol to water. Place the mixture away from light for about two weeks, shaking several times each day. Strain and store in a tightly capped, dark glass bottle. A standard dose is 0.14 oz (4 ml) of the tincture three times a day.

Precautions

Echinacea is considered safe in recommended doses. Pregnant or lactating women, however, are advised not to take echinacea in injection form. Because the plant has proven immuno-modulating properties, individuals with systemic lupus erythmatosus, **rheumatoid arthritis**, **tuberculosis**, leukemia, **multiple sclerosis**, or **AIDS** should consult their physician before using echinacea. Echinacea should not be given to children under two years of age, and it should only be given to children over two in consultation with a physician. Research indicates that echinacea is most effective when taken at first onset of symptoms of cold or flu, and when usage is continued no longer than eight weeks. There is some indication that the herb loses its effectiveness when used over a long period of time. It is necessary to interrupt use for a minimum of several weeks in order to give the body's immune system the opportunity to rest and adjust.

Side effects

No side effects are reported with oral administration of echinacea, either in tincture, capsule, or as a tea, when taken according to recommended doses. Chills, **fever**, and allergic reactions have been reported in some research studies using an injection of the plant extract.

Interactions

None reported. When used in combination with other herbs, dosage should be lowered.

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Clare Hanrahan

KEY TERMS

Allergenic—A substance capable of causing an allergic reaction.

Cholangitis—Infection or inflammation of the bile ducts; often causes abdominal pain, fever, and jaundice.

Computed tomography (CT) scan—A specialized x-ray procedure in which cross-sections of the area in question can be examined in detail.

Cyst—A protective sac that includes either fluid or the cell of an organism. The cyst enables many organisms to survive in the environment for long periods of time without need for food or water.

Embryo—The very beginning stages of development of an organism.

Jaundice—The yellow-greenish coloring of the skin and eyes due to the presence of bile pigments. The presence of jaundice is usually, but not always, a sign of liver disease.

Tapeworm—An intestinal parasite that attaches to the intestine or travels to other organs such as the liver and lungs.

Ultrasound—A noninvasive procedure based on changes in sound waves of a frequency that cannot be heard, but respond to changes in tissue composition.

Echinococcosis

Definition

Echinococcosis (Hydatid disease) refers to human infection by the immature (larval) form of tapeworm, *Echinococcus*. One of three forms of the *Echinococcus* spp., *E. granulosus*, lives on dogs and livestock, and infects humans through contact with these animals. Allergic reactions and damage to various organs from cyst formation are the most common forms of disease in humans.

Description

E. granulosus is found in many areas of Africa, China, South America, Australia, New Zealand, and Mediterranean and eastern Europe, as well as in parts of the western United States. The parasite lives in regions where dogs and livestock cohabitate. Direct exposure to infectious dogs as well as parasitic eggs released into the environment during shedding are both sources of human infection.

In humans, cysts containing the larvae develop after ingestion of eggs. Cysts form primarily in the lungs and liver. Cysts developing in the liver are responsible for about two-thirds of echinococcosis cases. Echinococcosis is a significant public health problem in many areas of the world, but control programs have decreased the rate of infection in some regions. In Kenya alone, the numbers of persons infected each year is as high as 220 per 100,000 population.

Causes and symptoms

After ingestion, the eggs develop into embryos within the intestines and then travel to the liver and lungs through major blood vessels. The embryos then begin to form cysts within the liver and lungs, causing damage as they enlarge over a period of five to 20 years. Cysts may become over 8 in (20.3 cm)or more in size and contain a huge amount of highly allergenic fluid. Studies show that while the liver is most often targeted, lungs, brain, heart, and bone can also be affected.

The major symptoms are due to compression damage, blockage of vessels and ducts (such as the bile ducts), and leakage of fluid from cysts. The following symptoms are frequent.

Infection with the larva of *Echinococcus granulosus* (shown above) is responsible for the disease echinococcosis. *(Illustration by Electronic Illustrators Group.)*

- Liver involvement causes **pain** and eventually **jaundice** or **cholangitis** due to blockage of bile ducts. Infection of cysts leads to abscesses in up to 20%.
- Lung cysts cause **cough** and chest pain.
- Bone cysts cause **fractures** and damage to bone tissue.
- Heart involvement leads to irregularities of heart beat and inflammation of the covering of the heart (pericardium).
- Allergic reactions occur from leakage of cyst fluid that contains antigens. **Itching**, **fever**, and **rashes** are frequent, and fatal allergic reactions (**anaphylaxis**) have been reported. Eosinophils, which are blood cells involved in allergic reactions, are increased in many patients.

Diagnosis

X rays, **computed tomography scans** (CT scans), and ultrasound are very helpful in detecting cysts. Some cysts will develop characteristic hardening of organ tissues from calcium deposits (calcifications). Blood tests to detect antibodies are useful when positive, but up to 50% of patients have negative results. Examination of aspirated cyst fluid for parasites can be diagnostic, but carries the danger of a fatal allergic reaction. Treatment with anti-parasitic medications before aspiration is reported to decrease allergic complications and decrease the risk of spread during the procedure.

Treatment

Treatment depends on the size and location of cysts, as well as the symptoms they are producing. Surgical removal of cysts and/or surrounding tissue is the accepted method of treatment, but carries a risk of cyst rupture with spread or allergic reactions. Recent studies using medication alongside aspiration and drainage of cysts instead of surgery are very encouraging.

The medication albenzadole can be taken before or after surgery or alone without surgery. However, its effectiveness as a single treatment is still not known. Multiple courses of medication are often necessary, with cure rates of only about 30%. Response to treatment is best monitored by serial CT scans or similar x-ray studies.

Prevention

Good hand washing, treating infected dogs, and preventing dogs access to slaughter houses discourage spread of the disease. Limiting the population of stray dogs has also been helpful.

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Echinococcus granulosus infection *see* **Echinococcosis**

Echocardiography

Definition

Echocardiography is a diagnostic test that uses ultrasound waves to create an image of the heart muscle. Ultrasound waves that rebound or echo off the heart can show the size, shape, and movement of the heart's valves and chambers as well as the flow of blood through the heart. Echocardiography may show such abnormalities as poorly functioning heart valves or damage to the heart tissue from a past **heart attack**.

Purpose

Echocardiography is used to diagnose certain cardiovascular diseases. In fact, it is one of the most widely used diagnostic tests for heart disease. It can provide a wealth of helpful information, including the size and shape of the heart, its pumping strength, and the location and extent of any damage to its tissues. It is especially useful for assessing diseases of the heart valves. It not only allows doctors to evaluate the heart valves, but it can detect abnormalities in the pattern of blood flow, such as the backward flow of blood through partly closed heart valves, known as regurgitation. By assessing the motion of the heart wall, echocardiography can help detect the presence and assess the severity of **coronary artery disease**, as well as help determine whether any chest **pain** is related to heart disease. Echocardiography can also help detect **hypertrophic cardiomyopathy**, in which the walls of the heart thicken in an attempt to compensate for heart muscle weakness. The biggest advantage to echocardiography is that it is noninvasive (doesn't involve breaking the skin or entering body cavities) and has no known risks or side effects.

Precautions

Echocardiography is an extremely safe procedure and no special precautions are required.

A patient getting an EKG. *(Photo Researchers. Reproduced by permission.)*

Description

Echocardiography creates an image of the heart using ultra-high-frequency sound waves—sound waves that are too high in frequency to be heard by the human ear. The technique is very similar to ultrasound scanning commonly used to visualize the fetus during **pregnancy**.

An echocardiography examination generally lasts between 15–30 minutes. The patient lies bare-chested on an examination table. A special gel is spread over the chest to help the transducer make good contact and slide smoothly over the skin. The transducer, a small hand-held device at the end of a flexible cable, is placed against the chest. Essentially a modified microphone, the transducer directs ultrasound waves into the chest. Some of the waves get echoed (or reflected) back to the transducer. Since different tissues and blood all reflect ultrasound waves differently, these sound waves can be translated into a meaningful image of the heart, which can be displayed on a monitor or recorded on paper or tape. The patient does not feel the sound waves, and the entire procedure is painless. In fact, there are no known side effects.

Occasionally, variations of the echocardiography test are used. For example, Doppler echocardiography employs a special microphone that allows technicians to measure and analyze the direction and speed of blood flow through blood vessels and heart valves. This makes it especially useful for detecting and evaluating regurgitation through the heart valves. By assessing the speed of blood flow at different locations around an obstruction, it can also help to precisely locate the obstruction.

An **exercise** echocardiogram is an echocardiogram performed during exercise, when the heart muscle must work harder to supply blood to the body. This allows doctors to detect heart problems that might not be evident when the body is at rest and needs less blood. For

KEY TERMS

Noninvasive—Pertaining to a diagnostic procedure or treatment that does not require the skin to be broken or a body cavity to be entered.

Regurgitation—Backward flow of blood through a partly closed heart valve.

Transducer—A device that converts electrical signals into ultrasound waves and ultrasound waves back into electrical impulses.

Ultrasound—Sound waves at a frequency of over 20,000 kHz, often used for diagnostic imaging.

patients who are unable to exercise, certain drugs can be used to mimic the effects of exercise by dilating the blood vessels and making the heart beat faster.

Preparation

The patient removes any clothing and jewelry above the chest.

Aftercare

No special measures need to be taken following echocardiography.

Risks

There are no known risks associated with the use of echocardiography.

Normal results

A normal echocardiogram shows a normal heart structure and the normal flow of blood through the heart chambers and heart valves. However, a normal echocardiogram does not rule out the possibility of heart disease.

Abnormal results

An echocardiogram may show a number of abnormalities in the structure and function of the heart, such as:

- thickening of the wall of the heart muscle (especially the left ventricle)
- abnormal motion of the heart muscle
- blood leaking backward through the heart valves (regurgitation)
- decreased blood flow through a heart valve (stenosis)

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American Heart Association. 7320 Greenville Ave. Dallas, TX 75231. (214) 373-6300. <http://www.americanheart.org>.

National Heart, Lung and Blood Institute. PO Box 30105, Bethesda, MD 20824-0105. (301) 251-1222. <http://www.nhlbi.nih.gov>.

Robert Scott Dinsmoor

Echovirus infections *see* **Enterovirus infections**

Eclampsia *see* **Preeclampsia and eclampsia**

ECT *see* **Electroconvulsive therapy**

Ectopic orifice of the ureter *see* **Congenital ureter anomalies**

Ectopic pregnancy

Definition

In an ectopic **pregnancy**, the fertilized egg implants in a location outside the uterus and tries to develop there. The word ectopic means "in an abnormal place or position." The most common site is the fallopian tube, the tube that normally carries eggs from the ovary to the uterus. However, ectopic pregnancy can also occur in the ovary, the abdomen, and the cervical canal (the opening from the uterus to the vaginal canal). The phrases tubal pregnancy, ovarian pregnancy, cervical pregnancy, and abdominal pregnancy refer to the specific area of an ectopic pregnancy.

Description

Once a month, an egg is produced in a woman's ovary and travels down the fallopian tube where it meets the male's sperm and is fertilized. In a normal pregnancy the fertilized egg, or zygote, continues on its passage down the fallopian tube and enters the uterus in three to five days. The zygote continues to grow, implanting itself securely in the wall of the uterus. The zygote's cells develop into the embryo (the organism in its first two months of develop-

ment) and placenta (a spongy structure that lines the uterus and nourishes the developing organism).

In a tubal ectopic pregnancy, the fertilized egg cannot make it all the way down the tube because of scarring or obstruction. The fallopian tube is too narrow for the growing zygote. Eventually the thin walls of the tube stretch and may burst (rupture), resulting in severe bleeding and possibly the **death** of the mother. More than 95% percent of all ectopic pregnancies occur in the fallopian tube. Only 1.5% develop in the abdomen; less than 1% develop in the ovary or the cervix.

Causes and symptoms

As many as 50% of women with ectopic pregnancies have a history of **pelvic inflammatory disease** (PID). This is an infection of the fallopian tubes (salpingitis) that can spread to the uterus or ovaries. It is most commonly caused by the organisms *Gonorrhea* and *Chlamydia* and is usually transmitted by sexual intercourse.

Other conditions also increase the risk of ectopic pregnancy. They include:

- **Endometriosis**. A condition in which the tissue that normally lines the uterus is found outside the uterus, and can block a fallopian tube.
- Exposure to diethylsilbestrol (DES) as a fetus. If a woman's mother took DES (a synthetic version of the hormone estrogen) during pregnancy, the woman may have abnormalities in her fallopian tubes that can make ectopic pregnancy more likely.
- Taking hormones. Estrogen and progesterone are hormones that regulate the menstrual cycle and may be in medications prescribed by a doctor for birth control or other reasons. Taking these hormones can affect the interior lining of the fallopian tubes and slow the movement of the fertilized egg down the tube. Women who become pregnant in spite of taking some progesterone-only contraceptives have a greater chance of an ectopic pregnancy. Ectopic pregnancy is also more likely when the ovaries are artificially stimulated with hormones to produce eggs for **in vitro fertilization** (a procedure in which eggs are taken from a woman's body, fertilized, and then placed in the uterus in an attempt to conceive a child).
- Use of an intrauterine device (**IUD**). These contraceptive devices are designed to prevent fertilized eggs from becoming implanted in the uterus, but they have only a minimal effect on preventing ectopic pregnancies. Therefore, if a woman becomes pregnant while using an IUD for **contraception**, the fertilized egg is more likely to be implanted someplace other than the uterus. For example, among women who become pregnant while using a progesterone-bearing IUD, about 15% have ectopic pregnancies.

In an ectopic pregnancy, the fertilized egg implants in a location outside the uterus and attempts to develop at that site. The most common site of an ectopic pregnancy is the fallopian tube, but it can occur in the ovary, the abdomen, and the cervical wall. More than 95% of all ectopic pregnancies occur in the fallopian tube. *(Illustration by Electronic Illustrators Group.)*

- Surgery on a fallopian tube. The risk of ectopic pregnancy can be as high as 60% after undergoing elective tubal sterilization, a procedure in which the fallopian tubes are severed to prevent pregnancy. Women who have successful surgery to reverse the procedure are also more likely to have an ectopic pregnancy.

Early symptoms

In an ectopic pregnancy all the hormonal changes associated with a normal pregnancy may occur. The early symptoms include: **fatigue**; nausea; a missed period; breast tenderness; **low back pain**; mild cramping on one side of the pelvis; and abnormal vaginal bleeding, usually spotting.

Later symptoms

As the embryo grows too large for the confined space in the tube, the first sign that something is wrong may be a stabbing **pain** in the pelvis or abdomen. If the tube has ruptured, blood may irritate the diaphragm and cause shoulder pain. Other warning signs are lightheadedness and **fainting**.

Diagnosis

To confirm an early diagnosis of ectopic pregnancy, the doctor must determine first that the patient is pregnant and that the location of the embryo is outside the uterus. If an ectopic pregnancy is suspected, the doctor

KEY TERMS

Embryo—In humans, the developing organism from conception until approximately the end of the second month.

Fallopian tube—The tube that carries the egg from the ovary to the uterus.

Human chorionic gonadotropin (hCG)—A hormone excreted during the development of an embryo or fetus.

Laparoscopy—Examination of the contents of the abdominal cavity with a fiberoptic tube inserted through a small incision.

Laparotomy—Surgical incision into the abdomen to locate, repair, and/or remove injured or diseased tissues.

Pelvic inflammatory disease (PID)—Acute or chronic inflammation in the pelvic cavity, particularly inflammation of the fallopian tubes (salpingitis) and its complications.

Rupture—A breaking apart of an organ or tissue.

Salpingitis—Inflammation of the fallopian tube.

Tubal pregnancy—Pregnancy in one of the fallopian tubes.

Zygote—The fertilized egg.

will perform a pelvic examination to locate the source of pain and to detect a mass in the abdomen.

Several laboratory tests of the patient's blood provide information for diagnosis. Measurement of the human chorionic gonadotropin (hCG) level in the patient's blood serum is the most useful laboratory test in the early stages. In a normal pregnancy, the level of this hormone doubles about every two days during the first 10 weeks. In an ectopic pregnancy, the rate of the increase is much slower and the low hCG for the stage of the pregnancy is a strong indication that the pregnancy is abnormal. (It could also represent a **miscarriage** in progress.) The level is usually tested several times over a period of days to determine whether or not it is increasing at a normal rate.

Progesterone levels in the blood are also measured. Lower than expected levels can indicate that the pregnancy is not normal.

An ultrasound examination may provide information about whether or not the pregnancy is ectopic. A device called a transducer, which emits high frequency sound waves, is moved over the surface of the patient's abdomen or inserted into the vagina. The sound waves bounce off of the internal organs and create an image on a screen. The doctor should be able to see whether or not there is a fetus developing in the uterus after at least five weeks of gestation. Before that point, a normal pregnancy is too small to see.

A culdocentesis may also help confirm a diagnosis. In this procedure a needle is inserted into the space at the top of the vagina, behind the uterus and in front of the rectum. Blood in this area may indicate bleeding from a ruptured fallopian tube.

A **laparoscopy** will enable the doctor to see the patient's reproductive organs and examine an ectopic pregnancy. In this technique, a hollow tube with a light on one end is inserted through a small incision in the abdomen. Through this instrument the internal organs can be observed.

Treatment

Ectopic pregnancy requires immediate treatment. The earlier the condition is treated, the better the chance to preserve the fallopian tube intact for future normal pregnancies.

Medical

If the ectopic pregnancy is discovered in a very early stage of development, the drug methotrexate may be given. The best results are obtained when the pregnancy is less than six weeks old and the tubal mass is no more than 1.4 in (3.5 cm) in diameter. Methotrexate, which has been used successfully since 1987, works by inhibiting the growth of rapidly growing cells. (It is also used to treat some cancers.) Most side effects are mild and temporary, but the patient must be monitored after treatment. Usually the medication is injected into the muscle in a single dose, but may also be given intravenously or injected directly into the fallopian tube to dissolve the embryonic tissue. Methotrexate has also been used to treat ovarian, abdominal, and cervical pregnancies that are discovered in the early stages.

Surgical

When a laparoscopy is done to visualize the ectopic pregnancy, the scope can be fitted with surgical tools and used to remove the ectopic mass immediately after it is identified. The affected fallopian tube can be repaired or removed as necessary. This procedure can be done without requiring the patient to stay in the hospital overnight.

When the pregnancy has ruptured, a surgical incision into the abdomen, or laparotomy, is performed to

stop the immediate loss of blood and to remove the embryo. This usually requires general anesthesia and a hospital stay. Every effort is made to preserve and repair the injured fallopian tube. However, if the fallopian tube has already ruptured, repair is extremely difficult and the tube is usually removed.

Alternative treatment

Ectopic pregnancy was first described in the eleventh century and was a potentially fatal condition until the advent of surgery and blood transfusions in the early twentieth century. The sophisticated diagnostic tools and surgical procedures developed since the 1970s have equipped modern medicine with the tools to not only save a woman's life, but also to preserve her future fertility.

Although there are herbal remedies for the temporary relief of the common symptoms of **anxiety** and abdominal discomfort, prompt medical treatment is the only sure remedy for ectopic pregnancy.

Prognosis

Ectopic pregnancies are the leading cause of pregnancy-related deaths in the first trimester and account for 9% of all pregnancy-related deaths in the United States. More than 1% of pregnancies are ectopic, and they are becoming more common. The reason for this increase is not clearly understood, though it is thought that the dramatic increase in **sexually transmitted diseases** (STD) is at least partly responsible.

The earlier an ectopic pregnancy is diagnosed and treated, the better the outcome. The chances of having a successful pregnancy are lower after an ectopic pregnancy, but depend on the extent of permanent fallopian tube damage. If the tube has been spared, chances are as high as 60%. The chances of a successful pregnancy after the removal of one tube are 40%.

Prevention

Many forms of ectopic pregnancy cannot be prevented. However, tubal pregnancies, which make up the majority of ectopic pregnancies, may be prevented by avoiding conditions that cause damage to the fallopian tubes. Since half of all women who experience ectopic pregnancy have a history of PID, avoiding this infection or getting early diagnosis and treatment for sexually transmitted diseases will decrease the risk of a future problem.

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ORGANIZATIONS

Resolve. 1310 Broadway, Somerville, MA 02144-1731. (617) 623-0744. <http://www.resolve.org>.

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Eczema *see* **Dermatitis**

ED *see* **Impotence**

Edema

Definition

Edema is a condition of abnormally large fluid volume in the circulatory system or in tissues between the body's cells (interstitial spaces).

Description

Normally the body maintains a balance of fluid in tissues by ensuring that the same of amount of water entering the body also leaves it. The circulatory system transports fluid within the body via its network of blood vessels. The fluid, which contains oxygen and nutrients needed by the cells, moves from the walls of the blood vessels into the body's tissues. After its nutrients are used up, fluid moves back into the blood vessels and returns to the heart. The lymphatic system (a network of channels in the body that carry lymph, a colorless fluid containing white blood cells to fight infection) also absorbs and transports this fluid. In edema, either too much fluid moves from the blood vessels into the tissues, or not enough fluid moves from the tissues back into the blood vessels. This fluid imbalance can cause mild to severe swelling in one or more parts of the body.

Causes and symptoms

Many ordinary factors can upset the balance of fluid in the body to cause edema, including:

- Immobility. The leg muscles normally contract and compress blood vessels to promote blood flow with walking or running. When these muscles are not used,

Gross lymphedema in the arm of an elderly woman following radiotherapy treatment for breast cancer. *(Photograph by Dr. P. Marazzi. Photo Researchers, Inc. Reproduced by permission.)*

blood can collect in the veins, making it difficult for fluid to move from tissues back into the vessels.

- Heat. Warm temperatures cause the blood vessels to expand, making it easier for fluid to cross into surrounding tissues. High humidity also aggravates this situation.
- Medications. Certain drugs, such as steroids, hormone replacements, **nonsteroidal anti-inflammatory drugs** (NSAIDs), and some blood pressure medications may affect how fast fluid leaves blood vessels.
- Intake of salty foods. The body needs a constant concentration of salt in its tissues. When excess salt is taken in, the body dilutes it by retaining fluid.
- Menstruation and **pregnancy**. The changing levels of hormones affect the rate at which fluid enters and leaves the tissues.

Some medical conditions may also cause edema, including:

- **Heart failure**. When the heart is unable to maintain adequate blood flow throughout the circulatory system, the excess fluid pressure within the blood vessels can cause shifts into the interstitial spaces. Left-sided heart failure can cause **pulmonary edema**, as fluid shifts into the lungs. The patient may develop rapid, shallow respirations, **shortness of breath**, and a **cough**. Right-sided heart failure can cause pitting edema, a swelling in the tissue under the skin of the lower legs and feet. Pressing this tissue with a finger tip leads to a noticeable momentary indentation.
- Kidney disease. The decrease in sodium and water excretion can result in fluid retention and overload.
- Thyroid or liver disease. These conditions can change the concentration of protein in the blood, affecting fluid movement in and out of the tissues. In advanced liver disease, the liver is enlarged and fluid may build-up in the abdomen.
- Malnutrition. Protein levels are decreased in the blood, and in an effort to maintain a balance of concentrations, fluid shifts out of the vessels and causes edema in tissue spaces.

Some conditions that may cause swelling in just one leg include:

- Blood clots. Clots can cause pooling of fluid and may be accompanied by discoloration and **pain**. In some instances, clots may cause no pain.
- Weakened veins. **Varicose veins**, or veins whose walls or valves are weak, can allow blood to pool in the legs. This is a common condition.
- Infection and inflammation. Infection in leg tissues can cause inflammation and increasing blood flow to the area. Inflammatory diseases, such as **gout** or arthritis, can also result in swelling.
- **Lymphedema**. Blocked lymph channels may be caused by infection, scar tissue, or hereditary conditions. Lymph that can't drain properly results in edema. Lymphedema may also occur after **cancer** treatments, when the lymph system is impaired by surgery, radiation, or **chemotherapy**.
- Tumor. Abnormal masses can compress leg vessels and lymph channels, affecting the rate of fluid movement.

Symptoms vary depending on the cause of edema. In general, weight gain, puffy eyelids, and swelling of the legs may occur as a result of excess fluid volume. Pulse rate and blood pressure may be elevated. Hand and neck veins may be observed as fuller.

Diagnosis

Edema is a sign of an underlying problem, rather than a disease unto itself. A diagnostic explanation should be sought. Patient history and presenting symptoms, along with laboratory blood studies, if indicated, assist the health professional in determining the cause of the edema.

Treatment

Treatment of edema is based on the cause. Simple steps to lessen fluid build-up may include:

- Reducing sodium intake. A high sodium level causes or aggravates fluid retention.
- Maintaining proper weight. Being overweight slows body fluid circulation and puts extra pressure on the veins.
- **Exercise**. Regular exercise stimulates circulation.
- Elevation of the legs. Placing the legs at least 12 in (30.5 cm) above the level of the heart for 10–15 minutes, three to four times a day, stimulates excess fluid re-entry into the circulatory system.
- Use of support stocking. Elastic stockings, available at most medical supply or drug stores, will compress the leg vessels, promoting circulation and decreasing pooling of fluid due to gravity.

KEY TERMS

Digitalis—A naturally occuring compound used in the preparation of the medication, digoxin, prescribed to increase the heart rate and strengthen the force of the heart's contractions.

Diuretics—Medications used in the treatment of fluid overload, to promote excretion of sodium and water.

Interstitial spaces—Areas of the body occuring outside the vessels or organs, between the cells.

Pitting edema—A swelling in the tissue under the skin, resulting from fluid accumulation, that is measured by the depth of indentation made by finger pressure over a boney prominence.

- Massage. Massaging the body part can help to stimulate the release of excess fluids, but should be avoided if the patient has blood clots in the veins.
- Travel breaks. Sitting for long periods will increase swelling in the feet and ankles. Standing and/or walking at least every hour or two will help stimulate blood flow.

The three "Ds"—diuretics, digitalis, and diet—are frequently prescribed for medical conditions that result in excess fluid volume. **Diuretics** are medications that promote urination of sodium and water. Digoxin is a digitalis preparation that is sometimes needed to decrease heart rate and increase the strength of the heart's contractions. Dietary recommendations include less sodium in order to decrease fluid retention. Consideration of adequate protein intake is also made.

For patients with lymphedema, a combination of therapies may prove effective. Combined decongestive therapy includes the use of manual lymph drainage (MLD), compression bandaging, garments and pumps, and physical therapy. MLD involves the use of light massage of the subcutaneous tissue where the lymph vessels predominate. Massage begins in an area of the body trunk where there is normal lymph function and proceeds to areas of lymphatic insufficiency, in an effort to stimulate new drainage tract development. (MLD should not be used for patients with active cancer, deep vein clots, congestive heart failure, or cellulitis.) MLD sessions are followed by application of compression garments or pumps. Physical therapy is aimed at strengthening the affected limb and increasing joint mobility.

Alternative treatment

Dietary changes, in addition to cutting back the amount of sodium eaten, may also help reduce edema. Foods that worsen edema, such as alcohol, **caffeine**, sugar, dairy products, soy sauce, animal protein, chocolate, olives, and pickles, should be avoided. Diuretic herbs can also help relieve edema. One of the best herbs for this purpose is dandelion (*Taraxacum mongolicum*), since, in addition to its diuretic action, it is a rich source of potassium. (Diuretics flush potassium from the body and it must be replaced to avoid potassium deficiency.) **Hydrotherapy** using daily contrast applications of hot and cold (either compresses or immersion) may also be helpful.

Resources

BOOKS

Monahan, Frances D., and Marianne Neighbors. *Medical-Surgical Nursing: Foundation for Clinical Practice.* 2nd ed. Philadelphia: W. B. Saunders Co., 1998.

ORGANIZATIONS

Lymphedema and Wound Care Clinic of Austin. 5750 Balcones Dr., Ste. 110, Austin, TX 78731. (512) 453-1930.

Kathleen D. Wright, RN

Edrophonium test *see* **Tensilon test**

Edwards' syndrome

Definition

Edwards' syndrome is caused by an extra copy of chromosome 18. For this reason, it is also called trisomy 18 syndrome. The extra chromosome is lethal for most babies born with this condition. It causes major physical abnormalities and severe **mental retardation**, and very few children afflicted with this disease survive beyond a year.

Description

Humans normally have 23 pairs of chromosomes. Chromosomes are numbered 1–22, and the 23rd pair is composed of the sex chromosomes, X and Y. A person inherits one set of 23 chromosomes from each parent. Occasionally, a genetic error occurs during egg or sperm cell formation. A child conceived with such an egg or sperm cell may inherit an incorrect number of chromosomes.

In the case of Edwards' syndrome, the child inherits three, rather than two, copies of chromosome 18. Trisomy 18 occurs in approximately one in every 3,000 newborns and affects girls more often than boys. Women older than their early thirties have a greater risk of conceiving a child with trisomy 18, but it can occur in younger women.

Causes and symptoms

A third copy of chromosome 18 causes numerous abnormalities. Most children born with Edwards' syndrome appear weak and fragile, and they are often underweight. The head is unusually small and the back of the head is prominent. The ears are malformed and low-set, and the mouth and jaw are small. The baby may also have a cleft lip or cleft palate. Frequently, the hands are clenched into fists, and the index finger overlaps the other fingers. The child may have clubfeet and toes may be webbed or fused.

Numerous problems involving the internal organs may be present. Abnormalities often occur in the lungs and diaphragm (the muscle that controls breathing), and heart defects and blood vessel malformations are common. The child may also have malformed kidneys and abnormalities of the urogenital system.

Diagnosis

Physical abnormalities point to Edwards' syndrome, but definitive diagnosis relies on karyotyping. Karyotyping involves drawing the baby's blood or bone marrow for a microscopic examination of the chromosomes. Using special stains and microscopy, individual chromosomes are identified, and the presence of an extra chromosome 18 is revealed.

Trisomy 18 can be detected before birth. If a pregnant woman is older than 35, has a family history of genetic abnormalities, has previously conceived a child with a genetic abnormality, or has suffered earlier miscarriages, she may undergo tests to determine whether her child carries genetic abnormalities. Potential tests include maternal serum analysis or screening, ultrasonography, **amniocentesis**, and **chorionic villus sampling**.

Treatment

There is no cure for Edwards' syndrome. Since trisomy 18 babies frequently have major physical abnormalities, doctors and parents face difficult choices regarding treatment. Abnormalities can be treated to a certain degree with surgery, but extreme invasive procedures may not be in the best interests of an infant whose lifespan is measured in days or weeks. Medical therapy often consists of supportive care with the goal of making the infant comfortable, rather than prolonging life.

KEY TERMS

Aminocentesis—A procedure in which a needle is inserted through a pregnant woman's abdomen and into her uterus to withdraw a small sample of amniotic fluid. The amniotic fluid can be examined for signs of disease or other problems afflicting the fetus.

Chorionic villus sampling—A medical test that is best done during weeks 10–12 of a pregnancy. The procedure involves inserting a needle into the placenta and withdrawing a small amount of the chorionic membrane for analysis.

Chromosome—A structure composed of deoxyribonucleic acid (DNA) contained within a cell's nucleus (center) in where genetic information is stored. Human have 23 pairs of chromosomes, each of which has recognizable characteristics (such as length and staining patterns) that allow individual chromosomes to be identified. Identification is assigned by number (1–22) or letter (X or Y).

Karyotyping—A laboratory test used to study an individual's chromosome make-up. Chromosomes are separated from cells, stained, and arranged in order from largest to smallest so that their number and structure can be studied under a microscope.

Maternal serum analyte screening—A medical procedure in which a pregnant woman's blood is drawn and analyzed for the levels of certain hormones and proteins. These levels can indicate whether there may be an abnormality in the unborn child. This test is not a definitive indicator of a problem and is followed by more specific testing such as amniocentesis or chorionic villus sampling.

Trisomy—A condition in which a third copy of a chromosome is inherited. Normally only two copies should be inherited.

Ultrasound—A medical test that is also called ultrasonography. Sound waves are directed against internal structures in the body. As sound waves bounce off the internal structure, they create an image on a video screen. An ultrasound of a fetus at weeks 16–20 of a pregnancy can be used to determine structural abnormalities.

Prognosis

Most children born with trisomy 18 die within their first year of life. The average lifespan is less than two months for 50% of the children, and 90–95% die before their first birthday. The 5–10% of children who survive their first year are severely mentally retarded. They need support to walk, and learning is limited. Verbal communication is also limited, but they can learn to recognize and interact with others.

Prevention

Edwards' syndrome cannot be prevented.

Resources

BOOKS

Gardner, R. J. McKinlay, and Grant R. Sutherland. *Chromosome Abnormalities and Genetic Counseling.* New York: Oxford University Press, 1996.

Jones, Kenneth Lyons. *Smith's Recognizable Patterns of Human Malformation.* 5th ed. W. B. Saunders Co., 1997.

ORGANIZATIONS

The Chromosome 18 Registry & Research Society. 6302 Fox Head, San Antonio, TX 78247. (210) 657-4968. <http://www.chromosome18.org>.

Support Organization for Trisomy 18, 13, and Related Disorders (SOFT). 2982 South Union St., Rochester, NY 14624. (800) 716-7638. <http://www.trisomy.org>.

Julia Barrett

EEG *see* **Electroencephalography**

Egyptian conjunctivitis *see* **Trachoma**

Ehlers-Danlos syndrome

Definition

The Ehlers-Danlos syndromes (EDS) refer to a group of inherited disorders that affect collagen structure and function. Genetic abnormalities in the manufacturing of collagen within the body affect connective tissues, causing them to be abnormally weak.

Description

Collagen is a strong, fibrous protein that lends strength and elasticity to connective tissues such as the

skin, tendons, organ walls, cartilage, and blood vessels. Each of these connective tissues requires collagen tailored to meet its specific purposes. The many roles of collagen are reflected in the number of genes dedicated to its production. There are at least 28 genes in humans that encode at least 19 different types of collagen. Mutations in these genes can affect basic construction as well as the fine-tuned processing of the collagen.

EDS was originally described by Dr. Van Meekeren in 1682. Dr. Ehlers and Dr. Danlos further characterized the disease in 1901 and 1908, respectively. Today, according to the Ehlers-Danlos National Foundation, one in 5,000 to one in 10,000 people are affected by some form of EDS.

EDS is a group of genetic disorders that usually affects the skin, ligaments, joints, and blood vessels. Classification of EDS types was revised in 1997. The new classification involves categorizing the different forms of EDS into six major sub-types, including classical, hypermobility, vascular, kyphoscoliosis, arthrochalasia, and dermatosparaxis, and a collection of rare or poorly defined varieties. This new classification is simpler and based more on descriptions of the actual symptoms.

Classical type

Under the old classification system, EDS classical type was divided into two separate types: type I and type II. The major symptoms involved in EDS classical type are the skin and joints. The skin has a smooth, velvety texture and **bruises** easily. Affected individuals typically have extensive scaring, particularly at the knees, elbows, forehead, and chin. The joints are hyperextensible, giving a tendency towards dislocation of the hip, shoulder, elbow, knee, or clavicle. Due to decreased muscle tone, affected infants may experience a delay in reaching motor milestones. Children may have a tendency to develop hernias or other organ shifts within the abdomen. Sprains and partial or complete joint dilocations are also common. Symptoms can range from mild to severe. EDS classical type is inherited in an autosomal dominant manner.

There are three major clinical diagnostic criteria for EDS classical type. These include skin hyperextensibility, unusually wide scars, and joint hypermobility. At this time there is no definitive test for the diagnosis of classical EDS. Both DNA and biochemical studies have been used to help identify affected individuals. In some cases, a **skin biopsy** has been found to be useful in confirming a diagnosis. Unfortunately, these tests are not sensitive enough to identify all individuals with classical EDS. If there are multiple affected individuals in a family, it may be possible to perform prenatal diagnosis using a DNA information technique known as a linkage study.

Hypermobility type

Excessively loose joints are the hallmark of this EDS type, formerly known as EDS type III. Both large joints, such as the elbows and knees, and small joints, such as toes and fingers, are affected. Partial and total joint dislocations are common, and particularly involve the jaw, knee, and shoulder. Many individuals experience chronic limb and joint **pain**, although x rays of these joints appear normal. The skin may also bruise easily. **Osteoarthritis** is a common occurrence in adults. EDS hypermobility type is inherited in an autosomal dominant manner.

There are two major clinical diagnostic criteria for EDS hypermobility type. These include skin involvement (either hyperextensible skin or smooth and velvety skin) and generalized joint hypermobility. At this time there is no test for this form of EDS.

Vascular type

Formerly called EDS type IV, EDS vascular type is the most severe form. The connective tissue in the intestines, arteries, uterus, and other hollow organs may be unusually weak, leading to organ or blood vessel rupture. Such ruptures are most likely between ages 20 and 40, although they can occur any time, and may be life-threatening.

There is a classic facial appearance associated with EDS vascular type. Affected individuals tend to have large eyes, a thin pinched nose, thin lips, and a slim body. The skin is thin and translucent, with veins dramatically visible, particularly across the chest.

The large joints have normal stability, but small joints in the hands and feet are loose, showing hyperextensibility. The skin bruises easily. Other complications may include collapsed lungs, premature **aging** of the skin on the hands and feet, and ruptured arteries and veins. After surgery there tends to be poor wound healing, a complication that tends to be frequent and severe. **Pregnancy** also carries the risk complications. During and after pregnancy there is an increased risk of the uterus rupturing and of arterial bleeding. Due to the severe complications associated with EDS type IV, **death** usually occurs before the fifth decade. A study of 419 individuals with EDS vascular type, completed in 2000, found that the median survival rate was 48 years, with a range of six to 73 years. EDS vascular type is inherited in an autosomal dominant manner.

There are four major clinical diagnostic criteria for EDS vascular type. These include thin translucent skin, arterial/intestinal/uterine fragility or rupture, extensive bruising, and characteristic facial appearance. EDS vascular type is caused by a change in the gene COL3A1,

which codes for one of the collagen chains used to build Collage type III. Laboratory testing is available for this form of EDS. A skin biopsy may be used to demonstrate the structurally abnormal collagen. This type of biochemical test identifies more than 95% of individuals with EDS vascular type. Laboratory testing is recommended for individuals with two or more of the major criteria.

DNA analysis may als be used to identify the change within the COL3A1 gene. This information may be helpful for **genetic counseling** purposes. Prenatal testing is available for pregnancies in which an affected parent has been identified and their DNA mutation is known or their biochemical defect has been demonstrated.

Kyphoscoliosis type

The major symptoms of kyphoscoliosis type, formerly called EDS type VI, are general joint looseness. At birth, the muscle tone is poor, and motor skill development is subsequently delayed. Also, infants with this type of EDS have an abnormal curvature of the spine (**scoliosis**). The scoliosis becomes progressively worse with age, with affected individuals usually unable to walk by age 20. The eyes and skin are fragile and easily damaged, and blood vessel involvement is a possibility. The bones may also be affected as demonstrated by a decrease in bone mass. Kyphoscoliosis type is inherited in an autosomal recessive manner.

There are four major clinical diagnostic criteria for EDS kyphoscoliosis type. These include generaly loose joints, low muscle tone at birth, scoliosis at birth (which worsens with age), and a fragility of the eyes, which may give the white area of the eye a blue tint or cause the eye to rupture. This form of EDS is caused by a change in the PLOD gene on chromosome 1, which encodes the enzyme lysyl hydroxylase. A laboratory test is available in which urinary hydroxylysyl pryridinoline is measured. This test, performed on urine is extremely senstive and specific for EDS kyphoscolios type. Laboratory testing is recommended for infants with three or more of the major diagnostic criteria.

Prenatal testing is available if a pregnancy is known to be at risk and an identified affected family member has had positive laboratory testing. An **amniocentesis** may be performed in which fetal cells are removed from the amniotic fluid and enzyme activity is measured.

Arthrochalasia type

Dislocation of the hip joint typically accompanies arthrochalasia type EDS, formerly called EDS type VIIB. Other joints are also unusually loose, leading to recurrent partial and total dislocations. The skin has a high degree of stretchability and bruises easily. Individuals with this type of EDS may also experience mildly diminished bone mass, scoliosis, and poor muscle tone. Arthrochalasia type is inherited in an autosomal dominant manner.

Elasticity of the skin is one characteristic of this rare disorder. *(Photograph by Biophoto Associates, Photo Researchers, Inc. Reproduced by permission.)*

There are two major clinical diagnostic criteria for EDS arthrochalasia type. These include sever generalized joing hypermobility and bilateral hip dislocation present at birth. This form of EDS is caused by a change in either of two components of Collage type I, called proa1(I) type A and proa2(I) type B. A skin biopsy may be preformed to demonstrate an abnormality in either components. Direct DNA testing is also available.

Dermatosparaxis type

Individuals with this type of EDS, once called type VIIC, have extremely fragile skin that bruises easily but does not scar excessively. The skin is soft and may sag, leading to an aged appearance even in young adults. Individuals may also experience hernias. Dermatosparaxis type is inherited in an autosomal recessive manner.

There are two major clinical diagnostic criteria for EDS dematosparaxis type. These include severe skin fragility and sagging or aged appearing skin. This form of EDS is caused by a change in the enzyme called procollagen I N-terminal peptidase. A skin biopsy may be preformed for a definitive diagnosis of Dermatosparaxis type.

Other types

There are several other forms of EDS that have not been as clearly defined as the aforementioned types. Forms of EDS within this category may present with soft, mildly stretchable skin, shortened bones, chronic **diarrhea**, joint hypermobility and dislocation, bladder rupture, or poor wound healing. Inheritance patterns within this group include X-linked recessive, autosomal dominant, and autosomal recessive.

KEY TERMS

Arthrochalasia—Excessive loosness of the joints.

Blood vessels—General term for arteries, veins, and capillaries that transport blood throughout the body.

Cartilage—Supportive connective tissue that cushions bone at the joints or which connects muscle to bone.

Collagen—The main supportive protein of cartilage, connective tissue, tendon, skin, and bone.

Connective tissue—A group of tissues responsible for support throughout the body; includes cartilage, bone, fat, tissue underlying skin, and tissues that support organs, blood vessels, and nerves throughout the body.

Dermatosparaxis—Skin fragility caused by abnormal collagen.

Hernia—A rupture in the wall of a body cavity, through which an organ may protrude.

Homeopathic—A holistic and natural approach to healthcare.

Hyperextensibility—The ability to extend a joint beyond the normal range.

Hypermobility—Unusual flexibility of the joints, allowing them to be bent or moved beyond their normal range of motion.

Joint dislocation—The displacement of a bone.

Kyphoscoliosis—Abnormal front-to-back and side-to-side curvature of the spine.

Ligament—A type of connective tissue that connects bones or cartilage and provides support and strength to joints.

Osteoarthritis—A degenerative joint disease that causes pain and stiffness.

Scoliosis—An abnormal, side-to-side curvature of the spine.

Tendon—A strong connective tissue that connects muscle to bone.

Uterus—A muscular, hollow organ of the female reproductive tract. The uterus contains and nourishes the embryo and fetus from the time the fertilized egg is implanted until birth.

Vascular—Having to do with blood vessels.

Causes and symptoms

There are numerous types of EDS, all caused by changes in one of several genes. The manner in which EDS is inherited depends on the specific gene involved. There are three patterns of inheritance for EDS: autosomal dominant, autosomal recessive, and X-linked (extremely rare).

Chromosomes are made up of hundreds of small units known as genes, which contain the genetic material necessary for an individual to develop and function. Humans have 46 chromosomes, which are matched into 23 pairs. Because chromosomes are inherited in pairs, each individual receives two copies of each chromosome and likewise two copies of each gene.

Changes or mutations in genes can cause genetic diseases in several different ways, many of which are represented within the spectrum of EDS. In autosomal dominant EDS, only one copy of a specific gene must be changed for a person to have EDS. In autosomal recessive EDS, both copies of a specific gene must be changed for a person to have EDS. If only one copy of an autosomal recessive EDS gene is changed the person is referred to as a carrier, meaning they do not have any of the signs or symptoms of the disease itself, but carry the possibility of passing on the disorder to a future child. In X-linked EDS a specific gene on the X chromosome must be changed. However, this affects males and females differently because males and females have a different number of X chromosomes.

As of 2001 the few X-linked forms of EDS fall under the category of X-linked recessive. As with autosomal recessive, this implies that both copies of a specific gene must be changed for a person to be affected. However, because males only have one X-chromosome, they are affected if an X-linked recessive EDS gene is changed on their single X-chromosome. That is, they are affected even though they have only one changed copy. On the other hand, that same gene must be changed on both of the X-chromosomes in a female for her to be affected.

Although there is much information regarding the changes in genes that cause EDS and their various inheritance patterns, the exact gene mutation for all types of EDS is not known.

Diagnosis

Clinical symptoms such as extreme joint looseness and unusual skin qualities, along with family history, can

lead to a diagnosis of EDS. Specific tests, such as skin biopsies are available for diagnosis of certain types of EDS, including vascular, arthrochalasia, and dermatosparaxis types. A skin biopsy involves removing a small sample of skin and examining its microscopic structure. A urine test is available for the Kyphoscoliosis type.

Management of all types of EDS may include genetic counseling to help the affected individual and their family understand the disorder and its impact on other family members and future children.

If a couple has had a child diagnosed with EDS the chance that they will have another child with the same disorder depends on with what form of EDS the child has been diagnosed and if either parent is affected by the same disease or not.

Individuals diagnosed with an autosomal dominant form of EDS have a 50% chance of passing the same disorder on to a child in each pregnancy. Individuals diagnosed with an autosomal recessive form of EDS have an extremely low risk of having a child with the same disorder.

X-linked recessive EDS is accompanied by a slightly more complicated pattern of inheritance. If a father with an X-linked recessive form of EDS passes a copy of his X chromosome to his children, the sons will be unaffected and the daughters will be carriers. If a mother is a carrier for an X-linked recessive form of EDS, she may have affected or unaffected sons, or carrier or unaffected daughters, depending on the second sex chromosome inherited from the father.

Prenatal diagnosis is available for specific forms of EDS, including kyphosocliosis type and vascular type. However, prenatal testing is only a possibility in these types if the underlying defect has been found in another family member.

Treatment

Medical therapy relies on managing symptoms and trying to prevent further complications. There is no cure for EDS.

Braces may be prescribed to stabilize joints, although surgery is sometimes necessary to repair joint damage caused by repeated dislocations. Physical therapy teaches individuals how to strengthen muscles around joints and may help to prevent or limit damage. Elective surgery is discouraged due to the high possibility of complications.

Alternative treatment

There are anecdotal reports that large daily doses 0.04–0.14 oz (1–4 g) of vitamin C may help decrease bruising and aid in wound healing. Constitutional homeopathic treatment may be helpful in maintaining optimal health in persons with a diagnosis of EDS. An individual with EDS should discuss these types of therapies with their doctor before beginning them on their own. Therapy that does not require medical consultation involves protecting the skin with sunscreen and avoiding activities that place **stress** on the joints.

Prognosis

The outlook for individuals with EDS depends on the type of EDS with which they have been diagnosed. Symptoms vary in severity, even within one sub-type, and the frequency of complications changes on an individual basis. Some individuals have negligible symptoms while others are severely restricted in their daily life. Extreme joint instability and scoliosis may limit a person's mobility. Most individuals will have a normal lifespan. However, those with blood vessel involvement, particularly those with EDS vascular type, have an increased risk of fatal complications.

EDS is a lifelong condition. Affected individuals may face social obstacles related to their disease on a daily basis. Some people with EDS have reported living with fears of significant and painful skin ruptures, becoming pregnant (especially those with EDS vascular type), their condition worsening, becoming unemployed due to physical and emotional burdens, and social stigmatization in general.

Constant bruises, skin **wounds**, and trips to the hospital take their toll on both affected children and their parents. Prior to diagnosis parents of children with EDS have found themselves under suspicion of **child abuse**.

Some people with EDS are not diagnosed until well into adulthood and, in the case of EDS vascular type, occasionally not until after death due to complications of the disorder. Not only may the diagnosis itself be devastating to the family, but in many cases other family members find out for the first time they are at risk for being affected.

Although individuals with EDS face significant challenges, it is important to remember that each person is unique with their own distinguished qualities and potential. Persons with EDS go on to have families, to have careers, and to be accomplished citizens, surmounting the challenges of their disease.

Resources

PERIODICALS

"Clinical and Genetic Features of Ehlers-Danlos Syndrome Type IV, the Vascular Type." *The New England Journal of Medicine* 342, no. 10 (2000).

"Ehlers-Danlos Syndromes: Revised Nosology, Villefranche, 1997." *American Journal of Medical Genetics* 77 (1998): 31–37.

"Living a Restricted Life with Ehlers-Danlos Syndrome." *International Journal of Nursing Studies* 37 (2000): 111–118.

ORGANIZATIONS

Elhers-Danlos National Foundation. 6399 Wilshire Blvd., Ste 203, Los Angeles, CA 90048 (323) 651-3038. Fax: (323) 651-1366. <http://www.ednf.org>.

Ehlers-Danlos Support Group- UK. PO Box 335, Farnham, Surrey, GU10 1XJ. UK. <http://www. atv.ndirect.co.uk>.

OTHER

GeneClinics. <http://www.geneclinics.org>.

Java O. Solis, MS

Ehrlichiosis

Definition

Ehrlichiosis is a bacterial infection that is spread by ticks. Symptoms include **fever**, chills, **headache**, muscle aches, and tiredness.

Description

Ehrlichiosis is a tick-borne disease caused by infection with *Ehrlichia* bacteria. Ticks are small, blood-sucking arachnids. Although some ticks carry disease-causing organisms, most do not. When an animal or person is bitten by a tick that carries bacteria, the bacteria are passed to that person or animal during the tick's feeding process. It is believed that the tick must remain attached to the person or animal for at least 24 hours to spread the infection.

There are two forms of ehrlichiosis in the United States; human monocytic ehrlichiosis and human granulocytic ehrlichiosis. Monocytic ehrlichiosis is caused by *Ehrlichia chaffeensis*, which is spread by the Lone Star tick, *Amblyomma americanum*. As of early 1998, about 400 cases of monocytic ehrlichiosis had been reported in 30 states, primarily in the southeastern and south central United States. The bacteria that causes granulocytic ehrlichiosis is not known, but suspected to be either *Ehrlichia equi* or *Ehrlichia phagocytophila*. Granulocytic ehrlichiosis is probably spread by the blacklegged tick *Ixodes scapularis* (which also spreads **Lyme disease**). About 100 cases of granulocytic ehrlichiosis have been reported in Connecticut, Massachusetts, Rhode Island, Minnesota, New York, and Wisconsin.

Causes and symptoms

Both forms of ehrlichiosis have similar symptoms, and the illnesses can range from mild to severe and life-threatening. Risk factors include old age and exposure to ticks through work or recreation. Symptoms occur seven to 21 days following a tick bite although patients may not recall being bitten. Fever, tiredness, headache, muscle aches, chills, loss of appetite, confusion, nausea, and vomiting are common to both diseases. A rash may occur.

Diagnosis

Ehrlichiosis may be diagnosed and treated by doctors who specialize in blood diseases (hematologists) or an infectious disease specialist. Because ehrlichiosis is not very common and the symptoms are not unique, it may be misdiagnosed. A recent history of a tick bite is helpful in the diagnosis. Blood tests will be done to look for antibodies to *Ehrlichia*. Staining and microscopic examination of the blood sample may show *Ehrlichia* bacteria inside white blood cells. Another test, called polymerase chain reaction (PCR), is a very sensitive assay to detect bacteria in the blood sample, but it is not always available.

Treatment

Antibiotic treatment should begin immediately if ehrlichiosis is suspected, even if laboratory results are not available. Treatment with either tetracycline (Sumycin, Achromycin V) or doxycycline (Monodox, Vibramycin) is recommended. Many patients with ehrlichiosis are admitted to the hospital for treatment.

Prognosis

For otherwise healthy people, a full recovery is expected following treatment for ehrlichiosis. Elderly patients are at a higher risk for severe disease, which may be fatal. Serious complications include lung or gastrointestinal bleeding. Two to 10 patients out of 100 die from the disease.

Prevention

The only prevention for ehrlichiosis is to minimize exposure to ticks by staying on the trail when walking through the woods, avoiding tall grasses, wearing long sleeves and tucking pant legs into socks, wearing insect

KEY TERMS

Tick-borne disease—A disease that is spread to animals by the bite of an infected tick.

repellent, and checking for ticks after an outing. Remove a tick as soon as possible by grasping the tick with tweezers and gently pulling.

Resources

BOOKS

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Belinda Rowland, PhD

EKG *see* **Electrocardiography**

Elder abuse *see* **Abuse**

Electric shock injuries

Definition

Electric shock injuries are caused by lightning or electric current from a mechanical source passing through the body.

Description

Electric shocks are responsible for about 1,000 deaths in the United States each year, or about 1% of all accidental deaths.

Causes and symptoms

The severity of injury depends on the current's pressure (voltage), the amount of current (amperage), the type of current (direct vs. alternating), the body's resistance to the current, the current's path through the body, and how long the body remains in contact with the current. The interplay of these factors can produce effects ranging from barely noticeable tingling to instant **death**; every part of the body is vulnerable. Although the severity of injury is determined primarily by the voltage, low voltage can be just as dangerous as high voltage under the right circumstances. People have been killed by shocks of just 50 volts.

How electric shocks affect the skin is determined by the skin's resistance, which in turn is dependent upon the wetness, thickness, and cleanliness of the skin. Thin or wet skin is much less resistant than thick or dry skin. When skin resistance is low, the current may cause little or no skin damage but severely burn internal organs and tissues. Conversely, high skin resistance can produce severe skin **burns** but prevent the current from entering the body.

The nervous system (the brain, spinal cord, and nerves) is particularly vulnerable to injury. In fact, neurological problems are the most common kind of nonlethal harm suffered by electric shock victims. Some neurological damage is minor and clears up on its own or with medical treatment, but some is severe and permanent. Neurological problems may be apparent immediately after the accident, or gradually develop over a period of up to three years.

Damage to the respiratory and cardiovascular systems is most acute at the moment of injury. Electric shocks can paralyze the respiratory system or disrupt heart action, causing instant death. Also at risk are the smaller veins and arteries, which dissipate heat less easily than the larger blood vessels and can develop blood clots. Damage to the smaller vessels is probably one reason why **amputation** is often required following high-voltage injuries.

Many other sorts of injuries are possible after an electric shock, including **cataracts**, kidney failure, and substantial destruction of muscle tissue. The victim may suffer a fall or be hit by debris from exploding equipment. An electric arc may set clothing or nearby flammable substances on fire. Strong shocks are often accompanied by violent muscle spasms that can break and dislocate bones. These spasms can also freeze the victim in place and prevent him or her from breaking away from the source of the current.

Diagnosis

Diagnosis relies on gathering information about the circumstances of the accident, a thorough **physical examination**, and monitoring of cardiovascular and kidney activity. The victim's neurological condition can fluctuate rapidly and requires close observation. A computed tomography scan (CT scan) or **magnetic resonance imaging** (MRI) may be necessary to check for brain injury.

Treatment

When an electric shock accident happens at home or in the workplace, the main power should immediately be

KEY TERMS

Antibiotics—Substances used against microorganisms that cause infection.

Cataract—Clouding of the lens of the eye or its capsule (surrounding membrane).

Computed tomography scan (CT scan)—A process that uses x rays to create three-dimensional images of structures inside the body.

Electrolytes—Substances that conduct electric current within the body and are essential for sustaining life.

Magnetic resonance imaging (MRI)—The use of electromagnetic energy to create images of structures inside the body.

Skin grafting—A technique in which a piece of healthy skin from the patient's body (or a donor's) is used to cover another part of the patient's body that has lost its skin.

shut off. If that cannot be done, and current is still flowing through the victim, the alternative is to stand on a dry, nonconducting surface such as a folded newspaper, flattened cardboard carton, or plastic or rubber mat and use a nonconducting object such as a wooden broomstick (never a damp or metallic object) to push the victim away from the source of the current. The victim and the source of the current must not be touched while the current is still flowing, for this can electrocute the rescuer. Emergency medical help should be summoned as quickly as possible. People who are trained to perform **cardiopulmonary resuscitation** (**CPR**) should, if appropriate, begin first aid while waiting for emergency medical help to arrive.

Burn victims usually require treatment at a burn center. Fluid replacement therapy is necessary to restore lost fluids and electrolytes. Severely injured tissue is repaired surgically, which can involve **skin grafting** or amputation. **Antibiotics** and antibacterial creams are used to prevent infection. Victims may also require treatment for kidney failure. Following surgery, physical therapy to facilitate recovery, and psychological counseling to cope with disfigurement, may be necessary.

Prognosis

Electric shocks cause death in 3–15% of cases. Many survivors require amputation or are disfigured by their burns. Injuries from household appliances and other low-voltage sources are less likely to produce extreme damage.

Prevention

Parents and other adults need to be alert to possible electric dangers in the home. Damaged electric appliances, wiring, cords, and plugs should be repaired or replaced. Electrical repairs should be attempted only by people with the proper training. Hair dryers, radios, and other electric appliances should never be used in the bathroom or anywhere else they might accidentally come in contact with water. Young children need to be kept away from electric appliances and should be taught about the dangers of electricity as soon as they are old enough. Electric outlets require safety covers in homes with young children.

During thunderstorms, people should go indoors immediately, even if no rain is falling, and boaters should return to shore as rapidly as possible. People who cannot reach indoor shelter should move away from metallic objects such as golf clubs and fishing rods and lie down in low-ground areas. Standing or lying under or next to tall or metallic structures is unsafe. An automobile is appropriate cover, as long as the radio is off. Telephones, computers, hair dryers, and other appliances that can act as conduits for lightning should not be used during thunderstorms.

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Electrical nerve stimulation

Definition

Electrical nerve stimulation, also called transcutaneous electrical nerve stimulation (TENS), is a noninvasive, drug-free **pain management** technique. By sending electrical signals to underlying nerves, the battery-powered TENS device can relieve a wide range of chronic and acute **pain**.

Purpose

TENS is used to relieve pain caused by a variety of chronic conditions, including:

- neck and lower back pain
- headache/migraine
- arthritis
- post-herpetic **neuralgia** (lingering chronic pain after an attack of **shingles**)

- sciatica (pain radiating from lower back, through the legs, to the foot)
- temporomandibular joint pain
- osteoarthritis
- amputation (phantom limb)
- fibromyalgia (a condition causing aching and stiffness throughout the body)

The device is also effective against short-term pain, such as:

- shingles (painful skin eruptions along the nerves)
- bursitis (inflammation of tissue surrounding a joint)
- childbirth
- post-surgical pain
- fractures
- muscle and joint pain
- sports injuries
- menstrual cramps

Precautions

Because TENS may interfere with pacemaker function, patients with **pacemakers** should consult a cardiologist before using a TENS unit. Patients should also avoid electrical stimulation in the front of the neck, which can be hazardous. The safety of the device during **pregnancy** has not been established.

TENS doesn't cure any condition; it simply eases pain. Patients who are not sure what is causing their pain should consult a physician before using TENS.

Description

The TENS device is a small battery-powered stimulator that produces low-intensity electrical signals through electrodes on or near a painful area, producing a tingling sensation that reduces pain. There is no dosage limitation, and the patient controls the amount of pain relief.

Some experts believe TENS works by blocking pain signals in the spinal cord, or by delivering electrical impulses to underlying nerve fibers that lessen the experience of pain. Others suspect that the electrical stimulation triggers the release of natural painkillers in the body.

Patients can rent a TENS unit before buying one, to see if it is effective against their pain.

Preparation

After TENS has been prescribed, a doctor will refer the patient to a TENS specialist, who will explain how to use the machine. The specialist works with the patient to determine the settings and electrode placements for the best pain relief.

KEY TERMS

Fibromyalgia—A condition characterized by aching and stiffness, fatigue and poor sleep, as well as tenderness at various sites on the body.

Osteoarthritis—A painful joint disease aggravated by mechanical stress.

Phantom limb—The perception that a limb is present (and throbbing with pain) after it has been amputated.

Post-herpetic neuralgia—Lingering pain that can last for years after an attack of shingles.

Sciatica—Pain that radiates along the sciatic nerve, extending from the buttock down the leg to the foot.

Temporomandibular joint pain (TMJ)—Pain and other symptoms affecting the head, jaw, and face that are caused when the jaw joints and muscles controlling them don't work together correctly.

Risks

TENS is nonaddictive and completely safe. The only side effect may be a slight skin irritation or redness in some people, which can be prevented by using different gels or electrodes.

Normal results

The amount of relief a person gets using TENS depends on the underlying cause of the pain, a person's mental state, and whether or not medication is also used. At least one study found that both a real TENS machine and a placebo were equally effective in reducing pain. This suggests that at least part of its effectiveness may be due to the patient's belief in its ability to ease pain.

Carol A. Turkington

Electrical stimulation of the brain

Definition

Electrical stimulation of the brain (ESB) is a relatively new technique used to treat chronic **pain** and

KEY TERMS

Infarction—A sudden insuffiency of local blood supply.

Neuralgia—Pain extending along one or more nerves.

Neuropathy—A functional disturbance or change in the nervous system.

Parkinson disease—A chronic neurological illness that causes tremors, stiffness, and difficulty in moving and walking.

tremors associated with **Parkinson disease**. ESB is administered by passing an electrical current through an electrode implanted in the brain.

Purpose

While the implantation of electrodes in the brain is used to treat or diagnose several disorders, the term ESB is limited here to the treatment of tremors, and as a **pain management** tool for patients suffering from back problems and other chronic injuries and illnesses.

Precautions

An ESB tremor control device, used in treating Parkinson patients, may interfere with or be affected by cardiac **pacemakers** and other medical equipment. As a result, patients with other implanted medical equipment may not be good candidates for the therapy.

Description

Electrical stimulation of the brain, or deep brain stimulation, is effective in treating tremors in up to 88% of Parkinson disease patients. An electrode is implanted into the thalamus (part of the brain) of the patient, and attached to an electric pulse generator via an extension wire. The pulse generator is implanted into the patient's pectoral, or chest area, and the extension wire is tunneled under the skin. The pulse generator sends out intermittent electrical stimulation to the electrode in the thalamus, which inhibits or partially relieves the tremor. The generator can be turned on and off with a magnet, and needs to be replaced every three to five years.

Similar methods have been used to treat chronic pain that responded unfavorably to conventional therapies. A remote transmitter allows these patients to trigger electric stimulation to relieve their symptoms on an as-needed basis. Patients with failed back syndrome, trigeminal neuropathy (pertaining to the fifth cranial nerve), and **peripheral neuropathy** fared well for pain control with this treatment, while patients with **spinal cord injury** and postherpetic neuralagia (pain along the nerves following herpes) did poorly.

Preparation

The patient should be free of any type of infection before undergoing an ESB procedure. He or she may be advised to discontinue any medication for a prescribed period of time before surgery.

Aftercare

After neurosurgery, patients should undergo regular head dressing changes, minimize exposure to others, and practice good personal hygiene in order to prevent a brain infection. The head may also be kept elevated for a prescribed period of time in order to decrease swelling of the brain.

Risks

The implantation of electrodes into the brain carries risks of hemorrhage, infarction, infection, and cerebral **edema**. These complications could cause irreversible neurological damage.

Patients with an implanted ESB tremor control device may experience headaches, disequilibrium (a disturbance of the sense of balance), burning or tingling of the skin, or partial **paralysis**.

Normal results

ESB is effective in pain control for specific conditions. It can provide long-term pain relief with few side effects or complications.

For the control of tremors a deep brain stimulator does provide some relief. It is recommended for patients with tremors severe enough to affect their quality of life.

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Electrocardiography

Definition

Electrocardiography is a commonly used, non-invasive procedure for recording electrical changes in the heart. The record, which is called an electrocardiogram (ECG or EKG), shows the series of waves that relate to the electrical impulses which occur during each beat of the heart. The results are printed on paper or displayed on a monitor. The waves in a normal record are named P, Q, R, S, and T and follow in alphabetical order. The number of waves may vary, and other waves may be present.

Purpose

Electrocardiography is a starting point for detecting many cardiac problems. It is used routinely in physical examinations and for monitoring the patient's condition during and after surgery, as well as during intensive care. It is the basic measurement used for tests such as **exercise** tolerance. It is used to evaluate causes of symptoms such as chest **pain**, **shortness of breath**, and **palpitations**.

This EKG strip shows evidence of Wolff-Parkinson-White syndrome. *(Custom Medical Stock Photo. Reproduced by permission.)*

An EKG strip indicting atrial flutter. *(Custom Medical Stock Photo. Reproduced by permission.)*

Precautions

No special precautions are required.

Description

The patient disrobes from the waist up, and electrodes (tiny wires in adhesive pads) are applied to specific sites on the arms, legs, and chest. When attached, the electrodes are called leads; three to 12 leads may be employed.

Muscle movement may interfere with the recording, which lasts for several beats of the heart. In cases where rhythm disturbances are suspected to be infrequent, the patient may wear a small Holter monitor in order to record continuously over a 24-hour period; this is known as ambulatory monitoring.

Preparation

The skin is cleaned to obtain good electrical contact at the electrode positions.

Aftercare

To avoid skin irritation from the salty gel used to obtain good electrical contact, the skin should be thoroughly cleaned after removal of the electrodes.

Risks

No complications from this procedure have been observed.

Normal results

When the heart is operating normally, each part contracts in a specific order. Contraction of the muscle is

A patient undergoing electrocardiography. *(Russell Curtis, Photo Researchers. Reproduced by permission.)*

triggered by an electrical impulse. These electrical impulses travel through specialized cells that form a conduction system. Following this pathway ensures that contractions will occur in a coordinated manner.

When the presence of all waves is observed in the electrocardiogram and these waves follow the order defined alphabetically, the heart is said to show a normal sinus rhythm, and impulses may be assumed to be following the regular conduction pathway.

The heart is described as showing arrhythmia or dysrhythmia when time intervals between waves, the order, or the number of waves do not fit this pattern. Other features that may be altered include the direction of wave deflection and wave widths.

In the normal heart, electrical impulses—at a rate of 60–100 times per minute—originate in the sinus node. The sinus node is located in the first chamber, known as the right atrium, where blood re-enters the heart. After traveling down to the junction between the upper and lower chambers, the signal stimulates the atrioventricular node. From here, after a delay, it passes by specialized routes through the lower chambers or ventricles. In many disease states, the passage of the electrical impulse can be interrupted in a variety of ways, causing the heart to perform less efficiently.

Abnormal results

Special training is required for interpretation of the electrocardiogram. To summarize the features used in interpretations in the simplest manner, the P wave of the electrocardiogram is associated with the contraction of the atria. The QRS series of waves, or QRS complex, is associated with ventricular contraction, with the T wave coming after the contraction. Finally, the P-Q or P-R interval gives a value for the time taken for the electrical impulse to travel from the atria to the ventricle (normally less than 0.2 sec).

KEY TERMS

Ambulatory monitoring—ECG recording over a prolonged period during which the patient can move around.

Arrhythmia or dysrhythmia—Abnormal rhythm in hearts that contract in an irregular way.

ECG or EKG—A record of the waves that relate to the electrical impulses produced at each beat of the heart.

Electrodes—Tiny wires in adhesive pads that are applied to the body for ECG measurement.

Fibrillation—Rapid, uncoordinated contractions of the upper or the lower chambers of the heart.

Lead—Name given the electrode when it is attached to the skin.

The cause of dysrhythmia is ectopic beats. Ectopic beats are premature heart beats that arise from a site other than the sinus node—commonly from the atria, atrioventricular node, or the ventricle. When these dysrhythmias are only occasional, they may produce no symptoms, or a feeling of the heart turning over or "flip-flopping" may be experienced. These occasional dysrhythmias are common in healthy people, but they also can be an indication of heart disease.

The varied sources of dysrhythmias provide a wide range of alterations in the form of the electrocardiogram. Ectopic beats that start in the ventricle display an abnormal QRS complex. This can indicate disease associated with insufficient blood supply to the muscle (myocardial **ischemia**). Multiple ectopic sites lead to rapid and uncoordinated contractions of the atria or ventricles. This condition is known as fibrillation. In atrial fibrillation, P waves are absent, and the QRS complex appears at erratic intervals, or "irregularly irregular."

When the atrial impulse fails to reach the ventricle, a condition known as **heart block** results. If this is partial, the P-R interval (the time for the impulse to reach the ventricle) is prolonged. If complete, the ventricles beat independently of the atria at about 40 beats per minute, and the QRS complex is mostly dissociated from the P wave.

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American Heart Association. 7320 Greenville Ave. Dallas, TX 75231. (214) 373-6300. <http://www.americanheart.org>.

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Electroconvulsive therapy

Definition

Electroconvulsive therapy (ECT) is a medical treatment for severe mental illness in which a small, carefully controlled amount of electricity is introduced into the brain. This electrical stimulation, used in conjunction with anesthesia and muscle relaxant medications, produces a mild generalized seizure or convulsion. While used to treat a variety of psychiatric disorders, it is most effective in the treatment of severe depression, and provides the most rapid relief currently available for this illness.

Purpose

The purpose of electroconvulsive therapy is to provide relief from the signs and symptoms of mental illnesses such as severe depression, **mania**, and **schizophrenia**. ECT is indicated when patients need rapid improvement because they are suicidal, self-injurious, refuse to eat or drink, cannot or will not take medication as prescribed, or present some other danger to themselves. Antidepressant medications, while effective in many cases, may take two to six weeks to produce a therapeutic effect. Antipsychotic medications used to treat mania and schizophrenia have many uncomfortable and sometimes dangerous side effects, limiting their use. In addition, some patients develop **allergies** and therefore are unable to take their medicine.

Precautions

The most common risks associated with ECT are disturbances in heart rhythm. Broken or dislocated bones occur very rarely.

Description

The treatment of severe mental illness, such as schizophrenia, using electroconvulsive therapy was introduced in 1938 by two Italian doctors named Cerletti and Bini. In those days many doctors believed that convulsions were incompatible with schizophrenia since, according to their obervations, this disease rarely occurred in individuals suffering from epilepsy. They concluded, therefore, that if convulsions could be artifically produced in patients with schizophrenia, the illness could be cured. Some doctors were already using a variety of chemicals to produce seizures, but many of their patients died or suffered severe injuries because the strength of the convulsions could not be well controlled.

Electroconvulsive therapy is among the most controversial of all procedures used to treat mental illness. When it was first introduced, many people were frightened simply because it was called "shock treatment." Many assumed the procedure would be painful, others thought it was a form of electrocution, and still others believed it would cause brain damage. Unfortunately, unfavorable publicity in newspapers, magazines, and movies added to these fears.

Indeed, in those early years, patients and families were rarely educated by doctors and nurses regarding this or other forms of psychiatric treatment. In addition, no anesthesia or **muscle relaxants** were used. As a result, patients had violent seizures, and even though they did not remember them, the procedure itself was frightening.

The way these treatments are given today is very different from the procedures used in the past. Currently, ECT is offered on both an inpatient and outpatient basis. Hospitals have specially equipped rooms with oxygen, suction, and **cardiopulmonary resuscitation** (**CPR**) in order to deal with the rare emergency.

The treatment is carried out as follows: approximately 30 minutes before the scheduled treatment time, the patient may receive an injection of a medication (such as atropine) that keeps the pulse rate from decreasing too much during the convulsion. Next, the patient is placed on a cot and hooked up to a machine that automatically takes and displays vital signs (temperature, pulse, respiration, and blood pressure) on a television-like monitor. A mild anesthetic is then injected into a vein, followed by a medication (such a Anectine) that relaxes all of the muscles in the body so that the seizure is mild, and the risk of broken bones is virtually eliminated.

When the patient is both relaxed and asleep, an airway is placed in the mouth to aid with breathing. Electrodes are placed on the sides of the head in the temple areas. An electric current is passed through the brain by means of a machine specifically designed for this pur-

pose. The usual dose of electricity is 70–150 volts for 0.1–0.5 seconds. In the first stage of the seizure (tonic phase), the muscles in the body that have not been paralyzed by medication contract for a period of five to 15 seconds. This is followed by the second stage (clonic phase) that is characterized by twitching movements, usually visible only in the toes or in a non-paralyzed arm or leg. These are caused by alternating contraction and relaxation of these same muscles. This stage lasts approximately 10–60 seconds. The entire procedure, from beginning to end, lasts about 30 minutes.

The total number of treatments a patient will receive depends upon many factors such as age, diagnosis, the history of illness, family support, and response to therapy. Patients with depression, for example, usually require six to 12 treatments. Treatments are usually administered every other day, three times a week.

The electrodes may be placed on both sides of the head (bilateral) or one side (unilateral). While bilateral ECT appears to be somewhat more effective, unilateral ECT is preferred for individuals who experience prolonged confusion or forgetfulness following treatment. Many doctors begin treatment with unilateral ECT, then change to bilateral if the patient is not improving.

Post-treatment confusion and forgetfulness are common, though disturbing symptoms associated with ECT. Doctors and nurses must be patient and supportive by providing patients with factual information about recovery. Elderly patients, for example, may become increasingly confused and forgetful as the treatments continue. These symptoms usually subside with time, but a small minority of patients state that they have never fully recovered from these effects.

With the introduction of antipsychotics in the 1950s, the use of ECT became less frequent. These new medications provided relief for untold thousands of patients who suffered greatly from their illness. However, there are a number of side effects associated with these drugs, some of which are irreversible. Another drawback is that some medications do not produce a therapeutic effect for two to six weeks. During this time the patient may present a danger to himself or others. In addition, there are patients who do not respond to medicine or who have severe allergic reactions. For these individuals, ECT may be the only treatment that will help.

Preparation

Patients and relatives are prepared for ECT by being shown video tapes that explain both the procedure and the risks involved. The physician then answers any questions these individuals may have, and the patient is asked to sign an "Informed Consent Form." This gives the doctor and the hospital permission to administer the treatment.

KEY TERMS

Mania—A mood disorder in which a person experiences prolonged elation or irritability characterized by overactivity that can lead to exhaustion and medical emergencies.

Relapse—A return of the signs and symptoms of an illness.

Schizophrenia—A severe mental illness in which a person has difficulty distinguishing what is real from what is not real. It is often characterized by hallucinations, delusions, and withdrawal from people and social activities.

Once the form is signed, the doctor performs a complete **physical examination**, and orders a number of tests that can help identify any potential problem. These tests may include a **chest x ray**, an electrocardiogram (ECG), **urinalysis**, spinal x ray, brain wave (EEG), and complete **blood count** (CBC).

Some medications, such as lithium and a type of antidepressant known as **monoamine oxidase inhibitors**, should be discontinued for some time before treatment. Patients are instructed not to eat or drink for at least eight hours prior to the procedure in order to reduce the possibility of vomiting and **choking**.

Aftercare

After the treatment, patients are moved to a recovery area. Vital signs are recorded every five minutes until the patient is fully awake, which may take 15–30 minutes. Some initial confusion may be present but usually disappears in a matter of minutes. There may be complaints of **headache**, muscle **pain**, or back pain. Such discomfort is quickly relieved by mild medications such as **aspirin**.

Risks

Advanced medical technology has substantially reduced the complications associated with ECT. These include slow heart beat (bradycardia), rapid heart beat (tachycardia), memory loss, and confusion. Persons at high risk for ECT include those with recent **heart attack**, uncontrolled blood pressure, brain tumors, and previous spinal injuries.

Normal results

ECT often produces dramatic improvement in the signs and symptoms of major depression, especially in

elderly individuals, sometimes during the first week of treatment. While it is estimated that 50% of these patients will experience a future return of symptoms, the prognosis for each episode of illness is good. Mania also often responds well to treatment. The picture is not as bright for schizophrenia, which is more difficult to treat and is characterized by frequent relapses.

A few patients are placed on maintenance ECT. This means they return to the hospital every one to two months, as needed, for an additional treatment. These individuals are thus able to keep their illness under control and lead a normal and productive life.

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National Institutes of Health. 5600 Fishers Lane. Room 7CO2, Rockville, MD 20857. (301) 496-4000. <http://www.nih.gov>.

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Electrocution *see* **Electric shock injuries**

Electroencephalography

Definition

Electroencephalography, or EEG, is a neurological test that uses an electronic monitoring device to measure and record electrical activity in the brain.

Purpose

The EEG is a key tool in the diagnosis and management of epilepsy and other seizure disorders. It is also used to assist in the diagnosis of brain damage and disease (e.g., **stroke**, tumors, **encephalitis**), **mental retardation**, **sleep disorders**, degenerative diseases such as **Alzheimer's disease** and **Parkinson's disease**, and certain mental disorders (e.g., **alcoholism**, **schizophrenia**, **autism**).

An EEG may also be used to monitor brain activity during surgery and to determine brain **death**.

Precautions

Electroencephalography should be administered and interpreted by a trained medical professional only. Data from an EEG is only one element of a complete medical and/or psychological patient assessment, and should never be used alone as the sole basis for a diagnosis.

Description

Before the EEG begins, a nurse or technician attaches approximately 16–20 electrodes to the patient's scalp with a conductive, washable paste. Depending on the purpose for the EEG, implantable or invasive electrodes are occasionally used. Implantable electrodes include sphenoidal electrodes, which are fine wires inserted under the zygomatic arch, or cheekbone; and depth electrodes, which are surgically-implanted into the brain. The EEG electrodes are painless, and are used to measure the electrical activity in various regions of the brain.

For the test, the patient lies on a bed, padded table, or comfortable chair and is asked to relax and remain still during the EEG testing period. An EEG usually takes no more than one hour. During the test procedure, the patient may be asked to breathe slowly or quickly; visual stimuli such as flashing lights or a patterned board may be used to stimulate certain types of brain activity. Throughout the procedure, the electroencephalograph machine makes a continuous graphic record of the patient's brain activity, or brainwaves, on a long strip of recording paper or on a computer screen. This graphic record is called an electroencephalogram.

The sleep EEG uses the same equipment and procedures as a regular EEG. Patients undergoing a sleep EEG are encouraged to fall asleep completely rather than just relax. They are typically provided a bed and a quiet room conducive to sleep. A sleep EEG lasts up to three hours.

In an ambulatory EEG, patients are hooked up to a portable cassette recorder. They then go about their normal activities, and take their normal rest and sleep for a period of up to 24 hours. During this period, the patient and patient's family record any symptoms or abnormal behaviors, which can later be correlated with the EEG to see if they represent seizures.

Many insurance plans provide reimbursement for EEG testing. Costs for an EEG range from $100 to more than $500, depending on the purpose and type of test (i.e., asleep or awake, and invasive or non-invasive electrodes). Because coverage may be dependent on the dis-

This woman is undergoing an electroencephalogram (EEG) to diagnose Alzheimer's disease. On the computer screen at the right are the colored scans of the electrical activity in her brain. Alzheimer's patients show a specific abnormality in their EEGs. *(Photograph by Catherine Pouedras, Photo Researchers, Inc. Reproduced by permission.)*

order or illness the EEG is evaluating, patients should check with their individual insurance plan.

Preparation

Full instructions should be given to EEG patients when they schedule their test. Typically, individuals on medications that affect the central nervous system, such as anticonvulsants, stimulants, or antidepressants, are told to discontinue their prescription for a short time prior to the test (usually one to two days). Patients may be asked to avoid food and beverages that contain **caffeine**, a central nervous system stimulant. However, any such request should be cleared by the treating physician. Patients may also be asked to arrive for the test with clean hair free of spray or other styling products.

Patients undergoing a sleep EEG may be asked to remain awake the night before their test. They may be given a sedative prior to the test to induce sleep.

Aftercare

If the patient has suspended regular medication for the test, the EEG nurse or technician should advise him when he can begin taking it again.

Risks

Being off medication for one to two days may trigger seizures. Certain procedures used during EEG may trigger seizures in patients with epilepsy. Those procedures include flashing lights and deep breathing. If the EEG is being used as a diagnostic for epilepsy (i.e., to determine the type of seizures an individual is suffering from), this may be a desired effect, although the patient needs to be monitored closely so that the seizure can be aborted if necessary. This type of test is known as an ictal EEG.

Normal results

In reading and interpreting brainwave patterns, a neurologist or other physician will evaluate the type of brainwaves and the symmetry, location, and consistency of brainwave patterns. He will also look at the brainwave response to certain stimuli presented during the EEG test (such as flashing lights or noise). There are four basic types of brainwaves: alpha, beta, theta, and delta. "Normal" brainwave patterns vary widely, depending on factors of age and activity. For example, awake and relaxed individuals typically register an alpha wave pattern of eight to 13 cycles per second. Young

KEY TERMS

Epilepsy—A neurological disorder characterized by recurrent seizures with or without a loss of consciousness.

Ictal EEG—Used to measure brain activity during a seizure. May be useful in learning more about patients who aren't responding to conventional treatments.

children and sleeping adults may have a delta wave pattern of under four cycles per second.

Abnormal results

The EEG readings of patients with epilepsy or other seizure disorders display bursts or spikes of electrical activity. In focal epilepsy, spikes are restricted to one hemisphere of the brain. If spikes are generalized to both hemispheres of the brain, multifocal epilepsy may be present.

The diagnostic brainwave patterns of other disorders varies widely. The appearance of excess theta waves (four to eight cycles per second) may indicate brain injury. Brain wave patterns in patients with brain disease, mental retardation, and brain injury show overall slowing. A trained medical specialist should interpret EEG results in the context of the patient's medical history, and other pertinent medical test results.

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Paula Anne Ford-Martin

Electrolyte disorders

Definition

An electrolyte disorder is an imbalance of certain ionized salts (i.e., bicarbonate, calcium, chloride, magnesium, phosphate, potassium, and sodium) in the blood.

Description

Electrolytes are ionized molecules found throughout the blood, tissues, and cells of the body. These molecules, which are either positive (cations) or negative (anions), conduct an electric current and help to balance pH and acid-base levels in the body. Electrolytes also facilitate the passage of fluid between and within cells through a process known as *osmosis* and play a part in regulating the function of the neuromuscular, endocrine, and excretory systems.

The serum electrolytes include:

- Sodium (Na). A positively charged electrolyte that helps to balance fluid levels in the body and facilitates neuromuscular functioning.
- Potassium (K). A main component of cellular fluid, this positive electrolyte helps to regulate neuromuscular function and osmotic pressure.
- Calcium (Ca). A cation, or positive electrolyte, that affects neuromuscular performance and contributes to skeletal growth and blood coagulation.
- Magnesium (Mg). Influences muscle contractions and intracellular activity. A cation.
- Chloride (CI). An anion, or negative electrolyte, that regulates blood pressure.
- Phosphate (HPO4). Negative electrolyte that impacts metabolism and regulates acid-base balance and calcium levels.
- Bicarbonate (HCO3). A negatively charged electrolyte that assists in the regulation of blood pH levels. Bicarbonate insufficiencies and elevations cause acid-base disorders (i.e., acidosis, alkalosis).

Medications, chronic diseases, and trauma (i.e., **burns**, **fractures, etc.**) may cause the concentration of certain electrolytes in the body to become too high (hyper-) or too low (hypo-). When this happens, an electrolyte imbalance, or disorder, results.

Causes and symptoms

Sodium

HYPERNATREMIA. Sodium helps the kidneys to regulate the amount of water the body retains or excretes. Consequently, individuals with elevated serum sodium levels also suffer from a loss of fluids, or **dehydration**. **Hypernatremia** can be caused by inadequate water intake, excessive fluid loss (i.e., **diabetes insipidus**, kidney disease, severe burns, and prolonged vomiting or **diarrhea**), or sodium retention (caused by excessive sodium intake or aldosteronism). In addition, certain drugs,

including loop **diuretics**, **corticosteroids**, and antihypertensive medications may cause elevated sodium levels.

Symptoms of hypernatremia include:

- thirst
- orthostatic hypotension
- dry mouth and mucous membranes
- dark, concentrated urine
- loss of elasticity in the skin
- irregular heartbeat (tachycardia)
- irritability
- fatigue
- lethargy
- heavy, labored breathing
- muscle twitching and/or seizures

HYPONATREMIA. Up to 1% of all hospitalized patients develop **hyponatremia**, making it one of the most common electrolyte disorders. Diuretics, certain psychoactive drugs (i.e., fluoxetine, sertraline, haloperidol), specific antipsychotics (lithium), vasopressin, chlorpropamide, the illicit drug "ecstasy", and other pharmaceuticals can cause decreased sodium levels, or hyponatremia. Low sodium levels may also be triggered by inadequate dietary intake of sodium, excessive perspiration, water intoxication, and impairment of adrenal gland or kidney function.

Symptoms of hyponatremia include:

- nausea, abdominal cramping, and/or vomiting
- headache
- edema (swelling)
- muscle weakness and/or tremor
- paralysis
- disorientation
- slowed breathing
- seizures
- **coma**

Potassium

HYPERKALEMIA. **Hyperkalemia** may be caused by ketoacidosis (diabetic coma), myocardial infarction (**heart attack**), severe burns, kidney failure, **fasting**, **bulimia nervosa**, gastrointestinal bleeding, adrenal insufficiency, or **Addison's disease**. Diuretic drugs, cyclosporin, lithium, heparin, ACE inhibitors, **beta blockers**, and trimethoprim can increase serum potassium levels, as can heavy **exercise**. The condition may also be secondary to hypernatremia (low serum concentrations of sodium). Symptoms may include:

- weakness
- nausea and/or abdominal pain
- irregular heartbeat (arrhythmia)
- diarrhea
- muscle pain

HYPOKALEMIA. Severe dehydration, aldosteronism, **Cushing's syndrome**, kidney disease, long-term diuretic therapy, certain **penicillins**, laxative abuse, congestive **heart failure**, and adrenal gland impairments can all cause depletion of potassium levels in the bloodstream. A substance known as glycyrrhetinic acid, which is found in licorice and chewing tobacco, can also deplete potassium serum levels. Symptoms of **hypokalemia** include:

- weakness
- paralysis
- increased urination
- irregular heartbeat (arrhythmia)
- orthostatic hypotension
- muscle pain
- tetany

Calcium

HYPERCALCEMIA. Blood calcium levels may be elevated in cases of thyroid disorder, **multiple myeloma**, metastatic **cancer**, multiple bone fractures, milk-alkali syndrome, and Paget's disease. Excessive use of calcium-containing supplements and certain over-the-counter medications (i.e., **antacids**) may also cause **hypercalcemia**. Symptoms include:

- fatigue
- constipation
- depression
- confusion
- muscle pain
- nausea and vomiting
- dehydration
- increased urination
- irregular heartbeat (arrhythmia)

HYPOCALCEMIA. Thyroid disorders, kidney failure, severe burns, **sepsis**, **vitamin D deficiency**, and medications such as heparin and glucogan can deplete blood calcium levels. Lowered levels cause:

- muscle cramps and spasms
- tetany and/or convulsions
- mood changes (depression, irritability)
- dry skin

- brittle nails
- facial twitching

Magnesium

HYPERMAGNESEMIA. Excessive magnesium levels may occur with end-stage renal disease, Addison's disease, or an overdose of magnesium salts. Hypermagnesemia is characterized by:

- lethargy
- hypotension
- decreased heart and respiratory rate
- muscle weakness
- diminished tendon reflexes

HYPOMAGNESEMIA. Inadequate dietary intake of magnesium, often caused by chronic **alcoholism** or **malnutrition**, is a common cause of hypomagnesemia. Other causes include malabsorption syndromes, **pancreatitis**, aldosteronism, burns, **hyperparathyroidism**, digestive system disorders, and diuretic use. Symptoms of low serum magnesium levels include:

- leg and foot cramps
- weight loss
- vomiting
- muscle spasms, twitching, and tremors
- seizures
- muscle weakness
- arrthymia

Chloride

HYPERCHLOREMIA. Severe dehydration, kidney failure, hemodialysis, traumatic brain injury, and aldosteronism can also cause hyperchloremia. Drugs such as boric acid and ammonium chloride and the intravenous (IV) infusion of sodium chloride can also boost chloride levels, resulting in hyperchloremic **metabolic acidosis**. Symptoms include:

- weakness
- headache
- nausea
- cardiac arrest

HYPOCHLOREMIA. Hypochloremia usually occurs as a result of sodium and potassium depletion (i.e., hyponatremia, hypokalemia). Severe depletion of serum chloride levels causes *metabolic alkalosis*. This alkalization of the bloodstream is characterized by:

- mental confusion
- slowed breathing
- paralysis
- muscle tension or spasm

Phosphate

HYPERPHOSPHATEMIA. Skeletal fractures or disease, kidney failure, **hypoparathyroidism**, hemodialysis, **diabetic ketoacidosis**, acromegaly, systemic infection, and intestinal obstruction can all cause phosphate retention and build-up in the blood. The disorder occurs concurrently with **hypocalcemia**. Individuals with mild hyperphosphatemia are typically asymptomatic, but signs of severe hyperphosphatemia include:

- tingling in hands and fingers
- muscle spasms and cramps
- convulsions
- cardiac arrest

HYPOPHOSPHATEMIA. Serum phosphate levels of 2 mg/dL or below may be caused by hypomagnesemia and hypokalemia. Severe burns, alcoholism, diabetic ketoacidosis, kidney disease, hyperparathyroidism, **hypothyroidism**, Cushing's syndrome, malnutrition, hemodialysis, vitamin D deficiency, and prolonged diuretic therapy can also diminish blood phosphate levels. There are typically few physical signs of mild phosphate depletion. Symptoms of severe hypophosphatemia include:

- muscle weakness
- weight loss
- bone deformities (osteomalacia)

Diagnosis

Diagnosis is performed by a physician or other qualified healthcare provider who will take a medical history, discuss symptoms, perform a complete **physical examination**, and prescribe appropriate laboratory tests. Because electrolyte disorders commonly affect the neuromuscular system, the provider will test reflexes. If a calcium imbalance is suspected, the physician will also check for Chvostek's sign, a reflex test that triggers an involuntary facial twitch, and Trousseau's sign, a muscle spasm that occurs in response to pressure on the upper arm.

Serum electrolyte imbalances can be detected through blood tests. Blood is drawn from a vein on the back of the hand or inside of the elbow by a medical technician, or phlebotomist, and analyzed at a lab.

Normal levels of electrolytes are:

- Sodium. 135–145 mEq/L (serum)
- Potassium. 3.5–5.5 mEq/L (serum)

KEY TERMS

Acid-base balance—A balance of acidity and alkalinity of fluids in the body that keeps the pH level of blood around 7.35–7.45.

Aldosteronism—A condition defined by high serum levels of aldosterone, a hormone secreted by the adrenal gland that is responsible for increasing sodium reabsorption in the kidneys.

Addison's disease—A disease characterized by a deficiency in adrenocortical hormones due to destruction of the adrenal gland.

Bulimia nervosa—An eating disorder characterized by binging and purging (self-induced vomiting) behaviors.

Milk-alkali syndrome—Elevated blood calcium levels and alkalosis caused by excessive intake of milk and alkalis. Usually occurs in the treatment of peptic ulcer.

Orthostatic hypotension—A drop in blood pressure that causes faintness or dizziness and occurs when one rises to a standing position. Also known as postural hypotension.

Osmotic pressure—Pressure that occurs when two solutions of differing concentrations are separated by a semipermeable membrane, such as a cellular wall, and the lower concentration solute is drawn across the membrane into the higher concentration solute (osmosis).

Tetany—A disorder of the nervous system characterized by muscle cramps, spasms of the arms and legs, and numbness of the extremities.

- Calcium. 8.8–10.4 mg/dL (total Ca; serum); 4.7–5.2 mg/dL (unbound Ca; serum)
- Magnesium. 1.4–2.1 mEq/L (plasma)
- Chloride. 100–108 mEq/L (serum)
- Phosphate. 2.5–4.5 mg/dL (plasma; adults)

Standard ranges for test results may vary due to differing laboratory standards and physiological variances (i.e., gender, age, and other factors). Other blood tests that determine pH levels and acid-base balance may also be performed.

Treatment

Treatment of electrolyte disorders depends on the underlying cause of the problem and the type of electrolyte involved. If the disorder is caused by poor diet or improper fluid intake, nutritional changes may be prescribed. If medications such as diuretics triggered the imbalance, discontinuing or adjusting the drug therapy may effectively treat the condition. Fluid and electrolyte replacement therapy, either intravenously or by mouth, can reverse electrolyte depletion.

Hemodialysis treatment may be required to reduce serum potassium levels in hyperkalemic patients with impaired kidney function. It may also be recommended for renal patients suffering from severe hypermagnesemia.

Prognosis

A patient's long-term prognosis depends upon the root cause of the electrolyte disorder. However, when treated quickly and appropriately, electrolyte imbalances in and of themselves are usually effectively reversed.

When they are mild, some electrolyte imbalances have few to no symptoms and may pass unnoticed. For example, transient hyperphosphatemia is usually fairly benign. However, long-term elevations of blood phosphate levels can lead to potentially fatal soft tissue and vascular calcifications and bone disease, and severe serum phosphate deficiencies (hypophosphatemia) can cause encephalopathy, coma, and **death**.

Severe hypernatremia has a mortality rate of 40–60%. Death is commonly due to cerebrovascular damage and hemorrhage resulting from dehydration and shrinkage of the brain cells.

Prevention

Physicians should use caution when prescribing drugs known to affect electrolyte levels and acid-base balance. Individuals with kidney disease, thyroid problems, and other conditions that may place them at risk for developing an electrolyte disorder should be educated on the signs and symptoms.

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Paula Ford-Martin

Electrolyte tests

Definition

Electrolytes are positively and negatively charged molecules, called ions, that are found within cells, between cells, in the bloodstream, and in other fluids throughout the body. Electrolytes with a positive charge include sodium, potassium, calcium, and magnesium; the negative ions are chloride, bicarbonate, and phosphate. The concentrations of these ions in the bloodstream remain fairly constant throughout the day in a healthy person. Changes in the concentration of one or more of these ions can occur during various acute and chronic disease states and can lead to serious consequences.

Purpose

Tests that measure the concentration of electrolytes are useful in the emergency room and to obtain clues for the diagnosis of specific diseases. Electrolyte tests are used for diagnosing dietary deficiencies, excess loss of nutrients due to urination, vomiting, and **diarrhea**, or abnormal shifts in the location of an electrolyte within the body. When an abnormal electrolyte value is detected, the physician may either act to immediately correct the imbalance directly (in the case of an emergency) or run further tests to determine the underlying cause of the abnormal electrolyte value. Electrolyte disturbances can occur with malfunctioning of the kidney (renal failure), infections that produce severe and continual diarrhea or vomiting, drugs that cause loss of electrolytes in the urine (**diuretics**), **poisoning** due to accidental consumption of electrolytes, or diseases involving hormones that regulate electrolyte concentrations.

Precautions

Electrolyte tests are performed from routine blood tests. The techniques are simple, automated, and fairly uniform throughout the United States. During the preparation of blood plasma or serum, health workers must take care not to break the red blood cells, especially when testing for serum potassium. Because the concentration of potassium within red blood cells is much higher than in the surrounding plasma or serum, broken cells would cause falsely elevated potassium levels.

Description

Electrolyte tests are typically conducted on blood plasma or serum, urine, and diarrheal fluids. Electrolytes can be classified in at least five different ways. One way is that some electrolytes tend to exist mostly inside cells, or are intracellular, while others tend to be outside cells, or are extracellular. Potassium, phosphate, and magnesium occur at much greater levels inside the cell than outside, while sodium and chloride occur at much greater levels extracellularly. A second classification distinguishes those electrolytes that participate directly in the transmission of nerve impulses and those that do not. Sodium, potassium, and calcium are the important electrolytes involved in nerve impulses, and disorders affecting them are most closely associated with neurological disorders. A third classification focuses on electrolytes that are able to form a tight union, or complex, with one another. Calcium and phosphate have the greatest tendency to form complexes with each other. Disorders that cause an increase in either plasma calcium or phosphate can result in the deposit of calcium-phosphate crystals in the soft tissues of the body. A fourth classification concerns those electrolytes that influence the acidity or alkalinity of the bloodstream, also known as the pH. The pH of the bloodstream is normally in the range of 7.35–7.45. A decrease below this range is called acidosis, while a pH above this range is called alkalosis. The electrolytes most closely associated with the pH of the bloodstream are bicarbonate, chloride, and phosphate.

Preparation

All electrolyte tests can be performed on plasma or serum. Plasma is prepared by withdrawing a blood sample and placing it in a test tube containing a chemical that prevents blood from clotting (an anticoagulant). Serum is prepared by withdrawing a blood sample, placing it in a test tube, and allowing it to clot. The blood spontaneously clots within a minute of withdrawing the blood from a vein. The serum or plasma is then rapidly spun with a centrifuge in order to remove the blood cells or clot.

Normal results

Electrolyte concentrations are similar whether measured in serum or plasma. Values can be expressed in terms of weight per unit volume (mg/deciliter; mg/dL) or in the number of molecules in a volume, or molarity (moles or millimoles/liter; M or mM). The range of normal values sometimes varies slightly between different age groups, for males and females, and between different analytical laboratories.

The normal level of serum sodium is in the range of 136–145 mM. The normal levels of serum potassium are 3.5–5.0 mM. Note that sodium occurs at a much higher concentration than potassium. The normal concentration of total serum calcium (bound calcium plus free calcium) is in the range of 8.8–10.4 mg/dL. About 40% of the total calcium in the plasma is loosely bound to proteins; this

calcium is referred to as bound calcium. The normal range of free calcium is 4.8–5.2 mg/dL. The normal concentration of serum magnesium is in the range of 2.0–3.0 mg/dL.

The normal concentration range of chloride is 350–375 mg/dL or 98–106 mM. The normal level of phosphate, as expressed as the concentration of phosphorus, is 2.0–4.3 mg/dL. Bicarbonate is an electrolyte that is freely and spontaneously interconvertable with carbonic acid and carbon dioxide. The normal concentration of carbonic acid (H_2CO_3) is about 1.35 mM. The normal concentration of bicarbonate (HCO_3^-) is about 27 mM. The concentration of total carbon dioxide is the sum of carbonic acid and bicarbonate; this sum is normally in the range of 26–28 mM. The ratio of bicarbonate/carbonic acid is more significant than the actual concentrations of these two forms of carbon dioxide. Its normal value is 27/1.35 (equivalent to 20/1).

Abnormal results

Positively charged electrolytes

High serum sodium levels (**hypernatremia**) occur at sodium concentrations over 145 mM, with severe hypernatremia over 152 mM. Hypernatremia is usually caused by diseases that cause excessive urination. In these cases, water is lost, but sodium is still retained in the body. The symptoms include confusion and can lead to convulsions and **coma**. Low serum sodium levels (**hyponatremia**) are below 130 mM, with severe hyponatremia at or below 125 mM. Hyponatremia often occurs with severe diarrhea, with losses of both water and sodium, but with sodium loss exceeding water loss. Hyponatremia provokes clinical problems only if serum sodium falls below 125 mM, especially if this has occurred rapidly. The symptoms can be as mild as tiredness but may lead to convulsions and coma.

High serum potassium (**hyperkalemia**) occurs at potassium levels above 5.0 mM; it is considered severe over 8.0 mM. Hyperkalemia is relatively uncommon, but sometimes occurs in patients with kidney failure who take potassium supplements. Hyperkalemia can result in abnormal beating of the heart (cardiac **arrhythmias**). Low serum potassium (**hypokalemia**) occurs when serum potassium falls below 3.0 mM. It can result from low dietary potassium, as during **starvation** or in patients with **anorexia nervosa**; from excessive losses via the kidneys, as caused by diuretic drugs; or by diseases of the adrenal or pituitary glands. Mild hypokalemia causes muscle weakness, while severe hypokalemia can cause **paralysis**, the inability to breathe, and cardiac arrhythmias.

High levels of calcium ions (**hypercalcemia**) occur at free calcium ion concentrations over 5.2 mg/dL or total serum calcium above 10.4 mg/dL. Hypercalcemia usually occurs when the body dissolves bone at an abnormally fast rate, increasing both serum calcium and serum phosphate. Sudden hypercalcemia can cause vomiting and coma, while prolonged and moderate hypercalcemia results in the deposit of calcium phosphate crystals in the kidneys and eye. **Hypocalcemia** occurs when serum free calcium ions fall below 4.4 mg/dL, or when total serum calcium falls below 8.8 mg/dL. Hypocalcemia can result from **hypoparathyroidism** (low parathyroid hormone), from failure to produce 1,25-dihydroxyvitamin D, from low levels of plasma magnesium, and from phosphate poisoning (the phosphate enters the bloodstream and forms a complex with the free serum calcium). Hypocalcemia can cause depression and muscle spasms.

Hypermagnesemia occurs at serum magnesium levels over 25 mM (60 mg/dL). Hypermagnesemia is rare but can occur with the excessive consumption of magnesium salts. Hypomagnesemia occurs when serum magnesium levels fall below 0.8 mM, and can result from poor **nutrition**. Chronic **alcoholism** is the most common cause of hypomagnesemia, in part because of poor diet. Magnesium levels below 0.5 mM (1.2 mg/dL) cause serum calcium levels to decline. Some of the symptoms of hypomagnesemia, including twitching and convulsions, actually result from the concurrent hypocalcemia. Hypomagnesemia can also result in hypokalemia and thereby cause cardiac arrhythmias.

Negatively charged electrolytes

Serum chloride levels sometimes increase to abnormal levels as an undesirable side effect of medical treatment with sodium chloride or ammonium chloride. The toxicity of chloride results not from the chloride itself, but from the fact that the chloride occurs as the acid, hydrogen chloride (more commonly known as hydrochloric acid, or HCl). An overdose of chloride may cause the accumulation of hydrochloric acid in the bloodstream, with consequent acidosis. **Renal tubular acidosis**, one of many kidney diseases, involves the failure to release acid into the urine. The acidosis produces weakness, **headache**, nausea, and cardiac arrest. Low plasma chloride leads to the opposite situation: a decline in the acid content of the bloodstream. This is known as alkalization of the bloodstream, or alkalosis. Hydrochloric acid, originally from extracellular fluids, can be lost by vomiting. At its most severe, alkalosis results in paralysis (tetany).

Hyperphosphatemia occurs at serum phosphate levels above 5 mg/dL. It can result from the failure of the kidneys to excrete phosphate into the urine, causing phosphate to accumulate in the bloodstream. Hyperphosphatemia can also be caused by the impaired action of parathyroid hormone and by phosphate poisoning. Severe hyperphos-

phatemia can cause paralysis, convulsions, and cardiac arrest. These symptoms result because the phosphate, occurring in elevated levels, complexes with free serum calcium, resulting in hypocalcemia. Tests for heart function (an electrocardiogram) and parathyroid hormone levels are used in the diagnosis of hyperphosphatemia. Hypophosphatemia occurs if serum phosphorus falls to 2.0 mg/dL or lower. It often results from a shift of inorganic phosphate from the bloodstream to various organs and tissues. This shift can be caused by a rise in pH (alkalization) of the bloodstream, which can occur during hyperventilation, a reaction in various disease states. A shift in phosphate to intracellular tissues may draw calcium away from the bloodstream via the formation of insoluble calcium phosphate crystals within cells, with consequent hypocalcemia. Thus, tests for abnormalities in phosphate metabolism also involve tests for serum calcium.

Bicarbonate metabolism involves several compounds. When dietary starches, sugars, and fats are broken down for energy production, carbon dioxide is created. Much of this carbon dioxide (CO_2) spontaneously converts to carbonic acid (H_2CO_3), and some of the carbonic acid spontaneously converts to bicarbonate (HCO_3^-) plus a hydrogen ion (H^+). Eventually, almost every molecule of carbon dioxide produced in the body, whether in the form of carbon dioxide, carbonic acid, or bicarbonate, must convert back to carbon dioxide in order to leave via the lungs during normal breathing.

If one holds one's breath, carbon dioxide cannot escape from the lungs, but continues to be generated within the body. This results in an increase in production of carbonic acid. A portion of the carbonic acid breaks apart (dissociates), causing an increase in hydrogen ions in the plasma, with a resulting acidosis. Tests for serum bicarbonate levels are accompanied by tests for acidosis (pH test). Conversely, when one breathes too rapidly (hyperventilation), the carbon dioxide is drawn off from the bloodstream and expelled in the breath at an increased rate. This results in an increase in the rate of combination of bicarbonate with hydrogen ions, resulting in alkalosis. Acidosis and alkalosis can be produced by means other than by altering the rate of breathing. The carbonic acid and bicarbonate in the bloodstream minimize (or buffer) any trend to acidosis or alkalosis. Tests for bicarbonate are generally accompanied by tests for blood pH and possibly tests for kidney malfunction, abnormal hormone function, or gastrointestinal disorders.

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Tom Brody, PhD

Electromyography

Definition

Electromyography (EMG) is an electrical recording of muscle activity that aids in the diagnosis of neuromuscular disease.

Purpose

Muscles are stimulated by signals from nerve cells called motor neurons. This stimulation causes electrical activity in the muscle, which in turn causes contraction. This electrical activity is detected by a needle electrode inserted into the muscle and connected to a recording device. Together, the electrode and recorder are called an electromyography machine. EMG can determine whether a particular muscle is responding appropriately to stimulation, and whether a muscle remains inactive when not stimulated.

EMG is performed most often to help diagnose different diseases causing weakness. Although EMG is a test of the motor system, it may help identify abnormalities of nerves or spinal nerve roots that may be associated with **pain** or numbness. Other symptoms for which EMG may be useful include numbness, atrophy, stiffness, fasciculation, cramp, deformity, and spasticity. EMG results can help determine whether symptoms are due to a muscle disease or a neurological disorder, and, when combined with clinical findings, usually allow a confident diagnosis.

EMG can help diagnose many muscle and nerve disorders, including:

- muscular dystrophy
- congenital **myopathies**
- mitochondrial myopathies

KEY TERMS

Motor neurons—Nerve cells that transmit signals from the brain or spinal cord to the muscles.

Motor unit action potentials—Spikes of electrical activity recorded during an EMG that reflect the number of motor units (motor neurons and the muscle fibers they transmit signals to) activated when the patient voluntarily contracts a muscle.

- metabolic myopathies
- myotonias
- peripheral neuropathies
- radiculopathies
- nerve lesions
- amyotrophic lateral sclerosis
- polio
- spinal muscular atrophy
- guillain-Barré syndrome
- ataxias
- myasthenias

Precautions

No special precautions are needed for this test. Patients with a history of bleeding disorder should consult with their treating physician before the test. If a muscle biopsy is planned as part of the diagnostic work-up, EMG should not be performed at the same site, as it may effect the microscopic appearance of the muscle.

Description

During an EMG test, a fine needle is inserted into the muscle to be tested. This may cause some discomfort, similar to that of an injection. Recordings are made while the muscle is at rest, and then during the contraction. The person performing the test may move the limb being tested, and direct the patient to move it with various levels of force. The needle may be repositioned in the same muscle for further recording. Other muscles may be tested as well. A typical session lasts from 30–60 minutes.

A slightly different test, the *nerve conduction velocity test*, is often performed at the same time with the same equipment. In this test, stimulating and recording electrodes are used, and small electrical shocks are applied to measure the ability of the nerve to conduct electrical signals. This test may cause mild tingling and discomfort similar to a mild **shock** from static electricity. Evoked potentials may also be performed for additional diagnostic information. Nerve conduction velocity and evoked potential testing are especially helpful when pain or sensory complaints are more prominent than weakness.

Preparation

No special preparation is needed. The doctor supervising and interpreting the test should be given information about the symptoms, medical conditions, suspected diagnosis, neuroimaging studies, and other test results.

Aftercare

Minor pain and bleeding may continue for several hours after the test. The muscle may be tender for a day or two.

Risks

There are no significant risks to this test, other than those associated with any needle insertion (pain, bleeding, bruising, or infection).

Normal results

There should be some brief EMG activity during needle insertion. This activity may be increased in diseases of the nerve and decreased in long-standing muscle disorders where muscle tissue is replaced by fibrous tissue or fat. Muscle tissue normally shows no EMG activity when at rest or when moved passively by the examiner. When the patient actively contracts the muscle, spikes (motor unit action potentials) should appear on the recording screen, reflecting the electrical activity within. As the muscle is contracted more forcefully, more groups of muscle fibers are recruited or activated, causing more EMG activity.

Abnormal results

The interpretation of EMG results is not a simple matter, requiring analysis of the onset, duration, amplitude, and other characteristics of the spike patterns.

Electrical activity at rest is abnormal; the particular pattern of firing may indicate denervation (for example, a nerve lesion, radiculopathy, or lower motor neuron degeneration), myotonia, or inflammatory myopathy.

Decreases in the amplitude and duration of spikes are associated with muscle diseases, which also show faster recruitment of other muscle fibers to compensate for weakness. Recruitment is reduced in nerve disorders.

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Richard Robinson

Electronic fetal monitoring

Definition

Electronic fetal monitoring (EFM) is a method for examining the condition of a baby in the uterus by noting any unusual changes in its heart rate. Electronic fetal monitoring is performed late in **pregnancy** or continuously during labor to ensure normal delivery of a healthy baby. EFM can be utilized either externally or internally in the womb.

Purpose

The heart rate of a fetus undergoes constant adjustment as it responds to its environment and other stimuli. The fetal monitor records an unborn baby's heart rate and graphs it on a piece of paper. Electronic fetal monitoring is usually advised for high-risk pregnancies, when the baby is in danger of distress. Specific reasons for EFM include: babies in a breech position, **premature labor**, and induced labor, among others.

When electronic fetal monitoring was originally introduced in the 1960s and 1970s, the hope was that it would help physicians diagnose fetal hypoxia, or lack of oxygen, in time to prevent damage to the baby. This lack of oxygen, also known as perinatal asphyxia or birth asphyxia, is an important cause of **stillbirth** and newborn deaths. It occurs when there are less than normal amounts of oxygen delivered to the body or an organ and there is build-up of carbon dioxide in the body or tissue. A lack of blood flow to an organ can cause asphyxia. Perinatal asphyxia can occur a long time before birth, shortly before birth, during delivery, or after birth. If the interruption to the supply of oxygen is short, the baby may recover without any damage. If the time is longer, there may be some injury that is reversible. If the time period without oxygen is very long, there may be permanent injury to one or more organs of the body. It is important, to detect any signs of asphyxia as soon as possible. One of the signs is an abnormal heart rate and rhythm in the unborn baby, which can be detected by electronic fetal monitoring.

Electronic fetal monitoring (EFM) is performed late in pregnancy or continuously during labor to ensure normal delivery of a healthy baby. EFM can be utilized either externally or internally in the womb. The illustration above shows the internal procedure, in which an electrode is attached directly to the baby's scalp to monitor the heart rate. Uterine contractions are recorded using an intrauterine pressure catheter which is inserted through the cervix into the uterus. *(Illustration by the Electronic Illustrators Group.)*

The fetal monitor is a more intricate version of the machine that a health care provider uses to listen to a baby's heartbeat. The monitor that is used during prenatal visits just picks up the sound of the baby's heart beating. The fetal monitor also keeps a continuous paper record of the heart rate. In addition, the fetal monitor can record uterine contractions on the lower part of the paper strip. This helps the doctor or midwife determine how a baby is handling the **stress** of contractions. The normal pattern is for the baby's heartbeat to drop slightly during a contraction and then go back to normal after the contraction is over. EFM looks for any changes from this normal pattern, particularly if there is a drastic drop in the baby's heart beat or if the heart rate does not recover immediately after a contraction.

Because it is an indirect test, it is not perfect. When an adult complains to a provider about not feeling well, checking the heart rate is only one of many things that the doctor will do. With an unborn baby, however, checking the heart rate is basically the only thing that a doctor or midwife can do.

Fetal monitoring can be helpful in a variety of different situations. During pregnancy, fetal monitoring can be used as a part of **antepartum testing**. If the practitioner

KEY TERMS

Breech presentation—Fetal position in which the buttocks come first.

A cesarean section—delivery of a baby through an incision in the mother's abdomen instead of through the vagina.

Hypoxia—An oxygen deficiency.

feels that a baby may be at increased risk of problems toward the end of pregnancy, a baby can be checked every week or every other week with a non-stress test. In this test, changes in the baby's heart rate are measured along with the fetus' own movements. The heart rate of a healthy baby should go up whenever she or he moves.

Fetal monitoring is used on and off during early labor. As labor progresses, more monitoring is often needed. Usually, as the time for delivery nears, the monitor is left on continuously since the end of labor tends to be the most stressful time for the baby.

A baby who is having trouble in labor will show characteristic changes in heart rate after a contraction (late decelerations). If a baby is not receiving enough oxygen to withstand the stress of labor and delivery is many hours away, a **cesarean section** (C-section) may be necessary.

Description

Using the external fetal monitor is simple and painless. Two elastic belts are placed around the mother's abdomen. One belt holds a listening device in place while the other belt holds the contraction monitor. The nurse or midwife adjusts the belts to get the best readings from each device.

Sometimes, it is difficult to hear the baby's heartbeat with the external monitoring device. Other times, the monitor may show subtle signs of a developing problem. In either case, the doctor or midwife may recommend that the external belt be replaced with an internal monitor.

The internal monitor is an electronic wire that rests directly on the baby's head. The provider can place it on the baby's head during an internal exam. The internal monitor can only be used when the cervix is already open. This device provides a more accurate record of the baby's heart rate.

Preparation

There are no special preparations needed for fetal monitoring.

Risks

External EFM poses no direct risks to the baby. However, because of being connected to the machine, the mother cannot walk around. This inactivity may prolong labor and reduce oxygen levels in the mother's blood, both of which can be detrimental to the unborn baby. Another problem is that electronic fetal monitoring seems to be associated with an increase in caesarian deliveries. There is a concern that EFM can give false alarms of distress in the baby, and that this can lead to unneeded caesarians. With internal monitoring, there is a higher risk for infection. For these and other reasons, the United States Preventive Services Task Force states that there is some evidence that using electronic fetal monitoring on low-risk women in labor might not be indicated. Many physicians, however, continue to use EFM routinely, and believe it to be of value in both low-risk and high-risk labors.

Normal results

An unborn baby's heart rate normally ranges from 120–160 beats per minute (bpm). A baby who is receiving enough oxygen through the placenta will move around. The monitor strip will show the baby's heart rate rising briefly as he/she moves (just as an adult's heart rate rises when he/she moves).

The baby's monitor strip is considered to be reactive when the baby's heart rate rises at least 20 bpm above the baseline heart rate for at least 20 seconds. This must occur at least twice in a 20-minute period. A reactive heart rate tracing (also known as a reactive non-stress test) is considered a sign of the baby's well being.

Abnormal results

If the baby's heart rate drops very low or rises very high, this signals a serious problem. In either of these cases it is obvious that the baby is in distress and must be delivered soon. However, many babies who are having problems do not give such clear signs.

During a contraction, the flow of oxygen (from the mother) through the placenta (to the baby) is temporarily stopped. It is as if the baby has to hold its breath during each contraction. Both the placenta and the baby are designed to withstand this condition. Between contractions, the baby should be receiving more than enough oxygen to do well during the contraction.

The first sign that a baby is not getting enough oxygen between contractions is often a drop in the baby's heart rate after the contraction (late deceleration). The baby's heart rate recovers to a normal level between contractions, only to drop again after the next contraction. This is also a more subtle sign of distress.

These babies will do fine if they are delivered in a short period of time. Sometimes, these signs develop long before delivery is expected. In that case, a C-section may be necessary.

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Electrophysiology study of the heart

Definition

An electrophysiology (EP) study of the heart is a nonsurgical analysis of the electrical conduction system (normal or abnormal) of the heart. The test employs cardiac catheters and sophisticated computers to generate electrocardiogram (EKG) tracings and electrical measurements with exquisite precision from within the heart chambers.

The EP study can be performed solely for diagnostic purposes. It also is performed to pinpoint the exact location of electrical signals (cardiac mapping) in conjunction with a therapeutic procedure called **catheter ablation**.

The test is simple, not painful, and performed in a special laboratory under controlled clinical circumstances by cardiologists and nurses who subspecialize in electrophysiology.

Purpose

A cardiologist may recommend an EP study when the standard EKG, Holter monitor, event recorder, **stress test**, echocardiogram, or angiogram cannot provide enough information to evaluate an abnormal heart rhythm, called an arrhythmia.

An EP study also may be beneficial in diagnosing a suspected arrhythmia in a patient who shows symptoms of an arrhythmia but in whom it could not be detected from other tests.

The purpose and great value of an EP study is that it offers more detailed information to the doctor about the electrical activity in the heart than the aforementioned noninvasive tests because electrodes are placed directly *on* heart tissue. This allows the electrophysiologist to determine the specific location of an arrhythmia and, oftentimes, correct it during the same procedure. This corrective treatment is permanent and considered a cure, and, in many cases, the patient may not need to take heart medications.

EP studies may be helpful in assessing:

- certain tachycardias or bradycardias of unknown cause.
- patients who have been resuscitated after experiencing **sudden cardiac death**.
- various symptoms of unknown cause, such as chest **pain**, **shortness of breath**, **fatigue**, or syncope (dizziness/fainting).
- response to anti-arrhythmic therapy.

Precautions

Pregnant patients should not undergo an EP study because of exposure to radiation during the study, which may be harmful to the growing baby.

Patients who have **coronary artery disease** may need to have that treated before having an EP study.

Description

The rhythmic pumping action of the heart, which is essentially a muscle, is the result of electrical impulses traveling throughout the walls of the four heart chambers. These impulses originate in the sinoatrial (SA) node, which are specialized cells situated in the top right chamber of the heart: the right atrium. Normally, the SA node, acting like a spark plug, spontaneously generates the impulses, which travel through specific pathways throughout the atria to the atrioventricular (AV) node. The AV node is a relay station, sending the impulses to more specialized muscle fibers throughout the bottom chambers of the heart: the ventricles. If these pathways become damaged or blocked or if extra (abnormal) pathways exist, the heart's rhythm may be altered (perhaps too slow, too fast, or irregular), which can seriously affect the heart's pumping ability.

The patient is transported to the x-ray table in the EP lab and connected to various monitors. Sterile sheets are placed over him or her. A minimum of two catheters are inserted into the right femoral (thigh) vein in the groin area. Depending on the type of arrhythmia, the number of catheters used in an EP test and their route to the heart may vary. For certain tachycardias, two more catheters may be inserted in the left groin and one in the internal jugular (neck) vein or in the subclavian (below the clavi-

An electrophysiologist nurse monitors a patient's heart rhythm during an electrophysiology study for tachycardia. *(Photograph by Collette Placek. Reproduced by permission.)*

cle) vein. The catheters are about 0.08 in (2 mm) in diameter, about the size of a spaghetti noodle. The catheters used in catheter ablation are slightly larger.

With the help of fluoroscopy (x rays on a television screen), all the catheters are guided to several specific locations in the heart. Typically, four to 10 electrodes are located on the end of the catheters, which have the ability to send electrical signals to stimulate the heart (called pacing) and to receive electrical signals from the heart—but not at the same time (just as a walkie-talkie cannot send and receive messages at the same time).

First, the electrodes are positioned to receive signals from inside the heart chambers. This allows the doctor to measure how fast the electrical impulses travel currently in the patient's heart. These measurements are called the patient's baseline measurements. Next, the electrodes are positioned to pace: The EP team actually tries to induce (sometimes in combination with various heart drugs) the arrhythmia that the patient has previously experienced so the team can observe it in a controlled environment, compare it to the patient's clinical or spontaneous arrhythmia, and decide how to treat it.

Once the arrhythmia is induced and the team determines it can be treated with catheter ablation, cardiac mapping is performed to locate precisely the origin and route of the abnormal pathway. When this is accomplished, the ablating electrode catheter is positioned directly against the abnormal pathway, and high radiofrequency energy is delivered through the electrode to destroy (burn) the tissue in this area.

Preparation

The following preparations are made for an EP study:

- the patient may be advised to stop taking certain medications, especially heart drugs, that may interfere with the test results.
- blood tests usually are ordered the week before the test.
- the patient undergoes conscious **sedation** (awake but relaxed) during the test. This is accomplished quite often with the anesthetic drugs VersedR (Roche laboratories) and fentanyl.
- a local anesthetic is injected at the site of catheter insertion.

Aftercare

The patient needs to rest flat in bed for several hours after the procedure to allow healing at the catheter insertion sites.

The patient often returns home either the same day of the test or the next day. Someone should drive him or her home.

The doctor may prescribe drugs and/or insert an AFCD to treat the arrhythmia and may do a possible follow-up EP study.

Risks

The EP diagnostic study and catheter ablation are low-risk procedures. There is a small risk of bleeding and/or infection at the site of catheter insertion, but this occurs less than 1% of the time. Blood clot formation occurs only two in 1,000 instances and is minimized with blood thinner medications administered during the procedure. Vascular injuries causing hemorrhage or **thrombophlebitis** are possible but occur less than 0.7% of the time. Cardiac perforations occur only in one or two per 1,000 instances. If the right internal jugular vein is accessed, the small possibility of puncturing the lung with the catheter exists, which, at worst, could cause a collapsed lung.

Because **ventricular tachycardia** or fibrillation (lethal **arrhythmias**) may be induced in the patient, the EP lab personnel must be prepared to defibrillate the patient as necessary.

Normal results

The heart initiates and conducts electrical impulses normally.

Abnormal results

Confirmation of arrhythmias, such as:

- supraventricular tachycardias
- ventricular arrhythmias
- accessory (extra) pathways
- bradycardias

KEY TERMS

Ablation—Remove or destroy, such as by burning or cutting.

Angiogram—X ray of a blood vessel after special x-ray dye has been injected into it.

Bradycardia—Slow heartbeat.

Cardiac catheter—Long, thin, flexible tube, that is threaded into the heart through a blood vessel.

Cardiologist—Doctor who specializes in diagnosing and treating heart diseases.

Echocardiogram—Ultrasound image of the heart.

Electrocardiogram—Tracing of the electrical activity of the heart.

Electrode—Medium for conducting an electrical current—in this case, platinum wires.

Electrophysiology—Study of how electrical signals in the body relate to physiologic function.

Event recorder—A small machine, worn by a patient usually for several days or weeks, that is activated by the patient to record his or her EKG when a symptom is detected.

Fibrillation—Rapid, random contraction (quivering).

Holter monitor—A small machine, worn by a patient usually for 24 hours, that continuously records the patient's EKG during usual daily activity.

Stress test—Recording a patient's EKG during exercise.

Supraventricular tachycardia—A fast heart beat that originates above the ventricles.

Tachycardia—Fast heartbeat.

Vascular—Pertaining to blood vessels.

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Medtronics Manufacturer of Therapeutic Devices. 710 Medtronic Parkway NE, Minneapolis, MN 55432-5604. (800) 328-2518. <http://www.medtronic.com>.

Midwest Heart Specialists. Physician Office Building, 3825 Highland Ave., Tower 2, Ste. 400, Downers Grove, IL 60515. (630) 719-4799. <http://www.midwestheart.com>.

United States Catheter Instruments (USCI). 129 Concord Road Billerica, MA 01821. (800) 826-2273.

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Electroshock therapy *see* **Electroconvulsive therapy**

Elephantiasis

Definition

The word elephantiasis is a vivid and accurate term for the syndrome it describes: the gross (visible) enlargement of the arms, legs, or genitals to elephantoid size.

Description

True elephantiasis is the result of a parasitic infection caused by three specific kinds of round worms. The long, threadlike worms block the body's lymphatic system—a network of channels, lymph nodes, and organs that helps maintain proper fluid levels in the body by draining lymph from tissues into the bloodstream. This blockage causes fluids to collect in the tissues, which can lead to great swelling, called "lymphedema." Limbs can swell so enormously that they resemble an elephant's foreleg in size, texture, and color. This is the severely disfiguring and disabling condition of elephantiasis.

There are a few different causes of elephantiasis, but the agents responsible for most of the elephantiasis in the world are filarial worms: white, slender round worms found in most tropical and subtropical places. They are transmitted by particular kinds (species) of mosquitoes, that is, bloodsucking insects. Infection with these worms is called "lymphatic filariasis" and over a long period of time can cause elephantiasis.

Lymphatic **filariasis** is a disease of underdeveloped regions found in South America, Central Africa, Asia, the Pacific Islands, and the Caribbean. It is a disease that has been present for centuries, as ancient Persian and Indian writings clearly described elephant-like swellings of the arms, legs, and genitals. It is estimated that 120 million people in the world have lymphatic filariasis, as of 1997. The disease appears to be spreading, in spite of decades of research in this area.

Other terms for elephantiasis are Barbados leg, elephant leg, morbus herculeus, mal de Cayenne, and myelolymphangioma.

Other situations that can lead to elephantiasis are:

- a protozoan disease called **leishmaniasis**
- a repeated streptococcal infection
- the surgical removal of lymph nodes (usually to prevent the spread of **cancer**)
- a hereditary birth defect

Causes and symptoms

Three kinds of round worms cause elephantiasis filariasis: *Wuchereria bancrofti*, *Brugia malayi*, and *Brugia timori*. Of these three, *W. bancrofti* makes up about 90% of the cases. Man is the only known host of *W. bancrofti*.

Culex, *Aedes*, and *Anopheles* mosquitoes are the carriers of *W. bancrofti*. *Anopheles* and *Mansonia* mosquitoes are the carriers of *B. malayi*. In addition, *Anopheles* mosquitoes are the carriers of *B. timori*.

Infected female mosquitoes take a blood meal from a human, and, in doing so, introduce larval forms of the particular parasite they carry to the person. These larvae migrate toward a lymphatic channel, then travel to various places within the lymphatic system, usually positioning themselves in or near lymph nodes throughout the body. During this time, they mature into more developed larvae and eventually into adult worms. Depending upon the species of round worm, this development can take a few months or more than a year. The adult worms grow to about 1 in (2.5 cm) to 4 in (10 cm) long.

The adult worms can live from about three to eight years. Some have been known to live to 20 years, and in one case 40 years. The adult worms begin reproducing numerous live embryos, called microfilariae. The microfilariae travel to the bloodstream, where they can be ingested by a mosquito when it takes a blood meal from the infected person. If they are not ingested by a mosquito, the microfilariae die within about 12 months. If they are ingested by a mosquito, they continue to mature. They are totally dependent on their specific species of mosquito to develop further. The cycle continues when the mosquito takes another blood meal.

Most of the symptoms an infected person experiences are due to the blockage of the lymphatic system by the adult worms and due to the substances (excretions and secretions) produced by the worms.

The body's allergic reactions may include repeated episodes of **fever**, shaking chills, sweating, headaches, vomiting, and **pain**. Enlarged lymph nodes, swelling of the affected area, skin ulcers, bone and joint pain, tiredness, and red streaks along the arm or leg also may occur. Abscesses can form in lymph nodes or in the lymphatic vessels. They may appear at the surface of the skin as well.

Long-term infection with lymphatic filariasis can lead to **lymphedema**, hydrocele (a buildup of fluid in any saclike cavity or duct) in the scrotum, and elephantiasis of the legs, scrotum, arms, penis, breasts, and vulvae. The most common site of elephantiasis is the leg. It typically begins in the ankle and progresses to the foot and leg. At first the swollen leg may feel soft to the touch but eventually becomes hard and thick. The skin may appear darkened or warty and may even crack, allowing bacteria to infect the leg and complicate the disease. The microfilariae usually don't cause injury. In some instances, they cause "eosinophilia," an increased number of eosinophils (a type of white blood cells) in the blood.

This disease is more intense in people who never have been exposed to lymphatic filariasis than it is in the native people of tropical areas where the disease occurs. This is because many of the native people often are immunologically tolerant.

Diagnosis

The only sure way to diagnose lymphatic filariasis is by detecting the parasite itself, either the adult worms or the microfilariae.

Microscopic examination of the person's blood may reveal microfilariae. But many times, people who have been infected for a long time do not have microfilariae in their bloodstream. The absence of them, therefore, does not mean necessarily that the person is not infected. In these cases, examining the urine or hydrocele fluid or performing other clinical tests is necessary.

Collecting blood from the individual for microscopic examination should be done during the night when the microfilariae are more numerous in the bloodstream. (Interestingly, this is when mosquitoes bite most frequently.) During the day microfilariae migrate to deeper blood vessels in the body, especially in the lung. If it is decided to perform the blood test during the day, the infected individual may be given a "provocative" dose of medication to provoke the microfilariae to enter the bloodstream. Blood then can be collected an hour later for examination.

Detecting the adult worms can be difficult because they are deep within the lymphatic system and difficult to get to. Biopsies usually are not performed because they usually don't reveal much information.

Man suffering from elephantiasis. *(Photograph by C. James Webb, Phototake NYC. Reproduced by permission.)*

Treatment

The drug of choice in treating lymphatic filariasis is diethylcarbamazine (DEC). The trade name in the United States is Hetrazan.

The treatment schedule is typically 2 mg/kg per day, three times a day, for three weeks. The drug is taken in tablet form.

DEC kills the microfilariae quickly and injures or kills the adult worms slowly, if at all. If all the adult worms are not killed, remaining paired males and females may continue to produce more larvae. Therefore, several courses of DEC treatment over a long time period may be necessary to rid the individual of the parasites.

DEC has been shown to reduce the size of enlarged lymph nodes and, when taken long-term, to reduce elephantiasis. In India, DEC has been given in the form of a medicated salt, which helps prevent spread of the disease.

KEY TERMS

Antigen—Any substance (usually a protein) that causes an immune response by the body to produce antibodies.

Filarial—Threadlike. The word "filament" is formed from the same root word.

Host—A person or animal in which a parasite lives, is nourished, grows, and reproduces.

Lymph—A watery substance that collects in the tissues and organs of the body and eventually drains into the bloodstream.

Lymphatic system—A network composed of vessels, lymph nodes, the tonsils, the thymus gland, and the spleen. It is responsible for transporting fluid and nutrients to the bloodstream and for maturing certain blood cells that are part of the body's immune system.

Lymphedema—The unnatural accumulation of lymph in the tissues of the body, which results in swelling in that area.

Protozoa—(Plural form of protozoan) Single-celled organisms (not bacteria) of which about 30 kinds cause disease in humans.

Streptococcal—Pertaining to any of the *Streptococcus* bacteria. These organisms can cause pneumonia, skin infections, and many other diseases.

The side effects of DEC almost all are due to the body's natural allergic reactions to the dying parasites rather than to the DEC itself. For this reason, DEC must be given carefully to reduce the danger to the individual. Side effects may include fever, chills, **headache**, **dizziness**, **nausea and vomiting**, **itching**, and joint pain. These side effects usually occur within the first few days of treatment. These side effects usually subside as the individual continues taking the drug.

There is an alternate treatment plan for the use of DEC. This plan is designed to kill the parasites slowly (to reduce allergic reactions to the dead microfilariae and dying adult worms within the body). Lower doses of DEC are taken for the first few days, followed by the higher dose of 2 mg/kg per day for the remaining three weeks. In addition, steroids may be prescribed to prevent the individual's body from reacting severely to the dead worms.

Another drug used is Ivermectin. Early research studies of Ivermectin show that it is excellent in killing microfilariae, but the effects of this drug on the adult worms are still being investigated. It is probable that patients will need to continue using DEC to kill the adult worms. Mild side effects of Ivermectin include headache, fever, and myalgia.

Other means of managing lymphatic filariasis are pressure bandages to wrap the swollen limb and elastic stockings to help reduce the pressure. Exercising and elevating a bandaged limb also can help reduce its size.

Surgery can be performed to reduce elephantiasis by removing excess fatty and fibrous tissue, draining the swelled area, and removing the dead worms.

Prognosis

With DEC treatment, the prognosis is good for early and mild cases of lymphatic filariasis. The prognosis is poor, however, for heavy parasitic infestations.

Prevention

The two main ways to control this disease are to take DEC preventively, which has shown to be effective, and to reduce the number of carrier insects in a particular area.

Avoiding mosquito bites with insecticides and insect repellents is helpful, as is wearing protective clothing and using bed netting.

Much effort has been made in cleaning the breeding sites (stagnant water) of mosquitoes near people's homes in areas where filariasis is found.

Before visiting countries where lymphatic filariasis is found, it would be wise to consult a travel physician to learn about current preventative measures.

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National Institute of Allergies and Infectious Diseases, Division of Microbiology and Infectious Diseases. Building 31, Room. 7A-50, 31 Center Drive MSC 2520, Bethesda, MD 20892. <http://www.niaid.nih.gov>.

National Lymphedema Network (NLN). 2211 Post St., Suite 404, San Francisco, CA 94115. (800) 541-3259. <http://www.hooked.net>.

National Organization for Rare Disorders. PO Box 8923, New Fairfield, CT 06812-8923. (800) 999-6673. <http://www.rarediseases.org>.

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Enzyme-linked Immunosorbant (ELISA) *see* **AIDS tests**

Embolism

Definition

An embolism is an obstruction in a blood vessel due to a blood clot or other foreign matter that gets stuck while traveling through the bloodstream. The plural of embolism is emboli.

Description

Emboli have moved from the place where they were formed through the bloodstream to another part of the body, where they obstruct an artery and block the flow of blood. The emboli are usually formed from blood clots but are occasionally comprised of air, fat, or tumor tissue. Embolic events can be multiple and small, or single and massive. They can be life-threatening and require immediate emergency medical care. There are three general categories of emboli: arterial, gas, and pulmonary. Pulmonary emboli are the most common.

Arterial embolism

In arterial emboli, blood flow is blocked at the junction of major arteries, most often at the groin, knee, or thigh. Arterial emboli are generally a complication of heart disease. An **arterial embolism** in the brain (cerebral embolism) causes **stroke**, which can be fatal. An estimated 5–14% of all strokes are caused by cerebral emboli. Arterial emboli to the extremities can lead to tissue **death** and **amputation** of the affected limb if not treated effectively within hours. Intestines and kidneys can also suffer damage from emboli.

Gas embolism

Gas emboli result from the compression of respiratory gases into the blood and other tissues due to rapid changes in environmental pressure, for example, while flying or scuba diving. As external pressure decreases, gases (like nitrogen) that are dissolved in the blood and other tissues become small bubbles that can block blood flow and cause organ damage.

Pulmonary embolism

In a **pulmonary embolism**, a common illness, blood flow is blocked at a pulmonary artery. When emboli block the main pulmonary artery, and in cases where there are no initial symptoms, a pulmonary embolism can quickly become fatal. According to the American Heart Association, an estimated 600,000 Americans develop pulmonary emboli annually and 60,000 die from it.

A pulmonary embolism is difficult to diagnose. Less than 10% of patients who die from a pulmonary embolism were diagnosed with the condition. More than 90% of cases of pulmonary emboli are complications of **deep vein thrombosis**, blood clots in the deep vein of the leg or pelvis.

Causes and symptoms

Arterial emboli are usually a complication of heart disease where blood clots form in the heart's chambers. Gas emboli are caused by rapid changes in environmental pressure that could happen when flying or scuba diving. A pulmonary embolism is caused by blood clots that travel through the blood stream to the lungs and block a pulmonary artery. More than 90% of the cases of pulmonary embolism are a complication of deep vein thrombosis, which typically occurs in patients who have had **orthopedic surgery** and patients with **cancer** or other chronic illnesses like congestive **heart failure**.

Risk factors for arterial and pulmonary emboli include: prolonged bed rest, surgery, **childbirth**, **heart attack**, stroke, congestive heart failure, cancer, **obesity**, a broken hip or leg, **oral contraceptives**, sickle cell anemia, chest trauma, certain congenital heart defects, and old age. Risk factors for gas emboli include: scuba diving, amateur plane flight, **exercise**, injury, obesity, **dehy-**

A close up view of a pulmonary embolism. *(Custom Medical Stock Photo. Reproduced by permission.)*

dration, excessive alcohol, colds, and medications such as narcotics and **antihistamines**.

Common symptoms of a pulmonary embolism include:

- labored breathing, sometimes accompanied by chest **pain**
- a rapid pulse
- a **cough** that may produce sputum
- a low-grade **fever**
- fluid build-up in the lungs

Less common symptoms include:

- coughing up blood
- pain caused by movement or breathing
- leg swelling
- bluish skin
- fainting
- swollen neck veins

Symptoms of an arterial embolism include:

- severe pain in the area of the embolism
- pale, bluish cool skin
- numbness
- tingling
- muscular weakness or **paralysis**

Diagnosis

An embolism can be diagnosed through the patient's history, a physical exam, and diagnostic tests. For arterial emboli, cardiac ultrasound and/or arteriography are ordered. For a pulmonary embolism, a **chest x ray**, lung scan, pulmonary **angiography**, **electrocardiography**, arterial blood gas measurements, and **venography** or venous ultrasound could be ordered.

Diagnosing an arterial embolism

Ultrasound uses sound waves to create an image of the heart, organs, or arteries. The technician applies gel to a hand-held transducer then presses it against the patient's body. The ultrasound's sound waves arteries are converted into an image that can be displayed on a monitor. Performed in an outpatient diagnostic laboratory, the test takes 30–60 minutes.

An arteriogram is an x ray in which a contrast medium is injected to make the arteries visible on the x ray. It can be performed in a radiology unit, outpatient clinic, or diagnostic center of a hospital.

Diagnosing a pulmonary embolism

A chest x ray can show fluid build-up and detect other respiratory diseases. The perfusion lung scan shows poor flow of blood in areas beyond blocked arteries. The patient inhales a small amount of radiopharmaceutical and pictures of airflow into the lungs are taken with a gamma camera. Then a different radiopharmaceutical is injected into an arm vein and lung blood flow is scanned. A normal result essentially rules out a pulmonary embolism. A lung scan can be performed in a hospital or an outpatient facility and takes about 45 minutes.

Pulmonary angiography is the most reliable test for diagnosing a pulmonary embolism but it is not used often because it is expensive, invasive, and not readily available in most hospitals. Pulmonary angiography is a radiographic test which involves injection of a radio contrast agent to show the pulmonary arteries. A cinematic camera records the blood flow through the patient, who lies on a table. Pulmonary angiography is usually performed in a hospital's radiology medicine department and takes 30–60 minutes.

An electrocardiograph shows the heart's electrical activity and helps distinguish a pulmonary embolism from a heart attack. Electrodes covered with conducting jelly are placed on the patient's chest, arms, and legs. Impulses of the heart's activity are traced on paper. The test takes about 10 minutes.

Arterial blood gas measurements are sometimes helpful but, alone, they are not diagnostic for pulmonary embolism. Blood is taken from an artery instead of a vein, usually in the wrist.

Venography is used to look for the most likely source of a pulmonary embolism, deep vein thrombosis. It is very accurate, but it is not used often, because it is painful, expensive, exposes the patient to a fairly high dose of radiation, and can cause complications. Venogra-

phy identifies the location, extent, and degree of attachment of the blood clots and enables the condition of the deep leg veins to be assessed. A contrast solution is injected into a foot vein through a catheter. The physician observes the movement of the solution through the vein with a fluoroscope while a series of x rays are taken. Venography takes between 30–45 minutes and can be done in a physician's office, a laboratory, or a hospital. Radionuclide venography, in which a radioactive isotope is injected, is occasionally used, especially if a patient has had reactions to contrast solutions. Venous ultrasound is the preferred evaluation of leg veins.

Treatment

Patients with emboli require immediate hospitalization. They are generally treated with clot-dissolving and/or clot-preventing drugs. **Thrombolytic therapy** to dissolve blood clots is the definitive treatment for a very severe pulmonary embolism. Streptokinase, urokinase, and recombinant tissue plasminogen activator (TPA) are used. Heparin is the anticoagulant drug of choice for preventing formation of blood clots. Warfarin, an oral anticoagulant, is sometimes used concurrently and is usually continued after the hospitalization.

In the case of an arterial embolism, the affected limb is placed in a dependent position and kept warm. Embolectomy is the treatment of choice in the majority of early cases of arterial emboli in the extremities. In this procedure, a balloon-tipped catheter is inserted into the artery to remove thromboembolic matter.

With a pulmonary embolism, oxygen therapy is often used to maintain normal oxygen concentrations. For people who can't take anticoagulants and in some other cases, surgery may be needed to insert a device that filters blood returning to the heart and lungs.

Prognosis

Of patients hospitalized with an arterial embolism, 25–30% die, and 5–25% require amputation of a limb. About 10% of patients with a pulmonary embolism die suddenly within the first hour of onset of the condition. The outcome for all other patients is generally good; only 3% of patients die who are properly diagnosed early and treated. In cases of an undiagnosed pulmonary embolism, about 30% of patients die.

Prevention

Embolism can be prevented in high risk patients through antithrombotic drugs such as heparin, venous interruption, gradient elastic stockings, and intermittent pneumatic compression of the legs. The combination of graduated compression stockings and low-dose heparin is significantly more effective than low-dose heparin alone.

Gradient elastic stockings, also called anti-embolism stockings, decrease the risk of blood clots by compressing superficial leg veins and forcing blood into the deep veins. They can be knee-, thigh-, or waist-length. Many physicians order the use of stockings before surgery and until there is no longer an elevated risk of developing blood clots. The risk of deep vein thrombosis after surgery is reduced 50% with the use of these stockings. The American Heart Association recommends that the use of graduated compression stockings be considered for all high-risk surgical patients.

Intermittent pneumatic compression involves wrapping knee- or thigh-high cuffs around the legs to prevent blood clots. The cuffs are connected to a pump which inflates and deflates, mimicking the heart's normal pumping action and reducing the pooling of blood. Intermittent pneumatic compression can be used during surgery and recovery and continues until there is no longer an elevated risk of developing blood clots. The American Heart Association recommends the use of intermittent pneumatic compression for patients who cannot take anticoagulants, for example, spinal cord and brain trauma patients.

KEY TERMS

Anticoagulants—Drugs that suppress, delay, or prevent blood clots. Anticoagulants are used to treat embolisms.

Artery—A blood vessel that carries blood from the heart to other body tissues. Embolisms obstruct arteries.

Deep vein thrombosis—A blood clot in the calf's deep vein. This frequently leads to pulmonary embolism if untreated.

Emboli—Clots or other substances that travel through the blood stream and get stuck in an artery, blocking circulation.

Thrombolytics—Drugs that dissolve blood clots. Thrombolytics are used to treat embolisms.

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Lori De Milto

EMG *see* **Electromyography**

Emollient bath *see* **Therapeutic baths**

Emphysema

Definition

Emphysema is a chronic respiratory disease where there is over-inflation of the air sacs (alveoli) in the lungs, causing a decrease in lung function, and often, breathlessness.

Description

Emphysema is the most common cause of **death** from respiratory disease in the United States, and is the fourth most common cause of death overall. There are 1.8 million Americans with the disease, which ranks fifteenth among chronic conditions that cause limitations of activity. The disease is usually caused by **smoking**, but a small number of cases are caused by an inherited defect.

Normally functioning lungs are elastic, efficiently expanding and recoiling as air passes freely through the bronchus to the alveoli, where oxygen is moved into the blood and carbon dioxide is filtered out. When a person inhales cigarette smoke or certain other irritants, his or her immune system responds by releasing substances that are meant to defend the lungs against the smoke. These substances can also attack the cells of the lungs, but the body normally inhibits such action with the release of other substances. In smokers and those with the inherited defect, however, no such prevention occurs and the lung tissue is damaged in such a way that it loses its elasticity. The small passageways (bronchioles) leading to the alveoli collapse, trapping air within the alveoli. The alveoli, unable to recoil efficiently and move the air out, over expand and rupture. As the disease progresses, coughing and **shortness of breath** occur. In the later stages, the lungs cannot supply enough oxygen to the blood. Emphysema often occurs with other respiratory diseases, particularly chronic **bronchitis**. These two diseases are often referred to as one disorder called chronic obstructive pulmonary disease (COPD).

Emphysema is most common among people aged 50 and older. Those with inherited emphysema may experience the onset as early as their thirties or fourties Men are more likely than women to develop emphysema, but female cases are increasing as the number of female smokers rises.

Causes and symptoms

Heavy cigarette smoking causes about 80–90% of all emphysema cases. However a few cases are the result of an inherited deficiency of a substance called alpha-1-antitrypsin (AAT). The number of Americans with this deficiency is relatively small, probably no greater than 70,000. Pipe, cigar, and marijuana smoking can also damage the lungs. While a person may be less likely to inhale cigar and pipe smoke, these types of smoke can also impair lung function. Marijuana smoke may be even more damaging because it is inhaled deeply and held in by the smoker.

The symptoms of emphysema develop gradually over many years. It is a common occurrence for many emphysema patients to have lost over half of their functioning lung tissue before they become aware that something is wrong. Shortness of breath, a chronic mild **cough** (which may be productive of large amounts of dark, thick sputum, and often dismissed as "smoker's cough"), and sometimes weight loss are associated with emphysema.

Initially, a patient may only notice shortness of breath when he or she is exercising. However, as the disease progresses, it will occur with less exertion or no exertion at all. Emphysema patients may also develop an enlarged, or "barrel," chest. Other symptoms may be skipped breaths, difficulty sleeping, morning headaches, increased difficulty breathing while lying down, chronic **fatigue**, and swelling of the feet, ankles, or legs. Those with emphysema are at risk for a variety of other complications resulting from weakened lung function, including **pneumonia**.

Diagnosis

A variety of pulmonary function tests may be ordered. In the early stages of emphysema, the only result may be dysfunction of the small airways. Patients with emphysema may show an increase in the total amount of air that is in the lungs (total lung capacity), but a decrease in the amount of air that can be breathed out after taking a deep breath (vital capacity). With severe emphysema, vital capacity is substantially below normal. Spirometry, a procedure that measures air flow and lung volume, helps in the diagnosis of emphysema.

A **chest x ray** is often ordered to aid in the diagnosis of emphysema, though patients in the early stages of the disease may have normal findings. Abnormal findings on the chest x ray include over-inflation of the lungs and an abnormally increased chest diameter. The diaphragm may appear depressed or flattened. In addition, patients with advanced emphysema may show a smaller or vertical heart. The physician may observe blisters in the lungs and bulging of the accessory muscles of the respiratory system. Late in the disease, an EKG will show signs of right ventricular failure in the heart and increased hemoglobin due to lower levels of oxygen in the patient's blood.

Treatment

Treatment methods for emphysema do not cure or reverse the damage to the lungs. However, they may slow the progression of the disease, relieve symptoms, and help control possibly fatal complications. The first step in treatment for smokers is to quit, so as to prevent any further deterioration of breathing ability. Smoking cessation programs may be effective. Consistent encouragement along with the help of health care professionals as well as family and friends can help increase the success rate of someone attempting to quit.

If the patient and the health care team develop and maintain a complete program of respiratory care, disability can be decreased, acute episodes of illness may be prevented, and the number of hospitalizations reduced. However, only quitting smoking has been shown to slow down the progression of the disease, and among all other treatments, only oxygen therapy has shown an increase in the survival rate.

A scanning electron microscopy (SEM) of lung tissue indicating emphysema. *(Photograph by Hossler, Ph.D., Custom Medical Stock Photo. Reproduced by permission.)*

Home oxygen therapy may improve the survival times in those patients with advanced emphysema who also have low blood oxygen levels. It may improve the patient's tolerance of **exercise**, as well as improve their performance in certain aspects of brain function and muscle coordination. The functioning of the heart may also improve with an increased concentration of oxygen in the blood. Oxygen may also decrease **insomnia** and headaches. Some patients may only receive oxygen at night, but studies have illustrated that it is most effective when administered at least 18, but preferably 24 hours per day. Portable oxygen tanks prescribed to patients carry a limited supply and must be refilled on a regular basis by a home health provider. Medicare and most insurance companies cover a large proportion of the cost of home oxygen therapy. Patients should be instructed regarding special safety issues involving the transport and presence of oxygen in the home.

A variety of medications may be used in the treatment of emphysema. Usually the patient responds best to a combination of medicines, rather than one single drug.

Bronchodilators are sometimes used to help alleviate the patient's symptoms by relaxing and opening the airways. They can be inhaled, taken by mouth, or injected. Another category of medication often used is **corticosteroids** or steroids. These help to decrease the

X ray showing emphysema in the lungs. *(Photo Researchers. Reproduced by permission.)*

inflammation of the airway walls. They are occasionally used if bronchodilators are ineffective in preventing airway obstruction. Some patients' lung function improves with corticosteroids, and inhaled steroids may be beneficial to patients with few side effects. A variety of **antibiotics** are frequently given at the first sign of a respiratory infection, such as increased amounts of sputum, or if there has been a change in the color of the sputum. **Expectorants** can help to loosen respiratory secretions, enabling the patient to more easily expel them from the airways.

Many of the medications prescribed involve the use of a metered dose inhaler (MDI) that may require special instruction to be used correctly. MDIs are a convenient and safe method of delivering medication to the lungs. However, if they are used incorrectly the medication will not get to the right place. Proper technique is essential for the medication to be effective.

For some patients, surgical treatment may be the best option. Lung volume reduction surgery is a surgical procedure in which the most diseased parts of the lung are removed to enable the remaining lung and breathing muscles to work more efficiently. Preliminary studies suggest improved survival rates and better functioning with the surgery. Another surgical procedure used for emphysema patients is **lung transplantation**. Transplantation may involve one or both lungs. However, it is a risky and expensive procedure, and donor organs may not be available.

For those patients with advanced emphysema, keeping the air passages reasonably clear of secretions can prove difficult. Some common methods for mobilizing and removing secretions include:

- Postural drainage. This helps to remove secretions from the airways. The patient lies in a position that allows gravity to aid in draining different parts of the lung. This is often done after the patient inhales an aerosol medication. The basic position involves the patient lying on the bed with his chest and head over the side and the forearms resting on the floor.
- Chest percussion. This technique involves lightly clapping the back and chest, and may help to loosen thick secretions.
- Coughing and deep breathing. These techniques may aid the patient in bringing up secretions.
- Aerosol treatments. These treatments may involve solutions of saline, often mixed with a bronchodilator, which are then inhaled as an aerosol. The aerosols thin and loosen secretions. A treatment normally takes 10 to 15 minutes, and is given three or four times a day.

Patients with COPD can learn to perform a variety of self-help measures that may help improve their symptoms and their ability to participate in everyday activities. These measures include:

- Avoiding any exposure to dusts and fumes.
- Avoiding air pollution, including the cigarette smoke of others.
- Avoiding other people who have infections like the cold or flu. Get a pneumonia **vaccination** and a yearly flu shot.
- Drinking plenty of fluids. This helps to loosen respiratory secretions so they can be brought up more easily through coughing.
- Avoiding extreme temperatures of heat or cold. Also avoiding high altitudes. (Special precautions can be taken that may enable the emphysema patient to fly on a plane.)
- Maintaining adequate nutritional intake. Normally a high protein diet taken in many small feedings is recommended.

Alternative treatment

Many patients are interested in whether any alternative treatments for emphysema are available. Some practitioners recommend supplements of antioxidant nutrients. There have also been some studies indicating a correlation between a low Vitamin A levels and COPD, with suggestions that supplements of vitamin A might be ben-

KEY TERMS

Alveoli—Small cells or cavities. In the lungs, these are air sacs where oxygen enters the blood and carbon dioxide is filtered out.

Pulmonary—Related to or associated with the lungs.

eficial. Aromatherapists have used essential oils like eucalyptus, lavender, pine, and rosemary to help relieve nasal congestion and make breathing easier. The herb elecampane may act as an expectorant to help patients clear mucus from the lungs. The patient should discuss these remedies with their health care practitioner prior to trying them, as some may interact with the more traditional treatments that are already being used.

Prognosis

Emphysema is a serious and chronic disease that cannot be reversed. If detected early, the effects and progression can be slowed, particularly if the patient stops smoking immediately. Complications of emphysema include higher risks for pneumonia and acute bronchitis. Overall, the prognosis for patients with emphysema is poor, with a survival rate for all those with COPD of four years, and even less for emphysema. However, individual cases vary and many patients can live much longer with supplemental oxygen and other treatment measures.

Prevention

The best way to prevent emphysema is to avoid smoking. Even patients with inherited emphysema should avoid smoking, as it especially worsens the onset and severity. If patients quit smoking as soon as evidence of small airway obstruction begins, they can significantly improve their prognosis.

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Deanna Swartout-Corbeil, RN

Empyema

Definition

Empyema is a condition in which pus and fluid from infected tissue collects in a body cavity. The name comes from the Greek word *empyein* meaning pus-producing (suppurate). Empyema is most often used to refer to collections of pus in the space around the lungs (pleural cavity), but sometimes refers to similar collections in the gall bladder or the pelvic cavity. Empyema in the pleural cavity is sometimes called empyema thoracis, or empyema of the chest, to distinguish it from empyema elsewhere in the body.

Description

Empyema may have a number of causes but is most frequently a complication of **pneumonia**. Its development can be divided into three phases: an acute phase in which the body cavity fills with a thin fluid containing some pus; a second stage in which the fluid thickens and a fibrous, coagulation protein (fibrin) begins to accumulate within the cavity; and a third or chronic stage in which the lung or other organ is encased within a thick covering of fibrous material.

Causes and symptoms

Empyema thoracis can be caused by a number of different organisms, including bacteria, fungi, and amebas, in connection with pneumonia, chest **wounds**, chest surgery, lung abscesses, or a ruptured esophagus. The infective organism can get into the pleural cavity either through the bloodstream or other circulatory system, in secretions from lung tissue, or on the surfaces of surgical instruments or objects that cause open chest wounds. The most common organisms that cause empyema are the following bacteria: *Streptococcus pneumoniae*, *Haemophilus influenzae,* and *Staphylococcus aureus*. *S. aureus* is the most common cause in all age groups, accounting for 90% of cases of empyema in infants and children. Pelvic empyema in

KEY TERMS

Abscess—An area of inflamed and injured body tissue that fills with pus.

Decortication—Surgical removal of the fibrous peel that covers the lungs in third-stage empyema.

Empyema—The collection of pus in a body cavity, particularly the lung or pleural cavity.

Fibrin—A fibrous blood protein vital to coagulation and blood clot formation.

Percussion—A diagnostic technique in which the back, chest, or abdomen is tapped to determine whether body cavities contain abnormal fluid.

Pleural cavity—The space surrounding the lungs, including the membranes covering the lungs and lining the inside of the chest wall.

Pneumonia—Inflammation of the lungs usually caused by a virus, bacteria, or other organism.

Resection—The surgical removal of part of an organ or body structure, as in rib resection.

Suppurate—To produce or discharge pus.

Thoracentesis—A procedure in which fluid is withdrawn from the pleural cavity through a needle inserted between the ribs. The fluid may be withdrawn either for diagnostic tests or to drain the cavity.

Video-assisted thoracic surgery (VATS)—A technique used to aid in the placement of chest tubes or when performing decortications when treating advanced empyema.

women is most often caused by *Bacteroides* strains or *Pseudomonas aeruginosa*. In elderly, chronically ill, or alcoholic patients, empyema is often caused by *Klebsiella pneumoniae* species of bacteria.

When the disease organisms arrive in the cavity surrounding the lungs, they infect the tissues that cover the lungs and line the chest wall. As the body attempts to fight off the infection, the cavity fills up with tissue fluid, pus, and dead tissue cells. Empyema of the gall bladder or pelvis results from similar reactions to infection in those parts of the body.

The signs and symptoms of empyema vary somewhat according to the location of the infection and its severity. In empyema thoracis, patients usually exhibit symptoms of pneumonia, including **fever**, **cough**, **fatigue**, **shortness of breath**, and chest **pain**. They may prefer to lie on the side of the body affected by the empyema. Family members may notice **bad breath**. In severe cases, the patient may become dehydrated, cough up blood or greenish-brown sputum, run a fever as high as 105°F (40.6°C), or fall into a **coma**.

Patients with thoracic empyema may develop potentially life-threatening complications if the condition is not treated. The infected tissues may develop large collections of pus (abscesses) that can rupture into the patient's airway, or the infection may spread to the tissues surrounding the heart. In extreme cases the empyema may spread to the brain by means of bacteria carried in the bloodstream.

In pelvic empyema, the infection produces large amounts of thick, foul-smelling pus that is rapidly replaced even after drainage. Empyema of the gallbladder is marked by intense pain on the upper right side of the abdomen, high fever, and rigidity of the muscles over the infected area.

Diagnosis

A physician may consider the possibility of empyema thoracis in patients with pneumonia or other symptoms of lung infection. When listening to sounds within the patient's chest with a stethoscope, the sounds of breathing will be partly muffled and harder to hear in the patients with empyema. The area of the chest over the infection will sound dull when tapped or thumped (percussed). On an x ray, empyema thoracis will appear as a cloudy or opaque area. The amount of fluid present in the pleural cavity can be estimated using an ultrasound imaging procedure. The diagnosis of empyema, however, has to be confirmed with laboratory tests because its symptoms can be caused by other disease conditions.

The diagnosis of empyema is usually confirmed by analyzing a sample of fluid taken from the pleural cavity. The sample is obtained by a procedure called **thoracentesis**. In this procedure, the patient is given a local anesthetic, a needle is inserted into the pleural cavity through the back between the ribs on the infected side, and a sample of fluid is withdrawn. If the patient has empyema, there will be a very high level of one particular kind of immune cell (white blood cells), a high level of protein, and a very low level of blood sugar. The fluid can also be tested for the specific disease organism by staining or tissue cultures. In some cases, the color, smell, or consistency of the tissue fluid also helps to confirm the diagnosis.

Treatment

Empyema is treated using a combination of medications and surgical techniques. Treatment with medication involves intravenously administering a two-week course

of **antibiotics**. It is important to give antibiotics as soon as possible to prevent first-stage empyema from progressing to its later stages. The antibiotics most commonly used are penicillin and vancomycin. Patients experiencing difficulty breathing are also given oxygen therapy.

Surgical treatment of empyema has two goals: drainage of the infected fluid and closing up of the space left in the pleural cavity. If the infection is still in its early stages, the fluid can be drained by thoracentesis. In second-stage empyema, the surgeon will insert a chest tube in the patient's rib cage or remove part of a rib (rib resection) in order to drain the fluid. In third-stage empyema, the surgeon may cut or peel away the thick fibrous layer coating the lung. This procedure is called decortication. When the fibrous covering is removed, the lung will expand to fill the space in the chest cavity. The doctor can use video-assisted **thoracic surgery** (VATS) techniques to position the chest tube or to perform a limited decortication. The VATS technique allows a physician to see within the body during certain surgical procedures. Empyema of the gallbladder is a serious condition that is treated with intravenous antibiotics and surgical removal of the gallbladder.

Prognosis

The prognosis for recovery is generally good, except in those cases with complications, such as a **brain abscess** or blood **poisoning**, or cases caused by certain types of streptococci.

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Rebecca J. Frey

Enalapril *see* **Angiotensin-converting enzyme inhibitors**

Encephalitis

Definition

Encephalitis is an inflammation of the brain, usually caused by a direct viral infection or a hypersensitivity reaction to a virus or foreign protein. Brain inflammation caused by a bacterial infection is sometimes called cerebritis. When both the brain and spinal cord are involved, the disorder is called encephalomyelitis. An inflammation of the brain's covering, or meninges, is called **meningitis**.

Description

Encephalitis is an inflammation of the brain. The inflammation is a reaction of the body's immune system to infection or invasion. During the inflammation, the brain's tissues become swollen. The combination of the infection and the immune reaction to it can cause **headache** and a **fever**, as well as more severe symptoms in some cases.

Approximately 2,000 cases of encephalitis are reported to the Centers for Disease Control in Atlanta, GA each year. The viruses causing primary encephalitis can be epidemic or sporadic. The **polio** virus is an epidemic cause. Arthropod-borne viral encephalitis is responsible for most epidemic viral encephalitis. The viruses live in animal hosts and mosquitos that transmit the disease. The most common form of non-epidemic or sporadic encephalitis is caused by the herpes simplex virus, type 1 (HSV-1) and has a high rate of **death**. **Mumps** is another example of a sporadic cause.

Causes and symptoms

Causes

There are more than a dozen viruses that can cause encephalitis, spread by either human-to human contact or by animal bites. Encephalitis may occur with several common viral infections of childhood. Viruses and viral diseases that may cause encephalitis include:

- **chickenpox**
- **measles**
- mumps
- Epstein-Barr virus (EBV)

- cytomegalovirus infection
- HIV
- herpes simplex
- herpes zoster (**shingles**)
- herpes B
- polio
- **rabies**
- mosquito-borne viruses (arboviruses)

Primary encephalitis is caused by direct infection by the virus, while secondary encephalitis is due to a post-infectious immune reaction to viral infection elsewhere in the body. Secondary encephalitis may occur with measles, chickenpox, mumps, **rubella**, and EBV. In secondary encephalitis, symptoms usually begin five to 10 days after the onset of the disease itself and are related to the breakdown of the myelin sheath that covers nerve fibers.

In rare cases, encephalitis may follow **vaccination** against some of the viral diseases listed above. **Creutzfeldt-Jakob disease**, a very rare brain disorder caused by an infectious particle called a prion, may also cause encephalitis.

Mosquitoes spread viruses responsible for equine encephalitis (eastern and western types), St. Louis encephalitis, California encephalitis, and **Japanese encephalitis**. **Lyme disease**, spread by ticks, can cause encephalitis, as can Colorado tick fever. Rabies is most often spread by animal bites from dogs, cats, mice, raccoons, squirrels, and bats and may cause encephalitis.

Equine encephalitis is carried by mosquitoes that do not normally bite humans but do bite horses and birds. It is occasionally picked up from these animals by mosquitoes that do bite humans. Japanese encephalitis and St. Louis encephalitis are also carried by mosquitoes. The risk of contracting a mosquito-borne virus is greatest in mid- to late summer, when mosquitoes are most active, in those rural areas where these viruses are known to exist. Eastern equine encephalitis occurs in eastern and southeastern United States; western equine and California encephalitis occur throughout the West; and St. Louis encephalitis occurs throughout the country. Japanese encephalitis does not occur in the United States, but is found throughout much of Asia. The viruses responsible for these diseases are classified as arbovirus and these diseases are collectively called **arbovirus encephalitis**.

Herpes simplex encephalitis, the most common form of sporadic encephalitis in western countries, is a disease with significantly high mortality. It occurs in children and adults and both sides of the brain are affected. It is theorized that brain infection is caused by the virus moving from a peripheral location to the brain via two nerves, the olfactory and the trigeminal (largest nerves in the skull).

Herpes simplex encephalitis is responsible for 10% of all encephalitis cases and is the main cause of sporadic, fatal encephalitis. In untreated patients, the rate of death is 70% while the mortality is 15–20% in patients who have been treated with acyclovir. The symptoms of herpes simplex encephalitis are fever, rapidly disintegrating mental state, headache, and behavioral changes.

Symptoms

The symptoms of encephalitis range from very mild to very severe and may include:

- headache
- fever
- lethargy (sleepiness, decreased alertness, and **fatigue**)
- malaise
- nausea and vomiting
- visual disturbances
- tremor
- decreased consciousness (drowsiness, confusion, **delirium**, and unconsciousness)
- stiff neck
- seizures

Symptoms may progress rapidly, changing from mild to severe within several days or even several hours.

Diagnosis

Diagnosis of encephalitis includes careful questioning to determine possible exposure to viral sources. Tests that can help confirm the diagnosis and rule out other disorders include:

- Blood tests. These are to detect antibodies to viral antigens, and foreign proteins.
- Cerebrospinal fluid analysis (spinal tap). This detects viral antigens, and provides culture specimens for the virus or bacteria that may be present in the cerebrospinal fluid.
- Electroencephalogram (EEG).
- CT and MRI scans.

A **brain biopsy** (surgical gathering of a small tissue sample) may be recommended in some cases where treatment to date has been ineffective and the cause of the encephalitis is unclear. Definite diagnosis by biopsy may allow specific treatment that would otherwise be too risky.

Treatment

Choice of treatment for encephalitis will depend on the cause. Bacterial encephalitis is treated with **antibiotics**. Viral encephalitis is usually treated with **antiviral drugs** including acyclovir, ganciclovir, foscarnet, ribovarin, and AZT. Viruses that respond to acyclovir include herpes simplex, the most common cause of sporadic (non-epidemic) encephalitis in the United States.

The symptoms of encephalitis may be treated with a number of different drugs. **Corticosteroids**, including prednisone and dexamethasone, are sometimes prescribed to reduce inflammation and brain swelling. **Anticonvulsant drugs**, including dilantin and phenytoin, are used to control seizures. Fever may be reduced with **acetaminophen** or other fever-reducing drugs.

A person with encephalitis must be monitored carefully, since symptoms may change rapidly. Blood tests may be required regularly to track levels of fluids and salts in the blood.

Prognosis

Encephalitis symptoms may last several weeks. Most cases of encephalitis are mild, and recovery is usually quick. Mild encephalitis usually leaves no residual neurological problems. Overall, approximately 10% of those with encephalitis die from their infections or complications such as secondary infection. Some forms of encephalitis have more severe courses, including herpes encephalitis, in which mortality is 15–20% with treatment, and 70–80% without. Antiviral treatment is ineffective for eastern equine encephalitis, and mortality is approximately 30%.

Permanent neurological consequences may follow recovery in some cases. Consequences may include personality changes, memory loss, language difficulties, seizures, and partial **paralysis**.

Prevention

Because encephalitis is due to infection, it may be prevented by avoiding the infection. Minimizing contact with others who have any of the viral illness listed above may reduce the chances of becoming infected. Most infections are spread by hand-to-hand or hand-to-mouth contact; frequent hand washing may reduce the likelihood of infection if contact cannot be avoided.

Mosquito-borne viruses may be avoided by preventing mosquito bites. Mosquitoes are most active at dawn and dusk, and are most common in moist areas with standing water. Minimizing exposed skin and use of mosquito repellents on other areas can reduce the chances of being bitten.

KEY TERMS

Cerebrospinal fluid analysis—A analysis that is important in diagnosing diseases of the central nervous system. The fluid within the spine will indicate the presence of viruses, bacteria, and blood. Infections such as encephalitis will be indicated by an increase of cell count and total protein in the fluid.

Computerized tomography (CT) Scan—A test to examine organs within the body and detect evidence of tumors, blood clots, and accumulation of fluids.

Electroencephalagram (EEG)—A chart of the brain waves picked up by the electrodes placed on the scalp. Changes in brain wave activity can be an indication of nervous system disorders.

Inflammation—A response from the immune system to an injury. The signs are redness, heat, swelling, and pain.

Magnetic Resonance Imaging (MRI)—MRI is diagnostic radiography using electromagnetic energy to create an image of the central nervous system (CNS), blood system, and musculoskeletal system.

Vaccine—A prepartation containing killed or weakened microorganisms used to build immunity against infection from that microorganism.

Virus—A very small organism that can only live within a cell. They are unable to reproduce outside that cell.

Vaccines are available against some viruses, including polio, herpes B, Japanese encephalitis, and equine encephalitis. Rabies vaccine is available for animals; it is also given to people after exposure. Japanese encephalitis vaccine is recommended for those traveling to Asia and staying in affected rural areas during transmission season.

Resources

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Office Practice of Neurology. Ed. Martin Samuels and Steven Feske. New York: Churchill Livingstone, 1996.

The Merck Manual. Whitehouse Station, NJ: Merck and Co. Inc., 1996.

ORGANIZATIONS

Centers for Disease Control and Prevention. 1600 Clifton Rd., NE, Atlanta, GA 30333. (800) 311-3435, (404) 639-3311. <http://www.cdc.gov>.

Richard Robinson

Encephalocele *see* **Congenital brain defects**

Endarterectomy

Definition

Endarterectomy is an operation to remove or bypass the fatty deposits, or blockage, in an artery narrowed by the buildup of fatty tissue (**atherosclerosis**).

Purpose

Removing the fatty deposits restores normal blood flow to the part of the body supplied by the artery. An endarterectomy is performed to treat cerebrovascular disease in which there is a serious reduction of blood supply to the brain (carotid endarterectomy), or to treat **peripheral vascular disease** (impaired blood supply to the legs).

Endarterectomy is most often performed on one of the two main arteries in the neck (the carotids) opening the narrowed arteries leading to the brain. When performed by an experienced surgeon, the practice is extremely effective, reducing the risk of **stroke** by up to 70%. Recent studies indicate it is effective in preventing stroke, even among those patients who had no warning signs except narrowed arteries detected by their doctors on a routine exam.

Precautions

Before the surgery, a full medical exam is usually done to assess any specific health problems, such as diabetes, high blood pressure, heart disease, or stroke. If possible, reversible health problems, such as cigarette **smoking** or being overweight, should be corrected.

Description

Carotid artery disease

Every person has four carotid arteries (the internal and external carotids on each side of the neck) through which blood from the heart moves into the brain. If one of these arteries becomes blocked by fat and cholesterol, the patient may have a range of symptoms, including:

In this procedure, surgeons are removing plaque from the carotid artery. *(Custom Medical Stock Photo. Reproduced by permission.)*

- weakness in one arm, leg, half of the face, or one entire side of the body
- numbness tingling
- **paralysis** of an arm, leg, or face
- slurred speech
- dizziness
- confusion, **fainting,** or **coma**
- stroke

Removing this fatty buildup, or bypassing a blocked segment, may restore blood flow to the brain, eliminate or decrease the symptoms, and lessen the risk of a stroke.

Peripheral vascular disease

When the blood vessels in the legs (and sometimes the arms) become narrowed, this can restrict blood flow and cause **pain** in the affected area. In severe cases, the tissue may die, requiring **amputation**.

The narrowing is usually caused by buildup of fatty plaques in the vessels, often as the result of smoking, high blood pressure, or poorly-controlled **diabetes mellitus**. The vessels usually narrow slowly, but it's possible for a blood clot to form quickly, causing sudden severe pain in the affected leg or arm.

Procedure

Endarterectomy is a delicate operation that may require several hours. The surgeon begins by making an

Plaque is removed from the carotid artery by clamping the artery, cutting the plaque out, and closing the opening back up. *(Illustration by Argosy Inc.)*

incision over the blocked artery and inserting a tube above and below the blockage to redirect the blood flow while the artery is opened.

Next, the surgeon removes the fat and cholesterol buildup, along with any blood clots that have formed, with a blunt dissecting instrument. Then the surgeon bathes the clean wall in salt solution combined with heparin, an anticoagulant. Then the surgeon stitches the artery just enough so that the bypass shunt tube can be removed, and then he/she stitches the artery completely closed. After checking to make sure no blood is leaking, the surgeon next closes the skin incision with stitches.

The operation should improve symptoms, although its long-term effects may be more limited, since arterial narrowing is rarely confined to one area of one artery. If narrowing is a problem throughout the body, arterial reconstructive surgery may be required.

The total cost of an endarterectomy, including diagnostic tests, surgery, hospitalization, and follow-up care, will vary according to hospital, doctor, and area of the country where the operation is performed, but a patient can expect to pay in the range of $15,000. Patients who are very young, very old, or very ill, or who need more extensive surgery, may require more expensive treatment.

Preparation

Before surgery, the doctor pinpoints the location of the narrowed artery with an x-ray procedure called **angiography**. For surgery to be effective, the degree of narrowing should be at least 70%, but it should not be total. Patients undergoing angiography are given a local anesthetic, but the endarterectomy itself requires the use of a general anesthesia.

Aftercare

After the surgery, the patient spends the first two days lying flat in bed. Patients who have had carotid endarterectomy should not bend the neck sharply during this time. Because the blood flow to the brain is now greatly increased, patients may experience a brief but severe **headache**, or lightheadedness. There may be a slight loss of sensation in the skin, or maybe a droop in

KEY TERMS

Carotid arteries—The four principal arteries of the neck and head. There are two common carotid arteries, each of which divides into the two main branches (internal and external).

Diabetes mellitus—A disorder in which the pancreas doesn't produce enough (or any) insulin. As a result, the blood levels of sugar become very high. Among other things, diabetes can lead to the breakdown of small blood vessels and a high risk of atherosclerosis and high blood pressure.

Stroke—Damage to the part of the brain caused by an interruption of the blood supply. In some cases, small pieces of plaque in the carotid artery may break loose and block an artery in the brain. A narrowed carotid artery also can be the source of blood clots travelling to the brain, or the artery can become completely clogged, blocking all blood flow to the brain.

the mouth, if any of the nerves in the neck were lightly bruised during surgery. In time, this should correct itself.

Risks

The amount of risk depends on the hospital, the skill of the surgeon, and the severity of underlying disease. Patients who have just had an acute stroke are at greatest risk. During carotid artery surgery, blood flow is interrupted through the artery, so that paralysis and other stroke symptoms may occur. These may resolve after surgery, or may result in permanent stroke. Paralysis is usually one-sided; other stroke symptoms may include loss of half the field of vision, loss of sensation, double vision, speech problems, and personality changes. Risks of endarterectomy to treat either carotid artery or peripheral vascular disease include:

- reactions to anesthesia
- bleeding
- infection
- blood clots

Normal results

The results after successful surgery are usually striking. The newly opened artery should help to restore normal blood flow. In carotid endarterectomy, surgery should prevent the risk of brain damage and stroke. However, the buildup of fat and cholesterol usually affects all arteries, not just the one that was operated on. Affected arteries in other parts of the body may be equally clogged and potentially dangerous. Even arteries that were operated electively will likely, begin to clog up again after the surgery.

For this reason, lifestyle changes (no smoking, low fat, low cholesterol diet) are important, especially if diet and lifestyle contributed to the development of the problem in the first place.

Resources

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"Better Blood Flow: Surgery May Strike Down Stroke Risk." *Prevention* 47 (1 Feb. 1995): 50-52.

ORGANIZATIONS

National Institute of Neurological Disorders and Stroke. PO Box 5801, Bethesda, MD 20824. (800) 352-9424. <http://www.ninds.nih.gov/index.htm>.

National Institute of Neurological Disorders at the Neurology Institute. PO Box 5801, Bethesda, MD 20824.

Carol A. Turkington

Endemic syphilis *see* **Bejel**

Endocardial resection *see* **Myocardial resection**

Endocarditis

Definition

The endocardium is the inner lining of the heart muscle, which also covers the heart valves. When the endocardium becomes damaged, bacteria from the blood stream can become lodged on the heart valves or heart lining. The resulting infection is known as endocarditis.

Description

The endocardium lines all four chambers of the heart—two at the top (the right and left atria) and two at the bottom (the right and left ventricles)—through which blood passes as the heart beats. It also covers the four valves (the tricuspid valve, the pulmonary valve, the mitral valve, and the aortic valve), which normally open

and close to allow the blood to flow in only one direction through the heart during each contraction.

For the heart to pump blood efficiently, the four chambers must contract and relax, and the four valves must open and close, in a well coordinated fashion. By damaging the valves or the walls of the heart chambers, endocarditis can interfere with the ability of the heart to do its job.

Endocarditis rarely occurs in people with healthy, normal hearts. Rather, it most commonly occurs when there is damage to the endocardium. The endocardium may be affected by a congenital heart defect, such as **mitral valve prolapse**, in which blood leaks through a poorly functioning mitral valve back into the heart. It may also be damaged by a prior scarring of the heart muscle, such as **rheumatic fever**, or replacement of a heart valve. Any of these conditions can damage the endocardium and make it more susceptible to infection.

Bacteria can get into the blood stream (a condition known as **bacteremia**) in a number of different ways: It may spread from a localized infection such as a urinary tract infection, **pneumonia**, or skin infection or get into the blood stream as a result of certain medical conditions, such as severe **periodontal disease**, **colon cancer**, or inflammatory bowel disease. It can enter the blood stream during minor procedures, such as periodontal surgery, tooth extractions, teeth cleaning, tonsil removal, prostate removal, or endoscopic examination. It can also be introduced through in-dwelling catheters, which are used for intravenous medications, intravenous feeding, or dialysis. In people who use intravenous drugs, the bacteria can enter the blood stream through unsterilized, contaminated needles and syringes. (People who are prone to endocarditis generally need to take prescribed **antibiotics** before certain surgical or dental procedures to help prevent this infection.)

If not discovered and treated, infective endocarditis can permanently damage the heart muscle, especially the valves. For the heart to work properly, all four valves must be functioning well, opening at the right time to let blood flow in the right direction and closing at the right time to keep the blood from flowing in the wrong direction. If the valve is damaged, this may allow blood to flow backward—a condition known as regurgitation. As a result of a poorly functioning valve, the heart muscle has to work harder to pump blood and may become weakened, leading to **heart failure**. Heart failure is a chronic condition in which the heart is unable to pump blood well enough to supply blood adequately to the body.

Another danger associated with endocarditis is that the vegetation formed by bacteria colonizing on heart valves may break off, forming emboli. These emboli may travel through the circulation and become lodged in blood vessels. By blocking the flow of blood, emboli can starve various tissues of nutrients and oxygen, damaging them. For instance, an embolus lodged in the blood vessels of the lungs may cause pneumonia-like symptoms. An embolus may also affect the brain, damaging nerve tissue, or the kidneys, causing kidney disease. Emboli may also weaken the tiny blood vessels called capillaries, causing hemorrhages (leaking blood vessels) throughout the body.

A close-up view of an infected artificial heart valve showing bacterial endocarditis (the granulated tissue at center of image). When infection occurs early after surgery, it is likely that organisms have gained entry during the operative period. This type of infection is usually caused by *Staphylococcus epidermidis* and *S. aureus* and is treated with antibiotic drugs. *(Photograph by Dr. E. Walker, Photo Researchers, Inc. Reproduced by permission.)*

Causes and symptoms

Most cases of infective endocarditis occur in people between the ages of 15 and 60, with a median age at onset of about 50 years. Men are affected about twice as often as women are. Other factors that put people at increased risk for endocarditis are congenital heart problems, heart surgery, previous episodes of endocarditis, and intravenous drug use.

While there is no single specific symptom of endocarditis, a number of symptoms may be present. The most common symptom is a mild **fever**, which rarely goes above 102°F (38.9°C). Other symptoms include chills, weakness, **cough**, trouble breathing, headaches, aching joints, and loss of appetite.

Emboli may also cause a variety of symptoms, depending on their location. Emboli throughout the body may cause Osler's nodes, small, reddish, painful bumps most commonly found on the inside of fingers and toes. Emboli may also cause petechiae, tiny purple

This echocardiogram shows an aortic regurgitation due to endocarditis, an infection of the lining membrane of the cardiac chambers. *(Custom Medical Stock Photo. Reproduced by permission.)*

or red spots on the skin, resulting from hemorrhages under the skin's surface. Tiny hemorrhages resembling splinters may also appear under the fingernails or toenails. If emboli become lodged in the blood vessels of the lungs, they may cause coughing or **shortness of breath**. Emboli lodged in the brain may cause symptoms of a mini-stroke, such as numbness, weakness, or **paralysis** on one side of the body or sudden vision loss or double vision. Emboli may also damage the kidneys, causing blood to appear in the urine. Sometimes the capillaries on the surface of the spleen rupture, causing the spleen to become enlarged and tender to the touch. Anyone experiencing any of these symptoms should seek medical help immediately.

Diagnosis

Doctors begin the diagnosis by taking a history, asking the patient about the symptoms mentioned above. During a **physical examination**, the doctor may also uncover signs such as fever, an enlarged spleen, signs of kidney disease, or hemorrhaging. Listening to the patient's chest with a stethoscope, the doctor may also hear a heart murmur. A heart murmur may indicate abnormal flow of blood through one of the heart chambers or valves.

Doctors take a sample of the patient's blood to test it for bacteria and other microorganisms that may be causing the infection. They usually also use a test called **echocardiography**, which uses ultrasound waves to make images of the heart, to check for abnormalities in the structure of the heart wall or valves. One of the telltale signs they look for in echocardiography is vegetation, the abnormal growth of tissue around a valve composed of blood platelets, bacteria, and a clotting protein called fibrin. Another tell-tale sign is regurgitation, or the backward flow of blood, through one of the heart valves. A normal echocardiogram does not exclude the possibility of endocarditis, but an abnormal echocardiogram can confirm its presence. If an echocardiogram cannot be done or its results are inconclusive, a modified technique called **transesophageal echocardiography** is sometimes performed. Transesophageal echocardiography involves passing an ultrasound device into the esophagus to get a clearer image of the heart.

Treatment

When doctors suspect infective endocarditis, they will admit the patient to a hospital and begin treating the infection before they even have the results of the **blood culture**. Their choice of antibiotics depends on what the most likely infecting microorganism is. Once the results of the blood culture become available, the doctor can adjust the medications, using specific antibiotics known to be effective against the specific microorganism involved.

Unfortunately, in recent years, the treatment of endocarditis has become more complicated as a result of antibiotic resistance. Over the past few years, especially as antibiotics have been overprescribed, more and more strains of bacteria have become increasingly resistant to a wider range of antibiotics. For this reason, doctors may need to try a few different types of antibiotics—or even a combination of antibiotics—to successfully treat the infection. Antibiotics are usually given for about one month, but may need to be given for an even longer period of time if the infection is resistant to treatment.

Once the fever and the worst of the symptoms have gone away, the patient may be able to continue antibiotic therapy at home. During this time, the patient should make regular visits to the health care team for further testing and physical examination to make sure that the antibiotic therapy is working, that it is not causing adverse side effects, and that there are no complications such as emboli or heart failure. The patient should alert the health-care team to any symptoms that could indicate serious complications: For instance, trouble breathing or swelling in the legs could indicate congestive heart failure. **Headache**, joint **pain**, blood in the urine, or **stroke** symptoms could indicate an embolus, and fever and chills could indicate that the treatment is not working and the infection is worsening. Finally, **diarrhea**, rash, **itching**, or joint pain may suggest a bad reaction to the antibiotics. Anyone experiencing any of these symptoms should alert the health care team immediately.

In some cases, surgery may be needed. These include cases of congestive heart failure, recurring

KEY TERMS

Aortic valve—The valve between the left ventricle of the heart and the aorta.

Bacteremia—An infection caused by bacteria in the blood.

Congestive heart failure—A condition in which the heart muscle cannot pump blood as efficiently as it should.

Echocardiography—A diagnostic test using reflected sound waves to study the structure and motion of the heart muscle.

Embolus—A bit of foreign material, such as gas, a piece of tissue, or tiny clot, that travels in the circulation until it becomes lodged in a blood vessel.

Endocardium—The inner wall of the heart muscle, which also covers the heart valves.

Mitral valve—The valve between the left atrium and the left ventricle of the heart.

Osler's nodes—Small, raised, reddish, tender areas associated with endocarditis, commonly found inside the fingers or toes.

Petechiae—Tiny purple or red spots on the skin associated with endocarditis, resulting from hemorrhages under the skin's surface.

Pulmonary valve—The valve between the right ventricle of the heart and the pulmonary artery.

Transducer—A device that converts electrical signals into ultrasound waves and ultrasound waves back into electrical impulses.

Transesophageal echocardiography—A diagnostic test using an ultrasound device, passed into the esophagus of the patient, to create a clear image of the heart muscle.

Tricuspid valve—The valve between the right atrium and the right ventricle of the heart.

Vegetation—An abnormal growth of tissue around a valve, composed of blood platelets, bacteria, and a protein involved in clotting.

emboli, infection that doesn't respond to treatment, poorly functioning heart valves, and endocarditis involving prosthetic (artificial) valves. The most common surgical treatment involves cutting away (debriding) damaged tissue and replacing the damaged valve.

Prognosis

If left untreated, infective endocarditis continues to progress and is always fatal. However, if it is diagnosed and properly treated within the first six weeks of infection, the infection can be completely cured in about 90% of the cases. The prognosis depends on a number of factors, such as the patient's age and overall physical condition, the severity of the diseases involved, the exact site of the infection, how vulnerable the microorganisms are to antibiotics, and what kind of complications the endocarditis may be causing.

Prevention

Some people are especially prone to endocarditis. These include people with past episodes of endocarditis, those with congenital heart problems or heart damage from rheumatic fever, and those with artificial heart valves. Intravenous drug users are also at increased risk. Anyone who falls into a high-risk category should alert his or her health-care professionals before undergoing any surgical or dental procedures. High-risk patients must be treated in advance with antibiotics before these procedures to minimize the risk of infection.

Resources

BOOKS

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PERIODICALS

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ORGANIZATIONS

American Heart Association. 7320 Greenville Ave. Dallas, TX 75231. (214) 373-6300. <http://www.americanheart.org>.

National Heart, Lung and Blood Institute. PO Box 30105, Bethesda, MD 20824-0105. (301) 251-1222. <http://www.nhlbi.nih.gov>.

Robert Scott Dinsmoor

Endocrine pancreatic cancer *see* **Pancreatic cancer, endocrine**

Endometrial biopsy

Definition

Endometrial biopsy is a procedure in which a sample of the endometrium (tissue lining the inside of the uterus) is removed for microscopic examination.

Purpose

The test is most often performed to find out the cause of abnormal uterine bleeding. Abnormal bleeding includes bleeding between menstrual periods, excessive bleeding during a menstrual period, or bleeding after **menopause**. Since abnormal uterine bleeding can indicate **cancer**, an endometrial biopsy is done to rule out **endometrial cancer** or hyperplasia (a potentially precancerous condition).

Endometrial biopsies are also done as a screening test for endometrial cancer in postmenopausal women on **hormone replacement therapy**. Hormone replacement therapy usually requires a woman to take estrogen and progesterone. An endometrial biopsy is particularly useful in cases where postmenopausal women take estrogen, but cannot take progesterone. Estrogen in the system without the balancing effect of progesterone has been linked to an increased risk of endometrial cancer.

An endometrial biopsy can also be used as part of an **infertility** exam to rule out problems with the development of the endometrium. This condition is called luteal phase defect and can cause the endometrium to not support a **pregnancy**. An endometrial biopsy can also be used to evaluate the problem of repeated early miscarriages.

Precautions

If the endometrial biopsy is being done to investigate why a woman is unable to get pregnant, the test must be performed at a specific time during the menstrual cycle. Since the test evaluates whether the endometrium is developed adequately to support implantation and growth of a fertilized egg, it is critical to perform the test approximately three days before the expected menstrual period.

Description

The test is performed by a doctor who specializes in women's reproductive health (an obstetrician/gynecologist). The test is performed either in the doctor's office or in a local hospital. The patient may be asked to take **pain** medication (like Motrin or Aleve) an hour or so before the procedure. A local anesthetic may be injected into the cervix in order to decrease pain and discomfort during the procedure.

KEY TERMS

Biopsy—The surgical removal and microscopic examination of living tissue for diagnostic purposes.

Cervix—The opening of the uterus extending into the vagina.

Endometrium—The layer lining the inner cavity of the uterus; this layer changes daily throughout the menstrual cycle.

Uterus—The hollow, muscular female organ that supports the development and nourishment of the unborn baby during pregnancy.

The woman will be asked to lie on her back with knees apart and feet in stirrups. The doctor will first conduct a thorough exam of the pelvic region, including the vulva (the external genitals), vagina, and uterus. A speculum (an instrument that is used to hold the walls of the vagina open) will be inserted into the vagina. A small, hollow plastic tube is then passed into the uterine cavity. A small piece of the uterine lining is sucked out with a plunger that is attached to the tube. Once the sample is obtained, the instruments are removed. The sample is sent to the laboratory for microscopic examination.

The patient may experience some pain when the cervix is grasped. The patient may also feel some cramping, pressure, and discomfort when the instruments are inserted into the uterus and the tissue sample is collected.

Preparation

For the small number of endometrial biopsies that are done as part of infertility testing, a pregnancy test is also often performed before the procedure. Since the biopsy is performed late in the menstrual cycle, it is possible that the woman may be pregnant.

Aftercare

The biopsy may cause a small amount of bleeding (spotting). The woman can resume normal activities right away. If cramping becomes severe, heavy bleeding occurs, or the woman develops a high temperature, the doctor should be notified immediately.

If the test is being done to determine the cause of infertility, the onset of the menstrual period following the biopsy should be reported to the doctor. This will allow the doctor to correctly predict if the endometrium has been developing at the expected rate.

A catheter is inserted into the uterus to remove uterine cells for further examination. *(Illustration by Argosy Inc.)*

Risks

The risks of an endometrial biopsy are very small. There is a possibility that prolonged bleeding may occur after the procedure. There is also a slight chance of an infection. Very rarely, there are instances when the uterus is pierced (perforated) or the cervix is torn because of the biopsy.

Normal results

Most biopsies are done to rule out endometrial cancer or endometrial hyperplasia. A normal result shows no cancerous or precancerous cells. Normal results also show that the uterine lining is changing at the proper rate. If it is, then the results of the biopsy are said to be "in-phase" because the tissue looks appropriate and has developed normally for the late phase of the menstrual cycle.

Abnormal results

If the endometrium is not developing at the appropriate rate, the results are said to be "out-of-phase" or abnormal. The endometrium has not developed appropriately and cannot support a pregnancy. This condition is called luteal phase defect and may need to be treated with progesterone.

Abnormal appearance of the cells forming the uterine tissue could also indicate uterine cancer, or the presence of fibroids or polyps in the uterus.

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ORGANIZATIONS

American Cancer Society. 1599 Clifton Rd., NE, Atlanta, GA 30329-4251. (800) 227-2345. <http://www.cancer.org>.

Cancer Research Institute. 681 Fifth Ave., New York, NY 10022. (800) 992-2623. <http://www.cancerresearch.org>.

Gynecologic Cancer Foundation. 401 North Michigan Ave., Chicago, IL 60611. (800) 444-4441.

National Cancer Institute. Building 31, Room 10A31, 31 Center Drive, MSC 2580, Bethesda, MD 20892-2580. (800) 422-6237. <http://www.nci.nih.gov>.

Lata Cherath, PhD

Endometrial cancer

Definition

Endometrial **cancer** develops when the cells that make up the inner lining of the uterus (the endometrium) become abnormal and grow uncontrollably.

Description

Endometrial cancer (also called uterine cancer) is the fourth most common type of cancer among women and the most common gynecologic cancer. Approximately 34,000 women are diagnosed with endometrial cancer each year. In 1998, approximately 6,300 women died from this cancer. Although endometrial cancer generally occurs in women who have gone through **menopause** and are 45 years of age or older, 30% of the women with endometrial cancer are younger than 40 years of age. The average age at diagnosis is 60 years old.

The uterus, or womb, is the hollow female organ that supports the development of the unborn baby during **pregnancy**. The uterus has a thick muscular wall and an inner lining called the endometrium. The endometrium is very sensitive to hormones and it changes daily during the menstrual cycle. The endometrium is designed to provide an ideal environment for the fertilized egg to implant and begin to grow. If pregnancy does not occur, the endometrium is shed causing the menstrual period.

More than 95% of uterine cancers arise in the endometrium. The most common type of uterine cancer is adenocarcinoma. It arises from an abnormal multiplication of endometrial cells (atypical adenomatous hyperplasia) and is made up of mature, specialized cells (well-differentiated). Less commonly, endometrial cancer arises without a preceding hyperplasia and is made up of poorly differentiated cells. The more common of these types are the papillary serous and clear cell carcinomas. Poorly differentiated endometrial cancers are often associated with a less promising prognosis.

The highest incidence of endometrial cancer in the United States is in Caucasians, Hawaiians, Japanese, and African Americans. American Indians, Koreans, and Vietnamese have the lowest incidence. African American and Hawaiian women are more likely to be diagnosed with advanced cancer and, therefore, have a higher risk of dying from the disease.

Causes and symptoms

Although the exact cause of endometrial cancer is unknown, it is clear that high levels of estrogen, when not balanced by progesterone, can lead to abnormal growth of the endometrium. Factors that increase a woman's risk of developing endometrial cancer are:

- Age. The risk is considerably higher in women who are over the age of 50 and have gone through menopause.
- **Obesity**. Being overweight is a very strong risk factor for this cancer. Fatty tissue can change other normal body chemicals into estrogen, which can promote endometrial cancer.
- Estrogen replacement therapy. Women receiving estrogen supplements after menopause have a 12 times higher risk of getting endometrial cancer if progesterone is not taken simultaneously.
- Diabetes. Diabetics have twice the risk of getting this cancer as nondiabetic women. It is not clear if this risk is due to the fact that many diabetics are also obese and hypertensive. One 1998 study found that women who were obese and diabetic were three times more likely to develop endometrial cancer than women who were obese but nondiabetic. This study also found that nonobese diabetics were not at risk of developing endometrial cancer.
- **Hypertension**. High blood pressure (or hypertension) is also considered a risk factor for uterine cancer.
- Irregular menstrual periods. During the menstrual cycle, there is interaction between the hormones estrogen and progesterone. Women who do not ovulate regularly are exposed to high estrogen levels for longer periods of time. If a woman does not ovulate regularly, this delicate balance is upset and may increase her chances of getting uterine cancer.
- Early first menstruation or late menopause. Having the first period at a young age (the mean age of menses is 12.16 years in African American girls and 12.88 years in caucasian girls) or going through menopause at a late age (over age 51) seem to put women at a slightly higher risk for developing endometrial cancer.
- Tamoxifen. This drug, which is used to treat or prevent **breast cancer**, increases a woman's chance of developing endometrial cancer. Tamoxifen users tend to have more advanced endometrial cancer with an associated poorer survival rate than those who do not take the drug. In many cases, however, the value of tamoxifen for treating breast cancer and for preventing the cancer from spreading far outweighs the small risk of getting endometrial cancer.
- Family history. Some studies suggest that endometrial cancer runs in certain families. Women with inherited mutations in the BRCA1 and BRCA2 genes are at a higher risk of developing breast, ovarian, and other gynecologic cancers. Those with the hereditary non-

Cancer located in the uterus. *(Illustration by Argosy Inc.)*

polyposis colorectal cancer gene have a higher risk of developing endometrial cancer.

- Breast, ovarian, or **colon cancer**. Women who have a history of these other types of cancer are at an increased risk of developing endometrial cancer.
- Low parity or nulliparity. Endometrial cancer is more common in women who have born few (low parity) or no (nulliparity) children. The high levels of progesterone produced during pregnancy has a protective effect against endometrial cancer. The results of one study suggest that nulliparity is associated with a lower survival rate.
- Infertility. Risk is increased due to nulliparity or the use of fertility drugs.
- Polycystic ovary syndrome. The increased level of estrogen associated with this abnormality raises the risk of cancers of the breast and endometrium.

The most common symptom of endometrial cancer is unusual vaginal spotting, bleeding, or discharge. In women who are near menopause (perimenopausal), symptoms of endometrial cancer could include bleeding between periods (intermenstrual bleeding), heavy bleeding that lasts for more than seven days, or short menstrual cycles (fewer than 21 days). For women who have gone through menopause, any vaginal bleeding or abnormal discharge is suspect. **Pain** in the pelvic region and the presence of a lump (mass) are symptoms that occur late in the disease.

Diagnosis

If endometrial cancer is suspected, a series of tests will be conducted to confirm the diagnosis. The first step will involve taking a complete personal and family medical history. A **physical examination**, which will include a thorough pelvic examination, will also be done.

The doctor may order an **endometrial biopsy**. This is generally performed in the doctor's office and does not require anesthesia. A thin, flexible tube is inserted through the cervix and into the uterus. A small piece of endometrial tissue is removed. The patient may experience some discomfort, which can be minimized by taking an anti-inflammatory medication (like Advil or Motrin) an hour before the procedure.

If an adequate amount of tissue was not obtained by the endometrial biopsy, or if the biopsy tissue looks abnormal but confirmation is needed, the doctor may perform a **dilatation and curettage** (D & C). This procedure is done in the outpatient surgery department of a hospital

KEY TERMS

Adjuvant therapy—A treatment done when there is no evidence of residual cancer in order to aid the primary treatment. Adjuvant treatments for endometrial cancer are radiation therapy, chemotherapy, and hormone therapy.

Atypical adenomatous hyperplasia—The overgrowth of the endometrium. This precancerous condition is estimated to progress to cancer in one third of the cases.

Dilation and curettage (D & C)—A procedure in which the doctor opens the cervix and uses a special instrument to scrape tissue from the inside of the uterus.

Endometrial biopsy—A procedure in which a sample of the endometrium is removed and examined under a microscope.

Endometrium—The mucosal layer lining the inner cavity of the uterus. The endometrium's structure changes with age and with the menstrual cycle.

Estrogen—A female hormone responsible for stimulating the development and maintenance of female secondary sexual characteristics.

Estrogen replacement therapy (ERT)—A treatment in which estrogen is used therapeutically during menopause to alleviate certain symptoms such as hot flashes. ERT has also been shown to reduce the risk of osteoporosis and heart disease in women.

Progesterone—A female hormone that acts on the inner lining of the uterus and prepares it for implantation of the fertilized egg.

Progestins—A female hormone, like progesterone, that acts on the inner lining of the uterus.

and takes about an hour. The patient may be given general anesthesia. The doctor dilates the cervix and uses a special instrument to scrape tissue from inside the uterus.

The tissue that is obtained from the biopsy or the D & C is sent to a laboratory for examination. If cancer is found, then the type of cancer will be determined. The treatment and prognosis depends on the type and stage of the cancer.

Trans-vaginal ultrasound may be used to measure the thickness of the endometrium. For this painless procedure, a wand-like ultrasound transducer is inserted into the vagina to enable visualization and measurement of the uterus, the thickness of the uterine lining, and other pelvic organs.

Other possible diagnostic procedures include sonohysterography and **hysteroscopy**. For sonohysteroscopy, a small tube is passed through the cervix and into the uterus. A small amount of a salt water (saline) solution is injected through the tube to open the space within the uterus and allow ultrasound visualization of the endometrium. For hysteroscopy, a wand-like camera is passed through the cervix to allow direct visualization of the endometrium. Both of these procedures cause discomfort, which may be reduced by taking an anti-inflammatory medication prior to the procedure.

Treatment

Clinical staging

The International Federation of Gynecology and Obstetrics (FIGO) has adopted a staging system for endometrial cancer. The stage of cancer is determined after surgery. Endometrial cancer is categorized into four stages (I, II, III, and IV) that are subdivided (A, B, and possibly C) based on the depth or spread of cancerous tissue. Seventy percent of all uterine cancers are stage I, 10–15% are stage II, and the remainder are stages III and IV. The cancer is also graded (G1, G2, and G3) based upon microscopic analysis of the aggressiveness of the cancer cells.

The FIGO stages for endometrial cancer are:

- Stage I. Cancer is limited to the uterus.
- Stage II. Cancer involves the uterus and cervix.
- Stage III. Cancer has spread out of the uterus but is restricted to the pelvic region.
- Stage IV. Cancer has spread to the bladder, bowel, or other distant locations.

The mainstay of treatment for most stages of endometrial cancer is surgery. **Radiation therapy**, hormonal therapy, and **chemotherapy** are additional treatments (called adjuvant therapy). The necessity of adjuvant therapy is a controversial topic which should be discussed with the patient's treatment team.

Surgery

Most women with endometrial cancer, except those with stage IV disease, are treated with a **hysterectomy**. A simple hysterectomy involves the removal of the uterus. In a bilateral **salpingo-oophorectomy** with total hysterectomy, the ovaries, fallopian tubes, and uterus are

removed. This may be necessary because endometrial cancer often spreads to the ovaries first. The lymph nodes in the pelvic region may also be biopsied or removed to check for metastasis. Hysterectomy is traditionally performed through an incision in the abdomen (laparotomy), however, endoscopic surgery (**laparoscopy**) with vaginal hysterectomy is also being used. Women with stage I disease may require no further treatment. However, those with higher grade disease will receive adjuvant therapy.

Radiation therapy

The decision to use radiation therapy depends on the stage of the disease. Radiation therapy may be used before surgery (preoperatively) and/or after surgery (postoperatively). Radiation given from a machine that is outside the body is called external radiation therapy. Sometimes applicators containing radioactive compounds are placed inside the vagina or uterus. This is called internal radiation therapy or brachytherapy and requires hospitalization.

Side effects are common with radiation therapy. The skin in the treated area may become red and dry. **Fatigue**, upset stomach, **diarrhea**, and nausea are also common complaints. Radiation therapy in the pelvic area may cause the vagina to become narrow (vaginal stenosis), making intercourse painful. **Premature menopause** and some problems with urination may also occur.

Chemotherapy

Chemotherapy is usually reserved for women with stage IV or recurrent disease because this therapy is not a very effective treatment for endometrial cancer. The **anticancer drugs** are given by mouth or intravenously. Side effects include stomach upset, vomiting, appetite loss, hair loss, mouth or vaginal sores, fatigue, menstrual cycle changes, and premature menopause. There is also an increased chance of infections.

Hormonal therapy

Hormonal therapy uses drugs like progesterone to slow the growth of endometrial cells. These drugs are usually available as pills. This therapy is usually reserved for women with advanced or recurrent disease. Side effects include fatigue, fluid retention, and appetite and weight changes.

Alternative treatment

Although alternative and complementary therapies are used by many cancer patients, very few controlled studies on the effectiveness of such therapies exist. Mind-body techniques, such as prayer, **biofeedback**, visualization, **meditation**, and **yoga**, have not shown any effect in reducing cancer, but they can reduce **stress** and lessen some of the side effects of cancer treatments. Clinical studies of hydrazine sulfate found that it had no effect on cancer and even worsened the health and well-being of the study subjects. One clinical study of the drug amygdalin (Laetrile) found that it had no effect on cancer. Laetrile can be toxic and has caused deaths. Shark cartilage, although highly touted as an effective cancer treatment, is an improbable therapy that has not been the subject of clinical study.

The American Cancer Society has found that the "metabolic diets" pose serious risk to the patient. The effectiveness of the macrobiotic, Gerson, and Kelley **diets** and the Manner metabolic therapy has not been scientifically proven. The FDA was unable to substantiate the anticancer claims made about the popular Cancell treatment.

There is no evidence for the effectiveness of most over-the-counter herbal cancer remedies. Some herbals have shown an anticancer effect. As shown in clinical studies, Polysaccharide krestin, from the mushroom *Coriolus versicolor*, has significant effectiveness against cancer. In a small study, the green alga *Chlorella pyrenoidosa* has been shown to have anticancer activity. In a few small studies, evening primrose oil has shown some benefit in the treatment of cancer.

Prognosis

Because it is possible to detect endometrial cancer early, the chances of curing it are excellent. The five year survival rates for endometrial cancer by stage are: 90%, stage I; 60%, stage II; 40%, stage III; and 5%, stage IV. Endometrial cancer most often spreads to the lungs, liver, bones, brain, vagina, and certain lymph nodes.

Prevention

Women (especially postmenopausal women) should report any abnormal vaginal bleeding or discharge to the doctor. Controlling obesity, blood pressure, and diabetes can help to reduce the risk of this disease. Women on estrogen replacement therapy have a substantially reduced risk of endometrial cancer if progestins are taken simultaneously. Long term use of birth control pills has been shown to reduce the risk of this cancer. Women who have irregular periods may be prescribed birth control pills to help prevent endometrial cancer. Women who are taking tamoxifen and those who carry the hereditary nonpolyposis colorectal cancer gene should be screened regularly, receiving annual pelvic examinations.

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ORGANIZATIONS

American Cancer Society, National Headquarters. 1599 Clifton Rd. NE, Atlanta, GA 30329. (800) 227-2345. <http://www.cancer.org/>.

Cancer Research Institute, National Headquarters. 681 Fifth Ave., New York, NY 10022. (800) 992-2623. <http://www.cancerresearch.org>.

Gynecologic Cancer Foundation. 401 North Michigan Ave., Chicago, IL 60611. (800) 444-4441. <http://www.wcn.org>.

National Cancer Institute, National Institutes of Health. 9000 Rockville Pike, Bethesda, MD 20892. (800) 422-6237. <http://cancernet.nci.nih.gov/>.

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Endometriosis

Definition

Endometriosis is a condition in which bits of the tissue similar to the lining of the uterus (endometrium) grow in other parts of the body. Like the uterine lining, this tissue builds up and sheds in response to monthly hormonal cycles. However, there is no natural outlet for the blood discarded from these implants. Instead, it falls onto surrounding organs, causing swelling and inflammation. This repeated irritation leads to the development of scar tissue and adhesions in the area of the endometrial implants.

Description

Endometriosis is estimated to affect 7% of women of childbearing age in the United States. It most commonly strikes between the ages of 25 and 40. Endometriosis can also appear in the teen years, but never before the start of menstruation. It is seldom seen in postmenopausal women.

Endometriosis was once called the "career woman's disease" because it was thought to be a product of delayed childbearing. The statistics defy such a narrow generalization; however, **pregnancy** may slow the progress of the condition. A more important predictor of a woman's risk is if her female relatives have endometriosis. Another influencing factor is the length of a woman's menstrual cycle. Women whose periods last longer than a week with an interval of less than 27 days between them seem to be more prone to the condition.

Endometrial implants are most often found on the pelvic organs—the ovaries, uterus, fallopian tubes, and in the cavity behind the uterus. Occasionally, this tissue grows in such distant parts of the body as the lungs, arms, and kidneys. Newly formed implants appear as small bumps on the surfaces of the organs and supporting ligaments and are sometimes said to look like "powder burns." **Ovarian cysts** may form around endometrial tissue (endometriomas) and may range from pea to grapefruit size. Endometriosis is a progressive condition that usually advances slowly, over the course of many years. Doctors rank cases from minimal to severe based on factors such as the number and size of the endometrial implants, their appearance and location, and the extent of the scar tissue and adhesions in the vicinity of the growths.

Causes and symptoms

Although the exact cause of endometriosis is unknown, a number of theories have been put forward. Some of the more popular ones are:

- Implantation theory. Originally proposed in the 1920s, this theory states that a reversal in the direction of menstrual flow sends discarded endometrial cells into the body cavity where they attach to internal organs and seed endometrial implants. There is considerable evidence to support this explanation. Reversed menstrual

flow occurs in 70–90% of women and is thought to be more common in women with endometriosis. However, many women with reversed menstrual flow do not develop endometriosis.

- Vascular-lymphatic theory. This theory suggests that the lymph system or blood vessels (vascular system) is the vehicle for the distribution of endometrial cells out of the uterus.
- Coelomic metaplasia theory. According to this hypothesis, remnants of tissue left over from prenatal development of the woman's reproductive tract transforms into endometrial cells throughout the body.
- Induction theory. This explanation postulates that an unidentified substance found in the body forces cells from the lining of the body cavity to change into endometrial cells.

In addition to these theories, the following factors are thought to influence the development of endometriosis:

- Heredity. A woman's chance of developing endometriosis is seven times greater if her mother or sisters have the disease.
- Immune system function. Women with endometriosis may have lower functioning immune systems that have trouble eliminating stray endometrial cells. This would explain why a high percentage of women experience reversed menstrual flow while relatively few develop endometriosis.
- Dioxin exposure. Some research suggests a link between the exposure to dioxin (TCCD), a toxic chemical found in weed killers, and the development of endometriosis.

While many women with endometriosis suffer debilitating symptoms, others have the disease without knowing it. Paradoxically, there does not seem to be any relation between the severity of the symptoms and the extent of the disease. The most common symptoms are:

- Menstrual **pain**. Pain in the lower abdomen that begins a day or two before the menstrual period starts and continues through to the end is typical of endometriosis. Some women also report lower back aches and pain during urination and bowel movement, especially during their periods.
- Painful sexual intercourse. Pressure on the vagina and cervix causes severe pain for some women.
- Abnormal bleeding. Heavy menstrual periods, irregular bleeding, and spotting are common features of endometriosis.
- **Infertility**. There is a strong association between endometriosis and infertility, although the reasons for this have not been fully explained. It is thought that the build up of scar tissue and adhesions blocks the fallopian tubes and prevents the ovaries from releasing eggs. Endometriosis may also affect fertility by causing hormonal irregularities and a higher rate of early **miscarriage**.

An endoscopic view of endometriosis on pelvic wall. *(Custom Medical Stock Photo. Reproduced by permission.)*

Diagnosis

If a doctor suspects endometriosis, the first step will be to perform a **pelvic exam** to try to feel if implants are present. Very often there is no strong evidence of endometriosis from a physical exam. The only way to make a definitive diagnosis is through minor surgery called a **laparoscopy**. A laparoscope, a slender scope with a light on the end, is inserted into the woman's abdomen through a small incision near her belly button. This allows the doctor to examine the internal organs for endometriotic growths. Often, a sample of tissue is taken for later examination in the laboratory. Endometriosis is sometimes discovered when a woman has abdominal surgery for another reason such as **tubal ligation** or **hysterectomy**.

Various imaging techniques such as ultrasound, computed tomography scan (CT scan), or **magnetic resonance imaging** (MRI) can offer additional information but aren't useful in making the initial diagnosis. A blood test may also be ordered because women with endometriosis have higher levels of the blood protein CA125. Testing for this substance before and after treatment can predict a recurrence of the disease, but the test is not reliable as a diagnostic tool.

Treatment

How endometriosis is treated depends on the woman's symptoms, her age, the extent of the disease, and her personal preferences. The condition cannot be fully eradicated without surgery. Conservative treatment focuses on managing the pain, preserving fertility, and delaying the progress of the condition.

Pain relief

Over-the-counter pain relievers such as **aspirin** and **acetaminophen** (Tylenol) are useful for mild cramping and menstrual pain. Prescription-strength and over-the-counter **nonsteroidal anti-inflammatory drugs** (NSAIDs), such as ibuprofen (Motrin, Advil) and naproxen (Naprosyn), are also effective. If pain is severe, a doctor may prescribe narcotic medications, although these can be addicting and are rarely used.

Hormonal treatments

Hormonal therapies effectively tame endometriosis but also act as contraceptives. A woman who is hoping to become pregnant would take these medications for a period of time, then try to conceive within several months of discontinuing treatment.

- Oral contraceptives. Continuously taking estrogen-progestin pills tricks the body into thinking it is pregnant. This state of pseudopregnancy means reduced pelvic pain and a temporary withering of endometrial implants.
- Danazol (Danocrine) and gestrinone are synthetic male hormones that lower estrogen levels, prevent menstruation, and shrink endometrial tissues. On the downside, they lead to weight gain and menopause-like symptoms, and cause some women to develop masculine characteristics.
- Progestins. Medroxyprogesterone (Depo-Provera) and related drugs may also be used in treating endometriosis. They have been proven effective in minimizing pain and halting the progress of the condition, but are rarely used because of the high rate of side effects.
- Gonadotropin-releasing hormone (GnHR) agonists. These estrogen-inhibiting drugs successfully limit pain and prevent the growth of endometrial implants. They can cause **menopause** symptoms, however, and doses have to be regulated to prevent bone loss associated with low estrogen levels.

Surgery

Removing the uterus, ovaries, and fallopian tubes is the only permanent method of eliminating endometriosis. This is an extreme measure that deprives a woman of her ability to bear children and forces her body into menopause. Endometrial implants and ovarian cysts can be removed with **laser surgery** performed through a laparoscope. For women with minimal endometriosis, this technique is usually successful in reducing pain and slowing the condition's progress. It may also help infertile women increase their chances of becoming pregnant.

Alternative treatment

Although severe endometriosis should not be self-treated, many women find they can help their condition through alternative therapies. Taking vitamin B complex combined with **vitamins** C, E, and the **minerals** calcium, magnesium, and selenium can help the depression and lack of energy that may accompany endometriosis. B vitamins also counteract the side effects of hormonal drugs. Other women have found relief when they turned to a macrobiotic diet. Less extreme **diets** that cut out sugar, salt, and processed foods are sometimes helpful as well. Mind-body therapies such as relaxation and visualization help women cope with pain. Other avenues to combat pain include **acupuncture** and **biofeedback** techniques. Still other women report positive results after being treated by chiropractors or homeopathic doctors.

Prognosis

Most women who have endometriosis have minimal symptoms and do well. Overall, endometriosis symptoms come back in an average of 40% of women over the five years following treatment. With hormonal therapy, pain returned after five years in 37% of patients with minimal symptoms and 74% of those with severe cases. The highest success rate from conservative treatment followed complete removal of implants using laser surgery. Eighty percent of these women were still pain-free five years later. In cases that don't respond to these treatments, a woman and her doctor may consider surgery to remove her reproductive organs.

Prevention

There is no proven way to prevent endometriosis. One study, however, indicated that girls who begin participating in aerobic **exercise** at a young age are less likely to develop the condition.

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KEY TERMS

Adhesions—Web-like scar tissue that may develop as a result of endometriosis and bind organs to one another.

Dioxin—A toxic chemical found in weed killers that has been linked to the development of endometriosis.

Endometrial implants—Growths of endometrial tissue that attach to organs, primarily in the pelvic cavity.

Endometrium—The tissue lining the uterus that grows and sheds each month during a woman's menstrual cycle.

Estrogen—A female hormone that promotes the growth of endometrial tissue.

Hormonal therapy—Use of hormone medications to inhibit menstruation and relieve the symptoms of endometriosis.

Laparoscopy—A diagnostic procedure for endometriosis performed by inserting a slender, wand-like instrument through a small incision in the woman's abdomen.

Menopause—The end of a woman's menstrual periods when the body stops making estrogen.

Retrograde menstruation—Menstrual flow that travels into the body cavity rather than being expelled through the uterus.

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ORGANIZATIONS

Endometriosis Association International Headquarters. 8585 North 76th Place, Milwaukee, WI 53223. (800) 992-3636. <http://EndometriosisAssn.org>.

Stephanie Slon

Endometritis *see* **Pelvic inflammatory disease**

Endorectal ultrasound

Definition

Endorectal ultrasound (ERUS) is a procedure where a probe is inserted into the rectum and high frequency sound waves (ultrasound waves) are generated. The pattern of echoes as they bounce off tissues is converted into a picture (sonogram) on a television screen.

Purpose

ERUS is used as a diagnostic procedure in **rectal cancer** to determine stage of the tumor and as a postradiation, presurgical examination to assess extent of tumor shrinkage. ERUS can also be used in cases of anal fistula (an abnormal passage) and problems with the anal sphincter muscles (muscles that control the opening and closing of the anus).

Precautions

Normal precautions should be taken with any diagnostic procedure. Since the population in which this procedure is normally done is elderly, the imaging staff should be extra cautious about stressing the patient. The procedure is invasive and may be embarrassing to some. Other patients may be anxious about their medical condition since endorectal ultrasounds are not routine. This places an added burden on already stressed hearts and nervous systems. Physicians, nurses, and technicians may need to be prepared for **stress** reactions that could include the heart, **asthma**, or anxious behaviors.

Description

ERUS has been used as a means to determine the depth of rectal cancers and to assess whether the tumor has affected surrounding tissues. This pre-treatment procedure has proven to be an accurate tool for tailoring surgery for patients.

Problems with interpretation of the sonograms after radiation and before surgery have resulted in tumors being identified that were merely the formation of fibrous tissues that remained after the tumors had been eliminated by the radiation. Yet, some of the fibrous areas actually hid residual tumors. Rectal anatomy itself can affect the accuracy of ultrasound reading. This makes ERUS problematic in determining the amount of tumor reduction a patient has after **radiation therapy**.

Preparation

The patient must evacuate the bowels completely before the procedure is done. This usually is assisted though the use of several **enemas**. The patient may be told to adhere to a liquid diet the day prior to doing this procedure. The probe is inserted, usually with little discomfort for the patient since it will only be examining the first few inches of the colon.

KEY TERMS

Anal sphincter muscles—Muscles that control the opening and closing of the anus.

Fistula—An abnormal passage.

Sonogram—The picture formed by the pattern of echoes from an ultra sound.

Ultrasound waves—High frequency sound waves.

Aftercare

Since ERUS is a minor invasive procedure, there is no aftercare.

Risks

There are no risks to having an ultrasound.

Normal results

Normal results after an endorectal ultrasound are normal, healthy tissues.

Abnormal results

Abnormal results range from any number of congenital deformities in the lining of the rectum to serious rectal cancers.

Resources

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Janie F. Franz

Endoscopic retrograde cholangiopancreatography

Definition

Endoscopic retrograde cholangiopancreatography (ERCP) is a technique in which a hollow tube called an endoscope is passed through the mouth and stomach to the duodenum (the first part of the small intestine). This procedure was developed to examine abnormalities of the bile ducts, pancreas, and gallbladder. It was developed during the late 1960s and is used today to diagnose and treat blockages of the bile and pancreatic ducts.

The term has three parts to its definition:

- endoscopic refers to the use of an endoscope
- retrograde refers to the injection of dye up into the bile ducts in a direction opposing, or against, the normal flow of bile down the ducts
- cholangiopancreatography means visualization of the bile ducts (cholangio) and pancreas (pancreato)

Purpose

Until the 1970s, methods to visualize the bile ducts produced images that were of relatively poor quality and often misleading; in addition, the pancreatic duct could not be examined at all. Patients with symptoms related to the bile ducts or pancreatic ducts frequently needed surgery to diagnose and treat their conditions.

Using ERCP, physicians can obtain high-quality x rays of these structures and identify areas of narrowing (strictures), cancers, and **gallstones**. This procedure can help determine whether bile or pancreatic ducts are blocked; it also identifies where they are blocked along with the cause of the blockage. ERCP may then be used to relieve the blockage. For patients requiring surgery or additional procedures for treatment, ERCP outlines the anatomical changes for the surgeon.

Precautions

The most important precaution is that the examination should be performed by an experienced physician. The procedure is much more technically difficult than many other gastrointestinal endoscopic studies. Patients

should seek physicians with experience performing ERCP. Patients should inform the physician about any **allergies** (including allergies to contrast dyes, iodine, or shellfish), medication use, and medical problems. Occasionally, patients may need to be admitted to the hospital after the procedure.

Description

After **sedation**, a specially adapted endoscope is passed through the mouth, through the stomach, then into the duodenum. The opening to ducts that empty from the liver and pancreas is identified, and a plastic tube or catheter is placed into the orifice (opening). Contrast dye is then injected into the ducts, and with the assistance of a radiologist, pictures are taken.

Preparation

The upper intestinal tract must be empty for the procedure, so patients should not eat or drink for at least six to 12 hours before the exam. Patients should ask the physician about taking their medications before the procedure.

Aftercare

Someone should be available to take the person home after the procedure and stay with them for a while; patients will not be able to drive themselves because they undergo sedation during this test. **Pain** or any other unusual symptoms should be reported to the physician.

Risks

ERCP-related complications can be broken down into those related to medications used during the procedure, the diagnostic part of the procedure, and those related to endoscopic therapy. The overall complication rate is 5–10%; most of those occur when diagnostic ERCP is combined with a therapeutic procedure. During the exam, the endoscopist can cut or stretch structures (such as the muscle leading to the bile duct) to treat the cause of the patient's symptoms. Although the use of sedatives carries a risk of decreasing cardiac and respiratory function, it is very difficult to perform these procedures without these drugs.

The major complications related to diagnostic ERCP are **pancreatitis** (inflammation of the pancreas) and **cholangitis** (inflammation of the bile ducts). **Bacteremia** (the passage of bacteria into the blood stream) and perforation (hole in the intestinal tract) are additional risks.

Normal results

Because certain standards have been set for the normal diameter or width of the pancreatic duct and bile ducts, measurements using x rays are taken to determine if the ducts are too large (dilated) or too narrow (strictured). The ducts and gallbladder should be free of stones or tumors.

Abnormal results

When areas in the pancreatic or bile ducts (including those in the liver) are too wide or too narrow compared with the standard, the test is considered abnormal. Once these findings are demonstrated using ERCP, symptoms are usually present; they generally do not change without treatment. Stones, identified as opaque or solid structures within the ducts, are also considered abnormal. Masses or tumors may also be seen, but sometimes the diagnosis is made not by direct visualization of the tumor, but by indirect signs, such as a single narrowing of one of the ducts. Overall, ERCP has an excellent record in diagnosing these abnormalities.

KEY TERMS

Endoscope, endoscopy—An endoscope used in the field of gastroenterology is a hollow, thin, flexible tube that uses a lens or miniature camera to view various areas of the gastrointestinal tract. When the procedure is performed to examine the bile ducts or pancreas, the organs are not viewed directly, but rather indirectly through the injection of contrast. The performance of an exam using an endoscope is referred to as endoscopy. Diagnosis through biopsies or other means and therapeutic procedures can also be done using these instruments.

Visualization—The process of making an internal organ visible. A radiopaque substance is introduced into the body, then an x-ray picture of the desired area is taken.

Resources

BOOKS

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David S. Kaminstein

Endoscopic sclerotherapy *see* **Sclerotherapy for esophageal varices**

Endoscopic sphincterotomy

Definition

Endoscopic sphincterotomy or endoscopic retrograde sphincterotomy (ERS) is a relatively new endoscopic technique developed to examine and treat abnormalities of the bile ducts, pancreas and gallbladder. The procedure was developed as an extension to the diagnostic examination, ERCP (**endoscopic retrograde cholangiopancreatography**); with the addition of "sphincterotomy," abnormalities found during the study could be treated at the same time without the need for invasive surgery.

The term ERS has three parts to its definition;

- endoscopic refers to the use of an endoscope
- retrograde refers to the insertion of the endoscope *up* into the ducts in a direction opposite to or against the normal flow of bile *down* the ducts
- sphincterotomy, which means cutting of the sphincter or muscle that lies at the juncture of the intestine with both the bile and pancreatic ducts

Purpose

Until the 1970s, patients with symptoms related to disease of the bile ducts or pancreas frequently needed surgery to diagnose the cause and treat any abnormalities. ERCP allowed physicians for the first time to obtain high quality x rays of the common bile and pancreatic ducts, and detect areas of narrowing (strictures), stones, and tumors. ERCP was not initially designed for treatment. ERS was developed shortly after and enabled physicians to treat the abnormalities identified by the injection of dye and x rays.

The revolutionary technique made possible the endoscopic removal of stones and stretching of areas of narrowing (strictures). It has since been expanded to include drainage of bile from blocked ducts and treatment of various abnormalities of the pancreas.

Precautions

The most important precaution related to both ERCP and ERS is to have the procedure performed by an experienced physician. ERS is technically more difficult than many other gastrointestinal endoscopic studies, including ERCP. Patients should inquire as to the physician's experience with the procedure. The physician should also be informed of any **allergies**, medication use, and medical problems.

Description

ERS is generally performed only after ERCP has been successfully accomplished and detail of the anatomy and abnormalities is known. During ERS, a number of various instruments are inserted through the endoscope in order to "cut" or stretch the sphincter. Once this is done, additional instruments are passed that enable the removal of stones and the stretching of narrowed regions of the ducts. Drains (stents) can also be used to prevent a narrowed area from rapidly returning to its previously narrowed state.

Preparation

The upper intestinal tract must be empty for the procedure, so patients must not eat or drink for at least six to 12 hours before the exam. Patients need to inquire about taking their medications before the procedure. Some patients may require **antibiotics** before and/or after the procedure. When possible, **aspirin** or NSAIDS should not be taken within several days before the procedure, because they interfere with blood clotting.

Aftercare

When ERS is performed, physicians will usually want to observe the patient closely for several hours to ensure that there are no signs of complications. **Pain** or any other unusual symptoms should be reported. Admission to the hospital may be advised.

Risks

ERS complications are related either to the drugs used during the procedure, or the results of dye injection or cutting of tissue. The overall complication rate is 5–10%. During the exam, the endoscopist can cut or

KEY TERMS

Endoscope, Endoscopy—An endoscope as used in the field of gastroenterology is a thin flexible tube which uses a lens or miniature camera to view various areas of the gastrointestinal tract. When the procedure is performed to examine certain organs such as the bile ducts or pancreas, the organs are not viewed directly, but rather indirectly through the injection of x-ray dye. The performance of an exam using an endoscope is referred by the general term endoscopy. Diagnosis through biopsies or other means and therapeutic procedures can be done with these instruments.

NSAIDS—This abbreviation stands for non-steroidal anti-inflammatory drugs, which are medications such as Ibufprofen that are used to control pain and inflammation. Most may be purchased over the counter. One of their major side effects is that they decrease the effect of the normal blood clotting factors in blood. In patients undergoing surgical or endoscopic procedures, this can lead to an increased risk of bleeding.

stretch structures (such as the muscle leading to the bile duct) to treat the cause of the patient's symptoms. Cutting or stretching of these structures can sometimes cause a hole or perforation. The use of sedatives also carries a risk of decreasing cardiac and respiratory function, however, it is very difficult to perform these procedures without these drugs.

Other major complications related to ERCP or ERS are **pancreatitis** (inflammation of the pancreas) and **cholangitis** (inflammation of the bile ducts). **Bacteremia** (the passage of bacteria into the blood stream) and bleeding are also risks.

Normal results

Certain standards have been set for the diameter or width of the pancreatic and bile ducts. Measurements by x ray are used to determine if the ducts are too large (dilated) or too narrow (strictured). Lastly, the ducts and gallbladder should be free of any solid particles, such as stones, and free of areas of narrowing.

Resources

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Enemas

Definition

An enema is the insertion of a solution into the rectum and lower intestine.

Purpose

Enemas may be given for the following purposes:

- to remove feces when an individual is constipated or impacted,
- to remove feces and cleanse the rectum in preparation for an examination,
- to remove feces prior to a surgical procedure to prevent contamination of the surgical area,
- to administer drugs or anesthetic agents.

Precautions

The rectal tube used for infusion of the enema solution should be smooth and flexible to decrease the possibility of damage to the mucous membrane that lines the rectum. Tap water is commonly used for adults but should not be used for infants because of the danger of electrolyte (substance that conducts electric current within the body and is essential for sustaining life) imbalance. The colon absorbs water, and repeated tap

Enemas may be given for the following purposes: to remove feces when an individual is constipated, or to remove feces and cleanse the rectum in preparation for an examination, or prior to surgery to prevent contamination. There are two types of enemas: the high enema, given to cleanse the large bowel, and the low enema, to cleanse only the lower bowel. *(Illustration by Electronic Illustrators Group.)*

water enemas can cause cardiovascular overload and electrolyte imbalance. Similarly, repeated saline enemas can cause increased absorption of fluid and electrolytes into the bloodstream, resulting in overload. Individuals receiving frequent enemas should be observed for overload symptoms that include **dizziness**, sweating, or vomiting.

Soap suds and saline used for cleansing enemas can cause irritation of the lining of the bowel, with repeated use or a solution that is too strong. Only white soap should be used; the bar should not have been previously used, to prevent infusing undesirable organisms into the individual receiving the enema. Common household detergents are considered too strong for the rectum and bowel. The commercially prepared castile soap is preferred, and should be used in concentration no greater than 5 cc soap to 1,000 cc of water.

Description

Cleansing enemas act by stimulation of bowel activity through irritation of the lower bowel, and by distention with the volume of fluid instilled. When the enema is administered, the individual is usually lying on the left side, which places the sigmoid colon (lower portion of bowel) below the rectum and facilitates infusion of fluid. The length of time it takes to administer an enema depends on the amount of fluid to be infused. The amount of fluid administered will vary depending on the age and size of the person receiving the enema, however general guidelines would be:

- Infant: 250 cc or less
- Toddler and preschooler: 500 cc or less
- School-aged child: 500–1,000 cc
- Adult: 750–1,000 cc

Some may differentiate between high and low enemas. A high enema, given to cleanse as much of the large bowel as possible, is usually administered at higher pressure and with larger volume (1,000 cc), and the individual changes position several times in order for the fluid to flow up into the bowel. A low enema, intended to cleanse only the lower bowel, is administered at lower pressure, using about 500 cc of fluid.

Oil retention enemas serve to lubricate the rectum and lower bowel, and soften the stool. For adults, about 150–200 cc of oil is instilled, while in small children, 75–150 cc of oil is considered adequate. Salad oil or liquid petrolatum are commonly used at a temperature of 91°F (32.8°C). There are also commercially prepared oil retention enemas. The oil is usually retained for one to three hours before it is expelled.

The rectal tube used for infusion of the solution, usually made of rubber or plastic, has two or more openings at the end through which the solution can flow into the bowel. The distance to which the tube must be inserted is dependent upon the age and size of the patient. For adult, insertion is usually 3–4 in (7.5–10 cm); for children, approximately 2–3 in (5–7.5 cm); and for infants, only 1–1.5 in (2.5–3.75 cm). The rectal tube is lubricated before insertion with a water soluble lubricant to ease insertion and decrease irritation to the rectal tissues.

The higher the container of solution is placed, the greater the force in which the fluid flows into the patient. Routinely, the container should be no higher than 12 in (30 cm) above the level of the bed; for a high cleansing enema, the container may be 12–18 in (30–45 cm) above the bed level, because the fluid is to be instilled higher into the bowel.

Preparation

The solution used in the procedure is measured, mixed, and warmed before administration of the enema.

Aftercare

If necessary, a specimen will be collected for diagnostic evaluation. If the enema was given to alleviate **constipation**, the better approach to combatting consti-

KEY TERMS

Electrolyte—A substance that conducts electric current within the body and is essential for sustaining life.

Intestine—Also called the bowels and divided into large and small intestine, they extend from the stomach to the anus, where waste products exit the body. The small intestine is about 20 ft (6.1 m) long and the large intestine, about 5 ft (1.5 m) long.

Rectum—The portion of bowel just before the anus. The prefix *recto* is used with a variety of words in relation to conditions that affect the rectum.

pation in the future is with a high fiber diet (five to six servings of whole grain foods) and adequate fluid intake (seven to eight glasses of water per day). Regular **exercise** and going to the bathroom when necessary will also help. If constipation is a chronic problem, medical help should be consulted to determine if there is underlying disorder.

Risks

Habitual use of enemas as a means to combat constipation can make the problem even more severe when their use is discontinued. Enemas should be used only as a last resort for treatment of constipation and with a doctor's recommendation. Enemas should not be administered to individuals who have recently had colon or rectal surgery, a **heart attack**, or who suffer from an unknown abdominal condition or an irregular heartbeat.

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Kathleen D. Wright, RN

Enlarged prostate

Definition

A non-cancerous condition that affects many men past 50 years of age, enlarged prostate makes urinating more difficult by narrowing the urethra, a tube running from the bladder through the prostate gland. It can be effectively treated by surgery and, today, by certain drugs.

Description

The common term for enlarged prostate is BPH, which stands for benign (non-cancerous) prostatic hyperplasia or hypertrophy. Hyperplasia means that the prostate cells are dividing too rapidly, increasing the total number of cells, and, therefore, the size of the organ itself. Hypertrophy simply means "enlargement." BPH is part of the **aging** process. The actual changes in the prostate may start as early as the 30s but take place very gradually, so that significant enlargement and symptoms usually do not appear until after age 50. Past this age the chances of the prostate enlarging and causing urinary symptoms become progressively greater. More than 40% of men in their 70s have an enlarged prostate. Symptoms generally appear between ages 55–75. About 10% of all men eventually will require treatment for BPH.

BPH has been viewed as a rare condition in African, Chinese and other Asian peoples for reasons that are not clear.

Causes and symptoms

The cause of BPH is a mystery, but age-related changes in the levels of hormones circulating in the blood may be a factor. Whatever the cause, an enlarging prostate gradually narrows the urethra and obstructs the flow of urine. Even though the muscle in the bladder wall becomes stronger in an attempt to push urine through the smaller urethra, in time, the bladder fails to empty completely at each urination. The urine that collects in the bladder can become infected and lead to stone formation. The kidneys themselves may be damaged by infection or by urine constantly "backing up."

When the enlarging prostate gland narrows the urethra, a man will have increasing trouble starting the urine stream. Because some urine remains behind in the bladder, he will have to urinate more often, perhaps two or three times at night (nocturia). The need to urinate can become very urgent and, in time, urine may dribble out to stain a man's clothing. Other symptoms of BPH are a weak and sometimes a split stream and general aching or **pain** in the perineum (the area between the scrotum and anus). Some men may have considerable enlargement of the prostate before even mild symptoms develop.

If a man must strain hard to force out the urine, small veins in the bladder wall and urethra may rupture,

An enlarged prostate is a non-cancerous condition in which the narrowing of the urethra makes the elimination of urine more difficult. It most often occurs in men over age 50. *(Illustration by Electronic Illustrators Group.)*

causing blood to appear in the urine. If the urinary stream becomes totally blocked, the urine collecting in the bladder may cause severe discomfort, a condition called acute urinary retention. Urine that stagnates in the bladder can easily become infected. A burning feeling during urination and **fever** are clues that infection may have developed. Finally, if urine backs up long enough it may increase pressure in the kidneys, though this rarely causes permanent kidney damage.

Diagnosis

When a man's symptoms point to BPH, the first thing the physician will want to do is a digital **rectal examination**, inserting a finger into the anus to feel whether—and how much—the prostate is enlarged. A smooth prostate surface suggests BPH, whereas a distinct lump in the gland might mean **prostate cancer**. The next step is a blood test for a substance called prostate-specific antigen or PSA. Between 30–50% of men with BPH have an elevated PSA level. This does not mean **cancer** by any means, but other measures are needed to make sure that the prostate enlargement is in fact benign. An ultrasound exam of the prostate, which is entirely safe and delivers no radiation, can show whether it is enlarged and may show that cancer is present.

If digital or ultrasound examination of the prostate raises the suspicion of cancer, most urologists will recommend that a prostatic tissue biopsy be performed. This is usually done using a lance-like instrument that is inserted into the rectum. It pierces the rectal wall and, guided by the physcian's finger, obtains six to eight pieces of prostatic tissue that are sent to the laboratory for microscopic examination. If cancer is present, the prognosis and treatment are changed accordingly.

A catheter placed through the urethra and into the bladder can show how much urine remains in the bladder after the patient urinates—a measure of how severe the obstruction is. Another and very simple test for obstruction is to have the man urinate into a uroflowmeter, which measures the rate of urine flow. A very certain—though invasive—way of confirming obstruction from an enlarged prostate is to pass a special viewing instrument called a cystoscope into the bladder, but this is not often necessary.

It is routine to check a urine sample for an increased number of white blood cells, which may mean there is infection of the bladder or kidneys. The same sample may be cultured to show what type of bacterium is causing the infection, and which **antibiotics** will work best. The state of the kidneys may be checked in two ways: imaging by either ultrasound or injecting a dye (the intra-

venous urogram, or pyelogram); or a blood test for creatinine, which collects in the blood when the kidneys cannot eliminate it.

Treatment

Drugs

A class of drugs called alpha-adrenergic blockers, which includes phenoxybenzamine and doxazosin, relax the muscle tissue surrounding the bladder outlet and lining the wall of the urethra to permit urine to flow more freely. These drugs improve obstructive symptoms, but do not keep the prostate from enlarging. Other drugs (finasteride is a good example) do shrink the prostate and may delay the need for surgery. Symptoms may not, however, improve until the drug has been used for three months or longer. Antibiotic drugs are given promptly whenever infection is diagnosed. Some medications, including **antihistamines** and some **decongestants**, can make the symptoms of BPH suddenly worse and even cause acute urinary retention, and therefore should be avoided.

Intermediate treatments

When drugs have failed to control symptoms of BPH but the physician does not believe that conventional surgery is yet needed, a procedure called transurethral needle ablation may be tried. In the office and using local anesthesia, a needle is inserted into the prostate and radiofrequency energy is applied to destroy the tissue that is obstructing urine flow. Another new approach is microwave hyperthermia, using a device called the Prostatron to deliver microwave energy to the prostate through a catheter. This procedure is done at an outpatient surgery center.

Surgery

For many years the standard operation for BPH has been transurethral resection (TUR) of the prostate. Under general or spinal anesthesia, a cystoscope is passed through the urethra and prostate tissue surrounding the urethra is removed using either a cutting instrument or a heated wire loop. The small pieces of prostate tissue are washed out through the scope. No incision is needed for TUR. There normally is some blood in the urine for a few days following the procedure. In a few men—less than 5% of all those having TUR—urine will continue to escape unintentionally. Other uncommon complications include a temporary rise in blood pressure with mental confusion, which is treated by giving salt solution. Impotence—the inability to achieve lasting penile erections—does occur, but probably in fewer than 10% of patients. A narrowing or stricture rarely develops in the urethra, but this can be treated fairly easily.

KEY TERMS

Catheter—A rubber or plastic tube placed through the urethra into the bladder to remove excess urine when the flow of urine is cut off, or to prevent urinary infection.

Creatinine—One of the "waste" substances normally excreted by the kidneys into the urine. When urine flow is slowed, creatinine may collect in the blood and cause toxic effects.

Hyperplasia—A condition where cells, such as those making up the prostate gland, rapidly divide abnormally and cause the organ to become enlarged.

Hypertrophy—A technical term for enlargement, as in BPH (benign prostatic hypertrophy).

Urethra—In males, the tube that conducts urine from the bladder through the penis to the outside of the body. When narrowed by an enlarging prostate, symptoms of BPH develop.

Urinary retention—The result of progressive obstruction of the urethra by an enlarging prostate, causing urine to remain in the bladder even after urination.

Alternatives to TUR, some only recently introduced, include:

- Laser ablation of the prostate. Laser energy is applied to the prostate through a special fiber passed through a cystoscope. The procedure is done in an operating room, and several patients have retained urine postoperatively.
- Transurethral incision of the prostate. Less invasive than standard TUR, an incision is made through the prostate to open up the part of the urethra passing through it. This may work well in men whose prostate is not grossly enlarged.
- Transurethral vaporization. A small roller ball is used to break up and vaporize the obstructing prostatic tissue, rather than cutting it away as in standard TUR. This is equally successful but patients usually can leave the hospital within 24 hours, and there is less blood loss.
- If the prostate is greatly enlarged—as is the case in about 5–10% of those diagnosed, an incision is made to perform an open **prostatectomy**, removing the entire gland under direct vision.

Alternative treatment

An extract of the **saw palmetto** (*Serenoa repens* or *S. serrulata*) has been shown to stop or decrease the hyperplasia of the prostate. Symptoms of BPH will improve after taking the herb for one to two months, but continued use is recommended.

Prognosis

In a man without symptoms whose prostate is enlarged, it is hard to predict when urinary symptoms will develop and how rapidly they will progress. For this reasons some specialists (urologists) advise a period of "watchful waiting." When BPH is treated by conventional TUR, there is a small risk of complications but, in the great majority of men, urinary symptoms will be relieved and their quality of life will be much enhanced. In the future, it is possible that the less invasive forms of surgical treatment will be increasingly used to achieve results as good as those of the standard operation. It also is possible that new medications will be developed that shrink the prostate and eliminate obstructive symptoms so that surgery can be avoided altogether.

Prevention

Whether or not BPH is caused by hormonal changes in aging men, there is no known way of preventing it. Once it does develop and symptoms are present that interfere seriously with the patient's life, timely medical or surgical treatment will reliably prevent symptoms from getting worse. Also, if the condition is treated before the prostate has become grossly enlarged, the risk of complications is minimal. One of the potentially most serious complications of BPH, urinary infection (and possible infection of the kidneys), can be prevented by using a catheter to drain excess urine out of the bladder so that it does not collect, stagnate, and become infected.

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ORGANIZATIONS

Prostate Health Council. American Foundation for Urologic Disease. 1128 N. Charles St., Baltimore, MD 21201. (800) 242-AFUD.

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Entamoeba histolytica infection *see* **Amebiasis**

Enteric fever *see* **Typhoid fever**

Enterically transmitted non-A non-B *see* **Hepatitis E**

Enterobacterial infections

Definition

Enterobacterial infections are disorders of the digestive tract and other organ systems produced by a group of gram-negative, rod-shaped bacteria called Enterobacteriaceae. Gram-negative means that the organisms do not retain the violet color of the dye used to make Gram stains. The most troublesome organism in this group is ***Escherichia coli***. Other enterobacteria are species of *Salmonella*, *Shigella*, *Klebsiella*, *Enterobacter*, *Serratia*, *Proteus*, and *Yersinia*.

Description

Enterobacterial infections can be produced by bacteria that normally live in the human digestive tract without causing serious disease, or by bacteria that enter from the outside. In many cases these infections are nosocomial, which means that they can be acquired in the hospital. *Klebsiella* and *Proteus* sometimes cause **pneumonia**, ear and sinus infections, and urinary tract infections. *Enterobacter* and *Serratia* often cause bacterial infection of the blood (**bacteremia**), particularly in patients with weakened immune systems.

Diarrhea caused by enterobacteria is a common problem in the United States. It is estimated that each person in the general population has an average of 1.5 episodes of diarrhea each year, with higher rates in children, institutionalized people, and Native Americans. This type of enterobacterial infection can range from a minor nuisance to a life-threatening disorder, especially in infants, elderly persons, **AIDS** patients, and malnourished people. Enterobacterial infections are one of the two leading killers of children in developing countries.

Causes and symptoms

Causes

Enterobacterial infections in the digestive tract typically start when the organisms invade the mucous tissues that line the digestive tract. They may be bacteria that are

already present in the stomach and intestines, or they may be transmitted by contaminated food and water. It is also possible for enterobacterial infections to spread by person-to-person contact. The usual incubation period is 12–72 hours.

***ESCHERICHIA COLI* INFECTIONS.** *E. coli* infections cause most of the enterobacterial infections in the United States. The organisms are categorized according to whether they are invasive or noninvasive. Noninvasive types of *E. coli* include what are called enteropathogenic *E. coli*, or EPEC, and enterotoxigenic *E. coli*, or ETEC. EPEC and ETEC types produce a bacterial poison (toxin) in the stomach that interacts with the digestive juices and causes the patient to lose large amounts of water through the intestines.

The invasive types of *E. coli* are called enterohemorrhagic *E. coli*, or EHEC, and enteroinvasive *E. coli,* or EIEC. These subtypes invade the stomach tissues directly, causing tissue destruction and bloody stools. EHEC can produce complications leading to **hemolytic-uremic syndrome** (HUS), a potentially fatal disorder marked by the destruction of red blood cells and kidney failure. EHEC has become a growing problem in the United States because of outbreaks caused by contaminated food. A particular type of EHEC known as O157:H7 has been identified since 1982 in undercooked hamburgers, unpasteurized milk, and apple juice. Between 2–7% of infections caused by O157:H7 develop into HUS.

Symptoms

The symptoms of enterobacterial infections are sometimes classified according to the type of diarrhea they produce.

WATERY DIARRHEA. Patients infected with ETEC, EPEC, some types of *Salmonella*, and some types of *Shigella* develop a watery diarrhea. These infections are located in the small intestine, result from bacterial toxins interacting with digestive juices, do not produce inflammation, and do not usually need treatment with **antibiotics**.

BLOODY DIARRHEA (DYSENTERY). Bloody diarrhea is sometimes called dysentery. It is produced by EHEC, EIEC, some types of *Salmonella*, some types of *Shigella*, and *Yersinia*. In dysentery, the infection is located in the colon, cells and tissues are destroyed, inflammation is present, and antibiotic therapy is usually required.

NECROTIZING ENTEROCOLITIS (NEC). **Necrotizing enterocolitis** (NEC) is a disorder that begins in newborn infants shortly after birth. Although NEC is not yet fully understood, it is thought that it results from a bacterial or viral invasion of damaged intestinal tissues. The disease organisms then cause the **death** (necrosis) of bowel tissue or **gangrene** of the bowel. NEC is primarily a disease of **prematurity**; 60–80% of cases occur in high-risk preterm infants. NEC is responsible for 2–5% of cases in newborn intensive care units (NICU). Enterobacteriaceae that have been identified in infants with NEC include *Salmonella*, *E. coli*, *Klebsiella*, and *Enterobacter*.

Diagnosis

Patient history

The diagnosis of enterobacterial infections is complicated by the fact that viruses, protozoa, and other types of bacteria can also cause diarrhea. In most cases of mild diarrhea, it is not critical to identify the organism because the disorder is self-limiting. Some groups of patients, however, should have stool tests. They include:

- patients with bloody diarrhea,
- patients with watery diarrhea who have become dehydrated,
- patients with watery diarrhea that has lasted longer than three days without decreasing in amount,
- patients with disorders of the immune system.

The patient history is useful for public health reasons as well as helping the doctor determine what type of enterobacterium may be causing the infection. The doctor will ask about the frequency and appearance of the diarrhea as well as other digestive symptoms. If the patient is nauseated and vomiting, the infection is more likely to be located in the small intestine. If the patient is running a **fever**, a diagnosis of dysentery is more likely. The doctor will also ask if anyone else in the patient's family or workplace is sick. Some types of enterobacteriaceae are more likely to cause group outbreaks than others. Other questions include the patient's food intake over the last few days and whether he or she has recently traveled to countries with **typhoid fever** or **cholera** outbreaks.

Physical examination

The most important parts of the **physical examination** are checking for signs of severe fluid loss and examining the abdomen to rule out typhoid fever. The doctor will look at the inside of the patient's mouth and evaluate the skin for signs of **dehydration**. The presence of a skin rash and an enlarged spleen suggests typhoid rather than a bacterial infection. If the patient's abdomen hurts when the doctor examines it, a diagnosis of dysentery is more likely.

Laboratory tests

The most common test that is used to identify the cause of diarrhea is the stool test. Examining a stool sample under a microscope can help to rule out parasitic and

protozoal infections. Routine stool cultures, however, cannot be used to identify any of the four types of *E. coli* that cause intestinal infections. ETEC, EPEC, and EIEC are unusual in the United States and can usually be identified only by specialists in research laboratories. Because of concern about EHEC outbreaks, however, most laboratories in the United States can now screen for O157:H7 with a test that identifies its characteristic toxin. All patients with bloody diarrhea should have a stool sample tested for *E. coli* O157:H7.

Treatment

The initial treatment of enterobacterial diarrhea is usually empiric. Empiric means that the doctor treats the patient on the basis of the visible symptoms and professional experience in treating infections, without waiting for laboratory test results. Since the results of stool cultures can take as long as two days, it is important to prevent dehydration. The patient will be given fluids to restore the electrolyte balance and paregoric to relieve abdominal cramping.

Newborn infants and patients with immune system disorders will be given antibiotics intravenously once the organism has been identified. Gentamicin, tobramycin, and amikacin are being used more frequently to treat enterobacterial infections because many of the organisms are becoming resistant to ampicillin and cephalosporin antibiotics.

Alternative treatment

Alternative treatments for diarrhea are intended to relieve the discomfort of abdominal cramping. Most alternative practitioners advise consulting a medical doctor if the patient has sunken eyes, dry eyes or mouth, or other signs of dehydration.

Herbal medicine

Herbalists may recommend cloves taken as an infusion or ginger given in drop doses to control intestinal cramps, eliminate gas, and prevent vomiting. Peppermint (*Mentha piperita*) or chamomile (*Matricaria recutita*) tea may also ease cramps and intestinal spasms.

Homeopathy

Homeopathic practitioners frequently recommend *Arsenicum album* for diarrhea caused by contaminated food, and *Belladonna* for diarrhea that comes on suddenly with mucus in the stools. *Veratrum album* would be given for watery diarrhea, and *Podophyllum* for diarrhea with few other symptoms.

KEY TERMS

Dysentery—A type of diarrhea caused by infection and characterized by mucus and blood in the stools.

Empirical treatment—Medical treatment that is given on the basis of the doctor's observations and experience.

Escherichia coli—A type of enterobacterium that is responsible for most cases of severe bacterial diarrhea in the United States.

Hemolytic-uremic syndrome (HUS)—A potentially fatal complication of *E. coli* infections characterized by kidney failure and destruction of red blood cells.

Necrotizing enterocolitis (NEC)—A disorder in newborns caused by bacterial or viral invasion of vulnerable intestinal tissues.

Nosocomial infections—Infections acquired in hospitals.

Toxin—A poison produced by certain types of bacteria.

Prognosis

The prognosis for most enterobacterial infections is good; most patients recover in about a week or 10 days without needing antibiotics. HUS, on the other hand, has a mortality rate of 3–5% even with intensive care. About a third of the survivors have long-term problems with kidney function, and another 8% develop high blood pressure, seizure disorders, and blindness.

Prevention

The World Health Organization (WHO) offers the following suggestions for preventing enterobacterial infections, including *E. coli* O157:H7 dysentery:

- Cook ground beef or hamburgers until the meat is thoroughly done. Juices from the meat should be completely clear, not pink or red. All parts of the meat should reach a temperature of 70°C (158°F) or higher.
- Do not drink unpasteurized milk or use products made from raw milk.
- Wash hands thoroughly and frequently, especially after using the toilet.
- Wash fruits and vegetables carefully, or peel them. Keep all kitchen surfaces and serving utensils clean.

- If drinking water is not known to be safe, boil it or drink bottled water.
- Keep cooked foods separate from raw foods, and avoid touching cooked foods with knives or other utensils that have been used with raw meat.

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Rebecca J. Frey

Enterobiasis

Definition

Enterobiasis, or pinworm infection as it is commonly called, is an intestinal infection caused by the parasitic roundworm called *Enterobius vermicularis*. The most common symptom of this irritating, but not particularly dangerous, disease is **itching** around the anal area.

The pinworm of the genus *Enterobius* pictured above is the source of this infestation occurring in children. *(Photo Researchers, Inc. Reproduced by permission.)*

Description

Enterobiasis is also called seatworm infection or oxyuriasis. In the United States, enterobiasis is the most common worm infection, and some estimate that approximately 10% of the United States population is infected. Worldwide, approximately 200 million people are infected. Enterobiasis can affect people of any age, but is most common among children ages 5–14 and particularly affects those in the daycare setting.

Causes and symptoms

The disease is highly contagious and is caused by a parasitic worm called *Enterobius vermicularis*. The adult female worm is about the size of a staple (approximately 0.4 in [1 cm] long and 0.02 in [0.5 mm] wide) and has a pointed tip. The disease is transmitted by ingesting the eggs of the pinworm. These eggs travel to the small intestine where, after approximately one month, they hatch and mature into adult worms. During the night, the female adult worms travel to the area around the anus and deposit eggs in the folds of the anal area. A single female pinworm can lay 10,000 eggs and, after laying eggs, dies. The eggs are capable of causing infection after six hours at body temperature.

Significant itching in the anal region is caused by the movement of the adult worm as the eggs are deposited. When an individual scratches the anal region, the tiny eggs get under the finger nails and in the underwear and night clothes. Anything the individual touches with the contaminated fingers, for example, toys, bedding, blankets, bathroom door knobs, or sinks, becomes contaminated. The eggs are very hardy and can live on surfaces for two to three weeks. Anyone touching these contaminated surfaces can ingest the eggs and become infected. An individ-

KEY TERMS

Anus—The opening through which feces are eliminated.

Hemorrhoid—An area around the anus where veins become dilated and the tissue swells, causing itching and pain.

Rectum—The end of the large intestine in which feces collects for elimination through the anus.

Vaginitis—Inflammation of the vagina.

ual can also become infected by inhaling and swallowing the eggs, for example, when the bedcovers are shaken.

Many individuals with enterobiasis exhibit no symptoms. When present, however, symptoms of the infection begin approximately two weeks after ingesting the pinworm eggs. The main symptom is itching around the anus. Because the itching intensifies at night, when the female worms comes to the anus to lay eggs, it often leads to disrupted sleep and irritability. Poor sleeping at night in small children can be related to pinworms. Occasionally, the itching causes some bleeding and bruising in the region, and secondary bacterial infections can occur. In females, the itching may spread to the vagina and sometimes causes an infection of the vaginal region (vaginitis). Enterobiasis usually lasts one to two months.

Diagnosis

First, a physician will rule out other potential causes of the itching, such as **hemorrhoids**, lice, or fungal or bacterial infection. Once these have been ruled out, an accurate diagnosis of enterobiasis will require that either the eggs or the adult worms are detected. Rarely, the adult worms are seen as thin, yellowish-white threads, about 0.4 in (1 cm) long, in the stools of the infected person. Usually, an hour or so after the individual goes to sleep, the adult female worms may be seen moving around laying eggs if a flashlight is shone at the rectal area.

An easier method is to observe the eggs under the microscope. In order to collect a specimen for laboratory diagnosis, the physician may provide a paddle with a sticky adhesive on one side, or an individual may be instructed to place a piece of shiny cellophane tape sticky side down against the anal opening. The best time to perform this test is at night or as soon as the individual wakes up in the morning, before having a bowel movement or taking a bath or shower. The pinworm eggs will stick to the tape, which can then be placed on a specimen slide. When under a microscope in the laboratory, the eggs will be clearly visible.

Treatment

In order to treat the disease, either mebendazole (Vermox) or pyrantel pamoate (Pin-X) will be given in two oral doses spaced two weeks apart. These medications eradicate the infection in approximately 90% of cases. Re-infection is common and several treatments may be required. Because the infection is easily spread through contact with contaminated clothing or surfaces, it is recommended that all family members receive the therapeutic dose. Sometimes a series of six treatments are given, each spaced two weeks apart. If family members continue to be infected, a source outside the house may be responsible.

To relieve the rectal itching, a shallow warm bath with either half a cup of table salt, or Epsom salts is recommended. Also, application of an ointment containing zinc oxide or regular petroleum jelly can be used to relieve rectal itching.

Prognosis

Pinworms cause little damage and can be easily eradicated with proper treatment. Full recovery is expected.

Prevention

The disease can be prevented by treating all the infected cases and thus eliminating the source of infection. Some ways to keep from catching or spreading the disease include the following recommendations:

- wash hands thoroughly before handling food and eating
- keep finger nails short and clean
- avoiding scratching the anal area
- take early morning showers to wash away eggs deposited overnight
- once the infection has been identified, and treatment is started, change the bed linen, night clothes, and underwear daily
- machine wash linens in hot water and dry with heat to kill any eggs
- open the blinds or curtains since eggs are sensitive to sunlight

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Lata Cherath, PhD

Enterohemorrhagic *E. coli* see ***Escherichia coli***

Enterostomy

Definition

An enterostomy is an operation in which the surgeon makes a passage into the patient's small intestine through the abdomen with an opening to allow for drainage or to insert a tube for feeding. The opening is called a stoma, from the Greek word for mouth. Enterostomies may be either temporary or permanent. They are classified according to the part of the intestine that is used to create the stoma. If the ileum, which is the lowest of the three sections of the small intestine, is used to make the stoma, the operation is called an ileostomy. If the jejunum, which is the middle section of the small intestine, is used, the operation is called a jejunostomy. Some people use the word *ostomy* as a word that covers all types of enterostomies.

Purpose

Enterostomies are performed in order to create a new opening for the passage of fecal matter when normal intestinal functioning is interrupted or when diseases of the intestines cannot be treated by medications or less radical surgery. Some situations that may require enterostomies include:

- Healing of inflamed bowel segments. Enterostomies performed for this reason are usually temporary.
- Emergency treatment of gunshot or other penetrating **wounds** of the abdomen. An enterostomy is needed to prevent the contents of the intestine from causing a serious inflammation of the inside of the abdominal cavity (**peritonitis**). These enterostomies are also often temporary.
- Placement of a tube for enteral feeding. Enteral feeding is a method for conveying nutritional solutions directly into the stomach or jejunum through a tube. Tube enterostomies may be long-term but are not permanent.
- Removal of diseased sections of the intestines. Ileostomies performed for this reason are permanent. The most common disorders requiring permanent ileostomy are **Crohn's disease**, **familial polyposis**, and **ulcerative colitis**. Familial polyposis and ulcerative colitis are serious health risks because they can develop into **cancer**.
- Treatment of advanced cancer or other causes of intestinal obstruction.

Precautions

Enterostomies are usually performed only as emergency treatments for traumatic injuries in the abdomen or as final measures for serious disorders of the intestines. Most patients do not refuse to have the operation performed when the need for it is explained to them. A small minority, however, refuse enterostomies because of strong psychological reactions to personal disfigurement and the need to relearn bowel habits.

Description

Ileostomy

Ileostomies represent about 25% of enterostomies. They are performed after the surgeon removes a diseased colon and sometimes the rectum as well. The most common ileostomy is called a Brooke ileostomy after the English surgeon who developed it. In a Brooke ileostomy, the surgeon makes the stoma in the lower right section of the abdomen. The ileum is pulled through an opening (incision) in the muscle layer. The surgeon then turns the cut end of the intestine inside out and sews it to the edges of the hole. He or she then positions an appliance for collecting the fecal material. The appliance consists of a plastic bag that fits over the stoma and lies flat against the abdomen. The patient is taught to drain the bag from time to time during the day. Ileostomies need to be emptied frequently because the digested food contains large amounts of water. Shortly after the operation, the ileostomy produces 1–2 qt (0.9–1.91) of fluid per day; after a month or two of adjustment, the volume decreases to 1–2 pt (0.5–0.9)per day.

KOCK POUCH (CONTINENT ILEOSTOMY). The Kock pouch is a variation of the basic ileostomy and is named for its Swedish inventor. In the Kock technique, the surgeon forms a pouch inside the abdominal cavity behind the stoma that collects the fecal material. The stoma is shaped into a valve to prevent fluid from leaking onto the patient's abdomen. The patient then empties the pouch several times daily by inserting a tube (catheter) through the valve. The Kock technique is sometimes called a continent ileostomy because the fluid is contained inside the abdomen. It is successful in 70–90% of patients who have it done.

KEY TERMS

Crohn's disease—A disease of the intestines that causes inflammation leading to scarring, thickening of the walls of the intestine, and eventual obstruction.

Duodenum—The first of the three segments of the small intestine. The duodenum connects the stomach and the jejunum.

Enteral nutrition—A technique for feeding patients with liquid formulas conveyed directly into the stomach or jejunum through tubes.

Enterostomal therapist (ET)—A specialized counselor, usually a registered nurse, who provides ostomy patients with education and counseling before the operation. After surgery, the ET helps the patient learn to take care of the stoma and appliance, and offers long-term emotional support.

Familial polyposis—A disease that runs in families in which lumps of tissue (polyps) form inside the colon. Familial polyposis may develop into cancer.

Ileum—The third segment of the small intestine, connecting the jejunum and the large intestine.

Jejunum—The second of the three segments of the small intestine, connecting the duodenum and the ileum.

Kock pouch—A type of ileostomy in which the surgeon forms an artificial rectum from a section of the ileum. A Kock pouch is sometimes called a continent ileostomy because it is drained with a tube.

Ostomy—A common term for all types of enterostomies.

Stoma—The surgically constructed mouth or passage between the intestine and the outside of the patient's body.

Tube enterostomy—An enterostomy performed to allow the insertion of a feeding tube into the jejunum or stomach.

Ulcerative colitis—A disease of the colon characterized by inflammation of the mucous lining, ulcerated areas of tissue, and bloody diarrhea.

Jejunostomy

A jejunostomy is similar to an ileostomy except that the stoma is placed in the second section of the small intestine rather than the third. Jejunostomies are performed less frequently than ileostomies. They are almost always temporary procedures.

Tube enterostomies

Tube enterostomies are operations in which the surgeon makes a stoma into the stomach itself or the jejunum in order to insert a tube for liquid nutrients. Tube enterostomies are performed in patients who need tube feeding for longer than six weeks, or who have had recent mouth or nose surgery. As long as the patient's intestinal tract can function, **tube feedings** are considered preferable to intravenous feeding. Enteral **nutrition** is safer than intravenous fluids and helps to keep the patient's digestive tract functioning.

Preparation

Preoperative preparation includes both patient education and physical preparation.

Patient education

If the patient is going to have a permanent ileostomy, the doctor will explain what will happen during the operation and why it is necessary. Most patients are willing to accept an **ostomy** as an alternative to the chronic **pain** and **diarrhea** of ulcerative colitis or the risk of cancer from other intestinal disorders. The patient can also meet with an enterostomal therapist (ET) or a member of the United Ostomy Association, which is a support group for people with ostomies.

Medical preparation

The patient is prepared for surgery with an evaluation of his or her nutritional status, possible need for blood transfusions, and **antibiotics** if necessary. If the patient does not have an intestinal obstruction or severe inflammation, he or she may be given a large quantity of a polyethylene glycol (PEG) solution to cleanse the intestines before surgery.

Aftercare

Aftercare of an enterostomy is both psychological and medical.

Medical aftercare

If the enterostomy is temporary, aftercare consists of the usual monitoring of surgical wounds for infection or bleeding. If the patient has had a permanent ileostomy, aftercare includes learning to use the appliance or empty the Kock pouch; learning to keep the stoma clean; and readjusting bathroom habits. Recovery takes a long time because major surgery is a **shock** to the system and the intestines take several days to resume normal functioning. The patient's fluid intake and output will be checked frequently to minimize the risk of **dehydration**.

Patient education

Ileostomy patients must learn to watch their fluid and salt intake. They are at greater risk of becoming dehydrated in hot weather, from **exercise**, or from diarrhea. In some cases they may need extra bananas or orange juice in the diet to keep up the level of potassium in the blood.

Patient education includes social concerns as well as physical self-care. Many ileostomy patients are worried about the effects of the operation on their close relationships and employment. If the patient has not seen an ET before the operation, the aftercare period is a good time to find out about self-help and support groups. The ET can also evaluate the patient's emotional reactions to the ostomy.

Risks

Enterostomies are not considered high-risk operations by themselves. About 40% of ileostomy patients have complications afterward, however; about 15% require minor surgical corrections. Possible complications include:

- skin irritation caused by leakage of digestive fluids onto the skin around the stoma, irritation is the most common complication of ileostomies
- diarrhea
- the development of abscesses
- gallstones or stones in the urinary tract
- inflammation of the ileum
- odors (can often be prevented by a change in diet)
- intestinal obstruction
- a section of the bowel pushing out of the body (prolapse)

Normal results

Normal results include recovery from the surgery with few or no complications. About 95% of people with ostomies recover completely, are able to return to work, and consider themselves to be in good health. Many ileostomy patients enjoy being able to eat a full range of foods rather than living on a restricted diet. Some patients, however, need to be referred to psychotherapists to deal with depression or other emotional problems after the operation.

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Enterovirus infections

Definition

Enteroviruses are so named because they reproduce initially in the gastrointestinal tract after infection occurs. Despite, this, they usually do not lead to intestinal symptoms; rather it is their spread to organs, such as the nervous system, heart, skin, and others that causes disease. Enteroviruses are part of a larger group of viruses known as Picornaviruses. The word comes from the combination of "pico" (Spanish, meaning "a little bit"), and RNA (ribonucleic acid, an important component of genetic material).

Description

There are four groups of enteroviruses: Coxsackievirus, Echovirus, ungrouped Enterovirus, and Y Poliovirus.

Viruses are generally divided into those that use DNA (desoxyribonucleic acid) or RNA as their genetic material; all enteroviruses are RNA viruses. They are found worldwide, but infection is more common in areas of poor hygiene and overcrowding.

Although most cases of enterovirus do not produce symptoms, some five to 10 million individuals in the United States each year suffer from one of the enteroviral diseases. Illness is more common in the very young. While there are close to seventy different strains of enteroviruses, over 70% of infections are caused by only 10 types.

The virus is most commonly transmitted by the fecal-oral route (contamination of fingers or objects by human waste material); in some instances transmission is through contaminated food or water. Passage of some strains of virus by way of air droplets can lead to respiratory illness. Infection of fetuses by way of the placenta has also been documented. Breast milk contains antibodies which can protect newborns.

The incubation period for most enteroviruses ranges from two to 14 days. In areas of temperate climate, infections occur mainly in the summer and fall.

Causes and symptoms

Enteroviruses are believed to be the cause of at least 10 distinct illnesses. Once they enter the body, they multiply in the cells that line the gastrointestinal tract, and eventually reach sites of lymphatic tissue (such as the tonsils). While most of these diseases are of short duration and do not cause significant injury, some can produce severe illness.

The main syndromes caused by the various enteroviruses are the following:

- Summer grippe (nonspecific febrile illness). This is the most common syndrome, and is characterized by flu-like symptoms of **fever**, **headache**, and weakness, that typically last three to four days. Many patients also develop upper respiratory symptoms and some **nausea and vomiting**. One of the major ways to distinguish this disease from **influenza**, is the fact that grippe most often occurs in the summer.
- Generalized disease of the newborn is a potentially serious infection in which infants from one week to three months of age develop a syndrome that can be difficult to distinguish from a severe bacterial infection. Fever, irritability, and decreased responsiveness or excessive sleepiness are the major symptoms. Inflammation of heart muscle (**myocarditis**), low blood pressure, hepatitis, and **meningitis** sometimes complicate the illness.
- Aseptic meningitis **encephalitis** is a well known syndrome caused by this group of viruses. In fact, enteroviruses are responsible for over 90% of cases of aseptic meningitis, and most often hits children and young adults. Headache, fever, avoidance of light, and eye **pain** are characteristic. Drowsiness may be prominent, and other symptoms include **sore throat**, **cough**, muscle pain, and rash. Occasionally, not only the meninges—the covering around the brain and spinal cord— is infected, but also brain tissue itself, producing encephalitis. The illness resolves after about a week or so, and permanent damage is unusual. Enteroviruses can also produce the Guillian-Barré syndrome, which involves weakness and **paralysis** of the extremities and even the muscles of respiration.
- Pleurodynia (Bornholm's disease) is due to viral infection and inflammation of the chest and abdominal muscles used for breathing. Pain occurs as acute episodes, lasting 30 minutes or so. Coxsackie B virus is the usual cause of the illness.
- Myocarditis and/or **pericarditis** involves infection of the heart muscle (myocardium) and the covering around the heart (pericardium). Infants and young adults are the most susceptible, and for some reason, over two-thirds of cases occur in males. The disease usually begins as an upper respiratory tract infection with cough, **shortness of breath,** and fever. Chest pain, increasing shortness of breath, irregularities of cardiac rhythm, and **heart failure** sometimes develop. Some patients wind up with long term heart failure if the heart muscle is significantly affected.
- Exanthems is the medical term for **rashes**, and enterovirus is the number one cause of summer and fall rashes in children. They occur anywhere on the body, and often resemble diseases such as **measles**.
- Hand-foot-and-mouth disease occurs initially as a sore throat (often involving the tongue as well), and is followed by a rash on the hands, and sometimes the feet. The rash often forms small blisters, which lead to ulcers. Symptoms generally resolve within a week. A specific Coxsackievirus (A16) is the most frequent cause of this highly infectious disease.
- Herpangina is most often caused by one of the Coxsackie A viruses, and appears as the acute onset of fever and sore throat. This last symptom is particularly severe, as the virus produces multiple ulcers in the throat. Swallowing becomes very painful; symptoms can persist for several weeks.
- Acute hemorrhagic **conjunctivitis** involves viral infection of the conjunctiva, which is a covering around the eye. Pain, blurred vision, aversion to light, and a discharge from the eye are the main symptoms. Headache

and fever occur in about one in five patients. The disease runs its course in about 10 days.

A number of other illnesses have been attributed to enteroviruses, including **pneumonia** and other respiratory infections, myositis or muscle inflammation, arthritis, and acute inflammation of the kidneys. It is clear then that these viruses produce a number of various illnesses, most often in younger age groups.

Diagnosis

In the majority of cases, diagnosis is based on the characteristic symptoms that the virus produces (such as the chest pain in pleurodynia). Rarely is it necessary to identify a specific strain of virus causing the illness. It is more important to be certain that the infection is due to a virus which does not require treatment with **antibiotics**.

Culture, or growing the organism outside of the body, is helpful only when obtained from areas that tend to indicate recent infection, such as from swollen joints, cerebrospinal fluid, or blood. Cultures from other areas, such as the throat, can be misleading. This is because the virus may remain for long periods of time in places with a large amount of lymphatic tissue. As a rule, cultures done early in the illness are more likely to identify the virus.

New techniques that involve identification of viral genetic material (PCR) are useful in certain cases, but are not indicated for routine testing.

Treatment

As noted above, enterovirus is capable of attacking many different organs and producing a variety of symptoms. Most infections are mild and improve without complications, and require no specific therapy. When the virus attacks critical organs however, such as the heart, respiratory muscles, nervous system, etc., then specialized care is often needed.

As of 2001, no effective antiviral medication for enterovirus has undergone investigation in patients, though some drugs appear promising for the future. In some patients who are unable to produce antibodies (hypogammaglobunemia), administrating antibodies themselves is helpful.

Prognosis

The overall outlook for enterovirus infection depends on the organs involved, and the immune condition of the individual patient. Unless vital organs are involved or immunity is abnormal, infection causes few problems. On the other hand, patients who have diseases that affect antibody production can develop chronic infection of the brain or meninges.

KEY TERMS

Antibodies—Proteins that are formed by the body and play a role in defense against infection.

Antibiotic—A medication that is designed to kill or weaken bacteria.

Meninges—Outer covering of the spinal cord and brain. Infection is called meningitis, which can lead to damage to the brain or spinal cord and lead to death.

Prevention

In the hospital setting, the best means of avoiding transmission of infection is the use of good hand-washing practices and other appropriate precautions (gowns and gloves for hospital staff). The virus is found in feces for up to one week after infection; therefore precautions that isolate waste material (enteric precautions) will help decrease the chance of spreading the illness.

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David Kaminstein, MD

Entropy *see* **Eyelid disorders**

Enuresis *see* **Bed-wetting**

Environmental medicine *see* **Wilderness medicine**

Enzyme therapy

Definition

Enyzme therapy is a plan of dietary supplements of plant and animal enzymes used to facilitate the digestive process and improve the body's ability to maintain balanced metabolism.

Purpose

In traditional medicine, enzyme supplements are often prescribed for patients suffering from disorders that affect the digestive process, such as **cystic fibrosis**, Gaucher's disease, and **celiac disease**. A program of enzyme supplementation is rarely recommended for healthy patients. However, proponents of enzyme therapy believe that such a program is beneficial for everyone. They point to enzymes' ability to purify the blood, strengthen the immune system, enhance mental capacity, cleanse the colon, and maintain proper pH balance in urine. They feel that by improving the digestive process, the body is better able to combat infection and disease.

Some evidence exists that pancreatic enzymes derived from animal sources are helpful in **cancer** treatment. The enzymes may be able to dissolve the coating on cancer cells and may make it easier for the immune system to attack the cancer.

A partial list of the wide variety of complaints and illnesses that can be treated by enzyme therapy includes:

- AIDS
- anemia
- alcohol consumption
- anxiety
- acute inflammation
- back pain
- cancer
- colds
- chronic **fatigue** syndrome
- colitis
- constipation
- **diarrhea**
- food **allergies**
- gastritis
- gastric duodenal ulcer
- gout
- headaches
- hepatitis
- hypoglycemia
- infections
- mucous congestion
- multiple sclerosis
- nervous disorders
- nutritional disorders
- obesity
- premenstrual syndrome (PMS)
- stress

Description

Origins

Enzymes are protein molecules used by the body to perform all of its chemical actions and reactions. The body manufactures several thousands of enzymes. Among them are the digestive enzymes produced by the stomach, pancreas, small intestine, and the salivary glands of the mouth. Their energy-producing properties are responsible for not only the digestion of nutrients, but their absorption, transportation, metabolization, and elimination as well.

Enzyme therapy is based on the work of Dr. Edward Howell in the 1920s and 1930s. Howell proposed that enzymes from foods work in the stomach to pre-digest food. He advocated the consumption of large amounts of plant enzymes, theorizing that if the body had to use less of its own enzymes for digestion, it could store them for maintaining metabolic harmony. Four categories of plant enzymes are helpful in pre-digestion: protease, amylase, lipase, and cellulase. Cellulase is particularly helpful because the body is unable to produce it.

Animal enzymes, such as pepsin extracted from the stomach of pigs, work more effectively in the duodenum. They are typically used for the treatment of nondigestive ailments.

The seven categories of food enzymes and their activities

- amylase breaks down starches
- cellulase breaks down fibers
- lactase breaks down dairy products
- lipase breaks down fats
- maltase breaks down grains
- protease breaks down proteins
- sucrase breaks down sugars

Enzyme theory generated further interest as the human diet became more dependent on processed and cooked foods. Enzymes are extremely sensitive to heat, and temperatures above 118°F (48°C) destroy them. Modern processes of pasteurization, canning, and microwaving are particularly harmful to the enzymes in food.

Enzyme supplements are extracted from plants like pineapple and papaya and from the organs of cows and pigs. The supplements are typically given in tablet or capsule form. Pancreatic enzymes may also be given by injection. The dosage varies with the condition being treated. For nondigestive ailments, the supplements are taken in the hour before meals so that they can be quickly absorbed into the blood. For digestive ailments, the supplements are taken immediately before meals accompanied by a large glass of fluids. Pancreatic enzymes may be accompanied by doses of vitamin A.

7Preparations

No special preparations are necessary before beginning enzyme therapy. However, it is always advisable to talk to a doctor or pharmacist before purchasing enzymes and beginning therapy.

Precautions

People with allergies to beef, pork, pineapples, and papaya may suffer allergic reactions to enzyme supplements. Tablets are often coated to prevent them from breaking down in the stomach, and usually shouldn't be chewed or crushed. People who have difficulty swallowing pills can request enzyme supplements in capsule form. The capsules can then be opened and the contents sprinkled onto soft foods like applesauce.

Side effects

Side effects associated with enzyme therapy include **heartburn**, **nausea and vomiting**, diarrhea, bloating, gas, and **acne**. According to the principles of therapy, these are temporary cleansing symptoms. Drinking eight to ten glasses of water daily and getting regular **exercise** can reduce the discomfort of these side effects. Individuals may also experience an increase in bowel movements, perhaps one or two per day. This is also considered a positive effect.

Plant enzymes are safe for pregnant women, although they should always check with a doctor before using enzymes. Pregnant women should avoid animal enzymes. In rare cases, extremely high doses of enzymes can result in a build up of uric acid in the blood or urine and can cause a break down of proteins.

KEY TERMS

Celiac disease—A chronic disease characterized by defective digestion and use of fats.

Cystic fibrosis—A genetic disease that causes multiple digestive, excretion, and respiratory complications. Among the effects, the pancreas fails to provide secretions needed for the digestion of food.

Duodenum—The first part of the small intestine.

Gaucher's disease—A rare genetic disease caused by a deficiency of enzymes needed for the processing of fatty acids.

Metabolism—The system of chemical processes necessary for living cells to remain healthy.

Research and general acceptance

In the United States, the Food and Drug Administration (FDA) has classified enzymes as a food. Therefore, they can be purchased without a prescription. However, insurance coverage is usually dependent upon the therapy resulting from a doctor's orders.

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Mary McNulty

Eosinophilic granuloma *see* **Histiocytosis X**

Eosinophilic pneumonia

Definition

Eosinophilic **pneumonia** is a group of diseases in which there is an above normal number of eosinophils in the lungs and blood.

Description

Eosinophilia is an increase in the number of eosinophils. Eosinophilic pneumonia is characterized by a large number of eosinophils in the lungs, usually in the absence of an infectious disease. Eosinophils are one of the white blood cells and are classified as a granulocyte. They are part of the non-specific immune system and participate in inflammatory reactions. Eosinophils contain cationic molecules that are useful for destroying infectious agents, especially heiminthic parasites (worms). There are several types of eosinophilic pneumonia. Loffler's pneumonia is a temporary infiltration of eosinophils into the lungs. The patient will feel tired, have a **cough**, spasms of the bronchial airway, and difficulty breathing. Loffler's pneumonia will clear spontaneously, but slowly over the course of about a month. Another form of eosinophilic pneumonia, pulmonary infiltrates with eosinophilia (PIE), is a more serious and potentially fatal disease. In PIE, the patient experiences **asthma**, pulmonary infiltrates, disorders of the peripheral nervous system, central nervous systems symptoms, and periarteritis nodosa.

Causes and symptoms

Pneumonia with eosinophils occurs as part of a hypersensitivity reaction. A hypersensitivity reaction is an over-reaction of the immune system to a particular stimulus. As part of the hypersensitive reaction, cells of the immune system are produced in increased numbers and migrate into areas targeted by the hypersensitivity reaction. In the case of eosinophilic pneumonia, the lungs are the target. Generally, eosinophilia pneumonia is not a reaction to an infection. There is a correlation between asthma and eosinophilic pneumonia. Eosinophilic pneumonia can also be caused by drugs and, in some people, by polluted air. The symptoms range from mild (coughing, **wheezing**, and **shortness of breath**) to severe and life threatening (severe shortness of breath and difficulty getting enough oxygen). The symptoms may resolve spontaneously or can persist for long periods of time. In a few cases, the disease may rapidly produce life-threatening pneumonia.

KEY TERMS

Infiltrates—Cells or body fluids that have passed into a tissue or body cavity.

Sputum—Material coughed up from the throat or lungs.

Diagnosis

Since eosinophilia is common to a number of conditions, the physician must rule out asthma and infection by helminths when diagnosing eosinophilic pneumonia. A whole **blood count** will reveal an increased number of eosinophils in the blood. An x ray of the lungs may show the presence of infiltrates (the eosinophils and fluid). If sputum is produced in coughing, eosinophils will be seen instead of the more normal profile of granulocytes seen when an infectious agent is present.

Treatment

Eosinophilic pneumonia may not respond to drugs used to treat asthma. Eosinophilic pneumonia is usually treated with steroids, particularly glucocorticosteroids. Steroids are not effective against infectious agents, but the main disease process in eosinophilic pneumonia is an inflammatory reaction, not a response to infection. When eosinophilia is produced as a consequence of asthma or an infection by helminths, treatment of the asthma or helminths will reduce the eosinophilia.

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John T. Lohr, PhD

Ephedrine *see* **Bronchodilators**

Epicondylitis *see* **Tennis elbow**

Epidemic icterus *see* **Hepatitis A**

Epidemic typhus *see* **Typhus**

Epidemic viral gastroenteritis *see* **Rotavirus infections**

Epidermolysis bullosa

Definition

Epidermolysis bullosa (EB) is a group of rare inherited skin diseases that are characterized by the development of blisters following minimal pressure to the skin. Blistering often appears in infancy in response to simply being held or handled. In rarer forms of the disorder, EB can be life-threatening. There is no cure for the disorder. Treatment focuses on preventing and treating **wounds** and infection.

KEY TERMS

Collagen—The main supportive protein of cartilage, connective tissue, tendon, skin, and bone.

Dermis—The layer of skin beneath the epidermis.

Epidermis—The outermost layer of the skin.

Keratin—A tough, nonwater-soluble protein found in the nails, hair, and the outermost layer of skin. Human hair is made up largely of keratin.

Description

Epidermolysis bullosa has three major forms and at least 16 subtypes. The three major forms are EB simplex, junctional EB, and dystrophic EB. These can range in severity from mild blistering to more disfiguring and life-threatening disease. Physicians diagnose the form of the disease based on where the blister forms in relation to the epidermis (the skin's outermost layer) and the deeper dermis layer.

The prevalence of epidermolysis varies among different populations. A study in Scotland estimated the prevalence to be one in 20,400. Researchers in other parts of the world estimate the prevalence to be one in 100,000. This variance is due to the variability of expression. Many cases of epidermolysis bullosa are often not accurately diagnosed and thus, are not reported.

Causes and symptoms

EB can be inherited as the result of a dominant genetic abnormality (only one parent carries the abnormal gene) or a recessive genetic abnormality (both parents carry the abnormal gene).

EB simplex results from mutations in genes responsible for keratin 5 and 14, which are proteins that give cells of the epidermis its structure. EB simplex is transmitted in an autosomal dominant fashion.

Dystrophic EB is caused by mutations in genes for type VII collagen, the protein contained in the fibers anchoring the epidermis to the deeper layers of the skin. The genetic mutations for junctional EB are found in the genes responsible for producing the protein Laminin-5. Dystrophic EB is an autosomal disorder and will only result if both parents transmit an abnormal gene during conception.

EB simplex, the most common form of EB, is the least serious form of the disease. In most affected individuals, the blisters are mild and do not scar after they heal. Some forms of EB simplex affect just the hands and feet. Other forms of EB simplex can lead to more widespread blistering, as well as hair loss and missing teeth. Recurrent blistering is annoying but not life threatening.

The second, or junctional, form of EB does not lead to scarring. However, skin on the areas prone to blistering, such as elbows and knees, often shrinks. In one variation of junctional EB, called gravis junctional EB of Herlitz, the blistering can be so severe that affected infants may not survive due to massive infection and **dehydration**.

The third form of EB, dystrophic EB, varies greatly in terms of severity, but more typically affects the arms and legs. In one variation, called Hallopeau-Siemens EB, repeated blistering and scarring of the hands and feet causes the fingers and toes to fuse, leaving them dysfunctional and with a mitten-like appearance.

Diagnosis

Physicians and researchers distinguish between the three major subtypes of EB based on which layer of the epidermis separates from the deeper dermis layer of the skin below. Patients suspected of having EB should have a fresh blister biopsied for review. This sample of tissue is examined under an electron microscope or under a conventional microscope using a technique called immunofluorescence, which helps to map the underlying structure.

Knowing that a family member has EB can help establish the diagnosis, but it is possible that parents or siblings will show no sign of the disease, either because it is caused by a new genetic mutation, or because the parents are carriers of the recessive trait and do not display the disease.

Treatment

The most important treatment for EB is daily wound care. Because the skin is very fragile, care must be taken to be certain that dressing changes do not cause further damage. Tape should not be applied directly to skin and

bandages should be soaked off. Infection is a major concern, so a topical antibiotic, such as bacitracin, mupirocin, or sulfadiazine, should be routinely applied. Among persons with recessive dystrophic EB, the anticonvulsant phenytoin is sometimes effective because it decreases production of an enzyme that breaks down collagen.

Prognosis

The prognosis of EB varies depending on the subtype of the disease. Individuals with EB simplex can live long, fulfilling lives. The severity of the junctional and dystrophic forms of EB can vary greatly. Infants affected with some forms of the disease often do not survive infancy; other forms can lead to severe scarring and disfigurement.

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Epididymitis

Definition

Epididymitis is inflammation or infection of the epididymis. In this long coiled tube attached to the upper part of each testicle, sperm mature and are stored before ejaculation.

Description

Epididymitis is the most common cause of **pain** in the scrotum. The acute form is usually associated with the most severe pain and swelling. If symptoms last for more than six weeks after treatment begins, the condition is considered chronic.

Epididymitis can occur any time after the onset of **puberty** but is most common between the ages of 18 and 40. It is especially common among members of the military who **exercise** for extended periods without emptying their bladders.

Factors that increase the risk of developing epididymitis include:

- infection of the bladder, kidney, prostate, or urinary tract
- other recent illness

- narrowing of the urethra (the tube that drains urine from the bladder)
- use of a urethral catheter.

Causes and symptoms

Although epididymitis can be caused by the same organisms that cause some **sexually transmitted diseases** (STDs) or occur after prostate surgery, the condition is generally due to pus-generating bacteria associated with infections in other parts of the body.

Epididymitis can also be caused by injury or infection of the scrotum or by irritation from urine that has accumulated in the vas deferens (the duct through which sperm travels after leaving the epididymis).

Epididymitis is characterized by sudden redness and swelling of the scrotum. The affected testicle is hard and sore, and the other testicle may feel tender. The patient has chills and **fever** and usually has acute **urethritis** (inflammation of the urethra).

Enlarged lymph nodes in the groin cause scrotal pain that intensifies throughout the day and may become so severe that walking normally becomes impossible.

Diagnosis

Laboratory tests used to diagnose epididymitis include:

- urinalysis and urine culture
- examination of discharges from the urethra and prostate gland
- blood tests to measure white-cell counts

Treatment

Because epididymitis that affects both testicles can make a man sterile, antibiotic therapy must be initiated as soon as symptoms appear. To prevent reinfection, medication must be taken exactly as prescribed, even if the patient's symptoms disappear or he begins to feel better. Over-the-counter anti-inflammatories can relieve pain but should not be used without the approval of a family physician or urologist.

Bed rest is recommended until symptoms subside, and patients are advised to wear athletic supporters when they resume normal activities. If pain is severe, a local anesthetic like lidocaine (Xylocaine) may be injected directly into the spermatic cord.

Self-care

A patient who has epididymitis should not drink beverages that contain **caffeine**. To prevent **constipation**, he should use stool softeners or eat plenty of fruit, nuts, whole grain cereals, and other foods with laxative properties.

An ice bag wrapped in a towel can reduce pain and swelling but should be removed from the inflamed area for a few minutes every hour to prevent **burns**.

Strenuous activity should be avoided until symptoms disappear. Sexual activity should not be resumed until a month after symptoms disappear.

If a second course of treatment doesn't eradicate stubborn symptoms, longterm anti-inflammatory therapy may be recommended. In rare instances, chronic symptoms require surgery.

Surgery

Each of the surgical procedures used to treat epididymitis is performed under local anesthesia on an outpatient basis. Both of them cause sterility.

Epididymectomy involves removing the inflamed section of the epididymitis through a small incision in the scrotum.

Bilateral **vasectomy** prevents fluid and sperm from passing through the epididymis. This procedure is usually performed on men who have chronic epididymitis or on elderly patients undergoing prostate surgery.

Prognosis

Pain generally subsides 24–72 hours after treatment begins. Complete healing may take weeks or months.

Prevention

Using condoms and not having sex with anyone who has an STD can prevent some cases of epididymitis.

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Epidural abscess *see* **Central nervous system infections**

Epidural anesthetic *see* **Anesthesia, local**

Epiglottitis

Definition

Epiglottitis is an infection of the epiglottis, which can lead to severe airway obstruction.

Description

When air is inhaled (inspired), it passes through the nose and the nasopharynx or through the mouth and the oropharynx. These are both connected to the larynx, a tube made of cartilage. The air continues down the larynx to the trachea. The trachea then splits into two branches, the left and right bronchi (bronchial tubes). These bronchi branch into smaller air tubes that run within the lungs, leading to the small air sacs of the lungs (alveoli).

Either food, liquid, or air may be taken in through the mouth. While air goes into the larynx and the respiratory system, food and liquid are directed into the tube leading to the stomach, the esophagus. Because food or liquid in the bronchial tubes or lungs could cause a blockage or lead to an infection, the airway is protected. The epiglottis is a leaf-like piece of cartilage extending upwards from the larynx. The epiglottis can close down over the larynx when someone is eating or drinking, preventing these food and liquids from entering the airway.

Epiglottitis is an infection and inflammation of the epiglottis. Because the epiglottis may swell considerably, there is a danger that the airway will be blocked off by the very structure designed to protect it. Air is then unable to reach the lungs. Without intervention, epiglottitis has the potential to be fatal.

Epiglottitis is primarily a disease of two to seven-year-old children, although older children and adults can also contract it. Boys are twice as likely as girls to develop this infection. Because epiglottitis involves swelling and infection of tissues, which are all located at or above the level of the epiglottis, it is sometimes referred to as supraglottitis (*supra,* meaning above). About 25% of all children with this infection also have **pneumonia**.

Causes and symptoms

The most common cause of epiglottitis is infection with the bacteria called *Haemophilus influenzae type b.* Other types of bacteria are also occasionally responsible for this infection, including some types of *Streptococcus* bacteria and the bacteria responsible for causing **diphtheria**.

A patient with epiglottitis typically experiences a sudden **fever**, and begins having severe throat and neck **pain**. Because the swollen epiglottis interferes significantly with air movement, every breath creates a loud, harsh, high-pitched sound referred to as **stridor**. Because the vocal cords are located in the larynx just below the area of the epiglottis, the swollen epiglottis makes the patient's voice sound muffled and strained. Swallowing becomes difficult, and the patient may drool. The patient often leans forward and juts out his or her jaw, while struggling for breath.

Epiglottitis strikes suddenly and progresses quickly. A child may begin complaining of a **sore throat**, and within a few hours be suffering from extremely severe airway obstruction.

Diagnosis

Diagnosis begins with a high level of suspicion that a quickly progressing illness with fever, sore throat, and airway obstruction is very likely to be epiglottitis. If epiglottitis is suspected, no efforts should be made to look at the throat, or to swab the throat in order to obtain a culture for identification of the causative organism. These maneuvers may cause the larynx to go into spasm (laryngospasm), completely closing the airway. These procedures should only be performed in a fully-equipped operating room, so that if laryngospasm occurs, a breathing tube can be immediately placed in order to keep the airway open.

An instrument called a laryngoscope is often used in the operating room to view the epiglottis, which will appear cherry-red and quite swollen. An x-ray picture taken from the side of the neck should also be obtained. The swollen epiglottis has a characteristic appearance, called the "thumb sign."

Treatment

Treatment almost always involves the immediate establishment of an artificial airway: inserting a breathing tube into the throat (intubation); or making a tiny opening toward the base of the neck and putting a breathing tube into the trachea (tracheostomy). Because the patient's apparent level of distress may not match the actual severity of the situation, and because the disease's progression can be quite surprisingly rapid, it is preferable to go ahead and place the artificial airway, rather than adopting a wait-and-see approach.

Because epiglottitis is caused by a bacteria, **antibiotics** such as cefotaxime, ceftriaxone, or ampicillin with sulbactam should be given through a needle placed in a vein (intravenously). This prevents the bacteria that are circulating throughout the bloodstream from causing infection elsewhere in the body.

KEY TERMS

Epiglottis—A leaf-like piece of cartilage extending upwards from the larynx, which can close like a lid over the trachea to prevent the airway from receiving any food or liquid being swallowed.

Extubation—Removal of a breathing tube.

Intubation—Putting a breathing tube into the airway.

Laryngospasm—Spasm of the larynx.

Larynx—The part of the airway lying between the pharynx and the trachea.

Nasopharynx—The part of the airway into which the nose leads.

Oropharynx—The part of the airway into which the mouth leads.

Supraglottitis—Another term for epiglottitis.

Trachea—The part of the airway that leads into the bronchial tubes.

Tracheostomy—A procedure in which a small opening is made in the neck and into the trachea. A breathing tube is then placed through this opening.

Prognosis

With treatment (including the establishment of an artificial airway), only about 1% of children with epiglottitis die. Without the artificial airway, this figure jumps to 6%. Most patients recover form the infection, and can have the breathing tube removed (extubation) within a few days.

Prevention

Prevention involves the use of a vaccine against *H. influenzae type b* (called the Hib vaccine). It is given to babies at two, four, six, and 15 months. Use of this vaccine has made epiglottitis a very rare occurrence.

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Epilepsy *see* **Seizure disorder**

Epinephrine *see* **Bronchodilators**

Episiotomy

Definition

An episiotomy is a surgical incision made in the area between the vagina and anus (perineum). This is done during the last stages of labor and delivery to expand the opening of the vagina to prevent tearing during the delivery of the baby.

Purpose

This procedure is usually done during the delivery or birthing process when the vaginal opening does not stretch enough to allow the baby to be delivered without tearing the surrounding tissue.

Precautions

Prior to the onset of labor, pregnant women may want to discuss the use of episiotomy with their care providers. It is possible that, with adequate preparation and if the stages of labor and delivery are managed with adequate coaching and support, the need for an episiotomy may be reduced.

Description

An episiotomy is a surgical incision, usually made with sterile scissors, in the perineum as the baby's head is being delivered. This procedure may be used if the tissue around the vaginal opening begins tearing or does not seem to be stretching enough to allow the baby to be delivered.

An episiotomy is a surgical incision made in the perineum, the area of tissue between the vaginal opening and the anus, during the birthing process. This procedure may be used if the tissue around the vaginal opening begins to tear or is not stretching enough to allow the baby to be delivered vaginally. In the United States, the rate of episiotomies being performed is estimated at 65–95%. *(Illustration by Electronic Illustrators Group.)*

In most cases, the physician makes a midline incision along a straight line from the lowest edge of the vaginal opening to toward the anus. In other cases, the episiotomy is performed by making a diagonal incision across the midline between the vagina and anus. This method is used much less often, may be more painful, and may require more healing time than the midline incision. After the baby is delivered through the extended vaginal opening, the incision is closed with stitches. A local anesthetic agent may be applied or injected to numb the area before it is sewn up (sutured).

Several reasons are cited for performing episiotomies. Some experts believe that an episiotomy speeds up the birthing process, making it easier for the baby to be delivered. This can be important if there is any sign of distress that may harm the mother or baby. Because tissues in this area may tear during the delivery, another reason for performing an episiotomy is that a clean incision is easier to repair than a jagged tear and may heal faster. Although the use of episiotomy is sometimes described as protecting the pelvic muscles and possibly preventing future problems with **urinary incontinence**, it is not clear that the procedure actually helps.

The use of episiotomy during the birthing process is fairly widespread in the United States. Estimates of episiotomy use in hospitals range from 65–95% of deliveries, depending on how many times the mother has given birth previously. This routine use of episiotomy is being reexamined in many hospitals and health care settings. However, an episiotomy is always necessary during a forceps delivery because of the size of the forceps.

Preparation

It may be possible to avoid the need for an episiotomy. Pregnant women may want to talk with their care providers about the use of episiotomy during the delivery. Kegel exercises are often recommended during the **pregnancy** to help strengthen the pelvic floor muscles. Prenatal perineal massage may help to stretch and relax the tissue around the vaginal opening. During the delivery process, warm compresses can be applied to the area along with the use of perineal massage. Coaching and support are also important during the delivery process. A slowed, controlled pushing during the second stage of labor (when the mother gets the urge to push) may allow the tissues to stretch rather than tear. Also, an upright birthing position (rather than one where the mother is lying down) may decrease the need for an episiotomy.

Aftercare

The area of the episiotomy may be uncomfortable or even painful for several days. Several practices can relieve some of the **pain**. Cold packs can be applied to the perineal area to reduce swelling and discomfort. Use of the **Sitz bath** available at the hospital or birth center can ease the discomfort, too. This unit circulates warm water over the area. A squirt bottle with water can be used to clean the area after urination or defecation rather

KEY TERMS

Kegel exercises—A series of contractions and relaxations of the muscles in the perineal area. These exercises are thought to strengthen the pelvic floor and may help prevent urinary incontinence in women.

Perineum—The area between the opening of the vagina and the anus in a woman, or the area between the scrotum and the anus in a man.

Sitz bath—A shallow tub or bowl, sometimes mounted above a toilet, that allows the perineum and buttocks to be immersed in circulating water.

Urinary incontinence—The inability to prevent the leakage or discharge of urine. This situation becomes more common as people age, and is more common in women who have given birth to more than one child.

than wiping with tissue. Also, the area should be patted dry rather than wiped. Cleansing pads soaked in witch hazel (such as Tucks) are very effective for cleaning the area and also feel soothing.

Risks

Several side effects of episiotomy have been reported, including infection, increased pain, prolonged healing time, and increased discomfort once sexual intercourse is resumed. There is also the risk that the episiotomy incision will be deeper or longer than is necessary to permit the birth of the infant. There is a risk of increased bleeding.

Normal results

In a normal and well managed delivery, an episiotomy may be avoided altogether. If an episiotomy is deemed to be necessary, a simple midline incision will be made to extend the vaginal opening without additional tearing or extensive trauma to the perineal area. Although there may be some pain associated with the healing of the episiotomy incision, relief can usually be provided with mild pain relievers and supportive measures, such as the application of cold packs.

Abnormal results

An episiotomy incision that is too long or deep may extend into the rectum, causing more bleeding and an increased risk of infection. Additional tearing or tissue damage may occur beyond the episiotomy incision, leaving a cut and a tear to be repaired.

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Altha Roberts Edgren

Epispadias *see* **Hypospadias and epispadias**

Epistaxis *see* **Nosebleed**

EPS *see* **Electrophysiology study of the heart**

Epstein-Barr virus test

Definition

The Epstein-Barr virus test is a blood test, or group of tests, to determine the presence or absence of antibodies in the blood stream directed against proteins of the Epstein-Barr virus, the cause of **infectious mononucleosis**.

Purpose

The test is primarily used to detect whether first time infection (called primary infection) with the Epstein-Barr virus is currently occurring, or has occurred within a short period of time. The pattern of the antibodies detected can, however, tell if the person has never been infected with the Epstein-Barr virus, or if the infection occurred in the more distant past. These tests are mostly utilized in the diagnosis of Epstein-Barr virus-associated infectious mononucleosis when the more common diagnostic test, the heterophile antibody, is negative, or in situations where the infection is manifesting unusual symptoms. Therefore, the tests are often not needed in a situa-

tion where a doctor believes that a person has mononucleosis and the heterophile test (also called the monospot test) is positive.

In addition, Epstein-Barr virus testing is usually not needed in the evaluation of a patient who has long-lasting **fatigue**, and may have the **chronic fatigue syndrome**. Initially, it was thought that discovering a particular pattern of antibodies to this virus was helpful in the diagnosis of chronic fatigue syndrome, but this no longer appears to be the case.

Precautions

As in any blood test, standard precautions should be performed to prevent infection at the site where the blood is obtained, and to prevent excess bleeding. Normally, the site is cleaned with an antiseptic liquid prior to the blood being obtained; a sterile non-reusable needle and syringe are used; and, once the needle is removed, pressure is placed at the site until bleeding has stopped.

Description

These tests are more often performed in a consulting laboratory than at a physician's office or in a hospital laboratory. Like most antibody tests, they are performed on serum, the liquid part of the blood obtained after the whole blood is allowed to clot in a tube. Antibodies can be detected against several components of the Epstein-Barr virus (EBV). These components are the EBV early antigen (EA), the viral capsid antigen (VCA), and the nuclear antigen (EBNA). These several antigens are different proteins that are produced in the process (stages) of the virus' growth.

At the time of infection with Epstein-Barr virus, antibodies to EA are found and usually last for four to six months only. This antibody, however, persists substantially longer in about 10% of persons who have had EBV infection in the more remote past. The absence of antibody to EA when other EBV antibodies are present strongly suggests that first time infection with EBV occurred in the past.

Antibody to VCA is found both early and late in EBV infection. At the time of infection, antibody of both the IgM and IgG types are detectable. After four to six months, usually, only the IgG antibody against VCA can be found.

Unlike antibodies to EA and VCA, antibody to EBNA does not usually develop until recovery from first time infection of this virus. Therefore, finding detectable amounts of antibody to EBNA during an illness which might be caused by EBV makes the causal relationship very unlikely.

Preparation

The skin area from which the blood sample will be obtained is wiped with an antiseptic such as alcohol or iodine.

Aftercare

The aftercare is similar to that for any blood test. Usually, pressure is applied to the area for several moments until bleeding stops. If the results are difficult to interpret, it may be necessary to re-test later, after waiting one to three weeks. The change in the amounts of antibody detected between the two tests can be particularly useful, at times, in helping to make a diagnosis.

Risks

There are no risks over and above those of having blood drawn for any other purpose. These tests are more expensive than many other blood tests but are usually covered by medical insurance.

Normal results

The pattern of the three antibodies can be used to determine whether the person has not had infection with EBV to this point (is susceptible to infection); is currently, or recently, infected with EBV for the first time; or has had first time infection with EBV sometime in the past (more than six months ago).

If one defines "normal" results as either not having EBV in the past, and call that category one; or having had it in the past, and call that category two. Most young children below the age of five will fall into category one, while most adults over the age of 20 years will fall into category two.

The results for susceptibility are:

- antibody to EA = negative
- antibody to VCA (either IgM or IgG) = negative
- antibody to EBNA = Negative

The results for past infection are:

- antibody to EA = negative (90% of time)
- antibody to VCA IgM = negative
- antibody to VCA IgG = positive
- antibody to EBNA = positive

It is important to realize that the Epstein-Barr virus, like all the human herpes viruses, does not totally leave the body after the patient recovers from illness. With EBV, the virus will intermittently recur in the saliva of people without any symptoms. Such people will have a

test pattern of previous infection. It is this group of people who can transmit EBV to others without themselves being ill.

Abnormal results

The results for current or recent infection are:

- antibody to EA = positive
- antibody to VCA IgM = positive
- antibody to VCA IgG = positive
- antibody to EBNA = negative

Without the pattern of the three antibodies, it can be difficult to be accurate in interpretation. The presence of antibody to VCA IgM is the best single test for current or recent first time infection.

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Larry Lutwick, MD, FACP

ERCP *see* **Endoscopic retrograde cholangiopancreatography**

Erectile disorder *see* **Impotence**

Ergotamine *see* **Antimigraine drugs**

Erosive gastritis *see* **Gastritis**

Erysipelas

Definition

Erysipelas is a skin infection that often follows **strep throat**.

Description

Erysipelas, also called St. Anthony's fire, is caused by infection by Group A *Streptococci*. This same type of bacteria is responsible for such infections as strep throat, and infections of both surgical and other kinds of **wounds** in the skin. The infection occurs most often in young infants and the elderly.

KEY TERMS

Bacteremia—The presence of bacteria in the blood.

Streptococcus—A bacteria that causes erysipelas and strep throat, as well as other infections.

Causes and symptoms

Erysipelas usually occurs rather abruptly. When the preceding infection was strep throat, the rash begins on the face. Occasionally, when the preceding infection was of a wound from an injury or operation, the rash will appear on an arm or leg.

Classically, the usual presentation is a bright-red, butterfly-shaped rash appearing across the bridge of the nose and the cheeks. It is hot to the touch, painful, shiny, and swollen, with clearly defined margins. The edges of the rash are a raised ridge, hard to the touch. There may be fluid-filled bumps scattered along the area. The rash spreads rapidly. Some patients have swelling of the eyelids, sometimes so severe that their eyes swell shut. The patient may have **fever**, chills, loss of energy, **nausea and vomiting**, and swollen, tender lymph nodes. In severe cases, walled-off areas of pus (abscesses) may develop beneath the skin. If left untreated, the streptococcal bacteria may begin circulating in the bloodstream (a condition called **bacteremia**). A patient may then develop an overwhelming, systemic infection called **sepsis**, with a high risk of **death**.

Diagnosis

The rash of erysipelas is very characteristic, raising the practitioner's suspicion towards that diagnosis, especially when coupled with a history of recent strep infection. Attempts to culture (grow) the bacteria from a sample of the rash usually fail. When the bacteria are present in the blood, they may be grown in a laboratory, and identified under a microscope. Other laboratory tests involve reacting fluorescently-tagged antibodies with a sample of the patient's infected tissue. This type of test may be successful in positively identifying the streptococcal bacteria.

Treatment

Penicillin is the drug of choice for treating erysipelas. It can usually be given by mouth, although in severe cases (or in cases of diagnosed bacteremia) it may be given through a needle placed in a vein (intravenously).

Even with antibiotic treatment, swelling may continue to spread. Other symptoms, such as fever, **pain**, and redness, usually decrease rapidly after penicillin is started. Cold packs and pain relievers may help decrease discomfort. Within about five to 10 days, the affected skin may begin drying up and flaking off.

Prognosis

With prompt treatment, the prognosis from erysipelas is excellent. Delay of treatment, however, increases the chance for bacteremia and the potential for death from overwhelming sepsis. This is particularly true of people with weakened immune systems (babies, the elderly, and people ill with other diseases, especially Acquired Immunodeficiency Syndrome, or **AIDS**). Frequently, an individual who has had erysipelas will have it occur again in the same location.

Prevention

Prevention involves appropriate and complete treatment of **streptococcal infections**, including strep throat and wound infections.

Resources

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Rosalyn Carson-DeWitt, MD

Erythema infectiosum *see* **Fifth disease**

Erythema multiforme

Definition

Erythema multiforme is a skin disease that causes lesions and redness around the lesions.

Description

Erythema multiforme appears on the skin and the mucous membranes (the lining of the mouth, digestive tract, vagina, and other organs). Large, symmetrical red blotches appear all over the skin in a circular pattern. On mucous membranes, it begins as blisters and progresses to ulcers. A more advanced form, called Stevens-Johnson syndrome, can be severe and even fatal.

Causes and symptoms

Erythema multiforme has many causes, most commonly are drugs. Penicillin, **sulfonamides**, certain epilepsy drugs, **aspirin**, and **acetaminophen** are the most likely medication-induced causes. Erythema multiforme can also be caused by certain diseases. Herpes virus and mycoplasma **pneumonia** are likely infectious causes.

Diagnosis

The appearance of the rash is sufficiently unique to identify it on sight. Having identified it, the physician will determine the underlying cause.

Treatment

Erythema multiforme is inadvertently treated when the causative agent, whether it be a drug or a disease, is treated. In severe cases, cortisone-like medication is often used along with general supportive measures and prevention of infection.

Prognosis

As a rule, the rash abates by itself without damaging the skin. Only in the case of infection, severe blistering, or continued use of an offending drug does complications occur.

Resources

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KEY TERMS

Herpes virus—Viruses that can infect the skin, mucous membranes, and brain, and they are responsible for such diseases as herpes simplex, chicken pox, and shingles.

Mycoplasma pneumonia—An incomplete bacterium that infects the lung.

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Erythema nodosum

Definition

Erythema nodosum is a skin disorder characterized by painful red nodules appearing mostly on the shins.

Description

Erythema nodosum is an eruption of tender red lumps on both shins and occasionally the arms and face. Bruising often accompanies the nodule formation. Erythema nodosum is most prevalent in young adults.

Causes and symptoms

Erythema nodosum can be caused by many important and treatable diseases. Among them are **tuberculosis**, several fungal lung infections, **leprosy**, inflammatory bowel disease, and some potentially dangerous bacterial infections. Drugs can also induce erythema nodosum. The most common are penicillin, **sulfonamides**, and birth control pills.

Diagnosis

There are a few other skin eruptions that mimic erythema nodosum, so the physician may have to perform a biopsy to sort them out. There are a few types of *panniculitis,* fat inflammation, that may signal a **cancer** somewhere in the body, and there are other kinds of inflammation that may confuse the diagnosis.

KEY TERMS

Biopsy—Surgical removal of tissue for diagnostic purposes.

Panniculitis—Inflammation of fatty tissue.

Once the skin problem has been diagnosed, its underlying cause must then be identified. A lengthy evaluation may ensue, and often times the cause remains unknown.

Treatment

Painful nodules can be treated with mild **pain** killers and local application of ice packs. Medical attention will be directed toward the underlying disease.

The nodules will eventually disappear, leaving no trace behind.

Resources

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Erythremia *see* **Polycythemia vera**

Erythroblastosis fetalis

Definition

Erythroblastosis fetalis refers to two potentially disabling or fatal blood disorders in infants: Rh incompatibility disease and ABO incompatibility disease. Either disease may be apparent before birth and can cause fetal **death** in some cases. The disorder is caused by incompatibility between a mother's blood and her unborn baby's blood. Because of the incompatibility, the mother's immune system may launch an immune response against the baby's red blood cells. As a result, the baby's blood

cells are destroyed, and the baby may suffer severe anemia (deficiency in red blood cells), brain damage, or death.

Description

Red blood cells carry several types of proteins, called antigens, on their surfaces. The A, B, and O antigens are used to classify a person's blood as type A, B, AB, or O. Each parent passes one A, B, or O antigen gene to their child. How the genes are paired determines the person's blood type.

A person who inherits an A antigen gene from each parent has type A blood; receiving two B antigen genes corresponds with type B blood; and inheriting A and B antigen genes means a person has type AB blood. If the O antigen gene is inherited from both parents, the child has type O blood; however, the pairing of A and O antigen genes corresponds with type A blood; and if the B antigen gene is matched with the O antigen gene, the person has type B blood.

Another red blood cell antigen, called the Rh factor, also plays a role in describing a person's blood type. A person with at least one copy of the gene for the Rh factor has Rh-positive blood; if no copies are inherited, the person's blood type is Rh-negative. In blood typing, the presence of A, B, and O antigens, plus the presence or absence of the Rh-factor, determine a person's specific blood type, such as A-positive, B-negative, and so on.

A person's blood type has no effect on health. However, an individual's immune system considers only that person's specific blood type, or a close match, acceptable. If a radically different blood type is introduced into the bloodstream, the immune system produces antibodies, proteins that specifically attack and destroy any cell carrying the foreign antigen.

Determining a person's blood type is very important if she becomes pregnant. Blood cells from the unborn baby (fetal red blood cells) can cross over into the mother's bloodstream, especially at delivery. If the mother and her baby have compatible blood types, the crossover does not present any danger. However, if the blood types are incompatible, the mother's immune system manufactures antibodies against the baby's blood.

Usually, this incompatibility is not a factor in a first **pregnancy**, because few fetal blood cells reach the mother's bloodstream until delivery. The antibodies that form after delivery cannot affect the first child. In later pregnancies, fetuses and babies may be in grave danger. The danger arises from the possibility that the mother's antibodies will attack the fetal red blood cells. If this happens, the fetus or baby can suffer severe health effects and may die.

There are two types of incompatibility diseases: Rh incompatibility disease and ABO incompatibility disease. Both diseases have similar symptoms, but Rh disease is much more severe, because anti-Rh antibodies cross over the placenta more readily than anti-A or anti-B antibodies. (The immune system does not form antibodies against the O antigen.) Therefore, a greater percentage of the baby's blood cells are destroyed by Rh disease.

Both incompatibility diseases are uncommon in the United States due to medical advances over the last 50 years. For example, prior to 1946 (when newborn blood transfusions were introduced) 20,000 babies were affected by Rh disease yearly. Further advances, such as suppressing the mother's antibody response, have reduced the incidence of Rh disease to approximately 4,000 cases per year.

Rh disease only occurs if a mother is Rh-negative and her baby is Rh-positive. For this situation to occur, the baby must inherit the Rh factor gene from the father. Most people are Rh-positive. Only 15% of the caucasian population is Rh-negative, compared to 5–7% of the african american population and virtually none of Asian populations.

ABO incompatibility disease is almost always limited to babies with A or B antigens whose mothers have type O blood. Approximately one third of these babies show evidence of the mother's antibodies in their bloodstream, but only a small percentage develop symptoms of ABO incompatibility disease.

Cause and symptoms

Rh disease and ABO incompatibility disease are caused when a mother's immune system produces antibodies against the red blood cells of her unborn child. The antibodies cause the baby's red blood cells to be destroyed and the baby develops anemia. The baby's body tries to compensate for the anemia by releasing immature red blood cells, called erythroblasts, from the bone marrow.

The overproduction of erythroblasts can cause the liver and spleen to become enlarged, potentially causing liver damage or a ruptured spleen. The emphasis on erythroblast production is at the cost of producing other types of blood cells, such as platelets and other factors important for blood clotting. Since the blood lacks clotting factors, excessive bleeding can be a complication.

The destroyed red blood cells release the blood's red pigment (hemoglobin) which degrades into a yellow substance called bilirubin. Bilirubin is normally produced as red blood cells die, but the body is only equipped to handle a certain low level of bilirubin in the bloodstream at one time. Erythroblastosis fetalis overwhelms the removal system, and high levels of bilirubin

KEY TERMS

Amniocentesis—A procedure in which a needle is inserted through a pregnant woman's abdomen and into her uterus to withdraw a small sample of amniotic fluid. The amniotic fluid can be examined for sign of disease or other problems afflicting the fetus.

Amniotic fluid—The fluid that surrounds a fetus in the uterus.

Anemia—A condition in which there is an abnormally low number of red blood cells in the bloodstream. Major symptoms are paleness, shortness of breath, unusually fast or strong heart beats, and tiredness.

Antibody—A protein molecule produced by the immune system in response to a protein that is not recognized as belonging in the body.

Antigen—A protein that can elicit an immune response in the form of antibody formation. With regard to red blood cells, the major antigens are A, B, O, and the Rh factor.

Bilirubin—A yellow-colored end-product of hemoglobin degradation. It is normally present at very low levels in the bloodstream; at high levels, it produces jaundice.

Cordocentesis—A procedure for delivering a blood transfusion to a fetus. It involves a fine needle being threaded through a pregnant woman's abdomen and into the umbilical cord with the aid of ultrasound imaging.

Hemoglobin—A molecule in red blood cells that transports oxygen and gives the cells their characteristic color.

Hydrops fetalis—A condition in which a fetus or newborn baby accumulates fluids, causing swollen arms and legs and impaired breathing.

Hyperbilirubinemia—A condition in which bilirubin accumulates to abnormally high levels in the bloodstream

Placenta—A protective membrane that surrounds and protects the fetus during pregnancy.

Platelet—A blood factor that is important in forming blood clots.

Rh factor—An antigen that is found on the red blood cells of most people. If it is present, the blood type is referred to as Rh-positive; if absent, the blood type is Rh-negative.

accumulate, causing hyperbilirubinemia, a condition in which the baby becomes jaundiced. The **jaundice** is apparent from the yellowish tone of the baby's eyes and skin. If hyperbilirubinemia cannot be controlled, the baby develops kernicterus. The term kernicterus means that bilirubin is being deposited in the brain, possibly causing permanent damage.

Other symptoms that may be present include high levels of insulin and low blood sugar, as well as a condition called hydrops fetalis. Hydrops fetalis is characterized by an accumulation of fluids within the baby's body, giving it a swollen appearance. This fluid accumulation inhibits normal breathing, because the lungs cannot expand fully and may contain fluid. If this condition continues for an extended period, it can interfere with lung growth. Hydrops fetalis and anemia can also contribute to heart problems.

Diagnosis

Erythroblastosis fetalis can be predicted before birth by determining the mother's blood type. If she is Rh-negative, the father's blood is tested to determine whether he is Rh-positive. If the father is Rh-positive, the mother's blood will be checked for antibodies against the Rh factor. A test that demonstrates no antibodies is repeated at week 26 or 27 of the pregnancy. If antibodies are present, treatment is begun.

In cases in which incompatibility is not identified before birth, the baby suffers recognizable characteristic symptoms such as anemia, hyperbilirubinemia, and hydrops fetalis. The blood incompatibility is uncovered through blood tests such as the Coombs test, which measures the level of maternal antibodies attached to the baby's red blood cells. Other blood tests reveal anemia, abnormal blood counts, and high levels of bilirubin.

Treatment

When a mother has antibodies against her unborn infant's blood, the pregnancy is watched very carefully. The antibodies are monitored and if levels increase, **amniocentesis**, fetal umbilical cord blood sampling, and ultrasound are used to assess any effects on the baby. Trouble is indicated by high levels of bilirubin in the amniotic fluid or baby's blood, or if the ultrasound

reveals hydrops fetalis. If the baby is in danger, and the pregnancy is at least 32–34 weeks along, labor is induced. Under 32 weeks, the baby is given blood transfusions while still in the mother's uterus.

There are two techniques that are used to deliver a blood **transfusion** to a baby before birth. In the first, a needle is inserted through the mother's abdomen and uterus, and into the baby's abdomen. Red blood cells injected into the baby's abdominal cavity are absorbed into its bloodstream. In early pregnancy or if the baby's bilirubin levels are gravely high, cordocentesis is performed. This procedure involves sliding a very fine needle through the mother's abdomen and, guided by ultrasound, into a vein in the umbilical cord to inject red blood cells directly into the baby's bloodstream.

After birth, the severity of the baby's symptoms are assessed. One or more transfusions may be necessary to treat anemia, hyperbilirubinemia, and bleeding. Hyperbilirubinemia is also treated with **phototherapy**, a treatment in which the baby is placed under a special light. This light causes changes in how the bilirubin molecule is shaped, which makes it easier to excrete. The baby may also receive oxygen and intravenous fluids containing electrolytes or drugs to treat other symptoms.

Prognosis

In many cases of blood type incompatibility, the symptoms of erythroblastosis fetalis are prevented with careful monitoring and blood type screening. Treatment of minor symptoms is typically successful and the baby will not suffer long-term problems.

Nevertheless, erythroblastosis is a very serious condition for approximately 4,000 babies annually. In about 15% of cases, the baby is severely affected and dies before birth. Babies who survive pregnancy may develop kernicterus, which can lead to deafness, speech problems, **cerebral palsy**, or **mental retardation**. Extended hydrops fetalis can inhibit lung growth and contribute to **heart failure**. These serious complications are life threatening, but with good medical treatment, the fatality rate is very low. According to the U.S. Centers for Disease Control and Prevention, there were 21 infant deaths in the United States during 1996 that were attributable to hemolytic disease (erythroblastosis fetalis) and jaundice.

Prevention

With any pregnancy, whether it results in a live birth, **miscarriage**, **stillbirth**, or abortion, blood typing is a universal precaution against blood compatibility disease. Blood types cannot be changed, but adequate forewarning allows precautions and treatments that limit the danger to unborn babies.

If an Rh-negative woman gives birth to an Rh-positive baby, she is given an injection of immunoglobulin G, a type of antibody protein, within 72 hours of the birth. The immunoglobulin destroys any fetal blood cells in her bloodstream before her immune system can react to them. In cases where this precaution is not taken, antibodies are created and future pregnancies may be complicated.

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Julia Barrett

Erythrocyte sedimentation rate

Definition

The erythrocyte sedimentation rate (ESR), or sedimentation rate (sed rate), is a measure of the settling of red blood cells in a tube of blood during one hour. The rate is an indication of inflammation and increases in many diseases.

Purpose

ESR is increased in rheumatoid diseases, most infections, and in **cancer**. An advanced rate doesn't diagnose a specific disease, but it does indicate that an underlying disease may be present.

A physician can use ESR to monitor a person with an associated disease. When the disease worsens, the ESR increases; when the disease improves, the ESR decreases. The ESR doesn't always follow the course of cancer.

ESR is called an acute-phase reactant test, meaning that it reacts to acute conditions in the body, such as infection or trauma. The rate increase follows a rise in temperature and white blood cells count, peaks after several days, and usually lasts longer than the elevated temperature or white blood cells count.

Precautions

The ESR should not be used to screen healthy persons for disease.

Description

The ESR test is a simple test dating back to the ancient Greeks. A specific amount of diluted, unclotted blood is placed in a special narrow tube and left undisturbed for exactly one hour. The red cells settle towards the bottom of the tube, and the pale yellow liquid (plasma) rises to the top. After 60 minutes, measurements are taken of the distance the red cells traveled to settle at the bottom of the tube. Two methods, the Westergren and the Wintrobe, are used by laboratories; each method produces slightly different results. Most laboratories use the Westergren method.

Normally red cells don't settle far toward the bottom of the tube. Many diseases make extra or abnormal proteins that cause the red cells to move close together, stack up, and form a column (rouleaux). In a group, red cells are heavier and fall faster. The faster they fall, the further they settle, and the higher the ESR.

The ESR test is covered by insurance when medically necessary. Results are usually available the same or following day.

Preparation

This test requires 7mL–10 mL of blood. A healthcare worker ties a tourniquet on the patient's upper arm, locates a vein in the inner elbow region, and inserts a needle into that vein. Vacuum action draws the blood through the needle into an attached tube. Collection of the sample takes only a few minutes.

Aftercare

Discomfort or bruising may occur at the puncture site. Pressure applied to the puncture site until the bleeding stops reduces bruising. Warm packs to the puncture site relieve discomfort. The patient may feel dizzy or faint.

Normal results

A normal value does not rule out disease. Normal values for the Westergren method are: Men 0 mm/hour–15 mm/hour; women 0 mm/hour–20 mm/hour; and children 0 mm/hour–10 mm/hour.

Abnormal results

The highest ESR levels are usually seen in a cancer of a certain type of white blood cell (**multiple myeloma**) and rheumatoid disease, such as **rheumatoid arthritis**. Many other diseases also increase the ESR: infection, kidney disease, anemia, diseases involving white blood cells, cancer, and autoimmune and inflammatory diseases.

Any disease that changes the shape and size of red blood cells decreases the ESR. Distorted cells, such as with **sickle cell disease**, do not stack, and consequently do not settle far, even in the presence of an ESR-associated disease. Diseases that cause the body to make less protein or extra red blood cells also decrease the ESR.

KEY TERMS

Acute phase reactant—A substance in the blood that increases as a response to an acute conditions such as infection, injury, tissue destruction, some cancers, burns, surgery, or trauma.

Erythrocyte sedimentation rate (ESR)—The distance that red blood cells settle in a tube of blood in one hour. It is an indication of inflammation.

Rouleaux—The stacking up of red blood cells, caused by extra or abnormal proteins in the blood that decrease the normal distance red cells maintain between each other.

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Erythromycins

Definition

Erythromycins are medicines that kill bacteria or prevent their growth.

Purpose

Erythromycins are **antibiotics**, medicines used to treat infections caused by microorganisms. Physicians

prescribe these drugs for many types of infections caused by bacteria, including **strep throat**, sinus infections, **pneumonia**, ear infections, **tonsillitis**, **bronchitis**, **gonorrhea**, **pelvic inflammatory disease** (PID), and urinary tract infections. Some medicines in this group are also used to treat **Legionnaires' disease** and ulcers caused by bacteria. These drugs will *not* work for colds, flu, and other infections caused by viruses.

Description

The drugs described here include erythromycins (Erythrocin, Ery-C, E-Mycin, and other brands) and medicines that are chemically related to erythromycins, such as azithromycin (Zithromax) and clarithromycin (Biaxin). They are available only with a physician's prescription and are sold in capsule, tablet (regular and chewable), liquid, and injectable forms.

Recommended dosage

The recommended dosage depends on the type of erythromycin, the strength of the medicine, and the medical problem for which it is being taken. Check with the physician who prescribed the drug or the pharmacist who filled the prescription for the correct dosage.

Always take erythromycins exactly as directed. Never take larger, smaller, more frequent, or less frequent doses. To make sure the infection clears up completely, it is very important to take the medicine for as long as it has been prescribed. Do not stop taking the drug just because symptoms begin to improve. This is important with all types of infections, but it is especially important in "strep" infections, which can lead to serious heart problems if they are not cleared up completely.

Erythromycins work best when they are at constant levels in the blood. To help keep levels constant, take the medicine in doses spaced evenly through the day and night. Do not miss any doses. Some of these medicines are most effective when taken with a full glass of water on an empty stomach, but they may be taken with food if stomach upset is a problem. Others work equally well when taken with or without food. Check package directions or ask the physician or pharmacist for instructions on how to take the medicine.

Precautions

Symptoms should begin to improve within a few days of beginning to take this medicine. If they do not, or if they get worse, check with the physician who prescribed the medicine.

Erythromycins may cause mild **diarrhea**, that usually goes away during treatment. However, severe diarrhea could be a sign of a very serious side effect. Anyone who develops severe diarrhea while taking erythromycin or related drugs should stop taking the medicine and call a physician immediately.

Special conditions

Taking erythromycins may cause problems for people with certain medical conditions or people who are taking certain other medicines. Before taking these drugs, be sure to let the physician know about any of these conditions:

ALLERGIES. Anyone who has had unusual reactions to erythromycins, azithromycin, or clarithromycin in the past should let his or her physician know before taking the drugs again. The physician should also be told about any **allergies** to foods, dyes, preservatives, or other substances.

PREGNANCY. Some medicines in this group may cause problems in pregnant women and have the potential to cause **birth defects**. Women who are pregnant or who may become pregnant should check with their physicians before taking these drugs.

BREASTFEEDING. Erythromycins pass into breast milk. Mothers who are breastfeeding and who need to take this medicine should check with their physicians.

OTHER MEDICAL CONDITIONS. Before using erythromycins, people with any of these medical problems should make sure their physicians are aware of their conditions:

- heart disease
- liver disease
- hearing loss

USE OF CERTAIN MEDICINES. Taking erythromycins with certain other drugs may affect the way the drugs work or may increase the chance of side effects.

Side effects

The most common side effects are mild diarrhea, nausea, vomiting, and stomach or abdominal cramps. These problems usually go away as the body adjusts to the drug and do not require medical treatment. Less common side effects, such as sore mouth or tongue and vaginal **itching** and discharge also may occur and do not need medical attention unless they persist or are bothersome.

More serious side effects are not common, but may occur. If any of the following side effects occur, check with a physician immediately:

- severe stomach **pain**, nausea, vomiting, or diarrhea

KEY TERMS

Bronchitis—Inflammation of the air passages of the lungs.

Gonorrhea—A sexually transmitted disease (STD) that causes infection in the genital organs and may cause disease in other parts of the body.

Inflammation—Pain, redness, swelling, and heat that usually develop in response to injury or illness.

Legionnaire's disease—A lung disease caused by a bacterium.

Microorganism—An organism that is too small to be seen with the naked eye.

Pelvic inflammatory disease (PID)—Inflammation of the female reproductive tract, caused by any of several microorganisms. Symptoms include severe abdominal pain, high fever, and vaginal discharge. Severe cases can result in sterility.

Pneumonia—A disease in which the lungs become inflamed. Pneumonia may be caused by bacteria, viruses, or other organisms, or by physical or chemical irritants.

Sinus—Any of several air-filled cavities in the bones of the skull.

Strep throat—A sore throat caused by infection with *Streptococcus* bacteria. Symptoms include sore throat, chills, fever, and swollen lymph nodes in the neck.

Tonsillitis—Inflammation of a tonsil, a small mass of tissue in the throat.

Urinary tract—The passage through which urine flows from the kidneys out of the body.

- **fever**
- skin rash, redness, or itching
- unusual tiredness or weakness

Although rare, very serious reactions to azithromycin (Zithromax) are possible, including extreme swelling of the lips, face, and neck, and **anaphylaxis** (a violent allergic reaction). Anyone who develops these symptoms after taking azithromycin should stop taking the medicine and get immediate medical help.

Other rare side effects may occur with erythromycins and related drugs. Anyone who has unusual symptoms after taking these medicines should get in touch with his or her physician.

Interactions

Erythromycins may interact with many other medicines. When this happens, the effects of one or both of the drugs may change or the risk of side effects may be greater. Anyone who takes erythromycins should let the physician know all other medicines he or she is taking. Among the drugs that may interact with erythromycins are:

- acetaminophen (Tylenol)
- medicine for overactive thyroid
- male hormones (androgens)
- female hormones (estrogens)
- other antibiotics
- blood thinners
- disulfiram (Antabuse), used to treat alcohol abuse
- antiseizure medicines such as valproic acid (Depakote, Depakene)
- caffeine
- the **antihistamines** astemizole (Hismanal)
- antiviral drugs such as (zidovudine) Retrovir

The list above does not include every drug that may interact with erythromycins. Be sure to check with a physician or pharmacist before combining erythromycins with any other prescription or nonprescription (over-the-counter) medicine.

Nancy Ross-Flanigan

Erythropoietin *see* **Cancer therapy, supportive; Immunologic therapies**

Erythropoietin test

Definition

Erythropoietin, also called EPO, is a type of protein called a glycoprotein that is formed mainly in the kidneys to stimulate the production of red blood cells.

KEY TERMS

Anemia—A condition in which the hemoglobin concentration in the blood is below normal.

Polycythemia vera—A condition characterized by an unusually large number of red blood cells in the blood due to increased production by the bone marrow. Symptoms include headaches, blurred vision, high blood pressure, dizziness, and night sweats.

Secondary polycythemia—Secondary polycythemia occurs when the excess of red blood cells is caused by a condition other than polycythemia vera. For example, when low levels of oxygen in the blood stimulate the bone marrow to produce more red blood cells, as in chronic lung disease.

Purpose

The erythropoietin (EPO) test is used to determine if hormonal secretion is causing changes in the red blood cells. The test has great value in evaluating low hemoglobin (anemia), and another disorder called polycythemia, in which unusually large numbers of red blood cells are found in the blood. The EPO test is also used to identify kidney tumors and to evaluate abuse by athletes who believe commercially prepared erythropoietin enhances performance.

Precautions

Not every laboratory is equipped to evaluate EPO, so the reference laboratory (a large commercial lab that does tests for hospitals not equipped to do them) performing the test may require as many as four days to complete the analysis. It should also be noted that EPO values increase in **pregnancy**, in which significantly higher levels are found before the twenty-fourth week.

Description

Erythropoietin is produced primarily in the kidneys but interacts with other factors in the bone marrow to increase red cell production. EPO is unique among the blood cell growth factors, because it is the only one that behaves like a hormone.

Erythropoietin acts as the principal regulator in the production of red blood cells (erythrocytes) by controlling the number, the kinds, and the survival of the cells. Because of this ability, it is being investigated for use in **cancer** patients to prevent anemia (hemoglobin concentration in the blood is lower than normal), or to treat anemia that has been induced by **chemotherapy** and **bone marrow transplantation** (BMT).

The correction of anemia can result in reduced **transfusion** requirements, so the erythropoietin test is used to diagnose anemia, including the anemia of end-stage renal disease. Erythropoietin determination is also valuable in diagnosing a condition known as polycythemia, when increased numbers of red blood cells occur. Levels of erythropoietin are extremely low in **polycythemia vera** but are normal or high in **secondary polycythemia**. It happens rarely, but cysts in the liver or kidneys, as well as tumors in the kidneys or brain, can also produce erythropoietin. Patients with these conditions can have high levels of erythropoietin and may develop secondary polycythemia.

Some athletes use EPO to enhance performance, as the increased red cell volume adds more oxygen-carrying capacity to the blood. Adverse reactions to this practice can include clotting abnormalities, **headache**, seizures, high blood pressure, nausea, vomiting, **diarrhea**, and rash.

Preparation

The EPO test requires a blood sample. The patient is to fast with nothing to eat or drink for at least eight hours before the test. It is also suggested that the patient lie down for 30 minutes before the test.

Risks

Risks for this test are minimal, but may include slight bleeding from the blood-drawing site, **fainting** or feeling lightheaded after venipuncture, and hematoma (blood accumulating under the puncture site).

Normal results

Reference values vary from laboratory to laboratory, but a general normal range is 11–48 mU/ml (milliunits per milliliter).

Abnormal results

Low levels of EPO are found in anemic patients with inadequate or absent production of erythropoietin. Severe kidney disease may decrease production of EPO, and congenital absence of EPO can occur.

Elevated levels of EPO can be found in some **anemias** when the body tries to overcompensate for reduced blood volume. Elevated levels are also seen in polycythemia, and erythropoietin-secreting tumors.

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ESB *see* **Electrical stimulation of the brain**

Escherichia coli

Definition

E. coli (Escherichia coli) is one of several types of bacteria that normally inhabit the intestine of humans and animals (commensal organism). Some strains of *E. coli* are capable of causing disease under certain conditions when the immune system is compromised or disease may result from an environmental exposure.

Description

E. coli bacteria may give rise to infections in **wounds**, the urinary tract, biliary tract, and abdominal cavity (**peritonitis**). This organism may cause septicemia, neonatal **meningitis**, infantile **gastroenteritis**, tourist **diarrhea**, and hemorrhagic diarrhea. An *E. coli* infection may also arise due to environmental exposure. Infections with this type of bacteria pose a serious threat to public health with outbreaks arising from food and water that has been contaminated with human or animal feces or sewage. This type of bacteria has been used as a biological indicator for safety of drinking water since the 1890s. Exposure may also occur during hospitalization, resulting in **pneumonia** in immunocompromised patients or those on a ventilator

Causes and symptoms

The symptoms of infection and resulting complications are dependent upon the strain of *E. coli* and the site of infection. These bacteria produce toxins that have a wide range of effects. Symptoms caused by some *E. coli* infections range from mild to severe, bloody diarrhea, acute abdominal **pain**, vomiting, and **fever**. Gastrointestinal complications that can cause *E. coli* infections include **irritable bowel syndrome** (IBS) ischemic colitis, **appendicitis**, perforation of the large bowel, and in some instances **gangrene** in the colon. Other known *E. coli*-causing infections may include chronic renal failure, **pancreatitis**, and **diabetes mellitus**. Some neurological symptoms such as drowsiness, seizure and **coma** may occur. In infants, *E. coli* infections are present in cases of infantile gastroenteritis and neonatal meningitis.

Strains of *E. coli* that produce diarrhea were initially distinguished by their O (somatic) antigens found on the bacterial surface. Although there is an overlap in characteristics between strains, they may be classified into four main groups; enterohemorrahagic (0157),enteropathogenic (055,0111), enterotoxigenic (06,078), and enteroinvasive (0124,0164).

E.coli O157 (VTEC)

The O157:H7 strain is the member of the group most often associated with a particularly severe form of diarrhea. (The O indicates the somatic antigen, while the H denotes the flagellar antigen, both of which are found on the cell surface of the bacteria.) The bacterium was discovered in 1977, and first reports of infections followed in 1982. *E. coli* O157:H7, as it is frequently referred to by researchers, causes bloody diarrhea in many infected patients. It accounts for about 2% of all cases of diarrhea in the western world, and at least one-third of cases of hemorrhagic colitis, or about 20,000 cases per year

E. coli O157:H7 is also the most common cause of unique syndromes, known as the **Hemolytic-Uremic Syndrome** (HUS) and thrombocytopenic purpura (TTP), which causes kidney failure, **hemolytic anemia**, and **thrombocytopenia**. Usually, infection with this strain of bacteria will subside without further complications. However, about 5% of people who are infected will develop HUS/TTP. This infection also accounts for the majority of episodes of HUS, especially in children.

This strain of bacteria produces a potent toxin called verotoxin, named for toxin's ability to kill green monkey kidney or "vero" cells. Bacteria that produce verotoxin are referred to as Verotoxin-producing *E. coli* (VTEC). The numbers of bacteria that are necessary to reproduce infectious levels of bacteria are quite small, estimated at 10-100 viable bacteria. These toxins are lethal for intestinal cells and those that line vessels (endothelial cells), inhibiting protein synthesis causing cell **death**. It is believed that the damage to blood vessels results in the formation of clots, which eventually leads to the Hemolytic-Uremic Syndrome. HUS/TTP is a serious, often fatal, syndrome that has other causes in addition to *E. coli* O157:H7; it is characterized by the breaking up of red blood cells (hemolysis) and kidney failure (uremia). The syndrome occurs most often in the very young and very old.

A magnified image of the *E. coli* bacterium. *(The Stock Market. Reproduced by permission.)*

E. coli O157:H7 is commonly found in cattle and poultry, and outbreaks have of disease have been associated with cattle and bovine products. There are reports of contamination from unpasteurized apple juice, hamburger meat, radish sprouts, lettuce, and potatoes, as well as other food sources. Environmental contamination may occur in water drained from cattle pastures or water containing human sewage used for drinking or swimming. Human to human transmission, through contact with fecal matter, has also been identified in daycare centers.

After an incubation period of three to four days on average, watery diarrhea begins, which rapidly progresses to bloody diarrhea in many victims, in which case the bowel movement may be mostly blood. Nausea, vomiting, and low-grade fever are also frequently present. Gastrointestinal symptoms last for about one week, and recovery is often spontaneous. Symptomatic infection may occur in about 10% of infected individuals. About 5-10% of individuals, usually at the extremes of age or elevated leukocyte count, develop HUS/TTP, and ultimately, kidney failure. Patients taking **antibiotics** or medications for gastric acidity may also be at risk. Neurological symptoms can also occur as part of HUS/TTP and consist of seizures, **paralysis**, and coma. **Rectal prolapse** may also be a complication, and in some cases colitis, appendicitis, perforation of the large bowel, and gangrene in the bowel. Systemically, the most prevalent complications of *E. coli* 157 infections are HUS and TTP.

E. coli non-O157 (VTEC)

These strains of *E. coli* produce verotoxin, but are strains other than O157. There have been as many as one hundred different types implicated in the development of disease. Strain OH111 was found to be involved in outbreaks in Australia, Japan, and Italy. The O128, O103, and O55 groups have also been implicated in diarrhea outbreaks. In Britain, cases of infantile gastroenteritis in maternity hospitals and neonatal units have been attributed to the *E. coli* non-0157 group. Many of these organisms have been identified in cattle.

Enterotoxigenic E. coli

Two toxins may be produced by this group, the heat-labile enterotoxin (LT) that can produce enteritis in infants, and a heat stable enterotoxin (ST), the action of which has yet to be determined.

Enteroinvasive E. coli

Some strains of the enteroinvasive *E. coli* have been involved in the development of gastroenteritis in infants. These organisms do not produce and enterotoxin. The cells of the intestine are affected, with the development of symptoms that are typical of a shigellae infection.

Diagnosis

Diagnosis of a specific type of infection is dependant upon the characteristics of the particular strain of the organism.

E. coli O157:H7 (HUS)

This particular strain of *E. coli* is suspected when bloody diarrhea, bloody stools, lack of fever, elevated leukocyte count, and abdominal tenderness are present. Stool cultures are used to tentatively identify the bacteria. Unfortunately, cultures are often negative or inconclusive if done after 48 hours of symptoms. Further tests are usually needed, however, for confirmation of infection. This may include a full **blood count**, blood film, and tests to determine urea, electrolyte, and LDH (lactate dehydrogenase) levels. Damaged red blood cells, and elevated levels of creatinine, urea, and LDH with a drop in **platelet count** may indicate that HUS will develop. Immunomagnetic separation is now being used for diagnosis as well.

E. coli non-O157 (VTEC)

Diagnosis is often difficult for these types of bacteria, but production of enterohemolysin (Ehly) is used as an indicator. Other diagnostic tests are used to detect verotoxins, including ELISA (enzyme-linked immunosorbent assays), colony immunoblotting, and DNA-based tests.

E. coli 0157 STEC

Methods for detection of this type of bacteria are under development, including culture growth media

selective for this organism. Immunomagnetic separation and specific ELISA, latex agglutination tests, colony immunoblot assays, and other immunological-based detection methods are being explored.

Treatment

Uncomplicated cases of the *E. coli* O157:H7 the infection clear up within ten days. It is not certain that antibiotics are helpful in treating *E. coli* O157:H7 and there is some evidence that they may be harmful. **Dehydration** resulting from diarrhea must be treated with either Oral Rehydration Solution (ORS) or intravenous fluids. Anti-motility agents that decrease the intestines' ability to contract, should not be used in any patient with bloody diarrhea. Treatment of HUS, if it develops, involves correction of clotting factors, plasma exchange, and **kidney dialysis**. Blood transfusions may be required. Treatment methods for other *E. coli* infections are similar. Antibiotics are often used in the treatment of *E. coli* infections, but their role is controversial. Some antibiotics may enhance the development of HUS/TTP depending upon their action, as well as the use of anti diarrhea medications that should be avoided. Phosphoenolpyruvate analogues may be helpful. Gentamicin, ampicillin, ceftazidime, or beta-lactamase-stable cephalosporin may be administered for neonatal meningitis. Antibiotic therapy is further complicated by the presence of antibiotic resistant organisms.

Alternative treatment

Studies have been conducted to determine if diarrhea symptoms can be reduced by alternative therapies such as the consumption of herbal teas, psyllium, and **acupuncture**. Patients should consult their doctors before using any alternative treatments, as *E. coli* can be life threatening and should be closely monitored.

Prognosis

In most cases of O157:H7, symptoms last for about a week and recovery is often spontaneous. Ten percent of individuals with *E. coli* O157:H7 infection develop HUS; 5% of those will die of the disease. Some who recover from HUS will be left with some degree of kidney damage and possibly irritable bowel syndrome. Additionally, there is a possibility of chronic *E. coli* infection.

Infants that develop *E. coli* infections may be permanently affected. Gastroenteritis may leave the child with **lactose intolerance**. Neonates developing meningitis from *E. coli* strains have a high morbidity and mortality rate

Prevention

Thorough cooking of all meat and poultry products and adhering to proper food preparation is the most effective way to avoid infection. More studies are needed to determine the appropriate safety margins for killing these bacteria. Food irradiation methods are also being developed to sanitize food. Vaccinations to *E. coli* 0157 are under development, as are medications aimed at limiting the effects of the verotoxin. The enforcement of regulations for meat production and water are critical. Steam pasteurization is used in the United States and is being explored in other countries.

Prevention of *E. coli* gastroenteritis in infants is best achieved by breast-feeding. The breast milk contains antibodies that combat the infection. For bottle-fed infants, care should be taken in the preparation of the milk and bottles. Good hygiene of the umbilical cord area is important. Keeping this area clean and dry may reduce infection.

KEY TERMS

Antigen—A substance, usually a protein, that causes the formation of an antibody and reacts specifically with that antibody.

Anti-motility medications—Medications such as loperamide (Imodium), dephenoxylate (Lomotil), or medications containing Codeine or narcotics which decrease the ability of the intestine to contract. This can worsen the condition of a patient with dysentery or colitis.

Colitis—Inflammation of the colon or large intestine, usually causing diarrhea which may be bloody.

Food irradiation methods—A process using radiant energy to kill microogranisms in food, to extend the amount of time in that food can be sold and eaten safely.

Oral Rehydration Solution (ORS)—A liquid preparation developed by the World Health Organization that can decrease fluid loss in persons with diarrhea. Originally developed to be prepared with materials available in the home, commercial preparations have recently come into use.

Urea—Chemical formed during the body's metabolism of nitrogen and normally excreted by the kidney. Urea levels rise in the blood when kidney failure occurs.

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Esophageal acidity test *see* **Esophageal function tests**

Esophageal aperistalsis *see* **Achalasia**

Esophageal atresia

Definition

Esophageal atresia is a serious birth defect in which the esophagus, the long tube that connects the mouth to the stomach, is segmented and closed off at any point. This condition usually occurs with **tracheoesophageal fistula**, a condition in which the esophagus is improperly attached to the trachea, the nearby tube that connects the nasal area to the lungs. Esophageal atresia occurs in approximately 1 in 4,000 live births.

Description

Failure of an unborn child (fetus) to develop properly results in **birth defects**. Many of these defects involve organs that do not function, or function only incidentally, before birth, and, as a result, go undetected until the baby is born. In this case, the digestive tract is unnecessary for fetal growth, since all **nutrition** comes from the mother through the placenta and umbilical cord.

During fetal development, the esophagus and the trachea arise from the same original tissue. Normally, the two tubes would form separately (differentiate); however, in cases of esphageal atresia and tracheoesophageal fistulas, they do not, resulting in various malformed configurations. The most common configuration is the "C" type, in which the upper part of the esophagus abruptly ends in a blind pouch, while the lower part attaches itself to the trachea. This configuration occurs in 85–90% of cases. Esophageal atresia without involvement of the trachea occurs in only 8% of cases.

Causes and symptoms

The cause of esophageal atresia, like that of most birth defects, is unknown.

An infant born with this defect will at first appear all right, swallowing normally. However, the blind pouch will begin to fill with mucus and saliva that would normally pass through the esophagus to the stomach. These secretions back up into the mouth and nasal area, causing the baby to drool excessively. When fed, the baby will also immediately regurgitate what he or she has eaten. **Choking** and coughing may also occur as the baby breaths in the fluid backing up from the esophagus. Aspiration **pneumonia**, an infection of the respiratory system caused by inhalation of the contents of the digestive tract, may also develop.

Diagnosis

Physicians who suspect esophageal atresia after being presented with the above symptoms diagnose the condition using x-ray imaging or by passing a catheter through the nose and into the esophagus. Esophageal atresia is indicated if the catheter hits an obstruction 4–5 in (10–13 cm) from the nostrils.

KEY TERMS

Fetal—Refers to the fetus, also known in the first two months after conception as an embryo.

Fistula—Unnatural connection between two hollow organs or one organ and the outside.

Treatment

Infants with esophageal atresia are unlikely to survive without surgery to reconnect the esophagus. The procedure is done as soon as possible; however, **prematurity**, the presence of other birth defects, or complications of apiration pneumonia may delay surgery. Once diagnosed, the baby will be fed intraveneously until he or she has recovered sufficiently from the operation. Mucus and saliva will also be continuously removed via a catheter until recovery has occured. When surgery is performed, the esophagus is reconnected and, if neccessary, separated from the trachea. If the two ends of the esophagus are too far apart to be reattached, tissue from the large intestine is used to join them.

Prognosis

Surgery to correct esophageal atresia is usually successful. Post-operative complications may include difficulty swallowing, since the esophagus may not contract efficiently, and gastrointestinal reflux, in which the acidic contents of stomach back up into the lower part of the esophagus, possibly causing ulcers.

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J. Ricker Polsdorfer, MD

Esophageal cancer

Definition

Esophageal **cancer** is a malignancy that develops in tissues of the hollow, muscular canal (esophagus) along which food and liquid travel from the throat to the stomach.

Description

Esophageal cancer usually originates in the inner layers of the lining of the esophagus and grows outward. In time, the tumor can obstruct the passage of food and liquid, making swallowing painful and difficult. Since most patients are not diagnosed until the late stages of the disease, esophageal cancer is associated with poor quality of life and low survival rates.

Squamous cell carcinoma is the most common type of esophageal cancer, accounting for 95% of all esophageal cancers worldwide. The esophagus is normally lined with thin, flat squamous cells that resemble tiny roof **shingles**. Squamous cell carcinoma can develop at any point along the esophagus but is most common in the middle portion.

Adenocarcinoma has surpassed squamous cell carcinoma as the most common type of esophageal cancer in the United States. Adenocarcinoma originates in glandular tissue not normally present in the lining of the esophagus. Before adenocarcinoma can develop, glandular cells must replace a section of squamous cells. This occurs in Barrett's esophagus, a precancerous condition in which chronic acid reflux from the stomach stimulates a transformation in cell type in the lower portion of the esophagus.

A very small fraction of esophageal cancers are melanomas, **sarcomas**, or lymphomas.

There is great variability in the incidence of esophageal cancer with regard to geography, ethnicity, and gender. The overall incidence is increasing. About 13,000 new cases of esophageal cancer are diagnosed in the United States each year. During the same 12-month period, 12,000 people die of this disease. It strikes between five and ten North Americans per 100,000. In some areas of China the cancer is endemic.

Squamous cell carcinoma usually occurs in the sixth or seventh decade of life, with a greater incidence in African-Americans than in others. Adenocarcinoma develops earlier and is much more common in white patients. In general, esophageal cancer occurs more frequently in men than in women.

Causes and symptoms

The exact cause of esophageal cancer is unknown, although many investigators believe that chronic irritation of the esophagus is a major culprit. Most of the identified risk factors represent a form of chronic irritation.

However, the wide variance in the distribution of esophageal cancer among different demographic groups raises the possibility that genetic factors also play a role.

Several risk factors are associated with esophageal cancer.

- Tobacco and alcohol consumption are the major risk factors, especially for squamous cell carcinoma. **Smoking** and alcohol abuse each increase the risk of squamous cell carcinoma by five-fold. The effects of the two are synergistic, in that the combination of smoking and alchohol increases the risk by 25- to 100- fold. It is estimated that drinking about 13 ounces of alcohol every day for an extended period of time raises the risk of developing esophageal cancer by 18%. That likelihood increases to 44% in individuals who also smoke one or two packs of cigarettes a day. Smokeless tobacco also increases the risk for esophageal cancer.

- Gastroesophageal reflux is a condition in which acid from the stomach refluxes backwards into the lower portion of the esophagus, sometimes causing symptoms of **heartburn**. In some cases of gastroesophageal reflux, the chronic exposure to acid causes the inner lining of the lower esophagus to change from squamous cells to glandular cells. This is called Barrett's esophagus. Patients with Barrett's esophagus are roughly 30 to 40 times more likely than the general population to develop adenocarcinoma of the esophagus.

- A diet low in fruits, vegetables, zinc, riboflavin, and other **vitamins** can increase risk of developing to esophageal cancer.

- Caustic injury to the esophagus inflicted by swallowing lye or other substances that damage esophageal cells can lead to the development of squamous cell esophageal cancer in later life.

- Achalasia is a condition in which the lower esophageal sphincter (muscle) cannot relax enough to let food pass into the stomach. Squamous cell esophageal cancer develops in about 6% of patients with achalasia.

- Tylosis is a rare inherited disease characterized by excess skin on the palms and soles. Affected patients have a much higher probability of developing esophageal cancer than the general population. They should have regular screenings to detect the disease in its early, most curable stages.

- Esophageal webs, which are protrusions of tissue into the esophagus, and diverticula, which are outpouchings of the wall of the esophagus, are associated with a higher incidence of esophageal cancer.

Symptoms

Unfortunately, symptoms generally don't appear until the tumor has grown so large that the patient cannot be cured. Dysphagia (trouble swallowing or a sensation of having food stuck in the throat or chest) is the most common symptom. Swallowing problems may occur occasionally at first, and patients often react by eating more slowly and chewing their food more carefully and, as the tumor grows, switching to soft foods or a liquid diet. Without treatment, the tumor will eventually prevent even liquid from passing into the stomach. A sensation of burning or slight mid-chest pressure is a rare, often-disregarded symptom of esophageal cancer. Painful swallowing is usually a symptom of a large tumor obstructing the opening of the esophagus. It can lead to regurgitation of food, weight loss, physical wasting, and **malnutrition**. Anyone who has trouble swallowing, loses a significant amount of weight without dieting, or cannot eat solid food because it is too painful to swallow should see a doctor.

Diagnosis

A barium swallow is usually the first test performed on a patient whose symptoms suggest esophageal cancer. After the patient swallows a small amount of barium, a series of x rays can highlight any bumps or flat raised areas on the normally smooth surface of the esophageal wall. It can also detect large, irregular areas that narrow the esophagus in patients with advanced cancer, but it cannot provide information about disease that has spread beyond the esophagus. A double contrast study is a barium swallow with air blown into the esophagus to improve the way the barium coats the esophageal lining. Endoscopy is a diagnostic procedure in which a thin lighted tube (endoscope) is passed through the mouth, down the throat, and into the esophagus. Cells that appear abnormal are removed for biopsy. Once a diagnosis of esophageal cancer has been confirmed through biopsy, staging tests are performed to determine whether the disease has spread (metastasized) to tissues or organs near the original tumor or in other parts of the body. These tests may include computed tomography, endoscopic ultrasound, **thoracoscopy**, **laparoscopy**, and **positron emission tomography**.

Treatment

Treatment for esophageal cancer is determined by the stage of the disease and the patient's general health. The most important distinction to make is whether the cancer is curable. If the cancer is in the early stages, cure may be possible. If the cancer is advanced or if the patient will not tolerate major surgery, treatment is usually directed at palliation (relief of symptoms only) instead of cure.

Staging

Stage 0 is the earliest stage of the disease. Cancer cells are confined to the innermost lining of the esophagus. Stage I esophageal cancer has spread slightly deeper, but still has not extended to nearby tissues, lymph nodes, or other organs. In Stage IIA, cancer has invaded the thick, muscular layer of the esophagus that propels food into the stomach and may involve connective tissue covering the outside of the esophagus. In Stage IIB, cancer has spread to lymph nodes near the esophagus and may have invaded deeper layers of esophageal tissue. Stage III esophageal cancer has spread to tissues or lymph nodes near the esophagus or to the trachea (windpipe) or other organs near the esophagus. Stage IV cancer has spread to distant organs like the liver, bones, and brain. Recurrent esophageal cancer is disease that develops in the esophagus or another part of the body after initial treatment.

Surgery

The most common operations for the treatment of esophageal cancer are esophagectomy and esophagogastrectomy. Esophagectomy is the removal of the cancerous part of the esophagus and nearby lymph nodes. This procedure is performed only on patients with very early cancer that has not spread to the stomach. Esophagogastrectomy is the removal of the cancerous part of the esophagus, nearby lymph nodes, and the upper part of the stomach. The resected esophagus is replaced with the stomach or parts of intestine so the patient can swallow. These procedures can significantly relieve symptoms and improve the nutritional status of more than 80% of patients with dysphagia. Although surgery can cure some patients whose disease has not spread beyond the esophagus, but more than 75% of esophageal cancers have spread to other organs before being diagnosed. Less extensive surgical procedures can be used for palliation.

Chemotherapy

Oral or intravenous **chemotherapy** alone will not cure esophageal cancer, but pre-operative treatments can shrink tumors and increase the probability that cancer can be surgically eradicated. Palliative chemotherapy can relieve symptoms of advanced cancer but will not alter the outcome of the disease.

Radiation

External beam or internal radiation, delivered by machine or implanted near cancer cells inside the body, is only rarely used as the primary form of treatment. Post-operative radiation is sometimes used to kill cancer cells that couldn't be surgically removed. Palliative radiation is effective in relieving dysphagia in patients who cannot be cured. However, radiation is most useful when combined with chemotherapy as either the definitive treatment or preoperative treatment.

A close-up view of a cancerous esophageal tumor. *(Custom Medical Stock Photo. Reproduced by permission.)*

Palliation

In addition to surgery, chemotherapy, and radiation, other palliative measures can provide symptomatic relief. Dilatation of the narrowed portion of the esophagus with soft tubes can provide short-term relief of dysphagia. Placement of a flexible, self-expanding stent within the narrowed portion is also useful in allowing more food intake.

Follow-up treatments

Regular barium swallows and other imaging studies are necessary to detect recurrence or spread of disease or new tumor development.

Alternative treatment

Photodynamic therapy (PDT) involves intravenously injecting a drug that is absorbed by cancer cells and kills them after they are exposed to specific laser beams. PDT can be used for palliation, but it also cured some early esophageal cancers during preliminary studies. Researchers are comparing its benefits with those of more established therapies.

Endoscopic laser therapy involves delivering short, powerful laser treatments to the tumor through an endoscope. It can improve dysphagia, but multiple treatments are required, and the benefit is seldom long-lasting.

Prognosis

Since most patients are diagnosed when the cancer has spread to lymph nodes or other structures, the prog-

KEY TERMS

Computed tomography—A radiology test by which images of cross-sectional planes of the body are obtained.

Endoscopic ultrasound—A radiology test utilizing high frequency sound waves, conducted via an endoscope.

Laparoscopy—Examination of the contents of the abdomen through a thin, lighted tube passed through a small incision.

Positron emission tomography—A radiology test by which images of cross-sectional planes of the body are obtained, utilizing the properties of the positron. The positron is a subatomic particle of equal mass to the electron, but of opposite charge.

Synergistic—The combined action of two or more processes is greater than the sum of each acting separately.

Thoracoscopy—Examination of the contents of the chest through a thin, lighted tube passed through a small incision.

nosis for esophageal cancer is poor. Generally, no more than half of all patients are candidates for curative treatment. Even if cure is attempted, the cancer can recur.

Prevention

There is no known way to prevent esophageal cancer.

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Esophageal diverticula *see* **Esophageal pouches**

Esophageal function tests

Definition

The esophagus is the swallowing tube through which food passes on its way from the mouth to the stomach. The main function of this organ is to propel food down into the stomach. There is also a mechanism to prevent food from coming back up or "refluxing" from the stomach into the esophagus. Esophageal function tests are used to determine if these processes are normal or abnormal.

Purpose

The esophagus is a long, muscular tube that also has two muscles (or sphincters) at the top and bottom. All of these muscular areas must contract in an exact sequence for swallowing to proceed normally. There are three main symptoms that occur when esophageal function is abnormal: difficulty with swallowing (dysphagia), **heartburn**, and chest **pain**.

Doctors perform a variety of tests to evaluate these symptoms. Endoscopy, which is not a test of esophageal function, is often used to determine if the lining of the esophagus has any ulcers, tumors, or areas of narrowing (strictures). Many times, however, endoscopy only shows the doctor if there is injury to the esophageal lining, and the procedure gives no information about the cause of the problem.

Therefore, in addition to endoscopy, several studies are available that measure esophageal function. There are three basic types of tests used to assess esophageal function:

- Manometry is used to study the way the muscles of the esophagus contract, and is most useful for the investigation of difficulty with swallowing.
- Esophageal pH monitoring measures changes in esophageal acidity, and is valuable for evaluating patients with heartburn or gastroesophageal reflux disease (GERD).
- X-ray studies investigate swallowing difficulties. They either follow the progress of barium during swallowing using a fluoroscope, or they use radioactive scanning techniques.

Precautions

Pregnant patients undergoing x-ray exams should carefully review the risks and benefits with their doctors. Most x-ray exams of the gastrointestinal tract do not involve radiation levels that are harmful to the unborn baby.

Description

Manometry

This study is designed to measure the pressure changes produced by contraction of the muscular portions of the esophagus. An abnormality in the function of any one of the segments of the swallowing tube causes difficulty in swallowing. Doctors call this symptom dysphagia. This exam is most useful in evaluating those patients whose endoscopy is negative.

During manometry, the patient swallows a thin tube carrying a device that senses changes in pressures in the esophagus. Readings are taken at rest and during swallowing. Medications are sometimes given during the study to help in the diagnosis. The results are then transmitted to recording equipment. Manometry can best identify diseases that produce disturbances of motility or contractions of the esophagus.

Esophageal pH monitoring

This procedure involves measuring the esophagus' exposure to acid that has "refluxed" from the stomach. The test is ideal for evaluating recurring heartburn or GERD. Too much acid produces not only heartburn, but also ulcers that can bleed or produce areas of narrowing (strictures) when they heal.

Normally, acid refluxes into the esophagus in only small amounts for short periods of time. A muscle called the lower esophageal sphincter prevents excessive reflux. Spontaneous contractions that increase esophageal emptying and production of saliva are other important protective mechanisms.

"pH" is the scientific term that tells just how acidic or alkaline a substance is. Researchers have shown that in the esophagus, the presence of acid is damaging only if it persists for prolonged periods. Therefore, the test has been designed to monitor the level of acidity over 24 hours, usually in the home. In this way, patients maintain their daily routine, documenting their symptoms, and at what point in their activities they occurred. During this period, a thin tube with a pH monitor remains in the esophagus to record changes. After the study, a computer is used to compare changes in acidity with symptoms reported by the patient.

Surgery is an effective and long-lasting treatment for symptoms of recurrent reflux and is the choice of many patients and doctors. pH monitoring is usually performed before surgery to confirm the diagnosis and to judge the effects of drug therapy.

X-ray tests

These fall into two categories: (1) those done with the use of barium and a fluoroscope; and (2) those performed with radioactive materials.

Studies performed with fluoroscopy are of greatest value in identifying a structural abnormality of the esophagus. Although this is not truly an esophageal function test, it does allow doctors to consider other diagnostic possibilities. Often a sandwich or marshmallow coated with barium is used to identify the site of an obstruction.

During fluoroscopy, the radiologist can observe the passage of material through the esophagus in real time, and video recordings can also be done. This is particularly useful when the swallowing symptoms appear to involve mainly the upper region of the esophagus. The most common cause of swallowing difficulties is a previous **stroke**, although other diseases of the neuromuscular system (like **myasthenia gravis**) can produce the same symptoms.

Scans using low-dose radioactive materials are useful because they are able not only to demonstrate that food passes through the esophagus more slowly than normal, but also how slow. These studies involve swallowing food coated with material that is followed by a nuclear medicine scanner. Scans are best used when other methods have failed to make a diagnosis, or if it is necessary to determine the degree of the abnormality. As of 1997, scans mainly served as research tools.

Preparation

Patients should not eat or drink for several hours before the exam. Many medications affect the esophagus; doses sometimes need to be adjusted or even stopped for a while. Patients must inform doctors of all medications taken, including over-the-counter medications (purchased without a doctor's prescription), and any known **allergies**.

Aftercare

For most of these studies, no special care is needed after the procedure. Patients can often go about normal daily activities following any of these tests. One exception is for those who undergo an x-ray exam with the use of barium. This can have a constipating effect and patients should ask about using a mild laxative later on.

Risks

Exposure of a fetus to x rays, especially in the first three months, is a potential risk.

Other studies of esophageal function are essentially free of any significant risk. The tubes passed during these procedures are small, and most patients adjust to them quite well. However, since medications cannot be used to relax patients, some may not tolerate the exam.

Abnormal results

Manometry is used to diagnose abnormalities related to contraction or relaxation of the various muscular regions of the esophagus. These studies cannot distinguish whether injury to either the muscle or nerves of the esophagus is producing the abnormal results. Only the final effect on esophageal muscle is identified. Results should be interpreted in light of the patient's entire medical history.

For example, there are many diseases that cause poor relaxation of the lower esophageal sphincter. When no cause is found, the disease is called **achalasia**.

Abnormal results of pH tests can confirm symptoms of heartburn or indicate a cause of chest pain (or rarely, swallowing difficulties). Doctors may want to start or change medications based on these results, or even repeat the test using different doses of medication. As noted above, these studies are indicated before surgical treatment of GERD.

X-ray tests can only serve to document an abnormality, and they are far from perfect. If they are negative, then other studies are often needed.

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David Kaminstein, MD

Esophageal laceration *see* **Mallory-Weiss syndrome**

Esophageal manometry *see* **Esophageal function tests**

Esophageal pouches

Definition

Esophageal pouches, also known as esophageal diverticula, are pocket-like structures formed when the interior space of the esophagus, the tube that connects the mouth to the stomach, protrudes into the walls that surround it.

Description

The esophagus is a muscular tube that propels food into the stomach. A defect in the wall of the esophagus may allow the lining to herniate, creating a space where food can be caught. Pouches can appear anywhere between the throat and the stomach. They occur primarily in men and usually later in life.

Different names for the condition apply to different locations along the esophagus:

- Zenker's diverticula are pharyngeal pouches, or ones that occur in the upper neck area at the top of the esophagus.
- **Traction** diverticula are a type of mid-esophageal pouch.
- Epiphrenic diverticula occur at the bottom of the esophagus near where it enters the stomach.

Causes and symptoms

To propel food into the stomach (or out of it during vomiting) the esophagus generates internal pressure just like the bowel. Under certain circumstances, that pressure can herniate the esophageal lining through a weakness in the wall, creating a pouch (a balloon squeezed in the hand will herniate through the fingers in the same way). Pouches are more common in people who have motility disorders of the esophagus, swallowing that is not well coordinated and may be spastic. A traction diverticulum can develop from a scar that pulls the esophagus out of shape. Food and saliva can collect in all of these pouches.

Pouches in the neck usually cause **bad breath** (halitosis) and the regurgitation of swallowed food and saliva. Some patients with Zenker's diverticula can push on their neck and make old food appear in their mouths. Pouches near the stomach may cause swallowing problems, conditions known as *achalasia* or *dysphagia*. Mid-esophageal pouches usually cause no symptoms.

In the most serious cases, a person may be unable to swallow because the esophagus is obstructed, or the esphagus may rupture, spilling its contents into the chest or neck.

A split x-ray image of the upper chest, neck, and esophagus (left), and chest and esophagus (right). *(Custom Medical Stock Photo. Reproduced by permission.)*

Diagnosis

Difficulty swallowing, bad breath, or food reappearing in the back of the mouth are among the signs physicians look for when diagnosing this condition. Sometimes the patient may also experience **pain** in the chest resembling a **heart attack**. A series of x rays taken while swallowing a contrast agent usually demonstrates the diverticulum clearly. An esophagoscopy may also be needed to gather more detail. Manometry, measuring pressures inside the esophagus using a balloon that is passed down it, may help determine the cause of the diverticula.

Treatment

Treatment for this condition is primarily aimed at alleviating symptoms. Physicians direct the patient to eat a bland diet, to chew his or her food thoroughly, and to drink water after eating to clean out the pouches. If the condition is severe, several types of surgery are available to remove the pouches and repair the defects. If a pouch is due to a stenosis (narrowing) in the esophagus it may be possible to relieve it by passing a dilator through it, a process called bougeinage.

KEY TERMS

Achalasia—Failure of the lower end of the esophagus (or another tubular valve) to open, resulting in obstruction, either partial or complete.

Contrast agent—A substance that produces shadows on an x ray so that hollow structures can be more easily seen.

Dysphagia—Difficult swallowing.

Esophagoscopy—Looking down the esophagus with a flexible viewing instrument.

Herniate—To protrude beyond usual limits.

Manometry—Pressure measurement.

Prognosis

The two complications that can render these nuisances dangerous, obstruction and rupture, are emergencies. Both require immediate medical attention. Other

than that, diverticula will usually grow slowly over the years, gradually increasing the symptoms they cause.

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Esophageal ulcers *see* **Ulcers (digestive)**

Esophagogastroduodenoscopy

Definition

An endoscope as used in the field of gastroenterology (the medical study of the stomach and intestines) is a thin, flexible tube that uses a lens or miniature camera to view various areas of the gastrointestinal tract. When the procedure is limited to the examination of the inside of the gastrointestinal tract's upper portion, it is called upper endoscopy or esphagogastroduodenoscopy (EGD). With the endoscope, the esophagus (swallowing tube), stomach, and duodenum (first portion of the small intestine) can be easily examined, and abnormalities frequently treated. Patients are usually sedated during the exam.

Purpose

EGD is performed to evaluate or treat symptoms relating to the upper gastrointestinal tract, such as:

- upper abdominal or chest **pain**
- nausea or vomiting
- difficulty swallowing (dysphagia)
- bleeding from the upper intestinal tract
- anemia (low **blood count**). EGD can be used to treat certain conditions, such as an area of narrowing or bleeding in the upper gastrointestinal tract

Upper endoscopy is more accurate than x rays for detecting inflammation, ulcers, or tumors. It is used to diagnose early **cancer** and can frequently determine whether a growth is benign (not cancerous) or malignant (cancerous).

KEY TERMS

Pathologist—A doctor who specializes in the anatomic (structural) and chemical changes that occur with diseases. These doctors function in the laboratory, examining biopsy specimens, and regulating studies performed by the hospital laboratories (blood tests, urine tests, etc). Pathologists also perform autopsies.

Biopsies (small tissue samples) of inflamed or "suspicious" areas can be obtained and examined by a pathologist. Cell scrapings can also be taken by the introduction of a small brush; this helps in the diagnosis of cancer or infections.

When treating conditions in the upper gastrointestinal tract, small instruments are passed through the endoscope that can stretch narrowed areas (strictures), or remove swallowed objects (such as coins or pins). In addition, bleeding from ulcers or vessels can be treated by a number of endoscopic techniques.

Recent studies have shown the usefulness of endoscopic removal of early tumors of the esophagus or stomach. This is done either with injection of certain materials (like alcohol), or with the use of instruments (like lasers) that burn the tumor. Other techniques combining medications and lasers also show promise.

Precautions

Patients should inquire as to the doctor's expertise with these procedures, especially when therapy is the main goal. The doctor should be informed of any **allergies**, medication use, and medical problems.

Description

First, a "topical" (local) medication to numb the gag reflex is given either by spray or is gargled. Patients are usually sedated for the procedure (though not always) by injection of medications into a vein. The endoscopist then has the patient swallow the scope, which is passed through the upper gastrointestinal tract. The lens or camera at the end of the instrument allows the endoscopist to examine each portion of the upper gastrointestinal tract; photos can be taken for reference. Air is pumped in through the instrument to allow proper observation. Biopsies and other procedures can be performed without any significant discomfort.

Esophagogastroduodenoscopy (EGD) is performed to evaluate or treat symptoms relating to the upper gastrointestinal tract. By inserting an endoscope into the mouth and guiding it through the gastrointestinal tract, the esophagus, stomach, and duodenum can be examined and abnormalities treated. *(Illustration by Electronic Illustrators Group.)*

Preparation

The upper intestinal tract must be empty for the procedure, so it is necessary NOT to eat or drink for at least 6–12 hours before the exam. Patients need to inquire about taking their medications before the procedure.

Aftercare

Someone should be available to take the person home after the procedure and stay with them for a while; patients will not be able to drive themselves due to **sedation**. Pain or any other unusual symptoms should be reported immediately.

It is important to recognize early signs of any possible complication. The doctor should be notified if the patient has **fever**, trouble swallowing, or increasing throat, chest, or abdominal pain.

Risks

EGD is safe and well tolerated; however, complications can occur as with any procedure. These are most often due to medications used during the procedure, or are related to endoscopic therapy. The overall complication rate of EGD is less than 2%, and many of these complications are minor (such as inflammation of the vein through which medication is given). However, serious ones can and do occur, and almost half of them are related to the heart or lungs. Bleeding or perforations (holes in the gastrointestinal tract) are also reported, especially when tumors or narrowed areas are treated or biopsied. Infections have also been rarely transmitted; improved cleaning techniques should be able to prevent them.

Resources

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Essential tremor *see* **Tremors**

Estradiol *see* **Hormone replacement therapy**

Estrogen *see* **Hormone replacement therapy**

Estrogen fractions test *see* **Sex hormones tests**

Estrogen replacement therapy *see* **Hormone replacement therapy**

Ethambutol *see* **Antituberculosis drugs**

Etodolac *see* **Nonsteroidal anti-inflammatory drugs**

Evoked potential studies

Definition

Evoked potential studies are a group of tests of the nervous system that measure electrical signals along the nerve pathways.

Purpose

Nerves convey information to the body by sending electrical signals down the length of the nerve. These signals can be recorded by wires placed over the nerves on the surface of the skin, in a procedure called an evoked potential (EP) study. The person conducting the test evokes the patient's neural activity by visual or auditory stimulation or using a mild electrical shock. This causes changes in the electrical potential in the nerves. Analysis of the signals can provide information about the condition of nerve pathways, especially those in the brain and spinal cord. They can indicate the presence of disease or degeneration, and can help determine the location of nerve lesions.

There are three major types of EP studies used regularly:

- Visual evoked potentials are used to diagnose visual losses due to optic nerve damage, especially from **multiple sclerosis**. They are also useful to diagnose "hysterical blindness," in which loss of vision is not due to any nerve damage.
- Auditory evoked potentials are used to diagnose hearing losses. They can distinguish damage to the acoustic nerve (which carries signals from the ear to the brain stem) from damage to the auditory pathways within the brainstem. Most auditory EPs record activity from the brainstem, and are therefore called "brainstem auditory evoked potentials." Disorders diagnosed with auditory EPs include **acoustic neuroma** (tumors of the inner ear) and multiple sclerosis (chronic disease in which nerves lose patches of their outer covering). They may also be used to assess high frequency hearing ability, to determine brain **death**, and to monitor brainstem function during surgery
- Somatosensory evoked potentials record transmission of nerve impulses from the limbs to the brain, and can be used to diagnose nerve damage or degeneration within the spinal cord or nerve roots from multiple sclerosis, trauma, or other degenerative disease. Somatosensory EPs can be used to distinguish central versus peripheral nerve disease, when combined with results from a nerve conduction velocity test, which measures nerve function in the extremities.

Precautions

Evoked potential studies are painless, noninvasive, and without any significant risk. Somatosensory EP tests involve very mild electric shocks, usually felt as a tingling.

Description

The person performing the test locates and marks specific spots on the patient's head for placement of electrodes. These spots are cleaned, and an adhesive conducting paste is applied. Cup electrodes are attached. For somatosensory EP, spots on the arm or leg are also marked and cleaned; electrodes may be taped in place. The patient sits or reclines in a chair throughout the tests.

For a visual EP, the patient focuses on a TV screen which displays a checkerboard pattern. The eye not being tested is covered with a patch. For children or others whose attention may wander, goggles are used which show the pattern to one eye at a time. Each eye is usually tested twice, and the entire procedure takes approximately 30–45 minutes.

For auditory EP, headphones are used to deliver a series of clicks to one ear at a time. A masking or static sound is played into the other ear. Each ear is usually tested twice, and the entire procedure takes approximately 30–45 minutes.

For somatosensory EP, mild electrical shocks are delivered to the arm or leg. This may cause some twitching and tingling. The stimulus lasts for about two minutes at a time, and the entire procedure takes approximately 30 minutes.

KEY TERMS

Nerve conduction velocity test—A test of the speed of conduction of nerves, performed on the nerves in the arm and leg.

After the tests, the electrodes are removed with acetone and the scalp is cleaned.

Preparation

Hair must be clean, dry, and free of any braids, pins, or jewelry. The patient should shampoo before the test, and must not use any hair spray, gel, or other hair care products after shampooing. Clothing should be loose and comfortable. The patient may eat and take some medications as usual before the test, although sedative medications should be avoided on the day of the test, if possible. It is best to check with the physician supervising the test for specific instructions.

Aftercare

This test is painless and has no residual effects. The patient may return to work or other activities immediately afterward.

Normal results

EP test results are displayed as jagged electrical tracings (wave forms), which have characteristic shapes, heights, and lengths, indicating the speed and intensity of signal transmission. Results are read by someone trained in evoked potential studies.

Abnormal results

Changes in the electrical tracings may indicate damage to or degeneration of nerve pathways to the brain from the eyes, ears, or limbs. Absence of any activity may mean complete loss of nerve function in that pathway. Other changes may provide evidence of the type and location of nerve damage.

Resources

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Richard Robinson

Evoked responses *see* **Evoked potential studies**

Exanthema subitum *see* **Roseola**

Exercise

Definition

Exercise is physical activity that is planned, structured, and repetitive for the purpose of conditioning any part of the body. Exercise is utilized to improve health, maintain fitness and is important as a means of physical **rehabilitation**.

Purpose

Exercise is useful in preventing or treating coronary heart disease, **osteoporosis**, weakness, diabetes, **obesity**, and depression. Range of motion is one aspect of exercise important for increasing or maintaining joint function. Strengthening exercises provide appropriate resistance to the muscles to increase endurance and strength. **Cardiac rehabilitation** exercises are developed and individualized to improve the cardiovascular system for prevention and rehabilitation of cardiac disorders and diseases. A well-balanced exercise program can improve general health, build endurance, and delay many of the effects of **aging**. The benefits of exercise not only improve physical health, but also enhance emotional well-being.

Precautions

Before beginning any exercise program, an evaluation by a physician is recommended to rule out any potential health risks. Once health and fitness are determined, and any or all physical restrictions identified, an individual's exercise program should be under the supervision of a health care professional. This is especially the case when exercise is used as a form of rehabilitation. If symptoms of **dizziness**, nausea, excessive **shortness of breath**, or chest **pain** are present during any exercise program, an individual should stop the activity and inform a physician about these symptoms before resuming activity. Exercise equipment must be checked to determine if it can bear the weight of people of all sizes and shapes.

Description

Range of motion exercise

Range of motion exercise refers to activity whose goal is improving movement of a specific joint. This

Exercise is utilized to improve health, maintain fitness, and is important as a means of physical rehabilitation. *(Illustration by Electronic Illustrators Group.)*

motion is influenced by several structures: configuration of bone surfaces within the joint, joint capsule, ligaments, and muscles and tendons acting on the joint. There are three types of range of motion exercises: passive, active, and active assists. Passive range of motion is movement applied to a joint solely by another person or persons or a passive motion machine. When passive range of motion is applied, the joint of an individual receiving exercise is completely relaxed while the outside force moves the body part, such as a leg or arm, throughout the available range. Injury, surgery, or **immobilization** of a joint may affect the normal joint range of motion. Active range of motion is movement of a joint provided entirely by the individual performing the exercise. In this case, there is no outside force aiding in the movement. Active assist range of motion is described as a joint receiving partial assistance from an outside force. This range of motion may result from the majority of motion applied by an exerciser or by the person or persons assisting the individual. It may also be a half-and-half effort on the joint from each source.

Strengthening exercise

Strengthening exercise increases muscle strength and mass, bone strength, and the body's metabolism. It can help attain and maintain proper weight and improve body image and self-esteem. A certain level of muscle strength is needed to do daily activities, such as walking, running and climbing stairs. Strengthening exercises increase this muscle strength by putting more strain on a muscle than it is normally accustomed to receiving. This increased load stimulates the growth of proteins inside each muscle cell that allow the muscle as a whole to contract. There is evidence indicating that strength training may be better than aerobic exercise alone for improving self-esteem and body image. Weight training allows one immediate feedback, through observation of progress in muscle growth and improved muscle tone. Strengthening exercise can take the form of isometric, isotonic and isokinetic strengthening.

ISOMETRIC EXERCISE. During isometric exercises, muscles contract. However, there is no motion in the affected joints. The muscle fibers maintain a constant length throughout the entire contraction. The exercises are usually performed against an immovable surface or object such as pressing one's hand against a wall. The muscles of the arm are contracting but the wall is not reacting or moving as a result of the physical effort. Isometric training is effective for developing total strength of a particular muscle or group of muscles. It is often used for rehabilitation since the exact area of muscle weakness can be isolated and strengthening can be administered at the proper joint angle. This kind of training can provide a relatively quick and convenient method

for overloading and strengthening muscles without any special equipment and with little chance of injury.

ISOTONIC EXERCISE. Isotonic exercise differs from isometric exercise in that there is movement of a joint during the muscle contraction. A classic example of an isotonic exercise is weight training with dumbbells and barbells. As the weight is lifted throughout the range of motion, the muscle shortens and lengthens. Calisthenics are also an example of isotonic exercise. These would include chin-ups, push-ups, and sit-ups, all of which use body weight as the resistance force.

ISOKINETIC EXERCISE. Isokinetic exercise utilizes machines that control the speed of contraction within the range of motion. Isokinetic exercise attempts to combine the best features of both isometrics and weight training. It provides muscular overload at a constant preset speed while a muscle mobilizes its force through the full range of motion. For example, an isokinetic stationary bicycle set at 90 revolutions per minute means that despite how hard and fast the exerciser works, the isokinetic properties of the bicycle will allow the exerciser to pedal only as fast as 90 revolutions per minute. Machines known as Cybex and Biodex provide isokinetic results; they are generally used by physical therapists and are not readily available to the general population.

Cardiac rehabilitation

Exercise can be very helpful in prevention and rehabilitation of cardiac disorders and disease. With an individually designed exercise program set at a level considered safe for that individual, people with symptoms of **heart failure** can substantially improve their fitness levels. The greatest benefit occurs as muscles improve the efficiency of their oxygen use, which reduces the need for the heart to pump as much blood. While such exercise doesn't appear to improve the condition of the heart itself, the increased fitness level reduces the total workload of the heart. The related increase in endurance should also translate into a generally more active lifestyle. Endurance or aerobic routines, such as running, brisk walking, cycling, or swimming, increase the strength and efficiency of the muscles of the heart.

Preparation

A **physical examination** by a physician is important to determine if strenuous exercise is appropriate or detrimental for an individual. Prior to the exercise program, proper stretching is important to prevent the possibility of soft tissue injury resulting from tight muscles, tendons, ligaments, and other joint-related structures.

KEY TERMS

Aerobic—Exercise training that is geared to provide a sufficient cardiovascular overload to stimulate increases in cardiac output.

Calisthenics—Exercise involving free movement without the aid of equipment.

Endurance—The time limit of a person's ability to maintain either a specific force or power involving muscular contractions.

Osteoporosis—A disorder characterized by loss of calcium in the bone, leading to thinning of the bones. It occurs frequently in postmenopausal women.

Aftercare

Proper cool down after exercise is important in reducing the occurrence of painful muscle spasms. It has been documented that proper cool down may also decrease frequency and intensity of muscle stiffness the day following any exercise program.

Risks

Improper warm up can lead to muscle strains. Overexertion with not enough time between exercise sessions to recuperate can also lead to muscle strains, resulting in inactivity due to pain. **Stress fractures** are also a possibility if activities are strenuous over long periods of time without proper rest. Although exercise is safe for the majority of children and adults, there is still a need for further studies to identify potential risks.

Normal results

Significant health benefits are obtained by including a moderate amount of physical exercise in the form of an exercise prescription. This is much like a drug prescription in that it also helps enhance the health of those who take it in the proper dosage. Physical activity plays a positive role in preventing disease and improving overall health status. People of all ages, both male and female, benefit from regular physical activity. Regular exercise also provides significant psychological benefits and improves quality of life.

Abnormal results

There is a possibility of exercise burnout if an exercise program is not varied and adequate rest periods are

not taken between exercise sessions. Muscle, joint, and cardiac disorders have been noted among people who exercise. However, they often have had preexisting or underlying illnesses.

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ORGANIZATIONS

American Alliance for Health, Physical Education, Recreation & Dance. 1900 Association Dr., Reston, VA 20191-1598. (800) 213-7193. Fax: (703) 476-9527. <aahperd@aahperd.org>. <http://www.aahperd.org>.

American College of Sports Medicine. 401 W. Michigan Street, Indianapolis, IN 46202-3233. (317) 637-9200. Fax: (317) 634-7817. <mkeckhaver@acsm.org>. <http://www.acsm.org/>.

American Council on Exercise. 5820 Oberlin Drive, Suite 102, San Diego, CA 92121-3787. (800) 825-3636. Fax: (858) 535-1778. <http://www.acefitness. org/>.

American Medical Association. 515 N. State Street, Chicago, IL 60610. (312) 464-5000. <http://www.ama-assn.org/>.

American Physical Therapy Association. 1111 North Fairfax Street Alexandria, VA 22314. (703) 684-2782. <http://www.apta.org>.

National Athletic Trainers' Association. 2952 Stemmons Freeway, Dallas, TX 75247-6916. (800) 879-6282. Fax: (214) 637-2206. <http://www.nata.org/>.

OTHER

American Diabetes Association. <http://www.diabetes.org/exercise/>.

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American Orthopaedic Society for Sports Medicine. <http://www.sportsmed.org/>.

American Society of Exercise Physiologists. <http://www.css.edu/asep/>.

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Exercise electrocardiogram *see* **Stress test**

Exercise stress test *see* **Stress test**

Exhibitionism *see* **Sexual perversions**

Exocrine pancreatic cancer *see* **Pancreatic cancer, exocrine**

Exophthalmos

Definition

When there is an increase in the volume of the tissue behind the eyes, the eyes will appear to bulge out of the face. The terms exophthalmos and proptosis apply. Proptosis can refer to any organ that is displaced forward, while exophthalmos refers just to the eyes.

Description

The eye socket (orbit) is made of bone and therefore will not yield to increased pressure within it. Only forward displacement of the eyeball (globe) will allow more room if tissue behind the eye is increasing.

Causes and symptoms

The most common cause of exophthalmos is Graves' disease, overactivity of the thyroid gland. The contents of the orbits swell due to inflammation, forcing the eyes forward. The inflammation affects primarily the muscles. This combination of muscle impairment and forward displacement reduces eye movement, causing double vision and crossed eyes (**strabismus**). The optic nerves can also be affected, reducing vision, and the clear membrane (conjunctiva) covering the white part of the eyes and lining the inside of the eyelids can swell. Finally, the eyes may protrude so far that the eyelids cannot close over them, leading to corneal damage.

Exophthalmos from Graves' disease is bilateral (occurring on both sides), but not necessarily symmetri-

A side view of the bulging eye (exophthalmos) of a person suffering from thytoxicosis. Exophthalmos is caused by swelling of the soft tissue in the eye socket, which forces the eyeball to be pushed forward and the eyelids stretched apart. *(Photograph by Dr. P. Marazzi, Photo Researchers, Inc. Reproduced by permission.)*

cal. In contrast, exophthalmos from orbital tumors or a blood clot in the brain happens on only one side.

Diagnosis

Exophthalmos is obvious when it is advanced enough to cause complications. When there is doubt in the early stages, a mechanical device called an exophthalmometer can measure the protrusion. **Computed tomography scans** (CT scans) are of great value in examining the bony components of the orbit. **Magnetic resonance imaging** (MRI) scanning is equally valuable for displaying the contents of the orbit, because it "sees through" the bone.

Treatment

If a tumor is growing behind the eye, it needs to be removed. If Graves' disease is the cause, it may subside with treatment of the overactive thyroid, but this is not guaranteed. Local care to the front of the eye to keep it moist is necessary if the eyelid cannot close.

Prognosis

Exophthalmos can be progressive. Its progress must be carefully followed, treating complications as they occur.

Prevention

Vision can usually be preserved with attentive treatment. There is currently no way to prevent any of the underlying conditions that lead to exophthalmos.

KEY TERMS

Conjunctivae—The clear membranes that line the inside of the eyelids and cover the white part (sclera) of the eyeballs.

Cornea—The clear, dome-shaped part of the front of the eye, through which light first enters the eye. It is located in front of the colored part of the eye (iris).

Inflammation—The body's reaction to invasion by foreign matter, particularly infection. The result is swelling and redness from an increase in water and blood, and pain from the chemical activity of the reaction.

Strabismus—Any deviation of the eyes from a common direction. Commonly called a turned eye.

Thyroid—A gland in the neck overlying the windpipe that regulates the speed of metabolic processes by producing a hormone, thyroxin.

Resources

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J. Ricker Polsdorfer, MD

Expectorants

Definition

Expectorants are drugs that loosen and clear mucus and phlegm from the respiratory tract.

Purpose

The drug described here, guaifenesin, is a common ingredient in **cough** medicines. It is classified as an expectorant, a medicine that helps clear mucus and other secretions from the respiratory tract. However, some debate exists about how effectively guaifenesin does this. In addition, some cough medicines contain other ingredi-

KEY TERMS

Asthma—A disease in which the air passages of the lungs become inflamed and narrowed.

Bronchitis—Inflammation of the air passages of the lungs.

Chronic—A word used to describe a long-lasting condition. Chronic conditions often develop gradually and involve slow changes.

Cough suppressant—Medicine that stops or prevents coughing.

Emphysema—An irreversible lung disease in which breathing becomes increasingly difficult.

Mucus—Thick fluid produced by the moist membranes that line many body cavities and structures.

Phlegm—Thick mucus produced in the air passages.

Respiratory tract—The air passages from the nose into the lungs.

Secretion—A substance, such as saliva or mucus, that is produced and given off by a cell or a gland.

ents that may cancel out guaifenesin's effects. **Cough suppressants** such as codeine, for example, work against guaifenesin because they discourage coughing up the secretions that the expectorant loosens.

There are other ways to loosen and clear the respiratory secretions associated with colds. These include using a humidifier and drinking six to eight glasses of water a day.

Description

Guaifenesin is an ingredient in many cough medicines, such as Anti-Tuss, Dristan Cold & Cough, Guaifed, GuaiCough, and some Robitussin products. Some products that contain guaifenesin are available only with a physician's prescription; others can be bought without a prescription. They come in several forms, including capsules, tablets, and liquids.

Recommended dosage

Adults and children 12 and over

200–400 mg every four hours. No more than 2,400 mg in 24 hours.

Children 6–11

100–200 mg every four hours. No more than 1,200 mg in 24 hours.

Children 2–5

50–100 mg every four hours. No more than 600 mg in 24 hours.

Children under two

Not recommended.

Precautions

Do not take more than the recommended daily dosage of guaifenesin.

Guaifenesin is not meant to be used for coughs associated with **asthma**, **emphysema**, chronic **bronchitis**, or **smoking**. It also should not be used for coughs that are producing a large amount of mucus.

A lingering cough could be a sign of a serious medical condition. Coughs that last more than seven days or are associated with **fever**, rash, **sore throat**, or lasting **headache** should have medical attention. Call a physician as soon as possible.

Some studies suggest that guaifenesin causes **birth defects**. Women who are pregnant or plan to become pregnant should check with their physicians before using any products that contain guaifenesin. Whether guaifenesin passes into breast milk is not known, but no ill effects have been reported in nursing babies whose mothers used guaifenesin.

Side effects

Side effects are rare, but may include vomiting, **diarrhea**, stomach upset, headache, skin rash, and **hives**.

Interactions

Guaifenesin is not known to interact with any foods or other drugs. However, cough medicines that contain guaifenesin may contain other ingredients that do interact with foods or drugs. Check with a physician or pharmacist for details about specific products.

Nancy Ross-Flanigan

Exstrophy of the urinary bladder *see* **Congenital bladder anomalies**

External fetal monitoring *see* **Electronic fetal monitoring**

External otitis *see* **Otitis externa**

External sphincter electromyography

Definition

External sphincter **electromyography** helps physicians determine how well the external urinary sphincter muscle is working by measuring the electrical activity in it during contraction and relaxation.

Purpose

The external sphincter muscle is the ring-like muscle that controls urine release from the bladder. When a patient cannot voluntarily control urination (incontinence), a physician may order this test to determine if the problem is caused by the failure of this muscle. The voluntary contraction or release of a muscle such as the external sphincter involves a complex process in which the nerves controlling the muscle signal it to move through the release and uptake of chemicals called neurotransmitters and the generation of electrical impulses. This test records the electrical impulses given off when the muscle contracts or relaxes and allows the physician to determine if the muscle is working properly, if it has been damaged by disease, or some other condition.

Precautions

Patients who are taking **muscle relaxants** or drugs that act like or have an effect on the neurotransmitter acetylcholine (cholinergic or anti-cholinergic drugs) should tell the doctor since they will change the test results. The results will also be altered if the patient moves during the test or if the electrodes are improperly placed.

Description

The patient puts on a surgical gown and lies down on the examining table. The procedure, which takes between 30–60 minutes, may be conducted one of three ways:

- Skin electrodes. This is the most commonly used method of recording information. The skin where the electrodes will be placed is cleaned and shaved and an electrically conductive paste is applied. The electrodes are then taped in place. For female patients, the electrodes are taped around the urethra, while for male patients they are placed between the scrotum and the anus.
- Needle electrodes. This is considered the most accurate method, since the electrodes are inserted directly into the muscle, using needles to guide placement. For male patients, a gloved finger is inserted in the rectum, then needles with wires attached are inserted through the skin between the anus and the scrotum. For female patients, the needles are inserted around the urethra. The discomfort of placing the needles is about the same as that of an injection. The needles are withdrawn, and the wires are taped to the thigh.
- Anal plug electrodes. The tip of an anal plug is lubricated and inserted into the rectum as the patient relaxes the anal sphincter. Electrodes are attached to the anal plug.

Once the electrodes are in place and attached to the recording device, the patient is asked to alternately contract and relax the external sphincter muscle. The electrical activity generated during these contractions and relaxations is recorded on a graph called an electromyogram.

KEY TERMS

Anti-cholinergic drug—A medication that blocks or subdues the action of the neurotransmitter acetylcholine.

Cholinergic drug—A medication that mimics or enhances the action of the neurotransmitter acetylcholine.

Sphincter—A circular muscle that aids in the opening or closing of an opening in the body.

Preparation

Before the test, the patient should discuss with the doctor whether it is necessary to temporarily discontinue any medications, and follow the doctor's orders. No changes in diet or activity are necessary.

Aftercare

Women may see some blood in their urine the first time they urinate after the test. Blood in the urine of men or blood in the urine of women after the first urination should be reported the doctor. The patient should take a warm bath and drink plenty of fluids to ease any discomfort after the test.

Risks

Complications of external sphincter electromyography are rare. Occasionally patients report blood in their urine after being tested with needle electrodes. Also, the urethra may become mildly irritated causing a change in the normal frequency of urination.

Normal results

In a normally functioning external sphincter muscle, the electromyogram will show increased electrical activi-

ty when the patient tightens the muscle and a little or no electrical activity when it is relaxed.

Abnormal results

A diseased external sphincter muscle will produce an abnormal pattern of electrical activity. Conditions that affect the external sphincter may include **multiple sclerosis**, **neurogenic bladder**, **Parkinson's disease**, **spinal cord injury**, and **stress** incontinence. However, additional tests must be done in order to confirm any of these diagnoses.

Resources

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Tish Davidson

Extracorporeal membrane oxygenation

Definition

Extracorporeal membrane oxygenation (ECMO) is a special procedure that uses an artificial heart-lung machine to take over the work of the lungs (and sometimes also the heart). ECMO is used most often in newborns and young children, but it also can be used as a last resort for adults whose heart or lungs are failing.

Purpose

In newborns, ECMO is used to support or replace an infant's undeveloped or failing lungs by providing oxygen and removing carbon dioxide waste products so the lungs can rest. Infants who need ECMO may include those with:

- meconium aspiration syndrome (breathing in of a newborn's first stool by a fetus or newborn, which can block air passages and interfere with lung expansion)
- persistent **pulmonary hypertension** (a disorder in which the blood pressure in the arteries supplying the lungs is abnormally high)
- respiratory distress syndrome (a lung disorder usually of premature infants that causes increasing difficulty in breathing, leading to a life-threatening deficiency of oxygen in the blood)
- congenital diaphragmatic **hernia** (the profusion of part of the stomach through an opening in the diaphragm).
- pneumonia
- blood **poisoning**

ECMO is also used to support a child or adult patient's damaged, infected, or failing lungs for a few hours to allow treatment or healing. It is effective for those patients with severe, but reversible, heart or lung problems who haven't responded to treatment with a ventilator, drugs, or extra oxygen. Adults and children who need ECMO usually have one of these problems:

- heart failure
- pneumonia
- **respiratory failure** caused by trauma or severe infection

The ECMO procedure can help a patient's lungs and heart rest and recover, but it will not cure the underlying disease. Any patient who requires ECMO is seriously ill and will likely die without the treatment. Because there is some risk involved, this method is used only when other means of support have failed.

Precautions

Typically, ECMO patients have daily chest x rays and blood work, and constant vital sign monitoring. They are usually placed on a special rotating bed that is designed to decrease pressure on the skin and help move secretions from the lungs.

After the patient is stable on ECMO, the breathing machine settings will be lowered to "rest" settings, which allows the lungs to rest without the risk of too much oxygen or pressure from the ventilator.

Description

There are two types of ECMO: Venoarterial (V-A) ECMO supports the heart and lungs, and is used for patients with blood pressure or heart functioning problems in addition to respiratory problems. Venovenous (V-V) ECMO supports the lungs only.

V-A ECMO requires the insertion of two tubes, one in the jugular and one in the carotid artery. In the V-V ECMO procedure, the surgeon places a plastic tube into the jugular vein through a small incision in the neck.

Once in place, the tubes are connected to the ECMO circuit, and then the machine is turned on. The patient's blood flows out through the tube and may look very dark because it contains very little oxygen. A pump pushes the blood through an artificial membrane lung, where oxygen is added and carbon dioxide is removed. The size of the

artificial lung depends on the size of the patient; sometimes adults need two lungs. The blood is then warmed and returned to the patient. A steady amount of blood (called the flow rate) is pushed through the ECMO machine every minute. As the patient improves, the flow rate is lowered.

Many patients require heavy **sedation** while they are on ECMO to lessen the amount of oxygen needed by the muscles.

As the patient improves, the amount of ECMO support will be decreased gradually, until the machine is turned off for a brief trial period. If the patient does well without ECMO, the treatment is stopped.

Typically, newborns remain on ECMO for three to seven days, although some babies need more time (especially if they have a diaphragmatic hernia). Once the baby is off ECMO, he or she will still need a ventilator (breathing machine) for a few days or weeks. Adults may remain on ECMO for days to weeks, depending on the condition of the patient, but treatment may be continued for a longer time depending on the type of heart or lung disease, the amount of damage to the lungs before ECMO was begun, and the presence of any other illnesses or health problems.

Preparation

Before ECMO is begun, the patient receives medication to ease **pain** and restrict movement.

Aftercare

Because infants on ECMO may have been struggling with low oxygen levels before treatment, they may be at higher risk for developmental problems. They will need to be monitored as they grow.

Risks

Bleeding is the biggest risk for ECMO patients, since blood thinners are given to guard against blood clots. Bleeding can occur anywhere in the body, but is most serious when it occurs in the brain. This is why doctors periodically perform ultrasound brain scans of anyone on ECMO. **Stroke**, which may be caused by bleeding or blood clots in the brain, has occurred in some patients undergoing ECMO.

If bleeding becomes a problem, the patient may require frequent blood transfusions or operations to control the bleeding. If the bleeding can't be stopped, ECMO will be withdrawn.

Other risks include infection or vocal cord injury. Some patients develop severe blood infections that cause irreversible damage to vital organs.

KEY TERMS

Carotid artery—Two main arteries (passageway carrying blood from the heart to other parts of the body) that carry blood to the brain.

Congenital diaphragmatic hernia—The profusion of part of the stomach through an opening in the diaphragm.

Meconium aspiration syndrome—Breathing in of meconium (a newborn's first stool) by a fetus or newborn, which can block air passages and interfere with lung expansion.

Membrane oxygenator—The artificial lung that adds oxygen and removes carbon dioxide.

Pulmonary hypertension—A disorder in which the blood pressure in the arteries supplying the lungs is abnormally high.

Respiratory distress syndrome—A lung disorder usually of premature infants that causes increasing difficulty in breathing, leading to a life-threatening deficiency of oxygen in the blood.

Venoarterial (V-A) bypass—The type of ECMO that provides both heart and lung support, using two tubes (one in the jugular vein and one in the carotid artery).

Venovenous (V-V) bypass—The type of ECMO that provides lung support only, using a tube inserted into the jugular vein.

There is a small chance that some part of the complex equipment may fail, which could introduce air into the system or affect the patient's blood levels, causing damage or **death** of vital organs (including the brain). For this reason, the ECMO circuit is constantly monitored by a trained technologist.

Normal results

Lungs and/or heart return to healthy functioning.

Abnormal results

Lungs and/or heart do not improve while on ECMO.

Resources

PERIODICALS

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ORGANIZATIONS

American Society of Extra-Corporeal Technology. 11480 Sunset Hills Rd., Ste. 210E, Reston, VA 20190. (703) 435-8556. <http://www.amsect.org>.

ECMO Moms and Dads. PO Box 53848, Lubbock, TX 79543. (806) 794-0259.

Extracorporeal Life Support Organization. 1327 Jones Dr., Ste. 101, Ann Arbor, MI 48105. (734) 998-6600. <http://www.elso.med.umich.edu>.

Carol A. Turkington

Extracorporeal shock-wave *see* **Lithotripsy**

Extrinsic allergic alveolitis *see* **Hypersensitivity pneumonitis**

Eye and orbit sonograms *see* **Eye and orbit ultrasounds**

Eye and orbit ultrasounds

Definition

Ultrasound imaging equipment allows eye specialists (ophthalmologists) to "see" the eye in great detail without the **pain** and risk of exploratory surgery, or the limitations and uncertainty inherent to traditional visual examination. Ultrasound is used to detect and diagnose many eye diseases and injuries, to measure the eye prior to corrective surgery, and directly as a treatment tool.

Purpose

An ophthalmologist uses ultrasonic imaging to help diagnose the underlying cause(s) of a patient's symptoms, to assess the general condition of an injured eye, and to measure the eye prior to corrective surgery. Situations that may call for ultrasonic imaging include:

- Excessive tearing or visible infection. These external symptoms could indicate a serious underlying problem such as a tumor, an internal infection, the presence of a deeply lodged irritant (foreign body), or the effects of a previously unrecognized injury. When presented with general symptoms, ultrasound can speed diagnosis if a serious condition is suspected.
- Impaired vision. Fuzzy vision, poor night vision, restricted (tunnel) vision, blind spots, extreme light sensitivity, and even blindness can all stem from inner eye conditions ranging from **glaucoma** and **cataracts**, to retinitis, detached retina, tumors, or impaired blood circulation. Again, high resolution ultrasound can quickly identify causes and pinpoint their location. A special type of ultrasound, known as Doppler, can even perceive and measure circulation in the tiny blood vessels of the eye.
- Eye trauma. The eye can be damaged by a direct impact or a puncture wound, as a result of a general head trauma, or by intense light exposure. Even when the cause of injury is obvious, ultrasound can reveal the exact type, extent, and location of damage, from deformations and ruptures to internal bleeding, and help to guide emergency care efforts.
- Lens replacement surgery. Exact measurement of the eye's optical dimensions with ultrasound greatly improves the visual outcome for cataract patients receiving permanent synthetic lenses; and for severely myopic patients receiving implanted corrective lenses.

Ophthalmic ultrasound imaging is also used routinely to guide the precise placement of instruments during surgery, and can be used directly for the treatment of glaucoma and tumors of the eye.

Precautions

Ultrasound of the eye, properly performed by qualified personnel using appropriate equipment, has no risks. There is no evidence to suggest that the procedure itself poses any threat to a healthy eye, or worsens the condition of a diseased or injured eye.

Description

Ophthalmic ultrasound equipment sends high frequency pulses of sound into the eye, where they bounce off the boundaries between different structures in the eye and produce a distinctive pattern of echoes. This echo pattern is received and interpreted by a computer to produce an image on a television screen. The time it takes an echo to return to the receiver corresponds to the depth it traveled into the eye.

Single transducer (the sound transmitter/receiver) ultrasound is used to measure distances within the eye. This is A-mode ultrasound. A linear array of transduc-

ers in a single small probe, B-mode, provides a picture of a cross section through the eye. Doppler mode ultrasound combines B-mode with the ability to detect and measure the flow of blood in the tiny vessels of the eye.

As a direct treatment tool, the vibrations of high intensity A-mode ultrasound can be used to heat and erode tumors. The same technique can be used to control glaucoma by selectively destroying the cells which produce the fluid that causes the internal pressure of the eye to rise.

The procedure followed in a regular ultrasonic **eye examination** is relatively simple. The patient relaxes in a comfortable chair in a darkened room. Mild anesthetic eye drops are administered and the head is held secure. The ultrasonic probe, coated with a sterile gel to ensure good contact, is lightly pressed against the eye as the images are made. The probe may be applied to the eyelid or directly to the eye, as necessary. The patient feels nothing else, and the whole office procedure takes about 15 minutes.

Preparation

Preparation by the patient is generally unnecessary, although under special circumstances an ophthalmologist may perform pretest procedures. The ophthalmologist and/or ultrasound technician will conduct all preparations at the time of the test.

Aftercare

Patients may experience partial and temporary blurred vision, as well as "eye strain" headaches. These symptoms usually fade within an hour of the procedure, during which time patients should rest their eyes and avoid all activities that require good eyesight, like driving.

Risks

Improperly focused, high-intensity ultrasound could burn and physically disrupt delicate eye tissue and cause injury. This risk is, however, slight and would arise only from improper use, or as a potential side effect of tumor or glaucoma treatment.

Normal results

A normal ultrasound scan would indicate a fully healthy eye. For therapeutic ultrasound, a normal result would be an improvement in the targeted condition, such as shrinking of a tumor or lessening of pressure inside the eye of a glaucoma patient.

KEY TERMS

Cataracts—A clouding of the lens of the eye or the material immediately surrounding it, causing blurred vision. For many people it occurs naturally with aging, but may also result from injury.

Glaucoma—A common eye disease characterized by increased fluid pressure in the eye that damages the optic nerve, which carries sensations to the brain. Glaucoma can be caused by another eye disorder, such as a tumor or congenital malformation, or appear without obvious cause, but if untreated it generally leads to blindness.

Intraocular—Literally, within the eye.

Ophthalmologist—A medical doctor specializing in eye care who is generally, but not necessarily, an eye surgeon.

Retina—The third and innermost membrane of the eye, which contains the light-sensitive nerve tissue that leads into the optic nerve and is the primary instument of vision. Inflammation of the retina (retinitis) has many causes, including over-exposure to intense light, diabetes, and syphilis.

Abnormal results

Because diagnostic ultrasound is generally used to investigate symptoms, the results of a scan will often be abnormal and they will detect evidence of an underlying condition.

Resources

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National Eye Institute. 2020 Vision Place, Bethesda, MD 20892-3655. (301) 496-5248. <http://www.nei.nih.gov>.

Kurt Richard Sternlof

Eye cancer

Definition

A cancerous growth in any part of the eye.

Description

Eye **cancer** can occur in many parts of the eye where a tumor can occur. Because of this there are several types of ocular cancer. Their occurrence varies in the age of the affected individual. This article will focus on **retinoblastoma**, the most common eye cancer in children, and intraocular melanoma, the most common eye cancer in adults.

Retinoblastoma can occur at any age but is most often seen in children younger than five. About 200 children a year are diagnosed with it in the United States. Retinoblastoma starts with a small tumor in the retina, the very back of the eye. In growing children, the retina originates from cells called retinoblasts that grow and divide very quickly. These cells eventually become the mature cells of the retina when they stop growing. In the case of retinoblastoma the retinoblasts don't stop growing and form a tumor that can continue to grow and cause further complications if not treated quickly.

Retinoblastoma typically has three classifications: intraocular, extraocular and recurrent retinoblastoma. In the intraocular form the cancer can be found in one or both eyes but not in tissue external of the eye. In the extraocular form the cancer has spread outside the eye. It can spread to the tissue surrounding the eye or it can invade other areas of the body. In the recurrent form the cancer returns after already being treated. It may recur in the eye, its surrounding tissues, or elsewhere in the body.

Intraocular melanoma is a rare cancer overall, yet it is the most common eye cancer seen in adults. It is when cancer cells are found in the uvea of the eye. The uvea includes the iris (the colored portion of eye), the ciliary body (an eye muscle that focuses the lens) and the choroid (found in the back of the eye next to the retina).

Intraocular cancer of the iris usually grows slowly and usually doesn't spread. The tumor is seen on the iris as a darker spot than the surrounding area. Intraocular cancer of the choroid or ciliary body occurs in the back of the eye. They are classified by size with a small tumor being 2-3 mm or smaller and a medium or large tumor being bigger than 3 mm.

Intraocular cancer can spread and become extraocular as well. If not found and treated early enough it can spread to the surrounding tissues, the optic nerve or into the eye socket.

Causes and symptoms

Genetics is thought to play a role in eye cancer. In regards to retinoblastoma, it is believed that if a tumor develops only in one eye then it isn't hereditary. However, if a tumor occurs in both eyes then it is hereditary. Those who have hereditary retinoblastoma have a rare risk of developing a tumor in the brain and should be monitored on a regular basis.

The cause of intraocular melanoma is still vague. Genetics could play a role, but age is also a factor. Interestingly enough, this type of cancer is seen most often in white people from a northern European descent.

The symptoms of this type of cancer usually begin with blurred vision and tenderness of the eye. Advanced symptoms may include loss of vision. If these symptoms persist a person should make an appointment with their ophthalmologist.

Diagnosis

An ophthalmologist makes a diagnosis. The doctor is usually able to see the tumor through the pupil or directly on the iris if the cancer is intraocular melanoma of the iris. Because the doctor can usually readily see the tumor a biopsy is rarely needed.

An ultrasound or a fluorescein **angiography** are two tests doctors use to further diagnose eye cancers. In an ultrasound sound waves are pointed at the tumor and depending on how they reflect off the tumor the doctor can better diagnose it. In a fluorescein angiography a fluorescent dye is injected into the patients arm. When this dye circulates through the body and reaches the eye a series of rapid pictures are taken through the pupil. The tumor will show up in these photos.

Once a diagnosis has been made, the treatment can begin.

Treatment

The treatment depends on how far advanced the tumor is. If the tumor is in the advanced stages and there is little hope of regaining vision the most effective treat-

ment is an enucleation, the removal of the eye. This obviously is a drastic treatment and is avoided if possible. Other eye surgeries include the following:

- choroidectomy-removal of part of the choroid,
- iridectomy-removal of part of the iris,
- iridocyclectomy-removal of parts of the ciliary body and parts of iris,
- iridotrabeculectomy-removal of parts of the supporting tissues around the cornea and iris.

In eye cancer where the tumor is small and there is a good chance that the vision will be restored less drastic measures than the above surgeries are taken. Radiation and **chemotherapy** are two courses of treatment that help in killing off the existing tumor and preventing its spread into other areas of the body.

Besides radiation and chemotherapy there are other methods of treating eye cancer. **Cryotherapy** uses extreme cold to destroy the cancer cells. Thermotherapy uses heat to destroy the cancer cells. Photocoagulation uses a laser to destroy blood vessels that supply the tumor with nutrients. If the tumor isn't advanced these are good options to treat it in order to avoid losing an eye.

A radiation/surgical treatment for eye cancer is brachytherapy. A small plaque with radioactive iodine on one side and gold on the other is stitched to the eye behind the tumor with the radioactive iodine facing the tumor. The gold is used to shield the other tissues from the radiation. It is left there for a period of time depending on the dosage of radiation needed and then it is removed. In this way the tumor is treated and hopefully will shrink and eventually die.

Alternative Treatment

Other than the treatments above, there aren't any alternative treatments. New clinical trials are constantly under way to further the treatment of the disease in the future.

Prognosis

All forms of retinoblastoma and intraocular melanoma are treatable. Enucleation can usually be avoided if found early enough. The outlook is positive for people with eye cancer.

Prevention

A good healthy diet and lifestyle are always recommended to prevent cancer. Known carcinogens should always be avoided.

KEY TERMS

Carcinogen—A substance that is known to cause cancer.

Cornea—The clear layer that covers the front part of the eye.

Enucleation—Surgical removal of the eye.

Pupil—The hole in the eye that allows light in.

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Eye examination

Definition

An eye examination is a series of tests that measure a person's ocular health and visual status, to detect abnormalities in the components of the visual system, and to determine how well the person can see.

Purpose

An eye examination is performed by an ophthalmologist M.D. or D.O. (doctor of **osteopathy**), or an optometrist (O.D.) to determine if there are any pre-existing or potential vision problems. Eye exams may also reveal the presence of many non-eye diseases. Many systemic diseases can affect the eyes, and since the blood vessels on the retina are observed during the exam, certain problems may be uncovered (e.g., high blood pressure or diabetes).

Infants should be examined by a physician to detect any physical abnormalities. Frequency of eye exams then generally differs with age and the health of the person. Eye exams can be performed in infants, and if a problem is

noted the infant can be seen, generally by a pediatric ophthalmologist. A child with no symptoms should have an eye exam at age three. Early exams are important because permanent decreases in vision (e.g., **amblyopia**, also called lazy eye) can occur if not treated early (usually by ages 6–9). Again, with no other symptoms, the second exam should take place before first grade. After first grade, the American Optometric Association recommends an eye exam every two years; ages 19–40, every two to three years; ages 41–60, every two years; and annually after that. However, these are recommendations for healthy people with no risk factors. Patients should ask their doctors how often they should come for exams. Some patients have risk factors for eye disease (e.g., people with diabetes or a family history of eye disease; African Americans, who are at higher risk for **glaucoma**) and may need more frequent checkups. Also, if children seem to be having trouble in school, problems with reading, rubbing their eyes when reading, etc., an eye exam may be necessary sooner.

Precautions

The examiner needs to know if the patient is taking any medications or has any existing health conditions. Some medications, even over-the-counter (OTC) medications can affect vision or even interfere with the eyedrops the doctor may use during the exam. Certain eyedrops would not be used if the patient has **asthma**, heart problems, or other conditions.

The patient may need someone to drive them home in case the eyes were dilated. Bringing sunglasses to the exam may also help decrease the glare from light until the dilating drops wear off.

Description

An eye examination, given by an ophthalmologist or optometrist, costs about $100. It may or may not be covered by insurance. It begins with information from the patient (case history) and continues with a set of primary tests, plus additional specialized tests given as needed, dictated by the outcomes of initial testing and the patient's age. The primary tests can be divided into two groups, those that evaluate the physical state of the eyes and surrounding areas, and those that measure the ability to see.

The order of the tests for the exam may differ from doctor to doctor, however, most exams will include the following procedures:

Information gathering and initial observations

The examiner will take eye and medical histories that include the patient's chief complaint, any past eye disorders, all medications being taken (e.g., OTC medications, **antibiotics**, and birth control pills), any blood relatives with eye disorders, and any systemic disorders the patient may have. The patient should also tell the doctor about hobbies and work conditions. This information helps in modifying prescriptions and lets the doctor know how the patient uses his or her eyes. For example, using a computer screen vs. construction work, the working distance of a computer screen may affect the prescription; the construction worker needs protective eyewear.

The patient should bring their current pair of glasses to the exam. The doctor can get the prescription from the glasses by using an instrument called a lensometer.

Visual acuity examination

Visual acuity measures how clearly the patient can see. It is measured for each eye separately, with and without the current prescription. It is usually measured with a Snellen eye chart, a poster with lines of different-sized letters, each line with a number at the side denoting the distance from which a person with normal vision can read that line. Other kinds of eye charts with identifiable figures are available for children or anyone unfamiliar with the Roman alphabet. These charts are made to be placed at a certain distance (usually 20 ft) from the person being tested. At this distance, people with normal vision can read a certain line (usually the lowest), marked the 20/20 line; these people are said to have 20/20 vision. For people who can't read the smallest line, the examiner assigns a ratio based on the smallest line they can read. The first number (numerator) of the ratio is the distance between the chart and the patient, and the second number (denominator) is the distance where a person with normal vision would be able to read that line. The ratio 20/40 means the patient can see at 20 ft. what people with normal vision can see at 40 ft. away.

When a patient is unable to read any lines on the chart, they are moved closer until they can read the line with the largest letters. The acuity is still measured the same way. A ratio of 5/200 means the person being tested can see at 5 ft what a normal person can see 200 ft.

When a patient can't read the chart at all, the examiner may hold up some fingers and ask the patient to count them at various distances, and records the result as "counting fingers" at the distance of recognition. If the patient cannot count the examiner's fingers at any distance, the examiner determines if the patient can see hand movements. If so, the result is recorded as "hand movements." If not, the examiner determines if the patient can detect light from a penlight. If the patient can detect the light but not its direction, the result is recorded at "light perception." If the patient can recognize its

direction, the result is recorded as "light projection." If the patient cannot detect the light at all, the result is recorded as "no light perception."

Eye movement examination and cover tests

The examiner asks the patient to look up and down, and to the right and left to see if the patient can move the eyes to their full extent. The examiner asks the patient to stare at an object, then quickly covers one eye and notes any movement in the eye that remains uncovered. This procedure is repeated with the other eye. This, and another similar cover test, helps to determine if there is an undetected eye turn or problem with fixation. The doctor may also have the patient look at a pen and follow it as it is moved close to the eyes. This checks convergence.

Iris and pupil examination

The doctor checks the pupil's response to light (if it dilates and constricts appropriately). The iris is viewed for symmetry and physical appearance. The iris is checked more thoroughly later using a slit lamp.

Refractive error determination-Refraction

The examiner will determine the refractive error and obtain a prescription for corrective lenses for people whose visual acuity is less than 20/20. An instrument called a phoropter, which the patient sits behind, is generally used (sometimes the refraction can be done with a trial frame that the patient wears). The phoropter is equipped with many lenses that allow the examiner to test many combinations of corrections to learn which correction allows the patient to see the eye chart most clearly. This is the part of the exam when the doctor usually says, "Which is better, one or two?" The phoropter also contains prisms, and sometimes the doctor will intentionally make the patient see double. This may help in determining a slight eye turn. The exam will check vision at distance and near (reading).

A prescription for corrective lenses can also be supplied by automated refracting devices, which measure the necessary refraction by shining a light into the eye and observing the reflected light. Another objective way to obtain a prescription is using a hand-held retinoscope. As in the automated method just mentioned, the doctor shines a light in the patient's eyes and can determine an objective prescription. This is helpful in young children or infants.

Sometimes drops will be instilled in the patient's eyes before this part of the exam. The drops may relax accommodation so that the refraction will be more accurate. This is helpful in children and people who are farsighted.

A woman looking through a refractor. *(Photograph by John Greim, Photo Researchers. Reproduced by permission.)*

After the refraction and other visual status tests, for example color tests or binocularity tests (can the patient see 3-D, or have depth perception), the doctor will check the health of the eyes and surrounding areas. The main instruments used are the ophthalmoscope and the slit lamp.

Ophthalmoscopic examination

These observations are best accomplished after dilating the pupils and require an ophthalmoscope. The ophthalmoscope most frequently used is a called a *direct ophthalmoscope*. It is a hand-held illuminated 15X multi-lens magnifier that lets the examiner view the inside back area of the eye (fundus). The retina, blood vessels, optic nerve, and other structures are examined.

Slit lamp examination

The slit lamp is a microscope with a light source that can be adjusted. This magnifies the external and some internal structures of the eyes. The lid and lid margin, cornea, iris, pupil, conjunctiva, sclera, and lens are examined. The slit lamp is also used in contact lens evaluations. A little probe called a tonometer may be used at this time to check the pressure of the eyes. A colored eyedrop may be instilled immediately prior to this test. The drop has a local anesthetic so the patient won't feel the probe touch the eye. It is a quick procedure.

Visual field measurement

A perimeter, the instrument for measuring visual fields, is a hollow hemisphere, equipped with a light source that projects dots of light over the inside surface. The patient's head is positioned so that the eye being tested is at the center of the sphere and 13 in (about 33

KEY TERMS

Amblyopia—Decreased visual acuity, usually in one eye, in the absence of any structural abnormality in the eye.

Conjunctiva—The mucous membrane that covers the white part of the eyes (sclera) and lines the eyelids.

Cornea—Clear outer covering of the front of the eye.

Floaters—Translucent specks that float across the visual field, due to small objects floating in the vitreous humor.

Fundus—The inside of an organ. In the eye, refers to the back area that can be seen with the ophthalmoscope.

Glaucoma—There are many types of glaucoma. Glaucoma results in optic nerve damage and a decreased visual field and blindness if not treated. It is usually associated with increased IOP, but that is not always the case. The three factors associated with glaucoma are increased IOP, a change in the optic nerve head, and changes in the visual field.

Gonioscope—An instrument used to inspect the eye (e.g., the anterior chamber). It consists of a magnifier and a lens equipped with mirrors; it's placed on the patient's cornea.

Iris—The colored ring just behind the cornea and in front of the lens that controls the amount of light sent to the retina.

Macula—The central part of the retina where the rods and cones are densest.

Ophthalmoscope—An instrument designed to view structures in the back of the eye.

Optic nerve—The nerve that carries visual messages from the retina to the brain.

Pupil—The circular opening that looks like a black hole in the middle of the iris.

Retina—The inner, light-sensitive layer of the eye containing rods and cones; transforms the image it receives into electrical messages which are then sent to the brain via the optic nerve.

Sclera—The tough, fibrous, white outer protective covering that surrounds the eye.

Slit lamp—A microscope that projects a linear slit beam of light onto the eye; allows viewing of the conjunctiva, cornea, iris, aqueous humor, lens, and eyelid.

Tonometer—An instrument that measures intraocular pressure (IOP).

Ultrasonography—A method of obtaining structural information about internal tissues and organs where an image is produced because different tissues bounce back ultrasonic waves differently.

cm) from all points on the inside surface of the hemisphere. The patient stares straight ahead at an image on the center of the surface and signals whenever he or she detects a flash of light. The perimeter records which flashes are seen and which are missed and maps the patient's field of vision and blindspots.

Intraocular pressure (IOP) measurement

Tonometers are used to measure IOP. Some tonometers measure pressure by expelling a puff of air (noncontact tonometer) towards the eyeball from a very short distance. Other tonometers are placed directly on the cornea. The noncontact tonometers are not as accurate as the contact tonometers and are sometimes used for screenings.

Completing the evaluation with additional tests

Depending upon the results other tests may be necessary. These can include, but are not limited to binocular indirect ophthalmoscopy, gonioscopy, color tests, contrast sensitivity testing, ultasonography, and others. The patient may have to return for additional visits.

Results

External observations

INITIAL OBSERVATIONS AND SLIT LAMP EXAM. Some general observations the doctor may be looking for include: head tilt; drooping eyelids (**ptosis**); eye turns; red eyes (injection); eye movement; size, shape, and color of the iris; clarity of the cornea, anterior chamber, and lens. The anterior chamber lies behind the cornea and in front of the iris. If it appears cloudy or if cells can be seen in it during the slit lamp exam an inflammation may be present. A narrow anterior chamber may put the patient at risk for glaucoma. A clouding of the normally clear lens is called a cataract.

Internal observations

OPHTHALMOSCOPIC EXAM. The observations include, but are not limited to the retina, blood vessels, and optic nerve. The optic nerve enters the back of the eye and can be checked for swelling or other problems. The blood vessels can be viewed as can the retina. The macula is a 3–5 mm area in the back of the eye and is responsible for central vision. The fovea is a small area located within the macula and is responsible for sharp vision. When a person looks at something, they are pointing the fovea at the object. Changes in the macular area can be observed with the ophthalmoscope. Retinal tears or detachments can also be seen.

Visual ability

VISUAL ACUITY. The refraction will determine the refractive status for each eye for distance and for near. A prescription for glasses is made after taking many things into consideration. The eye doctor may alter a prescription based upon many factors. Different materials for glasses may be suggested. For example, polycarbonate may be suggested for children or people active in sports because it is very impact resistant. Bifocals, trifocals, single-vision spectacles, and contact lenses are also options.

VISUAL FIELDS. A normal visual field extends about 60° upward, about 75° downward, about 65° toward the nose, and about 100° toward the ear and has one blind spot close to the center. Defects in the visual field signify damage to the retina, optic nerve, or the neurological visual pathway.

Seeing clearly does not necessarily mean the eyes are healthy or that the eyes are working together as a team. Regular checkups can detect abnormalities, hopefully before a problem arises. The eye doctor can suggest ways to help protect the eyes and vision (e.g., safety goggles, ultraviolet (UV) coatings on lenses). A person should also have an eye exam if they notice a change in vision, eyestrain, blur, flashes of light, a sudden onset of floaters (little dots), distortion of objects, double vision, redness, **pain** or discharge.

Resources

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ORGANIZATIONS

American Academy of Ophthalmology. 655 Beach Street, PO Box 7424, San Francisco, CA 94120-7424. <http://www.eyenet.org>.

American Optometric Association. 243 North Lindbergh Blvd., St. Louis, MO 63141. (314) 991-4100. <http://www.aoanet.org>.

Lorraine Lica, PhD

Eye exercises *see* **Vision training**

Eye glasses and contact lenses

Definition

Eyeglasses and contact lenses are devices that correct refractive errors in vision. Eyeglass lenses are mounted in frames worn on the face, sitting mostly on the ears and nose, so that the lenses are positioned in front of the eyes. Contact lenses appear to be worn in direct contact with the cornea, but they actually float on a layer of tears that separates them from the cornea.

Purpose

The purpose of eyeglasses and contact lenses is to correct or improve the vision of people with nearsightedness (**myopia**), farsightedness (**hyperopia**), **presbyopia**, and **astigmatism**.

Precautions

People allergic to certain plastics should not wear contact lenses or eyeglass frames or lenses manufactured from that type of plastic. People allergic to nickel should not wear Flexon frames. People at risk of being in accidents that might shatter glass lenses should wear plastic lenses, preferably polycarbonate. (Lenses made from polycarbonate, the same type of plastic used for the space shuttle windshield, are about 50 times stronger than other lens materials.) Also, people at risk of receiving electric shock should avoid metal frames.

People employed in certain occupations may be prohibited from wearing contact lenses, or may be required to wear safety eyewear over the contact lenses. Some occupations, such as construction or auto repair, may require safety lenses and safety frames. Physicians and employers should be consulted for recommendations.

Description

Eyes are examined by optometrists (O.D.) or by ophthalmologists (M.D. or D.O.—doctor of **osteopathy**). Prescriptions, if necessary, are then given to patients for

glasses. The glasses are generally made by an optician. A separate contact lens-fitting exam is necessary if the patient wants contact lenses, because an eyeglass prescription is not the same as a contact lens prescription.

Eyeglasses

Over 140 million people in the United States wear eyeglasses. People whose eyes have refractive errors do not see clearly without glasses, because the light emitted from the objects they are observing does not come into focus on their retinas. For people who are farsighted, images come into focus behind the retina; for people who are nearsighted, images come into focus in front of the retina.

LENSES. Lenses work by changing the direction of light so that images come into focus on the retina. The greater the index of refraction of the lens material and the greater the difference in the curvature between the two surfaces of the lens, the greater the change in direction of light that passes through it, and the greater the correction.

Lenses can be unifocal, with one correction for all distances, or they can be correct for more than one distance (multifocal). One type of multifocal, the bifocal, has an area of the lens (usually at the bottom) that corrects for nearby objects (about 14 in from the eyes); the remainder of the lens corrects for distant objects (about 20 ft from the eyes). Another type of multifocal, a trifocal, has an area in-between that corrects for intermediate distances (usually about 28 in). Conventional bifocals and trifocals have visible lines between the areas of different correction; however, lenses where the correction gradually changes from one area to the other, without visible lines, have been available since the 1970s. Such lenses are sometimes called progressives or no-line bifocals.

To be suitable for eyeglass lenses, a material must be transparent, without bubbles, and have a high index of refraction. The greater the index of refraction, the thinner the lens can be. Lenses are made from either glass or plastic (hard resin). The advantage of plastic is that it is lightweight and more impact resistant than glass. The advantage of glass is that it is scratch resistant and provides the clearest possible vision.

Glass was the first material to be used for eyeglass lenses, and was used for several hundred years before plastic was introduced. The crown glass used for eyeglass lenses has an index of refraction of 1.52.

Optical-quality acrylic was introduced for eyeglass use in the early 1940s, but because it was easily scratched, brittle, and discolored rapidly, it did not supplant glass as the material of choice. Furthermore, it had a relatively low index of refraction, so it wasn't suitable for people with large refractive errors. A plastic called CR-39, introduced in the 1960s, was more suitable. Today, eyeglass wearers can also choose between polycarbonate, which is the most impact-resistant material available for eyewear, and polyurethane, which has exceptional optical qualities and an index of refraction of up to 1.66, much higher than the conventional plastics used for lenses, and even higher than glass. Patients with high prescriptions should ask about high index material options for their lenses. Aspheric lenses are also useful for high prescriptions. They are flatter and lighter than conventional lenses.

There are many lenses and lens-coating options for individual needs, including coatings that block the ultraviolet (UV) light or UV and blue light which have been found to be harmful to the eyes. Such coatings are not needed on polycarbonate lenses, which already have UV protection. UV coatings are particularly important on sunglasses and ski goggles. Sunglasses, when nonprescription, should be labeled with an indication that they block out 99–100% of both UV-A and UV-B rays.

There are anti-scratch coatings that increase the surface hardness of lenses (an important feature when using plastic lenses) and anti-reflective (AR) coatings that eliminate almost all glare and allow other people to see the eyes of the wearer. AR coatings may be particularly helpful to people who use computers or who drive at night. Mirror coatings that prevent other people from seeing the wearer's eyes are also available. There is a whole spectrum of tints, from light tints to darker tints, used in sunglasses. Tint, however, does not block-out UV rays, so a UV coating is needed. Polaroid lenses that block out much of the reflected light also allow better vision in sunny weather and are helpful for people who enjoy boating. Photosensitive (photochromatic) lenses that darken in the presence of bright light are handy for people who don't want to carry an extra set of glasses. Photochromatic lenses are available in glass and plastic.

FRAMES. Frames can be made from metal or plastic, and they can be rimless. There is an almost unlimited variety of shapes, colors, and sizes. The type and degree of refractive correction in the lens determine to some extent the type of frame most suitable. Some lenses are too thick to fit in metal rims, and some large-correction prescriptions are best suited to frames with small-area lenses.

Rimless frames are the least noticeable type, and they are lightweight because the nosepiece and temples are attached directly to the lenses, eliminating the weight of the rims. They tend to not be as sturdy as frames with rims, so they are not a good choice for people who frequently

remove their glasses and put them on again. They are also not very suitable for lenses that correct a high degree of farsightedness, because such lenses are thin at the edges.

Metal frames are less noticeable than plastic, and they are lightweight. They are available in solid gold, gold-filled, anodized aluminum, nickel, silver, stainless steel, and now titanium and titanium alloy. Until the late 1980s, when titanium-nickel alloy and titanium frames were introduced, metal frames were, in general, more fragile than plastic frames. The titanium frames, however, are very strong and lightweight. An alloy of titanium and nickel, called Flexon, is not only strong and lightweight, but returns to its original shape after being twisted or dented. It is not perfect for everyone, though, because some people are sensitive to its nickel. Flexon frames are also relatively expensive.

Plastic frames are durable, can accommodate just about any lens prescription, and are available in a wide range of prices. They are also offered in a variety of plastics (including acrylic, epoxy, cellulose acetate, cellulose propionate, polyamide, and nylon) and in different colors, shapes, and levels of resistance to breakage. Epoxy frames are resilient and return to their original shape after being deformed, so they do not need to be adjusted as frequently as other types. Nylon frames are almost unbreakable. They revert to their original shape after extreme trauma and distortion; because of this property, though, they cannot be readjusted after they are manufactured.

FIT. The patient should have the distance between the eyes (PD) measured, so that the optical centers of the lenses will be in front of the patient's pupils. Bifocal heights also have to be measured with the chosen frame in place and adjusted on the patient. Again, this is so the lenses will be positioned correctly. If not positioned correctly, the patient may experience eyestrain or other problems. This can occur with over-the-counter reading glasses. The distance between the lenses is for a "standard" person. Generally, this will not be a problem, but if a patient is sensitive or has more closely set eyes, for example, it may pose a problem. Persons buying ready-made sunglasses or reading glasses should hold them up to see if they appear clear. They should also hold the lenses to see an object with straight lines reflected off of the lenses. If the lines don't appear straight, the lenses may be warped or inferior.

Patients may sometimes need a few days to adjust to a new prescription; however, problems should be reported, because the glasses may need to be rechecked.

Contact lenses

Over 32 million people in the United States wear these small lenses that fit on top of the cornea. They provide a field of view unobstructed by eyeglass frames; they do not fog-up or get splattered, so it is possible to see well while walking in the rain; and they are less noticeable than any eyeglass style. On the other hand, they take time to get accustomed to; require more measurements for fitting; require many follow-up visits to the eye doctor; can lead to complications such as infections and corneal damage; and may not correct astigmatism as well as eyeglasses, especially if the astigmatism is severe.

Originally, hard contact lenses were made of a material called PMMA. Although still available, the more common types of contact lenses are listed below:

- Rigid gas-permeable (RGP) daily-wear lenses are made of plastic that does not absorb water but allows oxygen to get from the atmosphere to the cornea. (This is important because the cornea has no blood supply and needs to get its oxygen from the atmosphere through the film of tears that moves beneath the lens.) They must be removed and cleaned each night.
- Rigid gas-permeable (RGP) extended-wear lenses are made from plastic that also does not absorb water but is more permeable to oxygen than the plastic used for daily-wear lenses. They can be worn up to a week.
- Daily wear soft lenses are made of plastic that is permeable to oxygen and absorbs water; therefore, they are soft and flexible. These lenses must be removed and cleaned each night, and they do not correct all vision problems. Soft lenses are easier to get used to than rigid lenses, but are more prone to tears and do not last as long.
- Extended-wear soft lenses are highly permeable to oxygen, are flexible by virtue of their ability to absorb water, and can usually be worn for up to one week. They do not correct all vision problems. There is more of a risk of infection with extended-wear lenses than with daily-wear lenses.
- Extended-wear disposable lenses are soft lenses worn continually for up to six days and then discarded, with no need for cleaning.
- Planned-replacement soft lenses are daily wear lenses that are replaced on a regular schedule, which is usually every two weeks, monthly, or quarterly. They must also be cleaned.

Soft contact lenses come in a variety of materials. There are also different kinds of RGP and soft multifocal contact lenses available. Monovision, where one contact lens corrects for distance vision while the other corrects for near vision, may be an option for presbyopic patients. Monovision, however, may affect depth perception and may not be appropriate for everyone. Contact lenses also

KEY TERMS

Astigmatism—Assymetric vision defects due to irregularities in the cornea.

Cornea—The clear outer covering of the front of the eye.

Index of refraction—A constant number for any material for any given color of light that is an indicator of the degree of the bending of the light caused by that material.

Lens—A device that bends light waves.

Permeable—Capable of allowing substances to pass through.

Polycarbonate—A very strong type of plastic often used in safety glasses, sport glasses, and children's eyeglasses. Polycarbonate lenses have approximately 50 times the impact resistance of glass lenses.

Polymer—A substance formed by joining smaller molecules. For example, plastic, acrylic, cellulose acetate, cellulose propionate, nylon, etc.

Presbyopia—A condition affecting people over the age of 40 where the system of accommodation that allows focusing of near objects fails to work because of age-related hardening of the lens of the eye.

Retina—The inner, light-sensitive layer of the eye containing rods and cones; transforms the image it receives into electrical messages sent to the brain via the optic nerve.

Ultraviolet (UV) light—Part of the electromagnetic spectrum with a wavelength just below that of visible light. It is damaging to living material, especially eyes and DNA.

come in a variety of tints. Soft contacts are available that can change dark-colored eyes a different color. Even though such lenses have no prescription, they must still be fitted and checked to make sure that an eye infection does not occur. People should NEVER wear someone else's contact lenses. This can lead to infection or damage to the eye.

Aftercare

Contact lens wearers must be examined periodically by their eye doctors to make sure that the lenses fit properly and that there is no infection. Both infection and lenses that do not fit properly can damage the cornea. Patients can be allergic to certain solutions that are used to clean or lubricate the lenses. For that reason, patients should not randomly switch products unless they speak with their doctor. Contact lens wearers should seek immediate attention if they experience eye **pain**, a burning sensation, red eyes, intolerable sensitivity to light, cloudy vision, or an inability to keep the eyes open.

To avoid infection, it is important for contact lens wearers to exactly follow their instructions for lens insertion and removal, as well as cleaning. Soft contact lens wearers should never use tap water to rinse their lenses or to make-up solutions. All contact lens wearers should also always have a pair of glasses and a carrying case for their contacts with them, in case the contacts have to be removed due to eye irritation.

Risks

Wearing contact lenses increases the risk of corneal damage and eye infections.

Normal results

The normal expectation is that people will achieve 20/20 vision while wearing corrective lenses.

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Lorraine Lica, PhD

Eye muscle surgery

Definition

Eye muscle surgery is surgery to weaken, strengthen, or reposition any of the muscles that move the eyeball (the extraocular muscles).

Purpose

The purpose of eye muscle surgery is generally to align the pair of eyes so that they gaze in the same direction and move together as a team, either to improve appearance or to aid in the development of binocular vision in a young child. To achieve binocular vision, the goal is to align the eyes so that the location of the image on the retina of one eye corresponds to the location of the image on the retina of the other eye.

In addition, sometimes eye muscle surgery can help people with other eye disorders (**nystagmus** and Duane syndrome, for example).

Precautions

Depth perception (stereopsis) develops around the age of three months old. For successful development of binocular vision and the ability to perceive three-dimensionally, the surgery should not be postponed past the age of four. The earlier the surgery the better the outcome, so an early diagnosis is important. Surgery may even be performed before two years old. After surgery, if binocular vision is to develop, corrective lenses and eye exercises (vision therapy) will probably be necessary.

Description

The extraocular muscles attach via tendons to the sclera (the white, opaque, outer protective covering of the eyeball) at different places just behind an imaginary equator circling the top, bottom, left, and right of the eye. The other end of each of these muscles attaches to a part of the orbit (the eye socket in the skull). These muscles enable the eyes to move up, down, to one side or the other, or any angle in between.

Normally both eyes move together, receive the same image on corresponding locations on both retinas, and the brain fuses these images into one three-dimensional image. The exception is in **strabismus** which is a disorder where one or both eyes deviate out of alignment, most often outwardly (exotropia) or toward the nose (esotropia). The brain now receives two different images, and either suppresses one or the person sees double (diplopia). This deviation can be adjusted by weakening or strengthening the appropriate muscles to move the eyes toward the center. For example, if an eye turns upward, the muscle at the bottom of the eye could be strengthened.

Rarely, eye muscle surgery is performed on people with nystagmus or Duane syndrome. Nystagmus is a condition where one or both eyes move rapidly or oscillate; it can sometimes be helped by moving the eyes to the position of least oscillation. Duane syndrome is a disorder where there is limited horizontal eye movement; it can sometimes be relieved by surgery to weaken an eye muscle.

There are two methods to alter extraocular muscles. Traditional surgery can be used to strengthen, weaken, or reposition an extraocular muscle. The surgeon first makes an incision in the conjunctiva (the clear membrane covering the sclera), then puts a suture into the muscle to prevent it from getting lost and loosens the muscle from the eyeball with a surgical hook. During a resection, the muscle is detached from the sclera, a piece of muscle is removed so the muscle is now shorter, and the muscle is reattached to the same place. This strengths the muscle. In a recession, the muscle is made weaker by repositioning it. More than one extraocular eye muscle might be operated on at the same time.

Another way of weakening eye muscles, using botulinum toxin injected into the muscle, was introduced in the early 1980s. Although the botulinum toxin wears off, the realignment may be permanent, depending upon whether neurological connections for binocular vision were established during the time the toxin was active. This technique can also be used to adjust a muscle after traditional surgery.

The cost of eye muscle surgery is about $2,000–$4,000, and about 700,000 surgeries are performed annually in the United States.

Preparation

Patients should make sure their doctors are aware of any medications that they are taking, even over-the-counter medications. Patients should not take **aspirin**, or any other blood-thinning medications for ten days prior to surgery, and should not eat or drink after midnight the night before.

Aftercare

Patients will need someone to drive them home after their surgery. They should continue to avoid aspirin and other non-steroidal anti-inflammatory agents for an additional three days, but they can take **acetaminophen** (e.g., Tylenol). Patients should discuss this with the surgeon to be clear what medications they can or cannot take. **Pain** will subside after two to three days, and patients can resume most normal activities within a few days. Again,

KEY TERMS

Botulinum toxin (botulin)—A neurotoxin made by *Clostridium botulinum*; causes paralysis in high doses, but is used medically in small, localized doses to treat disorders associated with involuntary muscle contraction and spasms, in addition to strabismus.

Conjunctiva—The mucous membrane that covers the eyes and lines the eyelids.

Extraocular muscles—The muscles (lateral rectus, medial rectus, inferior rectus, superior rectus, superior oblique, and inferior oblique) that move the eyeball.

Orbit—The cavity in the skull containing the eyeball; formed from seven bones: frontal, maxillary, sphenoid, lacrimal, zygomatic, ethmoid, and palatine.

Retina—The inner, light-sensitive layer of the eye containing rods and cones; transforms the image it receives into electrical messages sent to the brain via the optic nerve.

Sclera—The tough, fibrous, white outer protective covering of the eyeball.

Strabismus—A disorder where the two eyes do not point in the same direction.

this may vary with the patient and the patient should discuss returning to normal activity with the surgeon. They should not get their eyes wet for three to four days and should refrain from swimming for 10 days. Operated eyes will be red for about two weeks.

Risks

As with any surgery, there are risks involved. Eye muscle surgery is relatively safe, but very rarely a cut muscle gets lost and can not be retrieved. This, and other serious reactions, including those caused by anesthetics, can result in vision loss in the affected eye. Occasionally, retinal or nerve damage occurs. Double vision is not uncommon after eye muscle surgery. As mentioned earlier, glasses or vision therapy may be necessary.

Normal results

Cosmetic improvement is likely with success rate estimates varying from about 65–85%. According to the best statistics as of 1998, binocular vision is improved in young children about 35% of the time. There is no improvement, or the condition worsens 15–35% of the time. A second operation may rectify less-than-perfect outcomes.

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Eye training *see* **Vision training**

Eyelid disorders

Definition

An eyelid disorder is any abnormal condition that affects the eyelids.

Description

Eyelids consist of thin folds of skin, muscle, and connective tissue. The eyelids protect the eyes and spread tears over the front of the eyes. The inside of the eyelids are lined with the conjunctiva of the eyelid (the palpebral conjunctiva), and the outside of the lids are covered with the body's thinnest skin. Some common lid problems include the following: stye, blepharitis, chalazion, entropion, ectropion, eyelid **edema**, and eyelid tumors.

Stye

A stye is an infection of one of the three types of eyelid glands near the lid margins, at the base of the lashes.

Chalazion

A chalazion is an enlargement of a meibomian gland (an oil-producing gland in the eyelid), usually not associated with an infectious agent. More likely, the gland opening is clogged. Initially, a chalazion may resemble a stye, but it usually grows larger. A chalazion may also be located in the middle of the lid and be internal.

Blepharitis

Blepharitis is the inflammation of the eyelid margins, often with scales and crust. It can lead to eyelash loss, chalazia, styes, ectropion, corneal damage, excessive tearing, and chronic **conjunctivitis**.

Entropion

Entropion is a condition where the eyelid margin (usually the lower one) is turned inward; the eyelashes touch the eye and irritate the cornea.

Ectropion

Ectropion is a condition where one or both eyelid margins turn outward, exposing both the conjunctiva that covers the eye and the conjunctiva that lines the eyelid.

Eyelid edema

Eyelid edema is a condition where the eyelids contain excessive fluid.

Eyelid tumors

Eyelids are susceptible to the same skin tumors as the skin over the rest of the body, including noncancerous tumors and cancerous tumors (basal cell carcinoma, squamous cell carcinoma, **malignant melanoma**, and sebaceous gland carcinoma). Eyelid muscles are susceptible to sarcoma.

Causes and symptoms

Stye

Styes are usually caused by bacterial **staphylococcal infections**. The symptoms are **pain** and inflammation in one or more localized regions near the eyelid margin.

Chalazion

A chalazion is caused by a blockage in the outflow duct of a meibomian gland. Symptoms are inflammation and swelling in the form of a round lump in the lid that may be painful.

Blepharitis

Some cases of blepharitis are caused by bacterial infection and some by head lice, but in some cases, the cause is unclear. It may also be caused by an overproduction of oil by the meibomian glands. Blepharitis can be a chronic condition that begins in early childhood and can last throughout life. Symptoms can include **itching**, burning, a feeling that something is in the eye, inflammation, and scales or matted, hard crusts surrounding the eyelashes.

A chalazion on the eyelid. This condition is caused by an obstruction of one of the meibomian glands which lubricate the edge of the eyelid. *(Photo Researchers, Inc. Reproduced by permission.)*

Entropion

Entropion usually results from **aging**, but sometimes can be due to a congenital defect, a spastic eyelid muscle, or a scar on the inside of the lid that could be from surgery, injury, or disease. It is accompanied by excessive tearing, redness, and discomfort.

Ectropion

Similar to entropion, the usual cause of ectropion is aging. It also can be due to a spastic eyelid muscle or a scar, as in entropion. It also can be the result of **allergies**. Symptoms are excessive tearing and hardening of the eyelid conjunctiva.

Eyelid edema

Eyelid edema is most often caused by allergic reactions, for example, allergies to eye makeup, eyedrops or other drugs, or plant allergens such as pollen. **Trichinosis**, a disease caused by eating undercooked meat, also causes eyelid edema. However, swelling can also be caused by more serious causes, such as infection, and can lead to orbital **cellulitis** which can threaten vision. Symptoms can include swelling, itching, redness, or pain.

Eyelid tumors

Tumors found on the eyelids are caused by the same conditions that cause these tumors elsewhere on the

A close-up of the eye of an elderly patient showing ectropion of the lower eyelid. Ectropion is a condition in which the eyelid turns away from the eye. The most common type is senile ectropion (seen here), in which the droop of the eyelid is due to loss of tissue elasticity in old age and weakness in the muscles surrounding the eye. *(Photograph by Dr. P. Marazzi, Photo Researchers, Inc. Reproduced by permission.)*

body. They are usually painless and may or may not be pigmented. Some possible causes include **AIDS** (**Kaposi's sarcoma**) or increased exposure to ultraviolet (UV) rays which may lead to skin **cancer**.

Diagnosis

An instrument called a slit lamp is generally used to magnify the structures of the eyes. The doctor may press on the lid margin to see if oil can be expressed from the meibomian glands. The doctor may invert the lid to see the inside of the lid. Biopsy is used to diagnose cancerous tumors.

Treatment

Stye

Styes are treated with warm-hot compresses for 10–15 minutes, three to four times a day. Sometimes topical **antibiotics** may be prescribed. If the initial treatment is ineffective, styes are lanced and drained.

Chalazion

About 25% of chalazia will disappear spontaneously, but hot compresses may speed the process. Because chalazia are inside the lid, topical medications are generally of no benefit. Medication may need to be injected by the doctor into the chalazion or if that doesn't help the chalazion may need to be excised. If what appears to be a chalazion recurs on the same site as any previous one, the possibility of sebaceous gland carcinoma should be investigated by biopsy.

Blepharitis

Blepharitis is treated with hot compresses, with antibiotic ointment, and by cleaning the eyelids with a moist washcloth and then with baby shampoo. Good hygiene is essential. If the blepharitis doesn't clear up with treatment or if it seems to be a chronic problem, the patient may have **acnerosacea**. These patients may need to see a dermatologist as well.

Entropion and ectropion

Both entropion and ectropion can be surgically corrected. Prior to surgery, the lower lid of entropion can be taped down to keep the lashes off the eye, and both can be treated with lubricating drops to keep the cornea moist.

Eyelid edema

Patients with swollen eyelids should contact their eye doctor. A severely swollen lid can press on the eye and possibly increase the intraocular pressure. An infection needs to be ruled out. Or, something as simple as an allergy to nail polish and then touching the eyes can cause swelling. The best treatment for allergic eyelid edema is to find and remove the substance causing the allergy. When that is not possible, as in the case of plant allergens, cold compresses and immunosuppresesive drugs such as corticosteroid creams are helpful. However, steroids can cause **cataracts** and increase intraocular pressure and patients must be very careful not to get the cream in their eyes. This should not be done unless under a doctor's care. For edema caused by trichinosis, the trichinosis must be treated.

Eyelid tumors

Cancerous tumors should be removed upon discovery, and noncancerous tumors should be removed before they become big enough to interfere with vision or eyelid function. Eyelid tumors require special consideration because of their sensitive location. It is important that treatment not compromise vision, eye movement, or eyelid movement. Accordingly, eyelid reconstruction will sometimes accompany tumor excision.

Prognosis

The prognosis for styes and chalazia is good to excellent. With treatment, blepharitis, ectropion, and entropion usually have good outcomes. The prognosis for nonmalignant tumors, basal cell carcinoma, and squamous cell carcinoma is good once they are properly removed. Survival rate for malignant melanoma depends upon how early it was discovered and if it was completely removed. Sebaceous carcinomas are difficult to detect, so poor outcomes are more frequent.

All of these eyelid disorders, if not treated, can lead to other, possibly serious vision problems—dry eye, **astigmatism**, or even vision loss, for example. An ophthalmologist or optometrist should be consulted.

Prevention

Good lid hygiene is very important. Regular eyelid washing with baby shampoo helps prevent styes, chalazia, blepharitis, and eyelid edema. To avoid these problems, it's also important to refrain from touching and rubbing the eyes and eyelids, especially with hands that have not just been washed.

Blepharitis is associated with dandruff, which is caused by a kind of bacteria that is one of the causes of blepharitis. Controlling dandruff by washing the hair, scalp, and eyebrows with shampoo containing selenium sulfide to kill the bacteria helps control the blepharitis. When using anything near the eyes, it is important to read the label or consult with a doctor first.

Avoiding allergens helps prevent allergic eyelid edema. Staying inside as much as possible when pollen counts are high and eliminating the use of, or at least removing eye makeup thoroughly, or using hypo-allergenic makeup may help if the person is sensitive to those substances.

Sunscreen, UV-blocking sunglasses, and wide brimmed hats can help prevent eyelid tumors.

Entropian and ectropian seem to be unpreventable.

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KEY TERMS

Allergen—A substance capable of inducing an allergic response.

Allergic reaction—An immune system reaction to a substance in the environment; symptoms include rash, inflammation, sneezing, itchy watery eyes, and runny nose.

Conjunctiva—The mucous membrane that covers the white part of the eyes and lines the eyelids.

Edema—A condition where tissues contain excessive fluid.

Meibomian gland—Oil-producing glands in the eyelids that open near the eyelid margins.

Eyelid edema *see* **Eyelid disorders**

Eyelid plastic surgery *see* **Blepharoplasty**

F

Fabry's disease *see* **Lipidoses**

Face lift

Definition

Face lift surgery is a cosmetic procedure that involves redirecting some of the skin and muscle tissue of the face and neck to counter signs of **aging** produced by gravity.

Purpose

The purpose of face lift surgery, also known as facialplasty, rhytidoplasty, or cervicofacial rhytidectomy, is to improve the appearance of the face by repositioning the skin and tightening some of the underlying muscle and tissue. The procedure is designed to counter sagging and looseness in skin and muscle tissue caused by gravity as the patient ages. Face lift surgery will not erase all facial wrinkles, as the term rhytidectomy (which literally means "surgical removal of wrinkles") might imply. Wrinkles around the mouth and eyes, for example, may benefit little from face lift surgery. Other procedures, such as **blepharoplasty**, chemical peel, or dermabrasion, also may be necessary.

Precautions

Patients with other medical conditions should consult with their primary physician before undergoing face lift surgery. Lung problems, heart disease, and certain other conditions can lead to a higher risk of complications. Patients who take medications that can alter the way their blood clots (including female hormones, **aspirin**, and some non-aspirin **pain** relievers) should stop these medications prior to surgery to lower the risk that a hematoma will form. A hematoma, a pocket of blood below the skin, is the most frequent complication of face lift surgery.

Description

Face lift surgery can be performed on an outpatient basis with local anesthetics. Patients typically also receive "twilight anesthesia," an intravenous sedative that helps to lower their awareness of the procedure being performed.

There are a number of variations of face lift surgery. Which one is used will depend on the patient's facial structure, how much correction is needed, and the preferences of the surgeon performing the procedure. In a typical face lift surgery, the surgeon begins by making an incision within the hairline just above the ear. The incision continues down along the front edge of the ear, around the earlobe, and then up and behind the ear extending back into the hairline. The location of this incision is designed to hide any sign of the procedure later. The same procedure is repeated on the other side of the face. Using various instruments, the surgeon will then work to separate the skin of the face from its underlying tissue, moving down to the cheek and into the neck area and below the chin. Fat deposits over the cheeks and in the neck may be removed surgically or with **liposuction** at this time. The surgeon will then work to free up and tighten certain bands of muscle and tissue that extend up from the shoulder, below the chin, and up and behind the neck. If these muscles and tissue are not tightened, the looseness and sagging appearance of the skin will return. The surgeon then trims excess skin from the edges of the original incision, pulls the skin back, and staples or sutures it into place.

Preparation

Prior to the procedure, patients meet with their surgeon to discuss the surgery, clarify the results that can be achieved, and discuss the potential problems that can occur. Having realistic expectations is important in any cosmetic procedure. Patients will learn, for example, that although face lift surgery can improve the contour of the face and neck, other procedures will be necessary to reduce the appearance of many wrinkles. As mentioned

In a typical face lift surgery, the surgeon begins by making an incision within the hairline just above the ear. The incision continues down along the front of the ear, around the earlobe, and then up and behind the ear extending back into the hairline, as shown above. The same procedure is repeated on the other side of the face. The surgeon will then separate the skin from the tissue, remove fat deposits over the cheeks and neck, tighten up muscles and tissues below the chin and upwards behind the neck. The surgeon then trims excess skin from the original incision, pulls the skin back, and sutures it into place. *(Illustration by Electronic Illustrators Group.)*

earlier, patients will stop taking aspirin, birth control or female hormones, and other medications affecting blood clotting about two weeks before the procedure. Some physicians prescribe vitamin C and K in the belief that this promotes healing. Patients will also be advised to stop **smoking** and to avoid exposure to passive smoke before the procedure and afterward. Some surgeons also recommend **antibiotics** be taken beforehand to limit the risk of infection. Some surgeons also use a steroid injection before or after the procedure, to reduce swelling.

Aftercare

After the surgery, a pressure bandage will be applied to the face to reduce the risk of hematoma. The patient may spend a few hours resting in a recovery room to ensure no bleeding has occurred. The patient then returns home. Some surgeons recommend that the patient remain reclining for the next 24 hours, consuming a liquid diet, and avoiding any movements that lead the neck to flex. Ice packs for the first few days can help to reduce swelling and lower the risk of hematoma. Patients continue taking an antibiotic until the first stitches come out about five days after the procedure. The balance are removed seven to 10 days later. Many patients return to work and limited activities within two weeks of the procedure.

KEY TERMS

Hematoma—A complication of surgery in which a collection of blood forms below the skin.

Rhytidectomy—It literally means "wrinkle excision." It is another, misleading, term for face lift surgery.

Twilight anesthesia—An intravenous mixture of sedatives and other medications that decreases patients' awareness of the procedure being performed.

Risks

The major complication seen following face lift surgery is a hematoma. If a hematoma forms, the patient may have to return to have the stitches reopened to find the source of the bleeding. Most hematomas form within 48 hours of surgery. The typical sign is pain or swelling affecting one side of the face but not the other.

Another risk of face lift surgery is nerve damage. Sometimes it can affect the patient's ability to raise an eyebrow, or distort his smile, or leave him with limited feeling in his earlobe. Most of these nerve injuries, however, repair themselves within 2–6 months.

Normal results

Some swelling and bruising is normal following face lift surgery. After these disappear, the patient should see a noticeable improvement in the contour of his face and neck. Some fine wrinkling of the skin may be improved, but deep wrinkles are likely to require another cosmetic procedure to improve their appearance.

Abnormal results

In addition to the risks outlined above, other complications of face lift surgery include infection, scarring, and hair loss near incision lines.

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American Society of Plastic and Reconstructive Surgeons. 44 E. Algonquin Rd., Arlington Heights, IL 60005. (847) 228-9900. <http://www.plasticsurgery.org>.

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Facial nerve paralysis *see* **Bell's palsy**

Factitious disorders

Definition

Factitious disorders are a group of mental disturbances in which patients intentionally act physically or mentally ill without obvious benefits. The name factitious comes from a Latin word that means artificial. These disorders are not **malingering**, which is defined as pretending illness when the "patient" has a clear motive, such as financial gain.

Description

Patients with factitious disorders produce or exaggerate the symptoms of a physical or mental illness by a variety of methods, including contaminating urine samples with blood, taking hallucinogens, injecting themselves with bacteria to produce infections, and other similar behaviors.

There are no reliable statistics on the frequency of factitious disorders, but they are more common in men than in women. The following conditions are sometimes classified as factitious disorders:

Munchausen syndrome

Munchausen syndrome refers to patients whose factitious symptoms are dramatized and exaggerated. Many persons with Munchausen go so far as to undergo major surgery repeatedly, and, to avoid detection, at several locations. Many have been employed in hospitals or in health care professions. The syndrome's onset is in early adulthood.

Munchausen by proxy

Munchausen by proxy is the name given to factitious disorders in children produced by parents or other caregivers. The parent may falsify the child's medical history or tamper with laboratory tests in order to make the child appear sick. Occasionally, they may actually injure the child to assure that the child will be treated.

Ganser's syndrome

Ganser's syndrome is an unusual dissociative reaction to extreme **stress** in which the patient gives absurd or silly answers to simple questions. It has sometimes been labeled as psychiatric malingering, but is more often classified as a factitious disorder.

Causes and symptoms

No single explanation of factitious disorders covers all cases. These disorders are variously attributed to underlying **personality disorders**; **child abuse**; the wish to repeat a satisfying childhood relationship with a doctor; and the desire to deceive or test authority figures. Also, the wish to assume the role of patient and be cared for is involved. In many cases, the suffering of a major personal loss has been implicated.

The following are regarded as indications of a factitious disorder:

- dramatic but inconsistent medical history
- extensive knowledge of medicine and/or hospitals
- negative test results followed by further symptom development
- symptoms that occur only when the patient is not being observed
- few visitors
- arguments with hospital staff or similar acting-out behaviors
- eagerness to undergo operations and other procedures

When patients with factitious disorders are confronted, they usually deny that their symptoms are intentional. They may become angry and leave the hospital. In many cases they enter another hospital, which has led to the nickname "hospital hoboes."

KEY TERMS

Ganser's syndrome—An unusual factitious disorder characterized by dissociative symptoms and absurd answers to direct questions.

Malingering—Pretending to be sick in order to be relieved of an unwanted duty or obtain some other obvious benefit.

Munchausen by proxy—A factitious disorder in children produced by a parent or other caregiver.

Munchausen syndrome—A factitious disorder in which the patient's symptoms are dramatized and exaggerated.

Diagnosis

Diagnosis of factitious disorders is usually based on the exclusion of bona fide medical or psychiatric conditions, together with a combination of the signs listed earlier. In some cases, the diagnosis is made on the basis of records from other hospitals.

Treatment

Treatment of factitious disorders is usually limited to prompt recognition of the condition and the refusal to give unnecessary medications or to perform unneeded procedures. Factitious disorder patients do not usually remain in the hospital long enough for effective psychiatric treatment. Some clinicians have tried psychotherapeutic treatment for factitious disorder patients, and there are anecdotal reports that antidepressant or antipsychotic medications are helpful in certain cases.

Prognosis

Some patients have only one or two episodes of factitious disorders; others develop a chronic form that may be lifelong. Successful treatment of the chronic form appears to be rare.

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Rebecca J. Frey

Factor IX deficiency *see* **Hemophilia**

Factor VIII deficiency *see* **Hemophilia**

Failure to thrive

Definition

Failure to thrive (FTT) is used to describe a delay in a child's growth or development. It is usually applied to infants and children up to two years of age who do not gain or maintain weight as they should. Failure to thrive is not a specific disease, but rather a cluster of symptoms which may come from a variety of sources.

Description

Shortly after birth most infants loose some weight. After that expected loss, babies should gain weight at a steady and predictable rate. When a baby does not gain weigh as expected, or continues to loose weight, it is not thriving. Failure to thrive may be due to one or more conditions.

Organic failure to thrive (OFTT) implies that the organs involved with digestion and absorption of food are malformed or incomplete so the baby cannot digest its food. Non-organic failure to thrive (NOFTT) is the most common cause of FTT and implies the baby is not receiving enough food due to economic factors or parental neglect, or do to psychosocial problems.

Causes and symptoms

Occasionally, there may be an underlying physical condition that inhibits the baby's ability to take in, digest, or process food. These defects can occur in the esophagus, stomach, small or large intestine, rectum or anus. Usually the defect is an incomplete development of the organ, and it must be surgically corrected. Most physical defects can be detected shortly after birth.

Failure to thrive may also result from lack of available food or the quality of the food offered. This can be due to economic factors in the family, parental beliefs and concepts of **nutrition**, or neglect of the child. In addition, if the baby is being breast fed, the quality or quantity of the mother's milk may be the source of the problem.

Psychosocial problems, often stemming from a lack of nurturing parent-child relations can lead to a failure to thrive. The child may exhibit poor appetite due to depression from insufficient attention from parents.

Infants and toddlers, whose growth is substantially less than expected, are considered to be suffering from FTT.

Diagnosis

Most babies are weighed at birth and that weight is used as a base line for future well-baby check-ups. If the baby is not gaining weight at a predictable rate, the doctor will do a more extensive examination. If there are no apparent physical deformities in the digestive tract, the doctor will examine the child's environment. As part of that examination, the doctor will look at the family history of height and weight. In addition, the parents will be asked about feedings, illnesses, and family routines. If the mother is breastfeeding the doctor will also evaluate her diet, general health, and well being as it affects the quantity and quality of her milk.

Diagnosis of FTT is confirmed by a positive growth and behavioral response to increased nutrition.

Treatment

If there is an underlying physical reason for failure to thrive, such as a disorder of swallowing mechanism or intestinal problems, correcting that problem should reverse the condition. If the condition is caused by environmental factors, the physician will suggest several ways parents may provide adequate food for the child. Maternal education and parental counseling may also be recommended. In extreme cases, hospitalization or a more nurturing home may be necessary.

Prognosis

The first year of life is important as a foundation for growth and physical and intellectual development in the future. Children with extreme failure to thrive in the first year may never catch up to their peers even if their physical growth improves. In about one third of these extreme cases, mental development remains below normal and roughly half will continue to have psychosocial and eating problems throughout life.

KEY TERMS

Esophagus—The muscular tube which connects the mouth and stomach.

Psychosocial—A term referring to the mind's ability to, consciously or unconsciously, adjust and relate the body to its social environment.

When failure to thrive is identified and corrected early, most children catch up to their peers and remain healthy and well developed.

Prevention

Initial failure to thrive caused by physical defects cannot be prevented but can often be corrected before they become a danger to the child. Maternal education and emotional and economic support systems all help to prevent failure to thrive in those cases where there is no physical deformity.

Resources

ORGANIZATIONS

American Humane Association, Children's Division. 63 Inverness Drive East, Englewood, CO 80112-5117. (800) 227-4645. <www.americanhumane.org>.

Federation for Children With Special Needs. 1135 Tremont Street, Suite 420, Boston, MA 02120. (617) 236-7210. <http://www.fcsn.org>.

National Digestive Diseases Information Clearinghouse. 2 Information Way, Bethesda, MD 20892-3570. (800) 891-5389. <http://www.niddk.nih.gov/health/digest/nddic. htm>.

Dorothy Elinor Stonely

Fainting

Definition

Fainting is loss of consciousness caused by a temporary lack of oxygen to the brain. Known by the medical term "syncope," fainting may be preceded by **dizziness**, nausea, or a feeling of extreme weakness.

Description

When a person faints, the loss of consciousness is brief. The person will wake up as soon as normal blood flow is restored to the brain. Blood flow is usually

If a person is feeling faint, unconsciousness may be prevented by sitting with the head between the knees, as shown in the illustration above, or by lying flat with the legs raised. *Illustration by Electronic Illustrators Group.)*

restored by lying flat for a short time. This position puts the head on the same level as the heart so that blood flows more easily to the brain.

A fainting episode may be completely harmless and of no significance, but it can be a symptom of a serious underlying disorder. No matter how trivial it seems, a fainting episode should be treated as a medical emergency until the cause is determined.

Causes and symptoms

Extreme **pain**, fear, or **stress** may bring on fainting. This type of fainting is caused by overstimulation of the vagus nerve, a nerve connected to the brain that helps control breathing and circulation. In addition, a person who stands still or erect for too long may faint. This type of fainting occurs because blood pools in the leg veins, reducing the amount that is available for the heart to pump to the brain. This type of fainting is quite common in older people or those taking drugs to treat high blood pressure.

When an older person feels faint upon turning the head or looking upward suddenly, the cause could be **osteoarthritis** of the neck bones. Osteoarthritis damages the cartilage between the neck bones and causes pressure on blood vessels leading to the brain.

Fainting can be a symptom of a disease such as Stokes-Adams syndrome, a condition in which blood flow to the brain is temporarily reduced because of an irregular heartbeat. Some people may experience fainting associated with weakness in the limbs or a temporary problem in speaking caused by obstructed blood flow in vessels passing through the neck to the brain. Pregnant women frequently feel faint. Fainting may also occur as a result of low blood sugar. Low blood sugar can occur if a person skips a meal or has diabetes.

Fainting can also be caused by:

- prolonged coughing
- straining to defecate or urinate
- blowing a wind instrument too hard
- remaining in a stuffy environment with too little oxygen

Sometimes fainting may be caused by a temporary drop in the blood supply to the brain caused by a **transient ischemic attack** (TIA). A TIA, sometimes called a mini-stroke, is a disruption in the blood supply to the brain caused by a blocked or burst blood vessel. Seek help immediately if a fainting spell is followed by one or more of the symptoms listed below:

- numbness or tingling in any body part
- blurred vision
- confusion
- difficulty speaking
- loss of movement in arms or legs

A few seconds before fainting, a person may sweat or become pale, feel nauseated or dizzy, and have blurred vision or racing heartbeat. Once the person loses consciousness, the pupils may dilate as the heart rate slows down. There may be abnormal movements. Muscles may tighten or the back may arch. These movements do not last long and they are not violent.

In most cases, the patient regains consciousness within a few minutes, but the fainting spell may be followed by nervousness, **headache**, nausea, dizziness, pallor or sweating. The person may faint again, especially if he or she stands up within 30 minutes.

Diagnosis

Most episodes of fainting are a one-time occurrence. When a person experiences repeated fainting spells, a physician should be consulted.

Treatment

Most of the time, a person who faints ends up lying on the floor. If this happens, the patient should be rolled onto his or her back. Because someone who faints often vomits, bystanders should keep the airway open. A person who is fainting should not be held upright or in a sitting position. These positions prevent blood flow to the brain and may bring on a seizure.

KEY TERMS

Osteoarthritis—A disease characterized by damage to the cartilage in the joints. The joints become inflamed, deformed, and enlarged, and movement becomes painful.

Stokes-Adams syndrome—Recurrent episodes of temporary loss of consciousness (fainting) caused by an insufficient flow of blood from the heart to the brain. This syndrome is caused by a very rapid or a very slow heartbeat.

Transient ischemic attack (TIA)—A brief interruption of the blood supply to part of the brain that causes a temporary impairment of vision, speech, or movement. Usually, the episode lasts for just a few moments, but it may be a warning sign for a full-scale stroke.

Vagus nerve—A cranial nerve, that is, a nerve connected to the brain. The vagus nerve has branches to most of the major organs in the body, including the larynx, throat, windpipe, lungs, heart, and most of the digestive system.

Bystanders should check the patient's breathing and pulse rate. The pulse may be weak and slow. If there are no signs of breathing or heart rate, the problem is more serious than fainting, and **cardiopulmonary resuscitation** (**CPR**) must begin.

If breathing and pulse rates seem normal, the person's legs should be raised above the level of the head so that gravity can help the blood flow to the brain. Belts, collars or any other constrictive clothing should be loosened.

If the person does not regain consciousness within a minute or two after fainting, medical help should be summoned.

Prognosis

After a fainting spell, the person should regain normal color but may continue to feel weak for a short time. Lying down quietly for a few moments may help.

In most cases, an attack of fainting is not serious. As soon as the underlying pain or stress passes, the danger of repeated episodes also is eliminated.

Prevention

If a person is feeling faint, unconsciousness may be prevented by sitting with the head between the knees or lying flat with the legs raised.

A person who has fainted should lie flat for 10–15 minutes after regaining consciousness to give the system a chance to regain its balance. Standing up too soon may bring on another fainting spell.

Resources

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Carol A. Turkington

Falciparum malaria *see* **Malaria**

Fallopian tube ligation *see* **Tubal ligation**

Fallopian tube removal *see* **Salpingectomy**

Fallopian tube x rays *see* **Hysterosalpingography**

Famciclovir *see* **Antiviral drugs**

Familial Mediterranean fever

Definition

Familial Mediterranean **fever** (FMF) is an inherited disorder of the inflammatory response characterized by recurring attacks of fever, accompanied by intense **pain** in the abdomen, chest, or joints. Attacks usually last 12–72 hours, and can occasionally involve a skin rash. Kidney disease is a serious concern if the disorder is not treated. FMF is most prevalent in people of Armenian, Sephardic-Jewish, Arabic, and Turkish ancestry.

Description

FMF could be described as a disorder of "inappropriate" inflammation. That is, an event that in a normal situation causes a mild or unnoticeable inflammation might cause a severe inflammatory response in someone with FMF. Certain areas of the body are at risk for FMF-related symptoms. A serosa is a serous (fluid-producing) membrane that can be found inside the abdominal cavity (peritoneum), around the lungs (pleura), around the heart (pericardium), and inside the joints (synovium). The symptoms of FMF are due to inflammation of one or more of the serosal membranes (serositis). Thus, FMF is also sometimes called recurrent polyserositis.

During an attack, large numbers of neutrophils, a type of white blood cell, move into the affected areas

causing painful inflammation and fever. These episodes may be accompanied by a skin rash or joint pain. In a few cases, chronic arthritis is a problem. **Amyloidosis** is a potentially serious condition in which proteins called amyloids are mistakenly produced and deposited in organs and tissues throughout the body. Left untreated, amyloidosis often leads to kidney failure, which is the major long-term health risk in FMF.

In most cases, the attacks of fever and pain are first noticed in childhood or adolescence. The interval between these episodes may be days or months, and is not predictable. However, during these intervals people with FMF typically lead normal lives. It is not entirely clear what brings on an attack, but people with FMF often report mild physical trauma, physical exertion, or emotional **stress** just prior to the onset of symptoms. Treatment for FMF involves an oral medication called colchicine, which is highly effective for the episodes of fever and pain, as well as for amyloidosis and the kidney disease that can result from it.

FMF is most common in certain ethnic groups from the eastern Mediterranean region, but cases in other ethnic groups in other parts of the world are increasingly being reported. FMF is also known by many other names. They include: recurrent hereditary polyserositis, benign paroxysmal **peritonitis**, familial paroxysmal polyserositis, paroxysmal polyserositis, familial recurrent polyserositis, periodic fever, periodic amyloid syndrome, periodic peritonitis syndrome, Reimann periodic disease, Reimann syndrome, Siegel-Cattan-Mamou syndrome, and Armenian syndrome.

Estimates of the incidence of FMF in specific eastern Mediterranean populations range from 1 in 2000 to 1 in 100, depending on the population studied. Specific mutations in the MEFV gene are more common in certain ethnic groups, and may cause a somewhat different course of the disease. A few mutations in the MEFV gene likely became common in a small population in the eastern Mediterranean several thousand years ago. It is postulated that carrying a single copy of a mutated gene produced a modified (but not abnormal) inflammatory response that may have been protective against some infectious agent at that time. Those who carried a single "beneficial" mutation in the MEFV gene were more likely to survive and reproduce, which may explain the high carrier frequency (up to one in five) in some populations. People of Armenian, Sephardic-Jewish, Arabic, and Turkish ancestry are at greatest risk for FMF. However, a better understanding and recognition of the symptoms of FMF in recent years has resulted in more reports of the condition in other ethnic groups, such as Italians and Armenian-Americans.

Causes and symptoms

FMF is a genetic condition inherited in an autosomal recessive fashion. Mutations in the MEFV gene (short for Mediterranean Fever) on chromosome number 16 are the underlying cause of FMF. Autosomal recessive inheritance implies that a person with FMF has mutations in both copies of the MEFV gene. All genes come in pairs, and one copy of each pair is inherited from each parent. If neither parent of a child with FMF has the condition, it means they carry one mutated copy of the MEFV gene, but also one normal copy, which is enough to protect them from disease. If both parents carry the same autosomal recessive gene, there is a one in four chance in each **pregnancy** that the child will inherit both recessive genes, and thus have the condition.

The MEFV gene carries the instructions for production of a protein called pyrin, named for pyrexia, a medical term for fever. The research group in France that co-discovered the protein named it marenostrin, after ancient Latin words that referred to the Mediterranean Sea. The movement of neutrophils into an area of the body where trauma or infection has occurred is the major cause of inflammation, which is a normal process. Research has shown that pyrin has some function in controlling neutrophils. In a situation where minor trauma or stress occurs, some initial inflammation may follow, but a functional pyrin protein is responsible for shutting-down the response of neutrophils once they are no longer needed. An abnormal pyrin protein associated with FMF may be partly functional, but unstable. In some instances, the abnormal pyrin itself seems to be "stressed", and loses its ability to regulate neutrophils and inflammation. Left unregulated, a normal, mild inflammation spirals out of control. Exactly what causes pyrin in FMF to lose its ability to control neutrophils in some situations is not known.

The recurrent acute attacks of FMF typically begin in childhood or adolescence. Episodes of fever and painful inflammation usually last 12–72 hours. About 90% of people with FMF have their first attack by age 20. The group of symptoms that characterizes FMF includes the following:

Fever

An FMF attack is nearly always accompanied by a fever, but it may not be noticed in every case. Fevers are typically 100–104°F (38–40°C). Some people experience chills prior to the onset of fever.

Abdominal pain

Nearly all people with FMF experience abdominal pain at one point or another, and for most it is the most

KEY TERMS

Acute phase reactants—Blood proteins whose concentrations increase or decrease in reaction to the inflammation process.

Amyloid—A waxy translucent substance composed mostly of protein, that forms plaques (abnormal deposits) in the brain.

Amyloidosis—Accumulation of amyloid deposits in various organs and tissues in the body such that normal functioning of an organ is compromised.

Colchicine—A compound that blocks the assembly of microtubules–protein fibers necessary for cell division and some kinds of cell movements, including neutrophil migration. Side effects may include diarrhea, abdominal bloating, and gas.

Leukocyte—A white blood cell. The neutrophils are a type of leukocyte.

Leukocytosis—An increase in the number of leukocytes in the blood.

Neutrophil—The primary type of white blood cell involved in inflammation. Neutrophils are a type of granulocyte, also known as a polymorphonuclear leukocyte.

Pericarditis—Inflammation of the pericardium, the membrane surrounding the heart.

Peritonitis—Inflammation of the peritoneum, the membrane surrounding the abdominal contents.

Pleuritis—Inflammation of the pleura, the membrane surrounding the lungs.

Pyrexia—A medical term denoting fevers.

Serositis—Inflammation of a serosal membrane. Polyserositis refers to the inflammation of two or more serosal membranes.

Synovitis—Inflammation of the synovium, a membrane found inside joints.

common complaint. The pain can range from mild to severe, and can be diffuse or localized. It can mimic **appendicitis**, and many people with undiagnosed FMF have had appendectomies or exploratory surgery of the abdomen done, only to have the fever and abdominal pain return.

Chest pain

Pleuritis, also called **pleurisy**, occurs in up to half of the affected individuals in certain ethnic groups. The pain is usually on one side of the chest. **Pericarditis** would also be felt as chest pain.

Joint pain

About 50% of people with FMF experience joint pain during attacks. The pain is usually confined to one joint at a time, and often involves the hip, knee, or ankle. For some people, however, the recurrent joint pain becomes chronic arthritis.

Myalgia

Up to 20% of individuals report muscle pain. These episodes typically last less than two days, and tend to occur in the evening or after physical exertion. Rare cases of muscle pain and fever lasting up to one month have been reported.

Skin rash

A rash, described as erysipelas-like erythema, accompanies attacks in a minority of people, and most often occurs on the front of the lower leg or top of the foot. The rash appears as a red, warm, swollen area about 4–6 in (10–15 cm) in diameter.

Amyloidosis

FMF is associated with high levels in the blood of a protein called serum amyloid A (SAA). Over time, excess SAA tends to be deposited in tissues and organs throughout the body. The presence and deposition of excess SAA is known as amyloidosis. Amyloidosis may affect the gastrointestinal tract, liver, spleen, heart, and testes, but effects on the kidneys are of greatest concern. The frequency of amyloidosis varies among the different ethnic groups, and its overall incidence is difficult to determine because of the use of colchicine to avert the problem. Left untreated, however, those individuals who do develop amyloidosis of the kidneys may require a renal transplant, or may even die of renal failure. The frequency and severity of a person's attacks of fever and serositis seem to have no relation to whether they will develop amyloidosis. In fact, a few people with FMF have been described who have had amyloidosis but apparently no other FMF-related symptoms.

Other symptoms

A small percentage of boys with FMF develop painful inflammation around the testes, headaches are a common occurrence during attacks, and certain types of **vasculitis** (inflammation of the blood vessels) seem to be more common in FMF.

Diagnosis

Individually, the symptoms that define FMF are common. Fevers occur for many reasons, and nonspecific pains in the abdomen, chest, and joints are also frequent ailments. Several infections can result in symptoms similar to FMF (Mallaret **meningitis**, for instance), and many people with FMF undergo exploratory abdominal surgery and ineffective treatments before they are finally diagnosed. Membership in a less commonly affected ethnic group may delay or hinder the correct diagnosis.

In general, symptoms involving one or more of the following broad groups should lead to suspicion of FMF: Unexplained recurrent fevers, polyserositis, skin rash, and/or joint pain; abnormal blood studies (see below); and renal or other disease associated with amyloidosis. A family history of FMF or its symptoms would obviously be an important clue, but the recessive nature of FMF means there usually is no family history. The diagnosis may be confirmed when a person with unexplained fever and pain responds to treatment with colchicine since colchicine is not known to have a beneficial effect on any other condition similar to FMF. Abnormal results on a blood test typically include **leukocytosis** (elevated number of neutrophils in the blood), an increased **erythrocyte sedimentation rate** (rate at which red blood cells form a sediment in a blood sample), and increased levels of proteins associated with inflammation (called acute phase reactants) such as SAA.

Direct analysis of the MEFV gene for FMF mutations is the only method to be certain of the diagnosis. However, it is not yet possible to detect all MEFV gene mutations that might cause FMF. Thus, if DNA analysis is negative, clinical methods must be relied upon. If both members of a couple were proven to be FMF carriers through **genetic testing**, highly accurate prenatal diagnosis would be available in any subsequent pregnancy.

Similar syndromes of periodic fever and inflammation include familial Hibernian fever and hyperimmunoglobulinemia D syndrome, but both are more rare than FMF.

Treatment

Colchicine is a chemical compound that can be used as a medication, and is frequently prescribed for **gout**. Some years ago, colchicine was discovered to also be effective in reducing the frequency and severity of attacks in FMF. Treatment for FMF at this point consists of taking colchicine daily. Studies have shown that about 75% of FMF patients achieve complete remission of their symptoms, and about 95% show marked improvement when taking colchicine. Lower effectiveness has been reported, but there is some question about the number of FMF patients who choose not to take their colchicine between attacks when they are feeling well, and thus lose some of the ability to prevent attacks. Compliance with taking colchicine every day may be hampered by its side effects, which include **diarrhea**, nausea, abdominal bloating, and gas. There is a theoretical risk that colchicine use could damage chromosomes in sperms and eggs, or in an embryo during pregnancy, or that it might reduce fertility. However, studies looking at reproduction in men and women who have used colchicine have so far not shown any increased risks. Colchicine is also effective in preventing, delaying, or reversing renal disease associated with amyloidosis.

Other medications may be used as needed to deal with the pain and fever associated with FMF attacks. Dialysis and/or renal transplant might become necessary in someone with advanced kidney disease. Given its genetic nature, there is no cure for FMF, nor is there likely to be in the near future. Any couple that has a child diagnosed with FMF, or anyone with a family history of the condition (especially those in high-risk ethnic groups), should be offered **genetic counseling** to obtain the most up-to-date information on FMF and testing options.

Prognosis

For those individuals who are diagnosed early enough and take colchicine consistently, the prognosis is excellent. Most will have very few, if any, attacks of fever and polyserositis, and will likely not develop serious complications of amyloidosis. The problem of misdiagnosing FMF continues, but education attempts directed at both the public and medical care providers should improve the situation. Future research should provide a better understanding of the inflammation process, focusing on how neutrophils are genetically regulated. That information could then be used to develop treatments for FMF with fewer side effects, and might also assist in developing therapies for other diseases in which abnormal inflammation and immune response are a problem.

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ORGANIZATIONS

National Institute of Arthritis and Musculoskeletal and Skin Diseases. National Institutes of Health, One AMS Circle, Bethesda, MD 20892. <http://www.nih.gov/niams>.
National Organization for Rare Disorders (NORD). PO Box 8923, New Fairfield, CT 06812-8923. (203) 746-6518 or (800) 999-6673. Fax: (203) 746-6481. <http://www.rarediseases.org>.
National Society of Genetic Counselors. 233 Canterbury Dr., Wallingford, PA 19086-6617. (610) 872-1192. <http://www.nsgc.org/GeneticCounselingYou.asp>.

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Familial polyposis

Definition

Familial polyposis is an inherited condition which primarily affects the large intestine (colon and rectum). Large numbers of projecting masses of swollen and thickened or tumorous membrane (polyps) develop on the inner lining of this part of the bowel. The polyps eventually become malignant.

Description

Familial polyposis (FP) is known by many synonyms, most include some combination of words which reflect what is known about the disease. As the disease is inherited, the word, family, is often included. Because these mushroom-like growths are the most obvious manifestation of the disorder, the word, polyp, is usually in the term as well. Adenoma refers to the particular kind of polyp that is typically discovered. Some of the names found in medical texts and journals include polyposis coli, familial colonic polyposis, multiple familial polyposis, familial adenomatous colon polyposis, adenomatosis of the colon and rectum (ACR), and familial adenomatous polyposis (FAP). The last term and its abbreviation have been commonly used since the early 1990s. It will be used in this discussion.

Familial polyposis or familial adenomatous polyposis (FAP) is a premalignant disease. This means that a person with FAP, if left untreated, will invariably develop **cancer**. Individuals with this disorder grow hundreds of polyps throughout their large intestines. The polyps, which may also be called adenomas, commonly develop just after **puberty**. Approximately half of all FAP patients will have polyps by age 14. Ninety percent will have detectable polyps by age 25. Usually by age 35–40, one or more of these polyps will become cancerous.

FAP is a rare disease. One in 8,000 people in the United States have FAP. However, it may be very common in affected families. FAP is inherited in an autosomal dominant pattern. This means that a person with FAP has a 50% chance of passing the condition down to each of their children. FAP can also develop in someone with no family history of the disorder, due to a new genetic mutation in that individual. It is thought that approximately one percent of all colorectal cancers in the United States can be attributed to FAP.

Causes and symptoms

FAP is caused by a portion of a gene that mutates or changes. The original cause of the mutation is unknown. Its exact role in FAP is not completely clear. Researchers theorize that the normal gene directs the manufacture of a protein which helps control cell growth. The mutated gene section in FAP generates an abnormal protein which does not perform its normal function. Cells grow out of control, causing the development of multiple, sometimes hundreds, of polyps. One or more of these eventually becomes cancerous.

Many individuals develop polyps without displaying any symptoms. Others experience such gastrointestinal problems as **diarrhea**, **constipation**, abdominal cramps, blood in the stool, or weight loss. FAP patients may also develop nonmalignant tumors (desmoid tumors), and/or some bone and dental abnormalities. In addition, they may exhibit a "spot" on the retina of the eye (congenital hypertrophy of the retinal pigment epithelium, or CHRPE).

Relatives of individuals with diagnosed FAP are at high risk of having the disease themselves. There are no other known risk factors for this condition.

Diagnosis

The abnormal portion of the gene that causes FAP in most patients can be detected. A blood test can then be performed which identifies family members who have the same mutation. They will eventually develop the condition. Children who have a parent with FAP, and siblings of affected patients whose parental history is incomplete, should be evaluated. The polyps characteristic of FAP have been found in children as young as age five. Testing of appropriate individuals should take place as soon as the diagnosis of FAP is established in one member of a family.

Relatives of people with diagnosed FAP should **exercise** caution regarding where they seek advice and testing. One study of a commercially available blood test found that less than 20% of patients received any **genetic counseling**, and almost one third of their physicians misinterpreted the test results.

Registries for FAP patients can be found at many sites in the United States. Such a registry specializes in identification, assistance, and education of people with a particular disease, and is usually a separate department in a research hospital. A team of health professionals who have expertise in the disorder staff the registry.

Testing within a research setting and/or at a facility with a registry of patients with FAP is more likely to safeguard against problems, such as the misunderstanding of test results. As part of a research project, sometimes counseling as well as blood tests are available at no charge to the patient. Insurance coverage varies. Concerns about confidentiality, and future insurance and employment discrimination, may prompt individuals to pay for the examination out of pocket. Commercial blood tests cost approximately $250 per sample.

If the abnormal gene is found in a family member, annual screening for colon polyps is recommended, beginning at age 11. Flexible **sigmoidoscopy** is used for this examination. It is usually done in a physician's office, or in a hospital department, most often by a gastroenterologist or a surgeon. Food intake may be restricted for 24 hours prior to the procedure. Before the study, the intestine is cleared of stool by one or more small **enemas**. Some physicians prefer to sedate the patient, to help them relax. Then a flexible, lighted, hollow tube (sigmoidoscope) is inserted into the anus and maneuvered into the large intestine. The physician examines the wall of the colon to look for polyps. If polyps are found, one or more may be removed for biopsy.

Most patients report little discomfort during the examination. The procedure itself takes five to fifteen minutes. The patient may be at the facility an hour, or more, if recovery from **sedation** is needed. If no medication was administered, driving and resumption of normal activities are permitted immediately. The cost of the procedure varies widely, but, as of 1997, it was covered by Medicare, indicating the likelihood of other types of insurance coverage.

In some cases the portion of the gene responsible for FAP cannot be identified. Family members of these patients cannot have a predictive blood test. The current recommendation is for these patients to have the same annual examination with flexible sigmoidoscopy as patients with a diagnosed FAP gene. A noninvasive screening **eye examination** to detect CHRPE, associated with FAP, may also be performed.

Treatment

The only definitive treatment for FAP is surgical removal of the lower intestine. Since the goal is to prevent cancer, the operation is done as soon as adenomatous polyps are found on sigmoidoscopy. Waiting until a polyp becomes malignant is unsafe, as the cancer may invade surrounding tissues.

There are several choices about the type of surgery to treat this condition. Some authorities advocate removal of the colon, leaving the rectum or lowest portion of the intestine in place. The small intestine can be attached to the rectum, allowing normal bowel function. This is often called ileorectal anastomosis. Others argue that this section is also liable to develop polyps, needs to be monitored regularly, and may require eventual removal.

Excision of the entire lower intestine with preservation of normal bowel function is possible. This entails a more complex surgical procedure. The patient may experience more complications and a longer recovery period. However, the risk of polyp development in this area is very low. Periodic examination of the intestine may not be needed once healing is complete.

The more intricate surgery may be referred to as a J-pouch procedure, an ileal pouch-anal anastomosis, a restorative proctocolectomy, or an ileoanal reservoir procedure. It involves creating a "pouch" of tissue from the small intestine, which is attached to the anus. This serves as a reservoir or holding area for stool, much as the rectum does normally. The surgery is often done in several stages. A temporary ileostomy, which creates an opening of the small intestines onto the abdomen, is required. When all procedures are completed, and after a recuperation period, the patient regains normal bowel function through the anus.

Some researchers suggest that as **genetic testing** becomes more developed, the specific portion of the gene involved may dictate the type of surgery chosen. Those at high risk of developing **rectal polyps** may be

advised to have the more complex operation. FAP patients felt to be at lower risk for rectal polyps might be counseled to consider the less radical surgery.

Medical therapy to treat the adenomatous polyps has been attempted. Some **nonsteroidal anti-inflammatory drugs** have been effective in reducing the number and size of the polyps. It is possible that these agents will be used as an additional treatment for FAP, but they are unlikely to replace surgery.

Individuals with FAP are at increased risk for cancers of the upper digestive tract including the upper portion of the small bowel (dudodenum) and the channels where bile flows (biliary tract). Cancers of the thyroid, pancreas, and adrenal gland are also more commonly found among FAP patients. Periodic examination for the development of malignancy in these areas is considered part of the treatment of FAP. In some cases, such as cancer involving the duodenum, the tests themselves carry a chance of complications. The risk of the study must be weighed against the potential benefits of knowing the results. Non-malignant growths, called desmoid tumors, also occur more frequently in patients with FAP. Although they are not malignant, they grow quickly into surrounding tissues, causing many difficulties, even **death** in some cases.

Prognosis

The major cause of death in many patients with FAP remains colorectal cancer. One study suggested that even with improved disease recognition, social and emotional factors, such as fear of surgery, may significantly delay a patient's treatment. In recent years, the trend is towards mortality from other causes, such as desmoid tumors or cancers other than colorectal. It has been estimated that a patient with known FAP has a relative risk of dying over three times greater than that of the average population, at a given age.

Prevention

FAP cannot be prevented. Aggressive diagnosis, treatment, and follow-up monitoring are keys to successful management of the disease.

Resources

ORGANIZATIONS

Familial Polyposis Registry. Department of Colorectal Surgery. Cleveland Clinic Foundation. 9500 Euclid Ave., Cleveland OH 44195-5001. (216) 444-6470.

National Organization for Rare Disorders. PO Box 8923, New Fairfield, CT 06812-8923. (800) 999-6673. <http://www.rarediseases.org>.

Ellen S. Weber, MSN

KEY TERMS

Gene—The basic unit of heredity, made of DNA. Each gene occupies certain location on a chromosome.

Mutation—An alteration in a gene, especially one capable of producing a new trait, or a change in function.

Family therapy

Definition

Family therapy is a form of psychotherapy that involves all the members of a nuclear or extended family. It may be conducted by a pair or team of therapists. In many cases the team consists of a man and a woman in order to treat gender-related issues or serve as role models for family members. Although some forms of family therapy are based on behavioral or psychodynamic principles, the most widespread form is based on family systems theory. This approach regards the family, as a whole, as the unit of treatment, and emphasizes such factors as relationships and communication patterns rather than traits or symptoms in individual members.

Family therapy is a relatively recent development in psychotherapy. It began shortly after World War II, when doctors, who were treating schizophrenic patients, noticed that the patients' families communicated in disturbed ways. The doctors also found that the patients' symptoms rose or fell according to the level of tension between their parents. These observations led to considering a family as an organism or system with its own internal rules, patterns of functioning, and tendency to resist change. The therapists started to treat the families of schizophrenic patients as whole units rather than focusing on the hospitalized member. They found that in many cases the family member with **schizophrenia** improved when the "patient" was the family system. (This should not be misunderstood to mean that schizophrenia is caused by family problems, although family problems may worsen the condition.) This approach of involving the entire family in the treatment plan and therapy was then applied to families with problems other than the presence of schizophrenia.

Family therapy is becoming an increasingly common form of treatment as changes in American society are reflected in family structures. It has led to two further developments: couples therapy, which treats relationship

problems between marriage partners or gay couples; and the extension of family therapy to religious communities or other groups that resemble families.

Purpose

Family therapy is often recommended in the following situations:

- Treatment of a family member with schizophrenia or **multiple personality disorder** (MPD). Family therapy helps other family members understand their relative's disorder and adjust to the psychological changes that may be occurring in the relative.
- Families with problems across generational boundaries. These would include problems caused by parents sharing housing with grandparents, or children being reared by grandparents.
- Families that deviate from social norms (common-law relationships, gay couples rearing children, etc.). These families may not have internal problems but may be troubled by outsiders' judgmental attitudes.
- Families with members from a mixture of racial, cultural, or religious backgrounds.
- Families who are scapegoating a member or undermining the treatment of a member in individual therapy.
- Families where the identified patient's problems seem inextricably tied to problems with other family members.
- Blended families with adjustment difficulties.

Most family therapists presuppose an average level of intelligence and education on the part of adult members of the family.

Precautions

Some families are not considered suitable candidates for family therapy. They include:

- families in which one, or both, of the parents is psychotic or has been diagnosed with antisocial or paranoid personality disorder,
- families whose cultural or religious values are opposed to, or suspicious of, psychotherapy,
- families with members who cannot participate in treatment sessions because of physical illness or similar limitations,
- families with members with very rigid personality structures, (here, members might be at risk for an emotional or psychological crisis),
- families whose members cannot or will not be able to meet regularly for treatment,
- families that are unstable or on the verge of breakup.

Description

Family therapy tends to be short-term treatment, usually several months in length, with a focus on resolving specific problems such as eating disorders, difficulties with school, or adjustments to bereavement or geographical relocation. It is not normally used for long-term or intensive restructuring of severely dysfunctional families.

In family therapy sessions, all members of the family and both therapists (if there is more than one) are present at most sessions. The therapists seek to analyze the process of family interaction and communication as a whole; they do not take sides with specific members. They may make occasional comments or remarks intended to help family members become more conscious of patterns or structures that had been previously taken for granted. Family therapists, who work as a team, also model new behaviors for the family through their interactions with each other during sessions.

Family therapy is based on family systems theory, which understands the family to be a living organism that is more than the sum of its individual members. Family therapy uses "systems" theory to evaluate family members in terms of their position or role within the system as a whole. Problems are treated by changing the way the system works rather than trying to "fix" a specific member. Family systems theory is based on several major concepts:

The identified patient

The identified patient (IP) is the family member with the symptom that has brought the family into treatment. The concept of the IP is used by family therapists to keep the family from scapegoating the IP or using him or her as a way of avoiding problems in the rest of the system.

Homeostasis (balance)

The concept of homeostasis means that the family system seeks to maintain its customary organization and functioning over time. It tends to resist change. The family therapist can use the concept of homeostasis to explain why a certain family symptom has surfaced at a given time, why a specific member has become the IP, and what is likely to happen when the family begins to change.

The extended family field

The extended family field refers to the nuclear family, plus the network of grandparents and other members of the extended family. This concept is used to explain the intergenerational transmission of attitudes, problems, behaviors, and other issues.

Differentiation

Differentiation refers to the ability of each family member to maintain his or her own sense of self, while

remaining emotionally connected to the family. One mark of a healthy family is its capacity to allow members to differentiate, while family members still feel that they are "members in good standing" of the family.

Triangular relationships

Family systems theory maintains that emotional relationships in families are usually triangular. Whenever any two persons in the family system have problems with each other, they will "triangle in" a third member as a way of stabilizing their own relationship. The triangles in a family system usually interlock in a way that maintains family homeostasis. Common family triangles include a child and its parents; two children and one parent; a parent, a child, and a grandparent; three siblings; or, husband, wife, and an in-law.

Preparation

In some instances the family may have been referred to a specialist in family therapy by their pediatrician or other primary care provider. It is estimated that as many as 50% of office visits to pediatricians have to do with developmental problems in children that are affecting their families. Some family doctors use symptom checklists or psychological screeners to assess a family's need for therapy.

Family therapists may be either psychiatrists, clinical psychologists, or other professionals certified by a specialty board in marriage and family therapy. They will usually evaluate a family for treatment by scheduling a series of interviews with the members of the immediate family, including young children, and significant or symptomatic members of the extended family. This process allows the therapist(s) to find out how each member of the family sees the problem, as well as to form first impressions of the family's functioning. Family therapists typically look for the level and types of emotions expressed, patterns of dominance and submission, the roles played by family members, communication styles, and the locations of emotional triangles. They will also note whether these patterns are rigid or relatively flexible.

Preparation also usually includes drawing a genogram, which is a diagram that depicts significant persons and events in the family's history. Genograms also include annotations about the medical history and major personality traits of each member. Genograms help in uncovering intergenerational patterns of behavior, marriage choices, family alliances and conflicts, the existence of family secrets, and other information that sheds light on the family's present situation.

Risks

The chief risk in family therapy is the possible unsettling of rigid personality defenses in individuals, or couple relationships that had been fragile before the beginning of therapy. Intensive family therapy may also be difficult for psychotic family members.

KEY TERMS

Blended family—A family formed by the remarriage of a divorced or widowed parent. It includes the new husband and wife, plus some or all of their children from previous marriages.

Differentiation—The ability to retain one's identity within a family system while maintaining emotional connections with the other members.

Extended family field—A person's family of origin plus grandparents, in-laws, and other relatives.

Family systems theory—An approach to treatment that emphasizes the interdependency of family members rather than focusing on individuals in isolation from the family. This theory underlies the most influential forms of contemporary family therapy.

Genogram—A family tree diagram that represents the names, birth order, sex, and relationships of the members of a family. Therapists use genograms to detect recurrent patterns in the family history and to help the members understand their problem(s).

Homeostasis—The tendency of a family system to maintain internal stability and resist change.

Identified patient (IP)—The family member in whom the family's symptom has emerged or is most obvious.

Nuclear family—The basic family unit, consisting of father, mother, and their biological children.

Triangling—A process in which two family members lower the tension level between them by drawing in a third member.

Normal results

Normal results vary, but in good circumstances, they include greater insight, increased differentiation of individual family members, improved communication within the family, loosening of previously automatic behavior patterns, and resolution of the problem that led the family to seek treatment.

Resources

BOOKS

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Rebecca J. Frey

Famine fever *see* **Relapsing fever**

Fanconi's syndrome

Definition

Fanconi's syndrome is a set of kidney malfunctions brought about by a variety of seemingly unrelated disorders. Kidney malfunction leads to excessive urine production and excessive thirst, resulting in deficits of water, calcium, potassium, magnesium, and other substances in the body. It often leads to bone disease and stunted growth.

Description

Normally, kidneys cleanse the blood and keep its salt, water, and acidity in balance, leaving what the body needs in the blood and putting what the body doesn't need into the urine, which leaves the body. This task is performed in two steps. First, the blood is filtered through a kidney structure with small holes that keep the cells and large molecules in the blood. Second, some of the small molecules in the filtrate, needed by the body, are reabsorbed and returned to the bloodstream.

This reabsorption step is defective in Fanconi's syndrome. As a consequence, substances that are normally reabsorbed, like glucose, amino acids, small proteins, water, calcium, potassium, magnesium, bicarbonate, and phosphate, are lost and the body becomes overly acidic.

Fanconi's syndrome is also known as Fanconi syndrome, renal Fanconi syndrome, Fanconi renaltubular syndrome, and Lignac-de Toni-Debré-Fanconi syndrome. Fanconi's anemia is, however, a totally different disease.

Causes and symptoms

Causes

Fanconi's syndrome can be caused by a variety of genetic defects and by certain environmental assaults.

The genetic diseases known to give rise to Fanconi's syndrome are cystinosis (the most common cause in children), **galactosemia**, glycogen storage disease, **hereditary fructose intolerance**, Lowe syndrome, **Wilson disease**, tyrosinemia, medullary cystic disease, vitamin D dependency, and familial idiopathic Fanconi's syndrome.

Environmental assaults that cause Fanconi's syndrome include exposure to heavy metals (like cadmium, lead, mercury, platinum, uranium), certain drugs (like outdated tetracycline and gentamicin), other substances (like Lysol, paraquat, toluene, the amino acid lysine taken as a nutritional supplement), and **kidney transplantation**.

Symptoms

Fanconi's syndrome symptoms related directly to impaired absorption include excessive urine production and urination; excessive thirst; **dehydration**; **constipation**; **anorexia nervosa**; vomiting; elevated levels of glucose, phosphate, calcium, uric acid, amino acids, and protein (especially beta$_2$-microglobulin and lysozyme) in the urine; elevated levels of chloride and decreased levels of phosphate and calcium in the blood; and excessively acidic blood.

The most noticeable indirect consequences of impaired reabsorption are the bone diseases, rickets and osteomalacia. Rickets affects children and is associated with bone deformities, failure to grow, and difficulty walking. If a person acquires Fanconi's syndrome as an adult, the bone disease is termed osteomalacia and is accompanied by severe bone **pain** and spontaneous **fractures**. Unlike rickets due to **malnutrition**, these diseases cannot be reversed with vitamin D. Muscle weakness and occasional **paralysis** are other indirect consequences of the ineffective reabsorption.

Diagnosis

Diagnosis of Fanconi's syndrome can be made by urine and blood tests. It is also important to find the underlying cause to decide on the best treatment. Other symptoms specific to a particular patient will point to other useful diagnostic tests. For example, high levels of

blood galactose in conjunction with symptoms of Fanconi's syndrome indicate the patient is suffering from galactosemia, while high blood levels of cadmium indicate the patient is suffering from cadmium **poisoning**.

Treatment

Fanconi's syndrome is best treated by attacking the underlying cause whenever possible. For example, when cystinosis is treated with the drug cysteamine to lower cystine levels in the body or Wilson disease is treated with penicillamine to lower the levels of copper, accompanying symptoms of Fanconi's syndrome will subside. If the patient has acquired the disease from a heavy metal or another toxic agent, all contact with the toxic agent should stop; the condition will then likely disappear.

Nevertheless, additional treatment will be necessary either when it's not possible to treat the underlying cause or while waiting for the kidneys to resume normal function. This is done by restricting sodium chloride (table salt), giving **antacids** to counteract the excessive acidity of the blood, and supplying potassium supplements.

Kidney transplant is the treatment of last resort, used for patients whose kidneys have failed.

Prognosis

Fanconi's syndrome can be reversible. Fanconi's syndrome caused by kidney transplantation usually reverses itself within the first year after transplant surgery. When caused by a toxin in the environment, Fanconi's syndrome generally can be reversed by removing the causative agent from the patient's environment. If it is caused by a genetic disease, it can usually be reversed by treating the disease. However, if Fanconi's syndrome is not treated or if treatment is unsuccessful, the kidneys can fail.

Prevention

Fanconi's syndrome caused secondarily by the genetic diseases galactosemia, glycogen storage disease, hereditary fructose intolerance, and tyrosinemia is prevented by appropriate dietary restrictions to treat the genetic disease, starting in infancy.

Fanconi's syndrome caused by heavy metals and other toxins can be prevented by avoiding these substances.

Resources

BOOKS

Bergeron, Michael, André Gougoux, and Patrick Vinay. "The Renal Fanconi Syndrome." In *The Metabolic and Molecular Bases of Inherited Disease*. 7th ed. Ed. Charles R. Scriver, et al. New York: McGraw-Hill, Inc., 1995.

KEY TERMS

Acidosis—Condition where the body is more acidic than normal; associated with headache, nausea, vomiting, and visual disturbances.

Fanconi's anemia—An inherited form of aplastic anemia.

Filtrate—The part of filtered material that flows through the filter.

Idiopathic—Refers to a disease of unknown cause.

Polydipsia—Excessive thirst.

Polyuria—Excessive production of urine.

ORGANIZATIONS

The American Society of Nephrology. 2025 M Street NW #800, Washington, DC 20036. (202) 367-1190. <http://www.asn-online.com>.

National Kidney Foundation. 30 East 33rd St., New York, NY 10016. (800) 622-9010. <http://www.kidney.org>.

OTHER

"Online Mendelian Inheritance in Man." OMIM Homepage. <http://www.ncbi.nlm.nih.gov/Omim>.

Lorraine Lica, PhD

Farsightedness *see* **Hyperopia**

FAS *see* **Fetal alcohol syndrome**

Fasciotomy

Definition

Fasciotomy is a surgical procedure that cuts away the fascia to relieve tension or pressure

Purpose

The fascia is thin connective tissue covering, or separating, the muscles and internal organs of the body. It varies in thickness, density, elasticity, and composition, and is different from ligaments and tendons.

The fascia can be injured either through constant strain or through trauma. Fasciitis is an inflammation of the fascia. The most common condition for which fasciotomy is performed is plantar fasciitis, an inflammation of the fascia on the bottom of the foot that is sometimes called a heel spur or stone bruise.

Plantar fasciitis is caused by long periods on the feet, being overweight, and wearing shoes that do not support the foot well. Teachers, mail carriers, runners, and others who make heavy use of their feet are especially likely to suffer from plantar fasciitis.

Plantar fasciitis results in moderate to disabling heel **pain**. If nine to twelve months of conservative treatment (reducing time on feet, non-steroid anti-inflammatory drugs, arch supports) under the supervision of a doctor does not result in pain relief, a fasciotomy may be done. Fasciotomy removes a small portion of the fascia to relieve tension and pain. Connective tissue grows back into the cut space left by the cut, effectively lengthening the fascia.

When a fasciotomy is performed on other parts of the body, it is usually done to relieve pressure from a compression injury to a limb. This type of injury often occurs during contact sports. The blood vessels of the limb are damaged. They swell and leak, causing inflammation. Fluid builds up in the area contained by the fascia. A fasciotomy is done to relieve this pressure and prevent tissue **death**. Similar injury occurs in high voltage electrical **burns** where deep tissue damage occurs.

Precautions

In the case of injury, fasciotomy is done on an emergency basis, and the outcome of the surgery depends largely on the general health of the patient. Plantar fasciotomies are appropriate for most people whose foot problems cannot be resolved in any other way.

Description

Fasciotomy in the limbs is usually done by a surgeon under general or regional anesthesia. An incision is made in the skin, and a small area of fascia is removed where it will best relieve pressure. Then the incision is closed.

Plantar fasciotomy is an endoscopic (performed with the use of an endoscope) procedure. It is done by a foot specialist in a doctor's office or outpatient surgical clinic under local anesthesia and takes 20 minutes to one hour. The doctor makes two small incisions on either side of the heel. An endoscope is inserted in one to guide the doctor in where to cut. A tiny knife is inserted in the other. A portion of the fascia is cut from near the heel; then the incisions are closed.

Preparation

Little preparation is done before a fasciotomy. When the fasciotomy is related to burn injuries, the fluid and electrolyte status of the patient are constantly monitored.

KEY TERMS

Endoscope—A tube that contains a tiny camera and light, that is inserted in the body to allow a doctor to see inside without making a large incision.

Aftercare

Aftercare depends on the reason for the fasciotomy. People who have endoscopic plantar fasciotomy can walk without pain almost immediately, return to wearing their regular shoes within three to five days, and return to normal activities within three weeks. Most will need to wear arch supports in their shoes.

Risks

In endoscopic plantar fasciotomy, the greatest risk is that the arch will drop slightly as a result of this surgery, causing other foot problems. Risks involved with other types of fasciotomy are those associated with the administration of anesthesia and the development of blood clots.

Normal results

Fasciotomy in the limbs reduces pressure, thus reducing tissue death. Endoscopic plantar fasciotomy has a success rate of 90–95%.

Resources

BOOKS

"Blast Injuries." In *Current Surgical Diagnosis and Treatment*. 10th ed. Ed. Lawrence W. Way. Stamford: Appleton & Lange, 1994.

OTHER

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Tish Davidson

Fasting

Definition

Fasting is voluntarily not eating food for varying lengths of time. Fasting is used as a medical therapy for many conditions. It is also a spiritual practice in many religions.

Purpose

Fasting can be used for nearly every chronic condition, including **allergies**, **anxiety**, arthritis, **asthma**, depression, diabetes, headaches, heart disease, **high cholesterol**, low blood sugar, digestive disorders, mental illness, and **obesity**. Fasting is an effective and safe weight loss method. It is frequently prescribed as a **detoxification** treatment for those with conditions that may be influenced by environmental factors, such as **cancer** and **multiple chemical sensitivity**. Fasting has been used successfully to help treat people who have been exposed to high levels of toxic materials due to accident or occupation. Fasting is thought to be beneficial as a preventative measure to increase overall health, vitality, and resistance to disease. Fasting is also used as a method of mental and spiritual rejuvenation.

Description

Origins

Used for thousands of years, fasting is one of the oldest therapies in medicine. Many of the great doctors of ancient times and many of the oldest healing systems have recommended it as an integral method of healing and prevention. Hippocrates, the father of Western medicine, believed fasting enabled the body to heal itself. Paracelsus, another great healer in the Western tradition, wrote 500 years ago that "fasting is the greatest remedy, the physician within." **Ayurvedic medicine**, the world's oldest healing system, has long advocated fasting as a major treatment.

Fasting has also been used in nearly every religion in the world, including Christianity, Judaism, Buddhism, and Islam. Many of history's great spiritual leaders fasted for mental and spiritual clarity, including Jesus, Buddha, and Mohammed. In one of the famous political acts of the last century, the Indian leader Mahatma Gandhi fasted for 21 days to promote peace.

Fasting has been used in Europe as a medical treatment for years. Many spas and treatment centers, particularly those in Germany, Sweden, and Russia, use medically supervised fasting. Fasting has gained popularity in American alternative medicine over the past several decades, and many doctors feel it is beneficial. Fasting is a central therapy in detoxification, a healing method founded on the principle that the build up of toxic substances in the body is responsible for many illnesses and conditions.

The principle of fasting is simple. When the intake of food is temporarily stopped, many systems of the body are given a break from the hard work of digestion. The extra energy gives the body the chance to heal and restore itself, and burning stored calories gets rid of toxic substances stored in the body.

The digestive tract is the part of the body most exposed to environmental threats, including bacteria, viruses, parasites, and toxins. It requires the most immune system support. When food is broken down in the intestines, it travels through the blood to the liver, the largest organ of the body's natural detoxification system. The liver breaks down and removes the toxic by-products produced by digestion, including natural ones and the chemicals now present in the food supply. During fasting, the liver and immune system are essentially freed to detoxify and heal other parts of the body.

Many healers claim that fasting is a particularly useful therapy for Americans and for the modern lifestyle, subjected to heavy **diets**, overeating, and constant exposure to food additives and chemicals. Some alternative practitioners have gone so far as to estimate that the average American is carrying 5-10 pounds of toxic substances in their bodies, for which fasting is the quickest and most effective means of removal.

Physiology of fasting

Through evolution, the body became very efficient at storing energy and handling situations when no food was available. For many centuries, fasting was probably a normal occurrence for most people, and the body adapted to it. It is estimated that even very thin people can survive for 40 days or more without food. The body has a special mechanism that is initiated when no food is eaten. Fasting is not **starvation**, but rather the body's burning of stored energy. Starvation occurs when the body no longer has any stored energy and begins using essential tissues such as organs for an energy source. Therapeutic fasts are stopped long before this happens.

Many physiological changes occur in the body during fasting. During the first day or so, the body uses its glycogen reserves, the sugars that are the basic energy supply. After these are depleted, the body begins using fat. However, the brain, which has high fuel requirements, still needs glucose (sugars converted from glycogen). To obtain glucose for the brain, the body begins to break down muscle tissue during the second day of the fast. Thus, during fasting some muscle loss will occur. To fuel the brain, the body would need to burn over a pound of muscle a day, but the body has developed another way to create energy that saves important muscle mass. This protein-sparing process is called ketosis, which occurs during the third day of a fast for men and the second day for women. In this highly efficient state, the liver begins converting stored fat and other nonessential tissues into ketones, which can be used by the brain, muscles, and

heart as energy. It is at this point in the fast that sensations of hunger generally go away, and many people experience normal or even increased energy levels. Hormone levels and certain functions become more stable in this state as well. The goal of most fasts is to allow the body to reach the ketosis state in order to burn excess fat and unneeded or damaged tissue. Thus, fasts longer than three days are generally recommended as therapy.

Weight loss occurs most rapidly during the first few days of a fast, up to 2 pounds per day. In following days, the figure drops to around 0.5 pound per day. An average weight loss of a pound a day for an entire fast can be expected.

Performing a fast

Fasts can be performed for varying lengths of time, depending on the person and his or her health requirements. For chronic conditions, therapists recommend from two to four weeks to get the most benefits. Seven-day fasts are also commonly performed. A popular fasting program for prevention and general health is a three-day fast taken four times per year, at the change of each season. These can be easily performed over long weekends. Preventative fasts of one day per week are used by many people as well.

Juice fasts are also used by many people, although these are not technically fasts. Juice fasts are less intensive than water fasts because the body doesn't reach the ketosis stage. The advantage of juice fasts is that fruit and vegetable drinks can supply extra energy and nutrients. People can fit a few days of juice fasting into their normal schedules without significant drops in energy. Juice fasts are also said to have cleansing and detoxifying effects. The disadvantage of juice fasts is that the body never gets to the ketosis stage, so these fasters are thought to lack the deep detoxification and healing effects of the water fast.

Medical supervision is recommended for any fast over three days. Most alternative medicine practitioners, such as homeopaths, naturopathic doctors, and ayurvedic doctors, can supervise and monitor patients during fasts. Those performing extended fasts and those with health conditions may require blood, urine, and other tests during fasting. There are many alternative health clinics that perform medically supervised fasts as well. Some conventional medical doctors may also supervise patients during fasts. Costs and insurance coverage vary, depending on the doctor, clinic, and requirements of the patient.

Preparations

Fasts must be entered and exited with care. To enter a fast, the diet should be gradually lightened over a few days. First, heavy foods such as meats and dairy products should be eliminated for a day or two. Grains, nuts, and beans should then be reduced for several days. The day before a fast, only easily digested foods like fruits, light salads, and soups should be eaten. During the fast, only pure water and occasional herbal teas should be drunk.

Fasts should be ended as gradually as they are entered, going from lighter to heavier foods progressively. The diet after a fast should emphasize fresh, wholesome foods. Fasters should particularly take care not to overeat when they complete a fast.

Precautions

Fasting isn't appropriate for everyone and, in some cases, could be harmful. Any person undertaking a first fast longer than three days should seek medical supervision. Those with health conditions should always have medical support during fasting. Plenty of water should be taken by fasters since **dehydration** can occur. Saunas and sweating therapies are sometimes recommended to assist detoxification, but should be used sparingly. Those fasting should significantly slow down their lifestyles. Taking time off of work is helpful, or at least reducing the work load. Fasters should also get plenty of rest. **Exercise** should be kept light, such as walking and gentle stretching.

Side effects

Those fasting may experience side effects of **fatigue**, malaise, aches and pains, emotional duress, **acne**, headaches, allergies, swelling, vomiting, **bad breath**, and symptoms of colds and flu. These reactions are sometimes called *healing crises*, which are caused by temporarily increased levels of toxins in the body due to elimination and cleansing. Lower energy levels should be expected during a fast.

Research and general acceptance

The physiology of fasting has been widely studied and documented by medical science. Beneficial effects such as lowered cholesterol and improved general functioning have been shown. Fasting as a treatment for illness and disease has been studied less, although some studies around the world have shown beneficial results. A 1984 study showed that workers in Taiwan who had severe chemical **poisoning** had dramatic improvement after a ten-day fast. In Russia and Japan, studies have demonstrated fasting to be an effective treatment for mental illness. Fasting has been featured on the cover of medical journals, although mainstream medicine has generally ignored fasting and detoxification treatments as valid medical procedures.

KEY TERMS

Ayurvedic medicine—A traditional healing system developed in India.

Toxin—A substance that has poisonous effects on the body.

The majority of research that exists on fasting is testimonial, consisting of individual personal accounts of healing without statistics or controlled scientific experiments. In the alternative medical community, fasting is an essential and widely accepted treatment for many illnesses and chronic conditions.

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Douglas Dupler

Fasting blood sugar test *see* **Blood sugar tests**

Fasting plasma glucose test *see* **Blood sugar tests**

Fatigue

Definition

Fatigue is physical and/or mental exhaustion that can be triggered by **stress**, medication, overwork, or mental and physical illness or disease.

Description

Everyone experiences fatigue occasionally. It is the body's way of signaling its need for rest and sleep. But when fatigue becomes a persistent feeling of tiredness or exhaustion that goes beyond normal sleepiness, it is usually a sign that something more serious is amiss.

Physically, fatigue is characterized by a profound lack of energy, feelings of muscle weakness, and slowed movements or central nervous system reactions. Fatigue can also trigger serious mental exhaustion. Persistent fatigue can cause a lack of mental clarity (or feeling of mental "fuzziness"), difficulty concentrating, and in some cases, memory loss.

Causes and symptoms

Fatigue may be the result of one or more environmental causes such as inadequate rest, improper diet, work and home stressors, or poor physical conditioning, or one symptom of a chronic medical condition or disease process in the body. Heart disease, low blood pressure, diabetes, end-stage renal disease, iron-deficiency anemia, **narcolepsy**, and **cancer** can cause long-term, ongoing fatigue symptoms. Acute illnesses such as viral and bacterial infections can also trigger temporary feelings of exhaustion. In addition, mental disorders such as depression can also cause fatigue.

A number of medications, including **antihistamines**, **antibiotics**, and blood pressure medications, may cause drowsiness as a side-effect. Individuals already suffering from fatigue who are prescribed one of these medications may wish to check with their healthcare provider about alternative treatments.

Extreme fatigue which persists, unabated, for at least six months, is not the result of a diagnosed disease or illness, and is characterized by flu-like symptoms such as swollen lymph nodes, **sore throat**, and muscle weakness and/or **pain** may indicate a diagnosis of **chronic fatigue syndrome**. Chronic fatigue syndrome (sometimes called chronic fatigue immune deficiency syndrome), is a debilitating illness that causes overwhelming exhaustion and a constellation of neurological and immunological symptoms. Between 1.5 and 2 million Americans are estimated to suffer from the disorder.

Diagnosis

Because fatigue is a symptom of a number of different disorders, diseases, and lifestyle choices, diagnosis may be difficult. A thorough examination and patient history by a qualified healthcare provider is the first step in determining the cause of the fatigue. A physician can rule out physical conditions and diseases that feature fatigue as a symptom, and can also determine if prescription drugs, poor dietary habits, work environment, or other external stressors could be triggering the exhaustion. Several diagnostic tests may also be required to rule

out common physical causes of exhaustion, such as blood tests to check for iron-deficiency anemia.

Diagnosis of chronic fatigue syndrome is significantly more difficult. Because there is no specific biological marker or conclusive blood test to check for the disorder, healthcare providers must rely on the patient's presentation and severity of symptoms to make a diagnosis. In many cases, individuals with chronic fatigue syndrome go through a battery of invasive diagnostic tests and several years of consultation with medical professionals before receiving a correct diagnosis.

Treatment

Conventional medicine recommends the dietary and lifestyle changes outlined above as a first line of defense against fatigue. Individuals who experience occasional fatigue symptoms may benefit from short term use of caffeine-containing central nervous stimulants, which make people more alert, less drowsy, and improve coordination. However, these should be prescribed with extreme caution, as overuse of the drug can lead to serious **sleep disorders**, like **insomnia**.

Another reason to avoid extended use of **caffeine** is its associated withdrawal symptoms. People who use large amounts of caffeine over long periods build up a tolerance to it. When that happens, they have to use more and more caffeine to get the same effects. Heavy caffeine use can also lead to dependence. If an individual stops using caffeine abruptly, withdrawal symptoms may occur, including **headache**, fatigue, drowsiness, yawning, irritability, restlessness, vomiting, or runny nose. These symptoms can go on for as long as a week.

Alternative treatment

The treatment of fatigue depends on its direct cause, but there are several commonly prescribed treatments for non-specific fatigue, including dietary and lifestyle changes, the use of essential oils and herbal therapies, deep breathing exercises, **traditional Chinese medicine**, and color therapy.

Dietary changes

Inadequate or inappropriate nutritional intake can cause fatigue symptoms. To maintain an adequate energy supply and promote overall physical well-being, individuals should eat a balanced diet and observe the following nutritional guidelines:

- Drink plenty of water. Individuals should try to drink 9 to 12 glasses of water a day. **Dehydration** can reduce blood volume, which leads to feelings of fatigue.
- Eat iron-rich foods (i.e., liver, raisins, spinach, apricots). Iron enables the blood to transport oxygen throughout the tissues, organs, and muscles, and diminished oxygenation of the blood can result in fatigue.
- Avoid high-fat meals and snacks. High fat foods take longer to digest, reducing blood flow to the brain, heart, and rest of the body while blood flow is increased to the stomach.
- Eat unrefined carbohydrates and proteins together for sustained energy.
- Balance proteins. Limiting protein to 15–20 grams per meal and two snacks of 15 grams is recommended, but not getting enough protein adds to fatigue. Pregnant or breastfeeding women should get more protein.
- Get the recommended daily allowance of B complex **vitamins** (specifically, pantothenic acid, **folic acid**, thiamine, and vitamin B_{12}). Deficiencies in these vitamins can trigger fatigue.
- Get the recommended daily allowance of selenium, riboflavin, and niacin. These are all essential nutritional elements in metabolizing food energy.
- Control portions. Individuals should only eat when they're hungry, and stop when they're full. An overstuffed stomach can cause short-term fatigue, and individuals who are overweight are much more likely to regularly experience fatigue symptoms.

Lifestyle changes

Lifestyle factors such as a high-stress job, erratic work hours, lack of social or family support, or erratic sleep patterns can all cause prolonged fatigue. If stress is an issue, a number of relaxation therapies and techniques are available to help alleviate tension, including massage, **yoga**, **aromatherapy**, **hydrotherapy**, progressive relaxation exercises, **meditation**, and **guided imagery**. Some individuals may also benefit from individual or family counseling or psychotherapy sessions to work through stress-related fatigue that is a result of family or social issues.

Maintaining healthy sleep patterns is critical to proper rest. Having a set "bedtime" helps to keep sleep on schedule. A calm and restful sleeping environment is also important to healthy sleep. Above all, the bedroom should be quiet and comfortable, away from loud noises and with adequate window treatments to keep sunlight and streetlights out. Removing distractions from the bedroom such as televisions and telephones can also be helpful.

Essential oils

Aromatherapists, hydrotherapists, and other holistic healthcare providers may recommend the use of essential

oils of rosemary (*Rosmarinus officinalis*), eucalyptus blue gum (*Eucalyptus globulus*), peppermint, (*Mentha x piperata*), or scots pine oil (*Pinus sylvestris*) to stimulate the nervous system and reduce fatigue. These oils can be added to bathwater or massage oil as a topical application. Citrus oils such as lemon, orange, grapefruit, and lime have a similar effect, and can be added to a steam bath or vaporizer for inhalation.

Herbal remedies

Herbal remedies that act as circulatory stimulants can offset the symptoms of fatigue in some individuals. An herbalist may recommend an infusion of ginger (*Zingiber officinale*) root or treatment with cayenne (*Capsicum annuum*), balmony (*Chelone glabra*), damiana (*Turnera diffusa*), ginseng (*Panax ginseng*), or rosemary (*Rosmarinus officinalis*) to treat ongoing fatigue.

An infusion is prepared by mixing the herb with boiling water, steeping it for several minutes, and then removing the herb from the infusion before drinking. A strainer, tea ball, or infuser can be used to immerse loose herb in the boiling water before steeping and separating it. A second method of infusion is to mix the loose herbal preparation with cold water first, bringing the mixture to a boil in a pan or teapot, and then separating the tea from the infusion with a strainer before drinking.

Caffeine-containing **central nervous system stimulants** such as tea (*Camellia senensis*) and cola (*Cola nitida*) can provide temporary, short-term relief of fatigue symptoms. However, long-term use of caffeine can cause restlessness, irritability, and other unwanted side effects, and in some cases may actually work to increase fatigue after the stimulating effects of the caffeine wear off. To avoid these problems, caffeine intake should be limited to 300 mg or less a day (the equivalent of 4-8 cups of brewed, hot tea).

Traditional Chinese medicine

Chinese medicine regards fatigue as a blockage or misalignment of *qi*, or energy flow, inside the human body. The practitioner of Chinese medicine chooses **acupuncture** and/or herbal therapy to rebalance the entire system. The Chinese formula Minot Bupleurum soup (or Xiao Chia Hu Tang) has been used for nearly 2,000 years for the type of chronic fatigue that comes after the flu. In this condition, the person has low-grade **fever**, nausea, and fatigue. There are other formulas that are helpful in other cases. Acupuncture involves the placement of a series of thin needles into the skin at targeted locations on the body known as acupoints in order to harmonize the energy flow within the human body.

KEY TERMS

Aromatherapy—The therapeutic use of plant-derived, aromatic essential oils to promote physical and psychological well-being.

Guided imagery—The use of relaxation and mental visualization to improve mood and/or physical well-being.

Hydrotherapy—Hydrotherapy, or water therapy, is use of water (hot, cold, steam, or ice) to relieve discomfort and promote physical well-being.

Deep breathing exercises

Individuals under stress often experience fast, shallow breathing. This type of breathing, known as chest breathing, can lead to **shortness of breath**, increased muscle tension, inadequate oxygenation of blood, and fatigue. Breathing exercises can both improve respiratory function and relieve stress and fatigue.

Deep breathing exercises are best performed while laying flat on the back on a hard surface, usually the floor. The knees are bent, and the body (particularly the mouth, nose, and face) is relaxed. One hand should be placed on the chest and one on the abdomen to monitor breathing technique. With proper breathing techniques, the abdomen will rise further than the chest. The individual takes a series of long, deep breaths through the nose, attempting to raise the abdomen instead of the chest. Air is exhaled through the relaxed mouth. Deep breathing can be continued for up to 20 minutes. After the **exercise** is complete, the individual checks again for body tension and relaxation. Once deep breathing techniques have been mastered, an individual can use deep breathing at any time or place as a quick method of relieving tension and preventing fatigue.

Color therapy

Color therapy, also known as chromatherapy, is based on the premise that certain colors are infused with healing energies. The therapy uses the seven colors of the rainbow to promote balance and healing in the mind and body. Red promotes energy, empowerment, and stimulation. Physically, it is thought to improve circulation and stimulate red blood cell production. Red is associated with the seventh chakra, located at the root; or base of spine. In yoga, the chakras are specific spiritual energy centers of the body.

Therapeutic color can be administered in a number of ways. Practitioners of Ayurvedic, or traditional Indian

medicine, wrap their patients in colored cloth chosen for its therapeutic hue. Individuals suffering from fatigue would be wrapped in reds and oranges chosen for their uplifting and energizing properties. Patients may also be bathed in light from a color filtered light source to enhance the healing effects of the treatment.

Individuals may also be treated with color-infused water. This is achieved by placing translucent red colored paper or colored plastic wrap over and around a glass of water and placing the glass in direct sunlight so the water can soak up the healing properties and vibrations of the color. Environmental color sources may also be used to promote feelings of stimulation and energy. Red wall and window treatments, furniture, clothing, and even food may be recommended for their energizing healing properties.

Color therapy can be used in conjunction with both hydrotherapy and aromatherapy to heighten the therapeutic effect. Spas and holistic healthcare providers may recommend red color baths or soaks, which combine the benefits of a warm or hot water soak with energizing essential oils and the fatigue-fighting effects of bright red hues used in color therapy.

Prognosis

Fatigue related to a chronic disease or condition may last indefinitely, but can be alleviated to a degree through some of the treatment options outlined here. Exhaustion that can be linked to environmental stressors is usually easily alleviated when those stressors are dealt with properly.

There is no known cure for chronic fatigue syndrome, but steps can be taken to lessen symptoms and improve quality of life for these individuals while researchers continue to seek a cure.

Prevention

Many of the treatments outlined above are also recommended to prevent the onset of fatigue. Getting adequate rest and maintaining a consistent bedtime schedule are the most effective ways to combat fatigue. A balanced diet and moderate exercise program are also important to maintaining a consistent energy level.

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Paula Ford-Martin

Fatty liver

Definition

Fatty liver is the collection of excessive amounts of triglycerides and other fats inside liver cells.

Description

Also called steatosis, fatty liver can be a temporary or long-term condition, which is not harmful itself, but may indicate some other type of problem. Left untreated, it can contribute to other illnesses. It is usually reversible once the cause of the problem is diagnosed and corrected. The liver is the organ responsible for changing fats eaten in the diet to types of fat that can be stored and used by the body. Triglycerides are one of the forms of fat stored by the body and used for energy and new cell formation. The break down of fats in the liver can be disrupted by **alcoholism**, **malnutrition**, **pregnancy**, or **poisoning**. In fatty liver, large droplets of fat, containing mostly triglycerides, collect within cells of the liver. The condition is generally not painful and may go unnoticed for a long period of time. In severe cases, the liver can increase to over three times its normal size and may be painful and tender.

Causes and symptoms

The most common cause of fatty liver in the United States is alcoholism. In alcoholic fatty liver, over consumption of alcohol changes the way that the liver breaks down and stores fats. Often, people with chronic alcoholism also suffer from malnutrition by eating irregularly and not consuming a balanced diet. Conditions that can also cause fatty liver are other forms of malnutrition (especially when there is not enough protein in the diet), **obesity**, **diabetes mellitus**, and **Reye's syndrome** in children. Pregnancy can cause a rare, but serious form of fatty liver that starts late in pregnancy and may be associated with **jaundice** and liver failure. Some drug overdoses or toxic chemical poisonings, such as carbon tetrachloride, can also cause fatty liver.

Often, there are no symptoms associated with fatty liver. If there are symptoms, they can include **pain** under the rib cage on the right side of the body, swelling of the

abdomen, jaundice, and **fever**. Symptoms that occur less often in alcoholic fatty liver, but more often in pregnancy related fatty liver, are nausea, vomiting, loss of appetite, and abdominal pain.

Diagnosis

During a **physical examination**, a doctor might notice that the liver is enlarged and tender when the abdomen is palpated (examined with the tips of the fingers while the patient lies flat). Blood tests may be used to determine if the liver is functioning properly. A **liver biopsy**, where a small sample of liver tissue is removed with a long needle or though a very small incision, can be used to confirm fatty liver. In pregnant women, the fatty liver condition is usually associated with another serious complication, pre-eclampsia or eclampsia. In this condition, the mother has seriously high blood pressure, swelling, and possibly, seizures. Laboratory abnormalities include elevations of the SGOT (serum glutamic-oxaloacetic transaminase) and SGPT (serum glutamic pyruvic transaminase). In many cases the alkaline phosphatase will be significantly elevated due to **cholestasis** produced by the fatty infiltration.

Treatment

Treatment involves correcting the condition that caused fatty liver and providing supportive care. In fatty liver caused by alcoholism, the treatment is to give up drinking alcohol and to eat a healthy, well balanced diet. In fatty liver associated with pregnancy, the recommended treatment is to deliver the baby, if the pregnancy is far enough along. Vitamin and mineral supplements along with nutritional support may be useful.

Prognosis

Fatty liver is usually reversible if recognized and treated. There may be some long-term tendency toward other types of liver problems depending on how long and how severe the fatty liver condition was. In pregnant women with the condition, the situation can be life threatening for both the mother and the infant. Left untreated, there is a high risk of **death** for both the mother and baby. Severe liver damage that may require a liver transplant can occur in the mother if the condition is not recognized early.

Prevention

Prevention consists of maintaining a well balanced diet and healthy lifestyle with moderate or no alcohol consumption. Pregnant women require good prenatal care so that symptoms can be recognized and treated as early as possible. To prevent Reye's syndrome, children should not be given **aspirin** to treat symptoms of the flu or other viruses.

KEY TERMS

Jaundice—A condition where the skin and whites of the eyes take on a yellowish color due to an increase of bilirubin (a compound produced by the liver) in the blood.

Reye's syndrome—A serious, life-threatening illness in children, usually developing after a bout of flu or chickenpox, and often associated with the use of aspirin. In fatal cases, there is evidence of accumulation of fat in the liver.

Triglycerides—A type of fat consumed in the diet and produced by and stored in the body as an energy source.

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Altha Roberts Edgren

Febrile agglutination tests *see* **Fever evaluation tests**

Fecal fat test *see* **Stool fat test**

Fecal incontinence

Definition

Fecal incontinence is the inability to control the passage of gas or stools (feces) through the anus. For some

people fecal incontinence is a relatively minor problem, as when it is limited to a slight occasional soiling of underwear, but for other people it involves a considerable loss of bowel control and has a devastating effect on quality of life and psychological well-being. Fortunately, professional medical treatment is usually able to restore bowel control or at least substantially reduce the severity of the condition.

Description

Fecal incontinence, also called bowel incontinence, can occur at any age, but is most common among people over the age of 65, who sometimes have to cope with **urinary incontinence** as well. It was reported in 1998 that about 2% of adults experience fecal incontinence at least once a week whereas for healthy independent adults over the age of 65 the figure is about 7%. An extensive American survey, published in 1993, found fecal soiling in 7.1% of the surveyed population, with gross incontinence in 0.7%. For men and women the incidence of soiling was the same, but women were almost twice as likely to suffer from gross incontinence.

The wider public health impact of fecal incontinence is considerable. In the United States, more than $400 million is spent each year on disposable underwear and other incontinence aids. Fecal incontinence is the second most common reason for seeking a nursing home placement. One-third of the institutionalized elderly suffer from this condition. Incontinence sufferers, however, often hesitate to ask their doctors for help because they are embarrassed or ashamed. The 1993 American survey discovered that only one-sixth of those experiencing soiling had sought medical advice, and only one-half of those afflicted with gross incontinence.

Causes and symptoms

Fecal incontinence can result from a wide variety of medical conditions, including childbirth-related anal injuries, other causes of damage to the anus or rectum, and nervous system problems.

Vaginal-delivery **childbirth** is a major cause of fecal incontinence. In many cases, childbirth results in damage to the anal sphincter, which is the ring of muscle that closes the anus and keeps stools within the rectum until a person can find an appropriate opportunity to defecate. Nerve injuries during childbirth may also be a factor in some cases. An ultrasound study of first-time mothers found sphincter injuries in 35%. About one-third of the injured women developed fecal incontinence or an uncontrollable and powerful urge to defecate (urgency) within six weeks of giving birth. Childbirth-related incontinence is usually restricted to gas, but for some women involves the passing of liquid or solid stools.

The removal of **hemorrhoids** by surgery or other techniques (hemorrhoidectomies) can also cause anal damage and fecal incontinence, as can more complex operations affecting the anus and surrounding areas. Anal and rectal infections as well as **Crohn's disease** can lead to incontinence by damaging the muscles that control defecation. For some people, incontinence becomes a problem when the anal muscles begin to weaken in midlife or old age.

Dementia, **mental retardation**, strokes, brain tumors, **multiple sclerosis**, and other conditions that affect the nervous system can cause fecal incontinence by interfering with muscle function or the normal rectal sensations that trigger sphincter contraction and are necessary for bowel control. One study of multiple sclerosis patients discovered that about half were incontinent. Nerve damage caused by long-lasting **diabetes mellitus** (**diabetic neuropathy**) is another condition that can give rise to incontinence.

Diagnosis

Medical assessments in cases of fecal incontinence typically involve three steps: asking questions about the patient's past and current health (the medical history); a **physical examination** of the anal region; and testing for objective information regarding anal and rectal function.

Patient history

The medical history relies on questions that allow the doctor to evaluate the nature and severity of the problem and its effect on the patient's life. The doctor asks, for instance, how long the patient has been suffering from incontinence; how often and under what circumstances incontinence occurs; whether the patient has any control over defecation; and whether the patient has obstacles to defecation in his or her everyday surroundings, such as a toilet that can be reached only by climbing a long flight of stairs. For women who have given birth, a detailed obstetric history is also necessary.

Physical examination

The physical examination begins with a visual inspection of the anus and the area lying between the anus and the genitals (the perineum) for hemorrhoids, infections, and other conditions that might explain the patient's difficulties. During this phase of the examination the doctor asks the patient to bear down. Bearing down enables the doctor to check whether **rectal pro-**

lapse or certain other problems exist. Rectal prolapse means that the patient's rectum has been weakened and drops down through the anus. Next, the doctor uses a pin or probe to **stroke** the perianal skin. Normally this touching causes the anal sphincter to contract and the anus to pucker; if it does not, nerve damage may be present. The final phase of the examination requires the doctor to examine internal structures by carefully inserting a gloved and lubricated finger into the anal canal. This allows the doctor to judge the strength of the anal sphincter and a key muscle (the puborectalis muscle) in maintaining continence; to look for abnormalities such as scars and rectal masses; and to learn many other things about the patient's medical situation. At this point the doctor performs the anal wink test again and asks the patient to squeeze and bear down.

Laboratory tests

Information from the medical history and physical examination usually needs to be supplemented by tests that provide objective measurements of anal and rectal function. Anorectal manometry, a common procedure, involves inserting a small tube (catheter) or balloon device into the anal canal or rectum. Manometry measures, among other things, pressure levels in the anal canal, rectal sensation, and anal and rectal reflexes. Tests are also available for assessing nerve damage. An anal ultrasound probe can supply accurate images of the anal sphincter and reveal whether injury has occurred. **Magnetic resonance imaging**, which requires the insertion of a coil into the anal canal, is useful at times.

KEY TERMS

Anus—The opening at the lower end of the rectum.

Colostomy—A surgical procedure in which an opening is made in the wall of the abdomen to allow a part of the large intestine (the colon) to empty outside the body.

Crohn's disease—A disease marked by inflammation of the intestines.

Defecation—Passage of stools through the anus.

Hemorrhoids—Enlarged veins in the anus or rectum. They are sometimes associated with fecal incontinence.

Rectum—The lower section of the large intestine that holds stools before defecation.

Sphincter—A circular band of muscle that surrounds and encloses an opening to the body or to one of its hollow organs. Damage to the sphincter surrounding the anus can cause fecal incontinence.

Stools—Undigested food and other waste that is eliminated through the anus.

Suppository—A solid medication that slowly dissolves after being inserted into the rectum or other body cavity.

Treatment

Fecal incontinence arising from an underlying condition such as diabetic neuropathy can sometimes be helped by treating the underlying condition. When that does not work, or no underlying condition can be discovered, one approach is to have the patient use a suppository or enema to stimulate defecation at the same time every day or every other day. The goal is to restore regular bowel habits and keep the bowels free of stools. Medications such as loperamide (Imodium) and codeine phosphate are often effective in halting incontinence, but only in less severe cases involving liquid stools or urgency. Dietary changes and exercises done at home to strengthen the anal muscles may also help.

Good results have been reported for **biofeedback** training, although the subject has not been properly researched. In successful cases, patients regain complete control over defecation, or at least improve their control, by learning to contract the external part of the anal sphincter whenever stools enter the rectum. All healthy people have this ability. Biofeedback training begins with the insertion into the rectum of a balloon manometry device hooked up to a pressure monitor. The presence of stools in the rectum is simulated by inflating the balloon, which causes pressure changes that are recorded on the monitor. The monitor also records sphincter contraction. By watching the monitor and following instructions from the equipment operator, the patient gradually learns to contract the sphincter automatically in response to fullness in the rectum. Sometimes one training session is enough, but often several are needed. Biofeedback is not an appropriate treatment in all cases, however. It is used only with patients who are highly motivated; who are able, to some extent, to sense the presence of stools in the rectum; and who have not lost all ability to contract the external anal sphincter. One specialist suggests that possibly two-thirds of incontinence sufferers are candidates for biofeedback.

Some people may require surgery. Sphincter damage caused by childbirth is often effectively treated with surgery, however, as are certain other kinds of incontinence-related sphincter injuries. Sometimes surgical treat-

ment requires building an artificial sphincter using a thigh muscle (the gracilis muscle). At one time a **colostomy** was necessary for severe cases of incontinence, but is now rarely performed.

Prognosis

Fecal incontinence is a problem that usually responds well to professional medical treatment, even among elderly and institutionalized patients. If complete bowel control cannot be restored, the impact of incontinence on everyday life can still be lessened considerably in most cases. When incontinence remains a problem despite medical treatment, disposable underwear and other commercial incontinence products are available to make life easier. Doctors and nurses can offer advice on coping with incontinence, and people should never be embarrassed about seeking their assistance. Counseling and information are also available from support groups.

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National Association for Continence. PO Box 8310, Spartanburg, SC 29305-8310. (800) 252-3337. <http://www.nafc.org>.

National Digestive Diseases Information Clearinghouse. 2 Information Way, Bethesda, MD 20892-3570. (800) 891-5389. <http://www.niddk.nih.gov/health/digest/nddic.htm>.

Howard Baker

Fecal lipids test *see* **Stool fat test**

Fecal occult blood test

Definition

The fecal occult blood test (FOBT) is performed as part of the routine **physical examination** during the examination of the rectum. It is used to detect microscopic blood in the stool and is a screening tool for colorectal **cancer**.

Purpose

FOBT uses chemical indicators on stool samples to detect the presence of blood not otherwise visible. (The word "occult" in the test's name means that the blood is hidden from view.) Blood originating from or passing through the gastrointestinal tract can signal many conditions requiring further diagnostic procedures and, possibly, medical intervention. These conditions may be benign or malignant and some of them include:

- colorectal and gastric cancers
- ulcers
- hemorrhoids
- polyps
- inflammatory bowel disease
- irritations or lesions of the gastrointestinal tract caused by medications (such as **nonsteroidal anti-inflammatory drugs**, also called NSAIDs)
- irritations or lesions of the gastrointestinal tract caused by stomach acid disorders, such as reflux esophagitis

The FOBT is used routinely (in conjunction with a **rectal examination** performed by a physician) to screen for colorectal cancer, particularly after age 50. The ordering of this test should not be taken as an indication that cancer is suspected. The FOBT must be combined with regular screening endoscopy (such as a **sigmoidoscopy**) to detect cancers at an early stage.

Precautions

Certain foods and medicines can influence the test results. Some fruits contain chemicals that prevent the guaiac, the chemical in which the test paper is soaked, from reacting with the blood. **Aspirin** and some NSAIDs irritate the stomach, resulting in bleeding and should be avoided prior to the examination, along with red meat and many vegetables and fruits containing vitamin C. All of these factors could result in a false-positive test.

Description

Feces for the stool samples is obtained either by the physician at the rectal examination or by the patient at home, using a small spatula or a collection device. In most cases, the collection of stool samples can easily be done at home, using a kit supplied by the physician. The standard kit contains a specially prepared card on which

a small sample of stool will be spread, using a stick provided in the kit. The sample is placed in a special envelope and either mailed or brought in for analysis. When the physician applies hydrogen peroxide to the back of the sample, the paper will turn blue if an abnormal amount of blood is present.

Types of fecal occult blood tests

Hemoccult is one type of fecal occult blood test, and it is the most commonly used. The Hemoccult test takes less than five minutes to perform and may be performed in the physician's office or in the laboratory. The Hemoccult blood test can detect bleeding from the colon as low as 0.5 mg per day.

Tests that use anti-hemoglobin antibodies (or immunochemical tests) to detect blood in the stool are also used. Immunochemical tests can detect up to 0.7 mg of hemoglobin in the stool and do not require dietary restrictions. Immunochemical tests

- are not accurate for screening for stomach cancer
- are more sensitive than Hemoccult tests in detecting colorectal cancer
- are more expensive than Hemoccult tests

Hemoquant, another fecal occult blood test, is used to detect as much as 500 mg/g of blood in the stool. Like the Hemoccult, the Hemoquant test is affected by red meat. It is not affected by chemicals in vegetables.

Fecal blood may also be measured by measuring the chromium in the red blood cells in the feces. The stool is collected for three to ten days. The test is used in cases where the exact amount of the blood loss is required and it is the only test that can exclude blood loss from the gastrointestines with accuracy.

Preparation

For 72 hours prior to collecting samples, patients should avoid red meats, NSAIDs (including aspirin), **antacids**, steroids, iron supplements, and vitamin C, including citrus fruits and other foods containing large amounts of vitamin C. Foods like uncooked broccoli, uncooked turnips, cauliflower, uncooked cantaloupe, uncooked radish and horseradish and parsnips should be avoided and not eaten during the 72 hours prior to the examination. Fish, chicken, pork, fruits (other than melons) and many cooked vegetables are permitted in the diet.

Results

Many factors can result in false-positive and false-negative findings.

KEY TERMS

Occult—Not visible or easily detected.

Positive results

It is important to note that a true-positive finding only signifies the presence of blood—it is not an indication of cancer. The National Cancer Institute states that, in its experience, less than 10% of all positive results were caused by cancer. The FOBT is positive in 1–5% of the unscreened population and 2–10% of those are found to have cancer. The physician will want to follow up on a positive result with further tests, as indicated by other factors in the patient's history or condition.

Negative results

Alternatively, a negative result (meaning no blood was detected) does not guarantee the absence of **colon cancer**, which may bleed only occasionally or not at all. (Only 50% of colon cancers are FOBT-positive.)

Conclusions

Screening using the FOBT has been demonstrated to reduce colorectal cancer. However, because only half of colorectal cancers are FOBT-positive, FOBT must be combined with regular screening endoscopy to increase the detection of pre-malignant colorectal polyps and cancers. Since, through FOBT, cancer may be detected early, the benefits of possible early detection must be considered along with the likelihood of complications and costs for additional studies.

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Jill S. Lasker
Cheryl Branche, M.D.

Feldenkrais method

Definition

The Feldenkrais method is an educational system that allows the body to move and function more efficiently and comfortably. Its goal is to re-educate the nervous system and improve motor ability. The system can accomplish much more, relieving pressure on joints and weak points, and allowing the body to heal repetitive strain injuries. Continued use of the method can relieve **pain** and lead to higher standards of achievement in sports, the martial arts, dancing and other physical disciplines.

Pupils are taught to become aware of their movements and to become aware of how they use their bodies, thus discovering possible areas of **stress** and strain. The goal of Feldenkrais is to take the individual from merely functioning, to functioning well, free of pain and restriction of movement. Feldenkrais himself stated that his goal was, "To make the impossible possible, the possible easy, and the easy, elegant."

Purpose

This method of re-educating the nervous system can be beneficial to a wide range of people, including athletes, children, the elderly, martial artists, those who are handicapped, people with special needs, and those suffering from degenerative diseases. It has also proved popular with artists, particularly musicians, a number of whom have used Feldenkrais to improve their performance.

The Feldenkrais Guild of North America (FGNA) states that over half of the those who turn to Feldenkrais practitioners are seeking relief from pain. Many people who have pain from an injury compensate by changing their movements to limit pain. Often these changed movements remain after the pain from the original injury is gone, and new pain may occur. Feldenkrais helps students become aware of the changed movements and allows them to learn new movements that relieve their pain. Apart from the obvious physical benefits of more efficient movement and freedom from pain and restriction, Feldenkrais practitioners assert that there are other positive benefits for overall physical and mental health. Feldenkrais can result in increased awareness, flexibility, and coordination, and better relaxation. Feldenkrais practitioners have also noted other benefits in their students, including improvements in awareness, flexibility, coordination, breathing, digestion, sleep, mood, mental alertness, energy, and range of motion, as well as reduced stress and **hypertension**, and fewer headaches and backaches.

Musicians and athletes can improve their performance in many ways when they learn to use their bodies more efficiently. Feldenkrais can also help injured athletes regain lost potential and free them from pain and restriction of movement.

There are numerous accounts of the remarkable results obtained when Feldenkrais is taught to handicapped children so that they can learn to function despite their limitations. Handicapped people can learn to make full use of whatever potential they have, and to have more confidence in their abilities. Practitioners who specialize in teaching Feldenkrais to those who have handicaps have in many cases allowed the patient to discover ways of performing tasks which were previously thought to be impossible for them.

The elderly, whose movements are often restricted by pain and stiffness, can learn to overcome these obstacles with Feldenkrais instruction. In some instances even severe cases of arthritis have been conquered. Theoretically, Feldenkrais can make possible renewed levels of energy and freedom from restriction.

Description

Origins

Moshe Feldenkrais (1904–1984) was a Russian-born Israeli physicist and engineer who was also an active soccer player and judo master. He devised his system in response to his own recurring knee injury, which had restricted his movement and caused him great pain over a long period of time. Feldenkrais believed that repeated muscle patterns cause the parts of the brain controlling those muscles to stay in a fixed pattern as well. He thought that the more the muscles are used, the more parts of the brain can be activated.

He devised a method of re-educating the neuromuscular system and re-evaluating movement to increase efficiency and reduce stress, using his knowledge of mechanics and engineering, and applying some of his martial arts training.

Feldenkrais is described a being a dual system, with two components: "Awareness Through Movement" and "Functional Integration." The system aims to re-educate the body so that habitual movements that cause strain or pain can be relearned to improve efficiency and eliminate dangerous or painful action.

Feldenkrais helps to translate intention into action. In practice, an individual can learn to achieve his or her highest potential, while at the same time learning to avoid and eliminate stresses, strains, and the possibility of injury.

Functional integration

During this session, the patient wears comfortable clothing, and may sit, stand, walk, or lie on a low padded table. The practitioner helps the pupil by guiding him or her through a number of movements. The practitioner may use touch to communicate with the student, but touch is not used to correct any movements. The purpose of this session is to increase a student's awareness of his or her own movement and become open to different possibilities for movement. The instruction can be focused on a particular activity that the student does every day, or that causes him or her pain. The student can learn to alter habitual movements and re-educate the neuromuscular system. This type of session is particularly useful for those who suffer from limitations originating from misuse, stress, illness, or accident. It can also help athletes and musicians perform to the best of their ability by increasing their possibilities for movement. It offers students the potential for improving their physical and mental performance in addition to heightening the sense of well-being.

Awareness through movement

Feldenkrais's martial arts background can be clearly identified in many of the aspects of Awareness Through Movement (ATM). During group sessions, pupils are taught to become acutely aware of all their movements and to imagine them, so that they can improve the efficiency of their actions in their minds, and put them into practice. Pupils are encouraged to be disciplined about practicing their exercises, to achieve maximum benefit.

Awareness through movement is described as an exploratory, nonjudgmental process through which pupils are encouraged to observe and learn about themselves and their movements. The range of this therapy is wide, and there are thousands of different lessons designed to help specific areas.

MOSHE FELDENKRAIS (1904–1984)

Moshe Feldenkrais was born on the border between Russia and Poland. When he was only a boy of 13, he traveled to Palestine on foot. The journey took a year, and once there, young Feldenkrais worked as a laborer and cartographer, also tutoring others in mathematics. Moving to France in 1933, he graduated in mechanical and electrical engineering from the Ecole des Travaux Publiques de Paris.

Feldendrais became the first person to open a Judo center in Paris after meeting with Jigaro Kano. He was also one of the first Europeans to become a black belt in Judo, in 1936.

Obtaining his Ph.D. at the Sorbonne, he went on to assist Nobel Prize laureate, Frédéric Joliot-Curie at the Curie Institute. During World War II in England, he worked on the new sonar anti-submarine research.

Prompted by a recurring leg injury, he applied his knowledge of the martial arts and his training as an engineer to devise a method of re-integrating the body. The concept was that more efficient movement would allow for the treatment of pain or disability, and the better-functioning of the body as a whole. Later on, he would begin to teach what he had learned to others in Tel Aviv.

In addition to many books about judo, including *Higher Judo*, he wrote six books on his method.

Patricia Skinner

Preparations

No preparation is necessary for the practice of Feldenkrais, and all are encouraged to seek help from this system. No condition is considered a preclusion to the benefits of Feldenkrais.

Precautions

As with any therapy or treatment, care should be taken to choose a qualified practitioner. Feldenkrais practitioners stress that the body must not be forced to do anything, and if any movement is painful, or even uncomfortable, it should be discontinued immediately and the patient should seek professional help.

KEY TERMS

Neuromuscular—The body system of nerves and muscles as they function together.

Repetitive strain injury—Injury resulting from a repeated movement such as typing or throwing a ball.

Side effects

No known side effects are associated with the practice of Feldenkrais.

Research and general acceptance

Since Moshe Feldenkrais began to teach his method, it has gradually gained acceptance as an education system. Published research using the method can be found in United States and foreign publications.

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Feldenkrais Guild of North America. 3611 SW Hood Ave., Suite 100, Portland, OR 97201. (800) 775-2118. (503) 221-6612. Fax: (503) 221-6616. <http://www.feldenkrais.com/>.

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Female circumcision *see* **Female genital mutilation**

Female condom *see* **Condom**

Female genital mutilation

Definition

Female genital mutilation (FGM) is the cutting, or partial or total removal, of the external female genitalia for cultural, religious, or other non-medical reasons. It is usually performed on girls between the ages of four and 10. It is also called female **circumcision**.

Purpose

FGM results in the cutting or removal of the tissues around the vagina that give women pleasurable sexual feelings. This procedure is used for social and cultural control of women's sexuality. In its most extreme form, infibulation, where the girl's vagina is sewn shut, the procedure ensures virginity. In some cultures where female circumcision has been a tradition for hundreds of years, this procedure is considered a rite of passage for young girls. Families fear that if their daughters are left uncircumcised, they may not be marriageable. As in most cultures, there is also the fear that the girl might bring shame to the family by being sexually active and becoming pregnant before marriage.

Precautions

It is illegal to perform FGM in many countries, including the United States, Canada, France, Great Britain, Sweden, Switzerland, Egypt, Kenya, and Senegal. This procedure is usually done in the home or somewhere other than a medical setting. Often, it is performed by a family member or by a local "circumciser," using knives, razor blades, or other tools that may not be sterilized before use.

Description

Female circumcision includes a wide range of procedures. The simplest form involves a small cut to the clitoris or labial tissue. A Sunna circumcision removes the prepuce (a fold of skin that covers the clitoris) and/or the tip of the clitoris. A clitoridectomy removes the entire clitoris and some or all of the surrounding tissue; this procedure occurs in approximately 80% of cases. The most extreme form of genital mutilation is excision and infibulation, in which the clitoris and all of the surround tissue are cut away and the remaining skin is sewn together. Only a small opening is left for the passage of

urine and menstrual blood. Infibulation accounts for approximately 15% of FGM procedures.

The World Health Organization (WHO) estimates that between 100 million and 140 million girls and women have undergone some form of FGM. As a very deeply rooted cultural and religious tradition still practiced in over 28 African and Asian countries, up to two million girls per year are at risk. The following countries have the highest number of occurrences of FGM: Djibouti (98%), Egypt (97%), Eritrea (95%), Guinea (99%), Mali (94%), Sierra Leone (90%), and Somalia (98-100%). As more people move to Western countries from countries where female circumcision is performed, the practice has come to the attention of health professionals in the United States, Canada, Europe, and Australia.

In an effort to integrate old customs with modern medical care, some immigrant families have requested that physicians perform the procedure. While trying to be sensitive to cultural traditions, health care providers are sometimes put in the difficult position of choosing to perform this procedure in a medical facility under sanitary conditions, or refusing the request, knowing that it may be done anyway with no medical supervision. Some families who are intent on having this procedure done will take their daughters back to the country they immigrated from in order to have the girls circumcised.

Many national and international medical organizations including the American Medical Association (AMA), Canadian medical organizations, and WHO oppose the practice of female genital mutilation. The United Nations (UN) considers female genital mutilation a violation of human rights. WHO has undertaken a number of projects aimed at decreasing the incidence of FGM. These include the following activities:

- publishing a statement addressing the regional status of FGM and encouraging the development of national policy against its practice,
- organizing training for regional community workers,
- developing educational materials for local health care workers,
- providing alternative occupations for individuals who perform FGM procedures.

Aftercare

A girl or young woman who has recently had the procedure performed may require supportive care to control bleeding and **antibiotics** to prevent infection. Women who were circumcised as children may require medical care to treat complications. Pregnant women who have been infibulated may have to have the labial tissue cut open to allow the baby to be delivered. Aftercare should be provided with a supportive and nonjudgmental approach towards the girls and women who have undergone this procedure.

KEY TERMS

Circumcision—A procedure, usually with religious or cultural significance, where the prepuce or skin covering the tip of the penis on a boy, or the clitoris on a girl, is cut away.

Clitoridectomy—A procedure where the clitoris and possibly some of the surrounding labial tissue at the opening of the vagina is cut away.

Infibulation—A procedure where the tissue around the vagina is sewn shut, leaving only a small opening for the passage of urine and menstrual blood.

Risks

The immediate risks after the procedure are hemorrhage (excessive bleeding), severe **pain**, and infection (including abscesses, **tetanus**, and **gangrene**). The most severe consequence is **death** due to excessive blood loss. Long term complications include scarring, interference with the drainage of urine and menstrual blood, chronic urinary tract infections, pelvic and back pain, and **infertility**. Sexual intercourse can be painful. Complications of **childbirth** are also a risk. It is unclear whether it is related to the procedure itself, or related to the general condition of medical practice, but infant and maternal death rates are generally higher in those communities where female circumcision is practiced.

Resources

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Altha Roberts Edgren

Female sexual arousal disorder

Definition

Female sexual arousal disorder (FSAD) occurs when a woman is continually unable to attain or maintain arousal and lubrication during intercourse, is unable to reach orgasm, or has no desire for sexual intercourse.

Description

The disorder typically affects up to 25 percent of all American women, or an estimated 47 million women. Three-fourths of women with FSAD are postmenopausal. Women describe it as being "unable to get turned on," or being continually disinterested in sex. It is also called "frigidity." Other terms for the disorder include dyspareunia and vaginismus, both of which involve **pain** during intercourse.

Causes and symptoms

There are numerous causes of this disorder. They include:

- physical problems, such as **endometriosis**, **cystitis**, or vaginitis
- systemic problems, such as diabetes, high blood pressure, or **hypothyroidism**. Even **pregnancy** or the postpartum period (time after delivery of a child) may affect desire. **Menopause** is also known to reduce sexual desire.
- medications, including **oral contraceptives**, antidepressants, antihypertensives, and tranquilizers
- surgery, such as **mastectomy** or **hysterectomy** which may affect how a woman feels about her sexual self.
- stress
- depression
- use of alcohol, drugs, or cigarette **smoking**

Symptoms vary. A woman may have no desire for sex, or may not be able to maintain arousal, or may be unable to reach orgasm. She may also have pain during sex or orgasm, which interferes with her desire for intercourse.

Diagnosis

To make a diagnosis, a woman's physician - either family doctor, gynecologist, or even urologist — takes a complete medical history to determine when the problem started, how it presents, how severe it is, and what the patient thinks may be causing it. The doctor will also conduct a complete **physical examination**, looking for any abnormalities in the genital region

Treatment

The physician should start by providing education about the disorder and recommending various non-medical treatment strategies. These include:

- use of erotic materials, such as vibrators, books, magazines and videos
- sensual massage, avoiding the genitals
- position changes to reduce pain
- use of lubricants to moisten the vagina and genital area
- kegel exercises to strengthen the vagina and clitoris
- therapy to overcome any relationship or sexual **abuse** issues

Medical treatments include:

- estrogen replacement therapy, which may help with vaginal dryness, pain and arousal
- testosterone therapy in women who have low levels of this male hormone (side effects, however, may include deepening voice, hair growth, and acne)
- the EROS clitoral therapy device (EROS-CTD), recently approved by the Food and Drug Administration; a small vacuum pump, placed over the clitoris and gently activated to provide a gentle suction designed to increase blood flow to the region, which, in turn, helps with arousal
- using the herb yohimbine combined with nitric oxide has been found to increase vaginal blood flow in postmenopausal women and thus help with some forms of FSAD

Alternative treatment

Natural estrogens, such as those found in soy products and flax, may be effective. Herbal remedies include belladonna, gingko, and motherwort. However, there is no scientific evidence to prove these herbs actually help.

KEY TERMS

Dyspareunia— pain in the pelvic area during or after sexual intercourse.

Vaginismus —An involuntary spasm of the muscles surrounding the vagina, making penetration painful or impossible.

Some women squirt vitamin E in their vagina to increase lubrication.

Women may also want to see a sexual therapist for additional help.

Prognosis

Generally, once women seek the appropriate help they are quite likely to find a way to resolve their problems. Often, a holistic approach, using physical as well as emotional therapies, is required for success.

Prevention

Maintaining a close and open relationship with a partner is one way to avoid the emotional pain and isolation that can lead to **sexual dysfunction**. Additionally, women should learn if any medications they take affect sexual function, and should refrain from alcohol and drugs and quit smoking. Women who have anxieties and fears about sexual intercourse, whether because of earlier abuse, rape, or a prudish upbringing, should deal with those issues through therapy.

Resources

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ORGANIZATIONS

Female Sexual Medicine Center UCLA Medical Center 924 Westwood Blvd., Suite 520 Los Angeles, CA 90024. (310) 825-0025 <www.newshe.com>.

National Women's Health Resource Center, 120 Albany Street Suite 820 New Brunswick, NJ 08901. (877) 986-9472. <www.healthywomen.org>.

Debra Gordon

Female infertility *see* **Infertility**

Femoral hernia *see* **Hernia**

Fetal alcohol syndrome

Definition

Fetal alcohol syndrome (FAS) is a pattern of **birth defects**, learning, and behavioral problems affecting individuals whose mothers consumed alcohol during **pregnancy**.

Description

FAS is the most common preventable cause of **mental retardation**. This condition was first recognized and reported in the medical literature in 1968 in France and in 1973 in the United States. Alcohol is a teratogen, the term used for any drug, chemical, maternal disease or other environmental exposure that can cause birth defects or functional impairment in a developing fetus. Some features may be present at birth including low birth weight, **prematurity**, and microcephaly. Characteristic facial features may be present at birth, or may become more obvious over time. Signs of brain damage include delays in development, behavioral abnormalities, and mental retardation, but affected individuals exhibit a wide range of abilities and disabilities. It has only been since 1991 that the long-term outcome of FAS has been known. Learning, behavioral, and emotional problems are common in adolescents and adults with FAS. Fetal Alcohol Effect (FAE), a term no longer favored, is sometimes used to describe individuals with some, but not all, of the features of FAS. In 1996, the Institute of Medicine suggested a five-level system to describe the birth defects, learning and behavioral difficulties in offspring of women who drank alcohol during pregnancy. This system contains criteria including confirmation of maternal alcohol exposure, characteristic facial features, growth problems, learning and behavioral problems, and birth defects known to be associated with prenatal alcohol exposure.

The incidence of FAS varies among different populations studied, and ranges from approximately one in 200 to one in 2000 at birth. However, a recent study reported in 1997, utilizing the Institute of Medicine criteria, estimated the prevalence in Seattle, Washington from 1975–1981 at nearly one in 100 live births. Avoiding alcohol during pregnancy, including the earliest weeks of the pregnancy can prevent FAS. There is no amount of alcohol use during pregnancy that has been proven to be completely safe.

There is no racial or ethnic predilection for FAS. Individuals from different genetic backgrounds exposed to similar amounts of alcohol during pregnancy may exhibit different signs or symptoms of FAS. Several studies have estimated that between 25–45% of chronic alcoholic women will give birth to a child with FAS if they continue to drink during pregnancy. The risk of FAS appears to increase as a chronic alcoholic woman progresses in her childbearing years and continues to drink. That is, a child with FAS will often be one of the last born to a chronic alcoholic woman, although older siblings may exhibit milder features of FAS. Binge drinking, defined as sporadic use of five or more standard alcoholic drinks per occasion, and "moderate" daily drinking (two to four 12 oz bottles of beer, eight to 16 ounces of wine, two to four ounces of liquor) can also result in offspring with features of FAS.

Causes and symptoms

FAS is not a genetic or inherited disorder. It is a pattern of birth defects, learning, and behavioral problems that are the result of maternal alcohol use during the pregnancy. The alcohol freely crosses the placenta and causes damage to the developing embryo or fetus. Alcohol use by the father cannot cause FAS. If a woman who has FAS drinks alcohol during pregnancy, then she may also have a child with FAS. Not all individuals from alcohol exposed pregnancies have obvious signs or symptoms of FAS; individuals of different genetic backgrounds may be more or less susceptible to the damage that alcohol can cause. The dose of alcohol, the time during pregnancy that alcohol is used, and the pattern of alcohol use all contribute to the different signs and symptoms that are found.

Classic features of FAS include short stature, low birthweight and poor weight gain, microcephaly, and a characteristic pattern of facial features. These facial features in infants and children may include small eye openings (measured from inner corner to outer corner), epicanthal folds (folds of tissue at the inner corner of the eye), small or short nose, low or flat nasal bridge, smooth or poorly developed philtrum (the area of the upper lip above the colored part of the lip and below the nose), thin upper lip, and small chin. Some of these features are nonspecific, meaning they can occur in other conditions, or be appropriate for age, racial, or family background. Other major and minor birth defects that have been reported include cleft palate, congenital heart defects, **strabismus**, **hearing loss**, defects of the spine and joints, alteration of the hand creases, small fingernails, and toenails. Since FAS was first described in infants and children, the diagnosis is sometimes more difficult to recognize in older adolescents and adults. Short stature and microcephaly remain common features, but weight may normalize, and the individual may actually become overweight for his/her height. The chin and nose grow proportionately more than the middle part of the face and dental crowding may become a problem. The small eye openings and the appearance of the upper lip and philtrum may continue to be characteristic. Pubertal changes typically occur at the normal time.

Newborns with FAS may have difficulties with feeding due to a poor suck, have irregular sleep-wake cycles, decreased or increased muscle tone, seizures or **tremors**. Delays in achieving developmental milestones such as rolling over, crawling, walking and talking may become apparent in infancy. Behavior and learning difficulties typical in the preschool or early school years include poor attention span, hyperactivity, poor motor skills, and slow language development. Attention deficit-hyperactivity disorder is a common associated diagnosis. Learning disabilities or mental retardation may be diagnosed during this time. Arithmetic is often the most difficult subject for a child with FAS. During middle school and high school years the behavioral difficulties and learning difficulties can be significant. Memory problems, poor judgment, difficulties with daily living skills, difficulties with abstract reasoning skills, and poor social skills are often apparent by this time. It is important to note that animal and human studies have shown that neurologic and behavioral abnormalities can be present without characteristic facial features. These individuals may not be identified as having FAS, but may fulfill criteria for alcohol- related diagnoses, as set forth by the Institute of Medicine.

In 1991, Streissguth and others reported some of the first long-term follow-up studies of adolescents and adults with FAS. In the approximate 60 individuals they studied, the average IQ was 68, with 70 being the lower limit of the normal range. However, the range of IQ was quite large, as low as 20 (severely retarded) to as high as 105 (normal). The average achievement levels for reading, spelling, and arithmetic were fourth grade, third grade and second grade, respectively. The Vineland Adaptive Behavior Scale was used to measure adaptive functioning in these individuals. The composite score for this group showed functioning at the level of a seven-

year-old. Daily living skills were at a level of nine years, and social skills were at the level of a six-year-old.

In 1996, Streissguth and others published further data regarding the disabilities in children, adolescents and adults with FAS. Secondary disabilities, that is, those disabilities not present at birth and that might be preventable with proper diagnosis, treatment, and intervention, were described. These secondary disabilities include: mental health problems; disrupted school experiences; trouble with the law; incarceration for mental health problems, drug abuse, or a crime; inappropriate sexual behavior; alcohol and drug abuse; problems with employment; dependent living; and difficulties parenting their own children. In that study, only seven out of 90 adults were living and working independently and successfully. In addition to the studies by Streissguth, several other authors in different countries have now reported on long term outcome of individuals diagnosed with FAS. In general, the neurologic, behavioral and emotional disorders become the most problematic for the individuals. The physical features change over time, sometimes making the correct diagnosis more difficult in older individuals, without old photographs and other historical data to review. Mental health problems including attention deficit, depression, panic attacks, **psychosis** and suicide threats and attempts, and overall were present in over 90% of the individuals studied by Streissguth. A 1996 study in Germany reported more than 70% of the adolescents they studied had persistent and severe developmental disabilities and many had psychiatric disorders, the most common of which were emotional disorders, repetitive habits, **speech disorders**, and hyperactivity disorders.

Diagnosis

FAS is a clinical diagnosis, which means that there is no blood, x ray or psychological test that can be performed to confirm the suspected diagnosis. The diagnosis is made based on the history of maternal alcohol use, and detailed **physical examination** for the characteristic major and minor birth defects and characteristic facial features. It is often helpful to examine siblings and parents of an individual suspected of having FAS, either in person or by photographs, to determine whether findings on the examination might be familial, of if other siblings may also be affected. Sometimes, genetic tests are performed to rule out other conditions that may present with developmental delay or birth defects. Individuals with developmental delay, birth defects or other unusual features are often referred to a clinical geneticist, developmental pediatrician, or neurologist for evaluation and diagnosis of FAS. Psychoeducational testing to determine IQ and/or the presence of learning disabilities may also be part of the evaluation process.

KEY TERMS

Cleft palate—A congenital malformation in which there is an abnormal opening in the roof of the mouth that allows the nasal passages and the mouth to be improperly connected.

Congenital—Refers to a disorder which is present at birth.

IQ—Abbreviation for Intelligence Quotient. Compares an individual's mental age to his/her true or chronological age and multiplies that ratio by 100.

Microcephaly—An abnormally small head.

Miscarriage—Spontaneous pregnancy loss.

Placenta—The organ responsible for oxygen and nutrition exchange between a pregnant mother and her developing baby.

Strabismus—An improper muscle balance of the ocular musles resulting in crossed or divergent eyes.

Teratogen—Any drug, chemical, maternal disease, or exposure that can cause physical or functional defects in an exposed embryo or fetus.

Treatment

There is no treatment for FAS that will reverse or change the physical features or brain damage associated with maternal alcohol use during the pregnancy. Most of the birth defects associated with prenatal alcohol exposure are correctable with surgery. Children should have psychoeducational evaluation to help plan appropriate educational interventions. Common associated diagnoses such as attention deficit-hyperactivity disorder, depression, or **anxiety** should be recognized and treated appropriately. The disabilities that present during childhood persist into adult life. However, some of the secondary disabilities mentioned above may be avoided or lessened by early and correct diagnosis, better understanding of the life-long complications of FAS, and intervention. Streissguth has describe a model in which an individual affected by FAS has one or more advocates to help provide guidance, structure and support as the individual seeks to become independent, successful in school or employment, and develop satisfying social relationships.

Prognosis

The prognosis for FAS depends on the severity of birth defects and the brain damage present at birth. **Miscarriage**, **stillbirth** or **death** in the first few weeks of

life may be outcomes in very severe cases. Major birth defects associated with FAS are usually treatable with surgery. Some of the factors that have been found to reduce the risk of secondary disabilities in FAS individuals include diagnosis before the age of six years, stable and nurturing home environments, never having experienced personal violence, and referral and eligibility for disability services. The long-term data helps in understanding the difficulties that individuals with FAS encounter throughout their lifetime and can help families, caregivers and professionals provide the care, supervision, education and treatment geared toward their special needs.

Prevention of FAS is the key. Prevention efforts must include public education efforts aimed at the entire population, not just women of child bearing age, appropriate treatment for women with high-risk drinking habits, and increased recognition and knowledge about FAS by professionals, parents, and caregivers.

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Fetal Alcohol Syndrome Family Resource Institute. PO Box 2525, Lynnwood, WA 98036. (800) 999-3429. <http://www.fetalalcoholsyndrome.org>.

Institute of Medicine. National Academy Press, Washington, DC. <http://www.come-over.to/FAS/IOMsummary.htm>.

March of Dimes Birth Defects Foundation. 1275 Mamaroneck Ave., White Plains, NY 10605. (888) 663-4637. <resource center@modimes.org>. <http://www.modimes.org>.

Nofas. 216 G St. NE, Washington, DC 20002. (202) 785-4585. <http://www.nofas.org>.

Laurie Heron Seaver

Ferritin test *see* **Iron tests**

Fetal death *see* **Stillbirth**

Fetal hemoglobin test

Definition

Fetal hemoglobin (Hemoglobin F), Alkali-resistant hemoglobin, HBF (or Hb F), is the major hemoglobin component in the bloodstream of the fetus. After birth, it decreases rapidly until only traces are found in normal children and adults.

Purpose

The determination of fetal hemoglobin is an aid in evaluating low concentrations of hemoglobin in the blood (anemia), as well as the hereditary persistence of fetal hemoglobin, and a group of inherited disorders affecting hemoglobin, among which are the thalassemias and sickle cell anemia.

Description

At birth, the newborn's blood is comprised of 60%–90% of fetal hemoglobin. The fetal hemoglobin then rapidly decreases to 2% or less after the second to fourth years. By the time of adulthood, only traces (0.5% or less) are found in the bloodstream.

In some diseases associated with abnormal hemoglobin production (see Hemoglobinopathy, below), fetal hemoglobin may persist in larger amounts. When this occurs, the elevation raises the question of possible underlying disease.

For example, HBF can be found in higher levels in hereditary hemolytic **anemias**, in all types of leukemias, in **pregnancy**, diabetes, thyroid disease, and during anticonvulsant drug therapy. It may also reappear in adults when the bone marrow is overactive, as in the disorders of **pernicious anemia**, **multiple myeloma**, and metastatic **cancer** in the marrow. When HBF is increased after age four, it should be investigated for cause.

Hemoglobinopathy

Hemoglobin is the oxygen-carrying pigment found in red blood cells. It is a large molecule made in the bone marrow from two components, heme and globin.

Defects in hemoglobin production may be either genetic or acquired. The genetic defects are further subdivided into errors of heme production (porphyria), and those of globin production (known collectively as the **hemoglobinopathies**).

There are two categories of hemoglobinopathy. In the first category, abnormal globin chains give rise to abnormal hemoglobin molecules. In the second category, normal hemoglobin chains are produced but in abnormal amounts. An example of the first category is the disorder of sickle cell anemia, the inherited condition characterized by curved (sickle-shaped) red blood cells and chronic **hemolytic anemia**. Disorders in the second category are called the thalassemias, which are further divided into types according to which amino acid chain is affected (alpha or beta), and whether there is one defective gene (**thalassemia** minor) or two defective genes (thalassemia major).

Preparation

This test requires a blood sample. The patient is not required to be in a **fasting** state (nothing to eat or drink for a period of hours before the test).

Risks

Risks for this test are minimal, but may include slight bleeding from the blood-drawing site, **fainting** or feeling lightheaded after venipuncture, or hematoma (blood accumulating under the puncture site).

Normal results

Reference values vary from laboratory to laboratory but are generally found within the following ranges:

- six months to adult: up to 2% of the total hemoglobin
- newborn to six months: up to 75% of the total hemoglobin

Abnormal results

Greater than 2% of total hemoglobin is abnormal.

KEY TERMS

Anemia—A disorder characterized by a reduced blood level of hemoglobin, the oxygen-carrying pigment of blood.

Hemolytic anemia—A form of anemia caused by premature destruction of red cells in the blood stream (a process called hemolysis). Hemolytic anemias are classified according to whether the cause of the problem is inside the red blood cell (in which case it is usually an inherited condition), or outside the cell (usually acquired later in life).

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Janis O. Flores

Fetishes *see* **Sexual perversions**

Fever

Definition

A fever is any body temperature elevation over 100°F (37.8°C).

Description

A healthy person's body temperature fluctuates between 97°F (36.1°C) and 100°F (37.8°C), with the average being 98.6°F (37°C). The body maintains stability within this range by balancing the heat produced by the metabolism with the heat lost to the environment. The "thermostat" that controls this process is located in the hypothalamus, a small structure located deep within the brain. The nervous system constantly relays information about the body's temperature to the thermostat, which in turn activates different physical responses designed to

A dramatic rise in body temperature often includes the following symptoms: A. Loss of fluid results in dehydration. B. The hypothalamic set-point is increased, raising metabolism. C. Blood vessels in skin dilate. D. Sweat glands produce excess perspiration. E. Increased pulse rate. F. Increased hypothalmic set-point may introduce chills and shivering to promote heat production from muscles. G. Skin becomes more heat-sensitive. *(Illustration by Electronic Illustrators Group.)*

cool or warm the body, depending on the circumstances. These responses include: decreasing or increasing the flow of blood from the body's core, where it is warmed, to the surface, where it is cooled; slowing down or speeding up the rate at which the body turns food into energy (metabolic rate); inducing shivering, which generates heat through muscle contraction; and inducing sweating, which cools the body through evaporation.

A fever occurs when the thermostat resets at a higher temperature, primarily in response to an infection. To reach the higher temperature, the body moves blood to the warmer interior, increases the metabolic rate, and induces shivering. The "chills" that often accompany a fever are caused by the movement of blood to the body's core, leaving the surface and extremities cold. Once the higher temperature is achieved, the shivering and chills stop. When the infection has been overcome or drugs such as **aspirin** or **acetaminophen** (Tylenol) have been taken, the thermostat resets to normal and the body's cooling mechanisms switch on: the blood moves to the surface and sweating occurs.

Fever is an important component of the immune response, though its role is not completely understood. Physicians believe that an elevated body temperature has several effects. The immune system chemicals that react with the fever-inducing agent and trigger the resetting of the thermostat also increase the production of cells that fight off the invading bacteria or viruses. Higher temperatures also inhibit the growth of some bacteria, while at the same time speeding up the chemical reactions that help the body's cells repair themselves. In addition, the increased heart rate that may accompany the changes in blood circulation also speeds the arrival of white blood cells to the sites of infection.

Causes and symptoms

Fevers are primarily caused by viral or bacterial infections, such as **pneumonia** or **influenza**. However, other conditions can induce a fever, including allergic reactions; autoimmune diseases; trauma, such as breaking a bone; **cancer**; excessive exposure to the sun; intense

exercise; hormonal imbalances; certain drugs; and damage to the hypothalamus. When an infection occurs, fever-inducing agents called pyrogens are released, either by the body's immune system or by the invading cells themselves, that trigger the resetting of the thermostat. In other circumstances, the immune system may overreact (allergic reactions) or become damaged (autoimmune diseases), causing the uncontrolled release of pyrogens. A **stroke** or tumor can damage the hypothalamus, causing the body's thermostat to malfunction. Excessive exposure to the sun or intensely exercising in hot weather can result in heat stroke, a condition in which the body's cooling mechanisms fail. Malignant hyperthermia is a rare, inherited condition in which a person develops a very high fever when given certain anesthetics or **muscle relaxants** in preparation for surgery.

How long a fever lasts and how high it may go depends on several factors, including its cause, the age of the patient, and his or her overall health. Most fevers caused by infections are acute, appearing suddenly and then dissipating as the immune system defeats the infectious agent. An infectious fever may also rise and fall throughout the day, reaching its peek in the late afternoon or early evening. A low-grade fever that lasts for several weeks is associated with autoimmune diseases such as lupus or with some cancers, particularly leukemia and lymphoma.

KEY TERMS

Antipyretic—A drug that lowers fever, like aspirin or acetaminophen.

Autoimmune disease—Condition in which a person's immune system attacks the body's own cells, causing tissue destruction.

Febrile seizure—Convulsions brought on by fever.

Malignant hyperthermia—A rare, inherited condition in which a person develops a very high fever when given certain anesthetics or muscle relaxants in preparation for surgery.

Meningitis—A potentially fatal inflammation of the thin membrane covering the brain and spinal cord.

Metabolism—The chemical process by which the body turns food into energy, which can be given off as heat.

Pyrogen—A chemical circulating in the blood that causes a rise in body temperature.

Reye's syndrome—A disorder principally affecting the liver and brain, marked by the rapid development of life-threatening neurological symptoms.

Diagnosis

A fever is usually diagnosed using a thermometer. A variety of different thermometers are available, including traditional glass and mercury ones used for oral or rectal temperature readings and more sophisticated electronic ones that can be inserted in the ear to quickly register the body's temperature. For adults and older children, temperature readings are usually taken orally. Younger children who cannot or will not hold a thermometer in their mouths can have their temperature taken by placing an oral thermometer under their armpit. Infants generally have their temperature taken rectally using a rectal thermometer.

As important as registering a patient's temperature is determining the underlying cause of the fever. The presence or absence of accompanying symptoms, a patient's medical history, and information about what he or she may have ingested, any recent trips taken, or possible exposures to illness help the physician make a diagnosis. Blood tests can aid in identifying an infectious agent by detecting the presence of antibodies against it or providing samples for growth of the organism in a culture. Blood tests can also provide the doctor with white blood cell counts. Ultrasound tests, **magnetic resonance imaging** (MRI) tests, or computed tomography (CT) scans may be ordered if the doctor cannot readily determine the cause of a fever.

Treatment

Physicians agree that the most effective treatment for a fever is to address its underlying cause, such as through the administration of **antibiotics**. Also, because a fever helps the immune system fight infection, it usually should be allowed to run its course. Drugs to lower fever (antipyretics) can be given if a patient (particularly a child) is uncomfortable. These include aspirin, acetaminophen (Tylenol), and ibuprofin (Advil). Aspirin, however, should not be given to a child or adolescent with a fever since this drug has been linked to an increased risk of **Reye's syndrome**. Bathing a patient in cool water can also help alleviate a high fever.

A fever requires emergency treatment under the following circumstances:

- newborn (three months or younger) with a fever over 100.5°F (38°C)
- infant or child with a fever over 103°F (39.4°C)
- fever accompanied by severe **headache**, neck stiffness, mental confusion, or severe swelling of the throat

A very high fever in a small child can trigger seizures (febrile seizures) and therefore should be treated immediately. A fever accompanied by the above symptoms can indicate the presence of a serious infection, such as **meningitis**, and should be brought to the immediate attention of a physician.

Prognosis

Most fevers caused by infection end as soon as the immune system rids the body of the pathogen and do not produce any lasting effects. The prognosis for fevers associated with more chronic conditions, such as autoimmune disease, depends upon the overall outcome of the disorder.

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Bridget Travers

Fever blister *see* **Cold sore**

Fever evaluation tests

Definition

Fever evaluation tests, better known as febrile agglutinins tests, are performed to detect the presence of antibodies in the blood that are sensitive to temperature changes. Antibodies are proteins produced by the immune system in response to specific infectious agents, such as viruses or bateria. Febrile agglutinins are antibodies that cause red blood cells to clump, but only when the blood is warmed to temperatures higher than the average body temperature of 98.6°F (37°C).

Purpose

The febrile agglutinins test is used to confirm the diagonsis of certain infectious diseases that stimulate the body to produce febrile agglutinins. The disease most commonly diagnosed by this test is **brucellosis**, a infection caused by bacteria belonging to the genus *Brucella* and characterized by intermittent fever, sweating, chills, aches, and mental depression. The test is also used to diagnose certain other infectious diseases: salmonellosis, caused by *Salmonella* bacteria and marked by nausea and severe **diarrhea**; rickettsial infections, a group of diseases caused by the bacteria *Rickettsia*; and **tularemia**, also called rabbit fever, a bacterial infection characterized by a high fever and swollen lymph nodes. The febrile agglutinins test can also be used to confirm the presence of two types of **cancer**, leukemia and lymphoma; however, doctors rarely use the test for this purpose, since other diagnostic tests are more reliable.

Description

A febrile agglutinins test can be performed at a doctor's office or a hospital. A nurse or technician will collect a few drops of blood (about 7ml) in a small tube that has been cooled slightly. The specimen is then taken to a laboratory where it heated and examined for clumping. If the cells clump after warming and unclump as they cool, a febrile agglutinin titer (concentration) of greater than 1:80 is present.

Normal results

The results of febrile agglutinins tests require a doctor's interpretation. In general, however, a normal value is lower than 1:32.

Abnormal results

An value higher than 1:80 suggests a diagnosis for brucellosis or one of the other conditions indicated by this test.

Jill S. Lasker

Fever of unknown origin

Definition

Fever of unknown origin (FUO) refers to the presence of a documented fever for a specified time, for which a cause has not been found after a basic medical evaluation. The classic criteria developed in 1961 included: temperature greater than 101°F (38.3°C), for at least three weeks, and inability to find a cause after one week of study. Within the past decade, a revision has been proposed that categorizes FUO into classic, hospital acquired FUO, FUO associated with low white blood counts, and HIV associated FUO (**AIDS** related).

Description

Fever is a natural response of the body that helps in fighting off foreign substances, such as microorganisms, toxins, etc. Body temperature is set by the thermoregulatory center, located in an area in the brain called hypothalamus. Body temperature is not constant all day, but actually is lowest at 6 A.M. and highest around 4–6 P.M. In addition, temperature varies in different regions of the body; for example, rectal and urine temperatures are about one degree Fahrenheit higher than oral temperature and rectal temperature is higher than urine. It is also important to realize that certain normal conditions can effect body temperature, such as **pregnancy**, food ingestion, age, and certain hormonal changes.

Substances that cause fever are known as "pyrogens." There are two types of pyrogens; exogenous and endogenous. Those that originate outside the body, such as bacterial toxins, are called "exogenous" pyrogens. Pyrogens formed by the body's own cells in response to an outside stimulus (such as a bacterial toxin) are called "endogenous" pyrogens.

Researchers have discovered that there are several "endogenous" pyrogens. These are made up of small groups of amino acids, the building blocks of proteins. These natural pyrogens have other functions in addition to inducing fever; they have been named "cytokines". When cytokines are injected into humans, fever and chills develop within an hour. Interferon, tumor necrosis factor, and various interleukins are the major fever producing cytokines.

The production of fever is a very complex process; somehow, these cytokines cause the thermoregulatory center in the hypothalamus to reset the normal temperature level. The body's initial response is to conserve heat by vasoconstriction, a process in which blood vessels narrow and prevent heat loss from the skin and elsewhere. This alone will raise temperature by two to three degrees. Certain behavioral activities also occur, such as adding more clothes, seeking a warmer environment, etc. If the hypothalamus requires more heat, then shivering occurs.

Fever is a body defense mechanism. It has been shown that one of the effects of temperature increase is to slow bacterial growth. However, fever also has some downsides; the body's metabolic rate is increased and with it, oxygen consumption. This can have a devastating effect on those with poor circulation. In addition, fever can lead to seizures in the very young.

When temperature elevation occurs for an extended period of time and no cause is found, the term FUO is then used. The far majority of these patients are eventually found to have one of several diseases.

KEY TERMS

AIDS—Acquired immune deficiency syndrome is often represented by these initials. The disease is associated with infection by the human immunodeficiency virus (HIV), and has the main feature of repeated infections, due to failure of certain parts of the immune system. Infection by HIV damages part of the body's natural immunity, and leads to recurrent illnesses.

Antibiotic—A medication that is designed to kill or weaken bacteria.

Computed tomography scan (CT Scan)—A specialized x-ray procedure in which cross-sections of the area in question can be examined in detail. This allows physicians to examine organs such as the pancreas, bile ducts, and others which are often the site of hidden infections.

Magnetic Resonance Imaging (MRI)—This is a new technique similar to CT Scan, but based on the magnetic properties of various areas of the body to compose images.

NSAID—Nonsteroidal anti-inflammatory drugs are medications such as aspirin and ibuprofen that decrease pain and inflammation. Many can now be obtained without a doctor's prescription.

Ultrasound—A non-invasive procedure based on changes in sound waves of a frequency that cannot be heard, but respond to changes in tissue composition. It is very useful for diagnosing diseases of the gallbladder, liver, and hidden infections, such as abscesses.

Causes and symptoms

The most frequent cause of FUO is still infection, though the percentage has decreased in recent years. **Tuberculosis** remains an important cause, especially when it occurs outside the lungs. The decrease in infections as a cause of FUO is due in part to improved culture techniques. In addition, technological advances have made it easier to diagnose non-infectious causes. For example, tumors and autoimmune diseases in particular are now easier to diagnose. (An autoimmune disease is one that arises when the body tolerance for its own cell antigenic cell markers disappears.)

Allergies to medications can also cause prolonged fever; sometimes patients will have other symptoms suggesting an allergic reaction, such as a rash.

There are many possible causes of FUO; generally though, a diagnosis can be found. About 10% of patients will wind up without a definite cause, and about the same percentage have "factitious fevers" (either self induced or no fever at all).

Some general symptoms tend to occur along with fever; these are called constitutional symptoms and consist of myalgias (muscle aches), chills, and **headache**.

Diagnosis

Few symptoms in medicine present such a diagnostic challenge as fever. Nonetheless, if a careful, logical, and thorough evaluation is performed, a diagnosis will be found in most cases. The patient's past medical history as well as travel, social, and family history should be carefully searched for important clues.

Usually the first step is to search for an infectious cause. Skin and other screening tests for diseases such as tuberculosis, and examination of blood, urine, and stool, are generally indicated. Antibody levels to a number of infectious agents can be measured; if these are rising, they may point to an active infection.

Various x-ray studies are also of value. In addition to standard examinations, recently developed radiological techniques using ultrasound, computed tomography scan (CT scan) and **magnetic resonance imaging** (MRI) scans are now available. These enable physicians to examine areas that were once accessible only through surgery. Furthermore, new studies using radioactive materials (nuclear medicine), can detect areas of infection and inflammation previously almost impossible to find, even with surgery.

Biopsies of any suspicious areas found on an x-ray exam can be performed by either traditional or newer surgical techniques. Material obtained by biopsy is then examined by a pathologist to look for clues as to the cause of the fever. Evidence of infection, tumor or other diseases can be found in this way. Portions of the biopsy are also sent to the laboratory for culture in an attempt to grow and identify an infectious organism.

Patients with HIV are an especially difficult problem, as they often suffer from many unusual infections. HIV itself is a potential cause of fever.

Treatment

Most patients who undergo evaluation for FUO do not receive treatment until a clear-cut cause is found. **Antibiotics** or medications designed to suppress a fever (such as NSAIDs) will only hide the true cause. Once physicians are satisfied that there is no infectious cause, they may use medications such as NSAIDs, or **corticosteroids** to decrease inflammation and diminish constitutional symptoms.

The development of FUO in certain settings, such as that acquired by patients in the hospital or in those with a low white **blood count**, often needs rapid treatment to avoid serious complications. Therefore, in these instances patients may be placed on antibiotics after a minimal number of diagnostic studies. Once test results are known, treatment can be adjusted as needed.

Prognosis

The outlook for patients with FUO depends on the cause of the fever. If the basic illness is easily treatable and can be found rather quickly, the potential for a cure is quite good. Some patients continue with temperature elevations for six months or more; if no serious disease is found, medications such as NSAIDs are used to decrease the effects of the fever. Careful follow-up and reevaluation is recommended in these cases.

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David Kaminstein, MD

Fiber-modified diet *see* **Diets**

Fibrin degradation products *see* **Fibrin split products**

Fibrin split products

Definition

Fibrin split products (FSP) are fragments of protein released from a dissolving clot. The fibrin split products test is one of several tests done to evaluate a person with

blood clotting problems (coagulation), particularly disseminated intravascular coagulation (DIC).

Purpose

High levels of FSP in a person's blood are associated with DIC, a serious medical condition that develops when the normal balance between bleeding and clotting is disturbed. Excessive bleeding and clotting injures body organs, and causes anemia or **death**.

Description

Coagulation begins typically with an injury to some part of the body. The injury sets in motion a cascade of biochemical activities (the coagulation cascade) to stop the bleeding, by forming a clot from a mixture of the blood protein fibrin and platelets.

Once bleeding is stopped, another blood protein dissolves the clot by breaking down the fibrin into fragments. Measurement of these fragments gives information about the clot dissolving portion of coagulation, called fibrinolysis.

In DIC, the coagulation cascade is triggered in an abnormal way. A blood infection, a **transfusion** reaction, a large amount of tissue damage, such as a burn, a dead fetus, and some cancers can begin the chain of biochemical events leading to blood clots. The coagulation cascade becomes overwhelmed with excessive clotting followed by excessive bleeding. As the large number of clots dissolve, fibrin split products accumulate in the blood and encourage even more bleeding.

Laboratory tests for FSP are done on the yellow liquid portion left over after blood clots (serum). A person's serum is mixed with a substance that binds to FSP. This bound complex is measured, and the original amount of FSP is determined. Some test methods give an actual measurement of FSP; some give a titer, or dilution. Methods that provide a titer look for the presence or absence of FSP. If the serum is positive for FSP, the serum is diluted, or titered, and the test is done again. These steps are repeated until the serum is so dilute that it no longer gives a positive result. The last dilution that gives a positive result is the titer reported.

The FSP test is covered by insurance when medically necessary. Results are usually available within one to two hours. Other names for this test are fibrin degradation products, fibrin breakdown products, or FDP.

Preparation

This test requires 0.17 oz (5 ml) of blood. A healthcare worker ties a tourniquet on the patient's upper arm, locates a vein in the inner elbow region, and inserts a needle into that vein. Vacuum action draws the blood through the needle into an attached tube. Collection of the sample takes only a few minutes.

KEY TERMS

Coagulation—The entire process of blood clotting.

Coagulation cascade—A sequence of biochemical activities to stop bleeding by forming a clot.

Disseminated intravascular coagulation (DIC)—A serious medical condition that develops when the normal balance between bleeding and clotting is disturbed. Excessive bleeding and clotting injures body organs, and causes anemia or death.

Fibrin split products (FSP)—Pieces of the protein fibrin released from a dissolving clot.

Fibrinolysis—The clot dissolving portion of the coagulation process.

Titer—A dilution of a substance with an exact known amount of fluid. For example, one part of serum diluted with four parts of saline is a titer of 1:4.

Aftercare

Discomfort or bruising may occur at the puncture site. Pressure applied to the puncture site until the bleeding stops reduces bruising. Warm packs to the puncture site relieve discomfort. The patient may feel dizzy or faint.

Risks

People with coagulation problems may bleed longer than normal. The healthcare provider must make sure bleeding has stopped before leaving the patient unattended.

Normal results

Negative at a less than or equal to 1:4 dilution or less than 10 g/mL.

Abnormal results

High levels of FSP indicate DIC. Results of the test must be interpreted by the physician according to the person's clinical symptoms and medical history. Other conditions that increase blood clotting activity also increase FSP: venous thrombosis, surgery and trans-

plants, blood clots in the lung, certain cancers, and **heart attack** (myocardial infarction).

Resources

BOOKS

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Nancy J. Nordenson

KEY TERMS

Fibrin—The last step in the coagulation process. Fibrin forms strands that add bulk to a forming blood clot to hold it in place and help "plug" an injured blood vessel wall.

Platelet—An irregularly shaped cell-like particle in the blood that is an important part of blood clotting. Platelets are activated when an injury causes a blood vessel to break. They change shape from round to spiny, "sticking" to the broken vessel wall and to each other to begin the clotting process.

Prothrombin—A type of protein called a glycoprotein that is converted to thrombin during the clotting process.

Thrombin—An enzyme that converts fibrinogen into strands of fibrin.

Fibrinogen test

Definition

Fibrinogen (Factor I) is a protein that originates in the liver. It is converted to fibrin during the blood-clotting process (coagulation).

Purpose

The fibrinogen test aids in the diagnosis of suspected clotting or bleeding disorders caused by fibrinogen abnormalities.

Precautions

This test is not recommended for patients with active bleeding, acute infection or illness, or in those patients who have received blood transfusions within four weeks.

Drugs that may increase fibrinogen levels include estrogens and **oral contraceptives**. Drugs that may cause decreased levels include anabolic steroids, androgens, phenobarbital, urokinase, streptokinase, and valproic acid.

Description

Fibrinogen plays two essential roles in the body: it is a protein called an acute-phase reactant that becomes elevated with tissue inflammation or tissue destruction, and it is also a vital part of the "common pathway" of the coagulation process.

In order for blood to clot, fibrinogen must be converted to fibrin by the action of an enzyme called thrombin. Fibrin molecules clump together to form long filaments, which trap blood cells to form a solid clot.

The conversion of fibrinogen to fibrin is the last step of the "coagulation cascade," a series of reactions in the blood triggered by tissue injury and platelet activation. With each step in the cascade, a coagulation factor in the blood is converted from an inactive to an active form. The active form of the factor then activates several molecules of the next factor in the series, and so on, until the final step, when fibrinogen is converted into fibrin.

The factors involved in the coagulation cascade are numbered I, II, and V through XIII. Factor I is fibrinogen, while factor II (fibrinogen's immediate precursor) is called prothrombin. Most of the coagulation factors are made in the liver, which needs an adequate supply of vitamin K to manufacture the different clotting factors.

When fibrinogen acts as an "acute-phase reactant," it rises sharply during tissue inflammation or injury. When this occurs, high fibrinogen levels may be a predictor for an increased risk of heart or circulatory disease. Other conditions in which fibrinogen is elevated are cancers of the stomach, breast, or kidney, and inflammatory disorders like **rheumatoid arthritis**.

Reduced fibrinogen levels can be found in liver disease, **prostate cancer**, lung disease, bone marrow lesions, malnourishment, and certain bleeding disorders. The low levels can be used to evaluate disseminated intravascular coagulation (DIS), a serious medical condition that develops when there is a disturbed balance between bleeding and clotting. Other conditions related to decreased fibrinogen levels are those in which fibrino-

gen is completely absent (congenital afibrinogenemia), conditions in which levels are low (hypofibrinogenemia), and conditions of abnormal fibrinogen (dysfibrinogenemia). Obstetric complications or trauma may also cause low levels. Large-volume blood transfusions cause low levels because banked blood does not contain fibrinogen.

Preparation

This test is performed with a blood sample, which can be drawn at any time of day. The patient does not have to be **fasting** (nothing to eat or drink).

Aftercare

Because a fibrinogen test is often ordered when a bleeding disorder is suspected, the patient should apply pressure or a pressure dressing to the blood-drawn site site for a period of time after blood is drawn, and then reexamine the site for bleeding.

Risks

Risks for this test are minimal, but may include slight bleeding from the blood-drawing site, **fainting** or feeling lightheaded after procedure, or the seeing the accumulation of blood under the puncture site (hematoma).

Normal results

Normal reference ranges are laboratory-specific, but are usually within the following:

- adult: 200 mg/dL–400 mg/dL
- newborn: 125 mg/dL–300 mg/dL

Abnormal results

Spontaneous bleeding can occur with values less than 100 mg/dL.

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Janis O. Flores

Fibrocystic breast disease *see* **Fibrocystic condition of the breast**

Fibroadenoma

Definition

Fibroadenomas are benign breast tumors commonly found in young women. Fibroadenoma means "a tumor composed of glandular (related to gland) and fibrous (containing fibers) tissues."

Description

Breast fibroadenomas, abnormal growths of glandular and fibrous tissues, are most common between the ages of 15 and 30, and are found in 10% of all women (20% of African-American women). They are found rarely in postmenopausal women.

Described as feeling like marbles, these firm, round, movable, and "rubbery" lumps range from 1–5 cm in size. Giant fibroadenomas are larger, lemon-sized lumps. Usually single, from 10–15% of women have more than one.

While some types of breast lumps come and go during the menstrual cycle, fibroadenomas typically do not disappear after a woman's period, and should be checked by a doctor.

Causes and symptoms

The cause of breast fibroadenomas is unknown. They may be dependent upon estrogen, because they are common in premenopausal women, can be found in postmenopausal women taking estrogen, and because they grow larger in pregnant women.

Fibroadenomas usually cause no symptoms and may be discovered during **breast self-examination**, or during a routine check-up.

Diagnosis

When the doctor takes a complete medical history, they will ask when the lump was first noticed, if there were any symptoms or changes in lump size, and if there is any personal or family history of breast disease.

The doctor thoroughly feels the breasts (palpates). Tests are done, usually including **mammography** or ultrasound scans, or surgical removal of cells or tissue for examination under a the microscope (biopsy).

Diagnostic tests include:

- Mammogram. An x-ray examination of the breast.
- Ultrasound scan. A technique that uses sound waves to display a two-dimensional image of the breast, showing whether a lump is solid or fluid-filled (cystic).
- Fine-needle aspiration biopsy. A minor procedure wherein fluid or cells are drawn out of the lump through a small needle (aspirated).

KEY TERMS

Aspiration —To withdraw material with a needle and syringe.

Biopsy —To remove cells or tissue for microscopic examination.

Estrogen—Female sex hormone produced by the ovaries.

- Core biopsy. A procedure wherein a larger piece of tissue is withdrawn from the lump through a larger needle.
- Incisional biopsy. A surgical procedure wherein a piece of the lump is removed through an cut (incision).
- Excisional biopsy. A surgical procedure wherein the entire lump is removed through an cut (incision).

Most insurance plans cover the costs of diagnosing and treating fibroadenomas.

Treatment

Performed usually in outpatient settings, breast fibroadenomas are removed by **lumpectomy**, or surgical excision under local or general anesthesia. Sometimes lumps in younger women are not removed but are monitored by self-examination, yearly doctor check-ups, and mammograms. Surgery is generally recommended for women over 30, and for lumps that are painful or enlarging.

Alternative treatments

Alternative treatments for breast fibroadenomas include a low-fat, high-fiber, vegetarian-type diet; a reduction in **caffeine** intake; supplementation with evening primrose oil (Oenothera biennis), flax oil, or fish oil and **vitamins** E and C; and the application of hot compresses to the breast. In addition, a focus on liver cleansing is important to assist the body in conjugation and elimination of excess estrogens. Botanical remedies can be useful in hormone balancing, as can **acupuncture** and **homeopathy**. Massaging the breasts with castor oil, straight or infused with herbs or essential oils, can help fibroadenomas reduce and dissipate, as well as keep women in touch with changes in their breast tissue.

Prognosis

Breast fibroadenomas are not cancerous. The lumps recur in up to 20% of women. A small number of lumps disappear on their own.

Prevention

Breast fibroadenomas cannot be prevented. They can be discovered early by regular breast self-examination.

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ORGANIZATIONS

American College of Obstetricians and Gynecologists. 409 12th Street, S.W., PO Box 96920

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Fibrocystic condition of the breast

Definition

Fibrocystic condition of the breast is a term that may refer to a variety of symptoms: breast lumpiness or tenderness, microscopic breast tissue, and/or the x ray or ultrasound picture of the breast. It has been called a

"wastebasket" diagnosis because a wide range of vaguely defined benign breast conditions may be labeled as fibrocystic condition. It is not a **cancer**, and the majority of types of fibrocystic conditions do not increase the risk of **breast cancer**.

Description

There is no such thing as a normal or typical female breast. Breasts come in all shapes and sizes, with varying textures from smooth to extremely lumpy. The tissues of the female breast change in response to hormone levels, normal **aging**, nursing (**lactation**), weight fluctuations, and injury. To further complicate matters, the breast has several types of tissue; each of these tissue types may respond differently to changes in body chemistry.

Fibrocystic breast condition may be called fibrocystic disease, although it is clearly not a single, specific disease process. Variations or changes in the way the breast feels or looks on x ray may cause the condition to be called "fibrocystic change." Other names have been used to refer to this imprecise and ill-defined term: mammary dysplasia, mastopathy, chronic cystic **mastitis**, indurative mastopathy, mastalgia, lumpy breasts, or physiologic nodularity.

Estimates vary, but 40–90% of all women have some evidence of "fibrocystic" condition, change, or disease. It is most common among women between the ages 30 and 50, but may be seen at other ages.

Causes and symptoms

Fibrocystic condition of the breast refers to technical findings on diagnostic testing (signs); however, this discussion focuses on symptoms that may fall under the general category of the fibrocystic condition. First, a brief review of the structure and function of the breast may be useful.

The breast is not supposed to be a soft, smooth organ. It is actually a type of sweat gland. Milk, the breasts' version of sweat, is secreted when the breast receives appropriate hormonal and environmental stimulation.

The normal breast contains milk glands, with their accompanying ducts, or pipelines, for transporting the milk. These complex structures may not only alter in size, but can increase or decrease in number as needed. Fibrous connective tissue, fatty tissue, nerves, blood and lymph vessels, and lymph nodes, with their different shapes and textures, lie among the ever-changing milk glands. It is no wonder that a woman's breasts may not feel uniform in texture and that the "lumpiness" may wax and wane.

The fibrocystic condition refers to the tenderness, enlargement, and/or changing "lumpiness" that many women encounter just before or during their menstrual periods. At this time, female hormones are preparing the breasts for **pregnancy**, by stimulating the milk-producing cells, and storing fluid. Each breast may contain as much as three to six teaspoons of excess fluid. Swelling, with increased sensitivity or **pain**, may result. If pregnancy does not occur, the body reabsorbs the fluid, and the engorgement and discomfort are relieved.

Symptoms of fibrocystic breast condition range from mildly annoying in some women to extremely painful in others. The severity of discomfort may vary from month to month in the same woman. Although sometimes distressing, this experience is the body's normal response to routine hormonal changes.

This cycle of breast sensitivity, pain and/or enlargement, can also result from medications. Some hormone replacement therapies (estrogen and progesterone) used for postmenopausal women can produce these effects. Other medications, primarily, but not exclusively those with hormones may also provoke these symptoms.

Breast pain unrelated to hormone shifts is called "noncyclic" pain. "Trigger-zone breast pain" is a term that may also be used to describe this area-specific pain. This type of pain may be continuous, or it may be felt intermittently. Trauma, such as a blow to the chest area, a prior **breast biopsy**, or sensitivity to certain medications may also underlie this type of pain. Fibrocystic condition of the breast may be cited as the cause of otherwise unexplained breast pain.

Lumps, apart from those clearly associated with hormone cycles, may also be placed under the heading of fibrocystic condition. These lumps stand out from enlarged general breast tissue. Although noncancerous lumps may occur, the obvious concern with such lumps is cancer.

Noncancerous breast lumps include:

- Adenosis. This condition refers to the enlargement of breast lobules, which contain a greater number of glands than usual. If a group of lobules are found near each other, the affected area may be large enough to be felt.
- Cysts. These are fluid-filled sacs in the breast and probably develop as ducts that become clogged with old cells in the process of normal emptying and filling. Cysts usually feel soft and round or oval. However a cyst deep within the breast may feel hard, as it pushes up against firmer breast tissue. A woman with a cyst may experience pain, especially if it increases in size before her menstrual cycle, as is often the case. Women between the age of 30 and 50 are most likely to develop cysts.
- Epithelial hyperplasia. Also called proliferative breast disease, this condition refers to an overgrowth of cells lining either the ducts or the lobules.

A mammogram of a female breast indicating multiple cysts. *(Custom Medical Stock Photo. Reproduced by permission.)*

- Fibroadenomas. These are tumors that form in the tissues outside the milk ducts. The cause of fibroadenomas is unknown. They generally feel smooth and firm, with a somewhat rubber-like texture. Typically a **fibroadenoma** is not attached to surrounding tissue and moves slightly when touched. They are most commonly found in adolescents and women in their early twenties but can occur at any age.
- Fibrosis. Sometimes one area of breast tissue persistently feels thicker or more prominent than the rest of the breast. This feeling may be caused by old hardened scar tissue and/or dead fat tissue as a result of surgery or trauma. Often the cause of this type of breast tissue is unknown.
- Miscellaneous disorders. A number of other benign (noncancerous) breast problems may be placed under the heading of "fibrocystic condition." These problems include disorders that may lead to breast inflammation (mastitis), infection, and/or nipple discharge.

Atypical ductal hyperplasia

The condition known as atypical ductal hyperplasia (ADH) is a condition in which the cells lining the milk ducts of the breast are growing abnormally. This condition may appear as spots of calcium salts, or calcifications, on the mammogram. A biopsy removed from the breast would confirm the diagnosis. Atypical ductal hyperplasia is not a cancer. In most women, this condition will cause no problems. However, for some women, especially women with family histories of breast cancer, the risk of developing breast cancer is increased. (One study with over 3,000 female participants indicated that about 20% of the participants with atypical hyperplasia and a family history of breast cancer developed breast cancer, as compared to the 8% of participants who developed the disease with atypical hyperplasia and no family history of breast cancer.) For women with ADH and a family history of breast cancer, more frequent mammograms and closer monitoring may be required.

Diagnosis

Breast cancer is the most common concern of women who feel a breast lump or experience an abnormal breast symptom. For peace of mind, and to rule out any possibility of cancer, any newly discovered breast lumps should be brought to the attention of a family physician or an obstetrician-gynecologist. He or she will obtain a history and conduct thorough **physical examination** of the area. Depending on the findings on physical examination, the patient is usually referred for tests. The most common of these tests include:

- **Mammography**. A mammogram is an x-ray examination of the breasts. The two major types of abnormalities doctors look for are masses and calcifications; either abnormality may be benign or malignant. The size, shape, and edges of these masses help doctors determine whether or not cancer is present. Sometimes, however, this test may be difficult to interpret, however, due to dense breast tissue.
- Ultrasonography. If a suspicious lump is detected during mammography, an ultrasound (the use of high-frequency sound waves to outline the shape of various organs and tissues in the body) is useful (although not definitive) in distinguishing benign from cancerous growths.
- Ductography. A ductogram (also called a galactogram) is a test that is sometimes useful in evaluating nipple discharge. A very fine tube is threaded into the opening of the duct onto the nipple. A small amount of dye is injected, outlining the shape of the duct on an x ray, and indicates whether or not there is a mass in the duct.
- Biopsy. If a lump cannot be proven benign by mammography and ultrasound, a breast biopsy may be considered. Usually a tissue sample is removed through a needle (fine-needle aspiration biopsy, or FNAB) to obtain a sample of the lump. The sample is examined under the microscope by a pathologist, and a detailed diagnosis regarding the type of benign lesion or cancer is established. In some cases, however, FNAB may not provide a clear diagnosis, and another type of biopsy (such as a surgical biopsy, core-needle biopsy, or other stereotactic biopsy methods—such as the Mammotome or Advanced Breast Biopsy Instrument) may be required.

Other breast conditions such as inflammation or infection are usually recognized on the basis of suspicious history, breastfeeding, or characteristic symptoms such as pain, redness, and swelling. A positive response to appropriate therapies often confirms the diagnosis.

Treatment

Once a specific disorder within the broad category of fibrocystic condition is identified, treatment can be prescribed. There are a number of treatment options for women with a lump that has been diagnosed as benign. If it is not causing a great deal of pain, the growth may be left in the breast. However, some women may choose to have a lump such as a fibroadenoma surgically removed, especially if it is large. Another option to relieve the discomfort of a painful benign lump is to have the cyst suctioned, or drained. If there is any uncertainty regarding diagnosis, the fluid may be sent to the lab for analysis.

Symptoms of cycle breast sensitivity and engorgement may also be treated with diet, medication, and/or physical modifications. For example,

- Although there is no scientific data to support this claim, many women have reported relief of symptoms when **caffeine** was reduced or eliminated from their **diets**. Decreasing salt before and during the period when breasts are most sensitive may also ease swelling and discomfort. Low-fat diets and elimination of dairy products also appear to decrease soreness for some women. However, it may take several months to realize the effects of these various treatments.
- Over-the-counter **analgesics** such as **acetaminophen** (Tylenol) or ibuprofen (Advil) may be recommended. In some cases, treatment with prescription drugs such as hormones or hormone blockers may prove successful. **Oral contraceptives** may also be prescribed.
- Warm soaks or ice packs may provide comfort. A well-fitted support bra can minimize physical movement and do much to relieve breast discomfort. Breast massage may promote removal of excess fluid from tissues and alleviate symptoms. Massaging the breast with castor oil, straight or infused with herbs or essential oils, can help reduce and dissipate fibroadenomas as well as keep women in touch with changes in their breast tissue.
- Infections are often treated with warm compresses and **antibiotics**. Lactating women are encouraged to continue breastfeeding because it promotes drainage and healing. However, a serious infection may progress to form an **abscess** that may need surgical drainage.
- Some studies of alternative or complementary treatments, although controversial, have indicated that **vitamins** A, B complex and E, and mineral supplements may reduce the risk of developing fibrocystic condition of the breast. Evening primrose oil (*Oenothera biennis*), flaxseed oil, and fish oils have been reported to be effective in relieving cyclic breast pain for some women.

Prognosis

Most benign breast conditions carry no increased risk for the development of breast cancer. However, a small percentage of biopsies uncover overgrowth of tissue in a particular pattern in some women; this pattern indicates a 15–20% increased risk of breast cancer over the next 20 years. Strict attention to early detection measures, such as annual mammograms, is especially important for these women.

Prevention

There is no proven method of preventing the various manifestations of fibrocystic condition from occurring. Some alternative health care practitioners believe that eliminating foods high in methyl xanthines (primarily coffee and chocolate) can decrease or reverse fibrocystic breast changes.

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KEY TERMS

Advanced Breast Biopsy Instrument (ABBI)—Uses a rotating circular knife and thin heated electrical wire to remove a large cylinder of abnormal breast tissue.

Lobules—A small lobe or subdivision of a lobe (often on a gland) that may be seen on the surface of the gland by bumps or bulges.

Lymph nodes—Rounded, encapsulated bodies consisting of an accumulation of lymphatic tissue.

Mammotome—A method for removing breast biopsies using suction to draw tissue into an opening in the side of a cylinder inserted into the breast tissue. A rotating knife then cuts tissue samples from the rest of the breast; also known as a vacuum-assisted biopsy

Stereotactic biopsy—A biopsy taken by precisely locating areas of abnormal growth through the use of delicate instruments.

ORGANIZATIONS

American Cancer Society. 1599 Clifton Rd. NE, Atlanta, GA 30329. (800) ACS-2345 <http://www.cancer.org>.

American College of Obstetricians and Gynecologists. 409 12th St., S.W., P.O. Box 96920, Washington, DC 20090-6920. <http://www.acog.org>.

Cancer Information Service (CIS). 9000 Rockville Pike, Building 31, Suite 10A18, Bethesda, MD 20892. (800) 4-CANCER.

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Fibroids *see* **Uterine fibroids**

Fibromyalgia

Definition

Fibromyalgia is described as inflammation of the fibrous or connective tissue of the body. Widespread muscle **pain**, **fatigue**, and multiple tender points characterize these conditions. Fibrositis, fibromyalgia, and fibromyositis are names given to a set of symptoms believed to be caused by the same general problem.

Description

Fibromyalgia is more common than previously thought, with as many as 3–6% of the population affected by the disorder. Fibromyalgia is more prevalent in adults than children, with more women affected than men, particularly women of childbearing age.

Causes and symptoms

The exact cause of fibromyalgia is not known. Sometimes it occurs in several members of a family, suggesting that it may be an inherited disorder. People with fibromyalgia are most likely to complain of three primary symptoms: muscle and joint pain, stiffness, and fatigue.

Pain is the major symptom with aches, tenderness, and stiffness of multiple muscles, joints, and soft tissues. The pain also tends to move from one part of the body to another. It is most common in the neck, shoulders, chest, arms, legs, hips, and back. Although the pain is present most of the time and may last for years, the severity of the pain is changeable and dependent on individual patient perception.

Symptoms of fatigue may result from the individual's chronic pain coupled with **anxiety** about the problem and how to find relief. The inflammatory process also produces chemicals that are known to cause fatigue. Other common symptoms are tension headaches, difficulty swallowing, recurrent abdominal pain, **diarrhea**, and numbness or tingling of the extremities. **Stress**, anxiety, depression, or lack of sleep can increase symptoms. Intensity of symptoms is variable ranging from gradual improvement to episodes of recurrent symptoms.

Diagnosis

Diagnosis is difficult and frequently missed because symptoms of fibromyalgia are vague and generalized. Coexisting nerve and muscle disorders such as **rheumatoid arthritis**, spinal arthritis, or **Lyme disease** may further complicate the diagnostic process. Presently, there are no tests available to specifically diagnose fibromyalgia. The diagnosis is usually made after ruling out other medical conditions with similar symptoms.

Because of the emotional distress experienced by people with this condition and the influence of stress on the symptoms themselves, fibromyalgia has often been labeled a psychological problem. Recognition of the

underlying inflammatory process involved in fibromyalgia has helped promote the validity of this disease.

In 1990, the America College of Rheumatology developed standards for fibromyalgia that health care practitioners can use to diagnose this condition. According to these standards, a person is thought to have fibromyalgia if he or she has widespread pain in combination with tenderness in at least 11 of the 18 sites known as trigger points. Trigger point sites include the base of the neck, along the backbone, in front of the hip and elbow, and at the rear of the knee and shoulder.

KEY TERMS

Connective tissue—Tissue that supports and binds other body tissue and parts.

Lyme disease —An acute recurrent inflammatory disease involving one or a few joints, believed to be transmitted by a tickborne virus. The condition was originally described in the community of Lyme, Connecticut, but has also been reported in other parts of the United States and other countries. Knees, other large joints are most commonly involved with local inflammation and swelling.

Rheumatology—The study of disorders characterized by inflammation, degeneration of connective tissue, and related structures of the body. These disorders are sometimes collectively referred to as rheumatism.

Treatment

There is no known cure for fibromyalgia. Therefore, the goal of treatment is successful symptom management. Treatment usually requires a combination of therapies, **exercise**, proper rest, and diet. A patient's clear understanding of his or her role in the recovery process is imperative for successful management of this condition.

Treatments found to be helpful include heat and occasionally cold applications. A regular stretching program is often useful. Aerobic activities focusing on increasing the heart rate are the preferred forms of exercise over most other forms of exertion. Exercise programs need to include good warm-up and cool-down sessions, with special attention given to avoiding exercises causing joint pain. The diet should include a large variety of fruits and vegetables which provide the body with trace elements and **minerals** that are necessary for healthy muscles.

Adequate rest is essential in the treatment of fibromyalgia. Avoidance of stimulating foods or drinks (such as coffee) and medications like **decongestants** prior to bedtime is advised. If diet, exercise, and adequate rest do not relieve the symptoms of fibromyalgia, medications may be prescribed. Medications prescribed and found to have some benefit include **antidepressant drugs**, **muscle relaxants**, and anti-inflammatory drugs.

People with fibromyalgia often need a rheumatology consultation (a meeting with a doctor who specializes in disorders of the joints, muscles, and soft tissue) to decide the cause of various rheumatic symptoms, to be educated about fibromyalgia and its treatment, and to exclude other rheumatic diseases. A treatment program must be individualized to meet the patient's needs. The rheumatologist, as the team leader, enlists and coordinates the expertise of other health professionals in the care of the patient.

Alternative treatment

Massage therapy can be helpful, especially when a family member is instructed on specific massage techniques to manage episodes of increased symptoms. Specific attention to mental health, including psychological consultation, may also be important, since depression may precede or accompany fibromyalgia. Other alternative therapies, including **hellerwork**, **rolfing**, homeopathic medicine, Chinese traditional medicine (both **acupuncture** and herbs), **polarity therapy**, and Western botanical medicine, can assist the person with fibromyalgia to function day to day and can contribute to healing.

Prognosis

Fibromyalgia is a chronic problem. The symptoms sometimes improve and at other times worsen, but they often continue for months to years.

Prevention

There is no known or specific way to prevent fibromyalgia. However, similar to many other medical conditions, remaining as healthy as possible with a good diet, safe exercise, and adequate rest is the best prevention.

Resources

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ORGANIZATIONS

The American College of Rheumatology. 1800 Century Place, Suite 250, Atlanta, GA 30345. (404) 633-3777. <http://www.rheumatology.org>.

Arthritis Foundation.1300 W. Peachtree St., Atlanta, GA 30309. (800) 283-7800. <http://www.arthritis.org>.

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Fibromyomas *see* **Uterine fibroids**

Fibrous breast lumps *see* **Fibroadenoma**

Fifth disease

Definition

Fifth disease is a mild childhood illness caused by the human parvovirus B19 that causes flu-like symptoms and a rash. It is called fifth disease because it was fifth on a list of common childhood illnesses that are accompanied by a rash, including **measles**, **rubella** or German measles, **scarlet fever** (or scarlatina), and scarlatinella, a variant of scarlet **fever**.

Description

The Latin name for the disease is *erythema infectiosum*, meaning infectious redness. It is also called the "slapped cheek disease" because, when the bright red rash first appears on the cheeks, it looks as if the face has been slapped. Anyone can get the disease, but it occurs more frequently in school-aged children. The disease is usually mild, and both children and adults usually recover quickly without complications. In fact, some individuals exhibit no symptoms and never even feel ill. Outbreaks most often occur in the winter and spring.

Causes and symptoms

Fifth disease is caused by the human parvovirus B19, a member of the Parvoviridae family of viruses, that lives in the nose and throat of the infected person. The virus is spread through the air by coughing and sneezing. Because the virus needs a rapidly dividing cell in order to multiply, it attacks the red blood cells of the body. Once infected, a person is believed to be immune to reinfection.

Symptoms may appear four to 21 days after being exposed to the virus. Initial symptoms are flu-like and include **headache**, body ache, **sore throat**, a mild fever of 101°F (38.3°C), and chills. It is at this time, prior to the development of the rash, that individuals are contagious. These symptoms last for two to three days. In children, a bright red rash that looks like a slap mark develops suddenly on the cheeks. The rash may be flat or raised and may or may not be itchy. Sometimes, the rash spreads to the arms, legs, and trunk, where it has a lace-like or net-like appearance. The rash can also involve the palms of the hands and soles of the feet. By the time the rash appears, individuals are no longer infectious. On average, the rash lasts for 10–11 days, but may last for as long as five to six weeks. The rash may fade away and then reappear upon exposure to sunlight, hot baths, emotional distress, or vigorous **exercise**.

This infant has a rash caused by Fifth disease, or erythema infectiosum. *(Custom Medical Stock Photo. Reproduced by permission.)*

Adults generally do not develop a rash, but instead may have swollen and painful joints, especially in the hands and feet. In adults, symptoms such as sore throat, headache, muscle and joint **pain**, abdominal pain, **diarrhea**, and vomiting occur more frequently than in children and are usually more severe. The joint pain can be arthritis-like and last for several months, especially in women, but the disease does not appear to progress to **rheumatoid arthritis**.

The virus causes the destruction of red blood cells and, therefore, a deficiency in the oxygen-carrying capacity of the blood (anemia) can result. In healthy people, the anemia is mild and only lasts a short while. In people with weakened immune systems, however, either because they have a chronic disease like **AIDS** or **cancer** (immunocompromised), or are receiving medication to suppress the immune system (immunosuppressed), such as organ transplant recipients, this anemia can be severe and last long after the infection has subsided. Symptoms of anemia include **fatigue**, lack of color, lack of energy, and **shortness of breath**. Some individuals with sickle cell anemia, iron deficiency, a number of different hereditary blood disorders, and those who have received bone marrow transplantations may be susceptible to developing a potentially life-threatening complication called a transient aplastic crisis where the body is temporarily unable to form new red blood cells.

In very rare instances, the virus can cause inflammation of different areas of the body, including the brain (**encephalitis**), the covering of the brain and spinal cord (**meningitis**), the lungs (pneumonitis), the liver (hepatitis), and the heart muscle (**myocarditis**). The virus can also aggravate symptoms for people with an autoimmune disease called **systemic lupus erythematosus**.

There is some concern about fifth disease in pregnant women. Although no association with an increased number of **birth defects** has been demonstrated, there is concern that infection during the first three months of **pregnancy** may lead to a slight increase in the number of miscarriages. There is also some concern that infection later in pregnancy may involve a very small risk of premature delivery or stillbirths. As a result, women who get fifth disease while they are pregnant should be monitored closely by a physician.

KEY TERMS

Anemia—A congenital or acquired deficiency in the iron-carrying capacity of the blood.

Antibody—A specific protein produced by the immune system in response to a specific foreign protein or particle called an antigen.

Immunocompromised—A state in which the immune system is weakened or is not functioning properly due to chronic disease.

Immunosuppressed—A state in which the immune system is suppressed by medications during the treatment of other disorders, like cancer, or following an organ transplantation.

Reye's syndrome—A very serious, rare disease, most common in children, that involves an upper respiratory tract infection followed by brain and liver damage.

Sickle cell anemia—A hereditary blood disorder in which the red blood cells are misshapen into crescent or sickle shapes resulting in the reduced oxygen-carrying capacity of the lungs.

Diagnosis

Fifth disease is usually suspected based on a patient's symptoms, including the typical appearance of the bright red rash on the cheeks, patient history, age, and the time of year. The physician will also exclude other potential causes for the symptoms and rash, including rubella, **infectious mononucleosis**, bacterial infections like **Lyme disease**, allergic reactions, and lupus.

In addition, there is a blood test for fifth disease, but it is generally used only for pregnant women and for people who have weakened immune systems or who suffer from blood disorders, such as sickle cell anemia. The test involves measuring for a particular antibody or protein that the body produces in response to infection with the human parvovirus B19. The test is 92–97% specific for this disease.

Because fifth disease can pose problems for an unborn fetus exposed to the disease through the mother, testing may also be conducted while a fetus is still in the uterus. This test uses fluid collected from the sac around the fetus (amniotic fluid) instead of blood to detect the viral DNA.

Treatment

In general, no specific treatment for fifth disease is required. The symptoms can be treated using over-the counter medications, such as **acetaminophen** (Tylenol) or ibuprofen (Motrin, Advil). If the rash itches, calamine lotion can be applied. **Aspirin** is usually not given to children under the age of 18 to prevent the development of a serious illness called **Reye's syndrome**.

Patients who are receiving medications to suppress the immune system in the treatment of some other condition may be allowed to temporarily decrease the medications in order to allow the immune system to combat the infection and recover from the anemia. Those with weakened (not suppressed) immune systems, such as AIDS patients, may be given immunoglobulin intravenously to help the immune system fight the infection. People with severe anemia or who experience an aplastic crisis may require hospitalization and blood transfusions.

Prognosis

Generally, fifth disease is mild, and patients tend to improve without any complications. In cases where the patient is either immunocompromised or immunosuppressed, a life-threatening aplastic crisis can occur. With prompt treatment, however, the prognosis is good. Mothers who develop the infection while pregnant can pass the infection on to their fetus, and as such, stand an increased risk of **miscarriage** and **stillbirth**. There are tests and treatments, however, that can be performed on the fetus while still in the uterus that can reduce the risk of anemia or other complications.

Prevention

Currently, there is no vaccine against fifth disease. Avoiding contact with persons who exhibit symptoms of a cold and maintaining good personal hygiene by regularly washing hands may minimize the chances of an

infection. Pregnant women should avoid exposure to persons infected with the disease and notify their obstetrician immediately if they are exposed so that they can be tested and monitored closely.

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Lata Cherath, PhD

Filariasis

Definition

Filiariasis is the name for a group of tropical diseases caused by various thread-like parasitic round worms (nematodes) and their larvae. The larvae transmit the disease to humans through a mosquito bite. Filariasis is characterized by **fever**, chills, **headache**, and **skin lesions** in the early stages and, if untreated, can progress to include gross enlargement of the limbs and genitalia in a condition called **elephantiasis**.

Description

Approximately 170 million people in the tropical and subtropical areas of southeast Asia, South America, Africa, and the islands of the Pacific are affected by this debilitating parasitic disease. While filariasis is rarely fatal, it is the second leading cause of permanent and long-term disability in the world. The World Health Organization (WHO) has named filariasis one of only six "potentially eradicable" infectious diseases and has embarked upon a 20-year campaign to eradicate the disease.

In all cases, a mosquito first bites an infected individual then bites another uninfected individual, transferring some of the worm larvae to the new host. Once within the body, the larvae migrate to a particular part of the body and mature to adult worms. Filariasis is classified into three distinct types according to the part of the body that becomes infected: lymphatic filariasis affects the circulatory system that moves tissue fluid and immune cells (lymphatic system); subcutaneous filariasis infects the areas beneath the skin and whites of the eye; and serous cavity filariasis infects body cavities but does not cause disease. Several different types of worms can be responsible for each type of filariasis, but the most common species include the following: *Wucheria bancrofti, Brugia malayi* (lymphatic filariasis), *Onchocerca volvulus, Loa loa, Mansonella streptocerca, Dracunculus medinensis* (subcutaneous filariasis), *Mansonella pustans*, and *Mansonella ozzardi* (serous cavity filariasis).

The two most common types of the disease are Bancroftian and Malayan filariasis, both forms of lymphatic filariasis. The Bancroftian variety is found throughout Africa, southern and southeastern Asia, the Pacific islands, and the tropical and subtropical regions of South America and the Caribbean. Malayan filariasis occurs only in southern and southeastern Asia. Filariasis is occasionally found in the United States, especially among immigrants from the Caribbean and Pacific islands.

A larvae matures into an adult worm within six months to one year and can live between four and six years. Each female worm can produce millions of larvae, and these larvae only appear in the bloodstream at night, when they may be transmitted, via an insect bite, to another host. A single bite is usually not enough to acquire an infection, therefore, short-term travelers are usually safe. A series of multiple bites over a period of time is required to establish an infection. As a result, those individuals who are regularly active outdoors at night and those who spend more time in remote jungle areas are at an increased risk of contracting the filariasis infection.

Causes and symptoms

In cases of lymphatic filariasis, the most common form of the disease, the disease is caused by the adult worms actually living in the lymphatic vessels near the lymph nodes where they distort the vessels and cause local inflammation. In advanced stages, the worms can actually obstruct the vessels, causing the surrounding tissue to become enlarged. In Bancroftian filariasis, the legs and genitals are most often involved, while the Malayan variety affects the legs below the knees. Repeated episodes of inflammation lead to blockages of the lymphatic system, especially in the genitals and legs. This causes the affected area to become grossly enlarged, with thickened, coarse skin, leading to a condition called elephantiasis.

In conjunctiva filariasis, the worms' larvae migrate to the eye and can sometimes be seen moving beneath the skin or beneath the white part of the eye (conjunctiva). If untreated, this disease can cause a type of blindness known as onchocerciasis.

Symptoms vary, depending on what type of parasitic worm has caused the infection, but all infections usually

begin with chills, headache, and fever between three months and one year after the insect bite. There may also be swelling, redness, and **pain** in the arms, legs, or scrotum. Areas of pus (abscesses) may appear as a result of dying worms or a secondary bacterial infection.

Diagnosis

The disease is diagnosed by taking a patient history, performing a **physical examination**, and by screening blood specimens for specific proteins produced by the immune system in response to this infection (antibodies). Early diagnosis may be difficult because, in the first stages, the disease mimics other bacterial skin infections. To make an accurate diagnosis, the physician looks for a pattern of inflammation and signs of lymphatic obstruction, together with the patient's possible exposure to filariasis in an area where filariasis is common. The larvae (microfilariae) can also be found in the blood, but because mosquitos, which spread the disease, are active at night, the larvae are usually only found in the blood between about 10 pm and 2 am.

Treatment

Either ivermectin, albendazole, or diethylcarbamazine is used to treat a filariasis infection by eliminating the larvae, impairing the adult worms' ability to reproduce, and by actually killing adult worms. Unfortunately, much of the tissue damage may not be reversible. The medication is started at low doses to prevent reactions caused by large numbers of dying parasites.

While effective, the medications can cause severe side effects in up to 70% of patients as a result either of the drug itself or the massive **death** of parasites in the blood. Diethylcarbamazine, for example, can cause severe allergic reactions and the formation of pus-filled sores (abscesses). These side effects can be controlled using **antihistamines** and anti-inflammatory drugs (**corticosteroids**). Rarely, treatment with diethylcarbamazine in someone with very high levels of parasite infection may lead to a fatal inflammation of the brain (**encephalitis**). In this case, the fever is followed by headache and confusion, then stupor and **coma** caused when massive numbers of larvae and parasites die. Other common drug reactions include **dizziness**, weakness, and nausea.

Symptoms caused by the death of the parasites include fever, headache, muscle pain, abdominal pain, **nausea and vomiting**, weakness, dizziness, lethargy, and **asthma**. Reactions usually begin within two days of starting treatment and may last between two and four days.

No treatment can reverse elephantiasis. Surgery may be used to remove surplus tissue and provide a way to drain the fluid around the damaged lymphatic vessels. Surgery may also be used to ease massive enlargement of the scrotum. Elephantiasis of the legs can also be helped by elevating the legs and providing support with elastic bandages.

Prognosis

The outlook is good in early or mild cases, especially if the patient can avoid being infected again. The disease is rarely fatal, and with continued WHO medical intervention, even gross elephantiasis is now becoming rare.

Prevention

The best method of preventing filariasis is to prevent being repeatedly bitten by the mosquitoes that carry the disease. Some methods of preventing insect bites include the following:

- limit outdoor activities at night, particularly in rural or jungle areas
- wear long sleeves and pants and avoid dark-colored clothing that attracts mosquitoes
- avoid perfumes and colognes
- treat one or two sets of clothing ahead of time with permethrin (Duramon, Permanone)
- wear DEET insect repellent or, especially for children, try citronella or lemon eucalyptus, to repel insects
- if sleeping in an open area or in a room with poor screens, use a bed net to avoid being bitten while asleep
- use air conditioning, the cooler air makes insects less active

In addition, filariasis can be controlled in highly infested areas by taking ivermectin preventatively before being bitten. Currently, there is no vaccine available, but scientists are working on a preventative vaccine at this time.

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KEY TERMS

Abscess—An area of inflamed and injured body tissue that fills with pus.

Antibody—A specific protein produced by the immune system in response to a specific foreign protein or particle called an antigen.

Conjunctiva—The mucous membrane that lines the inside of the eyelid and the exposed surface of the eyeball.

Elephantiasis—A condition characterized by the gross enlargement of limbs and/or the genitalia that is also accompanied by a hardening and stretching of the overlying skin. Often a result of an obstruction in the lymphatic system caused by infection with a filarial worm.

Encephalitis—Inflammation of the brain.

Lymphatic system—The circulatory system that drains and circulates fluid containing nutrients, waste products, and immune cells, from between cells, organs, and other tissue spaces.

Microfilariae—The larvae and infective form of filarial worms.

Nematode—Round worms.

Subcutaneous—The area directly beneath the skin.

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National Institute of Allergies and Infectious Diseases, Division of Microbiology and Infectious Diseases. Building 31, Room. 7A-50, 31 Center Drive MSC 2520, Bethesda, MD 20892. <http://www.niaid.nih.gov>.

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Carol A. Turkington

Filgras *see* **Cancer therapy, supportive; Immunologic therapies**

Fingernail removal *see* **Nail removal**

Fingertip injuries

Definition

Fingertip trauma covers cuts, accumulation of blood (hematoma), bone breakage, or **amputation** in the fingertip.

Description

The fingertips are specialized areas of the hand with highly developed sensory and manipulative functions. Large sensory and motor areas located in the brain regulate the precise and delicate functions of fingertips. The fingertip is the site where extensor and flexor tendons insert. Fingertip injuries are extremely common since the hands hold a wide array of objects. In 2001, the approximately 10% of all accidents in the United States referred for Emergency Room consults involve the hand. Hand injuries are frequently the result of job injuries and account for 11–14% of on-the-job injuries and 6% of compensation paid injuries. Injury to the nail bed occurs in approximately 15–24% of fingertip injuries.

Fingertip injuries can result in amputation or tissue loss. The injury is assessed whether the bone and underlying tissue are intact and the size of the wound area. The pulp is the area of skin opposite the fingernail and is usually very vulnerable to injury. Pulp injuries commonly occur in persons who use or are in close contact with fast moving mechanical devices. These injuries can crush, cut, and puncture. The fingertips can also be injured by common crushing accidents. This could cause the development of a subungal hematoma (an accumulation of blood under the nail). At the base of the distal phalanx (the first circular skin fold from the tip) injuries can occur that can fracture the underlying bone in the area. Quite commonly

a hammer, closing a door, or sport accidents usually cause these injuries. These **fractures** can be simple, requiring little treatment or more complicated involving the joint. The accident may involve the point of insertion of a tendon. Usually this occurs when the terminal joint is being forced to flex while held straight. This motion typically occurs when tucking in sheets during bed making, a common cause of tendon injury. This injury causes a loss of extension (straightening the finger) ability.

Causes and symptoms

Accidental amputations will usually result in profuse bleeding and tissue loss. Injuries to the pulp can occur as from fast moving mechanical instruments, such as drills. These injuries may puncture the pulp. Injuries such as a subungal hematoma are caused by a crushing type injury. Fractures typically occur as the result of crushing injuries or tendon avulsion. These crushing injuries are frequently caused during sport injury and can be treated by simple interventions such as **immobilization** or more complex procedures if tendons are affected (the trauma is then treated as a tendon injury). Fractures can cause **pain** and, depending on the extent of swelling, there may be some restriction of movement. Tendon injuries can be caused when the terminal joint is exposed to force flexing motion (moving the finger toward the palm) while held straight.

Diagnosis

The attending clinician should evaluate the injury in a careful and systematic manner. The appearance of the hand can provide valuable information concerning presence of fractures, vascular status, and tendon involvement. Bones and joints should be evaluated for motion and tenderness. Nerves should be examined for sensory (feeling sensations) and motor (movement) functioning. Amputations usually profusely bleed and there is tissue loss. The wound is treated based on loss of tissue, bone, and wound area. Injuries to the pulp can be obvious during inspection. Subungal hematoma usually present a purplish-black discoloration under the nail. This is due to a hematoma underneath the nail. Radiographs may be required to assess the alignment of fractures or detect foreign bodies. Patients usually suffer from pain since injuries to the fingertip bone are usually painful and movement may be partially restricted due to swelling of the affected area. Tendon injuries usually result in the loss of ability to straighten or bend the finger.

Treatment

Amputation with bone and underlying tissue intact and a wound area 1 cm or less should be cleaned and treated with a dressing. With these types of **wounds** healthy tissue will usually grow and replace the injured area. Larger wounds may require surgical intervention. Puncture wounds should be cleaned and left open to heal. Patients typically receive **antibiotics** to prevent infection. A procedure called trephining treats subungal hematomas. This procedure is usually done with a straight cutting needle positioned over the nail. The clinician spins the needle with forefinger and thumb until a hole is made through the nail.

Patients who have extensive crush injuries or subungal hematomas involving laceration to skin folds or nail damage should have the nail removed to examine the underlying tissue (called the matrix). Patients who have a closed subungal hematoma with an intact nail and no other damage (no nail disruption or laceration) are treated conservatively. If the fracture is located two-thirds below the fingertip immobilization using a splint may be needed. Conservative treatment is recommended for crush injuries that fracture the terminal phalanx if a subungal hematoma is not present. Severe fractures near the fist circular skin crease may require surgical correction to prevent irregularity of the joint surface, which can cause difficulty with movement. Injury to a flexor tendon usually requires surgical repair. If this is not possible, the finger and wrist should be placed in a splint with specific positioning to prevent further damage.

Prognosis

Prognosis depends on the extent of traumatic damage to the affected area. Nail lacerations that are not treated may cause nail deformities. When amputation is accompanied with loss of two-thirds of the nail, half of the fingers develop beaking, or a curved nail. Aftercare and follow up are important components of treatment. The patient is advised to keep the hand elevated, check with a clinician two days after treatment, and to splint fractures for two weeks in the extended position. Usually a nail takes about 100 days to fully grow. Healing for an amputation takes about 21 to 27 days. This markedly

KEY TERMS

Distal—Movement away from the origin.

Flex—To bend.

Laceration—A cut in the skin

Phalanx—A bone of the fingers or toes.

Tendon—A structure that connects a skeletal muscle to bone.

decreases in elderly patients, primarily due to a compromised circulation normally part of advancing age.

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American Society of Plastic Surgeons. 444 E. Algonquin Rd., Arlington Heights, IL. (888) 475-2784.

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Fish and shellfish poisoning

Definition

Fish and shellfish **poisoning** is a common but often unrecognized group of illnesses related to food. Three of these illnesses include ciguatera, scombroid, and paralytic shellfish poisoning.

Ciguatera

Definition

Ciguatera (from the Spanish word for a poisonous snail) is a food-related illness that causes abdominal and neurological symptoms.

Causes and symptoms

Ciguatera is caused by eating fish that have a toxin called ciguatoxin. Scientists believe this toxin is acquired by the fish through the food chain, and is originally produced by small algae microorganisms (dinoflagellates). The fish most likely contaminated with ciguatoxin are those that feed close to tropical reefs, including red snapper, grouper, and barracuda. Larger fish are more likely to contain the toxin. Although not as common in the United States, ciguatera is commonly diagnosed on many of the islands in the Pacific Ocean.

Illness from ciguatera can occur in just a few minutes to about 30 hours after eating. Most cases occur one to six hours after eating the contaminated fish. Initial symptoms are abdominal cramps, nausea, vomiting, or watery **diarrhea**. The most characteristic symptoms of the illness are those involving the nervous system. These include **numbness and tingling** around the lips, tongue, and mouth; **itching**; **dry mouth**; metallic taste in the mouth; and blurry vision. In more prominent cases, patients may complain of temporary blindness, a slow pulse, and a feeling that their teeth are loose. Patients may also have the strange symptom of reversal of hot and cold sensations on the skin, where cold things feel very hot or painful to the touch. In very severe cases, there may be difficulties in breathing or low blood pressure.

Diagnosis

Ciguatera diagnosis is based on the typical combination of symptoms after eating fish. There are no readily available blood or urine tests to detect the poisoning, but some researchers have developed a test for the toxin left on any remaining fish. A person does not have to be in a tropical area to get ciguatera. Fish can be caught from one of these distant areas, and can then be shipped and eaten locally. It is important to report suspected cases to local public health officials because more cases may occur from other contaminated fish.

Treatment

The treatment for this illness is general. Patients are given fluids (by mouth or through a vein) and medications to decrease the itching or to treat vomiting and/or diarrhea. The neurological symptoms can cause discomfort and treatment with amitriptyline (a medicine that has been used for depression) may be useful. Other medications may also be given.

Prognosis

Although **death** can occur, almost all patients diagnosed with ciguatera will recover. Recovery, however, can be slow and some symptoms can last for weeks or even months. Symptoms can also be aggravated by other illnesses or alcohol.

Prevention

Knowing the kinds of fish linked to ciguatera can help a person avoid eating high-risk fish. However, over 400 different kinds of fish have been linked to the disease, even salmon. A particular fish in a given area may be more likely to cause ciguatera than other fish. For example, red snapper is most often the source of ciguatera in the Pacific, while barracuda is more likely to contain the toxin in Florida. This is why it is illegal to sell barracuda in Florida for human consumption. Cooking the fish does not prevent ciguatera.

Scombroid

Definition

Scombroid is a fish-associated illness caused by eating improperly handled fish. Fish linked to this disease are usually in the Scombridae family, which includes yellowfin tuna, skipjack, bonito, and mackerel.

Causes and symptoms

Scombroid occurs after eating fish that has not been properly refrigerated after capture. Unlike ciguatera, the toxins linked with scombroid are not contracted by the fish from its surroundings. Bacteria that are normally found in fish act directly on a chemical (called histidine) in the flesh of fish that are not properly cooled when stored. This interaction produces histamine and other chemicals that cause the illness when the fish is eaten.

Symptoms of scombroid occur quickly after eating the fish, as soon as 10 minutes. Since histamine is released by certain cells in the body during an allergic reaction, scombroid can be confused with a fish allergy. Scombroid causes flushing of the face, sweating, a burning feeling in the mouth or throat, vomiting, diarrhea, and headaches. A rash that looks like a **sunburn** may occur, and a small number of patients have **hives**. Some patients have a metallic or peppery taste in their mouths. In more severe cases, rapid pulse, blurred vision, and difficulty breathing can occur. Symptoms usually last about four hours.

Diagnosis

Like ciguatera, scombroid poisoning is diagnosed based on typical symptoms occurring after eating fish. There are usually no available tests for the patient. Experimentally, however, elevated levels of histamine-related products have been found in the urine. It may be possible for public health officials to test any remaining fish flesh for histamine levels. Improperly refrigerated fish caught in both temperate and tropical waters have been linked to the illness. An outbreak of similar cases may be helpful in correctly diagnosing the problem.

Treatment

The treatment for scombroid is usually general. **Antihistamines** like diphenhydramine (Benadryl) may shorten the duration of the illness, but the illness will go away on its own. Some doctors have found that cimetidine (Tagamet) given through a vein may be helpful as well. In rare, more severe cases, epinephrine (adrenaline) may be used.

KEY TERMS

Algae—Plants that have one cell.

Histamine—A chemical found naturally in the body that produces inflammation and increases blood flow; the uncomfortable symptoms of an allergy attack or an allergic reaction are generally caused by the release of histamine.

Toxin—A poisonous substance usually produced by a living thing.

Prognosis

Although sometimes dramatic and alarming symptoms can occur, scombroid is usually not serious. The patient should be reassured that scombroid is not a fish allergy.

Prevention

Adequate storage of the target fish will always prevent scombroid. Since the fish does not appear spoiled or smell bad, the consumer cannot detect the risk of the illness before eating the fish. Cooking the fish does not prevent scombroid. Suspected cases should be reported to public health officials.

Paralytic shellfish poisoning

Definition

Paralytic shellfish poisoning (PSP) is a nervous system disease caused by eating cooked or raw shellfish that contain environmental toxins. These toxins are produced by a group of algae (dinoflagellates). It is unclear whether these toxins are related to the "blooming" of the algae, also called red tide because the algae can turn the water reddish brown. PSP occurs mostly in May through November.

Causes and symptoms

PSP develops usually within minutes after eating a contaminated shellfish, most commonly a mussel, clam, or oyster. Symptoms include **headache**, a floating feeling, **dizziness**, lack of coordination, and tingling of the mouth, arms, or legs. Muscle weakness causing difficulty swallowing or speaking may occur. Abdominal symptoms such as nausea, vomiting, and diarrhea can also occur. Unlike ciguatera and scombroid, PSP may have a much more serious outcome. PSP may cause difficulty breathing related to weakness or **paralysis** of the breathing muscle. The symptoms may last for six to 12 hours, but a patient may continue to feel weak for a week or more.

Diagnosis

PSP diagnosis is based on symptoms after eating shellfish, even if the shellfish are adequately cooked. No blood or urine test is available to diagnose the illness, but tests in mice to detect the toxin from the eaten fish can be done by public health officials.

Treatment

The treatment of PSP is mostly supportive. If early symptoms are recognized, the doctor will try to flush the toxin from the gastrointestinal tract with medications that create diarrhea. Vomiting may be induced if the patient has no signs of weakness. In cases where the muscles of breathing are weakened, the patient may be placed on a respirator until the weakness goes away. However, this measure is not usually needed. Likewise, the use of a machine to clean the blood (dialysis) has been used in severe cases.

Prognosis

The prognosis for PSP is quite good, especially if the patient has passed the initial 12 hours of illness without needing breathing support. Most deaths occur during this period if breathing help is not available.

Prevention

Measures to control PSP require detecting rising numbers of algae in coastal waters by periodic microscopic examination. By law, shellfish beds are closed when levels of the toxin-producing organisms are above acceptable standards. Cooking the shellfish does not prevent this disease. Suspected cases should be reported to public health officials.

Resources

PERIODICALS

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Larry Lutwick, MD, FACP

5p- syndrome *see* **Cri du chat syndrome**

Flesh-eating disease

Definition

Flesh-eating disease is more properly called necrotizing fasciitis, a rare condition in which bacteria destroy tissues underlying the skin. This tissue **death**, called necrosis or **gangrene**, spreads rapidly. This disease can be fatal in as little as 12 to 24 hours.

Description

Although the term is technically incorrect, flesh-eating disease is an apt descriptor: the infection appears to devour body tissue. Media reports increased in the middle and late 1990s, but the disease is not new. Hippocrates described it more than three millennia ago and thousands of reports exist from the Civil War. Approximately 500 to 1,500 cases of necrotizing fasciitis occur in the United States each year.

Flesh-eating disease is divided into two types. Type I is caused by anaerobic bacteria, with or without the presence of aerobic bacteria. Type II, also called hemolytic streptococcal gangrene, is caused by group A streptococci; other bacteria may or may not be present. The disease may also be called synergistic gangrene.

Type I fasciitis typically affects the trunk, abdomen, and genital area. For example, Fournier's gangrene is a "flesh-eating" disease in which the infection encompasses the external genitalia. The arms and legs are most often affected in type II fasciitis, but the infection may appear anywhere.

Causes and symptoms

The two most important factors in determining whether or not a person will develop flesh-eating disease are: the virulence (ability to cause disease) of the bacteria and the susceptibility (ability of a person's immune system to respond to infection) of the person who becomes infected with this bacteria.

In nearly every case of flesh-eating disease, a skin injury precedes the disease. As bacteria grow beneath the skin's surface, they produce toxins. These toxins destroy superficial fascia, subcutaneous fat, and deep fascia. In some cases, the overlying dermis and the underlying muscle are also affected.

Initially, the infected area appears red and swollen and feels hot. The area is extremely painful, which is a prominent feature of the disease. Over the course of hours or days, the skin may become blue-gray, and fluid-filled blisters may form. As nerves are destroyed the area

becomes numb. An individual may go into **shock** and develop dangerously low blood pressure. Multiple organ failure may occur, quickly followed by death.

Diagnosis

The appearance of the skin, paired with **pain** and **fever** raises the possibility of flesh-eating disease. An x ray, **magnetic resonance imaging** (MRI), or **computed tomography scans** (CT scans) of the area reveals a feathery pattern in the tissue, caused by accumulating gas in the dying tissue. Necrosis is evident during exploratory surgery, during which samples are collected for bacterial identification.

Treatment

Rapid, aggressive medical treatment, specifically, antibiotic therapy and surgical **debridement**, is imperative. **Antibiotics** may include penicillin, an aminoglycoside or third-generation cephalosporin, and clindamycin or metronidazole. **Analgesics** are employed for pain control. During surgical debridement, dead tissue is stripped away. After surgery, patients are rigorously monitored for continued infection, shock, or other complications. If available, hyperbaric oxygen therapy has also be used.

Prognosis

Flesh-eating disease has a fatality rate of about 30%. Diabetes, arteriosclerosis, immunosuppression, kidney disease, **malnutrition**, and **obesity** are connected with a poor prognosis. Older individuals and intravenous drug users may also be at higher risk. The infection site also has a role. Survivors may require plastic surgery and may have to contend with permanent physical disability and psychological adjustment.

Prevention

Flesh-eating disease, which occurs very rarely, cannot be definitively prevented. The best ways to lower the risk of contracting flesh-eating disease are:

- take care to avoid any injury to the skin that may give the bacteria a place of entry
- when skin injuries do occur, they should be promptly washed and treated with an antibiotic ointment or spray
- people who have any skin injury should rigorously attempt to avoid people who are infected with streptococci bacteria. A bacteria that causes a simple **strep throat** in one person may cause flesh-eating disease in another
- have any areas of unexplained redness, pain, or swelling examined by a doctor, particularly if the affected area seems to be expanding

KEY TERMS

Aerobic bacteria—Bacteria that require oxygen to live and grow.

Anaerobic bacteria—Bacteria that require the absence of oxygen to live and grow.

CT scan (computed tomography scan)—Cross-sectional x rays of the body are compiled to create a three-dimensional image of the body's internal structures.

Debridement—Surgical procedure in which dead or dying tissue is removed.

Dermis—The deepest layer of skin.

Fascia, deep—A fibrous layer of tissue that envelopes muscles.

Fascia, superficial—A fibrous layer of tissue that lies between the deepest layer of skin and the subcutaneous fat.

Gangrene—An extensive area of dead tissue.

Hyperbaric oxygen therapy—A treatment in which the patient is placed in a chamber and breathes oxygen at higher-than-atmospheric pressure. This high-pressure oxygen stops bacteria from growing and, at high enough pressure, kills them.

Magnetic resonance imaging (MRI)—An imaging technique that uses a large circular magnet and radio waves to generate signals from atoms in the body. These signals are used to construct images of internal structures.

Necrosis—Abnormal death of cells, potentially caused by disease or infection.

Subcutaneous—Referring to the area beneath the skin.

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National Necrotizing Fascitis Foundation. PO Box 145, Niantic, CT 06357. (616) 261-2538. <http://www.nnff.org/>.

Paul A. Johnson

Flight medicine *see* **Aviation medicine**

Floppy mitral valve *see* **Mitral valve prolapse**

Flower remedies

Definition

Flower remedies are specially prepared flower essences, containing the healing energy of plants. They are prescribed according to a patient's emotional disposition, as ascertained by the therapist, doctor, or patients themselves.

Purpose

Flower remedies are more homeopathic than herbal in the way they work, effecting energy levels rather than chemical balances. They have been described as "liquid energy." The theory is that they encapsulate the flowers' healing energy, and are said to deal with and overcome negative emotions, and so relieve blockages in the flow of human energy that can cause illness.

Description

Origins

Perhaps the most famous and widely used system is the Bach flower remedies. This system originated in the 1920s when British physician and bacteriologist, Dr. Edward Bach (1886–1936), noticed that patients with physical complaints often seemed to be suffering from **anxiety** or some kind of negative emotion. He concluded that assessing a patient's emotional disposition and prescribing an appropriate flower essence could treat the physical illness. Bach was a qualified medical doctor, but he also practiced **homeopathy**.

As a result of his own serious illness in 1917, Bach began a search for a new and simple system of medicine that would treat the whole person. In 1930, he gave up his flourishing practice on Harley Street at the Royal London Homeopathic Hospital and moved to the countryside to devote his life to this research. It is known that at this point, he ceased to dispense the mixture of homeopathy and allopathic medicine that he had been using. Instead, he began investigating the healing properties of plant essences and discovered that he possessed an "intuition" for judging the properties of each flower. Accordingly, he developed the system of treatment that bears his name, and is also the foundation for all other flower-remedy systems.

The Bach Flower Remedies were ostensibly the only system of significance from the 1920s until in the 1970s, when there was a renewed interest in the subject by doctors working in the field of natural medicine. Perhaps the most notable was Dr. Richard Katz, who was seeking new methods of dealing with modern **stress** and the resulting ailments. He focused on the concept of a psychic, psychological effect and chose to pursue this line of research.

In 1979, Katz founded the Flower Essence Society in California, (FES). This society pledged to further the research and development of Bach's principles. As of 2000, FES hosts a database of over 100 flower essences from more than 50 countries. FES is now an international organization of health practitioners, researchers, students, and others concerned with flower essence therapy.

The Society has connections with an estimated 50,000 active practitioners from around the world, who use flower essence therapy as part of their treatment. FES encourages the study of the plants themselves to determine the characteristics of flower essences. They are compiling an extensive database of case studies and practitioner reports of the use of essences therapeutically, allowing verification and development of the original definitions. They are also engaged in the scientific study of flower essence therapy.

FES says they have developed the theories of Paracelsus and Goethe who researched the "signatures" and "gestures" of botanical specimens, on the premise that the human body and soul are a reflection of the system of nature. FES plant research interprets the therapeutic properties of flower essences according to these insights.

In this regard, they have devised 12 "windows of perception" for monitoring the attributes of plants. Each of these windows reveals an aspect of the plant's qualities, although they maintain that what they are seeking is a "whole which is greater than the sum of its parts." The 12 windows are not considered independent classifications, but more of a blended tapestry of views of the qualities that each plant possesses.

The first window is concerned with the "form" of a plant—its shape classification. The second focuses on its "gesture" or spatial relationship. The third window is a plant's botanical classification; the Flower Essence Society maintains that considering a plant's botanical family

is essential to obtaining an overview of its properties as a flower essence. The fourth window concerns the time orientation of a particular specimen regarding the daily and seasonal cycles. Why do some flowers bloom at different times of the day, while others, such as the evening primrose, respond to the moon? The fifth window observes a plant's relationship to its environment. Where a plant chooses to grow, and where it cannot survive, reveals much about its qualities. The sixth window observes a plant's relationship to the Four Elements and the Four Ethers, as FES maintains that plants exist in one of the elemental or etheric forces in addition to their physical life. "Elements" refers to those developed by the Greeks, as opposed to the modern concept of "molecular building blocks." It seems that commonly, two elements predominate in a plant, indicating a polarity of qualities, while two can be said to be recessive. The seventh window relates to a plant's relationship with the other kingdoms of nature: mineral, animal and human, while the eighth relates to the color and color variations of a plant. Katz explains how the language of color tells us so much about the "soul qualities" of a plant. The ninth window concerns all other sensory perceptions of a plant, such as fragrance, texture, and taste. The tenth window involves assessing the chemical substances and properties; the eleventh studies medicinal and herbal uses, as by studying the physical healing properties of plants, we can also understand something of their more subtle effects on the soul. Finally, the twelfth window involves the study of the lore, mythology, folk wisdom, and spiritual and ritual qualities associated with a particular plant. Katz relates how in the past, human beings were more in touch with the natural world, and the remnants of this unconscious plant wisdom live on in the form of folklore, mythology, and so on.

Because flower remedies operate on approximately the same principles as homeopathy, practitioners quite often prescribe the two therapies in conjunction with each other. They can also be used concurrently with allopathic medicine.

The system consists of 38 remedies, each for a different disposition. The basic theory is that if the remedy for the correct disposition is chosen, the physical illness resulting from the present emotional state can then be cured. There is a rescue remedy made up of five of the essences—cherry plum, clematis, impatiens, rock star, and star of Bethlehem—that is recommended for the treatment of any kind of physical or emotional shock. Therapists recommended that rescue remedy be kept on hand to help with all emergencies.

The 38 Bach Remedies

- agrimony: puts on a cheerful front, hides true feelings, and worries or problems
- aspen: feelings of apprehension, dark foreboding, and premonitions
- beech: critical, intolerant, picky
- centaury: easily comes under the influence of others, weak willed
- cerato: unsure, no confidence in own judgement, intuition, and seeks approval from others
- cherry plum: phobic, fear of being out of control, and tension
- chestnut bud: repeats mistakes, does not learn from experience
- chicory: self–centered, possessive, clingy, demanding, self pity
- clematis: absent minded, dreamy, apathetic, and lack of connection with reality
- crab apple: a "cleanser" for prudishness, self–disgust, feeling unclean
- elm: a sense of being temporarily overwhelmed in people who are usually capable and in control
- gentian: discouraged, doubting, despondent
- gorse: feelings of pessimism, accepting defeat
- heather: need for company, talks about self, and concentrates on own problems

EDWARD BACH (1886–1936)

Edward Bach was a graduate of University College Hospital (M.B., B.S., M.R.C.S.) in England. He left his flourishing Harley Street practice in favor of homeopathy, seeking a more natural system of healing than allopathic medicine. He concluded that healing should be as simple and natural as the development of plants, which were nourished and given healing properties by earth, air, water, and sun.

Bach believed that he could sense the individual healing properties of flowers by placing his hands over the petals. His remedies were prepared by floating summer flowers in a bowl of clear stream water exposed to sunlight for three hours.

He developed 38 remedies, one for each of the negative states of mind suffered by human beings, which he classified under seven group headings: fear, uncertainty, insufficient interest in present circumstances, loneliness, over-sensitivity to influences and ideas, despondency or despair, and overcare for the welfare of others. The Bach remedies can be prescribed for plants, animals, and other living creatures as well as human beings.

- holly: jealousy, envy, suspicion, anger, and hatred
- honeysuckle: reluctance to enter the present and let the past go
- hornbeam: reluctant to face a new day, weary, can't cope (mental fatigue)
- impatiens: impatience, always in a hurry, and resentful of constraints
- larch: feelings of inadequacy and apprehension, lack of confidence and will to succeed
- mimulus: fearful of specific things, shy, and timid
- mustard: beset by "dark cloud" and gloom for no apparent reason
- oak: courageous, persevering, naturally strong but temporarily overcome by difficulties
- olive: for physical and mental renewal, to overcome exhaustion from problems of long–standing
- pine: for self–reproach, always apologizing, assuming guilt
- red chestnut: constant worry and concern for others
- rock rose: panic, intense alarm, dread, horror
- rock water: rigid–minded, self–denial, restriction
- scleranthus: indecision, uncertainty, fluctuating moods
- star of Bethlehem: consoling, following shock or grief or serious news
- sweet chestnut: desolation, despair, bleak outlook
- vervain: insistent, fanatical, over–enthusiastic
- vine: dominating, overbearing, autocratic, tyrannical
- walnut: protects during a period of adjustment or vulnerability
- water violet: proud, aloof, reserved, enjoys being alone
- white chestnut: preoccupation with worry, unwanted thoughts
- wild oat: drifting, lack of direction in life
- wild rose: apathy, resignation, no point in life
- willow bitter: resentful, dissatisfied, feeling life is unfair

Originally, Bach collected the dew from chosen flowers by hand to provide his patients with the required remedy. This became impractical when his treatment became so popular that production could not keep up with demand. He then set about finding a way to manufacture the remedies, and found that floating the freshly picked petals on the surface of spring water in a glass bowl and leaving them in strong sunlight for three hours produced the desired effect. Therapists explain that the water is "potentized" by the essence of the flowers. The potentized water can then be bottled and sold. For more woody specimens, the procedure is to boil them in a sterilized pan of water for 30 minutes. These two methods produce "mother tinctures" and the same two methods devised by Bach are still used today. Flower essences do not contain any artificial chemical substances, except for alcohol preservative.

Bach Flower Remedies

Name	Remedy
Agrimony	Upset by arguments, nonconfrontational, conceals worry and pain
Aspen	Fear of the unknown, anxiety, prone to nightmares, and apprehension
Beech	Critical, intolerant, and negative
Centaury	Submissive and weak-willed
Cerato	Self doubting and overly dependent
Cherry Plum	Emotional thoughts and desparation
Chestnut	Repeats mistakes and has no hindsight
Chicory	Selfish, controlling, attention-seeking, and possessive
Clematis	Absorbed, impractical, and indifferent
Crab Apple	Shame and self-loathing
Elm	Overwelhmed and feelings of inadequacy
Gentian	Negative, doubt, and depression
Gorse	Pessimism, hopelessness, and despair
Heather	Self-centered and self-absorbed
Holly	Jealousy, hatred, suspicion, and envy
Honeysuckle	Homesick, living in the past, and nostalgic
Hornbeam	Procrastination, fatigue, and mental exhaustion
Impatiens	Impatience, irritability, and impulsive
Larch	No confidence, inferiority complex, and despondency
Mimulus	Timid, shy, and fear of the unknown
Mustard	Sadness and depression of unknown origin
Oak	Obstinate, inflexible, and overachieving
Olive	Exhaustion
Pine	Guilt and self blame
Red Chesnut	Fear and anxiety for loved ones
Rock Rose	Nightmares, hysteria, terror, and panic
Rock Water	Obsessive, repression, perfectionism, and self denial
Scleranthus	Indecision, low mental clarity, and confusion
Star-of-Bethlehem	Grief and distress
Sweet Chesnut	Despair and hopelessness
Vervain	Overbearing and fanatical
Vine	Arrogant, ruthless, and inflexible
Walnut	Difficulty accepting change
Water Violet	Pride and aloofness
White Chestnut	Worry, preoccupation, and unwanted thoughts
Wild Oat	Dissatisfaction
Wild Rose	Apathy and resignation
Willow	Self pity and bitterness

Bach remedies cost around $10 each, and there is no set time limit for treatment. It may take days, weeks, or in some cases months. Flower essences cost around $6 each, and there is also no set time for the length of treatment, or the amount of essences that may be taken. These treatments are not generally covered by medical insurance.

Precautions

Bach remedies and flower essences are not difficult to understand, and are considered suitable for self administration. The only difficulty may be in finding the correct remedy, as it can sometimes be tricky to pinpoint an

individual's emotional disposition. They are even safe for babies, children, and animals. An important aspect of treatment with flower remedies, is that if you feel instinctively that you need a particular remedy, you are encouraged to act on that instinct. However, it is advisable not to continue a particular remedy once you feel you no longer need it, and to try a different one if you feel that progress is not being made.

The remedies are administered from a stoppered bottle and need to be diluted. Individuals sensitive to alcohol can apply the concentrate directly to temples, wrists, behind the ears, or underarms. They should be kept in a cool dark place; like this they should last indefinitely. However, a diluted remedy should not be kept longer than three weeks. Two drops of each diluted remedy should be taken four times a day, including first thing in the morning and last thing at night. If the rescue remedy is being used, four drops should be used instead. Most therapists recommend that they be taken in spring water, but the remedy can be taken directly from the bottle, if care is taken that the dropper does not touch the tongue, as this would introduce bacteria that would spoil the remedy.

It is not recommended that more than six or seven Bach remedies be used at any one time. Instead, it is preferable to divide a larger amount up into two lots to ensure the optimum effectiveness of the remedies. No combination, or amount of combinations of the remedies can cause any harm, rather they become less effective.

Unlike FES, the Bach Centre does not encourage research to "prove" that the remedies work, preferring that people find out for themselves. They strive to keep the use of the Bach remedies as simple as possible, and to this end they do not keep case records. Bach warned before he died that others would try to change his work and make it more complicated. He was determined to keep it simple so that anyone could use it, and that is why he limited the system to only 38 remedies. The Centre points out that many who have used Bach's research as a starting point have added other remedies to the list, even some that Bach himself rejected.

Side effects

Flower remedies or essences are generally regarded as being totally safe, and there are no known side effects apart from the rare appearance of a slight rash, which is not a reason to discontinue treatment, says the Bach Centre.

Research and general acceptance

Bach flower remedies and flower essences have not yet officially won the support of allopathic medicine, despite the fact that more and more medical doctors are referring patients for such treatments on the strength of personal conviction. However, it is difficult to discount the scores of testimonials. Some practitioners refer skeptics to the research that has been done regarding the "auras" of living things. Theoretically, the stronger the aura, the more alive an organism is. Flower essences have very strong auras.

KEY TERMS

Aura—Emanation of light from living things (plants and animals) that can be recorded by Kirlian photography.

Essence—The constituent of a plant that determines its characteristics.

Potentize—The process of transferring the healing energy of a plant into spring water.

Window—A perspective adopted to assess the property of a given plant.

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ORGANIZATIONS

The Dr. Edward Bach Centre, Mount. Vernon, Bakers Lane, Sotwell, Oxon, OX10 OPX, UK. <centre@bachcentre.com>. <http://www.bachcentre.com>.

The Flower Essence Society. P.O. Box 459, Nevada City, CA 95959. (800) 736-9222. Fax: (530) 265-0584. <mail@flowersociety.org>. <http://www.flowersociety.org>.

Patricia Skinner

Flu *see* **Influenza**

Flucona *see* **Antifungal drugs, systemic**

Fluke infections

Definition

Fluke infections are diseases of the digestive tract and other organ systems caused by several different

A micrograph of adult intestinal blood flukes, *Schistosoma mansoni.* Humans can become infected while bathing or working in contaminated water. *(Photo Researchers, Inc. Reproduced by permission.)*

species of parasitic flatworms (Trematodes) that have complex life cycles involving hosts other than human beings. Trematode comes from a Greek word that means having holes and refers to the external suckers that adult flukes use to draw nourishment from their hosts. Fluke infections are contracted by eating uncooked fish, plants, or animals from fluke-infected waters. Symptoms vary according to the type of fluke infection.

Description

In humans, fluke infections can be classified according to those diseases caused by liver flukes and those caused by lung flukes. Diseases caused by liver flukes include fascioliasis, opisthorchiasis, and clonorchiasis. Cases of liver fluke infection have been reported in Europe and the United States, as well as the Middle East, China, Japan, and Africa. Diseases caused by lung flukes include paragonimiasis. Paragonimiasis is a common infection in the Far East, Southeast Asia, Africa, Central and South America, Indonesia, and the Pacific Islands. It is estimated that between 40 million and 100 million people worldwide suffer from either liver or lung fluke infections.

In their adult stage, liver and lung flukes are symmetrical in shape, ranging between 1/4–1 in in length, and look somewhat like long, plump leaves or blades of grass. They enter through the mouth and can infect any person at any age.

Causes and symptoms

The symptoms of fluke infection differ somewhat according to the type of fluke involved. All forms of liver and lung fluke infection, however, have the following characteristics:

- most persons who get infected do not develop symptoms (asymptomatic)
- the early symptoms of an acute fluke infection are not unique to these diseases alone (nonspecific symptoms)
- infection does not confer immunity against re-infection by the same species or infection by other species of flukes
- infection is usually associated with eating uncooked fish, plants, or animals that live in fresh water

Fascioliasis

Fascioliasis is caused by *Fasciola hepatica*, the sheep liver fluke. The fluke has a three-part life cycle that begins when eggs from a host's feces are deposited in water. The eggs release free-swimming larvae (miracidia) that infect snails. The snails then release free-swimming larvae with tails (cercariae) that form cysts containing larvae in the infective stage (metacercariae) on vegetation growing in fresh water. Humans become infected when they eat watercress, water chestnuts, or other plants covered with the encysted metacercariae.

When a person eats contaminated plants, the cysts are broken open in the digestive system, and the metacercariae leave their cysts, pass through the wall of the intestine, and enter the liver, where they cause inflammation and destroy tissue. After a period of 10–15 weeks in the liver, the adult flukes move to the bile ducts and produce eggs. Acute fascioliasis is marked by abdominal **pain** with **headache**, loss of appetite, anemia, and vomiting. Some patients develop **hives**, muscle pains, or a yellow-color to the skin and whites of the eyes (**jaundice**). Chronic forms of the disease may produce complications, including blockage of the bile ducts or the migration of adult flukes to other parts of the body.

Opisthorchiasis and clonorchiasis

These infections are caused by *Clonorchis sinensis*, the Chinese liver fluke, and *Opisthorchis viverrini* or *O. felineus*. The diseases are widespread, affecting more than 20 million people in Japan, China, Southeast Asia, and India. The life cycle of these liver flukes is similar to that of *F. hepatica* except that the etacercariae are encysted in freshwater fish rather than on plants. Dogs, cats, and other mammals that eat raw fish can be infected with opisthorchiasis and clonorchiasis.

KEY TERMS

Aspirator—A medical instrument that uses suction to withdraw fluids from the lungs, digestive tract, or other parts of the body for laboratory testing.

Asymptomatic—Persons who carry a disease and are usually capable of transmitting the disease but, who do not exhibit symptoms of the disease are said to be asymptomatic.

Cercaria (plural, cercariae)—An intermediate-stage of the fluke larva, released into water by infected snails.

Cross-reaction—A reaction that occurs in blood testing when a disease agent reacts to the specific antibody for another disease agent. Cross-reactions are common in blood tests for fluke infections because the different species are closely related.

Encysted—Enclosed in a cyst or capsule. Flukes spend part of their life cycle as encysted larvae.

Fluke—A parasitic flatworm that has external suckers. Flukes are sometimes called trematodes.

Host—The living animal that supplies nutrition to a parasite.

Jaundice—Yellowing of the skin and the whites of the eyes as a result of excess bile in the blood due to an improperly functioning liver.

Metacercaria (plural, metacercariae)—The encysted stage of a fluke larva that produces infection in human beings.

Miracidium (plural, miracidia)—The free-swimming larval form in the life cycle of the liver fluke.

Parasite—An organism that lives on or inside an animal of a different species and feeds on it or draws nutrients from it.

Trematode—Parasitic flatworms or another name for fluke, taken from a Greek word that means having holes.

The symptoms of opisthorchiasis and clonorchiasis are similar to those of fascioliasis and include both acute and chronic forms. In acute infection, the patient may be tired, have a low-grade **fever**, pains in the joints, a swollen liver, abdominal pain, and a skin rash. The acute syndrome may be difficult to diagnose because the fluke eggs do not appear in the patient's stool for three to four weeks after infection. Patients with the chronic form of the disease experience a loss of appetite, **fatigue**, low-grade fever, **diarrhea**, and an enlarged liver that feels sore when the abdomen is pressed.

Paragonimiasis

Paragonimiasis is caused by a lung fluke, either *Paragonimus westermani* or *P. skrjabini*. These flukes are larger than liver flukes and infect meat- or fish-eating animals as well as humans. Their life cycle is similar to that of liver flukes except that their encysted larvae infect crabs and crayfish rather than plants or fish. Humans can ingest the encysted metacercariae from drinking contaminated water or eating raw or undercooked crabs and crayfish.

In humans, the metacercariae are released from their cysts in the small intestine and migrate to the lungs or the brain in 1% of cases. In the lungs, the flukes lay their eggs and form areas of inflammation covered with a thin layer of fibrous tissue. These areas of infection may eventually rupture, causing the patient to **cough** up fluke eggs, blood, and inflamed tissue. The period between the beginning of the infection and the appearance of the eggs during coughing is about six weeks. Patients with lung infections may have chest pain and fever as well as rust-colored or bloody sputum. Lung infections can lead to **lung abscess**, **pneumonia**, or **bronchitis**. Patients with fluke infections of the brain may experience seizures or a fatal inflammation of brain tissue called **encephalitis**. Some patients also develop diarrhea and abdominal pain or lumps under the skin that contain adult flukes.

Diagnosis

Diagnosis of fluke infections is based on a combination of the patient's history, particularly travel or residence in areas known to have flukes, and identification of the fluke's eggs or adult forms. In some patients, the eggs are found in fluid from the lungs, bile duct, or small intestine. Samples of these fluids can be obtained with a suction instrument (aspirator). Because most types of fluke infections are rare in the United States, stool specimens or body fluid samples may need to be sent to a laboratory with experts in unusual diseases or conditions to identify the specific parasite. In some cases, adult flukes may be found in the patient's stools, vomit, sputum, or skin lumps (for lung flukes). In the case of lung flukes, it is important for the doctor to rule out **tuberculosis** as a possible diagnosis. A tuberculosis skin test and **chest x ray** will usually be sufficient to do this.

Blood tests may be useful in diagnosing fluke infections, but their usefulness is limited because of cross-reactions. A cross-reaction occurs in blood testing when a particular disease agent reacts with antibodies specific to another disease agent. This result means that the doctor may know that the person is infected by flukes but cannot tell from the blood test alone which specific type of fluke is causing the disease. In addition, blood tests for fluke infections cannot distinguish between past and current infections. In some cases, sophisticated imaging techniques, such as **computed tomography scans** (CT scans) or ultrasound scans of the patient's chest or brain (for lung flukes) or abdomen (for liver flukes), are useful in confirming a diagnosis of fluke infection.

Treatment

Liver and lung fluke infections are treated with medications. These include triclabendazole, praziquantel, bithionol, albendazole, and mebendazole. Praziquantel works by paralyzing the flukes' suckers, forcing them to drop away from the walls of the host's blood vessels. In the United States, bithionol is available only from the Centers for Disease Control (CDC). Depending on the species of fluke and the severity of infection, the course of treatment can vary from several days to several weeks. Cure rates vary from 50–95%. Most patients experience mild temporary side effects from these drugs, including diarrhea, **dizziness**, or headache.

Prognosis

The prognosis for recovery from liver fluke infections is good, although patients with serious infections may be more vulnerable to other diseases, particularly if significant liver damage has occurred. Most patients with lung fluke infections also recover, however, severe infections of the brain can cause **death** from the destruction of central nervous system or brain tissue.

Prevention

No vaccines have been developed that are effective against lung or liver fluke infections. Prevention of these infections includes the following measures:

- boiling or purifying drinking water
- avoiding raw or undercooked fish or salads made from fresh aquatic plants; all food eaten in areas with fluke infestations should be cooked thoroughly; pickling or **smoking** will not kill fluke cysts in fish or shellfish
- control or eradication of the snails that serve as the flukes' intermediate hosts

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Rebecca J. Frey

Fluoroquinolones

Definition

Fluoroquinolones are medicines that kill bacteria or prevent their growth.

Purpose

Fluoroquinolones are **antibiotics**, medicines used to treat infections caused by microorganisms. Physicians prescribe these drugs for bacterial infections in many parts of the body. For example, they are used to treat bone and joint infections, skin infections, urinary tract infections, inflammation of the prostate, serious ear infections, **bronchitis**, **pneumonia**, **tuberculosis**, some **sexually transmitted diseases** (STD), and some infections that affect people with **AIDS**.

Description

Fluoroquinolones are available only with a physician's prescription and are sold in tablet and injectable forms. Examples of these medicines are moxifloxacin (Avelox), ciprofloxacin (Cipro), ofloxacin (Floxin), levofloxacin (Levaquin), lomefloxacin (Maxaquin), nor-

floxacin (Noroxin), enoxacin (Penetrex), gatifloxacin (Tequin), and sparfloxacin (Zagam).

Recommended dosage

The recommended dosage depends on the type and strength of fluoroquinolone, and the kind of infection for which it is being taken. Check with the physician who prescribed the drug or the pharmacist who filled the prescription for the correct dosage.

To make sure the infection clears up completely, take the medicine for as long as it has been prescribed. Do not stop taking the drug just because symptoms begin to improve. Symptoms may return if the drug is stopped too soon.

Fluoroquinolones work best when they are at constant levels in the blood. To help keep levels constant, take the medicine in doses spaced evenly through the day and night. Do not miss any doses. For best results, take this medicine with a full glass of water and drink several more glasses throughout the day, every day during treatment with the drug. The extra water will help prevent some side effects. Some fluoroquinolones should be taken on an empty stomach; others may be taken with meals. Check package directions or ask the physician or pharmacist for instructions on how to take the medicine.

Precautions

Research suggests that fluoroquinolones may cause bone development problems in children and teenagers. Infants, children, teenagers, pregnant women, and women who are breastfeeding should not take this medicine unless directed to do so by a physician.

Although such side effects are rare, some people have had severe and life-threatening reactions to fluoroquinolones. Call a physician immediately if any of these signs of a dangerous reaction occur:

- swelling of the face and throat
- swallowing problems
- shortness of breath
- rapid heartbeat
- tingling of fingers or toes
- **itching** or **hives**
- loss of consciousness

Some fluoroquinolones may weaken the tendons in the shoulder, hand, or heel, making the tendons more likely to tear. Anyone who notices **pain** or inflammation in these or other tendon areas should stop taking the medicine immediately and call a physician. Rest and avoid **exercise** until the physician determines whether the tendons are damaged. If the tendons are torn, surgery may be necessary to repair them.

These medicines make some people feel drowsy, dizzy, lightheaded, or less alert. Anyone who takes these drugs should not drive, use machines or do anything else that might be dangerous until they have found out how the drugs affect them.

This medicine may increase sensitivity to sunlight. Even brief exposure to sun can cause a severe **sunburn** or a rash. While being treated with fluoroquinolones, avoid being in direct sunlight, especially between 10 A.M. and 3 P.M.; wear a hat and tightly woven clothing that covers the arms and legs; use a sunscreen with a skin protection factor (SPF) of at least 15; protect the lips with a sun block lipstick; and do not use tanning beds, tanning booths, or sunlamps.

KEY TERMS

Bacteria—Tiny, one-celled forms of life that cause many diseases and infections.

Bronchitis—Inflammation of the air passages of the lungs.

Digestive tract—The stomach, intestines, and other parts of the body through which food passes.

Inflammation—Pain, redness, swelling, and heat that usually develop in response to injury or illness.

Microorganism—An organism that is too small to be seen with the naked eye.

Pneumonia—A disease in which the lungs become inflamed. Pneumonia may be caused by bacteria, viruses, or other organisms, or by physical or chemical irritants.

Prostate—A donut-shaped gland in males below the bladder that contributes to the production of semen.

Sexually transmitted disease (STD)—A disease that is passed from one person to another through sexual intercourse or other intimate sexual contact.

Tendon—A tough band of tissue that connects muscle to bone.

Tuberculosis—An infectious disease that usually affects the lungs, but may also affect other parts of the body. Symptoms include fever, weight loss, and coughing up blood.

Urinary tract—The passage through which urine flows from the kidneys out of the body.

Do not take **antacids** that contain aluminum, calcium, or magnesium at the same time as fluoroquinolones. The antacids may keep the fluoroquinolones from working as they should. If antacids are needed, take them at least two hours before or two hours after taking norfloxacin or ofloxacin, at least four hours before or two hours after taking ciprofloxacin. Follow the same instructions for taking sucralfate (Carafate), a medicine used to treat stomach ulcers and other irritation in the digestive tract and mouth.

Anyone who has had unusual reactions to fluoroquinolones or related medicines such as cinoxacin (Cinobac) or nalidixic acid (NegGram) in the past should let his or her physician know before taking the drugs again. The physician should also be told about any **allergies** to foods, dyes, preservatives, or other substances.

Before using fluoroquinolones, people with any of these medical problems should make sure their physicians are aware of their conditions:

- kidney disease
- liver disease with kidney disease
- diseases of the brain or spinal cord, including hardening of the arteries in the brain, epilepsy, and other seizure disorders

Taking fluoroquinolones with certain other drugs may affect the way the drugs work or may increase the chance of side effects.

Side effects

The most common side effects are mild **diarrhea**, nausea, vomiting, stomach or abdominal pain, **dizziness**, drowsiness, lightheadedness, nervousness, sleep problems, and **headache**. These problems usually go away as the body adjusts to the drug and do not require medical treatment unless they are bothersome.

More serious side effects are not common, but may occur. If any of the following side effects occur, check with a physician immediately:

- skin rash or other skin problems such as itching, peeling, hives, or redness
- **fever**
- agitation or confusion
- hallucinations
- shakiness or **tremors**
- seizures or convulsions
- tingling of fingers or toes
- pain where the medicine was injected (lasting after the injection)
- pain in the calves, spreading to the heels
- swelling of the calves or lower legs
- swelling of the face or neck
- swallowing problems
- rapid heartbeat
- shortness of breath
- loss of consciousness

Other rare side effects may occur. Anyone who has unusual symptoms after taking fluoroquinolones should get in touch with his or her physician.

Interactions

Fluoroquinolones may interact with other medicines. When this happens, the effects of one or both of the drugs may change or the risk of side effects may be greater. Anyone who takes fluoroquinolones should let the physician know all other medicines he or she is taking. Among the drugs that may interact with fluoroquinolones are:

- antacids that contain aluminum, calcium, or magnesium
- medicines that contain iron or zinc, including multivitamin and mineral supplements
- sucralfate (Carafate)
- caffeine
- blood thinning drugs such as warfarin (Coumadin)
- airway opening drugs (**bronchodilators**) such as aminophylline, theophylline (Theo-Dur and other brands), and oxtriphylline (choledyl and other brands)
- didanosine (Videx), used to treat HIV infection.

The list above does not include every drug that may interact with fluoroquinolones. Be sure to check with a physician or pharmacist before combining fluoroquinolones with any other prescription or nonprescription (over-the-counter) medicine.

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Rosalyn Carson-DeWitt

Fluoxetine *see* **Selective serotonin reuptake inhibitors**

Flurbiprofen *see* **Nonsteroidal anti-inflammatory drugs**

Focal glomeruloscle *see* **Nephrotic syndrome**

Folic acid

Definition

Folic acid is a water-soluable vitamin belonging to the B-complex group of **vitamins**. These vitamins help the body break down complex carbohydrates into simple sugars to be used for energy. Excess B vitamins are excreted from the body rather than stored for later use. This is why sufficient daily intake of folic acid is necessary.

Description

Folic acid is also known as folate, or folacin. It is one of the nutrients most often found to be deficient in the Western diet, and there is evidence that deficiency is a problem on a worldwide scale. Folic acid is found in leafy green vegetables, beans, peas and lentils, liver, beets, brussel sprouts, poultry, nutritional yeast, tuna, wheat germ, mushrooms, oranges, asparagus, broccoli, spinach, bananas, strawberries, and cantaloupes. In 1998, the U.S. Food and Drug Administration (FDA) required food manufacturers to add folic acid to enriched bread and grain products to boost intake and to help prevent neural tube defects (NTD).

Purpose

Folic acid works together with vitamin B_{12} and vitamin C to metabolize protein in the body. It is important for the formation of red and white blood cells. It is necessary for the proper differentiation and growth of cells and for the development of the fetus. It is also used to form the nucleic acid of DNA and RNA. It increases the appetite and stimulates the production of stomach acid for digestion and it aids in maintaining a healthy liver. A deficiency of folic acid may lead to anemia, in which there is decreased production of red blood cells. This reduces the amounts of oxygen and nutrients that are able to get to the tissues. Symptoms may include **fatigue**, reduced secretion of digestive acids, confusion, and forgetfulness. During **pregnancy**, a folic acid deficiency may lead to preeclampsia, premature birth, and increased bleeding after birth.

People who are at high risk of strokes and heart disease may greatly benefit by taking folic acid supplements. An elevated blood level of the amino acid homocysteine has been identified as a risk factor for some of these diseases. High levels of homocysteine have also been found to contribute to problems with **osteoporosis**. Folic acid, together with vitamins B_6 and B_{12}, helps break down homocysteine, and may help reverse the problems associated with elevated levels.

Pregnant women have an increased need for folic acid, both for themselves and their child. Folic acid is necessary for the proper growth and development of the fetus. Adequate intake of folic acid is vital for the prevention of several types of **birth defects**, particularly NTDs. The neural tube of the embryo develops into the brain, spinal cord, spinal column, and the skull. If this tube forms incompletely during the first few months of pregnancy a serious, and often fatal, defect results in **spina bifida** or anencephaly. Folic acid, taken from one year to one month before conception through the first four months of pregnancy, can reduce the risk of NTDs by 50–70%. It also helps prevent a **cleft lip and palate**.

Research shows that folic acid can be used to successfully treat cervical dysplasia, a condition diagnosed by a Pap smear, of having abnormal cells in the cervix. This condition is considered to be a possible precursor to **cervical cancer**, and is diagnosed as an abnormal Pap smear. Daily consumption of 1,000 mcg of folic acid for three or more months has resulted in improved cervical cells upon repeat Pap smears.

Studies suggest that long-term use of folic acid supplements may also help prevent lung and **colon cancer**. Researchers have also found that alcoholics who have low folic acid levels face a greatly increased possibility of developing colon **cancer**.

Preparations

To correct a folic acid deficiency, supplements are taken in addition to food. Since the functioning of the B vitamins is interrelated, it is generally recommended that the appropriate dose of B-complex vitamins be taken in place of single B vitamin supplements. The Recommended Dietary Allowances (RDA) for folate is 400 mcg per day for adults, 600 mcg per day for pregnant women, and 500 mcg for nursing women. Medicinal dosages of up to 1,000-2,000 mcg per day may be prescribed.

Precautions

Folic acid is not stable. It is easily destroyed by exposure to light, air, water, and cooking. Therefore, the supplement should be stored in a dark container in a cold, dry place, such as a refrigerator. Many medications interfere with the body's absorption and use of folic acid. This includes sulfa drugs, sleeping pills, estrogen, anticonvulsants, birth control pills, **antacids**, quinine, and

KEY TERMS

Homocysteine—An amino aid involved in the breakdown and absorption of protein in the body.

Preeclampsia—A serious disorder of late pregnancy in which the blood pressure rises, there is a large amount of retained fluids, and the kidneys become less effective and excrete proteins directly into the urine.

Raynaud's disease—A symptom of various underlying conditions affecting blood circulation in the fingers and toes and causing them to be sensitive to cold.

Recommended Daily Allowance (RDA)—Guidelines for the amounts of vitamins and minerals necessary for proper health and nutrition established by the National Academy of Sciences in 1989.

Water-soluble vitamins—Vitamins that are not stored in the body and are easily excreted. They must, therefore, be consumed regularly as foods or supplements to maintain health.

some **antibiotics**. Using large amounts of folic acid (e.g., over 5,000 mcg per day) can mask a vitamin B_{12} deficiency and thereby risk of irreversible nerve damage.

Side effects

At levels of 5,000 mcg or less, folic acid is generally safe for use. Side effects are uncommon. However, large doses may cause nausea, decreased appetite, bloating, gas, decreased ability to concentrate, and **insomnia**. Large doses may also decrease the effects of phenytoin (Dilantin), a seizure medication.

Interactions

As with all B-complex vitamins, it is best to take folic acid with the other B vitamins. Vitamin C is important to the absorption and functioning of folic acid in the body.

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Patience Paradox

Folic acid deficiency anemia

Definition

Folic acid deficiency, an abnormally low level of one of the B **vitamins**, results in anemia characterized by red blood cells that are large in size but few in number.

Description

Folic acid is necessary for growth and cellular repair, since it is a critical component of DNA and RNA as well as essential for the formation and maturation of red blood cells. Folic acid deficiency is one of the most common of all vitamin deficiencies. Although it occurs in both males and females, folic acid deficiency anemia most often affects women over 30. It becomes increasingly common as age impedes the body's ability to absorb folic acid, a water-soluble vitamin that is manufactured by intestinal bacteria and stored for a short time in the liver. Folic acid deficiency has also been implicat-

ed as a cause of neural tube defects in the developing fetus. Recent research has shown that adequate amounts of folic acid can prevent up to half of these **birth defects**, if women start taking folic acid supplements shortly before conception.

A healthy adult needs at least 400 mcg of folic acid every day. Requirements at least double during **pregnancy**, and increase by 50% when a woman is breastfeeding. The average American diet, high in fats, sugar, and white flour, provides about 200 mcg of folic acid, approximately the amount needed to maintain tissue stores of the substance for six to nine months before a deficiency develops. Most of the folic acid in foods (with the exception of the folic acid added to enriched flour and breakfast cereals) occurs as folate. Folate is only about half as available for the body to use as is the folic acid in pills and supplements. Folate also is easily destroyed by sunlight, overcooking, or the storing of foods at room temperature for an extended period of time.

Good dietary sources of folate include:

- leafy green vegetables
- liver
- mushrooms
- oatmeal
- peanut butter
- red beans
- soy
- wheat germ

Causes and symptoms

This condition usually results from a diet lacking in foods with high folic acid content, or from the body's inability to digest foods or absorb foods having high folic acid content. Other factors that increase the risk of developing folic acid deficiency anemia are:

- age
- alcoholism
- birth-control pills, anticonvulsant therapy, sulfa **antibiotics**, and certain other medications
- illness
- smoking
- stress

Fatigue is often the first sign of folic acid deficiency anemia. Other symptoms include:

- anorexia nervosa
- pale skin
- paranoia
- rapid heart beat
- sore, inflamed tongue
- weakness
- weight loss

Diagnosis

Diagnostic procedures include blood tests to measure hemoglobin, an iron-containing compound that carries oxygen to cells throughout the body. Symptoms may be reevaluated after the patient has taken prescription folic acid supplements.

Treatment

Folic acid supplements are usually prescribed, and self-care includes avoiding:

- alcohol
- non-herbal tea, **antacids**, and phosphates (contained in beer, ice cream, and soft drinks), which restrict iron absorption
- tobacco

A person with folic acid deficiency anemia should rest as often as necessary until restored energy levels make it possible to resume regular activities. A doctor should be seen if **fever**, chills, muscle aches, or new symptoms develop during treatment, or if symptoms do not improve after two weeks of treatment.

Alternative treatment

Alternative therapies for folic acid deficiency anemia may include **reflexology** concentrated on areas that influence the liver and spleen. Increasing consumption of foods high in folate is helpful. Eating a mixture of yogurt (8 oz) and turmeric (1 tsp) also may help resolve symptoms. A physician should be contacted if the tongue becomes slick or smooth or the patient:

- bruises or tires easily
- feels ill for more than five days
- feels weak or out of breath
- looks pale or jaundiced

Prognosis

Although adequate folic acid intake usually cures this condition in about three weeks, folic acid deficiency anemia can make patients infertile or more susceptible to infection. Severe deficiencies can result in congestive **heart failure**.

Prevention

Eating raw or lightly cooked vegetables every day will help maintain normal folic acid levels, as will taking a folic acid supplement containing at least 400 mcg of this vitamin. Because folic acid deficiency can cause birth defects, all women of childbearing age who can become pregnant should consume at least 400 mcg of folic acid daily; a woman who is pregnant should have regular medical checkups, and take a good prenatal vitamin.

Resources

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Maureen Haggerty

Follicle-stimulating hormone test

Definition

The follicle-stimulating hormone (FSH) test measures the amount of FSH in the blood. FSH is a hormone that regulates the growth and development of eggs and sperm, and this test is used to diagnose or evaluate disorders involving the pituitary gland and reproductive system.

Purpose

FSH testing is performed if a physician suspects the patient may have a disorder involving the reproductive system or pituitary gland. The pituitary gland produces FSH, which stimulates the growth of the sacks (follicles) that surround the eggs in a woman's ovaries. This is important for the process of ovulation, in which the egg is released. In men, FSH stimulates production of sperm. If there are abnormal levels of FSH in the blood it may mean that one of several disorders are present. Normal fluctuations occur as a result of **puberty**, the menstrual cycle, **pregnancy**, and **menopause**.

The FSH test is performed more often on women than on men. In women, it is used to determine if menopause has begun, to diagnose **infertility** and **menstrual disorders** (such as anovulatory bleeding), to measure hormone levels in children who enter puberty at an early age, and to diagnose other disorders. In men, it can be used to determine early puberty, abnormal tissue growth on one or more of the hormone-secreting (endocrine) glands (called multiple endocrine neoplasia), or to diagnose other disorders.

Description

The FSH test is a blood test. Blood will be drawn from the patient and analyzed in a laboratory.

Preparation

In preparation for the test, there are no food or fluid intake restrictions. Patients may be advised to discontinue certain medications for 48 hours before the test. A menstruating woman having hot flashes or irregular periods should be tested on the second or third day of her menstrual cycle. A woman who has missed a period and is having other menopausal symptoms can be tested at any time.

Aftercare

No aftercare is necessary.

Risks

There are no risks associated with this test.

Normal results

Normal FSH test results vary according to age and sexual maturity. The phase of a woman's menstrual cycle or use of birth-control pills also affects test results.

For an adult male, normal results range from about 4–25 units of FSH in every liter of blood (U/L) or about 5–20 micro-international units in every milliliter.

For a premenopausal woman, normal values range from 4–30 U/L or 5–20 micro-international units per milliliter. In a pregnant woman, FSH levels are too low to measure. After menopause, normal values range from 40–250 U/L or 50–100 micro-international units per milliliter.

FSH levels fluctuate during premenopause. If no other symptoms are present, an elevated FSH level should not be interpreted as proof that menopause has begun.

Abnormal results

Anorexia nervosa and disorders of the hypothalamus or pituitary gland can result in abnormally low FSH levels.

Abnormal levels can also indicate:

- infertility
- hypopituitarism
- klinefelter syndrome (in men)

KEY TERMS

Anovulatory bleeding—Bleeding without release of an egg from an ovary.

Hypopituitarism—Underactivity of the pituitary gland.

Hypothalamus—The part of the brain that controls the endocrine system.

Klinefelter's syndrome—Chromosomal abnormality characterized by small testes and male infertility.

Multiple endocrine neoplasia—Abnormal tissue growth on one or more of the endocrine (hormone-secreting) glands.

Polycystic ovary disease—A condition in which a woman has little or no menstruation, is infertile, has excessive body hair, and is obese. The ovaries may contain several cysts.

Turner syndrome—Chromosomal abnormality characterized by immature reproductive organs in women.

- turner syndrome
- ovarian failure
- polycystic ovary syndrome

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Maureen Haggerty

Follicular cysts *see* **Ovarian cysts**

Folliculitis

Definition

Folliculitis is inflammation or infection of one or more hair follicles (openings in the skin that enclose hair).

Description

Folliculitis can affect both women and men at any age. It can develop on any part of the body, but is most likely to occur on the scalp, face, or parts of the arms, armpits, or legs not usually covered by clothing.

Small, yellowish-white blister-like lumps (pustules) surrounded by narrow red rings are usually present with both bacterial folliculitis and fungal folliculitis. Hair can grow through or alongside of the pustules, which sometimes ooze blood-stained pus.

Folliculitis can cause **boils** and, in rare instances, serious skin infections. Bacteria from folliculitis can enter the blood stream and travel to other parts of the body.

Causes and symptoms

Folliculitis develops when bacteria, such as *Staphylococcus,* or a fungus enters the body through a cut, scrape, surgical incision, or other break in the skin near a hair follicle. Scratching the affected area can trap fungus or bacteria under the fingernails and spread the infection to hair follicles on other parts of the body.

The bacteria that cause folliculitis are contagious. A person who has folliculitis can infect others who live in the same household.

Factors that increase the risk of developing folliculitis include:

- dermatitis
- diabetes
- dirty, crowded living conditions
- eczema
- exposure to hot, humid temperatures
- infection in the nose or other recent illness
- tight clothing

Diagnosis

Diagnosis is based on the patient's medical history and observations. Laboratory analysis of the substance drained from a pustule can be used to distinguish bacterial folliculitis from fungal folliculitis.

Treatment

Bacterial folliculitis may disappear without treatment, but is likely to recur. Non-prescription topical **antibiotics** like Bacitracin, Mycitracin, or Neomycin, gently rubbed on to affected areas three or four times a day, can clear up a small number of bacterial folliculitis pustules. Oral antibiotics such as erythromycin (Ery-

Acne folliculitis. *(Custom Medical Stock Photo. Reproduced by permission.)*

thocin) may be prescribed if the infection is widespread. The drug griseofulvin (Fulvicin) and topical antifungal medications are used to treat fungal folliculitis.

A doctor should be notified if:

- pustules spread after treatment has begun or reappear after treatment is completed
- the patient's **fever** climbs above 100°F (37.8°C)
- the patient develops boils or swollen ankles
- redness, swelling, warmth, or **pain** indicate that the infection has spread
- unexplained new symptoms appear

Alternative treatment

Eating a balanced diet, including protein, complex carbohydrates, healthy fats, fresh fruits and vegetables, and drinking eight to 10 glasses of water a day may stimulate the body's immune system and shorten the course of the infection. Garlic (*Allium sativum*) and goldenseal (*Hydrastis canadensis*), both antiseptic agents against staph infections, may be taken. The daily dosage would vary from person to person and is based on the severity of the infection. **Echinacea** (*Echinacea* spp.) is helpful in modulating immune function. Again, the dosage would vary.

Daily doses of 30–50 mg zinc and 1,000–5,000 mg Vitamin C (taken in equal amounts at several times during the day), and 300–2,000 mg bioflavinoids can also strengthen the body's infection-fighting ability. High doses of **vitamins** and **minerals** should not be used without a doctor's approval.

Prognosis

If properly treated, the symptoms of bacterial folliculitis generally disappear in about two weeks. Fungal folliculitis should clear up within six weeks. But it can worsen if the condition is misdiagnosed and inappropriately treated with steroid creams.

Prevention

Anyone who has a tendency to develop folliculitis should cleanse the skin with antibacterial soap twice a day and before shaving and should not use oily skin lotions. Men should not shave while the beard area is infected. When they begin shaving again, they should use a new blade each time. Women who have had fungal folliculitis should use depilatory creams instead of razors. Daily shampooing can help prevent folliculitis in the scalp. The spread of infection can be prevented by not sharing towels or washcloths

Resources

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Foot acupressure *see* **Reflexology**

Food poisoning

Definition

Food **poisoning** is a general term for health problems arising from eating contaminated food. Food may be contaminated by bacteria, viruses, environmental toxins, or toxins present within the food itself, such as the poisons in some mushrooms or certain seafood. Symptoms of food poisoning usually involve nausea, vomiting

and/or **diarrhea**. Some food-borne toxins can affect the nervous system.

Description

Every year millions of people suffer from bouts of vomiting and diarrhea each year that they blame on "something I ate." These people are generally correct. Each year in the United States, one to two bouts of diarrheal illness occur in every adult. The Centers for Disease Control and Prevention (CDC) estimates that there are from six to 33 million cases of food poisoning in the United States annually. Many cases are mild and pass so rapidly that they are never diagnosed. Occasionally a severe outbreak creates a newsworthy public health hazard.

Classical food poisoning, sometimes incorrectly called ptomaine poisoning, is caused by a variety of different bacteria. The most common are *Salmonella*, *Staphylococcus aureus*, ***Escherichia coli*** O157:H7 or other E. coli strains, *Shigella*, and *Clostridium botulinum*. Each has a slightly different incubation period and duration, but all except *C. botulinum* cause inflammation of the intestines and diarrhea. Sometimes food poisoning is called bacterial **gastroenteritis** or infectious diarrhea. Food and water can also be contaminated by viruses (such as the Norwalk agent that causes diarrhea and the viruses of **hepatitis A** and E), environmental toxins (heavy metals), and poisons produced within the food itself (**mushroom poisoning** or **fish and shellfish poisoning**).

Careless food handling during the trip from farm to table creates conditions for the growth of bacteria that make people sick. Vegetables that are eaten raw, such as lettuce, may be contaminated by bacteria in soil, water, and dust during washing and packing. Home canned and commercially canned food may be improperly processed at too low a temperature or for too short a time to kill the bacteria.

Raw meats carry many food-borne bacterial diseases. The United States Food and Drug Administration (FDA) estimates that 60% or more of raw poultry sold at retail carry some disease-causing bacteria. Other raw meat products and eggs are contaminated to a lesser degree. Thorough cooking kills the bacteria and makes the food harmless. However, properly cooked food can become re-contaminated if it comes in contact with plates, cutting boards, countertops, or utensils that were used with raw meat and not cleaned and sanitized.

Cooked foods can also be contaminated after cooking by bacteria carried by food handlers or from bacteria in the environment. It is estimated that 50% of healthy people have the bacteria *Staphylococcus aureus* in their nasal passages and throat, and on their skin and hair. Rubbing a runny nose, then touching food can introduce the bacteria into cooked food. Bacteria flourish at room temperature, and will rapidly grow into quantities capable of making people sick. To prevent this growth, food must be kept hot or cold, but never just warm.

Although the food supply in the United States is probably the safest in the world, anyone can get food poisoning. Serious outbreaks are rare. When they occur, the very young, the very old, and those with immune system weaknesses have the most severe and life-threatening cases. For example, this group is 20 times more likely to become infected with the *Salmonella* bacteria than the general population.

Travel outside the United States to countries where less attention is paid to sanitation, water purification, and good food handling practices increases the chances that a person will get food poisoning. People living in institutions such as nursing homes are also more likely to get food poisoning.

Causes and symptoms

The symptoms of food poisoning occur because food-borne bacteria release toxins or poisons as a byproduct of their growth in the body. These toxins (except those from *C. botulinum*) cause inflammation and swelling of the stomach, small intestine and/or large intestine. The result is abdominal muscle cramping, vomiting, diarrhea, **fever**, and the chance of **dehydration**. The severity of symptoms depends on the type of bacteria, the amount consumed, and the individual's general health and sensitivity to the bacterial toxin.

Salmonella

According to a 2001 report from the CDC, *Salmonella* caused almost 50,000 culture-confirmed cases of food poisoning in the United States annually. However, between two and four million probably occur each year. *Salmonella* is found in egg yolks from infected chickens, in raw and undercooked poultry and in other meats, dairy products, fish, shrimp, and many more foods. The CDC estimates that one out of every 50 consumers is exposed to a contaminated egg yolk each year. However, thorough cooking kills the bacteria and makes the food harmless. *Salmonella* is also found in the feces of pet reptiles such as turtles, lizards, and snakes.

About one out of every 1,000 people get food poisoning from *Salmonella*. Of these, two-thirds are under age 20, with the majority under age nine. Most cases occur in the warm months between July and October.

Symptoms of food poisoning begin eight to 72 hours after eating food contaminated with *Salmonella*. These include traditional food poisoning symptoms of abdomi-

nal **pain**, diarrhea, vomiting, and fever. The symptoms generally last one to five days. Dehydration can be a complication in severe cases. People generally recover without antibiotic treatment, although they may feel tired for a week after the active symptoms subside.

Staphylococcus aureus

Staphylococcus aureus is found on humans and in the environment in dust, air, and sewage. The bacteria is spread primarily by food handlers using poor sanitary practices. Almost any food can be contaminated, but salad dressings, milk products, cream pastries, and any food kept at room temperature, rather than hot or cold are likely candidates.

It is difficult to estimate the number of cases of food poisoning from *Staphylococcus aureus* that occur each year, because its symptoms are so similar to those caused by other foodborne bacteria. Many cases are mild and the victim never sees a doctor.

Symptoms appear rapidly, usually one to six hours after the contaminated food is eaten. The acute symptoms of vomiting and severe abdominal cramps without fever usually last only three to six hours and rarely more than 24 hours. Most people recover without medical assistance. Deaths are rare.

Escherichia coli (E. coli)

There are many strains of *E. coli*, and not all of them are harmful. The strain that causes most severe food poisoning is *E. coli O157:H7*. Food poisoning by *E. coli* occurs in three out of every 10,000 people. Foodborne *E. coli* is found and transmitted mainly in food derived from cows such as raw milk, raw or rare ground beef and fruit or vegetables that are contaminated.

Symptoms of food poisoning from *E. coli* are slower to appear than those caused by some of the other foodborne bacteria. *E. coli* produces toxins in the large intestine rather than higher up in the digestive system. This accounts for the delay in symptoms and the fact that vomiting rarely occurs in *E. coli* food poisoning.

One to three days after eating contaminated food, the victim with *E. coli O157:H7* begins to have severe abdominal cramps and watery diarrhea that usually becomes bloody within 24 hours. There is little or no fever, and rarely does the victim vomit. The bloody, watery diarrhea lasts from one to eight days in uncomplicated cases.

Campylobacter jejuni (C. jejuni)

According to the FDA, *C. jejuni* is the leading cause of bacterial diarrhea in the United States. It is responsible for more cases of bacterial diarrhea than *Shigella* and *Salmonella* combined. Anyone can get food poisoning from *C. jejuni*, but children under five and young adults between the ages of 15 and 29 are more frequently infected.

C. jejuni is carried by healthy cattle, chickens, birds, and flies. It is not carried by healthy people in the United States or Europe. The bacteria is also found ponds and stream water. The ingestion of only a few hundred *C. jejuni* bacteria can make a person sick.

Symptoms of food poisoning begin two to five days after eating food contaminated with *C. jejuni*. These symptoms include fever, abdominal pain, nausea, **headache**, muscle pain, and diarrhea. The diarrhea can be watery or sticky and may contain blood. Symptoms last from seven to 10 days, and relapses occur in about one quarter of people who are infected. Dehydration is a common complication. Other complications such as arthritis-like joint pain and **hemolytic-uremic syndrome** (HUS) are rare.

Shigella

Shigella is a common cause of diarrhea in travelers to developing countries. It is associated with contaminated food and water, crowded living conditions, and poor sanitation. The bacterial toxins affect the small intestine.

Symptoms of food poisoning by *Shigella* appear 36–72 hours after eating contaminated food. These symptoms are slightly different from those associated with most foodborne bacteria. In addition to the familiar watery diarrhea, nausea, vomiting, abdominal cramps, chills and fever occur. The diarrhea may be quite severe with cramps progressing to classical dysentery. Up to 40% of children with severe infections show neurological symptoms. These include seizures caused by fever, confusion, headache, lethargy, and a stiff neck that resembles **meningitis**.

The disease runs its course usually in two to three days but may last longer. Dehydration is a common complication. Most people recover on their own, although they may feel exhausted, but children who are malnourished or have weakened immune systems may die.

Clostridium botulinum (C. botulinum)

C. botulinum, which causes both adult **botulism** and infant botulism, is unlike any of the other foodborne bacteria. First, *C. botulinum* is an anaerobic bacterium in that it can only live in the absence of oxygen. Second, the toxins from *C. botulinum* are neurotoxins. They poison the nervous system, causing **paralysis** without the vomiting and diarrhea associated with other foodborne illnesses. Third, toxins that cause adult botulism are released when the bacteria grows in an airless environment outside the body. They can be broken down and made harm-

less by heat. Finally, botulism is much more likely to be fatal even in tiny quantities.

Adult botulism outbreaks are usually associated with home canned food, although occasionally commercially canned or vacuum packed foods are responsible for the disease. *C. botulinum* grows well in non-acidic, oxygen-free environments. If food is canned at too low heat or for too brief a time, the bacteria is not killed. It reproduces inside the can or jar, releasing its deadly neurotoxin. The toxin can be made harmless by heating the contaminated food to boiling for ten minutes. However, even a very small amount of the *C. botulinum* toxin can cause serious illness or **death**.

Symptoms of adult botulism appear about 18–36 hours after the contaminated food is eaten, although there are documented times of onset ranging from four hours to eight days. Initially a person suffering from botulism feels weakness and **dizziness** followed by double vision. Symptoms progress to difficulty speaking and swallowing. Paralysis moves down the body, and when the respiratory muscles are paralyzed, death results from asphyxiation. People who show any signs of botulism poisoning must receive immediate emergency medical care to increase their chance of survival.

Infant botulism is a form of botulism first recognized in 1976. It differs from food-borne botulism in its causes and symptoms. Infant botulism occurs when a child under the age of one year ingests the spores of *C. botulinum*. These spores are found in soil, but a more common source of spores is honey.

The *C. botulinum* spores lodge in the baby's intestinal tract and begin to grow, producing their neurotoxin. Onset of symptoms is gradual. Initially the baby is constipated. This is followed by poor feeding, lethargy, weakness, drooling, and a distinctive wailing cry. Eventually, the baby loses the ability to control its head muscles. From there the paralysis progresses to the rest of the body.

Diagnosis

One important aspect of diagnosing food poisoning is for doctors to determine if a number of people have eaten the same food and show the same symptoms of illness. When this happens, food poisoning is strongly suspected. The diagnosis is confirmed when the suspected bacteria is found in a **stool culture** or a fecal smear from the person. Other laboratory tests are used to isolate bacteria from a sample of the contaminated food. Botulism is usually diagnosed from its distinctive neurological symptoms, since rapid treatment is essential. Many cases of food poisoning go undiagnosed, since a definite diagnosis is not necessary to effectively treat the symptoms. Because it takes time for symptoms to develop, it is not necessarily the most recent food one has eaten that is the cause of the symptoms.

Common Pathogens Causing Food Poisoning

Pathogen	Common Host(s)
Campylobacter	Poultry
E.coli 0157:H7	Undercooked, contaminated ground beef
Listeria	Found in a variety of raw foods, such as uncooked meats and vegetables, and in processed foods that become contaminated after processing
Salmonella	Poultry, eggs, meat, and milk
Shigella	This bacteria is transmitted through direct contact with an infected person or from food or water that become contaminated by an infected person
Vibrio	Contaminated seafood

Treatment

Treatment of food poisoning, except that caused by *C. botulinum,* focuses on preventing dehydration by replacing fluids and electrolytes lost through vomiting and diarrhea. Electrolytes are salts and **minerals** that form electrically charges particles (ions) in body fluids. Electrolytes are important because they control body fluid balance and are important for all major body reactions. Pharmacists can recommend effective, pleasant-tasting, electrolytically balanced replacement fluids that are available without a prescription. When more fluids are being lost than can be consumed, dehydration may occur. Dehydration more likely to happen in the very young, the elderly, and people who are taking **diuretics**. To prevent dehydration, a doctor may give fluids intravenously.

In very serious cases of food poisoning, medications may be given to stop abdominal cramping and vomiting. Anti-diarrheal medications are not usually given. Stopping the diarrhea keeps the toxins in the body longer and may prolong the infection.

People with food poisoning should modify their diet. During period of active vomiting and diarrhea they should not try to eat and should drink only clear liquids frequently but in small quantities. Once active symptoms stop, they should eat bland, soft, easy to digest foods for two to three days. One example is the BRAT diet of bananas, rice, applesauce, and toast, all of which are easy to digest. Milk products, spicy food, alcohol and fresh fruit should be avoided for a few days, although babies should continue to breastfeed. These modifications are often all the treatment that is necessary.

Severe bacterial food poisonings are sometimes treated with **antibiotics**. Trimethoprim and sulfamethox-

KEY TERMS

Diuretic—Medication that increases the urine output of the body.

Electrolytes—Salts and minerals that produce electrically charged particles (ions) in body fluids. Common human electrolytes are sodium chloride, potassium, calcium, and sodium bicarbonate. Electrolytes control the fluid balance of the body and are important in muscle contraction, energy generation, and almost all major biochemical reactions in the body.

Lactobacillus acidophilus—This bacteria is found in yogurt and changes the balance of the bacteria in the intestine in a beneficial way.

Platelets—Blood cells that help the blood to clot.

azole (Septra, Bactrim), ampicillin (Amcill, Polycill) or ciprofloxacin (Ciloxan, Cipro) are most frequently used.

Botulism is treated in a different way from other bacterial food poisonings. Botulism antitoxin is given to adults, but not infants, if it can be administered within 72 hours after symptoms are first observed. If given later, it provides no benefit.

Both infants and adults require hospitalization, often in the intensive care unit. If the ability to breathe is impaired, patients are put on a mechanical ventilator to assist their breathing and are fed intravenously until the paralysis passes.

Alternative treatment

Alternative practitioners offer the same advice as traditional practitioners concerning diet modification. In addition they recommend taking charcoal tablets, *Lactobacillus acidophilus*, *Lactobacillus bulgaricus*, and citrus seed extract. An electrolyte replacement fluid can be made at home by adding one teaspoon of salt and four teaspoons of sugar to one quart of water. For food poisoning other than botulism, two homeopathic remedies, either *Arsenicum album* or *Nux vomica*, are strongly recommended.

Prognosis

Most cases of food poisoning (except botulism) clear up on their own within one week without medical assistance. The ill person may continue feel tired for a few days after active symptoms stop. So long as the ill person does not become dehydrated, there are few complications. Deaths are rare and usually occur in the very young, the very old and people whose immune systems are already weakened.

Complications of *Salmonella* food poisoning include arthritis-like symptoms that occur three to four weeks after infection. Although deaths from *Salmonella* are rare, they do occur. Most deaths caused by *Salmonella* food poisoning have occurred in elderly people in nursing homes.

Adults usually recover without medical intervention, but many children need to be hospitalized as the result of *E. coli* food poisoning. *E. coli* toxins may be absorbed into the blood stream where they destroy red blood cells and platelets. Platelets are important in blood clotting. About 5% of victims develop hemolytic-uremic syndrome which results in sudden kidney failure and makes dialysis necessary. (Dialysis is a medical procedure used to filter the body's waste product when the kidneys have failed).

Botulism is the deadliest of the bacterial food-borne illnesses. With prompt medical care, the death rate is less than 10%.

Prevention

Food poisoning is almost entirely preventable by practicing good sanitation and good food handling techniques. These include:

- keep hot foods hot and cold foods cold
- cook meat to the recommended internal temperature, use a meat thermometer to check and cook eggs until they are no longer runny
- refrigerate leftovers promptly, do not let food stand at room temperature
- avoid contaminating surfaces and other foods with the juices of uncooked meats
- wash fruits and vegetables before using
- purchase pasteurized dairy products and fruit juices
- throw away bulging or leaking cans or any food that smells spoiled
- wash hands well before and during food preparation and after using the bathroom
- sanitize food preparation surfaces regularly

Resources

PERIODICALS

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ORGANIZATION

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Foot care

Definition

Foot care involves all aspects of preventative and corrective care of the foot and ankle. Doctors specializing in foot care are called podiatrists.

Purpose

During an average lifetime, each person walks about 115,000 miles and three-quarters of people have foot problems at some point in their lives.

Foot problems can arise from wearing ill-fitting shoes, from general wear and tear, as a result of injury, or as a complication of disease. People with **diabetes mellitus** or circulatory diseases are 20 times more likely to have foot problems than the general public.

Podiatrists are doctors who specialize in treating the foot and ankle. Other doctors who have experience with foot problems are family physicians, orthopedists, sports medicine specialists, and those who care for diabetics. Problems with the feet include foot **pain**, joint inflammation, plantar **warts**, fungal infections (like **athlete's foot**), nerve disorders, torn ligaments, broken bones, bacterial infections, and tissue injuries (like frostbite).

Precautions

People with diabetes or circulatory disorders should be alert to even small foot problems. In these people, a break in the skin can lead to infection, **gangrene**, and **amputation**.

Description

Daily foot care for people likely to develop foot problems includes washing the feet in tepid water with mild soap and oiling the feet with vegetable oil or a lanolin-based lotion. Toenails should be cut straight across above the level of the skin after soaking the feet in tepid water. **Corns and calluses** should not be cut. If they need removal, it should be done under the care of a doctor. Athletes foot and plantar warts should also be treated by a doctor if they develop in high risk patients.

Many people with diabetes or circulatory disorders have problems with cold feet. These problems can be reduced by avoiding **smoking** tobacco (smoking constricts the blood vessels), wearing warm socks, not crossing the legs while sitting or not sitting in one position too long, or avoiding constricting stockings.

People with circulatory problems should not use heating pads or hot water bottles on their feet, as even moderate heat can damage the skin if circulation is impaired.

Preparation

No special preparation other than an understanding of the nature of foot problems is necessary to begin routine foot care.

Aftercare

Foot care is preventative and should be ongoing throughout a person's life.

Risks

There are no risks associated with foot care. The risks are in ignoring the feet and allowing problems to develop.

Normal results

With regular care, foot disorders such as infections, skin ulcers, and gangrene can be prevented.

Resources

BOOKS

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ORGANIZATIONS

American Diabetes Association. 1701 North Beauregard Street, Alexandria, VA 22311. (800) 342-2383. <http://www.diabetes.org>.

American Podiatry Association. 20 Chevy Chase Circle, NW, Washington, D.C. 20015.

Tish Davidson

Foreign bodies *see* **Foreign objects**

Foreign objects

Definition

"Foreign" means "originating elsewhere" or simply "outside the body." Foreign bodies typically become

X ray of swallowed spoon and blade in the intestine. *(Photo Researchers. Reproduced by permission.)*

lodged in the eyes, ears, nose, airways, and rectum of human beings.

Description

Both children and adults experience problems caused by foreign objects getting stuck in their bodies. Young children, in particular, are naturally curious and may intentionally put shiny objects, such as coins or button batteries, into their mouths. They also like to stick things in their ears and up their noses. Adults may accidentally swallow a non-food object or inhale a foreign body that gets stuck in the throat. Even if an object like a toothpick successfully passes through the esophagus and into the stomach, it can get stuck inside the rectum. Airborne particles can lodge in the eyes of people at any age.

Foreign bodies can be in hollow organs (like swallowed batteries) or in tissues (like bullets). They can be inert or irritating. If they irritate they will cause inflammation and scarring. They can bring infection with them or acquire it and protect it from the body's immune defenses. They can obstruct passageways either by their size or by the scarring they cause. Some can be toxic.

Causes and symptoms

Eyes

Dust, dirt, sand, or other airborne material can lodge in the eyes, causing minor irritation and redness. More serious damage can be caused by hard or sharp objects that penetrate the surface and become embedded in the cornea or conjunctiva (the mucous membranes around the inner surface of the eyelids). Swelling, redness, bleeding from the surface blood vessels, sensitivity to light, and sudden vision problems are all symptoms of foreign matter in the eyes.

Ears and nose

Children will sometimes put things into their noses, ears, and other openings. Beans, popcorn kernels, raisins, and beads are just a few of the many items that have been found in these bodily cavities. On occasion, insects may also fly into the ears and nose. **Pain**, **hearing loss**, and a sense of something stuck in the ear are symptoms of foreign bodies in the ears. A smelly, bloody discharge from one nostril is a symptom of foreign bodies in the nose.

Airways and stomach

At a certain age children will eat anything. A very partial list of items recovered from young stomachs includes the following: Coins, chicken bones, fish bones, beads, rocks, plastic toys, pins, keys, round stones, marbles, nails, rings, batteries, ball bearings, screws, staples, washers, a heart pendant, a clothespin spring, and a toy soldier. Some of these items will pass right on through and come out the other end. The progress of metal objects has been successfully followed with a metal detector. Others, like sharp bones, can get stuck and cause trouble. Batteries are corrosive and must be removed immediately.

Children eat things and stick things into their bodily openings of their own volition. But they inhale them unwittingly. The most commonly inhaled item is probably a peanut. A crayon and a cockroach have been found in a child's windpipes. These items always cause symptoms (difficulty swallowing and spitting up saliva, for instance) and may elude detection for some time while the child is being treated for **asthma** or recurring **pneumonia**.

Adults are not exempt from unorthodox inedibles. Dental devices are commonly swallowed. Adults with mental illness or subversive motives may swallow inappropriate objects, such as toothbrushes.

Rectum

Sometimes a foreign object will successfully pass throught the throat and stomach only to get stuck at the juncture between the rectum and the anal canal. Items may also be self-introduced to enhance sexual stimulation and then get stuck. Sudden sharp pain during elimination may signify that an object is lodged in the rectum. Other symptoms vary depending upon the size of the object, its location, how long it has been in place, and whether or not infection has set in.

Diagnosis

The symptoms are as diverse as the objects and their locations. The most common manifestation of a foreign object anywhere in the body is infection. Even if the object started out sterile, germs still seem to find it and are able to hide from the body's defenses there. Blockage of passageways—breathing, digestive or excretory—is another result. Pain is common.

Treatment

Eyes

Small particles like sand may be removable without medical help, but if the object is not visible or cannot be retrieved, prompt emergency treatment is necessary. Trauma to the eyes can lead to loss of vision and should never be ignored. Before attempting any treatment, the person should move to a well-lighted area where the object can be more easily spotted. Hands should be washed and only clean, preferably sterile, materials should make contact with the eyes. If the particle is small, it can be dislodged by blinking or pulling the upper lid over the lower lid and flushing out the speck. A clean cloth can also be used to pick out the offending particle. Afterwards, the eye should be rinsed with clean, lukewarm water or an opthalmic wash.

If the foreign object cannot be removed at home, the eye should be lightly covered with sterile gauze to discourage rubbing. A physician will use a strong light and possibly special eyedrops to locate the object. Surgical tweezers can effectively remove many objects. An antibiotic sterile ointment and a patch may be prescribed. If the foreign body has penetrated the deeper layers of the eye, an opthalmic surgeon will be consulted for emergency treatment.

Ears and nose

A number of ingenious extraction methods have been devised for removing foreign objects from the nose and ears. A bead in a nostril, for example, can be popped out by blowing into the mouth while holding the other nostril closed. Skilled practitioners have removed peas from the ears by tiny improvised corkscrews; marbles by q-tips with super glue. Tweezers often work well, too. Insects can be floated out of the ear by pouring warm (not hot) mineral oil, olive oil, or baby oil into the ear canal. Items that are lodged deep in the ear canal are more difficult to remove because of the possibility of damaging the ear drum. These require emergency treatment from a qualified physician.

Airways and stomach

Mechanical obstruction of the airways, which commonly occurs when food gets lodged in the throat, can be treated by applying the **Heimlich maneuver**. If the object is lodged lower in the airway, a bronchoscope (a special instrument to view the airway and remove obstructions) can be inserted. On other occasions, as when the object is blocking the entrance to the stomach, a fiberoptic endoscope (an illuminated instrument that views the interior of a body cavity) may be used. The physician typically administers a sedative and anesthetizes the throat. The foreign object will then either be pulled out or pushed into the stomach, depending on whether or not the physician

KEY TERMS

Bronchoscope—An illuminated instrument that is inserted into the airway to inspect and retrieve objects from the bronchial tubes.

Conjunctiva—Mucous membranes around the inner surface of the eyelid.

Cornea—The rounded, transparent portion of the eye that covers the pupil and iris and lets light into the interior

Endoscopy—The surgical use of long, thin instruments that have both viewing and operating capabilities.

Heimlich maneuver—An emergency procedure for removing a foreign object lodged in the airway that is preventing the person from breathing. To perform the Heimlich maneuver on a conscious adult, the rescuer stands behind the victim and encircles his waist. The rescuer makes a fist with one hand and places the other hand on top, positioned below the rib cage and above the waist. The rescuer then applies pressure by a series of upward and inward thrusts to force the foreign object back up the victim's trachea.

thinks it will pass through the digestive tract on its own. Objects in the digestive tract that are neither irritating, sharp nor large may be followed as they continue on through. Sterile objects that are causing no symptoms may be left in place. Surgical removal of the offending object is necessary if it is causing symptoms.

Rectum

A rectal retractor can remove objects that a physician can feel during **physical examination**. Surgery may be required for objects deeply lodged within the recturm.

Prevention

Using common sense and following safety precautions are the best ways to prevent foreign objects from entering the body. For instance, parents and grandparents should toddler-proof their homes, storing batteries in a locked cabinet and properly disposing of used batteries, so they are not in a location where curious preschoolers can fish them out of a wastebasket. To minimize the chance of youngsters inhaling food, parents should not allow children to eat while walking or playing. Adults should chew food thoroughly and not talk while chewing. Many eye injuries can be prevented by wearing safety glasses while using tools

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Fourn *see* **Flesh-eating disease**

47, XXY syndrome *see* **Klinefelter syndrome**

Fracture repair

Definition

Fracture repair is the process of rejoining and realigning the ends of broken bones. This procedure is usually performed by an orthopedist, general surgeon, or family doctor. In cases of an emergency, first aid measures should be evoked for temporary realignment and **immobilization** until proper medical help is available.

Purpose

Fracture repair is required when there is a need for restoration of the normal position and function of the broken bone. Throughout the stages of fracture healing, the bones must be held firmly in the correct position. In the event the fracture is not properly repaired, malalignment of the bone may occur, resulting in possible physical dysfunction of the bone or joint of that region of the body.

Precautions

Precautions for fracture repair are anything found to be significant with patients' medical diagnosis and history. This would include an individual's tolerance to anesthesia and the presence of bleeding disorders that may be present to complicate surgery.

Description

Fracture repair is applied by means of **traction**, surgery, and/or by immobilization of the bones. The bone fragments are aligned as close as possible to the normal position without injuring the skin. Metal wires or screws may be needed to align smaller bone fragments. Once the

broken ends of the bone are set, the affected area is immobilized for several weeks and kept rigid with a sling, plaster cast, brace or splint. With the use of traction, muscle pull on the fracture site is overcome by weights attached to a series of ropes running over pulleys. Strategically implanted electrical stimulation devices have proven beneficial in healing a fracture site, especially when the fracture is healing poorly and repair by other means is difficult.

Preparation

Emergency splinting may be required to immobilize the body part or parts involved. When fracture repair is necessary, the procedure is often performed in a hospital but can also be successfully done in an outpatient surgical facility, doctor's office or emergency room. Before any surgery for fracture repair, blood and urine studies may be taken from the patient. X rays may follow this if not previously acquired. It has been noted however, that not all **fractures** are immediately apparent on an initial x-ray examination. In this case, where a fracture is definitely suspected the extent of the fracture can be properly diagnosed by repeating the x rays 10–14 days later. Depending upon the situation, local or general anesthesia may be used for fracture repair.

Aftercare

After surgery, x rays may be again taken through the cast or splint to evaluate if rejoined pieces remain in good position for healing. This is usually performed either before the application of the splint or at least before the patient is awakened from the general anesthesia. The patient needs to be cautious not to place excess pressure on any part of the cast until it is completely dry. The patient also should avoid excess pressure on the operative site until complete healing has taken place and the injury has been re-examined by the physician. If the cast becomes exposed to moisture it may soften and require repair. The patient should also be instructed to keep the injured region propped up whenever possible to reduce the possibility of swelling.

Risks

Surgical risks of fracture repair are greater in patients over 60 years of age because the bones often taking longer to heal properly. **Obesity** may place extra **stress** on the healing site, affecting healing and possibly risking reinjury. **Smoking** may slow the healing process after fracture repair, as well as poor **nutrition**, **alcoholism**, and chronic illness. Some medications may affect the fracture site, causing poor union. Such medications include anti-hypertensives and cortisone.

An x-ray image of a healing fracture. *(Photograph by Bates, M.D., Custom Medical Stock Photo. Reproduced by permission.)*

Possible complications following fracture repair include excessive bleeding, improper fit of joined bone ends, pressure on nearby nerves, delayed healing, and a permanent incomplete healing of the fracture. If there is a poor blood supply to the fractured site with one of the portions of broken bone not properly supplied by the blood, the bony portion will die and healing of the fracture will not take place. This is called aseptic necrosis. Poor immobilization of the fracture from improper casting which permits motion between the bone parts may prevent healing and repair of the bone with possible deformity. Infection can interfere with bone repair. This risk is greater in the case of a compound fracture (a bone fracture causing an open wound) where ideal conditions are present for severe streptococcal and **staphylococcal infections**. Occasionally, fractured bones in the elderly may possibly never heal properly. The risk is increased when nutrition is poor.

Normal results

Once the procedure for fracture repair is completed, the body begins to produce new tissue to bridge the broken pieces. At first, this tissue (called a callus) is soft and easily injured. Later, the body deposits bone **minerals** until the callus becomes a solid piece of bone. The fracture site is thus strengthened further with extra bone. It usually takes about six weeks for a broken bone to heal together. The exact time required for healing depends on the type of fracture and the extent of damage. Before the use of x rays, fracture repair was not always accurate, resulting in crippling deformities. With modern x-ray technology, the physician can view the extent of the fracture, check the setting following the repair, and be certain after the procedure that the bones have not moved from their intended alignment. Children's bones usually heal relatively rapidly.

KEY TERMS

Compound fracture — A fracture in which the broken end or ends of the bone have torn through the skin. Compound fractures are also known as open fractures

Staphylococcal infection—An infection caused by any of several pathogenic species of staphylococcus, commonly characterized by the formation of abscesses of the skin or other organs.

Streptococcal infection—An infection caused by a pathogenic bacteria of one of several species of the genus streptococcus or their toxins. Almost any organ in the body may be involved.

Abnormal results

Abnormal results of fracture repair include damage to nearby nerves or primary blood vessels. Improper alignment causing deformity is also an abnormal outcome, however, with today's medical technology it is relatively rare.

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Fractures

Definition

A fracture is a complete or incomplete break in a bone resulting from the application of excessive force.

Description

A fracture usually results from traumatic injury to bones causing the continuity of bone tissues or bony cartilage to be disrupted or broken. Fracture classifications include simple, compound, incomplete and complete. Simple fractures (more recently called "closed") are not obvious as the skin has not been ruptured and remains intact. Compound fractures (now commonly called "open") break the skin, exposing bone and causing additional soft tissue injury and possible infection. A single fracture means that one fracture only has occurred and multiple fractures refer to more than one fracture occurring in the same bone. Fractures are termed complete if the break is completely through the bone and described as incomplete or "greenstick" if the fracture occurs partly across a bone shaft. This latter type of fracture is often the result of bending or crushing forces applied to a bone.

Fractures are also named according to the specific part of the bone involved and the nature of the break. Identification of a fracture line can further classify fractures. Types include linear, oblique, transverse, longitudinal, and spiral fractures. Fractures can be further subdivided by the positions of bony fragments and are described as comminuted, non-displaced, impacted, overriding, angulated, displaced, avulsed, and segmental. Additionally, an injury may be classified as a fracture-dislocation when a fracture involves the bony structures of any joint with associated dislocation of the same joint.

Fractures line identification

Linear fractures have a break that runs parallel to the bone's main axis or in the direction of the bone's shaft. For example, a linear fracture of the arm bone could extend the entire length of the bone. Oblique and transverse fractures differ in that an oblique fracture crosses a bone at approximately a 45° angle to the bone's axis. In contrast, a transverse fracture crosses a bone's axis at a 90° angle. A longitudinal fracture is similar to a linear fracture. Its fracture line extends along the shaft but is more irregular in shape and does not run parallel to the bone's axis. Spiral fractures are described as crossing a bone at an oblique angle, creating a spiral pattern. This break usually occurs in the long bones of the body such as the upper arm bone (humerus) or the thigh bone (femur).

Bony fragment position identification

Comminuted fractures have two or more fragments broken into small pieces, in addition to the upper and lower halves of a fractured bone. Fragments of bone that maintain their normal alignment following a fracture are described as being non-displaced. An impacted fracture is characterized as a bone fragment forced into or onto

Fractures usually result from a traumatic injury to a bone where the continuity of bone tissues or bony cartilage is disrupted or broken. The illustrations above feature common sites where fractures occur. *(Illustration by Electronic Illustrators Group.)*

another fragment resulting from a compressive force. Overriding is a term used to describe bony fragments that overlap and shorten the total length of a bone. Angulated fragments result in pieces of bone being at angles to each other. A displaced bony fragment occurs from disruption of normal bone alignment with deformity of these segments separate from one another. An avulsed fragment occurs when bone fragments are pulled from their normal position by forceful muscle contractions or resistance from ligaments. Segmental fragmented positioning occurs if fractures in two adjacent areas occur, leaving an isolated central segment. An example of segmental alignment is when the arm bone fractures in two separate places, with displacement of the middle section of bone.

Causes and symptoms

Individuals with high activity levels appear to be at greater risk for fractures. This group includes children and athletes participating in contact sports. Because of an increase in bone brittleness with **aging**, elderly persons are also included in this high-risk population. Up to the age of 50, more men suffer from fractures than women due to occupational hazards. However, after the age of 50, women are more prone to fractures than men. Specific diseases causing an increased risk for fractures include Paget's disease, rickets, **osteogenesis imperfecta**, **osteoporosis**, bone **cancer** and tumors, and prolonged disuse of a nonfunctional body part such as after a **stroke**.

Symptoms of fractures usually begin with **pain** that increases with attempted movement or use of the area and swelling at the involved site. The skin in the area may be pale and an obvious deformity may be present. In more severe cases, there may be a loss of pulse below the fracture site, such as in the extremities, accompanied by numbness, tingling, or **paralysis** below the fracture. An open or compound fracture is often accompanied by bleeding or bruising. If the lower limbs or pelvis are fractured, pain and resistance to movement usually accompany the injury causing difficulty with weight bearing.

Diagnosis

Diagnosis begins immediately with an individual's own observation of symptoms. A thorough medical his-

KEY TERMS

Avulsion fracture—A fracture caused by the tearing away of a fragment of bone where a strong ligament or tendon attachment forcibly pulls the fragment away from the bone tissue.

Axis—A line that passes through the center of the body or body part.

Comminuted fracture—A fracture where there are several breaks in a bone creating numerous fragments.

Compartment syndrome—Compartment syndrome is a condition in which a muscle swells but is constricted by the connective tissue around it, which cuts off blood supply to the muscle.

Contrast hydrotherapy—A series of hot and cold water applications. A hot compress (as hot as an individual can tolerate) is applied for three minutes followed by an ice cold compress for 30 seconds. These applications are repeated three times each and ending with the cold compress.

Osteogenesis imperfecta—A genetic disorder involving defective development of connective tissues, characterized by brittle and fragile bones that are easily fractured by the slightest trauma.

Osteoporosis—Literally meaning "porous bones," this condition occurs when bones lose an excessive amount of their protein and mineral content, particularly calcium. Over time, bone mass and strength are reduced leading to increased risk of fractures.

Paget's disease—Chromic disorder of unknown cause, usually affecting middle aged and elderly people, characterized by enlarged and deformed bones. Excessive breakdown and formation of bone tissue occurs with Paget's disease and can cause bone to weaken, resulting in bone pain, arthritis, deformities, and fractures.

Reduction—The restoration of a body part to its original position after displacement, such as the reduction of a fractured bone by bringing ends or fragments back into original alignment. The use of local or general anesthesia usually accompanies a fracture reduction. If performed by outside manipulation only, the reduction is described as closed; if surgery is necessary, it is described as open.

Rickets—A condition caused by the dietary deficiency of vitamin D, calcium, and usually phosphorus, seen primarily in infancy and childhood, and characterized by abnormal bone formation.

Traction—The process of placing a bone, limb, or group of muscles under tension by applying weights and pulleys. The goal is to realign or immobilize the part or to relieve pressure on that particular area to promote healing and restore function.

tory and physical exam by a physician often reveals the presence of a fracture. An x ray of the injured area is the most common test used to determine the presence of a bone fracture. Any x ray series performed involves at least two views of the area to confirm the presence of the fracture because not all fractures are apparent on a single x-ray. Some fractures are often difficult to see and may require several views at different angles to see clear fracture lines. In some cases, CT, MRI or other imaging tests are required to demonstrate fracture. Sometimes, especially with children, the initial x ray may not show any fractures but repeat x rays seven to 14 days later may show changes in the bone(s) of the affected area. If a fracture is open and occurs in conjunction with soft tissue injury, further laboratory studies are often conducted to determine if blood loss has occurred.

In the event of exercise-related **stress** fractures (micro-fractures due to excessive stress), a tuning fork can provide a simple, inexpensive test. The tuning fork is a metal instrument with a stem and two prongs that vibrate when struck. If an individual has increased pain when the tuning fork is placed on a bone, such as the tibia or shinbone, the likelihood of a stress fracture is high. Bone scans also are helpful in detecting stress fractures. In this diagnostic procedure, a radioactive tracer is injected into the bloodstream and images are taken of specific areas or the entire skeleton by CT or MRI.

Treatment

Treatment depends on the type of fracture, its severity, the individual's age and general health. The first priority in treating any fracture is to address the entire medical status of the patient. Medical personnel are trained not allow a painful, deformed limb to distract them from potentially life-threatening injury elsewhere or **shock**. If an open fracture is accompanied by serious soft tissue injury, it may be necessary to control bleeding and the shock that can accompany loss of blood.

First aid is the appropriate initial treatment in emergency situations. It includes proper splinting, control of blood loss, and monitoring vital signs such as breathing and circulation.

Immobilization

Immobilization of a fracture site can be done internally or externally. The primary goal of immobilization is to maintain the realignment of a bone long enough for healing to start and progress. Immobilization by external fixation uses splints, casts, or braces. This may be the primary and only procedure for fracture treatment. Splinting to immobilize a fracture can be done with or without **traction**. In emergency situations if the injured individual must be moved by someone other than a trained medical person, splinting is a useful form of fracture management. It should be done without causing additional pain and without moving the bone segments. In a clinical environment, plaster of Paris casts are used for immobilization. Braces are useful as they often allow movement above and below a fracture site. Treatments for stress fractures include rest and decreasing or stopping any activity that causes or increases pain.

Fracture reduction

Fracture reduction is the procedure by which a fractured bone is realigned in normal position. It can be either closed or open. Closed reduction refers to realigning bones without breaking the skin. It is performed with manual manipulation and/or traction and is commonly done with some kind of anesthetic. Open reduction primarily refers to surgery that is performed to realign bones or fragments. Fractures with little or no displacement may not require any form of reduction.

Traction is used to help reposition a broken bone. It works by applying pressure to restore proper alignment. The traction device immobilizes the area and maintains realignment as the bone heals. A fractured bone is immobilized by applying opposing force at both ends of the injured area, using an equal amount of traction and countertraction. Weights provide the traction pull needed or the pull is achieved by positioning the individual's body weight appropriately. Traction is a form of closed reduction and is sometimes used as an alternative to surgery. Since it restricts movement of the affected limb or body part, it may confine a person to bed rest for an extended period of time.

A person may need open reduction if there is an open, severe, or comminuted fracture. This procedure allows a physician to examine and surgically correct associated soft tissue damage while reducing the fracture and, if necessary, applying internal or external devices. Internal fixation involves the use of metallic devices inserted into or through bone to hold the fracture in a set position and alignment while it heals. Devices include plates, nails, screws, and rods. When healing is complete, the surgeon may or may not remove these devices. Virtually any hip fracture requires open reduction and internal fixation so that the bone will be able to support the patient's weight.

Alternative treatment

In addition to the importance of calcium for strong bones, many alternative treatment approaches recommend use of mineral supplements to help build and maintain a healthy, resilient skeleton. Some physical therapists use electro-stimulation over a fractured site to promote and expedite healing. Chinese traditional medicine may be helpful by working to reconnect chi through the meridian lines along the line of a fracture. **Homeopathy** can enhance the body's healing process. Two particularly useful homeopathic remedies are *Arnica* (*Arnica montana*) and *Symphytum* (*Symphytum officinalis*). If possible, applying contrast **hydrotherapy** to an extremity (e.g., a hand or foot) of a fractured area can assist healing by enhancing circulation.

Prognosis

Fractures involving joint surfaces almost always lead to some degree of arthritis of the joint. Fractures can normally be cured with proper first aid and appropriate aftercare. If determined necessary by a physician, the fractured site should be manipulated, realigned, and immobilized as soon as possible. Realignment has been shown to be much more difficult after six hours. Healing time varies from person to person with the elderly generally needing more time to heal completely. A non-union fracture may result when a fracture does not heal, such as in the case of an elderly person or an individual with medical complications. Recovery is complete when there is no bone motion at the fracture site, and x rays indicate complete healing. Open fractures may lead to bone infections, which delay the healing process. Another possible complication is compartment syndrome, a painful condition resulting from the expansion of enclosed tissue and that may occur when a body part is immobilized in a cast.

Prevention

Adequate calcium intake is necessary for strong bones and can help decrease the risk of fractures. People who do not get enough calcium in their **diets** can take a calcium supplement. **Exercise** can help strengthen bones by increasing bone density, thereby decreasing the risk of fractures from falls. A University of Southern California study reported that older people who exercised one or

more hours per day had approximately half the incidence of hip fractures as those who exercised fewer than 30 minutes per day or not at all.

Fractures can be prevented if safety measures are taken seriously. These measures include using seat belts in cars and encouraging children to wear protective sports gear. Estrogen replacement for women past the age of 50 has been shown to help prevent osteoporosis and the fractures that may result from this condition. In one study, elderly women on estrogen replacement therapy demonstrated the lowest occurrence of hip fractures when compared to similar women not on estrogen replacement therapy.

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Fragile X syndrome

Definition

Fragile X syndrome is the most common form of inherited **mental retardation**. Individuals with this condition have developmental delay, variable levels of mental retardation, and behavioral and emotional difficulties. They may also have characteristic physical traits. Generally, males are affected with moderate mental retardation and females with mild mental retardation.

Description

Fragile X syndrome is also known as Martin-Bell syndrome, Marker X syndrome, and FRAXA syndrome. It is the most common form of inherited mental retardation. Fragile X syndrome is caused by a mutation in the FMR-1 gene, located on the X chromosome. The role of the gene is unclear, but it is probably important in early development.

In order to understand fragile X syndrome it is important to understand how human genes and chromosomes influence this condition. Normally, each cell in the body contains 46 (23 pairs of) chromosomes. These chromosomes consist of genetic material (DNA) needed for the production of proteins, which lead to growth, development, and physical/intellectual characteristics. The first 22 pairs of chromosomes are the same in males and females. The remaining two chromosomes are called the sex chromosomes (X and Y). The sex chromosomes determine whether a person is male or female. Males have only one X chromosome, which is inherited from the mother at conception, and they receive a Y chromosome from the father. Females inherit two X chromosomes, one from each parent. Fragile X syndrome is caused by a mutation in a gene called FMR-1. This gene is located on the X chromosome. The FMR-1 gene is thought to play an important role in the development of the brain, but the exact way that the gene acts in the body is not fully understood.

Fragile X syndrome affects males and females of all ethnic groups. It is estimated that there are about one in 4,000 to one in 6,250 males affected with fragile X syndrome. There are approximately half as many females with fragile X syndrome as there are males. The carrier frequency in unaffected females is one in 100 to one in 600, with one study finding a carrier frequency of one in 250.

Causes and symptoms

For reasons not fully understood, the CGG sequence in the FMR-1 gene can expand to contain between 54 and 230 repeats. This stage of expansion is called a pre-

KEY TERMS

Amniocentesis—A procedure performed at 16-18 weeks of pregnancy in which a needle is inserted through a woman's abdomen into her uterus to draw out a small sample of the amniotic fluid from around the baby. Either the fluid itself or cells from the fluid can be used for a variety of tests to obtain information about genetic disorders and other medical conditions in the fetus.

CGG or CGG sequence—Shorthand for the DNA sequence: cytosine-guanine-guanine. Cytosine and guanine are two of the four molecules, otherwise called nucleic acids, that make up DNA.

Chorionic villus sampling (CVS)—A procedure used for prenatal diagnosis at 10-12 weeks gestation. Under ultrasound guidance a needle is inserted either through the mother's vagina or abdominal wall and a sample of cells is collected from around the early embryo. These cells are then tested for chromosome abnormalities or other genetic diseases.

Chromosome—A microscopic thread-like structure found within each cell of the body and consists of a complex of proteins and DNA. Humans have 46 chromosomes arranged into 23 pairs. Changes in either the total number of chromosomes or their shape and size (structure) may lead to physical or mental abnormalities.

FMR-1 gene—A gene found on the X chromosome. Its exact purpose is unknown, but it is suspected that the gene plays a role in brain development.

Mitral valve prolapse—A heart defect in which one of the valves of the heart (which normally controls blood flow) becomes floppy. Mitral valve prolapse may be detected as a heart murmur but there are usually no symptoms.

Premutation—A change in a gene that precedes a mutation; this change does not alter the function of the gene.

X chromosome—One of the two sex chromosomes (the other is Y) containing genetic material that, among other things, determine a person's gender.

mutation. People who carry a premutation do not usually have symptoms of fragile X syndrome; although there have been reports of individuals with a premutation and subtle intellectual or behavioral symptoms. Individuals who carry a fragile X premutation are at risk to have children or grandchildren with the condition. Female premutation carriers may also be at increased risk for earlier onset of **menopause**; however, premutation carriers may exist through several generations of a family and no symptoms of fragile X syndrome will appear.

The size of the premutation can expand over succeeding generations. Once the size of the premutation exceeds 230 repeats, it becomes a full mutation and the FMR-1 gene is disabled. Individuals who carry the full mutation may have fragile X syndrome. Since the FMR-1 gene is located on the X chromosome, males are more likely to develop symptoms than females. This is because males have only one copy of the X chromosome. Males who inherit the full mutation are expected to have mental impairment. A female's normal X chromosome may compensate for her chromosome with the fragile X gene mutation. Females who inherit the full mutation have an approximately 50% risk of mental impairment. The phenomenon of an expanding trinucleotide repeat in successive generations is called anticipation. Another unique aspect fragile X syndrome is that mosaicism is present in 15–20% those affected by the condition. Mosaicism is when there is the presence of cells of two different genetic materials in the same individual.

The mutation involves a short sequence of DNA in the FMR-1 gene. This sequence is designated CGG. Normally, the CGG sequence is repeated between six to 54 times. People who have repeats in this range do not have fragile X syndrome and are not at increased risk to have children with fragile X syndrome. Those affected by fragile X syndrome have expanded CGG repeats (over 200) in the first exon of the FMR1 gene (the full mutation)

Fragile X syndrome inherited in an X-linked dominant manner (characters are transmitted by genes on the X chromosome). When a man carries a premutation on his X chromosome, it tends to be stable and usually will not expand if he passes it on to his daughters (he passes his Y chromosome to his sons). Thus, all of his daughters will be premutation carriers like he is. When a woman carries a premutation, it is unstable and can expand as she passes it on to her children, therefore a man's grandchildren are at greater risk of developing the syndrome. There is a 50% risk for a premutation carrier female to transmit an abnormal mutation with each **pregnancy**. The likelihood for the premutation to expand is related to the number of

repeats present; the higher the number of repeats, the greater the chance that the premutation will expand to a full mutation in the next generation. All mothers of a child with a full mutation are carriers of an FMR-1 gene expansion. Ninety-nine percent of patients with fragile X syndrome have a CGG expansion, and less than one percent have a point mutation or deletion on the FMR1 gene.

Individuals with fragile X syndrome appear normal at birth but their development is delayed. Most boys with fragile X syndrome have mental impairment. The severity of mental impairment ranges from learning disabilities to severe mental retardation. Behavioral problems include attention deficit and hyperactivity at a young age. Some may show aggressive behavior in adulthood. Short attention span, poor eye contact, delayed and disordered speech and language, emotional instability, and unusual hand mannerisms (hand flapping or hand biting) are also seen frequently. Characteristic physical traits appear later in childhood. These traits include a long and narrow face, prominent jaw, large ears, and enlarged testes. In females who carry a full mutation, the physical and behavioral features and mental retardation tend to be less severe. About 50% of females who have a full mutation are mentally retarded. Other behavioral characteristics include whirling, spinning, and occasionally **autism**.

Children with fragile X syndrome often have frequent ear and sinus infections. Nearsightedness and lazy eye are also common. Many babies with fragile X syndrome may have trouble with sucking and some experience digestive disorders that cause frequent gagging and vomiting. A small percentage of children with fragile X syndrome may experience seizures. Children with fragile X syndrome also tend to have loose joints which may result in joint dislocations. Some children develop a curvature in the spine, flat feet, and a heart condition known as **mitral valve prolapse**.

Diagnosis

Any child with signs of developmental delay of speech, language, or motor development with no known cause should be considered for fragile X testing, especially if there is a family history of the condition. Behavioral and developmental problems may indicate fragile X syndrome, particularly if there is a family history of mental retardation. Definitive identification of the fragile X syndrome is made by means of a genetic test to assess the number of CGG sequence repeats in the FMR-1 gene. Individuals with the premutation or full mutation may be identified through **genetic testing**. Genetic testing for the fragile X mutation can be done on the developing baby before birth through **amniocentesis** or **chorionic villus sampling** (CVS), and is 99% effective in detecting the condition due to trinucleotide repeat expansion. Prenatal testing should only be undertaken after the fragile X carrier status of the parents has been confirmed and the couple has been counseled regarding the risks of recurrence. While prenatal testing is possible to do with CVS, the results can be difficult to interpret and additional testing may be required.

Treatment

Presently there is no cure for fragile X syndrome. Management includes such approaches as speech therapy, occupational therapy, and physical therapy. The expertise of psychologists, special education teachers, and genetic counselors may also be beneficial. Drugs may be used to treat hyperactivity, seizures, and other problems. Establishing a regular routine, avoiding over stimulation, and using calming techniques may also help in the management of behavioral problems. Children with a troubled heart valve may need to see a heart specialist and take medications before surgery or dental procedures. Children with frequent ear and sinus infections may need to take medications or have special tubes placed in their ears to drain excess fluid. Mainstreaming of children with fragile X syndrome into regular classrooms is encouraged because they do well imitating behavior. Peer tutoring and positive reinforcement are also encouraged.

Prognosis

Early diagnosis and intensive intervention offer the best prognosis for individuals with fragile X syndrome. Adults with fragile X syndrome may benefit from vocational training and may need to live in a supervised setting. Life span is typically normal.

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National Fragile X Foundation. PO Box 190488, San Francisco, CA 94119-0988. (800) 688-8765 or (510) 763-6030. Fax: (510) 763-6223. natlfx@sprintmail.com. <http://nfxf.org>.
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Nada Quercia, MS, CCGC

Frambesia *see* **Yaws**

Francisella tularensis infection *see* **Tularemia**

Fresh cell therapy *see* **Cell therapy**

Friedreich's ataxia

Definition

Friedreich's ataxia (FA) is an inherited, progressive nervous system disorder causing loss of balance and coordination.

Description

Ataxia is a condition marked by impaired coordination. Friedreich's ataxia is the most common inherited ataxia, affecting between 3,000–5,000 people in the United States. FA is an autosomal recessive disease, which means that two defective gene copies must be inherited to develop symptoms, one from each parent. A person with only one defective gene copy will not show signs of FA, but may pass along the gene to offspring. Couples with one child affected by FA have a 25% chance in each **pregnancy** of conceiving another affected child.

Causes and symptoms

Causes

The gene for FA codes for a protein called frataxin. Normal frataxin is found in the cellular energy structures known as mitochondria, where it is thought to be involved in regulating the transport of iron. In FA, the frataxin gene on chromosome 9 is expanded with nonsense information known as a "triple repeat." This extra DNA interferes with normal production of frataxin, thereby impairing iron transport. Normally, there are 10-21 repeats of the frataxin gene. In FA, this sequence may be repeated between 200-900 times. The types of symptoms and severity of FA seems to be associated with the number of repetitions. Patients with more copies have more severe symptomatology. Researchers are still wrestling with how frataxin and the repeats on chromosome 9 are involved in causing FA. One theory suggests that FA develops in part because defects in iron transport prevent efficient use of cellular energy supplies.

The nerve cells most affected by FA are those in the spinal cord involved in relaying information between muscles and the brain. Tight control of movement requires complex feedback between the muscles promoting a movement, those restraining it, and the brain. Without this control, movements become uncoordinated, jerky, and inappropriate to the desired action.

Symptoms

Symptoms of FA usually first appear between the ages of 8 and 15, although onset as early as 18 months or as late as age 25 is possible. The first symptom is usually gait incoordination. A child with FA may graze doorways when passing through, for instance, or trip over low obstacles. Unsteadiness when standing still and deterioration of position sense is common. Foot deformities and walking up off the heels often results from uneven muscle weakness in the legs. **Muscle spasms and cramps** may occur, especially at night.

Ataxia in the arms follows, usually within several years, leading to decreased hand-eye coordination. Arm weakness does not usually occur until much later. Speech and swallowing difficulties are common. **Diabetes mellitus** may also occur. **Nystagmus**, or eye tremor, is common, along with some loss of visual acuity. **Hearing loss** may also occur. A side-to-side curvature of the spine (**scoliosis**) occurs in many cases, and may become severe.

Heartbeat abnormalities occur in about two thirds of FA patients, leading to **shortness of breath** after exertion, swelling in the lower limbs, and frequent complaints of cold feet.

Diagnosis

Diagnosis of FA involves a careful medical history and thorough neurological exam. Lab tests include **electromyography**, an electrical test of muscle, and a nerve conduction velocity test. An electrocardiogram may be performed to diagnose heart arrhythmia.

Direct DNA testing is available, allowing FA to be more easily distinguished from other types of ataxia. The same test may be used to determine the presence of the genetic defect in unaffected individuals, such as siblings.

KEY TERMS

Ataxia—A condition marked by impaired coordination.

Scoliosis—An abnormal, side-to-side curvature of the spine.

Treatment

There is no cure for FA, nor any treatment that can slow its progress. Amantadine may provide some limited improvement in ataxic symptoms, but is not recommended in patients with cardiac abnormalities. Physical and occupational therapy are used to maintain range of motion in weakened muscles, and to design adaptive techniques and devices to compensate for loss of coordination and strength. Some patients find that using weights on the arms can help dampen the worst of the uncoordinated arm movements.

Heart **arrhythmias** and diabetes are treated with drugs specific to those conditions.

Prognosis

The rate of progression of FA is highly variable. Most patients lose the ability to walk within 15 years of symptom onset, and 95% require a wheelchair for mobility by age 45. Reduction in lifespan from FA complications is also quite variable. Average age at **death** is in the mid-thirties, but may be as late as the mid-sixties. As of mid-1998, the particular length of the triple repeat has not been correlated strongly enough with disease progression to allow prediction of the course of the disease on this basis.

Prevention

There is no way to prevent development of FA in a person carrying two defective gene copies.

Resources

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ORGANIZATIONS

Muscular Dystrophy Association. 3300 East Sunrise Drive, Tucson, AZ 85718. (520) 529-2000 or (800) 572-1717. <http://www.mdausa.org>.

Rosalyn Carson-DeWitt

Frostbite and frostnip

Definition

Frostbite is the term for damage to the skin and other tissues caused by freezing. Frostnip is a mild form of cold injury.

Description

In North America, frostbite is largely confined to Alaska, Canada, and the northern states. Recent years have witnessed a substantial decline in the number of cases, probably for several reasons, including better winter clothing and footwear and greater public understanding of how to avoid cold-weather dangers. At the same time, the nature of the at-risk population has changed as rising numbers of homeless people have made frostbite an urban as well as a rural public health concern. The growing popularity of outdoor winter activities has also expanded the at-risk population.

Causes and symptoms

Frostbite

Skin exposed to temperatures a little below the freezing mark can take hours to freeze, but very cold skin can freeze in minutes or seconds. Air temperature, wind speed, and moisture all affect how cold the skin becomes. A strong wind can lower skin temperature considerably by dispersing the thin protective layer of warm air that surrounds our bodies. Wet clothing readily draws heat away from the skin because water is a potent conductor of heat. The evaporation of moisture on the skin also produces cooling. For these reasons, wet skin or clothing on a windy day can lead to frostbite even if the air temperature is above the freezing mark.

The extent of permanent injury, however, is determined not by how cold the skin and the underlying tissues become but by how long they remain frozen. Consequently, homeless people and others whose self-preservation instincts may be clouded by alcohol or psychiatric illness face a greater risk of frostbite-related **amputation** because they are more likely to stay out in the cold when prudence dictates seeking shelter or medical attention. Alcohol also affects blood circulation in the extremities in a way that can increase the severity of injury (as does **smoking**). A review of 125 Saskatchewan frostbite cases found a tie to alcohol in 46% and to psychiatric illness in 17%. Other risk factors identified by researchers include inadequate clothing, previous cold injury, **fatigue**, wound infection, **atherosclerosis** (an arterial disease), and diabetes. Driving in poor weather can also be dan-

gerous: vehicular failure was a predisposing factor in 15% of the Saskatchewan cases.

Three nearly simultaneous physiological processes underlie frostbite injury: tissue freezing, tissue hypoxia, and the release of inflammatory mediators. Tissue freezing causes ice crystal formation and other changes that damage and eventually kill cells. Much of this harm occurs because the ice produces pressure changes that cause water (crucial for cell survival) to flow out of the cells. Tissue hypoxia (oxygen deficiency) occurs when the blood vessels in the hands, feet, and other extremities narrow in response to cold. Among its many tasks, blood transfers body heat to the skin, which then dissipates the heat into the environment. Blood vessel narrowing is the body's way of protecting vital internal organs at the expense of the extremities by reducing heat flow away from the core. However, blood also carries life-sustaining oxygen to the skin and other tissues, and narrowed vessels result in oxygen **starvation**. Narrowing also causes acidosis (an increase in tissue acidity) and increases blood viscosity (thickness). Ultimately, blood stops flowing through the capillaries (the tiny blood vessels that connect the arteries and veins) and blood clots form in the arterioles and venules (the smallest arteries and veins). Damage also occurs to the endothelial cells that line the blood vessels. Hypoxia, blood clots, and endothelial damage lead, in turn, to the release of inflammatory mediators (substances that act as links in the inflammatory process), which promote further endothelial damage, hypoxia, and cell destruction.

Frostbite is classified by degree of injury (first, second, third, or fourth), or simply divided into two types, superficial (corresponding to first- or second-degree injury) and deep (corresponding to third- or fourth-degree injury). Most frostbite injuries affect the feet or hands. The remaining 10% of cases typically involve the ears, nose, cheeks, or penis. Once frostbite sets in, the affected part begins to feel cold and, usually, numb; this is followed by a feeling of clumsiness. The skin turns white or yellowish. Many patients experience severe **pain** in the affected part during rewarming treatment and an intense throbbing pain that arises two or three days later and can last days or weeks. As the skin begins to thaw during treatment, **edema** (excess tissue fluid) often accumulates, causing swelling. In second- and higher-degree frostbite, blisters appear. Third-degree cases produce deep, blood-filled blisters and, during the second week, a hard black eschar (scab). Fourth-degree frostbite penetrates below the skin to the muscles, tendons, nerves, and bones. In severe cases of frostbite the dead tissue can mummify and drop off. Infection is also a possibility.

Frostnip

Like frostbite, frostnip is associated with ice crystal formation in the tissues, but no tissue destruction occurs and the crystals dissolve as soon as the skin is warmed. Frostnip affects areas such as the earlobes, cheeks, nose, fingers, and toes. The skin turns pale and one experiences numbness or tingling in the affected part until warming begins.

A human hand with frostbite. *(Photo Researchers, Inc. Reproduced by permission.)*

Diagnosis

Frostbite diagnosis relies on a **physical examination** and may also include conventional radiography (x rays), **angiography** (x-ray examination of the blood vessels using an injected dye to provide contrast), thermography (use of a heat-sensitive device for measuring blood flow), and other techniques for predicting the course of injury and identifying tissue that requires surgical removal. During the initial treatment period, however, a physician cannot judge how a case will progress. Diagnostic tests only become useful three to five days after rewarming, once the blood vessels have stabilized.

Treatment

Frostbite

Emergency medical help should always be summoned whenever frostbite is suspected. While waiting for help to arrive, one should, if possible, remove wet or tight clothing and put on dry, loose clothing or wraps. A splint and padding are used to protect the injured area. Rubbing the area with snow or anything else is dangerous. The key to prehospital treatment is to avoid partial thawing and refreezing, which releases more inflammatory mediators and makes the injury substantially worse. For this reason, the affected part must be kept away from heat sources such as campfires and car heaters. Experts advise rewarming in the field only when emergency help will take more than two hours to arrive and refreezing can be prevented.

Because the outcome of a frostbite injury cannot be predicted at first, all hospital treatment follows the same

route. Treatment begins by rewarming the affected part for 15–30 minutes in water at a temperature of 104–108°F (40–42.2°C). This rapid rewarming halts ice crystal formation and dilates narrowed blood vessels. Aloe vera (which acts against inflammatory mediators) is applied to the affected part, which is then splinted, elevated, and wrapped in a dressing. Depending on the extent of injury, blisters may be debrided (cleaned by removing foreign material) or simply covered with aloe vera. A **tetanus** shot and, possibly, penicillin, are used to prevent infection, and the patient is given ibuprofen to combat inflammation. Narcotics are needed in most cases to reduce the excruciating pain that occurs as sensation returns during rewarming. Except when injury is minimal, treatment generally requires a hospital stay of several days, during which **hydrotherapy** and physical therapy are used to restore the affected part to health. Experts recommend a cautious approach to tissue removal, and advise that 22–45 days must pass before a decision on amputation can safely be made.

Frostnip

Frostnipped fingers are helped by blowing warm air on them or holding them under one's armpits. Other frostnipped areas can be covered with warm hands. The injured areas should never be rubbed.

Alternative treatment

Alternative practitioners suggest several kinds of treatment to speed recovery from frostbite after leaving the hospital. Bathing the affected part in warm water or using contrast hydrotherapy can help enhance circulation. Contrast hydrotherapy involves a series of hot and cold water applications. A hot compress (as hot as the patient can stand) is applied to the affected area for three minutes followed by an ice cold compress for 30 seconds. These applications are repeated three times each, ending with the cold compress. Nutritional therapy to promote tissue growth in damaged areas may also be helpful. Homeopathic and botanical therapies may also assist recovery from frostbite. Homeopathic *Hypericum* (*Hypericum perforatum*) is recommended when nerve ending are affected (especially in the fingers and toes) and *Arnica* (*Arnica montana*) is prescribed for **shock**. Cayenne pepper (*Capsicum frutescens*) can enhance circulation and relieve pain. Drinking hot ginger (*Zingiber officinale*) tea also aids circulation. Other possible approaches include **acupuncture** to avoid permanent nerve damage and oxygen therapy.

Prognosis

The rapid rewarming approach to frostbite treatment, pioneered in the 1980s, has proved to be much more effective than older methods in preventing tissue loss and amputation. A study of 56 first-, second-, and third-degree frostbite patients treated with rapid rewarming in 1982–85 found that 68% recovered without tissue loss, 25% experienced some tissue loss, and 7% needed amputation. In a comparison group of 98 patients, treatment using older methods resulted in a tissue loss rate of nearly 35% and an amputation rate of nearly 33%. Although the comparison group included a higher proportion of second- and third-degree cases, the difference in treatment results was determined to be statistically significant.

The extreme throbbing pain that many frostbite sufferers endure for days or weeks after rewarming is not the only prolonged symptom of frostbite. During the first weeks or months, people often experience tingling, a burning sensation, or a sensation resembling shocks from an electric current. Other possible consequences of frostbite include skin—color changes, nail deformation or loss, joint stiffness and pain, **hyperhidrosis** (excessive sweating), and heightened sensitivity to cold. For everyone, a degree of sensory loss lasting at least four years—and sometimes a lifetime—is inevitable.

Prevention

With the appropriate knowledge and precautions, frostbite can be prevented even in the coldest and most challenging environments. Appropriate clothing and footwear are essential. To prevent heat loss and keep the blood circulating properly, clothing should be worn loosely and in layers. Covering the hands, feet, and head is also crucial for preventing heat loss. Outer garments need to be wind and water resistant, and wet clothing and footwear must be replaced as quickly as possible. Alcohol and drugs should be avoided because of their harmful effects on judgment and reasoning. Experts also warn against alcohol use and smoking in the cold because of the circulatory changes they produce. Paying close attention to the weather report before venturing outdoors and avoiding unnecessary risks such as driving in isolated areas during a blizzard are also important.

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Howard Baker

Frostnip *see* **Frostbite and frostnip**

FSH test *see* **Follicle-stimulating hormone test**

Fugue *see* **Dissociative disorders**

FUO *see* **Fever of unknown origin**

Furosemide *see* **Diuretics**

Furunculosis *see* **Boils**

Fusobacterium infection *see* **Anaerobic infections**

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LONG CASES IN CLINICAL MEDICINE

(Concerned with long cases, their presentation, related questions, answers and discussions)

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Foreword
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"He who studies medicine without books sails an uncharted sea, but he who studies medicine without patients does not go to sea at all."

—Sir William Osler

Dedicated to

My Parents,
Wife
and
Children

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Foreword

This is my pleasure and great honor to write a few words about *Long Cases in Clinical Medicine*. Professor Abdullah has written an excellent "made easy" book that will help both undergraduate and postgraduate students prepare themselves in a systematic manner. It is easy to understand, concise, and will help to learn many aspects of medicine. This will reflect the diseases of the region.

Medicine is a vast subject and ever-changing science, expanding and progressing day by day. New information is emerging all the time, making the textbooks bigger and harder to assimilate. Textbooks are a good source of knowledge, but many students, in spite of hours of tedious work, are often unable to acquire all the necessary information in a concise way.

Dr Abdullah has admirably succeeded in fulfilling this gap by preparing such a book in a concise and methodical way. This book is certainly the first of its kind to fulfill the long demand of students and doctors. I have no doubt that this book will be of immense benefit for the students who are appearing in any postgraduate and undergraduate examination in clinical medicine. This book has an excellent outline regarding presentation of long cases, answers of relevant questions and a brief discussion.

When I was a new student in clinical medicine, I found it difficult while talking to the patient, taking the history, physical examination, coming to the diagnosis, etc. I think every new student in clinical medicine used to feel the same problem. There is no book or clinical methods that will fill these difficulties. In that respect, I strongly appreciate and feel that this book will really be a good guide, written in a concise and rational manner that will greatly help the undergraduate students to establish the foundation of clinical medicine with ease and confidence.

I heartily appreciate and praise the author's effort, hard work, sincere endeavor, enthusiasm and patience in bringing out this book in a beautifully designed way for the benefit of the learners in medicine.

Pran Gopal Datta MCPS ACORL (Odessa)
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Vice-Chancellor
Bangabandhu Sheikh Mujib Medical University
Dhaka, Bangladesh

Preface

By the good grace of Almighty, I have succeeded to bring out the first edition of *Long Cases in Clinical Medicine*.

Long cases are an integral part of any examination in medicine. The idea is to assess the candidate's ability of gathering adequate information from thorough medical history and physical examination, interpreting them to come up with a probable diagnosis and formulating a management plan. A sound knowledge of medical science, optimum clinical skills, good interpersonal communication and adequate time management are all needed. A good preparation and adequate practice are vital for success.

From my experience as a teacher and an examiner in medicine, I feel that many candidates, even brilliant ones, fail to succeed in long cases due to lack of adequate technique of taking history from the patient, analysis of symptoms, inapt presentation and inability to answer questions related to the case. In spite of good theoretical knowledge, many of them are unable to effectively communicate with the patient. This is because they do not prepare themselves in an examination-oriented manner. It is important to acquire knowledge from textbooks, but it is equally vital to know what to expect in examinations, how to face them and to practice with that in mind. Goal-based preparation, systematic practice and repeated exposure to different cases and rehearsal of presentation in front of others is the secret to success. With this in mind, I have written this book to help students prepare themselves in an examination-oriented manner.

This book has been written to entertain a wide variety of readers from medical students to postgraduate examinees. It includes a complete outline of a comprehensive medical encounter including history taking and physical examination. It also gives valuable tips regarding interpretation of various clinical features to make a diagnosis. Successive chapters include long cases arranged according to body systems. In each case, the history and examination is presented first followed by the clinical diagnosis and possible differentials. Then the relevant questions and answers are provided.

The best way to get the most out of this book would be to practice a real case in the ward and then go through the relevant example given in the book. Students should notice how the case has been presented, the important clinical points that are mentioned and then familiarize themselves with the relevant questions and answers. They can make small groups where one will present a case in front of others and then answer questions asked by them. This will help them to be confident and fluent during the real examination.

In examination, a patient may have a single disease, or may be suffering from multiple diseases. For the purpose of preparation and simplicity, I have prepared this book using a prototype single case of a disease condition.

I do not claim that this book is enough for the whole clinical medicine and one should consult standard textbooks for learning. But for examination purpose, this book will be a valuable tool for optimum preparation.

A candidate needs to prove that he is not only knowledgeable but also competent. I hope that this book will help to promote such an approach.

I would like to invite constructive criticism from valued readers of this book, so that any error or omission may be corrected in future edition.

ABM Abdullah

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I would like to take the opportunity to extend my sincere gratitude to **Professor Pran Gopal Datta** MCPS, ACORL (Odessa), PhD (Kiev), MSc in Audiology (UK), FCPS, FRCS (Glasgow-UK), Vice-Chancellor, Bangabandhu Sheikh Mujib Medical University, for his encouragement and valuable suggestions in preparing this book.

I am also highly grateful to Dr Ahmed-al-Muntasir-Niloy for the computer composing and graphic designing of the entire book. He has also gone through the whole manuscript and made necessary corrections and modifications. I can, without any hesitation, mention that he has worked as the co-author.

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I must be grateful to my students who were repeatedly encouraging and demanding to write such a book.

Last but not least, I must express that no amount of appreciation is sufficient for my wife and children, whose untiring support and sacrifice has made it possible to bring such a book in the light of the day.

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"The good physician treats the disease; the great physician treats the patient who has the disease."

—Sir William Osler

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CHAPTER 1

Proforma of a Long Case

"Observe, record, tabulate, communicate. Use your five senses. Learn to see, learn to hear, learn to feel, learn to smell, and know that by practice alone you can become expert." **—Sir William Osler**

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HISTORY OF THE PATIENT

- Name, age, sex, address, marital status, occupation, religion
- Date of admission
- Date of examination
- Chief complaints (in chronological order, from longest to shortest duration)
- History of present illness
- History of past illness (including any operation)
- Family history
- Personal history
- Socioeconomic history
- Psychiatric history
- Drug and treatment history
- History of allergy (to drugs, diet or anything else, skin rash associated with allergy, treatment taken for allergy)
- History of immunization
- Menstrual and obstetric history (in female)
- Other history – Travelling to other places or abroad, working abroad (may be related to hepatitis B, HIV, etc.), contact with TB patient (mention, if relevant).

PHYSICAL EXAMINATION (INCLUDES GENERAL AND SYSTEMIC EXAMINATION)

General Examination

- Appearance
- Build
- Nutrition
- Decubitus
- Cooperation
- Anemia
- Jaundice
- Cyanosis
- Clubbing
- Koilonychia
- Leukonychia
- Edema
- Dehydration
- Bony tenderness
- Pigmentation
- Lymph nodes
- Thyroid gland
- Breasts
- Body hair
- Pulse
- Blood pressure
- Temperature
- Respiration

- Others (if relevant) – Neck, axilla, head (alopecia, large or small). Skin lesion (if any, such as butterfly rash in face, rash in body, scratch mark).

Systemic Examination

Cardiovascular System

1. Pulse:
   - Rate
   - Rhythm
   - Volume
   - Character
   - Condition of the vessel wall
   - Radio-femoral delay
   - Radio-radial delay
2. Neck veins (JVP), hepatojugular reflux (if needed)
3. Blood Pressure.

Precordium (Sequentially—Inspection, Palpation, Percussion and Auscultation)

Inspection:

- Any deformity of the chest
- Visible cardiac impulse
- Other impulses (epigastric, suprasternal, supraclavicular or other impulse)
- Any scar mark (midsternal or thoracotomy)
- Pacemaker or cardioverter defibrillator box (mention, if any).

Palpation:

1. Apex beat:
   - Site (that intercostal space)
   - Distance from midline (in cm)
   - Nature (normal, tapping, heaving, thrusting, diffuse or double apex).
2. Thrill:
   - Site (that intercostal space, apical or basal or other site)
   - Nature (systolic or diastolic or both).
3. Left parasternal heave
4. Palpable P_2
5. Epigastric pulsation.

Percussion:

- Area of cardiac dullness (Not a routine. However, it is important to diagnose pericardial effusion, where area of cardiac dullness is increased and in emphysema, where area of cardiac dullness is obliterated).

Auscultation:

1. 1st and 2nd heart sounds
2. Other heart sounds (3rd and 4th)

3. Murmur:
   - Site
   - Nature (systolic, diastolic or both)
   - Radiation (towards left axilla or neck)
   - Relation with respiration, posture (in left lateral position with breathing hold after expiration or bending forward with breathing hold after expiration)
   - Grading (1, 2, 3...)
4. Added sounds (pericardial rub, opening snap, ejection click, metallic plop)
5. Auscultate back of the chest (to see bilateral basal crepitations in pulmonary edema).

Respiratory System

Examination of the chest (systematically—inspection, palpation, percussion and auscultation).

Inspection:

- Shape of the chest
- Deformity (flattening of the chest, kyphosis, scoliosis, etc.)
- Drooping of the shoulder
- Movement of the chest
- Intercostal space (indrawing or fullness)
- Visible impulse
- Visible or engorged vein (if present, see flow)
- Others (scar marks, suprasternal and supraclavicular excavation, prominent accessory muscles, gynecomastia, needle puncture mark, tattooing, radiation mark).

Palpation:

- Position of trachea
- Apex beat
- Chest expansion
- Chest movement (symmetrical or asymmetrical)
- Tracheal tug
- Cricosternal distance
- Vocal fremitus
- Local rib tenderness.

Percussion:

- Percussion note
- Liver dullness
- Area of cardiac dullness (not done routinely, only if emphysema is suspected).

Auscultation:

- Breath sound
- Vocal resonance
- Added sounds (rhonchi, crepitations, pleural rub, post-tussive crepitations).

Note

Always examine the back of the chest, systematically.

Gastrointestinal System

(Always start examining from mouth and pharynx, then abdomen).

Mouth and pharynx:

- Lips
- Teeth and gum
- Oral mucous membrane
- Tongue
- Palate and movement of soft palate
- Tonsils
- Fauces.

Note

Look for pigmentation, white patch, ulceration.

Abdomen (Examine Systematically—Inspection, Palpation, Percussion and Auscultation)

Inspection:

- Shape of the abdomen
- Flanks
- Movement with respiration
- Visible peristalsis
- Visible pulsation
- Umbilicus
- Engorged veins (if present, see the direction of flow both above and below the umbilicus)
- Striae
- Any scar mark
- Pigmentation
- Swelling or mass (tell the site)
- Campbell de Morgan's spot
- Groin, pubic hair and genitalia (with permission of the patient)
- Cough impulse.

Palpation:

- Superficial palpation and local temperature
- Deep palpation (tenderness, rigidity, mass)
- Liver:
  - Size (in cm)
  - Margin
  - Surface
  - Tenderness
  - Consistency
  - Upper border of the liver dullness
  - Auscultation (to see bruit or rub).
- Spleen (size in cm)
- Kidneys

- Gallbladder (if palpable, mention the size, tenderness, consistency, surface, margin)
- Fluid thrill (if ascites is suspected)
- Any mass (if present, first see whether it is intra-abdominal or extra-abdominal). Then see the following points:
  - Site
  - Size
  - Shape
  - Surface
  - Consistency
  - Tenderness
  - Mobility
  - Others: (whether pulsatile, feel for get above the swelling).
- Para-aortic lymph nodes
- Hernial orifice
- Testis (with permission of the patient)
- Per-rectal examination (though it is a part of physical examination, usually it is never done in an examination setting).

Percussion:

- Liver dullness
- Splenic dullness
- Shifting dullness (if ascites is suspected or present).

Auscultation:

- Bowel sounds
- Hepatic bruit or rub
- Renal bruit
- Bruit of aortic aneurysm
- Splenic rub
- Venous hum.

Nervous System

Higher Psychic Functions (HPF):

- Appearance
- Behavior
- Consciousness
- Memory
- Intelligence
- Orientation of time, space and person
- Emotional state
- Hallucination
- Delusion
- Speech.

Motor functions:

- Bulk of the muscle

- Tone of the muscle
- Power of the muscle
- Fasciculation
- Involuntary movement (mention the type, e.g. tremor, chorea, athetosis, hemiballismus, etc.)
- Coordination test:
  - Finger nose test
  - Heel shin test
  - Romberg's sign
- Gait and posture.

Reflexes (Superficial and Deep)

Superficial reflexes:

- Plantar reflex
- Abdominal reflex
- Corneal reflex
- Palatal reflex
- Cremasteric reflex.

Deep reflexes:

Side	Biceps	Triceps	Supinator	Knee	Ankle
Right					
Left					

Clonus:

- Ankle
- Patellar.

Others: Gordon's sign and Oppenheim's sign (both in leg) and Hoffman's sign.

Sensory functions:

- Pain
- Touch
- Temperature
- Position sense
- Sense of vibration
- Tactile localization
- Tactile discrimination
- Recognition of size and shape, weight and form of object
- Romberg's sign.

Signs of meningeal irritation:

- Neck rigidity
- Kernig's sign
- Brudzinski's sign.

Examination of cranial nerves:

- Olfactory nerve (sense of smell or hallucination of smell)

- Optic nerve:
  - Visual acuity
  - Field of vision
  - Color vision
  - Light reflex (direct and consensual)
  - Fundoscopy (see last)
- Oculomotor, trochlear and abducent nerve:
  - Ptosis
  - Squint
  - Ocular movements
  - Diplopia
  - Nystagmus
  - Pupils (size, shape, light reflex)
  - Accommodation reflex.
- Trigeminal nerve:
  - Motor
  - Sensory
  - Corneal reflex.
- Facial nerve (both sensory and motor)
- Vestibulocochlear nerve: (ask about any hearing abnormality, vertigo or dizziness or giddiness).
  - Look at the external auditory meatus (for any wax, rash)
  - Rinne's test and Weber's test.
- Glossopharyngeal and vagus nerve:
  - Look for nasal voice, nasal regurgitation, hoarseness of voice, bovine cough
  - Movement of palate
  - Gag reflex
  - Taste sensation (in posterior 1/3 of tongue).
- Accessory nerve (spinal part): see the action of sternomastoid and trapezius
- Hypoglossal nerve (look at the tongue and see):
  - Wasting
  - Fasciculation
  - Movement of tongue.

Locomotor System

Bones:

- Shape
- Swelling
- Tenderness
- Deformity
- Sinus.

Joints:

- Inspection:
  - Swelling, local muscle wasting (unilateral or bilateral), any deformity
  - Redness
  - Skin change (psoriatic patch).
- Palpation:
  - Temperature

- Tenderness
- Dry or moist
- Fluctuation
- Crepitus.

- Movement:
  - Observe the range of active movement while gently palpating the joint for abnormal clicks or crepitus
  - If restricted, gently perform passive movement and check for crepitus
  - Perform passive stretching maneuvers to detect joint instability or ligament injury (when appropriate).

Spine:

- Look for any kyphosis, scoliosis, lordosis
- Any swelling of vertebral column (local swelling, Gibbus)
- Tenderness of vertebral column
- Movement of vertebrae (perform Schober's test, if appropriate).

Examination of nerve root compression:

- Straight leg raise: With the patient lying supine, flex the hip with legs extended. Normally, up to 90° hip flexion is possible. But when there is root compression, it will be restricted (patient will feel pain in the lumbar region)

Lasegue's sign: With the knee flexed, flex the hip up to 90°. Now gently extend the knee. The patient will feel pain.

Sacroiliac joint examination:

- With the patient in prone position, apply firm pressure over the sacrum with the hand
- With the patient lying on his side, press down on the pelvic brim.

Others (according to suspicion of cause, examine the individual joint accordingly. For example, in case of rheumatoid arthritis, examine the joints of hands, wrist, feet, etc.).

Genitourinary System

Inspection:

- Scar (nephrectomy)
- Scar of transplanted kidney in the right or left iliac fossa
- Visible mass (including mass of transplanted kidney)
- Small scar of dialysis
- Abdominal distension
- Inspection of scrotum for mass or swelling or edema and penis (with permission of the patient).

Palpation:

- Renal angle
- Kidneys
- Urinary bladder.

Percussion:

- Bladder.

Auscultation:

- Renal bruit.

After completing all of the above, proceed as follows:

Bedside investigations (if applicable):

- Urine for sugar (If diabetes mellitus)
- Urine for albumin (If nephrotic syndrome)

Salient features (Present in the following manner – mentioning the name, age, hailing from, smoker or nonsmoker, diabetic or nondiabetic, hypertensive or nonhypertensive, etc. One example is given below):

Mr. X, a 50-year-old businessman, smoker, nondiabetic, nonhypertensive, hailing from … was admitted in the hospital (or presented) with the complaints of:

1. … days/months
2. … days/months
3. … days/months

Then summarize the history of present illness, past history, social and other history with important negative points in the history.

On general examination—mention the important positive and important negative findings.

On systemic examination—tell the findings of the specific system. Then tell, "other systems reveal no abnormality".

My diagnosis is … (Tell the diagnosis if it is possible).

If the diagnosis is not clear, then tell in the following manner—"With this history and physical findings, I can tell some differential diagnoses".

Now, be ready to answer the questions asked by the examiner.

BRIEF DISCUSSION AND ELABORATION ABOUT PHYSICAL EXAMINATION

Always begin with the general examination, followed by systemic examination. Details history will suggest that system or parts of the body should be examined first.

General Examination

Remember, **"A doctor must be a good observer, like a detective"**. So, before starting general examination, look carefully from head to foot.

- **Appearance** (ill or well looking, depressed, anxious, Cushingoid, expressionless face)
- **Built** (obese, emaciated or cachexic, tall, short, normal)
- **Nutrition** (well nourished, poor, normal)
- **Decubitus** (on choice, propped up, lateral bending, Mohammedan's prayer position)
- **Anemia** (see in palpebral part of conjunctiva, tongue, palm, nails, body as a whole). Mention whether it is mild, moderate or severe
- **Jaundice** (see in sclera, under surface of the tongue, palm, body as a whole). Mention whether it is mild, moderate or severe (deep)
- **Cyanosis** (see in tip of the nose, lips, ear lobule, tongue, tip of the finger and toes). Comment whether the cyanosis is peripheral or central. Be aware of differential cyanosis (it means cyanosis in toes, not fingers)
- **Clubbing** (see fluctuation of nail base, angle between the nail and its base, curvature of the nails, look for hypertrophic osteoarthropathy by pressing the lower end of tibia-fibula or radius-ulna). Mention whether it is early clubbing, drum-stick or parrot-beak appearance. Be aware of differential clubbing (it means clubbing in toes, not fingers)
- **Koilonychia** (feel the nails for dryness, brittleness, flattening, thinning, spooning)
- **Leukonychia** (white spots in nail or white nail)
- **Edema** (in leg above the medial malleolus, in sacrum if the patient is recumbent)
- **Dehydration** (skin turgor, dry tongue)
- **Pigmentation** (exposed parts, face, neck, palmar creases, knuckles, inner side of the mouth, recent scars)
- **Lymph nodes** (examine systematically in different areas)
- **Thyroid gland** (palpable or enlarged)**.** If enlarged, examine in details
- **Breasts** (normal or enlarged or any mass)
- **Bony tenderness**
- **Body hair distribution** (including head, to see alopecia)
- **Pulse** (rate/min)
- **Blood pressure**
- **Temperature** (record in Centigrade or Fahrenheit)
- **Respiration** (number of respiration per minute, mention if any abnormality found)**.**

(Other findings, though not seen routinely, should be mentioned if present or relevant to individual cases. Examples are – xanthelasma, corneal arcus, xanthomatous nodules, skin rash, alopecia, scratch mark, rheumatoid nodule, Dupuytren's contracture, palmar erythema, Osler's node, splinter hemorrhage, Heberden's node, Bouchard's node, gangrene or nail fold infarct or nail fold telangiectasia, ulceration, wasting, skin rash or Gottron's patch, spider angioma, parotid gland enlargement, striae, Campbell de Morgan's spot, purpura, vitiligo, deformity like kyphosis, scoliosis, lordosis).

Note

Mention if the patient has any cannula, catheter, N-G tube, CV line, A-V fistula, etc. Remember to examine the lower limb to see unilateral leg swelling, DVT, differential cyanosis, clubbing, trophic ulcer or gangrene.

Systemic Examination

(From the history, once you get a clue of a particular disease, examine that system first. Then examine the other systems).

Cardiovascular System (First See Pulse, Neck Veins and BP, then Examine the Precordium)

1. Pulse (all the following features should be seen in radial pulse):
   - Rate (beat/min)
   - Rhythm (interval between two beats)
   - Volume—low, high or normal (make sure you lift the arm to see collapsing pulse)
   - Character (normal, slow rising, collapsing)
   - Condition of the vessel wall (if normal, tell, "neither thicken nor tortuous")
   - Radio-femoral delay and radio-radial delay (or inequality).

Compare all other pulses simultaneously (beware of the carotid pulse that should not be seen simultaneously). Volume and character of the pulse are better seen in the brachial and carotid artery. Collapsing pulse in aortic regurgitation and pulsus alternans in acute left ventricular failure are better seen in the radial artery.

2. Neck veins (JVP): The patient should lie at 45°.
   - Normal or engorged (internal jugular vein that lies medial to the sternomastoid). If visible, see any prominent wave. Always see hepatojugular reflux. Next, measure the height from the sternal angle (it indicates the mean pressure in the right atrium. Normally, it is at the level of the sternal angle and invisible).
   - Other signs in neck:
     - Tall, sinuous venous pulse, oscillating up to the ear lobule (indicates prominent V wave, found in tricuspid regurgitation)
     - Dancing carotid pulse (called Corrigan's sign found in aortic regurgitation)
     - Vigorous arterial pulsation in neck (found in coarctation of aorta)
     - Other pulsation in neck (carotid aneurysm or subclavian artery aneurysm).
3. Blood pressure (BP):
   - Measure BP (normal or high).
     - Low systolic, normal diastolic and narrow pulse pressure (found in aortic stenosis)
     - High systolic, low diastolic and wide pulse pressure (found in aortic regurgitation)

(If needed, see in both arms, also in standing and lying to see postural hypotension).

examination of Precordium

Inspection:

- Deformity of the chest wall (kyphosis, scoliosis, lordosis, pectus excavatum or carinatum)
- Visible cardiac impulse (visible apex beat)

- Other impulses: epigastric, suprasternal, supraclavicular
- Any scar mark: in the midline (valve replacement or coronary artery bypass), thoracotomy scar (valvotomy in mitral stenosis)
- Pacemaker or cardioverter defibrillator box may be seen (mention, if any).

Palpation:

1. Apex beat:
   - Site (localize the intercostal space. Beware of dextrocardia)
   - Distance from the midline (in cm)
   - Nature (normal, taping, heaving, thrusting, diffuse or double apex beat).
2. Thrill:
   - Site (apical, basal or any other space)
   - Nature (systolic or diastolic, by feeling the carotid pulse at the same time. If coincides with carotid pulse, it is systolic and if it does not coincide, it is diastolic).

Note

Always feel apical and basal thrill. Apical thrill is best felt by turning the patient to the left lateral position with breathing hold after expiration (apex comes close to the chest wall). Basal thrill is best felt with the patient sitting up and bending forward, breathing hold after expiration (base of the heart comes close to the chest wall).

3. Left parasternal heave: Place the flat of right palm in left parasternal area and feel by giving gentle sustain pressure (presence of left parasternal heave indicates RVH)
4. Palpable P_2 (in left second intercostal space): It indicates pulmonary hypertension
5. Epigastric pulsation.

Percussion:

Usually not done, may be helpful to diagnose pericardial effusion (area of cardiac dullness is increased) and emphysema (cardiac dullness is obliterated).

Auscultation:

1. First and second heart sounds in all four areas (mitral, aortic, pulmonary and tricuspid areas). At the same time, palpate the right carotid pulse with thumb simultaneously. **1st heart sound** coincides with carotid pulse, but **2nd sound** does not (comes before or after). See also other heart sounds, if present (3rd and 4th).
2. Murmur:
   - Site (apical, parasternal, aortic or pulmonary area)
   - Nature—systolic (pansystolic or ejection systolic), diastolic (mid diastolic or early diastolic)—by feeling carotid pulse at the same time (systolic coincides with carotid pulse and diastolic does not coincide)
   - Radiation (pansystolic murmur to left axilla, ejection systolic murmur to neck)
   - Relation with respiration (right sided murmur increases on inspiration and left sided murmur increases on expiration)
   - Grading of murmur (e.g. 2/6, 4/6).
3. Added sounds (pericardial rub, opening snap, ejection click, metallic plop.
4. Others:
   - Auscultate the back of the chest for crepitations (found in pulmonary edema).

- Palpate the liver (enlarged tender liver in CCF, pulsatile liver in tricuspid regurgitation)
- Splenomegaly (may be found in infective endocarditis).

Note: Remember the following points:

- If MDM—mid diastolic murmur is present in apex, always ask the patient to turn in left lateral position with breathing hold after expiration and auscultate with the bell of the stethoscope (MDM will be more prominent)
- If EDM—early diastolic murmur is present, ask the patient to sit up and bend forward, hold breathing after expiration. Now auscultate (EDM will be more prominent)
- If PSM—pansystolic murmur is present, put your stethoscope in left axilla to see the radiation
- If ESM—ejection systolic murmur is present, put your stethoscope in right carotid to see radiation.

Respiratory System

(Examine the chest from both front and back – **I**nspection, **P**alpation, **P**ercussion and **A**uscultation).

Inspection:

- Shape (asymmetry, deformity, barrel shaped, pectus excavatum or carinatum, kyphoscoliosis), flattening and drooping of the shoulder (due to fibrosis or collapse)
- Movement (unilateral or bilateral restriction), upward movement (in emphysema). See paradoxical inward motion of abdomen during inspiration with the patient in supine position (indicates diaphragmatic paralysis)
- Intercostal space (fullness, indrawing of lower ribs, Harrison's sulcus)
- Scar mark (thoracotomy scar, thoracoplasty, radiation marks)
- Visible impulse (cardiac, epigastric)
- Visible, engorged vein in chest (SVC obstruction). If present, see the flow
- Others: Suprasternal and supraclavicular excavation, prominent accessory muscles, gynecomastia, needle puncture mark, tattooing, bandage or gauge with tape.

Palpation:

- Position of trachea (deviated to the right or left or central). Normally, it is slightly deviated to the right
- Apex beat (shifted or not)
- Vocal fremitus (normal, increased, decreased or absent)
- Chest expansion (normal or reduced)
- Tracheal tug (descent of the trachea during inspiration. Examine by placing fingers over the trachea. It indicates hyperinflation of lung)
- Cricosternal distance: It is the distance between the suprasternal notch and cricoid cartilage (normally 3 fingers or more. If it is less, indicates hyperinflation)
- Rib tenderness (due to trauma or fracture, secondary deposit), tenderness in costochondral junction (due to Tietz's syndrome).

Percussion:

- Percussion note (normal resonance, hyper-resonance, stony dull, woody dull, impaired)
- Area of liver dullness (normally in 5th ICS in the right mid-clavicular line. It is obliterated or lower down because of emphysema or severe asthma).
- Area of cardiac dullness (obliterated because of emphysema or severe asthma).

Auscultation: (Turn the head of the patient to the left side and tell him, "Keep your mouth open, take deep breath in and out for me". Place the stethoscope. Auscultate in both right and left sides alternately).

- Breath sound (normal vesicular, vesicular with prolonged expiration, bronchial, diminished vesicular or absent)
- Vocal resonance (normal, increased, decreased or absent)
- Added sounds –
  - Rhonchi (high or low pitched, localized or generalized)
  - Crepitations (fine or coarse or end inspiratory. If crepitations are present, ask the patient to cough and auscultate again whether the crepitations are diminished, absent or same). Post-tussive crepitations that appear after cough may be found in tuberculosis
  - Pleural rub.

Ask the patient to sit forward, examine the back of chest systematically.

Finally see the following points:

- If your diagnosis is COPD, see FET (forced expiratory time), by asking the patient to exhale forcefully after full inspiration, while you listen by placing your stethoscope over the trachea. Normally, it is < 6 seconds. If > 6 seconds, indicates airway obstruction
- If any sputum cup is available nearby, look at the sputum and comment on it.

Gastrointestinal System

Mouth and pharynx:

- Lips (cyanosis, inflammation, any swelling, ulceration, angular stomatitis, pigmentation)
- Teeth (number, infection at the root, tartar, dental caries, Hutchinson's teeth)
- Gum (color, signs of inflammation, swelling or hypertrophy, ulceration, bleeding)
- Palate, movement of soft palate
- Tongue (color, papillae, dry or moist, ulceration, inflammation, presence or absence of fur, coating, white patch, candidiasis)
- Oral mucous membrane (colour, pigmentation, inflammation, ulceration, swelling, opening of the parotid duct)
- Tonsils (inflammation, swelling, pus formation, ulceration, membrane)
- Fauces (see any patch, redness, ulceration).

Abdomen (**I**nspection, **P**alpation, **P**ercussion and **A**uscultation).

Inspection:

- Shape of the abdomen—normal or distended or shrunken (scaphoid). If distended, whether generalized or localized (in epigastrium, right or left hypochondrium or iliac fossa, central part)
- Movement of the abdomen—ask the patient to take deep breath in and out, inspect from either leg or head end (to see whether the movement is equal in all sides)
- Visible peristalsis (present or absent)
- Visible pulsation (in the epigastrium)
- Umbilicus (inverted or everted)
- Visible veins—tell where (central part, flank, below or above the umbilicus, around the umbilicus). If present, **see the flow** both above and below the umbilicus
- Striae—tell where (color, size, vertical or horizontal)
- Any scar mark (because of surgery, trauma), fistula (Crohn's disease), stoma (colostomy, ileostomy, ileal conduit)

- Pigmentation (linea nigra from below umbilicus, erythema ab igne)
- Mass or swelling (tell the site, see whether it is intra-abdominal or extra-abdominal)
- Campbell de Morgan's spot (small, red, nodular lesion, common in middle age or elderly)
- Finally look to the groin (ask the patient to cough), pubic hair, genitalia (with permission of the patient).

Palpation:

- Inquire any pain in abdomen (examine that part last) and tell the patient, "Please tell me, if I hurt you"
- Ensure that your hand is warm, put the palm gently rather than the tip of the finger, keeping the hand flat on the abdominal wall with a gentle flexion of metacarpophalangeal (MCP) joints
- Better if you are in horizontal position with the patient, wrist and forearm in the same horizontal plane, by bending or kneeling by the side of the patient
- During palpation, look to the patient's face to see whether he or she **"winces"** with pain
- If ascites, do not forget to palpate by **dipping technique**.
  1. First, perform superficial palpation—feel for rigidity or any mass. Hard periumbilical lymph node (called **"Sister Marie Joseph's nodule"** is highly suggestive of metastasis from pelvic or GIT primary tumor)
  2. Tenderness (occasionally rebound tenderness may be seen—press the abdomen slowly, then release suddenly. Pain may be present that indicates peritonitis)
  3. Liver—start from right iliac fossa, ask the patient, "turn your face to left side, keep your mouth open, take deep breath in and out". Press and proceed during inspiration and look at the patient's face. If the liver is palpable, see the following points:
     - Measure in cm from the costal margin in the right mid-clavicular line. If left lobe is enlarged, measure from xiphoid process. Always measure with tape (not with fingers)
     - Margin (round or smooth or sharp)
     - Tenderness (tender or nontender)
     - Surface (smooth or irregular)
     - Consistency (soft or firm or hard)
     - Upper border of the liver dullness (using heavy percussion, but percussion of lower border using light percussion)
     - Auscultation (to hear bruit or rub).

Note

Pulsatile liver may be present. In such case, put your left hand on the back, right hand over the liver, press gently and see movement of right hand).

  4. Spleen (keep your left hand in lowermost part of left side of chest posterolaterally with slight pressure. Starting from the right iliac fossa, ask the patient, "turn your face to left side, keep your mouth open, take deep breath in and out". If it is not felt, turn the patient halfway toward right and palpate again. Once the spleen is palpable, see the following points:
     - Measure in cm along its long axis from costal margin in anterior axillary line towards right iliac fossa (also from costal margin in left midclavicular line downward)
     - Feel splenic notch (definitive sign of splenomegaly)
     - See – get above the swelling of spleen (insinuate right index finger between spleen and left costal margin)
     - See margin, surface, consistency and tenderness
     - Percuss over the spleen and continue up to left lower part of chest (to see the continuation of splenic dullness)
     - Auscultate over the spleen (to see splenic rub)

5. Palpate both right and left kidney (by ballottement)
6. Gallbladder
7. Any mass (see below)
8. Feel for para-aortic lymph nodes
9. Urinary bladder
10. Palpate the hernial orifice (ask the patient to cough, see and palpate)
11. Palpate the testis (with permission of the patient)
12. Finally per-rectal examination (tell if the examiner ask). **Never done in examination.**

Percussion:

- Usually a light percussion is done. Note the normal tympanic sound or any dullness
- If there is suspicion of ascites, elicit shifting dullness
- Fluid thrill (only necessary, if there is tense ascites).

Auscultation:

- Auscultate (normal bowel sound, increased borborygmi or reduced or absent bowel sound)
- Over liver (hepatic bruit or rub)
- Renal bruit (2 cm above the umbilicus and lateral to mid line)
- Bruit of aortic aneurysm (if any)
- Splenic rub (rarely present)
- Venous hum (heard between xiphisternum and umbilicus). It is a continuous, low pitch soft murmur. Presence of venous hum indicates portal hypertension (rare finding). It is because of large volume of blood flowing in umbilical or paraumbilical vein in falciparum ligament due to portosystemic shunt.

Note

When venous hum is present with prominent veins in anterior abdominal wall, it is called 'Cruveilhier-Baumgarten syndrome'.

If you get any mass, see the following points:

First, see whether it is intra-abdominal or extra-abdominal. Ask the patient to raise his head and press over the forehead. Now see and palpate the mass again. If it disappears or less prominent, it is intra-abdominal. If it is more prominent, likely to be extra-abdominal.

Next see the following points of a mass:

- Site
- Size
- Shape (round, regular or irregular)
- Surface (smooth or irregular)
- Consistency (soft, firm or hard)
- Tenderness
- Mobility (mobile or fixed).

Note

A fixed mass that does not move with respiration, suggest a retroperitoneal mass (such as retroperitoneal sarcoma) or colonic mass.

Nervous System

Higher psychic functions (HPF):

- Consciousness (conscious, semiconscious, unconscious or drowsy)
- Appearance and behavior (normal or violent)
- Memory – Recent and past (intact or not)
- Intelligence (normal or less)
- Orientation of time, space and person (normal or absent)
- Emotional state (normal or labile)
- Hallucination and delusion (present or absent)
- Speech (normal or dysarthria or aphasia or dysphasia or aphonia).

Motor functions:

- Bulk of the muscle (normal or wasted or hypertrophied)
- Tone of the muscle (normal, hypotonia or hypertonia)
- Power of the muscle (normal or diminished, mention the grading of weakness)
- Involuntary movement (present or absent. If present, mention the name, e.g. tremor, chorea, athetosis, etc.)
- Coordination:
  i. For upper extremity—finger nose test
  ii. For lower extremity—heel shin test
- Romberg's sign (positive or absent)
- Gait (mention the specific type of gait).

Reflexes:

1. Superficial reflexes:
   - Plantar reflex (normal flexor, extensor or equivocal).
   - Abdominal reflex (absent or exaggerated)—elicited by stroking upper and lower quadrant of the abdominal wall of each side. If present, there is contraction of abdominal muscles (It represents 7th and 12th thoracic segments)
   - Corneal reflex (present or absent)
   - Palatal reflex (present or absent)
   - Cremasteric reflex (present or absent)—elicited by stroking skin at upper and inner part of thigh. Normal response is an upward movement of testicle (It represents L_1 and L_2).
2. Deep reflex (mention whether it is normal, exaggerated, reduced or absent):

Side	B (Biceps)	T (Triceps)	S (Supinator)	K (Knee)	A (Ankle)
Right					
Left					

3. Clonus (sustained clonus indicates upper motor neuron lesion)-
   - Ankle
   - Patellar
4. Other reflexes:
   - Hoffman's sign (elicited by briskly flicking down the patient's tip of the middle finger with the examiner's thumb and index. If there is flexion of thumb or all fingers, it is positive. It indicates extensive upper motor neuron lesion)

- Gordon's sign (elicited by pinching the calcaneus tendon. If present, there is extensor plantar response)
- Oppenheim's sign (elicited by squeezing the calf or pressing heavily along the inner border of the tibia. If present, there is extensor plantar response).

Sensory functions:

1. Superficial sensations (normal, reduced or absent):
   - Touch (with cotton)
   - Temperature (with both cold and warm)
   - Pain (with pin).
2. Deep sensations:
   - Deep pain (elicited by squeezing a distal muscle or Achilles tendon. This sensation is particularly disturbed in tabes dorsalis)
   - Tactile localization
   - Tactile discrimination.
3. Position sense (intact or impaired)
4. Vibration sense (normal or decreased)
5. Recognition of size, shape, weight and form of object
6. Romberg's sign (positive or absent).

Signs of meningeal irritation:

- Neck rigidity—Normally chin can be flexed passively to touch the chest. It is not possible, if neck rigidity is present.
- Kernig's sign—Flex the knee and hip. Then gradually extend the knee. If meningeal irritation is present, patient will complain of pain (because of spasm of hamstring muscle).
- Brudzinski's sign—It is elicited with the patient in supine position and is positive when passive flexion of the neck results in spontaneous flexion of the hips and knees.

Examination of cranial nerves:

Ask the patient to sit at the edge of bed, face to face. See any obvious finding (ptosis, squint, asymmetry of face, dribbling of saliva). Now, examine the individual cranial nerve as follows:
1st Olfactory nerve:

- Examine the nasal cavity with a torch light to see any DNS, polyp
- Sense of smell (ask the patient, "Do you have any difficulty in your sense of smell?" Then examine the sense of smell, ideally by using a perfume. Put in each nostril and ask, "Do you get the smell?").

2nd Optic nerve (ask the patient whether he uses any glass. If so, ask to put it on and do the examination. Remember, each eye should be examined separately).

- Visual acuity: Both distant and near vision should be examined. Ideally, Snellen's chart should be used. If not available, proceed as follows:
  1. Distant vision—ask the patient, "look at the wall clock. What is the time now?" "Look at the window. How many rods in the window?"
  2. Near vision—tell the patient "read the newspaper or any small object".
- Color vision: Ideally it should be done with Ishihara chart. If not available, show different colors to the patient and ask, "what color is it?"
- Field of vision: Sit opposite to the patient, one meter apart at a same plane. Test each eye separately in the following way:

1. To examine right eye, ask the patient, "cover your left eye with left hand gently, look steadily at my left eye". You should cover your right eye. No one should move the eye and should look each other's tip of the nose.
2. Hold your index finger midway and from periphery, bring toward the center until you see it. Ask the patient "do you see my finger? Tell me when you see it."
3. If patient fails to see, continue to bring the finger and ask him, "tell me when you can see".
4. In this way, see in horizontal, upper and lower quadrant (temporal field).
5. Then, see nasal field in the same way.
6. Change your hand and repeat in other eye in the same manner.

- Test of central scotoma—Use a red headed pin, move it from temporal side to nasal side in the midway. Ask the patient, "Do you see it? Tell me, when it disappears".
- Fundoscopy (should be done at the end).

3rd, 4th and 6th Oculomotor, trochlear and abducent nerves:

- Look for ptosis or squint
- Ocular movements:
  1. Ask the patient, "Look at my finger. Follow it with your eyes with head fixed"
  2. See movements in horizontal and vertical directions like the pattern **"H"**
  3. See nystagmus. At extreme gaze, ask, "Do you see one or two fingers (diplopia)?"
- Pupils: size, shape, light reflex (both, direct and consensual—put light directly on one eye and see in other eye)
- Accommodation reflex (Ask the patient to look at a distant object. Then put your finger in front of his or her eyes. Now ask, "Look at my finger". See the movement of the eyeball and also pupil).

5th Trigeminal nerve (test both motor and sensory):

- Motor:
  1. Look for wasting of masseter and temporalis
  2. Ask the patient to clench his teeth and palpate the muscles. Then ask him to open the mouth, while you try to keep it closed (test for pterygoids). If paralysis is on one side, muscle of that side is less prominent and jaw deviates toward the side of lesion
  3. See jaw jerk (exaggerated or not).
- Sensory:
  1. Test along 3 divisions (ophthalmic, maxillary and mandibular) of nerve on each side using cotton and pin with eye closed
  2. See corneal reflex with a wisp of cotton. Touch the cornea (not conjunctiva), see if there is reflex blinking (afferent or sensory component is mediated by ophthalmic division of trigeminal nerve and efferent or motor component is mediated by facial nerve).

7th Facial nerve (perform both motor and sensory tests):

- Look at the face and see the following (which are present in 7th nerve palsy):
  1. Facial asymmetry and affected eye appears open and wide
  2. Drooping of corners of the mouth (unilateral or bilateral)
  3. Nasolabial fold (less pronounced).
- Motor tests:
  1. Ask the patient to look at the ceiling, keeping the head fixed and see any wrinkling of forehead, either unilateral or bilateral (frontal belly of occipitofrontalis)
  2. Ask the patient to close the eyes tightly and not to let you open it (orbicularis oculi). If failure to close, look for Bell's phenomenon
  3. Ask to whistle (orbicularis oris)

4. Ask the patient to puff cheeks out (buccinator). If paralysis, air is escaped easily on the affected side
5. Ask to show the teeth and to smile (levator anguli oris and risorius). If paralysis present, face is drawn to the healthy side.

- Sensory tests: Taste sensation of anterior 2/3rd of the tongue
- Finally, look at external auditory meatus and palate to see any rash (Ramsay Hunt's syndrome). Also, test for hyperacusis (nerve to the stapedius muscle).

8th Vestibulocochlear nerve:

- For vestibular division: Ask the patient about vertigo, dizziness or giddiness.
- For cochlear division:
  1. Look at the external ear and meatus (wax, rash)
  2. Rub hair or put the watch near the ear and ask the patient, whether he can hear or not
  3. Rinne's test and Weber's test may be necessary in some cases. Normally, air conduction is more than the bone conduction.

9th and 10th. Glossopharyngeal and Vagus nerves:

- While talking with the patient, observe any nasal voice or hoarseness. Presence of hoarseness indicates bilateral paralysis of superior laryngeal branch of vagus. If it is unilateral, usually the patient is asymptomatic
- Ask about nasal regurgitation
- Movement of the palate: Ask the patient, "open your mouth and say, **aah**". If one side remains flat and immobile, indicates paralysis of that side (soft palate is pulled to the normal side)
- Ask the patient to cough. If there is bovine cough, it indicates recurrent laryngeal nerve palsy
- Gag reflex (palatal reflex, 9th nerve): Touch the back of pharynx and see constriction
- Taste sensation in posterior 1/3rd of tongue (9th nerve).

11th Accessory nerve (spinal part):

- Ask the patient "Shrug your shoulder against resistance" (trapezius)
- Ask the patient "Turn your head to the other side against resistance". Feel sternocleidomastoid (test on both sides).

12th Hypoglossal nerve:

- Look at the tongue to see wasting, fasciculation or small and spastic or tight tongue
- Movement of tongue: Ask the patient to put out his tongue and observe the following:
  1. If small and spastic (unable to protrude)
  2. Deviation (toward the weak side).
- Ask the patient to waggle the tongue side to side. Feel the weak side.

HOW TO APPROACH A LONG CASE

"Practicing long case trains a physician to be a good clinician"

Vital parts of long cases include the following points:
- Detailed history taking
- Physical examination (general and systemic)
- Provisional diagnosis
- Differential diagnosis
- Investigations
- Management.

Proceed in a systematic way as above. Time allocation is very important. There is a fixed time given in any examination and a candidate should divide the time according to the case:
- Few minutes for history taking
- Few minutes for physical examination
- Few minutes for the formulation, plan of investigations, differential diagnosis and management
- Finally, few minutes for recapitulation of the case, as how to present the case and face the interpretation by the examiners.

Examiner usually asks:
- **Present** your case (mention the salient features)
- What is your **diagnosis**? (Remember this may be the first question. So, tell the diagnosis). Then you will be asked "**Why** do you think this is the diagnosis?" If the diagnosis is clear, then tell the brief history and important positive physical findings. From this history and physical findings my diagnosis is this. If no clear cut single diagnosis, then you can say, "with the history and physical findings, I can tell the differential diagnosis"
- What are the other possibilities (or **differential diagnoses**)? Why is it not a case of …? (Mention the points against that diagnosis)
- What **investigations** do you want to do in this case? What do you expect?
- How can you **confirm** the diagnosis?
- How will you **treat** the patient?
- What is the **prognosis**?

Remember, examiner usually interrupts at any point and you must be ready to interpret the history, physical findings, diagnosis, differential diagnosis, investigation and treatment.

Remember, during discussion of a long case, examiner usually expects or examines:
- Candidate's skill and art of taking history
- Candidate's ability to examine the patient systematically and gently
- Candidate's ability to come to a diagnosis and formulate management plan that includes investigations with interpretation of the result and treatment (symptomatic and specific).

BEFORE STARTING TO TAKE HISTORY

Careful history taking is the most fundamental and important aspect of a clinical case. Skill for good history taking can be achieved by regular practice, allocating time and having patience. Diagnosis is possible only by taking a good history, even without unnecessary investigations. A correct diagnosis is missed, not because of lack of knowledge, but because of not listening attentively to the patient or not asking the relevant questions.

- Always introduce yourself, in the following manner, "Good morning. I am Dr. … I would like to talk with you regarding your problems and if you kindly allow me, I would like to examine you" (In such a way, you can gain interest, confidence and cooperation of the patient. An intelligent patient may tell the diagnosis, treatment, etc.).
- Make a handshake and observe for any abnormality (like warm sweaty hand, tremor, slow relaxation of the handgrip).
- Check whether the patient is comfortable. Try to put the patient at ease (a good rapport may relieve distress on its own).
- Be polite, gentle, cordial and respectful to the patient (history taking is an art and beginning of doctor-patient relationship, depending on which the patient will develop confidence on the doctor).
- While you are appearing in an examination, explain to the patient that, "This is an important examination in my life. Your cooperation is very essential for me".
- While talking to the patient, watch him very carefully (patient may be anxious, apathetic or there may be obvious abnormality like myxedema, Graves' disease or Parkinsonism). Observe the nature of speech or any voice change during talking with the patient.
- Notice nonverbal clues for the diagnosis.

You must develop a good clinical eye that is extremely essential to be a good clinician. While taking history, listen to the patient carefully, and at the same time, keenly observe:

- From head to foot (gross abnormality may be obvious)
- Facial expression
- Posture
- Obvious pallor or jaundice
- Any swelling or goiter.

By observation, the diagnosis may become obvious or this will provide important clue for the diagnosis (e.g. thyrotoxicosis, myxedema, Parkinson's disease, Cushing's syndrome).

Remember the following points:

- Occasionally, if the patient is unable to give the history (such as elderly, very ill, children or aphasia), it is necessary to take history from the attendant or relative. This will also help to alert the physician, if anything is concealed by the patient. However, always try to take the patient's consent first.
- If there is possibility of drug abuse or alcoholism, ask the patient very gently and with confidentiality. Otherwise, the patient may either refuse or hide.
- Many a times, the patient tells his history in his own words. There may be irrelevant informations given by him. But you should listen attentively with patience. Unnecessary part of the history should be avoided.
- Sometimes, the patient is uncooperative, irritable or angry. In such a case, you must be more careful to make every effort to calm him down. Even if you feel irritated or angry, never show this to the patient.
- An intelligent patient may give a definite diagnosis. Even you can ask "Do you know the name of the disease from which you are suffering? What drugs are you taking? Can you mention if any procedure has been performed (e.g. aspiration of pleural fluid, peritoneal fluid, etc.)?" This will give valuable informations regarding the diagnosis, past and present problem.
- If the symptoms do not correlate with the real diagnosis, proceed with further questions. He may tell the symptoms that he has forgotten or failed to mention. However, you will have to formulate a final history of the patient before presenting to the examiner.

- Many patients may have multiple problems and multiple diagnoses. Organize to present the most important diagnosis first.
- At the end, always ask the patient, "Would you like to say anything else?"

Summary of difficulties in taking history (however, usually this type of cases are not selected for the examination):

- The patient may be very unwell (because of severe pain, vomiting, breathlessness, agitated, profuse bleeding)—take the help of the attendant.
- Unconscious, semiconscious, confused or psychiatric patient – take the history from the attendant.
- Communication difficulties (such as learning disability, deafness, mutism, aphasia or dysphasia)—take history from the attendant.
- Emotionally disturbed (angry, uncooperative)—try to calm the patient with good behavior. Let the patient relax. If the patient does not wish to speak at all, ask him – "Would you like to write it down?"
- Language may be a problem in many cases. Carefully take the history from interpreter.

HOW TO PROCEED WITH A LONG CASE

(Elaboration and description)

"A good history is the biggest and most important step towards the correct diagnosis."

After asking full name, age, sex, address, occupation, marital status, etc. start by the chief complaints.

Chief Complaints:

- Start by asking "Would you please tell me what's wrong with you?" Or, "Why are you admitted in the hospital?" Or, "What are your presenting problems?" Or, "What has been the trouble recently?"
- Try to elicit the main complaints with their time frame
- Precise chronology and sequence of events are very important
- Note the symptoms of longest duration, followed by the other symptoms in decreasing order, finally mentioning the symptom with shortest duration (suppose fever for 6 months, headache for 3 months, loss of appetite and weakness for 1 month).

History of present illness:

- Elaborate the chief complaints in details mentioning the following (mnemonic: OD PARA):
  - **O**nset—How did it start? When did it start?
  - **D**uration—How long?
  - **P**rogression—Is it progressive or static?
  - **A**ggravating factors—What makes it worse?
  - **R**elieving factors—What makes you feel better?
  - **A**nything else—Do you have anything else to mention?
- Elaboration of some common symptoms has been discussed as '**Description of symptoms'** on page no …
- Important negative parts of the history should be included if relevant.
- Information in patient's own words is more valuable, but sometimes leading questions are also necessary.
- Vague symptoms, such as "not feeling well", "head is hot", "stool is not clear", etc. should be precisely clarified. If a symptom is irrelevant, it may be ignored.
- Inquire whether the patient has been suffering from diabetes mellitus, hypertension or bronchial asthma or other chronic illness.
- Record the patient's own words, avoid using medical terms. For example, instead of "dyspnea", mention "difficulty in breathing", "vomiting of blood" should be noted instead of "hematemesis", instead of "anorexia" mention "loss of appetite".

History of past illness:

Every history of the past illness, including any event during childhood or infancy, should be recorded, as follows:

- Previous diseases with its details (duration, treatment taken, whether hospitalized).
- History of any operation, injury, trauma and procedure (catheterization, endoscopy, colonoscopy, biopsy).
- History of any investigation.
- Ask about diabetes mellitus, hypertension or other chronic illness. In case of CLD, enquire about past history of jaundice or if the patient has cardiac problem, enquire about history of rheumatic fever, hypertension, dyslipidemia.

- Ask about childhood illnesses including birth complications, immunization history, development and diseases.

Family History:

Detailed history of all the members of the family is very important. Ask about the following:

- Number of family members (parents, spouse, children, etc.)
- Their state of health. Ask – "Are they in good health?" "Do they have any illness? (e.g. ask about history of tuberculosis, hypertension, diabetes mellitus, dyslipidemia, ischemic heart disease, thyroid disorder, bronchial asthma, etc.)
- If death among family members, enquire the cause of death
- Ask about hereditary conditions (e.g. thalassemia), inquire regarding marriage among relatives (consanguinity)
- If X-linked disease is suspected, ask specifically about the health of maternal uncles.

Personal history:

Detailed personal history must be included:

- Occupation (exact nature of work)
- Marital status
- Dietary habit
- Hobby, pet keeping (cows, dog, rabbit, pigeon, etc.), interest, games, any source of entertainment
- Tea or coffee, betel nut
- Smoking (with number of sticks daily with duration) or tobacco chewing—ask technically specially in females who feel shy. If the patient is an ex-smoker, ask when he has stopped smoking and the number of sticks with duration that he used to smoke. Also, enquire any possibility of passive smoking.
- Alcohol (how much and how long, daily, weekly, occasional, place of drinking—home, outside, alone or socially). Be strategic as patient may not be forthcoming.
- History of drug abuse including alcohol, intravenous drug use, sharing of needles. Enquire about drug dependency, any social or physical problem arising from drug use. Again be careful regarding the confidentiality of the information.
- Sexual exposure or sexual practice including homosexuality, polygamy, etc. (ask strategically, without embarrassing the patient).

Socioeconomic history:

- Home and its surrounding environment—nature of house such as apartment, slum area, wooden house, living status, over-crowding, water supply and sanitation
- Office environment
- Income and employment
- Social and family relationship
- Any dependents at home? Who else at home?
- Who visits the house? (relatives, neighbor, friends).

Drug and treatment history:

- Details of drugs (previous and present)
- History of drug allergy, drug intolerance or reaction
- Treatment already received for present illness
- History of any transfusion (blood, plasma, blood product, normal saline or other fluid) received.

Immunization History:

- History of immunization is very relevant (hepatitis B, tuberculosis, tetanus).

Traveling history:

Travel or job outside the country (helpful for diagnosis of malaria, amebiasis, hepatitis B, HIV).

Psychiatric history:

Any symptoms related to anxiety, depression, dementia, hallucination, delusion, phobia, sleep pattern.

In female patient, always remember to ask 3 P –

- **P**eriod (menstrual history, such as amenorrhea, polymenorrhea, menorrhagia)
- **P**ill (oral contraceptive pill or other contraceptive method)
- **P**regnancy (obstetric history, e.g. number of child, age of last child, postpartum hemorrhage, abortion or repeated abortion).

To remember the format of history taking for long case, use the formula:

3P MAFTOSA:

- **P**resent history
- **P**ast history
- **P**ersonal history
- **M**edication (drug)
- **A**llergy
- **F**amily history
- **T**raveling history
- **O**ccupation
- **S**ocial history
- **A**nything else (psychiatric history, extra history in female patient, immunization history, etc.)

SYSTEMIC INQUIRY

(Review of Different Anatomical Systems)

Sometimes, the patient may forget to mention important symptoms or may feel it unimportant or feel shy or guilty about it. So, systematic symptom inquiry **(not mentioned by the patient)**, may give some clue to the diagnosis. Ask the questions in relation to particular anatomical systems of the body. Always begin with open questions without medical jargon. Some of the questions in different systems are given below. This may vary according to the state of patient, nature and severity of illness. Ask as follows:

General symptoms and others:

- Do you suffer from fever? If yes, ask details (see on page …).
- Do you have night sweats?
- Have you gained or lost weight? If yes, ask details (see on page …).
- Have you noticed any swelling on your body? If yes, ask details (see page …)?
- Do you feel unusually weak, lethargy, malaise or fatigue?
- Do you feel excessive sweaty or cold?
- Have you noticed any change in your complexion (pale, darkening, yellowish)?
- How is your sleep? Is there any change of sleep pattern, difficulty in getting to sleep, early awakening or feeling sleepy during the day? (Increased day time sleepiness occurs in hepatic precoma or obstructive sleep apnea).
- Do you have any skin rash or itching?

Cardiovascular system:

- Do you have chest pain or discomfort or tightness in your chest? If yes, ask details (see page …)
- Do you have difficulty in breathing? If yes, ask details (see page …)
- Do you have cough? If yes, ask details (see page …)
- Did you notice any swelling of your feet or ankle? (edema)
- Do you feel palpitation or irregular heartbeats? Do you sometimes miss a beat? Do you feel dizzy? Have you suffered from blackout?
- Do you feel pain on your legs or arms during exercise or work? (intermittent claudication)
- Do your hands or feet become blue or cold?

Note

From the history, if it is suggestive of ischemic heart disease—remember to ask about hypertension, diabetes mellitus, smoking, dyslipidemia and family history.

Respiratory system:

- Do you suffer or ever suffered from difficulty in breathing? If yes, ask details (page no. .....).
- Do you have cough? If yes, ask details (see page …).
- Did you notice blood with your sputum? If yes, ask about the amount.
- Do you feel any chest pain? (If any, ask details page no. .....).
- Have you noticed any wheezing?
- Do you snore? Or, Did anyone complain that you snore during sleep?

Alimentary and hepatobiliary system:

- Do you have heartburn?
- Do you have pain or discomfort in your abdomen? If yes, ask details (page no. .....).
- Do you feel abdominal bloating or distension?
- How is your appetite? If any change, such as loss or increased appetite, ask details.
- Do you feel nausea or vomiting? If yes ask details (see page no. .....).
- Do you feel difficulty in swallowing? If yes, ask details (see page …).
- Do you have diarrhea or constipation? If any, ask details regarding duration, frequency, amount, aggravating factors, etc.
- Is there any recent change in bowel habit or alteration of bowel habit?
- Have you seen blood or mucus in stool?
- Did you notice black tarry stool? (melena)
- Do you have pale stool with itching and dark urine? (obstructive jaundice)
- Do you have any mouth ulcer?

Genitourinary system:

- Do you have frequency of micturition?
- Are you passing larger amount of urine? (polyuria)
- Do you get up at night to pass urine? (nocturia)
- Do you feel pain during passing urine? (dysuria)
- If your bladder is full, do you have to void it immediately? (urgency)
- Do you notice narrow stream while passing urine? (poor stream)
- Does the flow stop on straining for micturition?
- Do you notice difficulty in starting micturition? (hesitancy)
- Is there any dribbling at the end of micturition? (terminal dribbling)
- Do you have incontinence of urine?
- What is the color of your urine? Is it mixed with blood? (hematuria)
- Do you have any loin pain? If any, does it go from loin to groin?
- Have you any problem with your sex life?
- Did you notice any ulcer, rash or lumps on your genitals?
- (In female) Do you have any discharge from your vagina or urethra?

Nervous system:

- Do you suffer from headache? If yes, ask details (see page …)
- Did you suffer from convulsion, fainting episodes, fits, blackout, vertigo or dizziness?
- Do you have problems with memory or concentration?
- Do you have trouble with your vision, hearing, taste or smell? Do you feel tinnitus?
- Do you have weakness (hemiplegia, paraplegia or monoplegia), tingling, numbness (pins and needles) or clumsiness in your arms or legs?
- Do you have tremor or any involuntary movement in any part of your body?
- Did you notice any problem with your balance?
- Did you ever have any head injury?

Locomotor system (musculoskeletal system):

- Do you have painful or stiff joints or swelling of joints? If yes, ask details (see page .....)
- Do you have backache or pain in the neck or muscular pain?
- Do you feel weak or have difficulty in standing up from sitting position or difficulty in raising hands above your head?

- Have you noticed any skin rash? (dermatomyositis)
- Have you ever had a dry mouth or mouth ulcer?
- Have your eyes been dry or red?

Hematological system:

- Do you have bleeding from anywhere? Or bruise easily?
- Have you noticed prolonged bleeding after a small cut?
- Have you noticed any lump under your armpit or in your neck or groin? (lymph nodes).
- Have you ever had blood clots in your legs or other parts of the body? DVT (deep venous thrombosis).
- Do you feel extreme weakness, dizziness, lassitude, dyspnea, palpitation? (anemia).
- Are you taking any drugs? Have you been exposed to chemicals or radiation? (aplastic anemia).

Endocrine system:

- Are you suffering from diabetes mellitus or do you have any thyroid problem?
- Have you noticed any neck swelling?
- Do you prefer hot or cold weather? Do you have excessive sweating? (cold intolerance indicates hypothyroidism, heat intolerance with excessive sweating indicates hyperthyroidism)
- Do you have tremor in your hands?
- Do you feel weak or fatigue?
- How is your appetite? (excessive appetite occurs in diabetes mellitus and thyrotoxicosis. Loss of appetite in malignancy, CKD, CLD, tuberculosis, hypothyroidism)
- Have you lost or gained weight? (weight gain in hypothyroidism, Cushing syndrome. Weight loss in hyperthyroidism, Addison's disease, diabetes mellitus). Also remember, a patient with a good appetite but weight loss is found in thyrotoxicosis and diabetes mellitus. Weight loss with poor appetite is because of malignancy, CKD, CLD, tuberculosis.
- Is there any change in your appearance, hair, skin or voice?
- Do you feel unusually thirsty? (excessive thirst may be because of diabetes mellitus, diabetes insipidus, hypercalcemia, psychogenic).

Reproductive system (in females):

- Did you have any miscarriage or abortion?
- During your past pregnancy, did you suffer from high blood pressure or diabetes mellitus?
- In your previous delivery (if any), did you suffer from prolonged bleeding?

Other questions in female patients:

- Do you feel any lump in your breast? If yes, ask – For how long do you have this lump? Is it getting larger? Is it painful or painless? Is it associated with any discharge, itching or skin change?

DESCRIPTION (OR ELABORATION) OF SYMPTOMS

(What else to know from patient's complaints or symptoms)

Once a patient complains of a symptom, you should ask certain important related questions regarding that symptom to determine the exact nature of the problem. You should also ask related questions in order to localize the disease to a system or organ of the body, understand the nature of the involvement (e.g. inflammatory, neoplastic) and find out the cause.

Usual symptoms related to anatomical systems of the body:

- General symptoms—fever, weight loss, weight gain, weakness, sleep pattern, malaise, itching, skin rash, excessive sweating.
- Gastrointestinal system—abdominal pain, nausea, vomiting, loss of appetite, heartburn, dysphagia, constipation, diarrhea, hematemesis, melena.
- Hepatobiliary system—jaundice, pain in the right hypochondrium, hematemesis, melena, abdominal distension (ascites), itching.
- Cardiovascular system—central chest pain, dyspnea, palpitation, cough, leg swelling, chorea, bluishness.
- Respiratory system—cough, chest pain, dyspnea, hemoptysis.
- Rheumatological system—arthritis, arthalgia, soft tissue swelling, bony deformity, skin rash, extra-articular features.
- Nervous system—headache, convulsion, weakness, vertigo, parsthesia, loss of consciousness, speech disturbance, memory disturbance, involuntary movements.
- Genitourinary system—dysuria, frequency, urgency, polyuria, retention, incontinence, loin pain, swelling of leg, puffiness of face, urethral discharge, impotence, premature ejaculation, infertility, abortion, miscarriage, menstrual irregularity, pelvic pain.
- Endocrine system—weight loss or gain, sweating, cold or heat intolerance, palpitation, tremor, pigmentation, polyuria, polydipsia.
- Dermatology—rash, itching, ulceration, blister, swelling or mass, pigmentation or depigmentation.
- Hematological system—prolonged bleeding, pallor, weakness, swelling over neck, axial or inguinal area.

Remember that different diseases involving different systems of the body may present with different symptoms. Here only the few common symptoms have been described:

- Fever
- Abdominal pain
- Chest pain
- Cough
- Dyspnea
- Vomiting
- Palpitation
- Jaundice
- Headache
- Joint pain
- Dysphagia
- Muscular weakness
- Weight loss
- Weight gain
- Vertigo
- Body swelling
- Cold or heat intolerance
- Polyuria
- Hematuria

If the patient complains of fever, ask:

What to be asked? See as follows:

- How long have you been suffering from fever?
- When does it start (morning, evening, night, etc.)? How long does it persist (few hours or throughout the day or night)? Is there any evening rise of temperature associated with night sweats?
- What was the highest recorded temperature?
- Is it associated with chills and rigors? Does it subside with sweating?
- Does it subside spontaneously or with antipyretic? If there is spontaneous remission, ask about the length of each episode of fever and the duration of the intervening afebrile period. However, if there is no spontaneous remission, ask if the temperature fluctuate more than 2ºC or not more than 1ºC? (to find whether the fever is continuous, remittent or intermittent).
- Is the fever punctuated by apyrexial period? (Undulant or Pel-Ebstein).
- Is the fever associated with skin rash or purpura?
- Is there any other associated symptom? (urinary complain, cough, chest pain, pain abdomen, headache, impaired or loss of consciousness, weight loss, polyarthritis).
- Is there any history of sexual exposure, homosexuality, travel abroad?
- Are you taking any drugs? (to exclude any drug fever).

Note Read the following features in relation to fever:

- Normal body temperature is 36.8ºC (mouth), 36.4ºC (axilla), 37.3ºC (rectum). Temperature > 37.3ºC in mouth or 37.7ºC in rectum is considered as fever.
- Temperature above 41.1ºC is called hyperthermia or hyperpyrexia. This may occur in severe infection, pontine hemorrhage, heat stroke, malignant hyperthermia, neuroleptic malignant syndrome, thyroid crisis, lobar pneumonia, datura poisoning.
- Hypothermia means temperature less than 35ºC.
- A recurrent bout of pyrexia followed by apyrexial period is called Pel-Ebstein fever. It is found in Hodgkin's disease (10% cases). This type of fever may be found in brucellosis (called undulant fever).
- Fever is of 3 types—intermittent, remittent and continued (other—hectic, Pel Ebstein).
- Intermittent: Fever that persists for several hours and always touches the baseline between attacks is called intermittent fever. It is of 3 types:
  a. Quotidian—It is characterized by paroxysm of fever that occurs daily (daily rise and fall). This type of fever may be found in tuberculosis, UTI, septicemia.
  b. Tertian—It is characterized by paroxysm of fever that occurs on alternate days. This may be found in benign tertian malaria (due to plasmodium vivax, rarely *P. ovale*).
  c. Quartan—It is characterized by paroxysm of fever that occurs with two days interval between consecutive attacks. This is found in quartan malaria due to *Plasmodium malariae* (rare).
- Remittent: If the fever fluctuates > 2ºC (3ºF) but does not touch the baseline, it is called remittent. This is found in any pyogenic infection (pyogenic liver abscess, acute bronchopneumonia, acute tonsillitis, septicemia, acute pyelonephritis), miliary tuberculosis, lymphoma.
- Continued: If the fluctuation of fever is not > 1ºC (1.5ºF) and the fever does not touch the baseline, it is called continued. This is found in typhoid, typhus, miliary tuberculosis, meningococcal meningitis, rheumatic fever, drug fever.
- Drug causing fever: A wide variety of drugs can cause drug fever. Common are—MAO inhibitor, tricyclic antidepressant, alpha-methyldopa, beta-lactam antibiotics, salicylate poisoning, LSD, ecstasy, procainamide, anticonvulsant, sulfonamide. Neuroleptic malignant syndrome may be caused by phenothiazine, butyrophenone, etc.
- Saddleback fever- Fever for few days, then no fever for one or two days followed by reappearance of fever. It occurs in dengue fever, Colorado tick fever, borreliosis, leptospira, yellow fever and influenza.
- Factitious fever: Sometimes patient purposefully show false rise of temperature. Usually found in young woman.

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- Fall by crisis and lysis:
  a. When temperature subsides quickly to subnormal level, it is called fall by crisis. This may be found in lobar pneumonia, septicemic shock, enteric fever associated with perforation or bleeding.
  b. When temperature falls gradually over several days, it is called fall by lysis. This may be found in enteric fever, rheumatic fever, acute bronchopneumonia.
- Hectic temperature: It means sudden rise of very high temperature usually associated with chill and rigor, persist for few hours and then fall with profuse sweating. This may be found if pus is anywhere in the body, e.g. lung abscess, pyogenic liver abscess, empyema thoracis, subphrenic abscess, empyema of gallbladder, perinephric abscess, etc. Sometimes in septicemia or pyemia.
- Aseptic (non-infectious) fever: Fever without infection. May be found in SLE, lymphoma, leukemia, pontine hemorrhage, drug fever, early stage of acute myocardial infarction, heat stroke, thyrotoxic crisis, acute gout, excessive use of atropine injection (in OPC poisoning), etc.

Causes of fever in different diseases:

- Low grade fever with evening rise—tuberculosis.
- Fever with chill and rigor—acute pyelonephritis, acute cholangitis, subacute bacterial endocarditis, subphrenic abscess, pyogenic lung abscess, septicemia, lobar pneumonia, pyrogenic reaction after infusion or transfusion.
- Fever with chill and rigor that subsides with sweating—malaria.
- Fever with unconsciousness—cerebral malaria, meningitis, encephalitis, pontine hemorrhage.
- Fever with neck rigidity—meningitis, encephalitis.
- Fever with drenching night sweat—lymphoma, tuberculosis.
- Patient feeling feverish with excessive sweating—thyrotoxicosis.
- Pel-Ebstein fever (undulant fever)—Hodgkin's lymphoma.
- Fever with double rise (or triple rise)—Kala-azar.
- Step ladder pattern of fever—enteric fever.
- Relapsing fever—malaria, borreliosis, occasionally lymphoma (HD).
- Fever with myalgia—viral infection (e.g. influenza, dengue).
- Fever with skin rash (according to the day of appearance of rash)—Remember: "**V**ery **s**ick **p**erson **m**ust **t**ake **d**ouble **e**ggs."
  - 1st day—Varicella (chicken pox)
  - 2nd day—Scarlet fever
  - 3rd day—Pox (small pox)
  - 4th day—Measles, german measles (rubella)
  - 5th day—Typhus
  - 6th day—Dengue
  - 7th day—Enteric fever (rose spot)
  - Drug rash may appear anytime.

Note Other cause of skin rash with fever are infectious mononucleosis, Stevens Johnson syndrome, leptospirosis, Lyme disease, meningococcal septicemia, SLE, Still's disease, adult Still's disease, erythema nodosum, erythema multiforme, toxic shock syndrome, staphylococcal scalded skin syndrome, Sweet's syndrome, anthrax, etc.

- High temperature with pink maculopapular skin rash that disappears with the fall of temperature —Still's disease.
- Transient rise of temperature may occur due to a recent hot drink, hot bath, smoking, etc.
- Hyperpyrexia and rigidity in patient taking antipsychotic—neuroleptic malignant syndrome.
- Fever may be because of malignancy, such as hepatocellular carcinoma, bronchial carcinoma, renal cell carcinoma or because of drugs (drug fever).

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- Fever with relative bradycardia: Normally, for 1°F rise in temperature, pulse increases by 10 beats per minute. If the rise of pulse rate is less than that, it is called relative bradycardia. It occurs in viral fever, 1st week of enteric fever, brucellosis, psittacosis, Weil's disease, etc.
- Fever with relative tachycardia: If rise in pulse rate is more than that is expected from increased temperature, it is called relative tachycardia. It occurs in acute rheumatic carditis, diphtheric myocarditis, severe tuberculosis, polyarteritis nodosa, etc.

If the patient complains pain, ask (formula- SOCRATES):

- **S**ite: Where is your pain?
- **O**nset: Was it gradual or sudden?
- **C**haracter: What is the nature of the pain? (dull ache, colicky, stabbing, compressive, crushing, agonizing, etc).
- **R**adiation: Does it radiate to anywhere?
- **A**ssociation (e.g. nausea, sweating, fever, skin rash).
- **T**iming of pain or duration: How long are you suffering from this pain? When does it come and how long does it persist?
- **E**xacerbating factor and relieving factor.
- **S**everity: How severe is it?

Note

Other questions will vary according to the site of pain, e.g. abdominal pain, chest pain, joint pain, etc. (see below).

Causes of pain in different diseases:

- Site: When localized to a part of the body, it gives a clue to the diagnosis. For example, pain in epigastrium may be because of peptic ulcer, cholecystitis, pancreatitis, etc. Central chest pain may be because of acute myocardial infarction, pericarditis, GERD, etc.
- Onset: May be sudden or gradual. Sudden onset usually indicates acute process. Gradual pain may occur in chronic cases.
- Character: Varies according to cause, e.g. peptic ulcer pain—hunger, boring or burning. Biliary or renal colic—severe, gripping, cramplike. Acute myocardial infarction—crushing, squeezing, compressing etc. Dissecting aneurysm—crushing or tearing. Pleuritic pain—sharp, stabbing. Tension headache—like a tight band around the head. Migraine—throbbing.
- Radiation—Pain may radiate to any part that will give a clue for specific diagnosis. For example, renal colic radiate from loin to groin, acute cholecystitis refer to right shoulder tip. Anginal pain may radiate to the inner aspect of left arm, neck and lower jaw.
- Duration—Pain lasting for seconds occurs in trigeminal neuralgia. Angina for 5 to 10 minutes, whereas pain of acute myocardial infarction last more than half an hour.
- Aggravating factor—Pleuritic pain is aggravated by coughing, change of posture, etc. Eating, exertion, activity, etc. aggravates anginal pain.
- Relieving factor—Rest relieves pain of angina pectoris. Food or drugs (like antacid) relieve duodenal ulcer pain. Rest in a dark room relieves migraine. Sitting up and leaning forward relieve pain of acute pancreatitis or pericarditis (Mohammedans prayer position). Lowering the arm relieves the pain of carpal tunnel syndrome. "Walking off" relieves the discomfort of restless leg syndrome.
- Severity—Very severe pain may be found in acute pancreatitis, biliary or renal colic, dissecting aneurysm, acute myocardial infarction, etc.

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- Associated factors: Excessive sweating, nausea, vomiting or sensation of impending death indicates acute myocardial infarction. Loin pain associated with temperature and hematuria indicates acute pyelonephritis. Premonitory symptoms (malaise and irritability followed by aura like fortification spectra) are common in migraine.

If the patient complains of abdominal pain, ask:

- **S**ite: What is the site of pain?
- **O**nset: Is it sudden or chronic? Does it disturb sleep at late night?
- **C**haracter: What is the character of pain?
- **R**adiation: Does it radiate to any site?
- **A**ssociation: Is it associated with diarrhea, vomiting, dyspepsia, altered bowel habit, urinary complaints, gynecological complaints, abdominal distension, etc.?
- **T**iming and duration – How long have you been suffering from this pain? When does it start? When does it go? Has it changed since it has begun?
- **E**xacerbating and relieving factors – What brings it on? What makes it worse? Is it related to meal? What makes it better?
- **S**everity—How severe is it?

Note Extra-abdominal cause or medical cause of abdominal pain:

- Diabetic ketoacidosis
- Henoch Schonlein purpura
- Addisonian crisis
- Acute intermittent porphyria
- Sickle cell crisis
- Hypercalcemic crisis (may be because of hyperparathyroidism)
- Polyarteritis nodosa
- Hyperlipidemia
- Hereditary angioedema (because of C1 esterase inhibitor deficiency)
- Paroxysmal nocturnal hemoglobinuria
- Chronic lead poisoning
- Familial Mediterranean fever
- Tabetic crisis in tabes dorsalis
- Others: Basal pneumonia (due to basal pleurisy), acute myocardial infarction (especially inferior wall infarction), Munchausen's syndrome, functional.

Causes of abdominal pain in different diseases according to site of pain:

- Epigastric pain: Peptic ulcer, acute pancreatitis, GERD, cholecystitis. (sometimes, there may be referred pain of acute myocardial infarction and basal pneumonia).
- Right iliac fossa pain: Acute appendicitis, Crohn's disease, salpingitis.
- Pain starts at mid abdomen and then shifts to right iliac fossa—Acute appendicitis.
- Left iliac fossa pain: Diverticulitis, volvulus, salpingitis, IBS.
- Right hypochondriac pain: Acute cholecystitis, liver abscess, acute viral hepatitis, enlarged tender liver in CCF, subphrenic abscess, perihepatitis (Fitz Hugh Curtis syndrome).
- Right hypochondriac colicky pain with jaundice: Gallstone in common bile duct.

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- Loin pain: Renal colic, acute pyelonephritis, perinephric abscess.
- Generalized abdominal pain: Peritonitis, inflammatory bowel disease, gastroenteritis.

Abdominal pain in different diseases according to onset:

- Acute pain: Acute cholecystitis, acute appendicitis, acute pancreatitis, intestinal obstruction, perforation of gas containing hollow viscus.
- Chronic pain: Peptic ulcer disease, irritable bowel syndrome.
- PUD may cause pain at late night.

Abdominal pain in different diseases according to severity and nature:

- Severe pain: Ureteric colic, acute pancreatitis, acute cholecystitis, burst appendicitis, perforation.
- Burning pain: Peptic ulcer disease.
- Colicky pain: Intestinal obstruction, ureteric stone, stone in common bile duct, ascariasis in common bile duct.

Abdominal pain in different diseases according to aggravating and relieving factors:

- Pain aggravated by smoking, alcohol, NSAIDs or steroid and relieved by antacids: Peptic ulcer disease. Duodenal ulcer is worse in empty stomach and relieved by taking food and gastric ulcer pain is worse after taking food.
- Pain aggravated by heavy meal and alcohol, but partially improved by bending forward: Acute pancreatitis.
- Pain aggravated by fatty food: Cholelithiasis.
- Pain aggravated by eating: Ischemic pain of gut.
- Pain aggravated by movement: Peritonitis.
- Pain relieved by vomiting: Gastric outlet obstruction.
- Pain relieved by spasmolytics or defecation: Intestinal obstruction.

Abdominal pain in different diseases according to radiation:

- Pain radiating to back: Acute pancreatitis, penetrating peptic ulcer.
- Pain radiating from loin to groin: Renal colic.
- Pain referred to right shoulder: Acute cholecystitis (because of diaphragmatic irritation), also diaphragmatic pleurisy.
- Pain referred to left shoulder: Splenic infarction, perisplenitis.
- Pain radiating to neck: Esophageal reflux.

If the patient complains of chest pain, ask:

- Site: Where is your pain? (central or peripheral part of the chest)
- Onset: How did the pain start? (sudden or gradual)
- Character: What is the nature of pain? (compressive, sharp, tearing, stabbing)
- Radiation: Does the pain radiate to any site?
- Timing (duration): How long does it persist?
- Exacerbating factors: What causes the pain? What makes it worse?
- Relieving factor: How the pain is relieved?
- Severity: How severe is it? (mild, moderate, severe)
- Associated features: Is there any other associated features?

Causes of chest pain in different diseases according to site and radiation:

- Central or retrosternal chest pain: Acute myocardial infarction, angina pectoris, pericarditis, myocarditis, dissecting aortic aneurysm, spontaneous pneumothorax, pulmonary embolism, reflux Esophagitis, Esophageal tear (Mallory Weis syndrome), mediastinitis, tracheitis, functional.
- Peripheral chest pain: Pleurisy, pneumonia, pneumothorax, pulmonary infarction, rib or chest wall involvement (injury, fracture or secondaries), costochondritis, herpes zoster, Bornholm disease.
- Pain radiating to inner part of left arm, neck or jaw occurs in IHD.

Chest pain in different diseases according to character:

- Compressing, crushing, constricting, squeezing or stabbing: Acute myocardial infarction.
- Sharp stabbing pain: Pleurisy or pericarditis.
- Burning pain: Gastroesophageal reflux disease (GERD).
- Discomfort or heaviness: Mediastinal compression due to tumor or lymphadenopathy.
- Atypical chest pain with no localization or no relation to coughing and breathing is psychogenic or due to anxiety.
- Very severe, tearing pain (sudden onset and radiates to back): Dissecting aortic aneurysm.

Chest pain in different diseases according to onset and duration:

- Sudden onset of pain: Acute MI, spontaneous pneumothorax, pulmonary embolism.
- Nocturnal chest pain: Heart failure, coronary artery spasm.
- Pain for less than 30 minutes: Angina pectoris.
- Pain for more than 30 minutes: Acute myocardial infarction.
- Long duration (weeks or months): Musculoskeletal, GIT disorder, cancer.

Chest pain in different diseases according to exacerbating and relieving factors:

- Pain on exertion, eating or emotion (3E) and relieved by rest or sublingual nitroglycerin: Angina pectoris.
- Pain precipitated by activity, persists for more than 30 minutes and is not relieved by rest or nitroglycerine: Acute myocardial infarction.
- Pain occurring after eating, lying flat, hot drinks or alcohol: Esophageal spasm or GERD.
- Unilateral sharp or stabbing pain aggravated by deep breathing, cough or change of posture: Pleuritic chest pain. This type of pain may also occur in chest wall disease (rib fracture, erosion, myalgia, etc.).
- Pain relieved by food: Duodenal ulcer.
- Pain relieved by sitting up and leaning forward: Pericarditis (not related to exertion).

Chest pain with other associated symptoms in different diseases:

- Pain with breathlessness: IHD, pulmonary embolism, pleurisy, anxiety.
- Pain with nausea, vomiting or sweating: Acute myocardial infarction.
- Pain with burning in chest or epigastrium: GERD.
- Sharp pain with cough: Pneumonia.
- Pain with difficulty in swallowing: Esophagitis, Esophageal carcinoma.
- Sudden pain (sharp and localized to a part of the chest) associated with severe dyspnea: Spontaneous pneumothorax.
- Central or retrosternal chest pain associated with repeated coughing: Tracheobronchitis.

Note If the pain is due to lesion in lung, pleura or chest wall, it is usually peripheral. Pain originating from centrally placed structure, such as heart, aorta, trachea, mediastinum, esophagus is usually central or retrosternal.

If the patient complains of cough, ask:

- How long have you been suffering from cough?
- Is it paroxysmal or persistent?

- Is it dry or productive?
- If productive of sputum, ask about its amount, color, odor, time of sputum production (morning), presence of blood and relation to posture change.
- Is it associated with hemoptysis? If yes, fresh or altered blood?
- Is it associated with chest pain, dyspnea?
- Is the cough aggravated by dust, cold air, smoke or pollen?
- Does it occur after eating or drinking?
- When does the cough get worse? (day or night).
- What is the character of cough?
- Are you taking any drug? (such as ACE inhibitor).
- Do you have diseases, such as rhinitis, asthma, heart disease, renal disorder?

Causes of cough in different diseases:

- Recent or acute onset: Respiratory infection, pneumonia, acute bronchitis.
- Chronic: COPD, bronchial asthma, bronchiectasis, ILD, tuberculosis.
- Occasional or paroxysmal cough: Bronchial asthma.
- Dry cough: ACE inhibitor (captopril, lisinopril), cough variant asthma, ILD, acute tracheobronchitis, tropical eosinophilia.
- Nocturnal cough: Bronchial asthma, LVF, tropical eosinophilia, post-nasal drip, aspiration.
- Cough with postural variation: Bronchiectasis, lung abscess, GERD.
- Painful cough or retrosternal pain: Tracheal involvement (tracheitis).
- Cough after eating or drinking: Esophageal reflux, tracheoesophageal Esophageal fistula.

Nature and character of cough indicate the following diagnosis:

- Croupy cough: Laryngitis (in children, diphtheria should be excluded).
- Harsh, barking, painful cough with stridor: Laryngeal disorder, such as laryngitis, tumor, etc.
- Barking cough: Acute epiglottitis.
- Loud and brassy cough: Pressure on trachea (by tumor).
- Hollow, bovine: Recurrent laryngeal nerve palsy (commonly due to bronchial carcinoma).
- Associated with whoop: Whooping cough.
- Cough with wheeze: Bronchial asthma, COPD.

Character of sputum may indicate the following diagnosis:

- Cough with profuse expectoration: Bronchiectasis, lung abscess, resolution stage of pneumonia.
- Yellowish or greenish or purulent sputum: Bronchiectasis, resolution stage of pneumonia.
- Foul smelling dark colored sputum: Lung abscess (usually with anaerobic infection).
- Rusty sputum: Pneumococcal pneumonia.
- Productive cough with frothy sputum occurs in pulmonary edema.

Sputum mixed with blood (hemoptysis):

- Respiratory cause: Bronchial carcinoma, pulmonary tuberculosis, pulmonary infarction, bronchiectasis.
- Cardiac cause: Mitral stenosis
- Blood dyscrasias: Hemophilia, Christmas disease, DIC, prolong use of anticoagulant, aspirin.

If the patient complains of dyspnea or difficulty in breathing, ask:

- Is the onset sudden (acute) or gradual (chronic)?
- Does it occur with exertion or at rest?
- If exertional, how much activity causes breathlessness? (Mild, moderate and severe. Ask how far he can walk or how many stairs he can climb or if he can undress himself without feeling breathlessness).

- Do you get breathless at night that wakes you up from sleep (PND)? How do you feel better?
- Do you feel breathless on lying flat? (orthopnea). How many pillows do you use at night?
- Is it paroxysmal or progressive?
- Is there any seasonal variation with breathlessness?
- Is there any history of recent travel abroad by air?
- Do you smoke? If yes, number of sticks per day.
- Is there any aggravating factor or occupational exposure to coal dust, silica, asbestos, animal dander?
- Is there any relieving factor? (drugs, rest, change of posture, after expectoration of sputum, etc).
- Is it associated with other symptoms? (cough, chest pain, wheeze or hemoptysis)?
- Is there any history of respiratory or cardiac disease or allergy or renal failure?

Note

Dyspnea may be defined as the subjective sensation of shortness of breath.

Causes of dyspnea in different diseases:

- Acute or sudden dyspnea—acute severe asthma, acute left ventricular failure (LVF), acute exacerbation of COPD, spontaneous pneumothorax, pulmonary embolism, ARDS, cardiac tamponade, acute laryngeal obstruction, diabetic ketoacidosis, conversion disorder.
- Chronic dyspnea—chronic bronchial asthma, COPD, DPLD.
- Dyspnea on mild exertion—COPD LVF.
- Orthopnea or PND—pulmonary edema (LVF, mitral stenosis).
- Dyspnea at rest—acute severe bronchial asthma, massive pneumothorax, ARDS, acute laryngeal edema, ILD (DPLD) in advanced stage, massive pulmonary embolism, cardiac cause (acute LVF), metabolic acidosis (diabetic ketoacidosis, lactic acidosis, salicylate poisoning, acute renal failure).
- Progressively increasing dyspnea—DPLD.
- Dyspnea with seasonal variation—bronchial asthma, chronic bronchitis.
- Dyspnea after air travel or immobilization – pulmonary embolism from DVT.
- Dyspnea aggravated by exposure to coal dust, silica, asbestos, animal dander—occupational asthma.
- Dyspnea may also be due to anxiety (or psychogenic) where the patient describes it to be an "inability to take a breath big enough to fill the lungs". The breathing is usually deep and punctuated with sighs.

Dyspnea with association:

- Dyspnea associated with wheezing—acute severe asthma, COPD, sometimes acute LVF, anaphylactic reaction.
- Dyspnea with stridor (indicates upper airway obstruction)—foreign body or tumor, acute epiglottitis, anaphylactic reaction, laryngeal trauma, laryngeal fracture.
- Dyspnea with crepitation—acute LVF (due to pulmonary edema), bilateral extensive bronchiectasis.
- Dyspnea but chest is clear—pulmonary embolism, metabolic acidosis (diabetic ketoacidosis, renal failure, lactic acidosis, salicylate poisoning), severe anemia, shock, pneumocystis jiroveci pneumonia, psychogenic.
- Dyspnea associated with unilateral chest pain—spontaneous pneumothorax.
- Dyspnea associated with shock—acute myocardial infarction.
- Dyspnea with high fever—pneumonia.

If the patient complains of vomiting, ask:

- How long have you been suffering from vomiting?
- How many times do you vomit a day?
- What are the contents of the vomitus?
- Does it contain blood (hematemesis)?
- What is the color of vomitus?
- Is it associated with nausea?
- Does it occur in the morning only?
- Do you induce vomiting?
- Is the vomiting projectile in nature?
- Does the vomiting relieve abdominal pain or discomfort?
- Is it associated with severe abdominal pain and absolute constipation followed by distension of abdomen?
- Is there any relation to food?
- Is there any history of head injury?
- Are you taking any drugs? Did you take radiation therapy?
- In female patient, ask about amenorrhea.
- Is it associated with chest pain, headache, tinnitus, vertigo, fever, jaundice, diarrhea weight loss?
- Ask about any other disease, such as hepatic, renal, migraine, carcinoma.

Note Non-gastrointestinal causes of vomiting – (A, B, C, D, E, F, G, H, I and P)

- **A**cute renal failure, Addison's disease
- **B**rain disease (raised ICP), Brainstem lesion
- **C**ardiac (acute myocardial infarction)
- **D**iabetic ketoacidosis
- **E**ar disease (labyrinthitis, Meniere's disease)
- **F**oreign substance (alcohol, drugs)
- **G**ravidity (hyperemesis gravidarum)
- **H**ypercalcemia
- **I**nfection (meningitis, encephalitis, appendicitis)
- **P**sychogenic.

Causes of vomiting in different diseases:

Contents of vomitus:

- Food taken on previous day (not stained with bile) indicates pyloric stenosis
- Bile stained contents indicate obstruction distal to the pylorus
- Fecal vomiting indicates distal small bowel obstruction, colonic obstruction or gastrocolic fistula
- Blood in vomitus indicates bleeding gastric ulcer, gastric erosion, carcinoma of stomach or ruptured esophageal varices.

Color of the vomitus:

- Coffee ground vomitus is because of conversion of hemoglobin to acid hematin by gastric acid. It indicates bleeding in the stomach.
- Bile stained (greenish) vomitus is because of obstruction distal to pylorus.

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Timing of vomiting:

- Early morning vomiting (before eating)—raised ICP, pregnancy, alcoholism
- Vomiting 1 hour after taking food—gastric outlet obstruction
- Vomiting occurring immediately after eating—psychogenic, peptic ulcer with pyloric spasm.

Vomiting with other associated features:

- Pregnancy is a common cause of vomiting (hyperemesis gravidarum)
- Vomiting without nausea—raised intracranial pressure (ICP)
- Projectile vomiting—gastric outlet obstruction
- Induced vomiting—gastric outlet obstruction and bulimia nervosa
- Pain abdomen relieved by vomiting—gastric outlet obstruction, gastric ulcer
- Vomiting with severe abdominal pain and absolute constipation—intestinal obstruction
- Acute vomiting with diarrhea and fever—infective gastroenteritis
- Vomiting with fever—inflammatory or infective origin (e.g. appendicitis)
- Vomiting with severe abdominal pain—renal or biliary colic
- Vomiting with jaundice—acute viral hepatitis
- Vomiting with chest pain—acute myocardial infarction
- Vomiting with unilateral headache—migraine, cluster headache
- Vomiting with tinnitus, vertigo—vestibular involvement
- Prolong history of vomiting with little or no weight loss—psychogenic.
- Vomiting may be because of many drugs, such as digoxin, opium, NSAIDs, chemotherapeutic drugs, aminophylline, etc. It may be because of radiotherapy as well.

If the patient complains of palpitation, ask:

- What do you really feel? (unexpected awareness of heartbeat)
- Did you check your pulse by yourself?
- How does it start? (spontaneous or with activity, anxiety, emotion, etc.)
- Is it paroxysmal or persistent?
- How long does it persist?
- How is it relieved?
- Have you ever missed a heartbeat?
- Do you get breathlessness, chest pain, dizziness or blackout with palpitation?

Note

Palpitation means sensation or abnormal awareness of heartbeat.

Causes of palpitation in various diseases:

- Sudden onset and termination of rapid, regular palpitation occurs in paroxysmal supraventricular tachycardia and atrial flutter with 2:1 block.
- Persistent palpitation may be because of anxiety neurosis, thyrotoxicosis, pregnancy, etc. Palpitation with anxiety occurs at night even.
- Sensation of a missed beat followed by a heavy beat occurs in premature atrial or ventricular contractions.
- Feeling of rapid palpitation followed by syncope indicates ventricular tachycardia.
- Rapid irregular palpitation indicates atrial fibrillation or flutter with variable block.
- Rapid regular palpitation indicates paroxysmal supraventricular tachycardia.
- Slow palpitation may be due to beta blocker or pulsus bigeminus.
- Other causes of palpitation are heart failure, ventricular tachycardia, AF, atrial flutter, etc.

If the patient complains of jaundice, ask:

- Did it start with anorexia, nausea and vomiting?
- Any history of contact with jaundiced patient or sexual exposure?
- What is the color of the stool? (yellowish, pale, dark)
- Do you have itching?
- Did you ever take any injection, infusion or blood transfusion? (HBV or HCV)
- Any history of IV drug abuse, tattooing or surgery? (HBV or HCV)
- Do you take alcohol or any drugs (look for hepatotoxic drugs)?
- Is there any family history of jaundice, consanguinity of marriage among parents?
- Did you suffer from recurrent jaundice?
- Any associated history of high fever, urinary complaints?
- Previous history of jaundice associated with any neurological abnormality?
- Have you traveled abroad?

Causes of jaundice in different diseases:

- Anorexia, nausea, vomiting—acute viral hepatitis, may be drug induced hepatitis.
- Itching with pale or dark pale stool—obstructive jaundice.
- Long standing jaundice with itching, pigmentation of skin—primary biliary cirrhosis.
- History of injection, infusion, blood or blood products transfusion, IV drug abuse and tattooing, homosexuality indicates probable infection with HBV or HCV.
- Family history of jaundice, consanguinity of marriage among parents and associated pallor indicates hereditary hemolytic anemia.
- Persistent mild jaundice indicates Gilbert's syndrome.
- Jaundice with high fever and urinary complain indicates leptospirosis.
- Recurrent jaundice with neurological abnormality—Wilson's disease.
- Jaundice with pregnancy—cholestatic jaundice of pregnancy.
- Painless progressive jaundice with palpable gallbladder—carcinoma of the head of the pancreas.
- Abdominal pain with fluctuating jaundice—bile duct stone or stricture, pancreatitis.

If the patient complains of headache, ask:

- What is the site of headache? (unilateral or diffuse, frontal, occipital or facial)
- What is the time of onset?
- How severe is it?
- What is the nature of headache? (throbbing, burning)
- How does it start?
- How long does it persist?
- Is it recurrent?
- Is there any aggravating factor, such as coughing, straining or change of posture?
- Is there any relieving factor?
- Is it preceded by any aura?
- Is it associated with fever, vomiting, weakness, blurring of vision, vertigo, nasal stuffiness, lacrimation, breathlessness?
- Are you taking any drug?
- Where have you been? (malaria endemic area)
- In female, ask about pregnancy (pre-eclampsia, especially if proteinuria and high blood pressure).

Note Worrying features or red flags in headache:

- First and worse headache—subarachnoid hemorrhage
- Thunderclap headache—subarachnoid hemorrhage
- Unilateral headache and eye pain—cluster headache, glaucoma
- Unilateral headache and ipsilateral symptoms—migraine, cerebral tumor, vascular headache
- Cough induced headache—raised ICP, cerebral venous sinus thrombosis
- Persistent unilateral headache with scalp tenderness over 50 years—temporal arteritis
- Headache with fever or neck stiffness—meningitis
- Changes in the pattern of usual headache—intracranial space occupying lesion, psychogenic
- Decreased level of consciousness—meningitis, encephalitis, cerebral malaria.

Causes of headache in different diseases:

Site of headache indicates:

- Unilateral headache preceded by flushing lights or zigzag lines—migraine.
- Headache over the occiput associated with neck stiffness—cervical spondylosis.
- Generalized headache, worse in the morning, associated with drowsiness and vomiting—raised intracranial pressure (ICP).
- Generalized headache with fever and photophobia and neck stiffness—meningitis.
- Persistent unilateral headache in temporal area—temporal arteritis (associated with temporal tenderness and blurring of vision).
- Pain on forehead, cheeks or behind the eyes—acute sinusitis.

Radiation of headache:

- Bilateral headache that extends to the top of the head, also unilateral headache radiating to neck with tenderness of neck muscles is suggestive of tension headache.
- Unilateral pain radiating to the throat, ear, eye, nose, cheeks, face is typical of neuralgia.

Time and mode of onset, severity and nature of headache:

- Headache at morning after waking up associated with vomiting—raised ICP
- Sudden, dramatic onset, severe headache associated with neck stiffness—subarachnoid hemorrhage
- Persistent headache for days or weeks—tension headache
- Persistent headache with scalp tenderness or tenderness over temporal artery—temporal arteritis
- Recurrent headache indicate migraine and cluster headache.

Duration of headache:

- Longer the history without progression is usually benign.
- Headache of migraine usually lasts less than 6 hours, but may persist for more than 24 hours.
- Episodes of cluster headache last less than an hour.
- In trigeminal neuralgia, each paroxysm last only seconds, recurring over several minutes.
- Tension headache may last for several days with or without disrupting sleep.

Nature of headache:

- Throbbing headache—migraine, cluster headache.
- Tight band-like around the head or pressure over the head—tension headache.
- Severe, thunderclap headache (like struck by a hammer)—subarachnoid hemorhage.
- Lancinating, paroxysmal pain indicates trigeminal neuralgia.

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Frequency and periodicity of headache:

- Sudden attack of pain in a repeated short burst with pain free interval lasting weeks or months are found in migraine, trigeminal neuralgia and cluster headache, angle closure glaucoma.
- Acute onset with rapid progression and continuous are found in meningitis and subarachnoid hemorrhage.
- Chronic daily headache—commonly due to cervical spondylosis, migraine, tension headache, drug (nitrates), chronic daily headache syndrome.

Special time of occurrence:

- Severe pain waking the patient from sleep in the early hours of morning is typical of cluster headache, also raised ICP.
- Pain precipitated by facial movement, such as eating, drinking, shaving, or brushing teeth are found in trigeminal or glossopharyngeal neuralgia.
- Pain in the jaw during chewing is typical of temporal arteritis.
- Headache at the onset of menarche and premenstrually is found in migraine.

Aggravating factor:

- Pain worse on coughing, bending, straining or posture change is due to raised ICP.
- Pain aggravated by hunger, intake of chocolate, cheese, alcohol or citrus fruit, contraceptive pill is suggestive of migraine.
- Idiopathic intracranial hypertension is associated with weight gain, use of corticosteroid, tetracycline, contraceptive pill, etc.

Relieving factor:

- Pain of migraine becomes less or improved in a dark place during acute attack, also improved or less severe during pregnancy.
- Rapid, dramatic response occurs in giant cell arteritis following steroid therapy.
- Headache usually responds to NSAIDs. But poor response occurs in tension headache.

Other disorders associated with headache:

- Headache with temporary visual loss or scintillating spots—migraine.
- Headache with nasal stuffiness or lacrimation—cluster headache.
- Headache with fever and neck stiffness—meningitis.
- Drug like nitrates may cause headache.
- Headache with fever and incoherent talk—cerebral malaria.

If the patient complains of joint pain, ask:

- Onset: Is it acute, gradual or chronic? Is it new or recurrent?
- Is there any history of trauma?
- How long are you suffering from joint pain?
- Is it associated with joint swelling?
- Which joints have been involved? Note the following:
  - Number of joints involved (mono, oligo or polyarthritis)
  - Symmetrical or asymmetrical.
  - Distribution of joint involvement (small or large joint involvement).
  - Upper or lower limb or both involvements.
- Does the pain move from one joint to other? (migratory or fleeting, additive)
- Does the pain worsen on activity or rest?
- Is there any morning stiffness? If present, how long does it persist? How does it subside? (improve with activity or exercise)

- Is it associated with redness, warmth and swelling? (suggest inflammation)
- Is there any deformity?
- Is there any extra-articular manifestation?
- Is this associated with dry mouth? (Sjogren syndrome)
- Do you have any skin or nail problem or is there any family history of such problem? (psoriatic arthritis)
- Is there any history of persistent bleeding?
- Is the arthritis preceded by urethritis, history of sexual contact, acute diarrhea (Reiter's syndrome, also may be eye problem)?
- Is there any history of frequent diarrhea? (IBD)
- Is there any history of tick bite in endemic area? (Lyme disease).

Note Remember the following points:

- Arthralgia means painful joint without swelling
- Arthritis means painful joint with swelling
- Seropositive means RA factor is positive (e.g. rheumatoid arthritis)
- Seronegative means RA factor is negative (e.g. ankylosing spondylitis, psoriatic arthritis, Reiter's syndrome, enteropathic arthritis)
- Monoarticular—single joint involved
- Oligoarticular or pauciarticular—2 to 4 joints involved
- Polyarticular—5 or more joints involved
- Migratory or fleeting—arthritis involving one joint then involving another
- Acute arthritis means < 6 weeks duration and chronic means > 6 weeks duration
- To remember, if any patient complains of arthritis—look for site or distribution of joint involvement, symmetry, joint swelling, deformity, movement, joint effusion, periarticular involvement, signs of inflammation (swelling, redness and warm), finally extra-articular manifestations
- Features of inflammatory arthritis are pain at rest, morning stiffness, joint inflammation and loss of function
- Non-inflammatory (mechanical) arthritis is more painful with activity and improves on rest.

Causes of joint pain in different diseases:

Monoarticular: (remember the formula – GRASP TH)

- **G**out, gonococcal arthritis
- **R**eactive arthritis
- **S**eptic arthritis
- **P**seudogout, psoriatic
- **T**ubercular
- **T**raumatic
- **H**emophilic (hemarthrosis)
- **A**ny polyarthritis may start as monoarthritis.

Polyarthritis:

- Rheumatic fever
- Rheumatoid arthritis (RA)
- Seronegative arthritis or spondyloarthropathy
- Osteoarthrosis (OA, commonly nodal OA)

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- Systemic lupus erythematisus (SLE)
- Gout, pseudogout
- Polymyalgia rheumatica.

Pattern of joint involvement:

- Distal interphalangeal joint (DIP) is involved in OA, psoriatic arthritis and gout
- Proximal interphalangeal joint (PIP) and metacarpophalangeal joints (MCP) are involved in rheumatoid arthritis
- First metatarsophalangeal (MTP) is involved in gout
- Sacroiliac (SI) joint is involved in ankylosing spondylitis
- Knee joint is involved in OA
- Bilateral symmetrical joint involvement— RA
- Asymmetrical joint involvement (also usually bigger joints)—seronegative arthritis
- Pain increased with activity, relieved by rest—mechanical arthritis
- Pain worse with rest, improved by activity—inflammatory arthritis
- Morning stiffness for more than 1 hour, relieved by activity indicates RA
- Fleeting arthritis—Rheumatic fever, gonococcal arthritis, others (SLE, Lyme arthritis, meningococcal arthritis, drug reaction or serum sickness, IBD, Whipple's disease).

Arthritis with deformity (deforming polyarthritis):

- Rheumatoid arthritis
- Seronegative spondyloarthropathy
- Chronic tophaceous gout
- Primary generalized osteoarthritis
- Infection – Lyme disease.

Note: In rheumatic fever, there is no deformity of the joint, "it licks the joint, kills the heart".

Extra-articular manifestations (when arthritis is associated with the following extra-articular findings, indicates the following diagnosis):

- Skin rash, oral ulcer—SLE
- Skin rash, heliotrope rash, muscular weakness—dermatomyositis
- Eye symptoms—RA, seronegative arthritis, SLE
- Dryness of mouth and eyes—Sjogren's syndrome
- Bowel symptoms—enteropathic arthritis (Crohn's disease, ulcerative colitis)
- Triad of urethritis, iritis and arthritis—Reiter's syndrome
- Psoriasis—psoriatic arthritis
- Renal stone—Gout, pseudogout
- Very high fever—septic arthritis
- Oral and genital ulcers, uveitis and skin lesion—Behcet's syndrome
- History of prolonged bleeding—hemophilic arthritis or Christmas disease
- History of sexual exposure indicates gonococcal or reactive arthritis
- History of tick bite indicates Lyme disease.

If the patient complains of dysphagia, ask:

- Can you show me with your finger at which level does the food get stuck?
- Is it due to solid or liquid or both?
- Is it painful or painless?
- Is it transient, intermittent or progressive?

- Do you have nasal regurgitation or cough during deglutition?
- Is it associated you heart burn or chest discomfort?
- Is there any difficulty to swallow?
- Did you notice bulging of the neck while eating or drinking?

Note Remember the following points:

- Dysphagia means difficulty in swallowing.
- Globus hystericus means feeling of a lump in the throat, without any organic cause. It does not interfere with swallowing and is not related to eating. It is found in conversion disorder (HCR).
- Odynophagia means painful swallowing. It is usually due to esophagitis. Causes are—esophageal ulceration due to candidiasis, herpes simplex infection, reflux esophagitis, corrosive poisoning, esophageal perforation.

Causes of dysphagia in different diseases:

According to nature of food:

- Difficulty more with solid food, less with liquid food—mechanical cause (because of esophageal stricture, tumor, pharyngeal web, esophagitis, dysmotility. Extrinsic compression on esophagus because of large retrosternal goiter, left atrial enlargement in MS, aortic aneurysm, posterior mediastinal mass.)
- Difficulty more with liquid, less with solid food—neurogenic cause, e.g. bulbar or pseudobulbar palsy (also called neurogenic dysphagia or motor dysphagia). It is associated with nasal regurgitation, choking or spluttering.
- Difficulty to both solid and liquid— indicates motility disorder (because of achalasia, diffuse esophageal spasm, pharyngeal causes, carcinoma esophagus, stricture of esophagus).

Association with pain:

- Painful dysphagia (odynophagia)—esophagitis (herpes simplex or candida), drug induced, ulceration, may be esophageal carcinoma, achalasia.
- Painless dysphagia—usually carcinoma of esophagus, achalasia or stricture.

According to site of obstruction:

- Lower retrosternal obstruction—carcinoma of esophagus, achalasia or stricture of esophagus.
- Obstruction at the level of cricoid cartilage—tumor, stricture, pharyngeal pouch.

According to duration or pattern:

- Transient dysphagia—esophageal infection.
- Progressive dysphagia—carcinoma, achalasia or stricture.
- Intermittent dysphagia or if present only with first few swallows of food—esophageal spasm or esophageal ring.

Dysphagia with other symptoms:

- Dysphagia with nasal regurgitation or dysphonia or choking on trying to swallow—suggestive of pharyngeal causes of dysphagia that are due to bulbar or pseudobulbar palsy. Also, left recurrent nerve palsy due to mitral stenosis (Ortner syndrome).
- Dysphagia with chest discomfort and heart burn—hiatus hernia, GERD, diffuses esophageal spasm.
- Dysphagia with nocturnal cough and dyspnea—GERD, achalasia.
- Neck bulge or gurgle during drinking—pharyngeal pouch.
- Dysphagia with anemia and koilonychia—Plummer Vinson syndrome (iron deficiency anemia).
- Dysphagia with palmar hyperkeratosis—tylosis.

If the patient complains of muscular weakness, ask:

- Is it generalized or localized?
- Distribution: Is it proximal or distal?
- Onset: Is it sudden or gradual?
- Progression: Is it ascending or descending?
- Does it worsen or improve with activity?
- Is there other features, such as muscle pain, skin rash, sensory loss, loss of bowel or bladder control?
- Do you take any drug or alcohol?

Note Remember the following points:

- Myopathy is associated with proximal muscular weakness, except myotonia dystrophica that involves distal muscles.
- Neuropathy is associated with distal muscular weakness, except diabetic amyotrophy (that involves the proximal muscles).

Causes of muscular weakness in different diseases:

Group of muscles involved:

- Generalized: Hypokalemia, hyperkalemia, malnutrition, chronic illness.
- Localized: Usually neurological (hemiplegia, paraplegia, monoplegia).
- Proximal weakness: All myopathy (except myotonia dystrophica that causes distal weakness)—dermatomyositis or polymyositis, myasthenia gravis, myasthenic myopathic syndrome (Eaton-Lambert syndrome), Cushing's syndrome, diabetic amyotrophy, thyrotoxicosis (also hypothyroidism), polymyalgia rheumatica, osteomalacia, hyperparathyroidism, periodic paralysis, alcohol and drugs, McArdle's syndrome (myophosphorylase deficiency, there is stiffness and cramps of muscle after exercise, that is hard and painful on movement).
- Distal weakness: Peripheral neuropathy, myotonia dystrophica, Charcot-Marie-tooth disease.

Onset and progression:

- Sudden onset, generalized weakness: Hypokalemic periodic paralysis, thyrotoxic periodic paralysis.
- Sudden onset, localized weakness: Stroke (usually hemiparesis), spinal cord compression (usually paraparesis).
- Weakness that progress over hours to days: GBS, spinal cord lesion.
- Gradual onset and slowly progressive weakness: Peripheral neuropathy, spinal cord lesion, motor neuron disease, myasthenia gravis, myopathy.
- Weakness worsens with activity: Myasthenia gravis.
- Weakness improves with activity: Eaton Lambert syndrome.
- Weakness worsen on exposure to heat (e.g. hot bath): Multiple sclerosis.
- Sudden ascending paralysis occurs in GBS.

Weakness with associated symptoms:

- Weakness with skin rash: Dermatomyositis.
- Weakness associated with muscle pain: Polymyalgia rheumatica, polymyositis or dermatomyositis, hypothyroidism (Hoffman's syndrome), diabetic myopathy, hypoparathyroidism.
- If there is fasciculation: Indicates lesion involving the anterior horn cell or root (in motor neuron disease).
- Drugs causing muscular weakness: Statins, steroids, chloroquine, zidovudine, vincristine, alcohol, cocaine.

- Weakness with preserved reflex: Myotonia dystrophica, also myasthenia.
- Weakness with loss of reflex: Neuropathy, also in case of myopathy, lower motor neuron lesion.
- Weakness with exaggerated reflex: Upper motor neuron lesion (MND, typically in amyotrophic lateral sclerosis).

If the patient complains of weight loss, ask:

- How much weight did you lose? Over what period?
- How is your appetite?
- How is your bowel habit? (If frequent diarrhea or loose motion, ask details regarding color, amount, presence of blood, etc.).
- Do you feel excessively thirsty and micturate frequently?
- Do you have other symptoms, such as cough, fever, night sweat?
- Do you have palpitation?
- Do you prefer hot or cold environment?
- Do you feel that you are getting darker than before? (any change in your complexion?)
- Do you have vomiting? If yes, is it spontaneous or induced?
- Do you take alcohol or any other substance?

Note Also remember the following points:

- A detailed systematic enquiry should be made to find out any malignancy.
- History regarding intravenous drug intake, blood or blood product transfusion, extramarital sexual contact, traveling abroad and other high-risk behavior for HIV infection should be sought.
- Weight loss means reduction of 5% of body weight or 5 kg within 6 months is considered significant.
- Weight loss may be physiological because of dieting, exercise, starvation or less intake in old age.

Causes of weight loss in different diseases:

- Weight loss with low grade evening fever, cough and night sweats indicates tuberculosis.
- Weight loss in spite of good appetite or high food intake—thyrotoxicosis or diabetes mellitus. Also, may be in malabsorption syndrome or bulimia (binge eating).
- Weight loss with heat intolerance, diarrhea, palpitation, etc.—thyrotoxicosis.
- Weight loss with polyphagia, polyuria and polydipsia (3P)—diabetes mellitus.
- Weight loss with diarrhea or steatorrhea indicates malabsorption syndrome.
- Weight loss with pigmentation and hypotension—Addison's disease.
- Extreme cachexia in young female with history of diet control, heavy exercise, induced vomiting and amenorrhea – anorexia nervosa.
- Any malignancy, chronic debilitating illness like cardiac, pulmonary or renal failure or malnutrition may cause weight loss.
- HIV infection should be ruled out.

If the patient complains of weight gain, ask:

- How much weight did you gain? Over what period?
- How is your appetite?
- Do you feel weak or fatigue?
- How is your bowel habit?

- Do you prefer hot or cold environment?
- Do you take any drugs or alcohol?
- How is your menstrual cycle? Any growth of excessive hair? (For female).
- Do you have headache?

Causes of weight gain in different diseases:

- Weight gain with loss of appetite indicates hypothyroidism (other features of hypothyroidism are cold intolerance, fatigul and constipation.
- Weight gain with increased appetite—Cushing's syndrome, hypoglycemia (occurs in insulinoma), hypothalamic disease.
- Weight gain with central obesity indicates Cushing syndrome (other features of Cushing syndrome are moon face, plethora, hypertension, easy bruising, etc. The most common cause is prolong use of steroid). Drugs, such as corticosteroid, TCA, sulfonylurea, beta blocker, estrogen containing OCP may cause weight gain.
- Young obese female patient with irregular cycle or amenorrhea and hirsutism indicates polycystic ovarian syndrome.
- Headache indicates pituitary cause of weight gain.
- If only weight gain with more food intake without any other complain—simple obesity. Also, may be familial.
- Some congenital anomalies may cause weight gain, such as Prader Willi syndrome, Laurence Moon Biedl syndrome, Klinefelter syndrome, Kallman syndrome, Noonan syndrome.

If the patient complains of vertigo, ask:

- Onset—is it sudden or gradual?
- Is it recurrent, persistent or progressively increasing?
- If recurrent, what is the frequency and duration?
- Do you feel that the surrounding is moving or do you feel yourself to be moving?
- What causes the vertigo? (movement of the head, standing from sitting position, traveling in a motor vehicle, anxiety, stress, menstruation, etc.).
- Does it relate to change in head posture?
- How severe is it?
- Did you ever suffer any head injury or trauma to the head?
- Is it associated with symptoms, such as hearing loss, tinnitus, headache, nausea, vomiting, pallor, sweating, double vision, frequent fall, ataxia, focal weakness, confusion or loss of taste sensation?
- Do you take any drugs? (aminoglycoside).

Note Remember the following points:

- **Dizziness:** It means a sensation of faintness, light-headedness, spinning or giddiness. But the term may be used by the patient to describe other inappropriate sensations, such as confusion, blurring of vision, tingling, etc. Even the sensation of ataxia is sometimes described as dizziness. Causes of recurrent dizzy spells over 65 years of age are—postural hypotension, vertebrobasilar insufficiency or cerebrovascular disease, arrhythmia, hyperventilation due to acute anxiety or panic attack.
- **Syncope:** It means transient loss of consciousness due to reduction in cerebral blood flow.
- **Vertigo:** It is a sense of unsteadiness and loss of balance with a feeling of rotation of the body or environment, due to impaired vestibular function of either central or peripheral origin.

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- **Drop attack:** Sudden fall to the ground while walking or standing with transient loss of consciousness. The patient does not remember the actual fall. It is common in middle age or elderly woman. It is due to vertebrobasilar TIA, but no evidence of vascular disease.
- Vertigo may be due to **central lesion** (brainstem or cerebellum) or **peripheral lesion** (labyrinthine lesion).
- **Peripheral vertigo** is usually sudden in onset, severe in nature, unilateral, lasting for few seconds or few days and often recurrent. It is usually associated with unilateral deafness or tinnitus. There may be ear pain or discharge. There may be unidirectional nystagmus with slow phase toward the affected side and fast component toward the opposite side. Common cause is labyrinthine disorder.
- **Central vertigo** is usually chronic and mild, often bidirectional and associated with other central abnormalities. Patient with central vertigo cannot stand or walk. Direction of fall is variable. Vertical nystagmus (up or down beat) is pathognomonic of central vertigo (brainstem lesion). Central vertigo is commonly because of vascular insufficiency of brainstem or basilar artery insufficiency supplying cerebellum.
- **Vertigo due to vascular cause** (vertebrobasilar insufficiency) occurs in elderly and is usually associated with hypertension, CVA, IHD, smoking, diabetes mellitus and dyslipidemia.
- **Common causes of vertigo:**
  - Central vertigo—brainstem ischemia or infarction, migraine, multiple sclerosis.
  - Peripheral vertigo—Meniere's disease, benign positional vertigo, vestibular neuronitis, drugs (gentamicin, anticonvulsant), trauma.

Causes of vertigo in different diseases:

- Acute or sudden vertigo—vestibular neuronitis, labyrinthitis, multiple sclerosis, skull fracture, Meniere's disease, CVD involving brainstem or cerebellum.
- Recurrent vertigo lasting less than a minute—benign positional vertigo, post-traumatic vertigo, psychogenic.
- Recurrent vertigo lasting for minutes to hours—migraine, vertebrobasilar insufficiency, Meniere's disease.
- Spontaneous attack of prolong vertigo for a day or more—labyrinthitis, multiple sclerosis, brainstem infarction.
- Vertigo with hearing loss and tinnitus indicates peripheral disorder, e.g. Meniere's disease, labyrinthitis. This may be due to ototoxic drugs like aminoglycoside.
- Vertigo associated with neurological disorders or chronic vertigo without any cochlear symptom suggests a central lesion, e.g. lesion in brainstem, cerebellum, CP , etc.
- Vertigo precipitated by movement of the head in a specific direction—benign positional vertigo.
- Vertigo with slowly progressive unilateral hearing loss, tinnitus, dizziness and disequilibrium—acoustic neuroma.
- Intermittent brief vertigo with occasional drop attack, ataxia, visual loss, double vision and confusion—vertebrobasilar insufficiency.
- Episodic, recurrent vertigo with auditory symptoms, headache, photophobia, aura—migraine.
- Vertigo with facial weakness and loss of taste sensation—Ramsay Hunt syndrome.
- Triad of episodic vertigo, tinnitus and progressive deafness—Meniere's disease.
- Psychogenic vertigo is usually associated with agoraphobia (fear of large open space or crowd). It differs from organic vertigo in which, despite discomfort, patient attempts to work. Also, there is no nystagmus in psychogenic vertigo (nystagmus is usually present in organic disease).

If the patient complains of swelling of the body, ask:

- Is it generalized, involving the whole body or localized to a part?
- If generalized, where did it first appear? (Face, feet, abdomen).

- If localized, is the swelling painful?
- What is the amount of urine you pass everyday? Is there any pain or burning?
- What is the color of your urine?
- Do you feel palpitation, cough, chest pain or breathlessness on exertion?
- Any history of sore throat or skin infection?
- Do you have diabetes mellitus or hypertension?
- Do you have cold intolerance, constipation, lethargy?
- Do you take any drugs? (steroid, amlodipine, nifedipine).
- How is your bowel habit?

Note Remember the following points:

- Generalized edema indicates hypoalbuminemia (because of less intake, nephrotic syndrome, CLD, malabsorption, etc.) or fluid overload (CCF, glomerulonephritis, etc.).
- Localized edema indicates venous (DVT) or lymphatic obstruction (lymphedema, allergic) or inflammatory (cellulitis).

Causes of body swelling in different diseases:

Generalized swelling:

- Generalized swelling starting at the face (especially periorbital puffiness mostly at the morning) with oliguria indicates a renal cause (glomerulonephritis or nephrotic syndrome). If history of skin or throat infection, followed by smoky or cloudy urine, it indicates post streptococcal glomerulonephritis.
- Generalized swelling with anemia in a hypertensive patient indicates CRF.
- Swelling starting at the legs, ascending upwards and exertional dyspnea indicates cardiac cause, commonly CCF.
- Gradual swelling of whole body with non-pitting edema, cold intolerance, lethargy—hypothyroidism.
- Generalized swelling may also occur in wet beri beri, also in cyclical edema.
- Swelling with steatorrhea indicates hypoalbuminemia due to malabsorption.

Abdominal swelling:

- In CLD (cirrhosis of liver), abdominal swelling (ascites) starts first.
- Abdominal swelling associated with pain in abdomen, anorexia and weight loss indicates abdominal malignancy with metastasis in the peritoneum.
- In constrictive pericarditis, abdominal swelling occurs first, followed by swelling of the leg in advanced stage.

Localized swelling:

- Unilateral leg swelling with non-pitting edema (lymphedema in filariasis).
- Unilateral painful leg swelling of sudden onset—DVT.
- Pitting unilateral lower limb edema may be due to DVT, compression of large veins by tumor or lymph nodes.
- Non pitting lower limb edema may be due to hypothyroidism or lymphedema (filariasis, malignancy, congenital, allergic or Milroy's disease).
- Localized swelling—angioedema.
- Unilateral painful and red swelling in a limb with fever in a toxic patient—cellulitis.
- Gradual truncal swelling in a patient taking steroid—Cushing's syndrome.
- Drugs causing pedal edema—nifedipine, amlodipine.
- Unilateral edema of the arm may occur following surgery or removal of axillary lymph node (in breast carcinoma).

If patient complains excessive cold or heat intolerance, ask:

- If the patient has cold intolerance ask, features of hypothyroid, such as weight gain, lethargy, increased sleepiness, constipation, etc.
- If patient has heat intolerance or excessive sweating, ask to exclude thyrotoxicosis, e.g. increased appetite, weight loss, palpitation, diarrhea, irritability.

Causes of heat or cold intolerance in different diseases:

- Causes of cold intolerance are hypothyroidism, old age, excessive environmental cold.
- Causes of heat intolerance are thyrotoxicosis, menopausal syndrome.
- Excess sweating is called hyperhidrosis. Causes are—anxiety neurosis, thyrotoxicosis, pheochromocytoma, acromegaly, autonomic neuropathy (gustatory hyperhidrosis), excess use of antipyretic, exposure to hot environment, fever, severe pain, menopausal syndrome, malignancy, amyloidosis, neuroleptic malignant syndrome, cholinergic or parasympathomimetic drug side effect, drugs, such as thyroxin, somatostatin analog, vasopressin, epinephrine, withdrawal of drugs like gabapentin or opiate.
- Less or no sweating is called anhidrosis. Causes are—hypothyroidism, hypothermia, autonomic neuropathy, Sjogren's syndrome, anticholinergic drug therapy, vitamin A deficiency, hypoadrenalism.

If patient complains of polyuria, ask:

- What is the amount of water you take and void everyday?
- Are you suffering from diabetes mellitus?
- Is it associated with excessive thirst?
- Do you have excessive thirst with polyphagia?
- Are you taking any drugs? (diuretic, lithium, analgesic, cidofovir, foscarnet)
- Do you take alcohol or excessive coffee?
- Do you have excess thirst, abdominal pain, constipation, etc.?
- Do you have history of head trauma, pituitary surgery or stroke?
- (Take history of psychiatric illness).

Note Remember the following points:

- **Polyuria** means passage of large volume of urine, usually more than 3 L per day in the absence of excess intake of water. Causes are—diabetes mellitus, diabetes insipidus (cranial and nephrogenic), psychogenic polydipsia, hypercalcemia due to any cause, CRF, excessive intake of water, drugs (diuretic, alcohol), renal tubular disease, adrenal insufficiency.
- **Anuria** means urine output less than 50 mL per day. The patient may not pass urine at all.
- **Oliguria** means passage of less than 400 mL urine daily.
- **Nocturia** means the need to get up during night to pass urine.
- **Normal** urine output is 800 to 2500 mL per day in temperate climate.
- **Frequency** of micturition means frequent passage of small amounts of urine (not increased volume). Causes are—urethritis, cystitis, enlarged prostate, bladder neoplasm, pregnancy.
- **Urgency:** It means immediate desire to pass urine.
- **Hesitancy:** It is defined as difficulty in initiating the process of micturition.
- **Dysuria:** It is a specific form of discomfort arising from the urinary tract, in which there is pain immediately before, during or immediately after micturition.

Causes of polyuria in different diseases:

- Polyuria associated with polyphagia and polydipsia is highly suggestive of diabetes mellitus (may be also in thyrotoxicosis, obesity and bulimia).
- Polyuria with excessive thirst—diabetes insipidus, anxiety, also diabetes mellitus.
- History of head injury or surgery suggests cranial diabetes insipidus.
- Polyuria with constipation, abdominal pain and excess thirst indicates hypercalcemia.
- History of psychiatric disease indicates psychogenic polydipsia.
- Drugs causing polyuria—diuretic, lithium, analgesic, cidofovir, foscarnet, etc.

If the patient complains of hematuria, ask:

- Is it at the beginning of micturition or at the end or throughout? (initial, terminal or total)
- Do you feel pain or burning during micturition? (dysuria)
- Is this associated with frequency, urgency or hesitancy?
- Do you have loin pain? Does it radiate to the groin? Do you have pain in lower abdomen or generalized abdominal pain? (If the patient complains of any pain, take detailed history as given in page …).
- Have you noticed bleeding from any other part of the body?
- Do you have fever? (If yes, take detailed history of fever).
- Is it associated with nausea or vomiting?
- Have you noticed any rash? Is it associated with joint pain and swelling?
- Do you take any drugs? (anticoagulant, antiplatelet, analgesic, cyclophosphamide, antibiotic).
- Did you ever pass stones previously?
- Did you suffer from any kind of trauma?
- Did you suffer from skin infection or sore throat recently?
- Do you have hypertension, exertional breathlessness and swelling of the body?
- Is there any history of renal disease in your family?
- In female, enquire whether she is menstruating.
- Take occupational history specially looking for exposure to radiation or industrial chemicals like benzene.
- Have you recently traveled to any Middle Eastern country (to exclude bilharziasis or schistosomiasis)?

Note Remember the following points:

- Causes of high colored or dark or red urine are—hematuria, hemoglobinuria, myoglobinuria, porphyria and deep jaundice. Also, drugs like rifampicin, phenolphthelein, clofazimine, phenindione and some food like beet root, senna, rhubarb, and blackberry.
- Hematuria is the presence of fresh blood (intact RBC) in urine.
- Presence of hemoglobin in urine is called hemoglobinuria (no RBC). It indicates intravascular hemolysis.
- Loss of muscle pigment in urine is called myoglobinuria (no RBC in urine microscopy). This is found in rhabdomyolysis.
- Presence of porphobilinogen in urine is found porphyria. Here the urine is normal in color when it is voided but becomes dark (Burgundy-wine) on standing for few hours. It is detected by Ehrlich's aldehyde test. This type of urine may be found in alkaptonuria. It is due to presence of homogentisic acid in urine.
- Blood appearing at the beginning of micturition indicates a lower urinary tract cause (urethra). Uniform blood staining throughout the stream points to a cause higher up (bladder and above). Terminal hematuria indicates severe bladder irritation by stone or infection or neoplasm, also disease of prostate.

Contd...

Contd...

- Hematuria may be detected by dipstick. False positive may occur in hemoglobinuria, myoglobinuria, beet root, porphyria, alkaptonuria, rifampicin, phenindione, phenolphthalein.
- Presence of red cell cast in urine indicates bleeding from kidney, usually glomerulonephritis.
- Macroscopic hematuria is more likely due to tumors of renal tract. Sometimes, it may be found in severe infection and renal infarction.

Causes of hematuria in different diseases:

- Hematuria with dysuria indicates cystitis or urethritis (UTI).
- Hematuria with more than trace of protein in urine suggests that the blood is of renal origin.
- Hematuria with loin pain, high grade fever with chill and rigor, nausea or vomiting indicates acute pyelonephritis.
- Hematuria with fever may also be found in infective endocarditis with renal involvement, collagen vascular disease (SLE).
- Hematuria with loin to groin pain indicates renal stone. If stone in urinary bladder, there may be pain in lower abdomen.
- Painful hematuria may be found in loin pain hematuria syndrome.
- Hematuria either painful or painless may be found in UTI, adult polycystic kidney disease, reflux nephropathy and renal scarring, renal stone without obstruction.
- Painless hematuria may be due to tumor of kidney, ureter, bladder and prostate, renal tuberculosis, glomerulonephritis, schistosomiasis (bilharziasis), bleeding disorders, benign enlargement of prostate, IgA nephropathy, infective endocarditis, hypertensive nephrosclerosis, interstitial nephritis, drugs like heparin and oral anticoagulant.
- Bilharziasis should be strongly suspected in any patient who has been to Middle East recently.
- Hematuria with obstructive features in elderly male indicates benign enlargement of prostate or carcinoma of prostate.
- Hematuria with previous history of skin infection or sore throat, hypertension and generalized body swelling indicates acute glomerulonephritis.
- Hematuria due to drugs—analgesic (papillary necrosis or analgesic nephropathy), cyclophosphamide (haemorrhagic cystitis), antibiotic (interstitial nephritis), anticoagulant, antiplatelet.
- Hematuria with hypertension—renovascular disease..
- There may be family history of renal disease in patient with polycystic kidney disease.
- Bleeding from multiple sources indicates bleeding disorder, also may be drug induced.
- Hematuria with bruise or purpura may be due to coagulation disorder, Henoch Schonlein purpura or vasculitis.
- Hematuria with abdominal pain and vasculitic rash over lower limbs indicate Henoch Schonlein purpura.
- In young fit athlete, hematuria may be due to exercise induced hematuria.
- Hematuria associated with diabetes mellitus or sickle cell disease or trait—papillary necrosis.

CHAPTER 2

Respiratory System

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BRONCHIAL ASTHMA

CHIEF COMPLAINTS

- Difficulty in breathing for … years
- Cough for … months
- Wheeze and tightness in the chest … months.

HISTORY

History of present illness: According to the statement of the patient, he has been suffering from difficulty in breathing for the last … years. Initially, for a few years, it was episodic, occurring mainly during the winter seasons, and he was asymptomatic in between the attacks. But for the last … years, it is persistent with occasional exacerbations. His breathlessness is worse at night and sometimes during the daytime. It is aggravated by cold, dust and activity. There is no history of orthopnea or paroxysmal nocturnal dyspnea.

The patient also complains of cough which is usually dry, with occasional scanty mucoid sputum expectoration, but no history of hemoptysis. Cough is present throughout the day and night, more on exposure to dust or cold. He also experiences wheeze and tightness of the chest during coughing. For severe attack of breathlessness and cough, he was hospitalized twice within the last ... months.

On query, the patient agreed that he has occasional attack of running nose and sneezing, more marked on exposure to dust. There is no history of chest pain, weight loss or fever. His bowel and bladder habits are normal.

History of past illness: He is non-hypertensive, no history suggestive of cardiac illness or reflux esophagitis.

Family history: His brother is suffering from bronchial asthma and food allergy.

Personal history: He is a school teacher, smokes 10 to 15 cigarettes daily for the last 10 years. There is no history of exposure to cotton, coal, etc.

Drug history: He uses bronchodilator and steroid inhalers, and used to take tablets like aminophylline, ketotifen and montelukast.

GENERAL EXAMINATION

- The patient is dyspneic
- Decubitus is propped up
- No anemia, jaundice, cyanosis, edema, clubbing, koilonychia or leukonychia
- No lymphadenopathy or thyromegaly
- Neck vein: Not engorged
- Purse lip: Absent
- Nasal polyp: Present on both sides
- Pulse: 120/min
- BP: 120/70 mm Hg
- Respiratory rate: 24/min.

SYSTEMIC EXAMINATION

Respiratory System

Inspection:

- Shape of the chest—Normal
- There is indrawing of intercostal spaces, suprasternal and supraclavicular excavation and prominent accessory muscles of respiration.

Palpation:

- Trachea: Central. Tracheal tug absent
- Apex beat: In the left 5th intercostal space in midclavicular line, 8 cm from midsternal line, normal in character
- Chest expansion: Reduced
- Vocal fremitus: Normal.

Percussion:

- Percussion note: hyperresonance in both sides
- Area of liver dullness: In 5th ICS in the right midclavicular line
- Area of cardiac dullness: Normal.

Auscultation:

- Breath sound: Vesicular with prolonged expiration
- Vocal resonance: Normal
- Added sounds: High pitched rhonchi are present in both sides of the chest, more marked on expiration.

FET (forced expiratory time): > 6 seconds (normally <6 seconds).

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 50 years old, school teacher, normotensive, nondiabetic, hailing from …, presented with difficulty in breathing, cough, wheeze and tightness of the chest for the last … years. Initially, for few years, it was episodic, occurring mainly during the winter seasons, and he was asymptomatic in between the attacks. But for the last … years, it is persistent with occasional exacerbations. His breathlessness is worse at night and sometimes during the daytime. It is aggravated by cold, dust and activity. There is no history of orthopnea or paroxysmal nocturnal dyspnea. The patient also complains of cough which is usually dry, with occasional scanty mucoid sputum expectoration, but no history of hemoptysis. Cough is present throughout the day and night, more on exposure to dust or cold. He also experiences wheeze and tightness of the chest during coughing. For severe attack of breathlessness and cough, he was hospitalized twice within the last ... months. On query, the patient agreed that he has occasional attack of running nose and sneezing, most marked on exposure to dust. There is no history of chest pain, weight loss or fever. His bowel and bladder habits are normal. There is no history suggestive of cardiac illness or reflux oesophagitis. His brother is suffering from bronchial asthma and food allergy. He smokes 10 to 15 cigarettes daily for the last 10 years. There is no history of exposure to cotton, coal, etc. He uses bronchodilator and steroid inhalers, and used to take tablets like aminophylline, ketotifen and montelukast.

On examination, general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is chronic bronchial asthma.

Q. What is your **differential diagnosis**?

A. COPD (Chronic obstructive pulmanary disease).

Q. Why not **chronic bronchitis**?

A. In chronic bronchitis, there is presence of cough with sputum production not attributable to other causes, on most of the days for at least 3 consecutive months in a year for at least 2 successive years.

Q. Why not **cardiac asthma**?

A. Cardiac asthma means left ventricular failure in which the patient usually presents with sudden severe dyspnea and cough with profuse mucoid expectoration. On examination, there are bilateral basal crepitations and no rhonchi or wheeze.

Q. What **investigations** do you want to do in bronchial asthma?

A. As follows:

1. Full blood count.
2. X-ray chest of PA view.
3. Sputum for eosinophil count.
4. Lung function tests:
   - Spirometry with reversibility test: Forced expiratory volium income second (FEV1) and Forced vital capacity (FVC) are reduced. Ratio of FEV1/FVC is also reduced. FEV1 or FVC shows >15% and 200 mL improvement after inhalation of bronchodilator (reversibility test). According to Global Initiative for Asthma (GINA), a >12% increase in FEV1 after bronchodilator indicates asthma.
   - PEFR: Reduced. It improves >15% after reversibility test. It may show diurnal variation (seen on waking and before bronchodilator, at afternoon and before going to bed. It shows wide diurnal variation, characteristic of bronchial asthma. Fall of PEF > 20% in early morning is known as morning dipping. It is characteristic of uncontrolled bronchial asthma).
   - Exercise test (fall of FEV1 or PEFR > 15% after 6 minutes exercise indicates exercise induced asthma).
   - Carbon monoxide transfer test (normal in asthma).
5. Blood gas analysis: PaO_2 (reduced)and $PaCO_2$ (raised or normal).
6. Bronchoprovocation test (with methacholine or histamine or hypertonic saline – fall of FEV1 > 20% indicates hyperresponsiveness of airways. This is found in cough variant asthma, mild intermittent asthma, chronic bronchitis with hyperresponsive airways). It is useful when asthma is suspected, but spirometry is not diagnostic.
7. Skin prick test.
8. Allergen provocation tests.
9. Serum IgE level.
10. ECG (to exclude RVH in cor pulmonale).

RELATED QUESTIONS AND ANSWERS

Q. What is **bronchial asthma**?

A. It is a chronic airway inflammatory disorder characterized by hyper-responsiveness of the airways to various stimuli, presenting as breathlessness, cough, chest tightness and wheeze. It is reversible.

Q. What are the **cardinal pathophysiologic features** of bronchial asthma?

A. Three cardinal features:

- Airflow limitation – it is usually reversible spontaneously or with treatment
- Airway hyper-responsiveness – airway is hyper-responsive to a wide range of nonspecific stimuli like exercise, cold air
- Airway inflammation – there is inflammation of the bronchi with infiltration of eosinophils, T cells and mast cells. Also there is plasma exudation, edema, smooth muscle hypertrophy, matrix deposition, mucus plugging and epithelial damage

(In chronic asthma, inflammation may lead to irreversible airflow limitation due to airway wall remodeling, involving the large and small airways with mucus impaction.)

Q. How can you **diagnose** a case of bronchial asthma?

A. Typical history (cardinal features like paroxysmal breathlessness, cough, wheeze and chest tightness) **plus** any of the following:

- FEV1 ≥ 15 % (and 200 mL) increase following the inhalation of bronchodilator. (Global Initiative for Asthma accepts an increase of 12%).
- FEV1 ≥ 15 % decrease after 6 minutes of exercise.
- PEFR shows > 20% of diurnal variation on ≥ 3 days in a week for 2 weeks.

Q. What are the **types** of bronchial asthma?

A. Four groups based on frequency of symptoms, severity of attack and pulmonary function tests abnormality:

1. **Intermittent asthma**: About 2 or less than 2 nocturnal symptoms (cough, wheeze, shortness of breath at night or early morning) in a month. Between the episodes, the patient remains symptom free and lung function tests are normal.
2. **Persistent asthma**: Frequent attacks at least more than two occasions in a month. In between the attack, the patient may or may not have symptoms and lung function tests are abnormal, except in mild case. It may be:
   - Mild – usually the patient has nocturnal attack of dyspnea more than 2 times per month and baseline (i.e. during symptom free state) PEFR or FEV1 is usually < 80 to 65% of predicted value. Occasionally, lung function tests may be normal in between attacks.
   - Moderate – usually the patient has almost daily attack of dyspnea and baseline PEFR or FEV1 is < 65 to 50% of predicted value.
   - Severe – usually the patient has dyspnea to some extent continuously for 6 months or more and baseline PEFR or FEV1 is less than 50% of predicted value.
3. **Acute exacerbation**: Loss of control of any class or variant of asthma. It is again classified as –
   - Mild – The patient is dyspneic, but can complete a sentence in one breath.
   - Moderate – The patient is more dyspneic and cannot complete a sentence in one breath.
   - Severe (severe acute asthma) – The patient is severely dyspneic, talks in words and may be restless, even unconscious.
4. **Special variants**. There are **5** types:
   - Cough variant asthma
   - Exercise induced asthma
   - Occupational asthma
   - Drug-induced asthma (aspirin, other NSAID, β blocker)
   - Seasonal asthma.

Q. What is **cough variant** asthma?

A. It is a type of asthma in which there is chronic dry cough with or without sputum eosinophilia, but no abnormalities in airway function. It is also called eosinophilic bronchitis, common in

young children. Cough is the only symptom, mostly at night. Examination during day may not reveal any abnormality. Cough may be increased with exercise, exposure to dust, strong fragrances or cold air. Methacholine challenge test is positive.

Clinical criteria for diagnosis:

- Dry cough persisting more than 6 to 8 weeks
- Presence of bronchial hyper-responsiveness
- Absence of dyspnea and wheeze.

Treatment: Should be according to the stepwise approach for long-term. Nedocromil sodium is effective. Also consider the following points:

- Allergic rhinitis should be treated, if present.
- Gastroesophageal reflux disease should be treated with proton pump inhibitor (e.g. omeprazole) and/or gastric prokinetic agent (e.g. domperidone).
- Any environmental factors like cold, dust, fume, etc. should be avoided.
- β blocker, aspirin should also be avoided.

Q. What is **exercise-induced asthma**?

A. When exercise produces asthma, it is known as exercise-induced asthma. 10% or more reduction of FEV1 after exercise is diagnostic.

Cold dry air that enters into the lungs during exercise is the main trigger factor. Increased ventilation results in water loss from the pericellular lining fluid of the respiratory mucosa trigger mediator release. Heat loss from the respiratory mucosa is also involved.

Treatment:

- Single dose short acting β_2 agonist, sodium chromoglycate or nedocromil sodium immediately before exercise should be used.
- Inhaled corticosteroid twice daily for 8 to 12 weeks reduces severity.
- If abnormal spirometry and persistent symptoms- inhaled corticosteroid with long acting β_2 agonist.
- Leukotriene receptor antagonist may be used.

Q. What is **occupational asthma**?

A. It may be defined as "asthma induced at work by exposure to occupation related agents, which are mainly inhaled at the workplace". The most characteristic feature is symptoms that worsen on work days and improves on holidays.

Atopic individual and smoker are at increased risk. Commonly found in chemical workers, farmers, grain handlers, cigarette manufacturers, fabric, dye, press and printing workers, laboratory workers, poultry breeders, wood and bakery workers.

Measurement of 2 hourly peak at and away from work is helpful for diagnosis.

Treatment:

- Avoidance of further exposure
- Using mask at work
- If no response, step care asthma management plan.

Q. What is **drug induced asthma**?

A. Symptoms of asthma that occurs after use of certain drugs such as aspirin, beta blocker, some nonsteroidal anti-inframmatory drugs (NSAIDs), etc. These drugs can cause bronchospasm.

Treatment: Avoidance of triggering drugs**.** Safe NSAIDs are paracetamol, tramadol, also etoricoxib.

Q. What is **intrinsic asthma** and **extrinsic asthma**?

A. As follows:

- Intrinsic asthma (non atopic or late onset asthma): When no causative agent can be identified. It is not allergic, usually begins after the age of 30 years, tends to be more continuous and more severe.
- Extrinsic asthma (atopic or early onset asthma): When a definite external cause is present. There is history of allergy to dust, mite, animal danders, pollens, fungi, etc. It occurs commonly in childhood and usually shows seasonal variations.

Q. What are the **differences** between extrinsic and intrinsic bronchial asthma?

A. As follows:

Points	Extrinsic	Intrinsic
1. Age	Early or childhood	Middle age or late onset
2. History of allergy	Usually present	Absent
3. Precipitating allergen	Present	Absent
4. Atopy	Atopic individual	Non atopic
5. Family history of asthma, rhinitis, eczema, etc.	Usually present	Usually absent
6. Skin prick test	Usually positive	Usually negative
7. Serum IgE	High	Normal

Q. What is **acute severe asthma**?

A. It is defined as "severe acute persistent attack of asthma without any remission in between and not controlled by conventional bronchodilator". Previously it was called status asthmaticus.

Q. How to **assess the severity** of acute bronchial asthma?

A. Acute severe asthma is assessed by the following points:

- Inability to complete a sentence in one breath
- Respiratory rate > 25/min
- Pulse rate > 110/min
- PEFR 33 to 50% of predicted (< 200 L/min).

Note

Pulsus paradoxus may be found in up to 45% of acute severe asthma.

Q. What are the features of **life threatening or very severe asthma**?

A. As follows:

- Exhaustion, confusion or coma
- Cyanosis
- Silent chest
- Feeble respiratory effort
- Bradycardia or hypotension or arrhythmia
- PEFR < 33% of predicted (< 100 L/min)
- Blood gas analysis – SpO_2 < 92% or PaO_2 <8 κPa (60 mm Hg) even with O_2
- Normal or raised $PaCO_2$ (> 6 κPa) and low or falling blood pH.

Note

If a patient has raised $PaCO_2$ and/or requires mechanical ventilation with raised inflation pressure, it is called **near fatal asthma.**

Q. How to **treat acute severe bronchial asthma**?

A. As follows:

- High flow O_2—40 to 60% (to maintain O_2 saturation above 92%).
- Nebulized sulbutamol 5 mg or terbutaline 10 mg. May be repeated 2 to 4 hourly.
- Nebulized ipratropium bromide 0.5 mg may be added with nebulized sulbutamol.
- Injection hydrocortison 200 mg IV 4 hourly. After 24 hour, oral prednisolone 60 mg daily should be given for two weeks, then taper.
- If no response, IV infusion sulbutamol 3 to 20 μg/min or terbutaline 1.5 to 5 μg/min or magnesium sulphate IV 1.2 to 2 gm over 20 minutes may be given.
- In some cases, injection aminophyllin 5 mg/kg loading dose over 20 minutes, then continuous infusion at 1 mg/kg/h.
- Correction of fluid and electrolytes (repeated use of salbutamol may cause hypokalemia).
- If no response with this regime, the patient may be shifted ICU for assisted ventilation.

Note Remember the following points:

- Arterial blood gases are measured. If $PaCO_2 > 7$ κPa, ventilation should be considered. Chest X-ray should be done in acute severe asthma to exclude pneumothorax
- 2.5 mL of isotonic magnesium sulphate may be given as a nebulizer.

Q. How to monitor a patient with acute severe bronchial asthma?

A. As follows:

- Repeated PEFR in every 15 to 30 min
- Pulse oxymetry (SaO_2 should be kept > 92%)
- Repeat arterial blood gas analysis
- X-ray chest to exclude pneumothorax.

Q. What are the **indications of assisted ventilation?**

A. As follows:

1. Coma, severe exhaustion, confusion, drowsiness, respiratory arrest.
2. Deterioration of arterial blood gas despite optimal therapy:
   - $PaO_2 < 8$ κPa (< 60 mm Hg) and falling
   - $PaCO_2 > 6$ κPa (> 45 mm Hg) and rising
   - P^H low and falling (H^+ high and rising)
   - Failure to maintain above 92% (or O_2 saturation <90%).

Note. Remember the following points:

- Sedative is contraindicated in acute severe asthma
- No role of chest physiotherapy, antihistamine, antitussive drugs in acute attack.

Q. What is the **stepwise management** of asthma?

A. As follows:

Step	PEFR	Treatment
Step 1. Occasional symptoms (less than once in a week for three months and fewer than two nocturnal symptoms/ month)	100% predicted	Inhaled short acting β_2 agonist as required.If used more than once daily, move to step 2
Step 2. Daily symptoms. Also indicated- – exacerbation of asthma in the last 2 years – uses inhaled â2 agonist 3 times a week or more – symptoms 3 times a week or more – awakened by asthma one night per week	≤ 80% predicted	Add any of the following –· » Low dose inhaled corticosteroid (ICS) – started at 400 µg beclometasone (BDP) or equivalent (budesonide, fluticasone, ciclesonide) daily and may be raised up to 800 µg daily » Leukotriene receptor antagonist (LTRA), theophylline or sodium cromoglicate (these are less effective) » If not controlled, move to step 3
Step 3. Severe symptoms or poorly controlled despite regular use of ICS	50 to 80% predicted	Add one of the following (add on therapy) –· » Low dose ICS + long acting β_2 agonist like salmeterol, formeterol, etc. » Low dose ICS + LTRA » Low dose ICS + sustained release theophylline » Medium or high dose ICS If not controlled, move to step 4
Step 4. Severe symptoms or poorly controlled with high dose inhaled corticosteroids	50 to 80% predicted	High dose inhaled corticosteroid, up to 2000 µg daily Plus regular long acting β_2 agonist Plus either LTRA or modified release theophylline or β_2 agonist.
Step 5. Severe symptoms deteriorating	≤ 50% predicted	Regular oral corticosteroid – add prednisolone 40 mg daily to step 4 and or Anti-IgE treatment
Step 6. Severe symptoms deteriorating inspite of prednisolone	≤ 30% predicted	Hospital admission

Q. What are the **criteria for discharge?**

A. As follows:

- Stable on discharge medication
- Without nebulisation for at least 24 hours
- PEFR 75% of predicted or personal best.

Q. How to **step down**?

A. If patient's asthma is under control, then at every 3 months interval, reduce the dose of inhaled corticosteroids by 25 to 50%.

Q. What are the **steroid sparing** drugs?

A. As follows:

- Methotrexate
- Cyclosporine
- Intravenous immunoglobulin
- Etanercept
- Anti-IgE monoclonal antibody (omalizumab).

Q. What **new therapy** is available for bronchial asthma?

A. As follows:

- Omalizumab, a monoclonal antibody directed against IgE, can be given subcutaneously 2 to 4 weekly
- Bronchoplasty – a stent is applied to dilate constricted bronchi
- Bronchothermoplasty – hyperplastic bronchial smooth muscle is reduced by thermal coagulation.

Q. What is **rescue therapy?**

A. If the patient develops severe asthma or loss of control at any step during therapy, a short course of oral corticosteroid is given. This is called rescue therapy. Tablet prednisolone 30 to 60 mg daily (1 to 2 mg/kg daily for children) is given in a single morning dose or two divided doses for 3 to 14 days. Tapering is not necessary, if it is not given for more than 3 weeks. **Indication**s are:

- Morning symptoms persist till mid-day
- Onset or worsening of sleep disturbance by asthma
- Progressively diminishing response to inhaled bronchodilators
- Symptoms severe enough to require treatment with nebulized or injected bronchodilators
- Symptoms and PEF get progressively worse day by day
- PEFR falls below 60% of patient's personal best recording.

Q. What are the **home management** of acute severe asthma?

A. The patient should follow the rule of 5:

1. The patient should be sitting comfortably in up right position.
2. Give 5 puffs of bronchodilator inhaler with a large volume spacer. Initially 5 puffs (1 puff and 5 sucks) at 5 minutes interval through spacer up to 5 times (25 puffs) within 1 hour. If no improvement, the patient should go to the nearby hospital.
3. If spacer is not available, the patient should take the puffs in the above rule but hold breath for 5 seconds for each puff.

Q. What is **refractory asthma?**

A. Some patients with asthma have more troublesome disease reflected by:

- High medication requirements to maintain disease control or
- Persistent symptoms, asthma exacerbation, or airflow obstruction despite high medication use.

This group is called refractory asthma:

Treatment:

- Home nebulization—continuous or as required
- Vaccination—influenza, measles, pneumococcal vaccine
- Anti-IgE (omalizumab), sublingual immunotherapy
- Disease modifying agent—methotrexate, cyclosporine, gold salt
- Patient's education
- Identifying pitfalls of management.

Q. What is **brittle asthma**?

A. This is an unusual variant of asthma characterized by severe, life-threatening attacks that may occur within hours or even minutes without little or no warning symptoms. Patients are at risk of sudden death although their asthma may be well controlled in between attacks.

Management:

- The patient should be advised to keep emergency supplies of medications at home, in the car and at work.
- There should be oxygen and resuscitation equipments at home and at work.
- Nebulized β_2 agonists should be available at home and at work. Inhaled long acting β_2 agonists with a corticosteroid can be very effective.
- Self injectable epinephrine should be kept at home, at work and should be carried by the patent at all times.
- Prednisolone 60 mg.
- Medic Alert bracelet.

On developing wheeze, patient should attend the nearest hospital immediately. Direct admission to ICU may be required.

Q. What are the **differences** between bronchial asthma and COPD?

A. Key distinguishing feature is the reversibility test. Bronchial asthma is fully reversible with use of bronchodilator which leads to >15% and 200 mL increase in FEV_1 (except in severe persistent asthma). COPD is not fully reversible and the increase in FEV_1 after bronchodilator is < 15%.

The **differences** between bronchial asthma and COPD are:

Parameter	COPD	Bronchial asthma
1. Age of onset	Middle age, usually >40 years	Any age
2. Smoking history	Common, >20 pack years	May or not be present
3. Allergy	Uncommon	Common—rhinitis, eczema, skin prick positive, eosinophilia
4. Family history	Not common	Common
5. Cardinal features	Cough, expectoration and dyspnea	Dyspnea, cough, wheeze, and chest tightness
6. Sputum	Often copious	Infrequent
7. Symptom free period	It is chronic and progressive without any symptom free period	There is recurrent attack but the patient is usually symptom free in between attacks. However, in chronic bronchial asthma, the features may be persistent
8. Dyspnea	Progressive, persistent (with exacerbation)	Intermittent and variable, vary from day to day and peak at night and in early morning
9. Spirometry	Airway obstruction is irreversible	Airway obstruction is reversible
10. Durnal variation of PEFR	Less	More
11. Sputum microscopy	Increased neutrophil and helper T lymphocyte (CD4)	Increased eosinophil and cytotoxic T lymphocyte (CD8)

Contd...

Contd...

12. Bronchodilator response	May not be satisfactory	Usually satisfactory
13. Airway hyper-responsiveness	Absent in 50% cases	Present
14. Destruction of lung parenchyma	Common	Uncommon

Q. What are the **differences** between bronchial asthma and cardiac asthma?

A. As follows:

Features	Cardiac Asthma	Bronchial Asthma
1. History	» Hypertension, IHD, vulvular disease » Family history of hypertension	» History of previous attack of asthma, allergy or rhinitis » Family history of asthma or allergy
2. Age	Usually elderly	Young, but may be any age
3. Symptoms	» Dyspnea » Cough with frothy sputum, often mixed with blood » Wheeze – rare » Sweating – common	» Dyspnea » Cough with little mucoid sputum » Wheeze – common » Sweating – less
4. Signs	» Pulse—pulsus alternans » BP—high (if hypertensive) » Heart— – Cardiomegaly (apex is shifted) – Gallop rhythm may be present – Primary cause (mitral or aortic valvular disease) may be present » Lungs— – Bilateral basal crepitations. In severe case, extensive crepitations – No or little rhonchi	» Pulse—may be pulsus paradoxus » BP—Normal, low in severe case » Heart— – Absent – No – No » Lungs— – Plenty of rhonchi all over the lungs – No or little crepitations
5. CXR	» Pulmonary edema – perihilar opacities (Bat's wing appearance) » Cardiomegaly	» Relatively clear, evidence of infection may be present
6. ECG	Left ventricular hypertrophy, MI, arrhythmia	Normal, only tachycardia may be present

Q. What are the **differences** between wheeze and stridor?

A. As follows:

- **Stridor** is a high pitched, loud sound produced by partial obstruction of major airways like larynx, trachea or large bronchi. It is heard both in inspiration and expiration. Causes are—foreign body in larynx or trachea, laryngeal edema (angioedema), laryngeal tumor, vocal cord palsy due to recurrent laryngeal nerve paralysis, tumor, infection (e.g. epiglottitis, acute laryngitis, diphtheria, whooping cough) or inflammation, paratracheal and subcarinal lymphadenopathy pressing over the main bronchi, laryngismus stridulus in tetany. This indicates an emergency condition.

- **Wheezes** are a musical sound heard from a distance, due to small airways obstruction. High pitched wheezes are produced by obstruction in smaller bronchi and low pitched wheezes are produced in larger bronchi. It is present both during inspiration and expiration but prominent during expiration. Wheezes are caused by severe bronchial asthma, chronic bronchitis or COPD or airways obstruction by a foreign body or tumor.

READ THE FOLLOWING TOPICS

Asthma with Diabetes Mellitus

Drugs are used as in other cases of bronchial asthma. However, the following points should be remembered:

- Corticosteroid can be used if necessary, but regular sugar monitoring should be done.
- In severe acute asthma, insulin therapy may be necessary.
- Metformin should be avoided in uncontrolled asthma and contraindicated in acute severe asthma.
- Dose of oral hypoglycemic drugs like sulfonylurea and pioglitazone should be adjusted if used with aminophylline, as it may cause hypoglycemia.

Asthma in Pregnancy

1. Unpredictable clinical course:
   - One third worsen
   - One third improve
   - One third remain stable.
2. Uncontrolled asthma is associated with:
   - Maternal complications – hyperemesis gravidarum, hypertension, pre-eclampsia, vaginal hemorrhage, complicated labor.
   - Fetal complications – IUGR, low birth weight, preterm baby, increased perinatal mortality, neonatal hypoxia.
3. Management of asthma in pregnancy:
   - All inhalers are safe and effective.
   - β_2 agonist (both short and long acting), inhaled steroids, theophylline, oral prednisolone, chromone are safe.
   - If the patient was getting leukotriene receptor blockers, it can be continued.
4. Management during labor: Treatment as usual should be continued. If the patient is on maintenance prednisolone > 7.5 mg/day for > 2 weeks prior to delivery, it should be changed to parenteral hydrocortisone, 100 mg 6 to 8 hourly during labor.
5. Breastfeeding should be continued. Very little drug is excreted in breast milk (<1% of maternal theophylline is excreted in milk).

Note

Acute attack during delivery is rare, probably due to endogenous steroid production. If prostaglandin $F_{2\alpha}$ is needed, it should be used with extreme caution as it may induce bronchospasm.

Asthma with Hypertension

Management of asthma is same. Regarding antihypertensive drugs, remember the following points:

- Avoid β blocker. However, cardioselective β blocker can be used.
- Drug of choice—calcium channel blocker or ARB (losartan, valsartan). ACE inhibitor is avoided as it may induce cough.

Asthma with Arrhythmia

- Digoxin and amiodarone may be used
- Aminophylline or theophylline should be avoided.

Asthma with Pain

- Paracetamol and tramadol are preferred for pain management. COX 2 inhibitor can be used.
- NSAIDs like aspirin, diclofenac, etc. should be avoided
- Steroid may be given, if needed
- DMARDs are safe.

Asthma with Heart Failure

- Diuretic is the drug of choice
- ACE inhibitors should be continued, if tolerated
- Digoxin may be given
- Carvedilol may be used in low doses.

Asthma with IHD

- Antianginal nitrates, calcium channel blocker (diltiazem and verapamil) are drug of choice
- Clopidogrel is preferred than aspirin (as it may trigger or aggravate asthma)
- Sometimes, cardioselective β blocker (like metoprolol) may be given
- Asthma should be well controlled.

CHRONIC BRONCHITIS

CHIEF COMPLAINTS

- Cough with sputum for … years
- Tightness in the chest for … months
- Breathlessness on exertion for … months.

HISTORY

History of present illness: The patient was alright … years back. Since then, he has been suffering from frequent attack of cough with profuse expectoration of mucoid sputum. Initially, cough was present during winter only and persisted for 2 to 3 months. For the last … month, it is present throughout day and night, more marked in the morning and also on exposure to cold and dust. The patient also complains of occasional tightness all over the chest, which is worse on coughing. He also complains of difficulty in breathing, more marked during moderate to severe exertion, relieved by taking rest. There is no history of chest pain, hemoptysis, and paroxysmal nocturnal dyspnea. He does not give any history of fever, swelling of the ankle or weight loss. His bowel and bladder habits are normal.

History of past illness: 2 years back, he was admitted in the hospital due to severe attack of cough and breathlessness.

Family history: Nothing contributory.

Personal history: He is a truck driver, smokes 30 sticks per day for last 35 years.

Drug history: He used to take tablet aminophylline, cough syrup, salbutamol inhaler, beclomethacin inhaler and sometimes local doctor prescribed antibiotics, the name of which he cannot mention.

GENERAL EXAMINATION

- The patient is emaciated
- Central cyanosis present
- No anamia, jaundice, edema, clubbing, koilonychia or leukonychia
- No lymphadenopathy or thyromegaly
- Pulse: 120/min, high volume
- BP: 120/70 mm Hg
- Respiratory rate: 20/min
- JVP: not raised
- (Look at the sputum pot, if available at the bedside).

SYSTEMIC EXAMINATION

Respiratory System

Inspection:

- Shape of the chest: Normal
- Movement of the chest: Bilaterally restricted
- Intercostal space: Appears full.

Palpation:
- Trachea: Central
- Apex beat: in the left 5th intercostal space in the midclavicular line, normal in character
- Chest expansion: Reduced
- Vocal fremitus: Normal.

Percussion:
- Percussion note: Normal resonance
- Area of liver dullness: In the right 5th ICS in midclavicular line
- Area of cardiac dullness: Impaired

Auscultation:
- Breath sounds: Vesicular with prolonged expiration
- Added sounds: Plenty of rhonchi, in both lung fields, present in both inspiration and expiration
- Vocal resonance: Normal

FET (forced expiratory time): 8 seconds (normally <6 seconds).

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr. …, 52 years old, truck driver, normotensive, nondiabetic, smoker, hailing from …, presented with frequent attack of cough with profuse expectoration of mucoid sputum for … years. Initially, cough was present during winter only and persisted for 2 to 3 months. For the last … month, it is present throughout day and night, more marked in the morning and also on exposure to cold and dust. The patient also complains of occasional tightness all over the chest, which is worse on coughing. He also complains of difficulty in breathing, more marked during moderate to severe exertion, relieved by taking rest. There is no history of chest pain, hemoptysis, paroxysmal nocturnal dyspnea. He does not give any history of fever, swelling of the ankle or weight loss. His bowel and bladder habits are normal. 2 years back he was admitted in the hospital due to severe attack of cough and breathlessness. He smokes 30 sticks a day for last 35 years. All the family members are in good health. No such illness in family. He used to take tablet aminophylline, cough syrup, salbutamol inhaler, beclomethasone inhaler and sometimes local doctor prescribed antibiotics, the name of which he cannot mention.

On examination – general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is chronic bronchitis.

Q. What are your **differential** diagnoses?

A. As follows:
- COPD
- Chronic persistent bronchial asthma
- Emphysema
- Bilateral extensive bronchiectasis.

Q. Why not this is COPD?

A. Because in the history, there is frequent attack of cough with profuse expectoration 2 to 3 months in a year during winter. But in COPD, usually there should be breathlessness which is progressive and not fully reversible.

Q. What **investigations** should be done in chronic bronchitis?

A. As follows:

1. Full blood count
2. Chest X-ray PA views (no significant abnormality)
3. ECG (usually normal. In cor pulmonale, there may be features of RVH)
4. Lung function tests:
   - FEV_1 (reduced)
   - FVC (reduced)
   - Ratio of FEV_1: FVC is also reduced (indicates obstructive airway disease).
   - Other tests – residual volume (RV is increased), total lung capacity (TLC is increased), gas transfer (either normal or mildly reduced).
5. PEFR (reduced).
6. Blood gas analysis:
   - PO_2 (reduced)
   - PCO_2 (normal or increased)
   - PH (acidosis).
7. CT scan in some cases.

RELATED QUESTIONS AND ANSWERS

Q. What is **chronic bronchitis?**

A. It is defined as "presence of cough with sputum, not attributable to other causes, on most of the days of at least 3 consecutive months for 2 successive years".

Q. What are the **causes** of chronic bronchitis?

A. Multiple factors are responsible:

- Smoking.
- Exposure to dust, fume, foggy environment (may be occupational). Dampness, sudden change in temperature—all exaggerate chronic bronchitis.
- Infection (*H. influenzae*, *Streptococcus pneumoniae*, *Moraxella catarrhalis* – all of these exaggerate chronic bronchitis).

Q. What are the **presentations** of chronic bronchitis?

A. Usual presentations are:

- Cough with sputum expectoration, more marked in the morning, on exposure to cold and during winter. The sputum is mucoid or mucopurulent, usually not associated with hemoptysis.
- Tightness of the chest, and breathlessness on exertion.
- In advanced stage, features of pulmonary hypertension and cor pulmonale are present. The patient looks cyanosed and edematous (blue bloater).

Q. What are the **complications** of chronic bronchitis?

A. As follows:

- Respiratory failure, both type I and type II
- Emphysema
- Secondary polycythemia
- Secondary infection
- Pulmonary hypertension
- Cor pulmonale.

Q. How to **treat** chronic bronchitis?

A. As follows:

1. Smoking must be stopped
2. Avoid air pollution (dust, fume)
3. Control of infection with appropriate antibiotic
4. Bronchodilator:
   - Inhaled β agonist—salbutamol (200 µg 4 to 6 hourly), terbutaline
   - Inhaled antimuscarinic—ipratropium (40 µg 4 hourly), tiotropium (18 µg daily), oxitropium (200 µg BD)
   - Long acting β agonist - salmeterol, formeterol
   - Oral theophylline (in some cases).
5. Inhaled corticosteroid beclomethasone (400 µg BD) or budensonide or fluticasone. In severe case, oral prednisolone 30 mg for 2 weeks, followed by maintenance dose.
6. Mucolytic agents like bromhexine or N-acetylcysteine (200 mg 8 hourly orally for 8 weeks) may be given.
7. Other measures:
   - Chest physiotherapy
   - Exercise and weight reduction, if obese
   - Long-term domiciliary oxygen
   - Pulmonary rehabilitation
   - Annual influenza vaccine, 5 yearly pneumococcal vaccine and *Haemophilus influenzae* vaccine may be given.

Q. What are the indications of **long-term domiciliary oxygen therapy** in COPD?

A. As follows:

1. PaO_2 < 7.3 κPa (55 mm Hg) irrespective of $PaCO_2$ and FEV_1 < 1.5 L.
2. PaO_2 7.3 to 8 κPa (55 to 60 mm Hg) associated with:
   - Pulmonary hypertension
   - Peripheral edema
   - Nocturnal hypoxemia
   - Secondary polycythemia.
3. Carboxyhemoglobin < 3% (in patient who have stopped smoking).
4. Terminally ill patient of whatever cause with PaO_2 < 7.3 κPa.

Note

Arterial blood gases should be measured in clinically stable patients on optimal medical therapy on at least two occasions, 3 weeks apart.

Q. How to **treat** acute exacerbations?

A. As follows:

- Nebulized bronchodilators like terbutaline, ipratropium bromide.
- IV antibiotic to control infection.
- Oxygen inhalation (24%, 1 to 3 L/min).
- IV hydrocortisone and oral steroid (steroid is only used in acute exacerbations and unlike in asthma, it does not influence the course of chronic bronchitis).

Q. How to **differentiate** between emphysema and chronic bronchitis?

A. As follows:

Topic	Emphysema	Chronic bronchitis
1. Definition	It is the permanent distension of alveoli with destruction of their walls distal to the terminal bronchioles	It is defined as the presence of cough with sputum, not attributable to other causes, on most of the days of at least 3 consecutive months for 2 successive years
2. Age	50 to 75 years	Middle age (45 to 50)
3. Appearance	Pink puffer	Blue bloater
4. Body built	Lean and thin	Normal
5. Dyspnea	Severe	Less or no
6. Pursed lip	Present	Absent
7. Cough	Not a feature	Main feature
8. Sputum	No sputum	Mucoid expectoration
9. Cyanosis	Absent	Prominent
10. Hyperinflation	Common	Uncommon
11. Shape of the chest	Barrel shaped	Normal
12. Examination of the lung	On percussion, hyperresonant lungs with obliteration of liver and cardiac dullness and on auscultation, no rhonchi or wheeze	Percussion is normal. On auscultation, plenty of rhonchi
13. Pulmonary hypertension with cor pulmonale	Late feature	Early feature
14. Respiratory failure	Late	Common
15. Secondary polycythemia	Absent or late	Common
16. Arterial blood gas analysis	Normal or low PaO_2, normal $PaCO_2$	Low PaO_2, high $PaCO_2$
17. Diffusing capacity	Reduced	Normal
18. X-ray chest	Hyperinflated lung field, low flat diaphragm, horizontal ribs, tubular heart, bulla	Normal

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

CHIEF COMPLAINTS

- Cough with sputum for … years
- Breathlessness on exertion for … months.

HISTORY

History of present illness: The patient was alright … years back. Since then, he has been suffering from frequent attack of cough with profuse expectoration of mucoid sputum. Cough is present throughout the day and night, more marked in the morning and also on exposure to cold and dust. It is progressively increasing day by day. He also complains of difficulty in breathing, more marked during moderate to severe exertion, relieved by taking rest. His breathlessness is progressively increasing. There is no history of chest pain, hemoptysis, paroxysmal nocturnal dyspnea. He does not give any history of fever, swelling of the ankle or weight loss. His bowel and bladder habits are normal.

History of past illness: The patient was admitted in the hospital 4 times with severe breathlessness in the last 3 years.

Family history: Nothing contributory.

Personal history: He is a shopkeeper, smokes 20 sticks a day for last 30 years.

Drug history: He used to take tablet aminophylline, salbutamol, ketotifen frequently. Sometimes, he used to take different types of inhalers.

GENERAL EXAMINATION

- The patient is ill looking, dyspneic. There is suprasternal and supraclavicular excavation.
- No anemia, cyanosis, jaundice, edema, clubbing, koilonychia or leukonychia.
- No lymphadenopathy or thyromegaly.
- Pulse: 100/min, high volume.
- BP: 110/60 mm Hg.
- Respiratory rate: 30/min.
- JVP: Not raised.
- (Look at the sputum pot, if available at the bedside).

SYSTEMIC EXAMINATION

Respiratory System

Inspection:

- Shape of the chest: Barrel shaped.
- Movement of the chest: Bilaterally restricted.
- Intercostal space: Full.

Palpation:

- Trachea: Central
- Apex beat: Difficult to localize
- Chest expansion: Reduced
- Vocal fremitus: Normal.

Percussion:
- Percussion note: Hyperresonant
- Area of liver dullness: In the right 7th ICS in midclavicular line
- Area of cardiac dullness: Impaired.

Auscultation:
- Breath sounds: Vesicular with prolonged expiration
- Added sounds: Plenty of rhonchi, in both lung fields, present in both inspiration and expiration
- Vocal resonance: Normal.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 48 years old, shopkeeper, normotensive, nondiabetic, smoker, hailing from …, presented with frequent attack of cough with profuse expectoration of mucoid sputum for … years. Cough is present throughout the day and night, more marked in the morning and also on exposure to cold and dust. It is progressively increasing day by day. He also complains of difficulty in breathing, more marked during moderate to severe exertion, relieved by taking rest. His breathlessness is progressively increasing. There is no history of chest pain, hemoptysis, paroxysmal nocturnal dyspnea. He does not give any history of fever, swelling of the ankle or weight loss. His bowel and bladder habits are normal. He was admitted in the hospital 4 times with severe breathlessness in the last 3 years. He smokes 30 sticks a day for last 35 years. He used to take tablet aminophylline, salbutamol, ketotifen frequently. Sometimes, he used to take different types of inhalers. There is no history of such illness in the family.

On examination – general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is chronic obstructive pulmonary disease

Q. Why it is **COPD?**

A. The patient is a heavy smoker, taking ... cigarettes a day for ... years, there is chronic cough with breathlessness, which is progressively increasing day by day.

Q. What are the **differential diagnoses** of COPD?

A. As follows:
- Chronic severe or persistent bronchial asthma
- Bronchiectasis
- Chronic bronchitis
- Congestive cardiac failure.

Q. Why not this is a case of chronic bronchitis?

A. Because chronic bronchitis is defined as the presence of cough with sputum, not attributable to other causes, on most of the days of at least 3 consecutive months for 2 successive years.

Q. What is the basic **difference** between bronchial asthma and COPD?

A. Bronchial asthma is reversible, but COPD is not fully reversible and it is progressive.

Q. How to **confirm** your diagnosis?

A. By spirometry and reversibility test.

Q. What are the **findings** in spirometry?

A. As follows:

- FEV_1 < 80% predicted
- FEV_1: FVC < 70% predicted
- Bronchodilator reversibility test shows <15% increase in FEV_1 after giving bronchodilator.

Q. What **investigations** should be done in COPD?

A. As follows:

1. Complete blood count (there may be polycythemia and increased PCV due to persistent hypoxemia).
2. Chest X-ray PA view (there may be features of hyperinflation – increased translucency, low flat diaphragm, tubular heart, widening of intercostal space, emphysematous bullae).
3. ECG (usually normal. In cor pulmonale, there may be features of RVH).
4. Echocardiogram (may show features of cor pulmonale).
5. Lung function tests:
   - FEV_1 and FVC are reduced. Ratio of FEV_1: FVC is also reduced (indicates obstructive airway disease)
   - Post bronchodilator FEV_1 < 80% of the predicted value and FEV_1/FVC is < 70%
   - Other tests: Lung volumes may be normal or increased. Gas transfer coefficient of carbon monoxide is low, when significant emphysema is present
6. PEFR (reduced).
7. Blood gas analysis:
   - Often normal at rest
   - PO_2 (reduced)
   - PCO_2 (normal or increased)
   - P^H (acidosis).
8. High resolution CT—assessment of COPD, characters of emphysema, particularly bullae.
9. Sputum examination (if superadded infection).
10. β_1 antitrypsin deficiency—may be done in young, nonsmoker patient with basal emphysema.

BRIEF DISCUSSIONS ABOUT CHORONIC OBSTRUCTIVE PULMONARY DISEASE

Q. What is **COPD?**

A. COPD is characterized by airflow limitation, which is not fully reversible. It is usually progressive, and associated with an abnormal inflammatory response of the lung to noxious particles or gases.

FEV_1< 80% predicted and FEV_1: FVC < 70% predicted. Bronchodilator reversibility test shows <15% increase in FEV_1 after giving bronchodilator.

Q. What are the **mechanisms of airflow limitation** in COPD?

A. As follows:

- Increased mucus production and reduced mucocilliary clearance
- Loss of elastic recoil
- Increased muscle tone
- Pulmonary hyperinflation.

Q. What are the **presentations** of COPD?

A. Usually the patient is above 40 years, male and smoker. There is:

- Chronic cough and sputum production, which is progressively increasing
- Progressive breathlessness
- There may be hemoptysis, edema and morning headache (due to hypercapnia).

Q. What are the systemic features in COPD?

A. Muscular weakness, peripheral edema due to impaired salt and water excretion, weight loss due to altered fat metabolism, increased osteoporosis, increased circulating inflammatory markers.

Q. What are the risk factors or causes of COPD?

A. Multiple factors may be responsible for COPD, such as:

1. Exposure to:
- Smoking (the most common)—active or passive
- Indoor and outdoor air pollution
- Occupation—exposure to dust, fumes, smokes, chemicals, etc. (e.g. coal miners and those who work with cadmium)
- Urban dweller
- Low socioeconomic status
- Low birth weight
- Poor lung growth which may be due to childhood infections or maternal smoking
- Infections—recurrent lung infection, persistent adenovirus in lung tissue, HIV infection is associated with emphysema
- Cannabis smoking (controversial).

2. Host factors:
- Genetic factors—α_1 antitrypsin deficiency
- Airway hyper-reactivity
- More in male and Caucasians
- Biofuel mass.

Q. What organisms are associated with acute exacerbation of COPD?

A. Common organisms: *Haemophilus influenzae* and *Streptococcus pneumoniae*. Other less common organisms are *Moraxella catarrhalis*, *Chlamydia pneumoniae* and *Pseudomonas aeruginosa*.

Q. What are the complications of COPD?

A. As follows:
- Pulmonary hypertension
- Cor pulmonale
- Respiratory failure
- Secondary infection
- Polycythemia.

Q. What are the stages or classification of COPD?

A. According to the GOLD criteria, classification COPD is as follows:

Stage	Spirometry	Symptoms
0. At risk	Normal	Presence of chronic symptoms (cough, sputum production)
I. Mild	$FEV_1/FVC < 70\%$ $FEV_1 \leq 80\%$ predicted	None or mild
II. Moderate	$FEV_1/FVC < 70\%$ $FEV_1 \leq 50\%$, but $< 80\%$ predicted	Mild to moderate symptoms
III. Severe	$FEV_1/FVC < 70\%$ $FEV_1 \leq 30\%$, but $< 50\%$ predicted	Breathlessness on minimal exertion, e.g. dressing
IV. Very severe	$FEV_1/FVC < 70\%$ $FEV_1 < 30\%$ predicted or $FEV_1 < 50\%$ predicted plus chronic respiratory failure	Breathlessness at rest

Q. How to **manage** COPD?

A. As follows:

1. Smoking must be stopped
2. Avoidance of dust, fume, smoke, etc
3. Drug therapy according to the stage:

I: Mild	» Avoid of risk factors, influenza vaccination » Short acting inhaled bronchodilator like β_2 agonist (salbutamol, terbutaline) or anticholinergic (ipratropium) when needed
II: Moderate	Above treatment plus: » Regular treatment with one or more long acting bronchodilator like β_2 agonist (e.g. salmeterol, formeterol) or anticholinergic (tiotropium) when needed » Rehabilitation
III: Severe	Above treatment plus: » Inhaled steroid (fluticasone)
IV: Very severe	Above treatment plus: » Long-term oxygen, if chronic respiratory failure » Surgical treatment, if needed

4. Other therapy:
   - Oxygen, if needed
   - Mucolytic (acetylcysteine)
   - Antibiotic (if infection)
   - Diuretic (if edema)
   - Pulmonary rehabilitation
   - Pneumococcal vaccination.
   - Reduction of obesity.
5. Surgical intervention:
   - Bullectomy: If young patient, large bullae compressing surrounding lung tissue, no generalized emphysema
   - Lung volume reduction surgery (LVRS): Predominant upper lobe emphysema, preserved gas transfer, no evidence of pulmonary hypertension
   - Lung transplantation.

Q. How **domiciliary oxygen** is given? What is the **aim** of the therapy?

A. Oxygen O_2 is given 2 to 4 L/min for 15 hours/day by nasal prongs. The aim is to increase the PaO_2 to at least 8 kPa (60 mm Hg) at sea level during rest or SaO_2 to at least 90% (greater benefit may be seen in patients who receive > 20 hours per day).

Note Regarding air travel:

- Preflight assessment should be done by spirometry and hypoxic challenge test with 15% oxygen. If saturation is maintained >90%, the patient can be allowed to travel. If not, air travel should be avoided or undertaken only with inspired oxygen therapy.
- Sufficient supplementary oxygen should be given during flight to keep the PaO_2 above 50 mm Hg, which is achieved by increasing the flow by 1 to 2 L/min.
- Patient who use to take continuous oxygen at home will require this supplementation.

Q. What is the role of **inhaled steroid** in COPD?

A. Inhaled steroid is recommended for symptomatic patient with moderate to severe COPD and for patients with frequent exacerbations, but not in mild COPD. It reduces the frequency and severity of exacerbation. There is small improvement of FEV_1, but it does not alter the natural history of FEV_1 decline.

Q. What is the role of **oral steroid** in COPD? What are the indications of steroid in COPD?

A. Oral steroid is useful during exacerbation, but maintenance therapy should be avoided.

Indications are:

- Stage III or IV disease
- In stage II if oral steroid trial shows responsiveness
- Severe exacerbations of COPD
- Frequent episodes of exacerbations.

Q. What is the **prognosis** of COPD?

A. Prognosis of COPD is predicted by **BODE** index:

Variable	Points on BODE index			
	0	1	2	3
1. Body mass index	> 21	≤ 21		
2. Obstruction to airflow (FEV_1 % predicted)	≥ 65	50 to 64	36 to 49	≥ 35
3. Dyspnea (MMRC scale)	0 to 1	2	3	4
4. Exercise capacity (metres walked in 6 minutes)	≥ 350	250 to 349	150 to 249	≤ 149

4 years mortality rate for BODE index 0 to 2 is 10%, while that of BODE index 7 to 10 is 80%.

Note

Poor prognostic factors are increasing age (inversely related), fall of FEV_1 over time, weight loss and pulmonary hypertension.

Q. How to manage **acute exacerbation** of COPD (type II respiratory failure)?

A. As follows:

- Oxygen: Continuous low concentration oxygen via Venturi mask to raise $PaO_2 > 8$ κPa (60 mm Hg). Initially 24% or 28% oxygen is given and increased gradually provided $PaCO_2$ does not rise unacceptably. If $PaCO_2$ rises and pH falls below 7.25, artificial ventilation or a respiratory stimulant should be given.
- Bronchodilator nebulized short acting β_2 agonist (e.g. salbutamol) with an anticholinergic agent (e.g. ipratropium).
- Oral prednisolone 30 mg daily for 10 days.
- Antibiotic: Given if infection is suspected.
- Diuretic: If peripheral edema.
- Chest physiotherapy. Secretions should be removed by suction.

- Respiratory support: If above treatment fails or there is tachypnea and acidosis (pH < 7.35). Noninvasive ventilatory technique like BiPAP is used first. CPAP is occasionally needed.
- Respiratory stimulant: Less used. Doxapram 1.5 to 4.0 mg/min by slow IV infusion may be helpful.

Note

Many patients with exacerbation of COPD can be managed at home with increased bronchodilator, short course of oral steroid and antibiotic.

Indications of hospitalization are:

- Severe symptoms or acute worsening that fail to respond to outpatient management
- Presence of cyanosis
- Peripheral edema
- Alteration of consciousness
- Co-morbidity and poor social circumstances.

Q. Why **low concentration O_2** given in COPD? Or what happens when high flow O_2 given**?**

A. In COPD, the patient is dependent on hypoxic drive for respiration. High flow oxygen blunts the chemoresponsiveness of the respiratory center in the medulla (part of the brainstem) and thus aggravates respiratory failure (Type 2 respiratory failure). To avoid this, low flow oxygen is given.

Q. What are the **discharge criteria** of COPD patient?

A. As follows:

- The patient should be clinically stable and no parenteral therapy for 24 hours
- Inhaled bronchodilators are required less than 4 hourly
- Oxygen delivery has ceased for 24 hours
- The patient is able to eat and sleep without significant episodes of dyspnea
- The patient or caretaker understands and is able to administer medications
- Follow up and home care arrangements (As for example home oxygen, home care, Meals on Wheels, community nurse, allied health, GP, specialist) have been completed
- The patient is ambulating safely and independently, and performing activities of daily living.

CHRONIC BRONCHITIS WITH EMPHYSEMA

CHIEF COMPLAINTS

- Cough with sputum for … years
- Breathlessness on exertion for … months.

HISTORY

History of present illness: The patient was alright … years back. Since then, he has been suffering from frequent cough with profuse expectoration of mucoid sputum. Initially, cough was present during winter only and persisted for 2 to 3 months. For the last … months, it is present during the day and night, more marked in the morning and also on exposure to cold and dust. He also complains of difficulty in breathing, which was more marked during moderate to severe exertion. But for the last ... months, breathlessness is more even during mild exertion, such as undressing, going to the toilet, climbing upstairs, etc. There is no history of chest pain, hemoptysis, and paroxysmal nocturnal dyspnea. He does not give any history of fever, swelling of the ankle or weight loss. His bowel and bladder habits are normal.

History of past illness: He is suffering from chronic bronchitis for the last 10 years but non-hypertensive, nondiabetic.

Family history: There is no such illness in his family.

Personal history: He was a previous smoker, but stopped for the last 2 years. He works in a jute mill.

Drug history: He used to take tablet aminophylline, salbutamol, etc. Also he took some inhalers, the name of which he cannot mention.

GENERAL EXAMINATION

- The patient is emaciated and dyspneic with pursing of lips.
- There is suprasternal and supraclavicular recession with prominent accessory muscles of respiration.
- No anaemia, cyanosis, edema, clubbing, koilonychia, leukonychia.
- Pulse:124/min.
- BP: 120/75 mm Hg.
- Respiratory rate: 30/min.

SYSTEMIC EXAMINATION

Respiratory System

Inspection:

- Chest is barrel-shaped
- Indrawing of the lower intercostal space on inspiration (due to low flat diaphragm, called Harrison's sulcus).

Palpation:

- Trachea is central, tracheal tug (descent of trachea during inspiration) is present.
  - Cricosternal distance (distance between suprasternal notch and cricoid cartilage): Reduced (normally 3 fingers or more)
  - Apex beat is not felt
  - Chest expansion: Reduced (tell in centimeter)
  - Vocal fremitus: Reduced in both sides.

Percussion:
- Hyper-resonance in both the lung fields.
- Obliteration of the liver and cardiac dullness (liver dullness may be lowered down).

Auscultation:
- Breath sound – Diminished and vesicular with prolonged expiration.
- Plenty of rhonchi are present in both lung fields.
- Vocal resonance—reduced.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 49 years old, jute mill worker for 25 years, normotensive, nondiabetic, ex-smoker, hailing from …, presented with frequent cough with profuse expectoration of mucoid sputum for ... years. Initially, cough was present during winter only and persisted for 2 to 3 months. For the last … month, it is present during the day and night, more marked in the morning and also on exposure to cold and dust. He also complains of difficulty in breathing, which was more marked during moderate to severe exertion. But for the ... months, breathlessness is more even during mild exertion such as undressing, going to the toilet, climbing upstairs etc. There is no history of chest pain, haemoptysis, paroxysmal nocturnal dyspnoea. He does not give any history of fever, swelling of the ankle or weight loss. His bowel and bladder habits are normal. He used to take tablet aminophylline, salbutamol etc. Also he took some inhalers, the name of which he cannot mention. He was a previous smoker, but stopped for the last 2 years. There is no history of similar illness in his family.

On examination – general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is chronic bronchitis with emphysema

Q. What are your **differential diagnoses?**

A. As follows:
- COPD
- Bronchial asthma
- Cardiac failure.

Q. Why not COPD?

A. Because, COPD is characterized by airflow limitation, which is not fully reversible. It is usually progressive, and associated with an abnormal inflammatory response of the lung to noxious particles or gases.

Q. Why not CCF?

A. Because, in CCF, there should be engorged and pulsatile neck veins, enlarged tender liver, dependent pitting oedema.

Q. What **investigations** should be done in emphysema?

A. As follows**:**

1. X-ray chest P/A view (shows features of emphysema):
   - Increased translucency of both lung fields with loss of peripheral vascular markings
   - Low flat diaphragm
   - Tubular heart
   - Widening of intercostal space and ribs appear horizontal
   - Bulla may be present (which is pathognomonic)
   - Prominent pulmonary arterial shadow in both hilum (due to pulmonary hypertension).

2. Lung function tests:
   - FEV_1 and FVC are reduced. Ratio of FEV_1: FVC is reduced (obstructive type)
   - Post-bronchodilator FEV_1 is <80% predicted, and ratio of FEV1:FVC is <70% predicted
   - PEFR: reduced
   - Lung volume with increased TLC and RV.
3. Arterial blood gas analysis:
   - Low PCO_2 (due to hyperventilation)
   - Low PO_2
   - Impaired gas transfer of CO.
4. Other investigations:
   - TC, DC, Hb%, ESR (polycythemia may be present).
   - CT scan of the chest, especially HRCT (high resolution CT)—highly suggestive.
   - To confirm—biopsy of the lung tissue (not a routine test).
   - In young patient, serum level of α_1 antitrypsin may be done.
   - ECG may show tall P, RVH, RAD in patient with corpulmonale.
   - Echocardiography.

Q. What is the **definitive diagnosis** of emphysema?

A. Histopathological.

RELATED QUESTIONS AND ANSWERS

Q. What is emphysema?

A. It is the permanent distension of alveoli with destruction of their walls distal to the terminal bronchioles.

Q. What are the **presentations** of emphysema?

A. Breathlessness on exertion and minimum cough with lip pursing.

Q. What are the **types** of emphysema?

A. Four types:
- Centriacinar: Involves the proximal part of acini, limited to respiratory bronchiole with relatively less change in acinus.
- Panacinar: All the alveoli and alveolar ducts in acinus are involved, both central and peripheral portion. It occurs mostly in α_1-antitrypsin deficiency.
- Paraseptal: Along the septa, blood vessels and pleura.
- Scar or irregular emphysema: Scarring and damage affecting the lung parenchyma without involving acinus structure.

Q. What are the **causes** of emphysema?

A. As follows:
- Smoking
- Cold, dust (causes centrilobular emphysema)
- α_1-antitrypsin deficiency
- Macleod's syndrome (unilateral emphysema).

Q. How **smoking** cause emphysema?

A. Certain mechanisms are responsible:
- Prolonged smoking causes inflammation in airways, release of oxidants and proteinase from inflammatory cells, which are responsible for irreparable damage to the supporting connective tissue of alveolar septa
- There is increased proteinase synthesis and inactivation of anti-proteinase due to enzymes responsible for inactivating anti-proteinase
- Imbalance between proteinase and anti-proteinase.

Q. Why **lip pursing** is present in emphysema?

A. By this in expiration through partly closed lips, there is increased end-expiratory pressure that keeps airway open, helping to minimize air trapping.

Q. What are the **complications** of emphysema?

A. As follows:
- Pulmonary hypertension
- Cor pulmonale
- Respiratory failure type 1
- Bullae, which may rupture causing pneumothorax
- Secondary infection
- Polycythemia.

Q. What are the **signs** of emphysema**?**

A. As follows:
- Patient is dyspneic with lip pursing
- Barrel shaped chest
- Suprasternal and supraclavicular excavation during inspiration
- Prominent sternomastoid and scalene muscles
- Tracheal tug
- Reduced cricosternal distance (length of trachea above suprasternal notch)
- Indrawing of lower intercostal space during inspiration
- Horizontal ribs with wide intercostal spaces
- Wide subcostal angle
- Obliteration of liver and cardiac dullness.

Q. How to **treat** emphysema?

A. As follows:
1. Smoking must be stopped.
2. For breathlessness:
   - Inhaled salbutamol (200 mg 4 to 6 hourly) or ipratropium (40 mg 4 hourly) or tiotropium (18 mg daily) or oxitropium (200 mg BD)
   - If no response, inhaled corticosteroid beclomethasone (400 ìgm BD)
   - In severe case, oral prednisolone 30 mg for 2 weeks, followed by maintenance dose.
3. Antibiotic, if secondary infection.
4. In chronic cough: Mucolytic therapy (acetylcysteine 200 mg 8 hourly orally for 8 weeks).
5. Domiciliary O_2 may be given
6. Vaccination, such as annual influenza vaccine, 5 yearly pneumococcal vaccine and *Haemophilus influenzae* vaccine may be given.
7. Other treatment:
   - α_1-antitrypsin in case of deficiency
   - Lung transplantation in young patient
   - Surgical intervention (if large bullae)
   - Weight reduction, if obese
   - Exercise.

Q. What is bullae? What are the **causes**? What is the **treatment**?

A. It is the thinwalled air space produced by rupture of alveolar walls. Bullae may be single or multiple, large or small, and usually associated with emphysema. It is usually situated subpleurally. Rupture may lead to pneumothorax. Large bullae may compress the lung tissue and impair lung function. Causes of bullae are:

- Emphysema
- Congenital (rare).

Treatment:

- Small bullae: No treatment, treatment of primary cause
- Large bullae with impaired lung function requires surgical ablation of bullae.

Q. What is **pink puffer** and **blue bloater**?

A. As follows:

Pink puffer:

- The patient is not cyanosed (pink), but dyspneic with lip pursing (puffer). No edema
- Usually lean and thin
- It is found in emphysema, commonly panacinar, age 50 to 75 years
- Usually there is no cor pulmonale
- Exertional dyspnea is the main feature, and cough less common
- Arterial PO_2 and PCO_2 are relatively normal.

Blue bloater:

- The patient is cyanosed (blue) and edematous (bloater). But not dyspneic (or mild dyspnea)
- It is found in chronic bronchitis, age 40 to 45 years. Edema is due to cor pulmonale
- Cough with sputum is the main feature, dyspnoea is less common
- Pulmonary hypertension, right ventricular hypertrophy, cor pulmonale and secondary polycythemia may develop (patient may appear plethoric)
- There is marked arterial hypoxemia and hypercapnia (low PO_2 and increased PCO_2).

Q. What are the **indications** of long term domiciliary (home) oxygen therapy?

A. As follows:

- Severe hypoxemic patients, $PO_2 < 7.3$ κPa (55 mm Hg) or $SaO_2d < 88\%$, with or without hypercapnia, FEV1 < 1.5 L
- PO_2 between 7.3 to 8.0 κPa (55 to 60 mm Hg) or SaO_2 at 89% with evidence of cor pulmonale, CCF or polycythemia (Hct >55%).

Note

Oxygen is given 2 to 4 L/min, 15 hours/day. The patient must stop smoking.

Q. What is **Macleod's syndrome?**

A. It is a type of unilateral emphysema due to childhood bronchitis or bronchiolitis, resulting in subsequent impairment of alveolar growth. It is a rare disease (also called **Swyer-James syndrome**).

Q. What are the causes of **dyspnea on exertion?**

A. As follows:

- COPD
- Bronchial asthma
- DPLD (Interstitial lung disease)
- LVF
- Valvular diseases of the heart
- Anemia.

CHRONIC BRONCHITIS WITH COR PULMONALE

CHIEF COMPLAINTS

- Cough with sputum for … months.
- Breathlessness for … months.
- Swelling of both legs for … months.

HISTORY

History of present illness: The patient was alright … months back. Since then, he has been suffering from cough, which is more marked in the morning. There is expectoration of copious amount of sputum, which is mucoid or mucopurulent in nature but not mixed with blood. The patient mentioned that he has been experiencing episodic attack of such illness for almost 10 years, mostly during the winter seasons and each episode persisted for 3 to 4 months. Along with cough, he is also experiencing breathlessness which was initially associated with moderate to severe exertion, but now with even mild exertion. There is no history of paroxysmal nocturnal dyspnea or orthopnea. For … months, he noticed gradual swelling of his feet, more marked with prolonged standing and disappears on waking in the morning. He also complains of upper abdominal discomfort associated with loss of appetite. There is no history of fever, burning micturition, yellow coloration of urine or sclera, abdominal swelling and weight loss. His bowel and bladder habits are normal.

History of past illness: He has been suffering from chronic bronchitis for the last ... year.

Family history: There is no such illness in his family.

Personal history: He smokes 20 sticks per day for last 15 years, but nonalcoholic

Drug history: He took tablet aminophylline, salbutamol, occasional cough syrup and sometimes inhalers.

GENERAL EXAMINATION

- The patient looks anxious, emaciated
- Central cyanosis: Present
- Bilateral pitting pedal edema: Present
- No anemia, jaundice, clubbing, koilonychia or leukonychia
- No lymphadenopathy or thyromegaly
- Pulse: 120/min, bounding pulse
- BP: 120/70 mm Hg
- Respiratory rate: 30/min
- JVP: Raised with prominent "a" wave.

SYSYEMIC EXAMINATION

Respiratory System

Inspection:

- Shape of the chest: Barrel shaped
- Movement of the chest: Bilaterally restricted
- Suprasternal and intercostal recession present.

Palpation:
- Chest expansion: Reduced
- Trachea: Central
- Tracheal tug: Present
- Apex beat: Difficult to localize
- Vocal fremitus: Reduced.

Percussion:
- Percussion note: Hyperresonant in both sides of chest
- Area of liver dullness: In the right 7th ICS in midclavicular line
- Area of cardiac dullness: Impaired.

Auscultation:
- Breath sound: Vesicular with prolonged expiration
- Added sound: Plenty of rhonchi, in both lung fields, both in inspiration and expiration. There are a few coarse crepitations present
- Vocal resonance: Reduced.

SYSTEMIC EXAMINATION

Cardiovascular System

- **JVP:** Engorged and pulsatile JVP, prominent 'a' wave
- **Pulse:** 120/min
- **BP:** 120/70 mm Hg.

Examination of precordium:

Inspection:
- Visible epigastric impulse.

Palpation:
- Apex beat: In left 5th intercostal space ... cm from midline.
- Thrill: Absent
- Palpable P_2, left parasternal lift and epigastric pulsation: Present.

Percussion: area of cardiac dullness is impaired.

Auscultation:
- 1st heart sound: Normal in all the areas
- 2nd heart sound: P_2 is loud in pulmonary area.

Abdomen

Inspection:
- Visible peristalsis.

Palpation:
- Liver is enlarged 4 cm from right costal margin in right midclavicular line, soft, tender, margin is sharp, surface is smooth, no hepatic bruit
- Spleen is not palpable.

Percussion:
- No abnormality.

Auscultation:
- Bowel sound present
- No hepatic bruit.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 52 years old, businessman, normotensive, nondiabetic, smoker, hailing from …, presented with cough for … months, which is more marked in the morning. There is expectoration of copious amount of sputum, which is mucoid or mucopurulent in nature but not mixed with blood. The patient mentioned that he has been experiencing episodic attack of such illness for almost 10 years, mostly during the winter seasons and each episode persisted for 3 to 4 months. Along with cough, he is also experiencing breathlessness which was initially associated with moderate to severe exertion, but now with even mild exertion. There is no history of paroxysmal nocturnal dyspnea or orthopnea. For … months, he noticed gradual swelling of his feet, more marked with prolonged standing and disappears on waking in the morning. He also complains of upper abdominal discomfort associated with loss of appetite. There is no history of fever, burning micturition, yellow coloration of urine or sclera, abdominal swelling and weight loss. His bowel and bladder habits are normal. He smokes 20 sticks a day for last 15 years. He took tablet aminophylline, salbutamol, occasional cough syrup and sometimes inhalers. There is no such illness in his family.

On examination – general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is chronic bronchitis with cor pulmonale.

Q. What are the **differential diagnoses?**

A. As follows
- CCF
- CLD
- Nephrotic syndrome.

Q. Why **cor pulmonale**?

A. Because he has been suffering from chronic bronchitis for the last ... years, and there are features of right sided heart failure. So his failure is secondary to the disease of the lung, which indicates cor pulmonale.

Q. Why not **CLD**?

A. In the history, there is no history of jaundice or other liver disease and on physical examination there are no stigmata of CLD.

Q. Why not **nephrotic syndrome**?

A. Nephrotic syndrome is characterized by generalized edema, massive proteinuria and hypoalbuminemia. In this case, there is no history of generalized edema. In contrast, there is history of chronic bronchitis and also there are features of right sided heart failure, which are not consistent with nephrotic syndrome.

Q. What **investigations** are done in cor pulmonale?

A. As follows:
- X-ray chest PA view: May show right ventricular enlargement and right atrial dilatation. Pulmonary arteries are prominent, peripheral lung fields are oligemic
- ECG: May show RVH and right atrial hypertrophy
- Echocardiogram: Shows right ventricular dilatation and/or hypertrophy
- Lung function tests
- Others: CBC, arterial blood gas analysis, CT scan of chest, pulmonary artery wedge pressure.

RELATED QUESTIONS AND ANSWERS

Q. What is **cor pulmonale**?

A. Cor pulmonale may be defined as "right ventricular hypertrophy or dilatation with or without right sided heart failure due to causes of lung parenchyma, pulmonary vasculature or chest wall".

Q. What are the **types** of cor pulmonale?

A. Acute and chronic.

- Acute: It occurs following massive pulmonary embolism with acute pulmonary hypertension causing right ventricular dilatation and failure (no RVH). May occur in ARDS.
- Chronic: It is defined as "right ventricular hypertrophy or dilatation with or without right sided heart failure due to causes of lung parenchyma, pulmonary vasculature or chest wall".

Q. What are the **causes** of chronic cor pulmonale?

A. As follows:

1. Respiratory disorders:
   - Obstructive: COPD or chronic bronchitis with emphysema, chronic persistent asthma
   - Restrictive: DPLD (interstitial lung disease).
2. Pulmonary vascular disorders:
   - Primary pulmonary hypertension
   - Vasculitis of the small pulmonary arteries.
3. Chest wall or bony abnormality: kyphoscoliosis, ankylosing spondylitis, obesity (Pickwickian syndrome).

Q. What are the **signs of pulmonary hypertension** (PH)?

A. Signs of pulmonary hypertension are:

- Low volume pulse
- JVP is raised
- Prominent 'a' wave in JVP
- Left parasternal heave (indicates RVH)
- Palpable P_2
- Loud P_2 on auscultation
- Epigastric pulsation (indicates RVH)
- Early diastolic murmur (Graham Steel murmur due to pulmonary regurgitation).

Q. What are the **signs** of chronic cor pulmonale?

A. Signs of primary disease like COPD, emphysema, etc. **plus**:

1. Without failure:
   - Signs of pulmonary hypertension and RVH (palpable P2, left parasternal heave, epigastric pulsation).
2. With failure:
   - Engorged and pulsatile neck vein
   - Enlarged tender liver
   - Dependent edema (pitting, pedal edema).

Q. What are the causes of **right heart failure**?

A. As follows:

- Secondary to left sided failure (the most common cause)
- Secondary to mitral stenosis
- Cor pulmonale

- Myocardial infarction
- Pulmonary valvular disease (PS, PR)
- Tricuspid regurgitation
- Eisenmenger's syndrome (pulmonary hypertension with reversal of shunt in ASD, VSD, PDA)
- Cardiomyopathy
- Chronic constrictive pericarditis.

Q. How to **manage** cor pulmonaly?

A. As follows:

1. Treatment of cardiac failure:
   - Diuretic (frusemide)
   - Fluid and salt restriction
   - Vasodilator drug
   - Digoxin is some cases.
2. Treatment of the underlying cause, as for example COPD.
3. Sildenofil in primary pulmonary hypertension.
4. Venesection: If hematocrit is more than 55%.
5. Domiciliary oxygen.

Q. What is the **prognosis** of cor pulmonale?

A. Approximately 50% patients die within 5 years.

Q. What is **Pack-year**?

A. It is a way to measure the amount a person has smoked over a long period of time. It is calculated by multiplying the number of packs of cigarettes smoked per day by the number of years the person has smoked.

For example, 1 pack year is equal to smoking 20 cigarettes (1 pack) per day for 1 year, or 40 cigarettes per day for half a year, and so on.

One pack year equals 365 packs of cigarettes.

BRONCHIECTASIS

CHIEF COMPLAINTS

- Cough with copious sputum for … months
- Occasional hemoptysis for … months
- Weight loss, weakness and malaise for … months.

HISTORY

History of present illness: The patient was alright … months back. Since then, he has been suffering from frequent cough with profuse expectoration of mucoid sputum, which is more marked in the morning after waking from sleep. Occasionally, the sputum is purulent or yellowish and foul smelling, relieved after taking antibiotics. The patient also noticed small amount of blood occasionally mixed with sputum. For the last ... months, he also complains of loss of about 5 kg body weight, weakness, malaise, occasional fever and night sweats. There is no history of chest pain, breathlessness or swelling of the ankle. His bowel and bladder habits are normal.

History of past illness: He was suffering from measles at the age of 6 and also from recurrent chest infection for the last 2 years. There is no history of whooping cough, pulmonary TB or foreign body impaction.

Family history: There is no family history of such illness.

Personal history: He smokes about 30 sticks a day for last 10 years, but nonalcoholic.

Drug history: He used to take cough syrup frequently, treated with antibiotics several times due to chest infection.

GENERAL EXAMINATION

- The Patient is slightly emaciated
- There is generalized clubbing involving both toes and fingers, but no hypertrophic osteoarthropathy
- No anemia, jaundice, cyanosis, edema, koilonychia or leukonychia
- No thyromegaly or lymphadenopathy
- Pulse: 88/min
- BP: 120/75 mm Hg
- Respiratory rate: 30/min
- (Examination of the sputum cup: Always look at the cup at the side of the patient, if any).

SYSTEMIC EXAMINATION

Respiratory System

Inspection:

- Chest movement slightly restricted (mention where). Or, no abnormality.

Palpation:

- Trachea: Central
- Apex beat: In left 5th intercostal space 9 cm from the midsternal line, normal in character
- Vocal fremitus: Slightly increased on both base
- Chest expansion: Normal.

Percussion:
- Percussion note: Normal
- Liver and cardiac dullness: In normal area.

Auscultation:
- Breath sound: Normal vesicular (may be bronchial over the involved area).
- There are multiple coarse crepitations on the base of both lungs, both in inspiration and expiration, reduced (or disappeared) after coughing.
- Vocal resonance: Slightly increased (mention where).

Other systemic examination reveals no abnormalities.

SALIENT FEATURES

Mr. …, 28 years old, day laborer, normotensive, nondiabetic, smoker, hailing from …, presented with frequent cough with profuse expectoration of mucoid sputum for ... months. It is more marked in the morning after waking from sleep. Occasionally, the sputum is purulent or yellowish and foul smelling, relieved after taking antibiotics. The patient also noticed small amount of blood occasionally mixed with sputum. For the last ... months, he also complains of loss of about 5 kg body weight, weakness, malaise, occasional fever and night sweating. There is no history of chest pain, breathlessness or swelling of the ankle. His bowel and bladder habits are normal. There is history of measles during childhood. He also gives history of recurrent chest infection for the last 2 years. There is no history of whooping cough, pulmonary TB or foreign body impaction. There is no family history suggestive of such illness. He smokes about 30 sticks a day for last 10 years but nonalcoholic. He used to take cough syrup frequently, treated with antibiotics several times due to chest infection.

On examination – general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is bilateral bronchiectasis.

Note

All the above signs may be on the left or right side. Then the diagnosis will be left or right sided bronchiectasis.

Q. What are your **differential diagnoses?**

A. As follows:
- DPLD (IPF)
- Pulmonary TB.

Q. Why it is bronchiectasis**?**

A. The patient is complaining of cough with profuse expectoration of sputum, more marked in the morning after waking up from sleep. On examination, there are generalized clubbing and bilateral basal coarse crepitations, altered by coughing. All are highly suggestive of bronchiectasis.

Q. Why not IPF?

A. In such case, usually there is history of persistent cough may or may not be with profuse expectoration, progressively increasing breathlessness or exertional dyspnea. There are bibasal fine late inspiratory crepitation (like unfastening of Velcro).

Q. What **investigations** do you suggest in bronchiectasis?

A. As follows:

1. Chest X-ray PA view (may be normal). There may be:
- Ring with clear centre (like honeycomb)
- Ring with or without fluid level, may be multiple (cystic bronchiectasis)
- Linear streaks (tram line)
- Thick bronchi, signet ring or patchy opacity.

2. High-resolution CT scan: Definitive (preferred investigation).

3. Others:
- CBC with ESR (may be neutrophilic leucocytosis)
- X-ray PNS (in Kartagener's syndrome)
- Lung function tests (obstructive type usually, may be restrictive in advanced case)
- Sputum for Gram staining, C/S, AFB, malignant cell (mention if necessary according to the history)
- Sometimes bronchoscopy to locate the site of obstruction
- Aspergillus precipitin antibody or skin prick test (if ABPA is suspected)
- Serum immunoglobulin: If hypogammaglobulinemia is suspected (10% of adults with bronchiectasis have antibody deficiency, mainly IgA)
- Sweat test for sodium and chloride content: If cystic fibrosis is suspected (sweat chloride content > 60 mEq/L is suggestive of cystic fibrosis)
- Mucociliary clearance (nasal clearance of saccharin): Normally less than 30 minutes. If more, it indicates ciliary dysfunction
- Urine for proteinuria (if amyloidosis is suspected)
- USG of whole abdomen (if situs inversus is suspected).

Q. If a patient with bronchiectasis develops **nephrotic syndrome** (or urine shows proteinuria), what is the likely diagnosis?

A. Amyloidosis (in amyloidosis, there may be splenomegaly). In long standing bronchiectasis, amyloidosis may occur as a complication.

Q. What is the **role of CT scan** in the diagnosis of bronchiectasis?

A. Conventional CT scan has sensitivity of 60 to 80% while high resolution CT scan has a sensitivity of more than 90% (previously bronchography was done).

Q. What is the **difference** between standard CT scan and HRCT?

A. In standard CT scan, the resolution is 10 mm thick. But in HRCT, resolution is 1 to 2 mm thick.

RELATED QUESTIONS AND ANSWERS

Q. What is **bronchiectasis** and what are the **causes** of it?

A. It is the abnormal, permanent dilatation of one or more bronchi with destruction of bronchial wall proximal to the terminal bronchiole. Causes are:

1. Congenital or hereditary:
- Cystic fibrosis
- Kartagener's syndrome (triad of bronchiectasis, dextrocardia and sinusitis or frontal sinus agenesis)
- Primary ciliary dyskinesia (including immotile ciliary syndrome)
- Hypogammaglobulinemia (of IgA and IgG. It causes recurrent infection and bronchiectasis)
- Yellow nail syndrome

- Young's syndrome (obstructive azoospermia and chronic sinopulmonary infection, thought to be due to mercury intoxication)
- Sequestrate segment of lung.

2. Acquired:
   - In children, pneumonia complicating measles, whooping cough, primary TB and foreign body
   - In adults, bronchial neoplasm, pulmonary TB, recurrent aspiration or suppurative pneumonia
   - Allergic bronchopulmonary aspergillosis (causes proximal bronchiectasis)

Note

In children, post-measles or whooping cough are commonly associated with bronchiectasis. In adult, post-tubercular bronchiectasis is the common one.

Q. What are the **types** of bronchiectasis?

A. Three types:
- Saccular or cystic (more severe form).
- Cylindrical.
- Fusiform.

Q. What is the **most common site** of bronchiectasis?

A. Left lower lobe and lingula.

Q. What are the **presentations** of bronchiectasis?

A. Cough with profuse expectoration of sputum, usually more marked in the morning after waking from sleep. Occasionally, hemoptysis and breathlessness in advance cases. Features of secondary infection may be present.

Q. What are the **typical signs of bronchiectasis?**

A. On general examination, there is generalized clubbing. On examination of the chest, there are coarse crepitations that reduce or disappear after coughing. The signs are usually better found on the back of the chest and are mostly basal.

Q. Why **hemoptysis?**

A. It is due to bronchial wall hypertrophy, hence mucosa becomes friable, slough out, capillary opens and bleeding occurs. Erosion of hypertrophic bronchial artery may result in massive hemoptysis.

Q. What is **dry bronchiectasis** (bronchiectasis sicca)?

A. It is a type of bronchiectasis in which dry cough is associated with intermittent episodes of hemoptysis. It may be massive, even life-threatening as bleeding is from bronchial vessels with systemic pressure. Common in patient with granulomatous infection, especially TB and usually involves upper lobe.

Q. What are the **characteristics of sputum** in bronchiectasis?

A. If the sputum is kept in a bottle, there are three layers:
- Lower sediment (epithelial debris and bacteria) layer
- Middle thick or liquid layer
- Upper frothy layer.

Q. What are the **causes** of basal crepitations?

A. As follows:

1. Unilateral basal crepitation:

- Unilateral bronchiectasis
- Resolution stage of pneumonia
- Lung abscess
- Localized fibrosis of lung.

2. Bilateral basal crepitation:
   - Bilateral bronchiectasis
   - IPF (fibrosing alveolitis or ILD)
   - Pulmonary edema.
3. Causes of bilateral crepitation with clubbing:
   - Bilateral bronchiectasis
   - IPF (fibrosing alveolitis or ILD).

Q. What is **post-tussive** crepitation? What is its **significance?**

A. Crepitation which appears after cough is called posttussive crepitation. It is usually at the apex, indicates TB.

Q. What **abnormalities** may be associated with bronchiectasis?

A. As follows:

- Situs inversus or dextrocardia and frontal sinusitis or agenesis (Kartagener's syndrome)
- Obstructive azoospermia and chronic sinopulmonary infection (Young's syndrome).

Q. What are the **complications** of bronchiectasis?

A. As follows:

- Secondary infection (pneumonia and pleurisy), common organisms are *Staphylococcus aureus*, *Haemophilus influenzae* and *Pseudomonas aeruginosa*
- Lung abscess
- Pleural effusion, empyema or pneumothorax
- Pulmonary hypertension and cor pulmonale
- Respiratory failure
- Amyloidosis (commonly involving spleen or kidney) in long standing case
- Brain abscess (metastatic cerebral abscess)
- Aspergiloma in the bronchiectatic cavity.

Q. How will you **treat** bronchiectasis?

A. As follows:

- Postural drainage, keeping the affected part remaining up and percussion over it. It is done for 5 to 10 minutes, once or twice daily
- Antibiotic, if infection
- Chest physiotherapy
- Surgery (lobectomy)
- Bronchodilator drugs. Also, nebulized salbutamol may be used in asthma, COPD, cystic fibrosis and ABPA
- Inhaled or oral steroid can decrease the rate of progression. Also, helpful in ABPA
- In bilateral extensive bronchiectasis, lung transplantation is required.

Indications of surgery: Usually in young patient. Indications are –

- Unilateral and localized to a single lobe or segment
- Severe and recurrent hemoptysis.

PLEURAL EFFUSION (TUBERCULAR)

CHIEF COMPLAINTS

- Cough with slight expectoration for … weeks
- Breathlessness for … days
- Fever for … days
- Weight loss for … days.

HISTORY

History of present illness: According to the statement of the patient, he was alright … weeks back. Since then, he has been suffering from frequent cough, which is present throughout day and night. The cough is usually dry with occasional slight expectoration of mucoid sputum, but no hemoptysis. He is also complaining of breathlessness, which is more marked during moderate to severe exertion, but there is no history of orthopnea or paroxysmal nocturnal dyspnea. The patient also complains of low grade continued fever for … days, more marked in the evening and associated with night sweats. During this period, he lost about 15 kg of body weight. There is no history of chest pain, joint pain or swelling, skin rash or any contact with patient with pulmonary TB. His bowel and bladder habits are normal.

History of past illness

Family history

Personal history

Socioeconomic history: Mention according to the patient's statement.

GENERAL EXAMINATION

- The patient is ill-looking and emaciated
- Mildly anemic
- No jaundice, cyanosis, clubbing, edema, koilonychia or leukonychia
- No lymphadenopathy or thyromegaly
- Pulse: 100/min
- BP: 130/75 mm Hg
- Temperature: 100ºF
- Respiratory rate: 24/min.

SYSTEMIC EXAMINATION

Respiratory System: (Supposing Right Sided)

Inspection:

- Movement is restricted on lower part of right side of the chest with fullness of intercostal spaces
- (Mention, if any puncture mark, gauze and tape indicating aspiration of pleural fluid).

Palpation:

- Trachea is shifted to the left side

- Apex is shifted to the left (in 6th intercostal space in the anterior axillary line), normal in character
- Vocal fremitus is reduced in right lower chest up to … ICS (tell where)
- Chest expansion is restricted over the right lower chest.

Percussion:

- There is stony dullness in the right lower chest up to … ICS (tell where).

Auscultation:

- Breath sound—diminished (or absent) in the right lower chest
- Vocal resonance—diminished (or absent) in the right lower part of chest
- No added sound.

Note Just above the upper level of effusion, the following findings may be present (mention, if any)

- Bronchial sound
- Increased vocal resonance
- Whispering pectoriloquy
- Pleural rub.

Examination of the other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 30 years, rickshawpuller, normotensive, nondiabetic, smoker, hailing from …, presented with frequent cough for … weeks, which is present throughout day and night. The cough is usually dry with occasional slight expectoration of mucoid sputum, but no hemoptysis. He is also complaining of breathlessness, which is more marked during moderate to severe exertion but there is no history of orthopnea or paroxysmal nocturnal dyspnea. The patient also complains of low grade continued fever for … days, more marked in the evening and associated with night sweats. During this period, he lost about 15 kg of body weight. There is no history of chest pain, joint pain or swelling, skin rash or any contact with patient with pulmonary TB. His bowel and bladder habits are normal. There is no history of such illness in his family.

He smokes 30 to 40 sticks per day for 15 years. He was treated by local physicians with antibiotic and paracetamol without any response.

On examination – general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is right sided pleural effusion.

Q. What is the **likely cause** of pleural effusion?

A. This is more likely to be tubercular, because:

- In the history, there is low grade fever with evening rise and night sweating
- Marked weight loss
- Cough with slight mucoid sputum.

Q. What may be the **other causes** in this case?

A. This may be due to:

- Post-pneumonic
- Lymphoma
- SLE (in female).

Q. Why not **bronchial carcinoma**?

A. The patient is young, bronchial carcinoma is less common (but he is a heavy smoker for 15 years, so carcinoma should be excluded.)

Q. Why not **thickened pleura?**

A. In this case, there is history of breathlessness, weight loss and fever which are not present in thickened pleura. Also, on examination, there is mediastinal shifting with stony dullness on the affected side. These are not found in thickened pleura.

Q. Why not **consolidation?**

A. There is stony dullness and reduced breath sound and vocal resonance in the affected area along with mediastinal shifting. These are against consolidation (In consolidation, there is woody dullness, bronchial breath sound, increased vocal resonance and no shifting of the mediastinum).

Q. Why not **collapse?**

A. In case of collapse, the apex beat and trachea will be shifted to the same side. In addition, if there is collapse with patent bronchus, there will be bronchial breath sound and increased vocal resonance.

Q. Why not **pneumothorax?**

A. In pneumothorax, there is hyper-resonance on percussion.

Q. What **investigations** do you suggest?

A. As follows:

1. X-ray chest P/A view
2. Hb%, TC, DC, ESR (high ESR in TB, leukocytosis in pneumonia)
3. Mantoux test (MT)
4. Aspiration of pleural fluid for analysis-
   - Physical appearance (straw colored, serous, hemorrhagic, chylous)
   - Gram-staining, cytology (routine) and exfoliative cytology (malignant cells)
   - Biochemistry (protein and sugar), also a simultaneous blood sugar, protein and lactate dehydrogenase (LDH) may be done
   - ADA (high in tuberculosis)
   - Culture and sensitivity (C/S)
   - AFB and mycobacterial C/S
5. Pleural biopsy by Abram's or Cope's needle
6. Other investigation of pleural fluid (according to suspicion of cause):
   - Cholesterol, LDH and rheumatoid factor (in rheumatoid arthritis)
   - Amylase (high in acute pancreatitis, esophageal rupture, malignancy)
   - Trigycerides (in chylothorax)
7. Sputum (if present) for Gram staining, C/S, AFB, mycobacterial C/S and malignant cells (exfoliative cytology)
8. If palpable lymph node: FNAC or biopsy (for lymphoma, metastasis)
9. Other investigations according to suspicion of causes include:
   - ANF, anti-ds DNA (SLE)
   - Liver function tests
   - Urine for protein and serum total protein (nephrotic syndrome)
   - CT scan in some cases (it helps to clarify pleural abnormalities more readily than chest X-ray and ultrasonogram, and also helps to distinguish between benign and malignant diseases).

Note

In tuberculosis, AFB is positive in pleural fluid in 20% cases and pleural biopsy is positive in 80% cases. In malignancy, pleural biopsy is positive in 40% cases (may be up to 60% cases).

RELATED QUESTIONS AND ANSWERS

Q. What is **pleural effusion?**

A. Accumulation of excessive amount of fluid in pleural cavity is called pleural effusion.

Q. What are the **definitive signs** of pleural effusion?

A. Stony dullness on percussion and reduced or absent breath sound (confirmed by aspiration).

Q. How to **confirm** if there is small effusion? (if not detected by chest X-ray PA view.)

A. By doing:
- X-ray in lateral decubitus position
- Ultrasonogram (USG) of lower part of the chest
- Occasionally, CT scan of chest may be needed.

Q. What are the **characteristics** of pleuritic chest pain?

A. Pleuritic chest pain is localized, sharp or lancinating in nature, worse on coughing, deep inspiration or movement.

Q. **What are the causes of** dullness on percussion **over lower chest?**

A. As follows:
- Pleural effusion (stony dullness)
- Thickened pleura
- Consolidation (woody dullness)
- Collapse of the lung
- Raised right hemidiaphragm (due to hepatomegaly or liver pushed up)
- Mass lesion.

Note Remember the following points in pleural effusion:
- Pleural fluid normally present: 5 to 15 mL
- At least 500 mL of fluid is necessary to detect clinically
- At least 300 mL of fluid is necessary to detect radiologically in PA view
- At least 100 mL of fluid is necessary to detect radiologically in lateral decubitus position
- Less than 100 mL or small amount of fluid is detected by ultrasonography (even 20 to 25 mL fluid can be detected).

Q. Supposing, clinically it is pleural effusion but **no fluid** is coming after aspiration. What are the **possibilities?**

A. As follows:
- Fluid may be thick (empyema)
- Thickened pleura
- Mass lesion.

Q. What are the common causes of pleural effusion?

A. Four common causes are:

- Pulmonary tuberculosis
- Parapneumonic (also called postpneumonic)
- Bronchial carcinoma
- Pulmonary infarction.

If the patient is young, common causes are

- Pulmonary tuberculosis
- Parapneumonic
- Others—Lymphoma and SLE in female (also pulmonary infarction).

If the patient is middle age or elderly, common causes are:

- Pulmonary tuberculosis
- Parapneumonic
- Bronchial carcinoma.

Q. What are the causes of predominantly **right** or **left** sided pleural effusion?

A. As follows:

Causes of right-sided pleural effusion

- Liver abscess
- Meig's syndrome
- Dengue hemorrhagic fever.

Causes of left-sided pleural effusion

- Acute pancreatitis
- Rheumatoid arthritis
- Dressler's syndrome
- Esophageal rupture (Boerhaave's syndrome)
- Dissecting aneurysm.

Q. What are the causes of bilateral effusion?

A. **As follows:**

- All causes of transudative effusion (CCF, nephrotic syndrome, cirrhosis of liver, malabsorption or malnutrition or hypoproteinemia).
- Collagen diseases (rheumatoid arthritis and SLE).
- Lymphoma.
- Bilateral extensive pulmonary TB.
- Pulmonary infarction.
- Malignancy (usually multiple metastases involving both lungs).

Q. What are the **causes** of exudative and transudative pleural effusion?

A. As follows:

1. **Exudative** (protein **>3 g%**):
   - Pulmonary tuberculosis
   - Pneumonia
   - Bronchial carcinoma
   - Pulmonary infarction
   - Collagen disease (SLE, rheumatoid arthritis)
   - Lymphoma.

- Dressler's syndrome (post-myocardial infarction syndrome characterised by pain, pyrexia, pericarditis, pleurisy and pneumonitis).
- Others—acute pancreatitis, subphrenic abscess, liver abscess, pleural mesothelioma, secondaries in the pleura, yellow nail syndrome, etc.

2. **Transudative** (protein **<3 g%**):
   - Congestive cardiac failure (CCF)
   - Nephrotic syndrome
   - Cirrhosis of liver
   - Malnutrition
   - Hypothyroidism
   - Meig's syndrome (ovarian fibroma, ascites and right sided pleural effusion)
   - Chronic constrictive pericarditis
   - Acute rheumatic fever.

Q. How to **differentiate** between exudative and transudative pleural effusion?

A. As follows:

Criteria	Exudative	Transudative
1. Appearance	Straw, purulent, hazy, chylus or blood-stained	Clear or serous
2. Protein	>3 g%	<3 g%
3. Glucose	Low	Normal
4. Cholesterol	> 60 mg/dL	< 60 mg/dL
5. LDH	> two thirds of the upper limit of normal serum LDH	< two thirds of the upper limit of normal serum LDH
6. Pleural fluid LDH : serum LDH	>0.6	<0.6
7. Pleural fluid protein : serum protein	>0.5	<0.5
8. Serum-effusion albumin gradient (serum albumin minus pleural fluid albumin)	< 1.2 g/dL >1.2 g/dL	

Note Remember the following:

- Pleural fluid cholesterol level < 60 mg/dl indicates transudate. In all malignant effusion, pleural fluid cholesterol > 60 mg/dL. So, this test is useful to separate these two types of effusion.
- High pleural fluid ADA indicates tubercular pleural effusion.

Q. What are the **types** of pleural effusion according to the color?

A. According to color, pleural effusion may be:

- Serous (hydrothorax)
- Straw
- Purulent (empyema or pyothorax)
- Hemorrhagic (hemothorax)
- Milky or chylous (chylothorax)

Note

Clinically, only pleural effusion should be mentioned. After drawing the fluid and according to its color, other diagnosis may be done. e.g. if pus, it is empyema.

Q. What are the causes of **hemothorax (blood stained fluid)?**

A. As follows:

- Chest injury or trauma
- Bronchial carcinoma
- Pleural mesothelioma
- Pulmonary infarction
- Others – SLE, lymphoma, acute pancreatitis.

Q. What are the **differences** between traumatic hemothorax and hemorrhagic pleural effusion?

A. As follows:

Traumatic hemothorax	Hemorrhagic pleural effusion
1. Less uniform	1. Uniformly mixed
2. Usually clots on standing	2. Does not clot
3. Gross hemorrhage, RBC >100,000/mm^3	3. RBC > 10,000/mm^3
4. RBC not crenated (fresh RBC)	4. RBC may be crenated

Q. What are causes of **empyema?**

A. As follows:

- Bacterial pneumonia
- Lung abscess (bursting in pleural cavity)
- Bronchiectasis
- Tuberculosis
- Secondary infection after aspiration
- Rupture of subphrenic abscess or liver abscess
- Infected hemothorax.

Q. How to diagnose **empyema thoracis** clinically?

A. As follows:

From history:

- High fever, sometimes hectic, may be associated with chill, rigor and sweating. Fever is persistent or recurrent despite treatment with a suitable antibiotic.
- Malaise, weight loss.
- Pleuritic chest pain, breathlessness.
- Copious purulent sputum if empyema rubtures into a bronchus (bronchopleural fistula).

On examination:

- Toxic, emaciated.
- Tachypnea.
- Tachycardia.
- Features of pleural effusion.
- Clubbing.
- To be confirmed—aspiration which shows pus or purulent fluid.

Q. What is empyema necessitans?

A. In empyema thoracis, fluid may come out subcutaneously in the chest wall. This is called empyema necessitans.

Characteristics of empyema fluid:

- Fluid is purulent
- Thick
- Biochemical—glucose low, < 3.3 mmol/L, protein exudative, LDH > 1000 U/L
- C/S—organism may be found
- Pleural biopsy may be done to exclude tuberculosis.

Q. How to treat empyema thoracis?

A. According to cause:

1. Non-tuberculus:
   - Drainage of pus with wide bore intercostal tube using water seal drainage.
   - Antibiotic for 2 to 6 weeks. IV Co-amoxiclav or cefuroxime plus metronidazole. May be given according to C/S.
   - Surgical intervention if pus is thick or loculated. Surgical decortication of the lung may be needed, if visceral pleura is grossly thickened.
2. Tuberculous empyema:
   - Antitubercular drug
   - Wide bore needle aspiration or intercostal tube drainage
   - Sometimes surgical ablation of pleura.

Q. What are causes of chylothorax (milky or whitish fluid due to lymph)?

A. Injury or obstruction of thoracic duct due to any of the following causes:

- Traumatic (surgery and trauma to the thoracic duct)
- Neoplastic (bronchial carcinoma and metastasis)
- Infective (tuberculosis and filariasis)
- Lymphoma involving thoracic duct.

Q. How to differentiate between chylothorax and empyema?

A. In both cases, fluid may be cloudy. It is centrifuged and following is observed:

- If clear, empyema
- If persistent cloudy or milky, chylothorax.

Q. What is hydrothorax? How to diagnose it clinically?

A. When the pleural effusion is transudative, it is called hydrothorax. It is usually bilateral due to any cause causing transudative pleural effusion.

Clinically this can be diagnosed by:

- Presence of primary cause like CCF, nephrotic syndrome, cirrhosis of liver, etc.
- Associated edema which may be generalized, also ascites, pericardial effusion.
- No history of fever or acute infection.
- Aspiration of fluid shows transudative in nature (serous in color and protein < 3 g%).

Q. What are the causes of recurrent pleural effusion? How to treat recurrent pleural effusion?

A. As follows:

- Bronchial carcinoma
- Pleural mesothelioma

- Lymphoma
- Collagen disease (SLE)
- All causes of transudate (CCF, nephrotic syndrome, cirrhosis of liver).

Treatment of recurrent pleural effusion is done by pleurodesis in the following way:
- A plain rubber tube is introduced in the intercostal space, and fluid is removed as far as possible. Introduce the drug, tetracycline (500 mg) or kaolin or talc through the tube, clamp it and keep for 4 to 8 hours (may be overnight). In malignant pleural effusion, bleomycin 30 to 60 mg is introduced.
- Patients' posture should be changed 2 hourly to allow the drug to spread in pleural space.
- After 4 to 8 hours, remove any remaining fluid and take out the drainage tube at the height of inspiration.
- The patient usually complains of severe chest pain after pleurodesis. In such case, analgesic should be given.

Q. How can you suspect malignant effusion?

A. As follows:
- Clincally—elderly emaciated or cachexic patient having clubbing with nicotine stain, palpable lymph node, radiation mark on the chest, etc.
- Pleural fluid is hemorrhagic and there is rapid accumulation after aspiration.

Q. What are causes of high eosinophil in the pleural fluid (also high in the blood)?

A. As follows:
- Pulmonary eosinophilia
- Polyarteritis nodosa
- Rarely lymphedema.

Note

High eosinophil in the pleural fluid but not in the blood is likely due to pulmonary embolism. High eosinophil in pleural fluid is unlikely to be malignant.

Q. What is subpulmonary pleural effusion?

A. Effusion between the lower surface of lung and upper surface of diaphragm. Confused with subphrenic abscess. Detected by chest X-ray in lateral decubitus position or USG or CT scan.

Q. What is pseudotumor (phantom tumor)?

A. It is the accumulation of fluid in interlobular fissure, usually found along the lateral chest wall. Chest X-ray shows rounded homogeneous opacity, misdiagnosed as a tumor. It is confirmed by USG (localized or encysted effusion) or CT scan. It disappears with resolution of effusion. It is commonly found in CCF.

Q. What is yellow nail syndrome?

A. It is a congenital disorder characterized by:
- Nails—yellow, thick, onycholysis
- Lymphedema of legs
- Pleural effusion or bronchiectasis.

Q. What are the mechanisms of pleural effusion?

A. Excess pleural fluid accumulation occurs when pleural fluid formation exceeds absorption or normal pleural fluid formation with reduced absorption. Probable mechanisms are:
- Increased hydrostatic pressure (as in CCF)

- Reduced plasma colloidal osmotic pressure (as in hypoproteinemia)
- Involvement of pleura causing increased permeability (as in TB and tumor)
- Impaired lymphatic drainage of pleural space (as in obstruction of lymphatic system by tumor, TB and radiation)
- Transdiaphragmatic passage of fluid (in liver disease, ascites and acute pancreatitis).

Q. What is the **mechanism** of tuberculous pleural effusion?

A. Hypersensitivity to tuberculous protein in pleural space.

Q. What are the **characteristics** of tuberculous pleural effusion?

A. As follows:

- Straw or amber color
- Exudative
- High lymphocyte in pleural fluid
- AFB is found in 20% cases
- Culture for AFB is found in one-third cases
- Pleural biopsy is positive in 80% cases.

Q. What are the causes of **low pH and low glucose** in pleural fluid?

A. As follows:

- Infection (empyema)
- Tuberculosis
- Advanced malignancy
- SLE
- Rheumatoid arthritis
- Esophageal rupture.

Q. What is the role of **pleural fluid amylase?**

A. Pleural fluid amylase may be higher than serum amylase in acute pancreatitis, bacterial pneumonia, esophageal rupture and malignancy. It is high in adenocarcinoma of lung and may be useful in differentiating it from mesothelioma.

Q. What is the **treatment** of pleural effusion?

A. Treatment should be according to cause. For example:

- If tuberculosis: Full course antitubercular therapy. Prednisolone 20 to 30 mg daily may be given for 4 to 6 weeks, especially in large effusion.
- If parapneumonic: Aspiration of fluid, may be repeated if necessary. Antibiotic should be given. If complicated case, especially empyema, thoracostomy may be done. Sometimes, if all fails, thoracotomy with decortication may be necessary.

Q. **How much fluid** may be drawn at a time?

A. Usually up to 1500 mL. If more is drawn, there may be risk of re-expansion pulmonary edema. The mechanism is because of effusion, lung is compressed and there is ischemia to lung parenchyma and necrosis of pulmonary vessels. If more fluid is drawn, there is rapid expansion of the lung, as no regeneration of necrotic vessels. As a result, more leakage of fluid causing pulmonary edema.

Q. What is the role of **steroid** in pleural effusion?

A. Steroid is mostly given in tubercular pleural effusion. Although its role is controversial, some evidences suggest that it promotes rapid absorption of pleural fluid and gives the patient quick symptomatic relief. It also prevents pleural fibrosis and adhesion. Steroid should be used along with antitubercular therapy.

LUNG ABSCESS

CHIEF COMPLAINTS

- Cough with profuse foul smelling sputum for … days
- Hemoptysis for … days
- Fever for … days
- Chest pain for … days
- Malaise, weakness, loss of weight for … days.

HISTORY

History of present illness: According to the statement of the patient, he was reasonably well … days back. Since then, he has been suffering from severe cough with production of copious foul smelling purulent sputum. It is occasionally associated with scanty amount of blood. He also complains of high grade continuous fever, highest recorded 104°F. The fever is associated with chills and rigors and profuse sweating, subsides only with paracetamol. The patient also complains of right sided chest pain, which is compressive in nature, worse with inspiration and during coughing, but there is no radiation. For the last ... days, he is also suffering from malaise, weakness, anorexia and loss of approximately 15 kg of body weight. His bowel and bladder habits are normal.

History of past illness: He was suffering from pneumonia 6 months back from which there is complete recovery.

Family history: Nothing significant.

Personal history: He smokes about 25 sticks a day for 25 years. He is also an alcoholic.

Socioeconomic history: He is a day laborer and lives in a slum area with poor sanitation.

Drug history: The patient was treated by local physicians with antibiotics, cough syrup and paracetamol, but no improvement.

GENERAL EXAMINATION

- The patient looks toxic and emaciated
- Generalized clubbing is present in all the fingers and toes
- Moderately anemic
- No jaundice, cyanosis, koilonychia, leukonychia or edema
- No thyromegaly or lymphadenopathy
- Pulse: 110/min
- BP: 110/75 mm Hg
- Temperature: 103º F
- Respiratory rate: 28/min.

SYSTEMIC EXAMINATION

Respiratory System

(Supposing right sided)

Inspection:

- Movement is restricted in the right side of the chest.

Palpation:
- Trachea is central in position
- Apex beat is in the left 5th intercostal space in the midclavicular line
- Vocal fremitus is increased on the right side of the chest
- Chest expansion is reduced on the right side.

Percussion:
- Percussion note is woody dull over right side of chest from … to … intercostal space
- Upper border of the liver dullness is in the right 5th intercostal space in midclavicular line
- Cardiac dullness is normal.

Auscultation:
- Breath sound is bronchial in … intercostal space on the right side. In other places, it is vesicular.
- Vocal resonance is increased over the same area.
- There are coarse crepitations over the right side of the chest in … intercostal space, reduces on coughing.

Examination of the other systems reveals no abnormalities.

SALIENT FEATURES

Mr. …, 42 years old, day laborer, normotensive, nondiabetic, smoker and alcoholic, hailing from …, presented with severe cough with production of copious foul smelling purulent sputum for … days. It is occasionally associated with scanty amount of blood. He also complains of high grade continuous fever, highest recorded 104°F. The fever is associated with chills and rigors and profuse sweating, subsides only with paracetamol. The patient also complains of right sided chest pain, which is compressive in nature, worse with inspiration and during coughing, but there is no radiation. For the last ... days, he is also suffering from malaise, weakness, anorexia and loss of approximately 15 kg of body weight. His bowel and bladder habits are normal. He was suffering from pneumonia 6 months back from which there is complete recovery. He smokes about 25 sticks a day for 25 years. He was treated by local physicians with antibiotics, cough syrups and paracetamol, but no improvement.

On examination—general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is right sided lung abscess.

Q. What are the **differential diagnoses**?

A. As follows:
- Consolidation (during resolution stage)
- Bronchiectasis
- Bronchial carcinoma
- Pulmonary TB.

Q. Why lung abscess and **not** consolidation?

A. Because:
- The patient is toxic with high temperature. There is cough with foul smelling purulent sputum.
- Clubbing is present (it is usually present in 10% cases after 3 weeks.)

To be confirmed—chest X-ray should be done (which shows cavity with air fluid level).

Q. With these findings, can it be **consolidation** only?

A. Yes, it may be during resolution stage.

Q. Could it be **bronchiectasis?**

A. Yes, because there is clubbing with coarse crepitations. However, in bronchiectasis, crepitations are mostly on the basal area. Also, there is no fever and patient is not toxic in bronchiectasis (until there is secondary infection).

Also, in the history of bronchiectasis, there is profuse expectoration of sputum after waking up from sleep in the morning.

Q. **What** investigations **should be done in lung abscess?**

A. As follows:

- CBC (leukocytosis)
- X-ray chest (cavity with air fluid level)
- Sputum examination—Gram staining, C/S (both aerobic and anaerobic), AFB, fungus, malignant cells
- Bronchoscopy (to exclude mass and foreign body)
- CT or MRI (in some cases)
- Blood sugar.

RELATED QUESTIONS AND ANSWERS

Q. What is **lung abscess?** What are the **causes?**

A. It is a localized area of suppuration within the lung parenchyma that leads to parenchymal destruction and is manifested radiologically as a cavity with air fluid level.

Causes of lung abscess:

- Aspiration of nasopharyngeal or oropharyngeal contents, such as in vomiting, anesthesia, tooth extraction, tonsillectomy, unconscious patient, alcoholism and achalasia of cardia. Organisms are aerobic and anaerobic.
- Specific infections (*Streptococcus pneumoniae* type 3, *Staphylococcus aureus, Klebsiella pneumoniae* and fungal). In HIV, *Pneumocystis jiroveci, Cryptococcus neoformans* and *Rhodococcus equi.*
- Obstruction by bronchial carcinoma, adenoma and foreign body.
- Infection in pulmonary infarction (by *Streptococcus pneumoniae, Staphylococcus aureus, Haemophilus influenzae* and anaerobic).
- Spread from liver abscess and subphrenic abscess (due to transdiaphragmatic spread).
- Hematogenous from other infection as septic emboli (pelvic abscess and salpingitis, right sided endocarditis, IV drug abuse).

Q. How the patient of lung abscess usually **presents?**

A. As follows

- Severe cough with profuse foul smelling sputum, may be fetid (anaerobic)
- Hemoptysis
- Chest pain (pleuritic)
- Fever, usually high with chill and rigor, with profuse sweating
- Malaise, weakness and loss of weight.

Q. What are the **physical findings** in lung abscess?

A. It depends on site. If deep seated within the lung parenchyma, there may not be any physical findings. If it is near the surface, findings are:

- Features of consolidation, usually

- Rarely, features of cavitation
- Sometimes, combined features of consolidation and cavitation, if large abscess.

Q. What is the **common site** of lung abscess?

A. As follows:

1. Lung abscess is common in right middle lobe.
2. If it is due to aspiration, then the commonest site depends on the posture of the patient during aspiration.
   - If the patient is lying down, abscess forms in the posterior segment of upper lobe or superior segment of lower lobe
   - If the patient is in upright position, the common site is basal segment.

Q. Why lung abscess is more common on the **right side**?

A. Lung abscess is more common in right side due to less obliquity of the right major bronchus.

Q. What are the **complications** of lung abscess?

A. As follows:

- Pleurisy
- Empyema
- Bronchiectasis
- Fibrosis
- Septicemia
- Cerebral abscess (common in parietal lobe or posterior frontal region)
- Amyloidosis (rare), in chronic cases.

Q. What are the **characteristics of sputum** in lung abscess?

A. If the sputum is kept in a bottle, there are three layers (as in bronchiectasis):

- Lower—sediment (epithelial debris and bacteria)
- Middle—thick liquid
- Upper—frothy.

Q. What are the other causes of **cavitary lesion in lung?**

A. As follows:

- Tuberculosis
- Cavitating bronchial carcinoma
- Pulmonary infarction
- Fungal infection (histoplasmosis)
- Wegener's granulomatosis
- Rheumatoid nodules
- Consolidation (*Streptococcus pneumoniae* serotypes 3).

Q. What are the causes of **multiple cavitary lesions** in the lung?

A. As follows:

- Tuberculosis
- Staphylococcal lung abscess (in children)
- Fungal infection
- Klebsiella
- Amebiasis.

Q. What are the causes of **multiple lung abscess**?

A. As follows:

- Aspiration of infected material
- *Staphylococcus aureus* (in children)
- Klebsiella infection
- Fungal infection
- Amebiasis.

Q. How to **treat** lung abscess?

A. Sputum is sent for C/S and broad-spectrum antibiotic should be started.

- Broad-spectrum antibiotic—amoxicillin or co-amoxiclav or erythromycin **plus** metronidazole. **Or,** cefuroxime 1 g IV 6 hourly **plus** metronidazole 500 mg IV 8 hourly for 5 days, followed by cefaclor **plus** metronidazole (in 70% cases anaerobic organisms are present, but mixed organisms are also common).
- If improves, continue as above. If no response, antibiotic is given according to C/S. Treatment should be continued for 4 to 6 weeks.
- Postural drainage and chest physiotherapy.
- If no response to medical therapy (occurs in 1 to 10% cases), percutaneous aspiration (USG or CT guided).
- Sometimes, surgery (lobectomy) may be done.
- Treatment of the cause, if present.

Indications of surgery:

- No clinical response
- Increasing size of the abscess.
- Massive hemorrhage or hemoptysis.

BRONCHIAL CARCINOMA

CHIEF COMPLAINTS

- Cough with expectoration for … months
- Occasional haemoptysis for … months
- Chest pain for … days
- Weight loss, malaise, weakness, loss of appetite for … days.

HISTORY

History of present illness: The patient was alright … months back. Since then, he has been suffering from frequent cough, which is present throughout the day and night. The cough is usually dry, sometimes associated with slight mucoid sputum expectoration. Occasionally, the patient noticed streaks of frank blood with sputum during coughing. There is one episode of massive hemoptysis … days back. For the last … days, he is also complaining of right sided chest pain, which becomes worse with deep inspiration, coughing and also on lying down on right side. The patient also complains of loss of appetite, substantial loss of weight, weakness and malaise for ... days. His bowel and bladder habits are normal. There is no history of fever, hoarseness of voice, difficulty in deglutition, contact with TB patients.

History of past illness: Nothing significant.

Family history: Nothing contributory.

Personal history: He smokes about 25 sticks per day for 30 years.

Socioeconomic history: He is a clerk and comes from a middle class family.

Drug history: He used to take some cough syrup and occasionally antibiotics, the name of which he cannot mention.

GENERAL EXAMINATION

- Ill-looking and emaciated
- Moderately anemic
- Generalized clubbing present involving all the fingers and toes (mention hypertrophic osteoarthropathy is present or not)
- Nicotine stain present in right finger nail (mention if any)
- Right supraclavicular lymph nodes are enlarged, hard in consistency, nontender, fixed with underlying structure and overlying skin
- No jaundice, cyanosis, edema, koilonychias or leukonychia
- No thyromegaly
- Pulse: 84/min
- BP: 110/70 mm Hg
- Respiratory rate: 20/min
- Temperature: Normal.

SYSTEMIC EXAMINATION

Respiratory System

(Supposing right sided)

Inspection:

- Movement is restricted on right upper chest
- There is radiation mark on the chest (if any).

Palpation:

- Trachea is central in position
- Apex beat is in left 5th intercostal space, just medial to the midclavicular line
- Vocal fremitus is reduced (or absent) in right upper chest
- Pleural rub is present (mention where).

Percussion:

- Percussion note is dull in right upper chest (mention up to which space)
- Upper border of the liver dullness is in the right 5th intercostal space in the midclavicular line
- Cardiac dullness is normal.

Auscultation:

- Breath sound is reduced (or absent)
- Vocal resonance is reduced (or absent)
- Few crepitations (may be present)
- Pleural rub is present (mention where).

Examination of the other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 52 years old, a clerk, normotensive, nondiabetic, smoker, hailing from …, presented with frequent cough for … months, which is present throughout the day and night. The cough is usually dry, sometimes associated with slight mucoid sputum expectoration. Occasionally, the patient noticed streaks of frank blood with sputum during coughing. There is one episode of massive hemoptysis … days back. For the last … days, he is also complaining of right sided chest pain, which becomes worse with deep inspiration, coughing and also on lying down on right side. The patient also complains of loss of appetite, substantial loss of weight, weakness and malaise for ... days. His bowel and bladder habits are normal. There is no history of fever, hoarseness of voice, difficulty in deglutition, contact with TB patients. He smokes about 25 sticks a day for the last 30 years. He used to take some cough syrup and occasionally antibiotics, the name of which he cannot mention.

On examination – general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is bronchial carcinoma with metastasis (in right supracalvicular LN).

Q. Why bronchial carcinoma?

A. The patient is elderly and heavy smoker. There is history of cough with hemoptysis and marked loss of weight. On examination, the patient is emaciated, has generalized clubbing with nicotine stain and examination of chest shows evidence of mass lesion. All the features are suggestive of bronchial carcinoma.

Q. What are your differential diagnoses?

A. As follows:

- Pulmonary TB
- Other mass lesion (hydatid cyst, dermoid cyst, neurofibroma).

Q. Why pulmonary TB is not your primary diagnosis?

A. This may be pulmonary tuberculosis, because all the features like cough, hemoptysis and weight loss are present in tuberculosis. However in this case, there is no history of fever or contact with TB patient. The patient has gross clubbing, enlarged supraclavicular lymph node, which is hard in consistency and evidence of mass lesion in chest. All these are against pulmonary tuberculosis.

Q. Why not this is collapse?

A. In collapse, trachea and apex beat are shifted to the same side.

Q. Why not consolidation?

A. In consolidation, there is bronchial breath sound and increased vocal resonance.

Q. What investigations do you suggest in bronchial carcinoma?

A. **As follows:**

1. X-ray chest P/A view (homogeneous irregular opacity, with **sun-ray** appearance may be seen. There may be collapse, pleural effusion, hilar lymphadenopathy, widening of mediastinum, raised hemidiaphragm, and rib erosion or destruction).
2. Sputum for malignant cells (exfoliative cytology).
3. CT scan of chest (MRI is not helpful for primary lesion).
4. CT guided FNAC.
5. FNAC (or biopsy) of lymph nodes (if present).
6. Fiber optic bronchoscopy and biopsy (or bronchial washing and brushing).
7. PET-CT scan is the investigation of choice (highly sensitive and specific for mediastinal staging).
8. To see evidence of metastasis: USG of whole abdomen, X-ray skull, isotope bone scan, etc. Sometimes, CT scan of chest and abdomen, even MRI may be needed.
9. Others:
   - Complete blood count, ESR
   - If pleural effusion, then fluid cytology. Pleural biopsy may also be done
   - Liver function test, renal function test (before chemotherapy, if needed)
   - Pulmonary function test specially FEV_1 (DLCO below 60% predicted is associated with a mortality rate of 25% due to pulmonary complications).

Q. Why bronchoscopy should be done?

A. Bronchoscopy should be done:

- To see the mass and to take biopsy for tissue diagnosis. This will guide further management.
- If the carcinoma involves first 2 centimeter of either main bronchus, it indicates the tumor is inoperable.
- If carina is wide and there is loss of sharp angle of carina, it indicates presence of enlarged madiastinal lymph nodes (may be malignant or reactive). Biopsy can be taken by passing a needle through bronchial wall.
- Vocal cord paralysis on the left indicates left recurrent laryngeal nerve palsy and indicates an inoperable case.

Q. Have you examined the eyes of the patient? What did you look for?

A. I have examined the eyes for partial ptosis, miosis and enophthalmos, which indicates Horner's syndrome. It is commonly found in Pancoast's tumor. Fundoscopy may show papilledema, if secondary metastasis in the brain.

Q. If **sputum** shows malignant cells, would you do **bronchoscopy** and **biopsy**?

A. Yes, to see histological type. This is helpful for therapy and prognosis. If squamous cell carcinoma, radiotherapy is the treatment. If small cell carcinoma, chemotherapy is necessary.

RELATED QUESTIONS AND ANSWERS

Q. What are the **types** of bronchial carcinoma?

A. Two types:

- Non-small-cell carcinoma in 80%
- Small-cell carcinoma in 20%.

Q. What are the **histological types** of bronchial carcinoma?

A. Four types:

- Squamous cell carcinoma in 35%
- Small cell carcinoma in 20%
- Adenocarcinoma in 30%
- Large cell carcinoma in 15%.

Features of adenocarcinoma:

- Ten percent of bronchial carcinoma
- Arises from mucous cells in the bronchial epithelium
- Occurs in the periphery of lung
- Usually develops in or around old scar
- More in elderly
- More in female
- More in nonsmokers
- More in far east
- More in asbestosis
- Invasion to pleura and mediastinal lymph nodes is common
- Metastasis to brain, bone and adrenal gland is common.

Features of small cell carcinoma:

- About 20 to 30% of bronchial carcinoma
- Arises from endocrine cells called Kulchitsky cells. These cells are members of APUD system, which secretes many polypeptide hormones. Some of these hormones act in an autocrine fashion, they feedback on the cells and cause cell growth
- Highly malignant, rapidly growing, early metastasis and inoperable at presentation
- Usually responds to chemotherapy and radiotherapy, less likely to be cured by surgery
- Overall prognosis is poor. Survival is short, 3 months to 1 year.

Features of bronchoalveolar cell carcinoma:

- Found in 1 to 2% of bronchial carcinoma
- Occurs as peripheral solitary nodule or diffuse nodular lesion of multicentric origin
- It may be associated with profuse mucoid sputum expectoration.

Q. What are the **causes or risk factors** of bronchial carcinoma?

A. As follows:

- Cigarette smoking is the major risk factor. Even passive smoking causes 1.5 times increase in the risk of bronchial carcinoma.
- Other factors are exposure to asbestos, silica, beryllium, cadmium, chromium, arsenic, iron oxide, radon, radiation, petroleum products and oils, coal tar, products of coal combustion.
- Adenocarcinoma may develop in nonsmokers and in old scar.

Q. What are the **presentations** of bronchial carcinoma?

A. Usually in elderly patients with history of smoking:

1. Due to lung lesion:
- Cough—dry or sputum production. Changing pattern of regular cough in a smoker is highly suspicious. Bovine cough due to left recurrent laryngeal nerve palsy.
- Hemoptysis, commonly in central lesion. Sometimes, involvement of large blood vessels causes massive hemoptysis.
- Breathlessness (due to bronchial obstruction, collapse or massive pleural effusion or compression of phrenic nerve causing paralysis of the diaphragm).
- Chest pain (due to involvement of pleura, rib or chest wall, intercostal nerve and brachial plexus).
- Recurrent pneumonia at the same site or pneumonia with slow resolution is highly suspicious.
- Apical tumor (called Pancoast's tumor) involves cervical sympathetic chain at or above the stellate ganglia, causing Horner's syndrome (characterized by ipsilateral partial ptosis, enophthalmos, miosis and anhydrosis of the face). Also, there is pain in shoulder and inner aspect of arm due to the involvement of lower trunk of brachial plexus, called Pancoast's syndrome.

2. Due to local spread in mediastinum:
- Hoarseness of voice and a bovine cough (due to involvement of left recurrent laryngeal nerve by left hilar lesion).
- Dysphagia (esophageal obstruction, also cardiac tamponade).
- SVC obstruction (with right sided mass or mediastinal lymphadenopathy).
- If pericardium is invaded, there may be pericardial effusion or arrhythmia.
- Stridor, when lower trachea, carina and main bronchi are narrowed by primary tumor or compression by subcarinal and paratracheal lymph nodes.

3. Distant metastasis (in liver, brain, bone, adrenal, contralateral lung and lymph nodes. Metastatic features usually common in adenocarcinoma).

4. Nonmetastatic extrapulmonary manifestations (see below).

5. General features of malignancy—anorexia, weight loss, malaise, fatigue.

Q. Why **chest pain** in bronchial carcinoma?

A. Due to metastasis in the rib or chest wall invasion.

Q. What is **Pancoast's tumor** and **Pancoast's syndrome**?

A. As follows:
- Pancoast's tumor (superior sulcus tumor): It is the tumor that arises from apex of the lung. It may involve the cervical sympathetic chain, causing Horner's syndrome.
- Pancoast's syndrome**:** This is characterized by pain in the shoulder or inner aspect of arm along the ulnar nerve distribution due to the involvement of lower part of brachial plexus (C_8, T_1 and T_2). There may be wasting of small muscles of hand due to C_8 and T_1 nerve involvement. Local invasion by the tumor may cause pain and tenderness of the first and second ribs with evidence of rib destruction radiologically. Horner's syndrome may occur due to involvement of the sympathetic pathway as it passes through T_1 root. In Pancoast's syndrome, treatment is by combined surgery and radiotherapy.

Non-metastatic extra-pulmonary manifestations (paraneoplastic syndrome) -

Occur in 15 to 20% cases of bronchial carcinoma due to secretory products by the tumor. These may precede, coincide or follow after the cancer. Treatment of carcinoma improves the features.

1. Endocrine (10%, usually in small cell carcinoma):
   - SIADH (syndrome of inappropriate ADH, usually in small cell carcinoma)
   - ACTH secretion causing Cushing's syndrome (usually in small cell carcinoma)
   - Carcinoid syndrome (usually in small cell carcinoma)
   - Hypercalcemia due to release of parathormone-like substance (usually in squamous cell carcinoma)
   - Gynecomastia due to excess estrogen (in large cell)
   - Rarely, hypoglycemia and thyrotoxicosis.
2. Neurological (in any type):
   - Peripheral neuropathy (usually sensorimotor)
   - Cerebellar degeneration
   - Cortical degeneration (dementia)
   - Myelopathy—motor neuron disease like feature
   - Retinal blindness (small cell carcinoma).
3. Musculoskeletal:
   - Polymyositis or dermatomyositis (in all types)
   - Myasthenic myopathic syndrome (Eaton-Lambert syndrome)
   - Clubbing and hypertrophic osteoarthropathy (non-small-cell type).
4. Hematological (in all types):
   - Migrating thrombophlebitis
   - DIC
   - Thrombotic thrombocytopenic purpura
   - Normocytic normochromic anemia and occasionally, hemolytic
   - Eosinophilia.
5. Heart (in adenocarcinoma):
   - Marantic endocarditis (non-bacterial, thrombotic or verrucous endocarditis).
6. Skin (in all types):
   - Acanthosis nigricans
   - Dermatomyositis
   - Herpes zoster.
7. Renal:
   - Nephrotic syndrome due to membranous glomerulonephritis (rare).
8. Metabolic (universal at some stage):
   - Loss of weight
   - Lassitude
   - Anorexia.

Q. How to **treat** bronchial carcinoma?

A. As follows:

1. Non-small-cell carcinoma:
- Surgery should be done, if the tumor is localized to lobe or segment. (It is curative if the stage is T1N0M0)
- If surgery is not possible, radiotherapy or chemotherapy or combined therapy should be given.
- In squamous cell type, radiotherapy is advised (it is especially indicated in SVC obstruction, repeated hemoptysis and chest pain caused by chest wall invasion or skeletal metastasis).
- Chemotherapy is less helpful in non-small-cell type.

2. Small-cell-carcinoma:
- Even small, metastasis occurs early. Surgery is less helpful. Chemotherapy is usually given. Radiotherapy may be added (continuous hyperfractionated accelerated radiotherapy, CHART, in which total dose is given in smaller, but more frequent fractions offer the best survival).

- Usual chemotherapy—intravenous CDV (cyclophosphamide, doxorubicin and vincristine) or CE (cisplatin plus etoposide). Chemotherapy is given every 3 weeks for 3 to 6 cycles.

3. Other treatments: These are usually palliative.
- Laser therapy with fiberoptic bronchoscopy.
- Endobronchial therapy—tracheobronchial stent, cryotherapy, laser, brachytherapy (a radioactive source is placed closed to the tumor).
- RFT (radiofrequency thermal ablation).
- Pleural drainage or pleurodesis (in pleural effusion).
- Drug—steroid to improve appetite, morphine or diamorphine for pain (along with laxatives if constipated). Oral candidiasis should be treated.
- Short courses of palliative radiotherapy are helpful for bone pain, severe cough or hemoptysis.

The RFT is helpful in some malignancy, such as bronchial carcinoma and hepatocellular carcinoma. It is done by placing special needle into the tumor under guidance of CT scan. Electric current from radiofrequency current generator is passed through the needle, which results in generation of heat causing destruction of tumor. RFT is helpful, if the tumor size is < 4 cm. Also, sometimes used in large tumor.

Complications of RFT:
- Bleeding
- Pneumothorax
- Skin burn
- Secondary infection and lung abscess.

TNM classification of lung cancer (it is for non-small-cell carcinoma):
- T—extent of primary tumor
- N—involvement of lymph node
- M—presence of distant metastasis.

Stages for T:
- Tx—Positive cytology only
- T1—< 3 cm in diameter
- T2—> 3 cm in diameter or extends to hilar region or invades visceral pleura or partial atelectasis or extend into main bronchus, but remains 2 cm or more distal to carina
- T3—Involvement of chest wall, diaphragm, pericardium, mediastinum, pleura, total atelectasis, main bronchus < 2 cm distal to carina
- T4—Involvement of heart, great vessels, trachea, esophagus, malignant effusion, vertebral body, carina. Separate tumor nodules.

Stages for N:
- N0—No nodal involvement
- N1—Peribronchial, ipsilateral hilar or intrapulmonary lymph node involvement
- N2—Ipsilateral mediastinal or subcarinal
- N3—Contralateral mediastinal, scalene or supraclavicular.

Stages for M:
- M0—No distant metastasis
- M1—Distant metastasis.

Q. What is the **role of staging?**

A. Staging is done to see the possibility of surgical resection of the carcinoma. TNM staging is done for non small cell cancer only. In early stage, surgery may be curative. In advanced stages, surgery may not be possible. Small cell carcinoma is treated according to whether it is limited or extensive.

Q. What is the **role of surgery** in lung carcinoma?

A. In non-small-cell carcinoma without metastasis, surgery is the treatment of choice. But it has limited role in small cell carcinoma, as more then 90% patient has metastasis at the time of presentation.

Q. What are the **contraindications** of surgery?

A. As follows:

- Distant metastasis (M1)
- Invasion of central mediastinal structures including heart, great vessels, trachea and esophagus (T4)
- Malignant pleural effusion (T4)
- Contralateral mediastinal lymph node involvement (N3)
- $FEV_1 < 0.8$ L
- Poor general condition, severe or unstable cardiac or other medical problem.

Note Remember the following points:

- In a fit individual, surgery is not absolutely contraindicated in case of direct extension of tumor into the chest wall, diaphragm, mediastinal pleura or pericardium or to within 2 cm of the main carina.
- Surgery is rarely appropriate in patients over 65 years as the operative mortality rate exceeds the 5-year survival rate.

Q. What are the **indications of radiotherapy?**

A. As follows:

1. As the main treatment in:
   - Localized tumor where surgery is not possible
   - Along with chemotherapy in small cell carcinoma
   - Before and after surgery in selected patients.
2. As a palliative therapy in:
   - Pain (local or metastasis)
   - Superior vena caval obstruction
   - Pancoast's tumor
   - Obstruction of trachea and main bronchi
   - Recurrent hemoptysis.

Q. What is the role of **chemotherapy**?

A. Small cell carcinoma is usually treated with chemotherapy. Drugs used are cisplatin, etoposide, cyclophosphamide, vinblastine, vindesine, carboplatin. Newer drugs are docetaxel, paclitaxel, irinotecan, vinorelbine, gemcitabine.

Q. What is the **prognosis**?

A. If it is localized and surgical resection is possible, the prognosis is good. Otherwise:

- Non-small-cell carcinoma—50% 2 year survival without spread, 10% with spread
- Small cell carcinoma—median survival is 3 months if untreated, 1 to 1½ year with treatment.

Remember the tumour markers of different tumour

Biochemical markers of tumor—Some biochemical markers in the serum indicates presence of specific carcinoma. Examples are:

- α-fetoprotein—HCC, non seminomatous germ cell tumor of gonads
- β human chorionic gonadotrophin (β-HCG)—choriocarcinoma (100%), hydatidiform mole (97%), ovarian non-seminomatous germ cell tumor (50 to 80%), seminoma, lung cancer
- Prostate specific antigen (PSA)—carcinoma of prostate
- Carcinoembryonic antigen (CEA)—colorectal cancer (commonly with liver metastasis)
- CA-125 (cancer antigen 125)—ovarian cancer (75%), gastrointestinal cancer (10%), lung cancer (5%), breast (5%)
- CA-19-9—pancreatic cancer, may be other gastrointestinal cancer
- CA-15-3—breast cancer
- Osteopontin—mesothelioma and many other cancers
- Thyroglobulin—papillary and follicular thyroid carcinoma
- Calcitonin—medullary carcinoma of thyroid
- Placental alkaline phosphatase (PLAP)—seminoma (40%), ovarian dysgerminoma (50%)
- β_2 microglobullin—myeloma, NHL.

CONSOLIDATION

CHIEF COMPLAINTS

- Fever for … days
- Cough for … days
- Chest pain for … days
- Malaise, generalized bodyache, weakness for ... days.

HISTORY

History of present illness: According to the statement of the patient, he was alright … days back. Since then, he has been suffering from high grade continued fever, highest recorded temperature is 104^0F. The fever is associated with chill and rigor, sometimes with profuse sweating, subsides with paracetamol. The patient also complains of cough for … days, which was initially dry, but for the last few days, the cough is productive with purulent or yellowish sputum. He also complains of left sided chest pain, which is sharp, stabbing in nature, more marked on coughing, and deep inspiration, also on lying on the left side, and there is no radiation of pain. For the last ... days, he is experiencing malaise, generalized bodyache and weakness. There is no history of breathlessness, hemoptysis or contact with TB patient. His bowel and bladder habits are normal. There is no history of traveling, exposure to firm animals or birds.

History of past illness: There is no history of previous lung disease. He is nondiabetic.

Family history

Personal history

Socioeconomic history

Drug history: No history of taking steroid, antibiotic, etc. (immunosuppressive drugs). (Mention according to the patient's statement).

GENERAL EXAMINATION

- Ill looking and toxic
- Pulse: 120/min
- BP: 110/70 mm Hg
- Temperature: 104°F
- Respiratory rate: 30/min
- Herpes labialis in the right angle of mouth (mention if present)
- No anemia, jaundice, cyanosis, clubbing, koilonychia, leukonychia and edema
- No lymphadenopathy or thyromegaly.

SYSTEMIC EXAMINATION

Respiratory System (Supposing in Left Side)

Inspection:

- Movement restricted on the left side.

Palpation:
- Trachea—central in position
- Apex beat—in the left fifth intercostal space medial to the midclavicular line, normal in character
- Vocal fremitus- increased over left side from … to ….
- Chest expansibility—slightly reduced on left side
- Pleural rub is palpable in the left side (mention if any).

Percussion:
- Percussion note is woody dull over … to … spaces on left side of the chest
- Upper border of liver dullness is in right 5th intercostal space in midclavicular line
- Area of cardiac dullness—normal.

Auscultation:
- Breath sound—high pitched bronchial sound over in … spaces in left side
- Vocal resonance is increased and there is whispering pectoriloquy in the same area
- (There are few crepitations and pleural rub on the same area, mention if any).

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 42 years old, Government service holder, normotensive, nondiabetic, nonsmoker, hailing from …, presented with high grade continued fever for … days. The highest recorded temperature is 104°F. The fever is associated with chill and rigor, sometimes with profuse sweating, subsides with paracetamol. The patient also complains of cough for … days, which was initially dry, but for the last few days, the cough is productive with purulent or yellowish sputum. He also complains of left sided chest pain, which is sharp, stabbing in nature, more marked on coughing, and deep inspiration, also on lying on the left side, and there is no radiation of pain. For the last ... days, he is experiencing malaise, generalized bodyache and weakness. There is no history of breathlessness, hemoptysis or contact with TB patient. His bowel and bladder habits are normal. There is no history of traveling, exposure to firm animals or birds. There is no history of previous lung disease. For his illness he took some paracetamol and cough syrup. No history of taking steroid, antibiotic, etc.

On examination – general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is left sided consolidation

Q. What are your **differential diagnoses?**

A. As follows:
- Lung abscess
- Bronchiectasis with secondary infection
- Pleural effusion
- Pulmonary infarction.

Q. Why not lung abscess?

A. In case of lung abscess, there will be more profuse foul smelling sputum. Clubbing may be present. Auscultation may show more coarse crepitations. X-ray will show cavity with air fluid level.

Q. Why not **tuberculosis**?

A. With short history, very high temperature and signs of consolidation, tuberculosis is unlikely. In case of TB, there will be low grade continued fever with evening rise, weight loss, anorexia, night sweat, etc.

Q. What is the typical character of **sputum** in consolidation?

A. The sputum is usually rusty.

Q. Why **crepitations** in consolidation?

A. Because of resolution.

Q. What **investigations** should be done in consolidation?

A. As follows:

1. Hb%, TC, DC, ESR:
   - In bacterial pneumonia—polymorphonuclear leukocytosis.
   - In atypical pneumonia—normal or slightly increased leukocytes.
   - In viral pneumonia—leukopenia.
2. X-ray chest: Homogenous opacity with air bronchogram (usually found after 12 to 18 hours). If it is associated with hilar adenopathy, suggestive of *Mycoplasma pneumoniae.*
3. Sputum: Gram staining, C/S (aerobic and anaerobic).
4. Blood C/S (positive in pneumococcal pneumonia).
5. Arterial blood gas analysis.
6. Others (according to etiology):
   - Pneumococcal antigen in serum.
   - Mycoplasma antibody detection (agglutination, CFT), Coomb's test, C/S in special media
   - Antibody against virus, chlamydia, legionella
   - Urinary legionella pneumophila antigen
   - CRP (high).

Note

Chest X-ray may reveal complications, such as pleural effusion and cavitation (found in infection by *Staphylococcus aureus* and pneumococcal serotype 3).

RELATED QUESTIONS AND ANSWERS

Q. What is consolidation?

A. It means pneumonia which is defined as "inflammation in the lung characterized by accumulation of secretion and inflammatory cells in alveoli".

Q. What are the types **of pneumonia?**

A. As follows:

1. Anatomically 2 types:
   - Lobar: Commonly involves one or more lobe.
   - Lobular (bronchopneumonia): It is characterized by nonpatchy alveolar opacity with bronchial and bronchiolar inflammation. Commonly, involves both lower lobes.

2. Clinically 4 types:
   - Community acquired pneumonia (CAP)
   - Nosocomial pneumonia (hospital acquired)
   - Pneumonia in immunocompromised
   - Suppurative and aspiration pneumonia.

Q. What are the causes of **community acquired pneumonia (CAP)?**

A. It is caused by:

- Common organism: Streptococcus pneumoniae (50%), *Mycoplasma pneumoniae*, *Chlamydia pneumoniae* and *Legionella pneumophila.*
- Others: *Staphylococcus aureus*, *Haemophilus influenzae*, *Chlamydia psittaci*, *Coxiella burnetii* (Q fever), *Klebsiella*, *Actinomyces* israelii and viral (influenza, parainfluenza, measles, respiratory syncytial virus in infancy and varicella) infections.

Note Remember the following points:

- CAP usually spread by droplet infection and most cases occur in previously healthy individual
- Physical signs of consolidation develops in 2 days, disappears after 2 weeks
- Radiological signs develop 12 to 18 hours after the onset and usually disappear within 4 weeks.

Q. What are the **precipitating factors** of pneumonia?

A. As follows:

- *Streptococcus pneumonia* often follows viral infection with influenza or parainfluenza virus
- Hospitalized ill patient
- Smoking
- Alcohol excess
- Bronchiectasis (e.g. in cystic fibrosis)
- Bronchial obstruction
- Immunosuppression
- IV drug abuser
- Inhalation from esophageal obstruction.

Q. **What are the** pathological stages **of CAP?**

A. Four stages:

- Stage of congestion—persists for 1 to 2 days
- Stage of red hepatization (red and solid like liver)—persists for 2 to 4 days
- Stage of grey hepatization—persists for 4 to 8 days
- Stage of resolution—8 to 9 days or more.

Q. What are the **presentations** of lobar pneumonia?

A. The patient may present with:

- Fever, may be with chill and rigor
- Cough, initially short, painful and dry. Later on, expectoration (during resolution). Rusty sputum (due to *Streptococcus pneumoniae*)
- May be hemoptysis
- Chest pain, pleuritic (may radiate to shoulder or abdomen)
- Other features—dyspnea, anorexia, nausea and vomiting.

Q. What are the **complications** of pneumonia?

A. As follows:

- Pulmonary—lung abscess, pleurisy, pleural effusion, empyema thoracis, pneumothorax by *Staphylococcus aureus*, fibrosis of lung, collapse, adult respiratory distress syndrome (ARDS), delayed or slow resolution
- Cardiovascular—pericarditis, myocarditis, endocarditis, arrhythmia, thromboembolic disease and peripheral circulatory failure
- Neurological—meningism, meningoencephalitis
- Musculoskeletal—septic arthritis

- GIT—meteorism (gaseous distension of stomach, intestine or abdomen).
- Others—septicemia, renal failure, hepatitis, ectopic abscess formation by *Staphylococcus aureus*.

Q. How to **differentiate** between bacterial and viral pneumonia?

A. As follows:

Topic	Bacterial pneumonia	Viral pneumonia
1. Onset	Abrupt, high fever with chill and rigor	Less abrupt, history of upper respiratory tract infection and low-grade fever, headache and malaise
2. Cough	Initially dry, later rusty sputum or purulent	Usually dry (extrathoracic complains are more)
3. Pleuritic chest pain	Common.	Less common (respiratory complaints are less common, constitutional symptoms predominate)
4. Physical signs of consolidation	Well marked	Minimal
5. Blood count	Leukocytosis	Normal or leukopenia.
6. Chest X-ray	Lobar or segmental homogeneous opacity with air bronchogram	Mottling or reticular pattern or patchy opacity or streaky
7. C/S	Organism found	No organism

Q. What are the causes of **slow or delayed resolution** of pneumonia?

A. Delayed resolution means when the physical signs persist for more than 2 weeks and radiological features persist for more than 4 weeks after antibiotic therapy. Causes are:

- Incorrect microbiological diagnosis
- Fungal, tubercular or atypical pneumonia
- Improper antibiotic or insufficient dose
- Bronchial obstruction (bronchial carcinoma, adenoma, foreign body)
- Empyema or atelectasis
- Immunocompromised patient (HIV, DM, lymphoma, leukemia, multiple myeloma).

Note Remember the following points:

- Physical signs of consolidation may appear within 2 days, and disappear within 2 weeks with proper treatment
- Radiological opacity appears within 12 to 18 hours, and disappears within 4 weeks with proper treatment
- If radiological opacity persists after 8 weeks (with treatment), it is called non-resolution

Q. What are the causes of **recurrent pneumonia** (3 or more separate attack)?

A. As follows:

- Bronchial obstruction (bronchial carcinoma, adenoma, foreign body)
- Lung disease (bronchiectasis, lung abscess, cystic fibrosis, sequestrate segment of lung—commonly left lower lobe)

- Aspiration (achalasia cardia, scleroderma, pharyngeal pouch)
- Immunocompromised patient (HIV, DM, lymphoma, leukemia, multiple myeloma).

Q. What are the **criteria** of assessment of severity of CAP?

A. CURB-65 criteria may be used for the assessment of severity of CAP. 1 point is scored for each of the following features:

- **C**onfusion (mini mental score 8 or less or new disorientation in person, place or time)
- **U**rea > 7 mmol/L or > 20 mg/dL
- **R**espiratory rate > 30 /min
- **B**lood pressure (systolic BP < 90 mm Hg and diastolic BP < 60 mm Hg)
- Age > **65** years.

This score is used for management:

- Score 0 or 1—home treatment
- Score 2—hospitalization
- Score 3 or more—manage in hospital, may require ICU.

Other markers of severity of pneumonia

- Chest X-ray—more than one lobe involved
- PaO_2 < 8 κPa
- Low albumin (<35 g/L)
- White cell count (<4,000/cmm or >20,000/cmm)
- Blood culture positive.

Q. What are the **indications** for referral for ITU?

A. As follows:

- CURB score 4 to 5
- Persistent hypoxia despite high concentration of oxygen (PO_2 < 8 κPa or 60 mm Hg)
- Progressive hypercapnia
- Severe acidosis
- Shock
- Depressed consciousness.

Q. What is **nosocomial pneumonia?** What are the **causes** and **predisposing factors**?

A. New episode of pneumonia occurring at least 2 days after admission in the hospital is called nosocomial pneumonia.

Causes are: If it occurs within 4 to 5 days of admission (early onset), organisms are similar to CAP. However, if it occurs later (late onset), common organisms are:

- Gram-negative enterobacteriaceae *(Escherichia coli, Klebsiella and Pseudomonas aeruginosa)* are common
- *Staphylococcus aureus* including methicillin-resistant *Staphylococcus aureus* (MRSA)
- Anaerobic organism.

Predisposing factors:

- Elderly patient
- Bed bound, unconscious (e.g. CVA)
- Postoperative case (thoracic or abdominal surgery)
- Malignancy
- Diabetes mellitus
- Use of steroid, cytotoxic drugs, antibiotics
- Prolonged anesthesia, intubation, tracheostomy, IV canula

- Achalasia of cardia, dysphagia due to any cause, vomiting
- Bulbar or vocal cord palsy
- Nasogastric intubation
- Abdominal sepsis, infected emboli.

Q. How to **diagnose** nosocomial pneumonia?

A. After admission in the hospital, associated with predisposing factors, if the patient develops purulent sputum, fever associated with radiological infiltrate, leukocytosis or leukopenia unexplained increase in oxygen requirement.

Q. How to treat **nosocomial pneumonia?**

A. Empirical antibiotic therapy should be started which should cover Gram-negative organisms:

- A third generation cephalosporin (e.g. cefotaxime) with an aminoglycoside (gentamicin)
- Meropenem or
- A monocyclic beta lactam (e.g. aztreonam) and flucloxacillin
- MRSA is treated with IV vancomycin. When possible, oral therapy may be considered with doxycycline, rifampicin or linezolid
- If pseudomonas infection is suspected: IV ciprofloxacin or ceftazidime should be given.

Note

Aspiration pneumonia is also common in hospital and involves multiple organism with anaerobe. Treatment—IV co-amoxiclav or cefuroxime plus metronidazole.

Physiotherapy and oxygen therapy, fluid support and monitoring are also essential.

Q. What is **bronchopneumonia**?

A. It is defined as wide spread diffuse patchy alveolar opacity associated with bronchial and bronchiolar inflammation, often affecting both lower lobes. In children, it occurs as a complication of measles or whooping cough and in elderly, a complication following bronchitis or influenza.

Q. What is **typical pneumonia?**

A. Typical pneumonia is characterized by high temperature with cough, pleuritic chest pain, features of consolidation, caused by *Streptococcus pneumoniae*, *Staphylococcus aureus*, etc. Respiratory symptoms are more with constitutional symptoms.

Q. What is **atypical pneumonia?**

A. When pneumonia is caused by mycoplasma, legionella, coxiella, chlamydia. In these cases, constitutional symptoms are more than respiratory symptoms. Features are:

- Gradual onset
- Dry cough
- Low grade fever
- Constitutional symptoms are more than respiratory symptoms (headache, myalgia, fatigue, nausea, vomiting)
- Less physical finding in the chest.

Q. How to **diagnose and treat** *Mycoplasma pneumoniae?*

A. It is common in children and young adult and is usually associated with headache, malaise and severe cough. Physical signs are less marked. Epidemics occur in cycle every 3 to 4 years.

Investigations**:**

- WBC (normal)
- Chest X-ray (commonly lower lobe involvement), may show bilateral patchy consolidation
- Cold agglutinin (positive in 50% cases)
- Rising antibody titer for *Mycoplasma pneumoniae*
- Others (CFT and hemagglutination test).

Extrapulmonary complications of *Mycoplasma pneumonia:*

- Maculopapular skin rash, erythema multiforme and Stevens Johnson syndrome
- Myocarditis and pericarditis
- Hemolytic anemia (Coombs test may be positive) and thrombocytopenia
- Meningoencephalitis, GBS and other neurological abnormalities
- Myalgia and arthralgia
- Gastrointestinal symptoms like vomiting, diarrhea.

Treatment:

- Clarithromycin 500 mg twice daily orally or IV or
  Erythromycin 500 mg 6 hourly orally or IV for 7 to 10 days
- **Or,** Doxycycline 100 mg twice daily
- Rifampicin 600 mg 12 hourly.

Note

The term atypical pneumonia is abandoned

Q. How to **diagnose and treat** *Legionella pneumophila?*

A. Three patterns of Legionnaires' disease may occur:

- Outbreak of infection is usually associated with contaminated water supply or cooling system, or from stagnant water in cistern or shower head.
- Sporadic case, where source is unknown. It is usually common in middle aged and elderly, more in smokers.
- Outbreaks may occur in immunocompromised patients as for example those on corticosteroid therapy. Diabetes and CKD also increase risk.

Features are: Initially viral-like illness with high fever, chill and rigor, malaise, myalgia and headache. Dry cough, which is later productive and purulent. There may be nausea, vomiting, diarrhea and pain abdomen. Mental confusion and other neurological signs, even coma may be present. Occasionally, renal failure and hematuria may be seen.

Investigations:

- WBC—lymphopenia without marked leukocytosis.
- Chest X-ray—usually shows lobar and then multilobar shadowing. A small pleural effusion may be present. Cavitation is rare
- Hyponatremia
- Hypoalbuminemia
- High serum aminotransferases, creatine phosphokinase
- Direct immunofluorescent for Legionella in pleural fluid, sputum or bronchial washings. Culture on special media can be done, but takes 3 weeks
- Legionella serology—4 fold rise is highly suggestive
- Urine for antigen (highly specific)
- Urine R/E shows hematuria.

Treatment:
- Clarithromycin 500 mg twice daily orally or IV or
  Erythromycin 500 mg 6 hourly orally or IV for 7 to 10 days
- Rifampicin 600 mg 12 hourly.

Prognosis: 10% mortality (may be up to 30% in elderly).

Q. How to **treat** pneumonia?

A. Sputum should be sent for C/S and antibiotic should be started. The treatment involves:

1. General treatment—rest, O_2 therapy, adequate hydration and chest physiotherapy

2. Antibiotic (empirically with suspicion of cause).

Community acquired pneumonia (CAP):

1. Mild CAP:
- Amoxicillin 500 mg 8 hourly orally or erythromycin 500 mg 6 hourly or clarithromicin 500 mg twice daily or azithromycin 500 mg daily
- If *Staphylococcus aureus* is suspected—clarithromycin 500 mg twice daily orally or IV, **plus** flucloxacillin 1 to 2 g 6 hourly IV
- If *Klebsiella* is suspected—ciprofloxacin 200 mg IV 12 hourly, **plus** gentamycin 60 to 80 mg IV 8 hourly (see serum creatinine level) or gentamicin plus ceftazidime 1 g IV 8 hourly

Duration of treatment: 7 to 10 days (up to 14 days):
- If *Mycoplasma, Legionella* or atypical organism is suspected—clarithromycin 500 mg twice daily orally or erythromycin 500 mg 6 hourly orally, or tetracycline or doxycycline may be used.

Duration of treatment: 2 to 3 weeks.

2. Severe CAP:
- Clarithromycin 500 mg twice daily IV or erythromycin 500 mg 6 hourly IV
- **Plus** add one of the following:
  i. Co-amoxiclav 1 to 2 g 8 hourly IV
  ii. Cefuroxime 1.5 g 8 hourly IV
  iii. Ceftriaxone 1 to 2 g IV daily
  iv. Amoxicillin 1 g 6 hourly IV.
  v. If *Staphylococcus aureus* is suspected—flucloxacillin 2 g 6 hourly IV or sodium fusidate is added.

Q. What are the criteria for **discharge** of a patient with pneumonia from hospital?

A. To discharge, the patient should be clinically stable with no more than one of the following clinical signs:
- Temperature > 37.8 ºC
- Heart rate > 100/min
- Respiratory rate > 24/min
- Systolic BP < 90 mm Hg
- SaO_2 < 90%
- Inability to maintain oral intake
- Abnormal mental status.

PNEUMOTHORAX

CHIEF COMPLAINTS

- Breathlessness for … days
- Right sided chest pain for … days
- Cough for … days.

HISTORY

History of present illness: According to the statement of the patient, he was alright … days back. Since then, he suddenly felt severe breathlessness associated with pain in right side of his chest. Breathlessness is present in rest, more marked on lying on right side and also on lying flat. It is non-progressive, not associated with wheeze and does not relieve by taking rest or drugs. He also complains of right sided chest pain, which is sharp and stabbing in nature, aggravated by deep breathing, coughing, with movement and lying on right side but no radiation. The patient also complains of cough with slight mucoid expectoration but no hemoptysis. There is no history of trauma or fever.

History of past illness: There is no history suggestive of COPD, or chronic bronchitis or bronchial asthma. There is no previous attack of such illness.

Family history: Nothing contributory.

Socioeconomic history: He is a laborer, living in a slum area with poor sanitary facilities.

Personal history: He smokes 30 to 40 sticks/day for 20 years, but nonalcoholic.

GENERAL EXAMINATION

- The patient appears anxious and slightly dyspneic
- Decubitus: patient prefers to lie on left lateral position
- He is mildly anemic
- No jaundice, cyanosis, edema, clubbing, koilonychia or leukonychia
- No lymphadenopathy or thyromegaly
- Respiratory rate: 34/min
- BP: 110/80 mm Hg
- Pulse: 108/min.

SYSTEMIC EXAMINATION

Respiratory System (Supposing Right Side)

Inspection:
- Restricted movement on right side of the chest
- Intercostal spaces appear full.

Palpation:
- Trachea—deviated to the left
- Apex beat—in left 6th intercostal space in anterior axillary line (shifted to left), normal in character
- Vocal fremitus—reduced in right side but normal on the left side
- Chest expansion—reduced on the right side of the chest.

Percussion:
- Hyper-resonance in right side (tell where), but normal on the left side
- Upper border of the liver dullness—in the right 6th intercostal space in the midclavicular line.

Auscultation:
- Breath sound—diminished (or absent) on the right side of the chest (tell up to which space), but vesicular on the left side.
- Vocal resonance—diminished (or absent) on the right side of the chest (tell up to which space), but normal on the left side.

Examination of other systems reveals nothing abnormal.

SALIENT FEATURES

Mr …, 38 years, laborer, normotensive, nondiabetic, heavy smoker, hailing from …, presented with sudden severe breathlessness associated with right sided chest pain for … days. Breathlessness is present in rest, more marked on lying on right side and also on lying flat. It is non-progressive, not associated with wheeze and does not relieve by taking rest or drugs. He also complains of right sided chest pain, which is sharp and stabbing in nature, aggravated by deep breathing, coughing, with movement and lying on right side but no radiation. The patient also complains of cough with slight mucoid expectoration but no hemoptysis. There is no history of trauma or fever. There is no history suggestive of COPD, or chronic bronchitis or bronchial asthma. There is no such illness in the past. He smokes 30 to 40 sticks a day for last 20 years. There is no family history of such illness.

On examination, general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is right sided pneumothorax

Q. What are your **differential diagnoses?**
A. As follows:
- Big pulmonary cavity
- Giant bullae.

Q. Mention **one single** investigation for your diagnosis.
A. X-ray chest P/A view.

Q. What **investigations** do you suggest?
A. As follows:
- Complete blood count and ESR
- Chest X-ray P/A view
- Sometimes, CT scan of chest.

RELATED QUESTIONS AND ANSWERS

Q. What is **pneumothorax?**
A. Pneumothorax means presence of air in the pleural cavity.

Q. What is the **usual presentation** of pneumothorax?
A. The patient usually presents with sudden onset of unilateral pleuritic chest pain and breathlessness.

Q. What are the **definitive signs** of pneumothorax?
A. Hyper-resonance on percussion and diminished or absent breath sound.

Q. What are the types of pneumothorax?

A. As follows:

1. Spontaneous: It may be primary and secondary

2. Traumatic.

Q. What are the causes of pneumothorax?

A. As follows:

1. Spontaneous:

a. Primary: Without underlying lung disease. It is due to:
   - Rupture of apical subpleural bleb due to congenital defect in connective tissue of alveolar walls. Common in young, 15 to 30 years of age. M:F ratio is 4:1. The patient is tall, lean and thin, there is 25% chance of recurrence.
   - Rupture of emphysematous bullae or pulmonary end of pleural adhesion.

b. Secondary: Occurs in pre-existing lung disease. Causes are:
   - Commonly COPD and tuberculosis.
   - Others—lung abscess, acute severe asthma, bronchial carcinoma, pulmonary infarction, all forms of fibrotic and cystic lung disease, Marfan's syndrome, Ehlers-Danlos syndrome and eosinophilic granuloma.

2. Traumatic:

a. Iatrogenic—during aspiration of pleural fluid, thoracic surgery, lung biopsy or pleural biopsy, positive pressure ventilation, thoracocentesis and subclavian vein catheterization.

b. Chest wall injury.

Note Remember the following points:

- In young patient, common cause is rupture of subpleural bleb
- In patient > 40 years of age, common cause is chronic bronchitis with emphysema

Q. What are the types of spontaneous pneumothorax?

A. Three types (anatomical):

1. Closed—communication between the lung and pleural space is sealed off. Intrapleural pressure is less than atmospheric pressure. Trapped air is slowly reabsorbed, lung reexpands in 2 to 4 weeks. Closed pneumothorax may be mild, moderate and large.
2. Open—communication between the lung and pleural space persists (bronchopleural fistula). Intrapleural pressure and atmospheric pressure are equal throughout the respiratory cycle, which prevents re-expansion of the collapsed lung. Hydropneumothorax develops. Infection is common and empyema develops. Physical examination shows features of hydropneumothorax. Causes are:
   - Rupture of emphysematous bullae
   - Small pleural bleb
   - Tuberculous cavity
   - Lung abscess bursting into pleural cavity.
3. Valvular—There is a communication between the pleura and the lung which acts as a one-way valve allowing air to enter into the pleural space during inspiration, but does not let air escape on expiration. Intrapleural pressure becomes greater than the atmospheric pressure. It results in compression of the lung, shifting of mediastinum to the opposite side, compression of heart and the opposite lung also. It reduces the venous return by compressing the SVC. There is rapidly progressing breathlessness, cyanosis, shock, etc. It is a medical emergency, death may occur within minutes.

Note Remember the following:

Normal intrapleural pressure is negative (subatmospheric), usually – 2.5 to – 6.0 mm Hg.

Q. How would you **grade** pneumothorax?

A. According to British Thoracic Society:

- Mild—small rim of air around the lung, <20% of the radiographic volume
- Moderate—lung collapse, >20 to 50% of the radiographic volume
- Large—lung collapse, >50% of the radiographic volume
- Tension—pneumothorax with cardiorespiratory distress, features of shock.

Q. What are the **causes of recurrent pneumothorax** (more than twice)? How to **treat**?

A. Causes are:

- Apical subpleural bleb or cyst (congenital)
- Emphysematous bullae
- Cystic fibrosis
- Others—Marfan's syndrome, catamenial pneumothorax, Ehlers-Danlos syndrome, α_1- antitrypsin deficiency and histiocytosis X, honeycomb lung.

Treatment:

1. Chemical pleurodesis. Done by injecting tetracycline (500 mg), kaolin or talc into the pleural cavity through intercostal tube.
2. Surgical pleurodesis. Done by parietal pleurectomy or pleural abrasion during thoracotomy or thoracoscopy. Indications are:
   - All patients after a second pneumothorax
   - Considered after first episode of secondary pneumothorax, if there is low respiratory reserve
   - Patient who plan to continue activity, where pneumothorax would be particularly dangerous (e.g. flying or diving) should undergo definitive treatment after first episode of primary spontaneous pneumothorax.

Note Remember the following:

Pleurodesis is avoided in patient with cystic fibrosis, as lung transplantation may be required and pleurodesis may make this condition technically not feasible.

Q. What are the indications of **surgery (open thoracotomy)?**

A. As follows:

- Failure of the lung to re-expand after 5 days of tube thoracotomy
- Recurrence (usually on third recurrence)
- Bilateral pneumothorax.

Q. What is **coin test?**

A. In this test, one coin is placed on the front or back of the chest and struck with edge of another coin. At the same time auscultated on the opposite side of the chest at the same level. There will be a metallic, bell-like sound if pneumothorax is present.

Q. What is **catamenial pneumothorax?**

A. If pneumothorax develops at the time of menstruation, it is called catamenial pneumothorax. It is usually on the right side, occurs within 48 hours of onset of menstruation, common in 25 to 30 year old female and is due to intrapleural endometriosis.

It is treated by hormone therapy to suppress ovulation (by progesterone or androgen therapy) or simply by oral contraceptive pills. Sometimes, surgical exploration and pleurodesis may be needed.

Q. What is **tension pneumothorax?** What are the **causes?** How to **treat?**

A. It is a valvular-type of pneumothorax, in which there is a communication between lung and pleural cavity with one-way valve, which allows air to enter during inspiration and prevents to leave during expiration. It causes shifting of mediastinum to the opposite side and compresses the heart and opposite lung.

Features of tension pneumothorax:
- Severe chest pain (pain is worse with cough and relieve on sitting position)
- Severe and progressively increasing dyspnea
- Cough
- Tachypnea, tachycardia, pulsus paradoxus
- Features of shock (hypotension, central cyanosis and tachycardia)
- Raised JVP, engorged neck vein due to compression of the heart
- Shifting of mediastinum to the opposite side.

Note

Cardinal features are progressively increasing dyspnea and features of shock.

Causes of tension pneumothorax:
- Traumatic
- Mechanical ventilation at high pressure
- Rarely, spontaneous pneumothorax.

Treatment:
- Immediate insertion of wide bore needle in second intercostal space in midclavicular line, with the patient is sitting position.
- Intrathoracic tube is inserted in fourth, fifth or sixth intercostal space in midaxillary line, and the tip of the tube should be advanced in apical direction. It is connected to a underwater seal or one-way Heimlich valve.
- The patient should be kept propped up with oxygen inhalation.
- Morphine 5 to 10 mg subcutaneously.
- If bubbling ceases, repeat chest X-ray. If the lung re-expands, tube may be removed after 24 hours. Tube should be removed during expiration or Valsalva maneuver (the tube need not be clamped before removing).
- If no response or continued bubbling for 5 to 7 days, surgical treatment may be necessary.

Q. How do you know that the **water seal drainage** is working properly or not?

A. As follows:
- Bubbling of air in water
- During expiration or coughing, more bubbling occurs
- During inspiration, water column ascends within the tube, which remains under water.

Q. What **advice** is given to the patient with **water seal drainage?**

A. Never raise the bottle above the chest wall. The bottle must be kept below the level of thorax. The patient is also advised to inflate air pillows or balloons which will help in the expansion of collapsed lung.

Q. What are the **indications** of chest tube or IT tube drainage?

A. As follows:

- Tension pneumothorax
- Large second spontaneous pneumothorax if > 50 years
- Malignant pleural effusion
- Empyema thoracis or complicated parapneumonic effusion
- Hydropneumothorax
- Traumatic hemopneumothorax
- Postoperatively as for example thoracotomy, esophagectomy, cardiothoracic surgery.

Q. How to **follow-up** a patient after chest tube insertion?

A. As follows:

- Bubbling—whether it disappears or persistent (indicates leaking)
- Blockage of the tube by clot or kinking
- Malposition
- Retrograde flow back into the chest.

Q. How to **treat** pneumothorax?

A. Depends on whether it is primary or secondary, open, closed or tension or presence of symptoms.

1. In primary small pneumothorax:
   - Spontaneous resolution occurs. Follow-up at 2-week interval (repeat chest X-ray)
   - Normal activity
   - Avoid strenuous exercise
2. In primary moderate to large with breathlessness: Percutaneous needle aspiration of air (2 to 5 litre. Stop, if resistance to suction is felt or patient coughs).
3. In secondary pneumothorax: Patient with COPD, even small pneumothorax can cause respiratory failure. Hence, water seal drainage should be given.
4. Open pneumothorax: Surgery (as is due to bronchopleural fistula).
5. Tension pneumothorax (described as above).

Advice to the patient:

- Must stop smoking
- Avoid air travel for 6 weeks after normal chest X-ray
- Diving should be permanently avoided.

Q. If you are working in a **remote place** and a patient presents with tension pneumothorax, what measures should you take?

A. Immediately I shall insert a wide bore needle (may be cannula/venflon) in the second intercostal space in midclavicular line. This will allow the trapped air to escape (producing an audible hiss). Then I shall send the patient to the nearest hospital (do not remove the cannula, tape it securely).

Q. How long the lung takes to **re-expand?**

A. Air is absorbed at the rate of 1.25% of the total radiographic volume/day. So, if there is 50% lung collapse, it will take 40 days to expand.

Q. What are the possible causes of **failure of re-expansion** of lung?

A. As follows:

- Water seal drainage is not working properly or may be blocked.
- Presence of bronchopleural fistula.
- A major bronchus may be obstructed.
- Lung is completely fibrosed with permanent damage.

Q. What is **hydropneumothorax?** What are the **causes?** How to **manage?**

A. When there is accumulation of fluid and air in pleural cavity, it is called hydropneumothorax.

Its **causes** are:

- Iatrogenic (during aspiration of pleural fluid)
- Pulmonary tuberculosis
- Bronchopleural fistula
- Trauma (penetrating chest injury and thoracic surgery)
- Rupture of lung abscess
- Esophageal rupture
- Erosion of bronchial carcinoma.

Management**:** Water seal drainage and treatment of primary cause.

Q. What is the **bedside test** of hydropneumothorax?

A. Succusion splash.

Q. What are the **signs** of hydropneumothorax?

A. In lower part, signs of pleural effusion and in upper part, signs of pneumothorax.

COLLAPSE OF THE LUNG

CHIEF COMPLAINTS

- Frequent cough for … months
- Breathlessness for … days
- Weight loss, malaise, anorexia for … days.

HISTORY

History of present illness: According to the statement of the patient, he was alright … months back. Since then, he has been suffering from severe dry cough, which is present throughout the day and night. Cough is worse on lying position, also occasionally it is aggravated on exposure to cold and dust. The patient also complains of breathlessness, which is usually on moderate to severe exertion, but there is no history of orthopnea or paroxysmal nocturnal dyspnea. For last … days, he also complains of loss of appetite and marked weight loss. There is no history of fever or haemoptysis or contact with TB patients.

History of past illness: He was suffering from some lung disease, the nature of which he could not mention.

Family history: Nothing significant.

Personal history: He smokes about 20 sticks/day for 20 years, but nonalcoholic.

Socioeconomic history: He works in a pillow shop where he sorts cotton and makes pillows and blankets.

Drug history: Nothing significant.

GENERAL EXAMINATION

- The patient is ill-looking and emaciated, dyspneic
- Mildly anemic
- Clubbing: There are generalized clubbing involving toes and fingers, but no hypertrophic osteoarthropathy
- No jaundice, cyanosis koilonychia, leukonychia or edema
- No lymphadenopathy or thyromegaly
- Pulse:100/min
- BP: 100/60 mm Hg
- Respiratory rate: 28/min.

SYSTEMIC EXAMINATION

Respiratory System (Supposing Right of Chest)

Inspection:

- Restricted movement on the right side
- Flattening on the upper part and crowding of ribs
- Drooping of the right shoulder.

Palpation:
- Trachea: Shifted to the right
- Apex beat: Shifted to the right (tell where)
- Vocal fremitus: Reduced (or increased) in the right side (tell up to where).

Percussion:
- Dullness in the right upper part of the chest (tell up to where)
- Upper border of liver dullness is in the right 4th intercostal space in the midclavicular line.

Auscultation:
- Breath sound: Bronchial (or reduced) on right side of the chest (tell up to where).
- Added sound: Some coarse crepitations are found on the right side of the chest (tell which spaces).
- Vocal resonance: Increased in right upper chest (or decreased), there is whispering pectoriloquy (present, if bronchial sound is present).

Note Signs of collapse depend on patency of the bronchus:
- If bronchus is completely obstructed (usually central collapse), all the signs will be collapsed (absent or reduced). Breathsound is diminished or absent. Vocal resonance is diminished or absent.
- If bronchus is patent (peripheral collapse), there is bronchial sound and increased vocal resonance.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 45 years, cotton sorter, normotensive, nondiabetic, smoker, hailing from …, presented with severe dry cough for … months. The cough is present throughout the day and night. It is worse on lying position, also occasionally it is aggravated on exposure to cold and dust. The patient also complains of breathlessness, which is usually on moderate to severe exertion, but there is no history of orthopnea or paroxysmal nocturnal dyspnea. For last … days, he also complains of loss of appetite and marked weight loss. There is no history of fever or hemoptysis or contact with TB patients. He was suffering from some lung disease, the nature of which he could not mention. He smokes about 20 sticks/day for 20 years.

On examination, general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is right sided lung collapse.

Q. What are your differential diagnoses?

A. Fibrosis of the lung.

Q. Why not fibrosis?

A. It may be fibrosis, but there are certain differentiating points. As fibrosis is a chronic process, the following findings are highly suggestive of fibrosis:
- Flattening of chest on the affected side
- Crowding of the ribs
- Drooping of the shoulder

These findings may be present in collapse as well, if it is prolonged. All other signs of collapse are same as in fibrosis, but with less degree.

Q. How to **confirm** your diagnosis?

A. X-ray chest PA view**:**

- In collapse: There is homogenous opacity with clear lung margin. Evidence of bronchial obstruction (mass lesion) may be seen, diaphragm may be elevated.
- In fibrosis: Nonhomogenous opacity, rib crowding and ring shadow due to dilatation of bronchi within fibrosis may be seen.

Q. Why not this is a case of **consolidation?**

A. In consolidation, trachea and apex beat will not be shifted and percussion is woody dull.

Q. Why not this is a case of **pleural effusion?**

A. In pleural effusion, trachea and apex beat are shifted to the opposite side.

Q. Why not this is a case of **thickened pleura?**

A. In thickened pleura, there is no shifting of the trachea and the apex beat.

Q. What **investigations** should be done in collapse of lung?

A. As follows:

- CBC
- Chest X-ray, PA view (homogenous opacity, heart and lung shifted to the affected side), and lateral view, if needed
- CT scan of chest
- Bronchoscopy (to see any obstruction, removal of foreign body, aspiration of any material, biopsy).

RELATED QUESTIONS AND ANSWERS

Q. What are the **types** of collapse?

A. As follows:

I. Etiologically:

1. Compression collapse (passive)—due to pleural effusion, pneumothorax and hydropneumothorax. Trachea and apex beat are shifted to the opposite side.
2. Absorption collapse (active)—caused by bronchial obstruction due to any cause. Air is absorbed distal to the obstruction and affected part is collapsed. Causes are:
   - Neoplasm (bronchial carcinoma, adenoma)
   - Foreign body (inert object and artificial teeth)
   - Mucous plug (due to bronchial asthma, cystic fibrosis, postoperative)
   - Aspergilloma
   - Pressure on bronchus from outside (enlarged lymph node, aortic aneurysm, pericardial effusion causing collapse of left lung and enlarged left atrium in mitral stenosis)
   - Rarely, congenital collapse due to absence of surfactant.

II. Anatomically:

1. Central—mass lesion (shows more signs and symptoms).
2. Peripheral—usually small collapse (shows less signs and symptoms).

Causes of collapse according to age:

- Neonate—congenital due to low or absent surfactant, aspiration of meconium.
- Children—foreign body.
- Young—bronchial adenoma and foreign body.
- Elderly—bronchial carcinoma and foreign body (artificial tooth).

Q. How can you **differentiate** central and peripheral collapse clinically?

A. As follows:

- In central collapse—bronchus is completely obstructed. So, breath sound is diminished or absent. Vocal resonance is diminished or absent.
- In peripheral collapse—bronchus is patent. So, breath sound is bronchial and vocal resonance is increased.

Note The most Common cause of collapse:

- Central – brochial carcinoma or adenoma, enlarged lymph node or foreign body.
- Peripheral – mucus plugging, bronchial cast.

Q. What is **middle lobe syndrome?**

A. Middle lobe syndrome is the recurrent or persistent atelectasis of right middle lobe.

The right middle lobe originates at an acute angle and is completely surrounded by lymph nodes. It is frequently obstructed by the enlarged lymph nodes due to malignancy or TB causing collapse of the lobe. There may be bronchiectatic changes. Foreign body may also be responsible.

Diagnosis:

- CT scan or MRI may be done
- Bronchoscopy is also helpful.

SUPERIOR VENA CAVA (SVC) OBSTRUCTION

CHIEF COMPLAINTS

- Cough with mild expectoration for … months
- Loss of appetite and weight loss for … months
- Gradual swelling of the face and arms for … days
- Headache for ... days.

HISTORY

History of present illness: According to the statement of the patient, he was alright … months back. Since then, he has been suffering from frequent cough which is present throughout the day and night. The cough is usually dry, sometimes associated with scanty mucoid expectoration. He also noticed small amount of blood with sputum several times. The patient also complains of loss of appetite and substantial weight loss for the same duration. There is no history of fever, chest pain or contact with TB patients. For the last … days, he noticed gradual swelling of the face and arms along with shortness of breath, which is more marked on exertion. The patient also complains of headache, mostly the vertex, which is aggravated by cough and movement of the head for the same duration. He denies any change of voice, back pain, yellow coloration of urine and sclera. His bowel and bladder habits are normal.

History of past illness: Nothing significant.

Family history: Nothing significant.

Personal history: He smokes about 30 sticks/day for 25 years, but nonalcoholic.

Socioeconomic history: Mention according to the patient's statement.

Drug history: Nothing significant.

GENERAL EXAMINATION

- The patient is dyspneic and emaciated.
- Face is edematous, red, plethoric and cyanosed.
- Eyes are red with congested conjunctiva (blood shot eyes), conjunctival edema (chemosis) and periorbital edema.
- Neck is swollen with engorged, non-pulsatile neck veins.
- Visible tortuous veins in chest wall and abdomen, flow is downwards.
- Upper limbs are edematous with prominent engorged veins.
- Generalized clubbing involving toes and fingers, but no hypertrophic osteoarthropathy.
- No anemia, jaundice, cyanosis, koilonychia, leukonychia or pedal edema.
- No lymphadenopathy or thyromegaly.
- Pulse: 110/min.
- BP: 90/60 mm Hg.
- Respiratory rate: 28/min.

SYSTEMIC EXAMINATION

Respiratory System

(Supposing right sided)

Inspection:

- Shape—normal
- Movement is restricted on right upper chest
- Dilated veins visible on chest and back, flow is above downward.

Palpation:

- Trachea is central in position
- Apex beat—on left 5th intercostal space, 9 cm from midline, normal in character
- Vocal fremitus is reduced in right upper chest.

Percussion:

- Percussion note is dull in right upper chest
- Upper border of liver dullness is in the right 5th intercostal space in the midclavicular line
- Cardiac dullness is normal.

Auscultation:

- Breath sound is reduced on right upper chest
- Vocal resonance is reduced
- Few crepitations (may be present, mention where).

Fundoscopy shows dilated vessels, hemorrhage, exudate, rarely papilledema.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr ..., 65 years old, smoker, normotensive, nondiabetic, hailing from ..., presented with frequent cough for ... months, which is present throughout the day and night. The cough is usually dry, sometimes associated with scanty mucoid expectoration. He also noticed small amount of blood with sputum several times. The patient also complains of loss of appetite and substantial weight loss for the same duration. There is no history of fever, chest pain or contact with TB patients. For the last … days, he noticed gradual swelling of the face and arms along with shortness of breath, which is more marked on exertion. The patient also complains of headache, mostly the vertex, which is aggravated by cough and movement of the head for the same duration. He denies any change of voice, back pain, yellow coloration of urine and sclera. His bowel and bladder habits are normal. He smokes about 30 sticks/day for 25 years.

On examination, general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is superior vena cava obstruction.

Q. What do you think the **cause** of SVC obstruction in this case?

A. Mention according to the age of the patient:

- In elderly or middle aged—causes are bronchial carcinoma, lymphoma
- In young or early age—common cause is lymphoma.

Q. Tell one **single investigation** which will help the diagnosis of SVC obstruction.

A. Chest X-ray (which may show bronchial carcinoma and lymphoma).

Q. What **investigations** should be done in SVC obstruction?

A. As follows:

1. Chest X-ray
2. CBC, ESR
3. Sputum for malignant cells
4. CT or MRI of chest
5. Others (according to suspicion of cause or physical findings):
   - If palpable lymph nodes FNAC or biopsy
   - Bronchoscopy and mediastinoscopy, venography and occasionally thoracotomy may be needed
   - Echocardiography in some cases.

RELATED QUESTIONS AND ANSWERS

Q. What **physical findings** did you look for to find out the cause of SVC obstruction?

A. As follows:

- Chest (bronchial carcinoma)
- Lymph nodes (lymphoma and metastasis)
- Liver and spleen (lymphoma)
- Clubbing, nicotine stain (bronchial carcinoma)
- Thyroid (to see retrosternal thyroid).

Q. What are the **presentations** of SVC obstruction?

A. The patient may complain of:

- Breathlessness, cough, hoarseness of voice and dysphagia
- Flushing, red, puffy and edematous face
- Headache (early morning), which is severe with coughing. May be syncope, dizziness or blackout, stupor, seizure (due to increased intracranial pressure)
- Symptoms are aggravated on lying down or bending forward (indicates mediastinal involvement)
- The patient may have stridor (tracheal compression), hoarseness of voice (recurrent laryngeal nerve involvement), Horner's syndrome (cervical sympathetic chain involvement).

Features of mediastinal compression—according to the involvement of structure:

1. Trachea: breathlessness, cough, stridor.
2. Esophagus: Dysphagia.
3. Bronchus: Features of collapse of lung.
4. Recurrent laryngeal nerve: Hoarseness of voice, bovine cough.
5. Phrenic nerve: Breathlessness (X-ray chest shows raised diaphragm).
6. Cervical sympathetic chain involvement: Horner's syndrome.
7. SVC:
   - Face is puffy, edematous and red
   - Neck is swollen with engorged, non-pulsatile neck veins
   - Visible tortuous veins in chest wall and abdomen, flow is downwards
   - Upper limbs are edematous with prominent engorged veins.

Q. What are the **causes of death** in SVC obstruction?

A. Death is due to:

- Respiratory obstruction
- Intracranial hemorrhage.

Q. What are the **causes of SVC obstruction?**

A. As follows:

1. Bronchial carcinoma (common cause, in 75%)
2. Lymphoma (early age, also in elderly)
3. Other causes:
   - Retrosternal thyroid
   - Thymoma
   - Mediastinal fibrosis (its causes include idiopathic, radiation, methysergide used in migraine and histoplasmosis)
   - Metastasis to the mediastinum
   - Chronic constrictive pericarditis
   - Giant aortic aneurysm
   - Carcinoma of esophagus
   - Rarely thrombosis, invasion by malignancy, germ cell tumor.

Q. What is **Pemberton's test?**

A. On lifting the arms over the head for more then 1 minute, there is increased facial plethora or cyanosis, raised JVP (non-pulsatile) and inspiratory stridor.

Q. How will you **treat** the case?

A. Treatment is according to cause:

1. General treatment:
   - To relieve edema—intravenous frusemide, head should be raised, dexamethasone may be used
   - To relieve severe obstruction—expandable metallic stent may be used (placed in SVC) as palliative measure. Venoplasty may be considered
   - Anticoagulant may be given, if needed
   - Ventilatory support, if needed.
2. Treatment of cause:
   - The most common cause is bronchial carcinoma. Radiotherapy in non-small cell carcinoma and chemotherapy for small cell carcinoma.
   - If lymphoma—treat accordingly (usually chemotherapy).

Note Remember the following points:

- SVC obstruction of recent onset is likely to be due to malignancy
- SVC obstruction of long-standing is due to nonmalignant origin.

DIFFUSE PARENCHYMAL LUNG DISEASE (DPLD)

CHIEF COMPLAINTS

- Breathlessness for … months
- Cough for … months
- Weight loss for ... months.

HISTORY

History of present illness: According to the statement of the patient, he was alright … months back. Since then, he has been suffering from frequent cough which is usually non-productive, but sometimes with scanty mucoid expectoration. Cough is aggravated on exposure to dust and fume. He also complains of breathlessness. Initially, it was present during moderate to severe exertion, but for the last ... months, it is progressively increasing, becoming worse with mild exertion such as going to toilet, dressing, etc. There is no history of orthopnea or paroxysmal nocturnal dyspnea. He does not give any history of chest pain, hemoptysis, fever, joint swelling or pain, skin rash, oral ulcer. For the last ... months, he is experiencing malaise, marked loss of appetite and body weight. His bowel and bladder habits are normal. He denies any history of contact with birds at home or at work or with tuberculosis patient.

History of past illness: Nothing significant.

Family history: Nothing significant.

Personal history: He smokes about 15 sticks per day for 30 years, nonalcoholic.

Socioeconomic history: He works in a pillow shop where his job involves sorting cotton and making pillows, blankets, etc.

Drug history: He used to take cough syrup, salbutamol, aminophylline etc, for his cough.

GENERAL EXAMINATION

- The patient is dyspneic
- There is central cyanosis involving tongue, lips and finger tips
- Generalized clubbing is present involving all the fingers and toes. But no hypertrophic osteoarthropathy
- He is mildly anemic
- No jaundice, koilonychia, leukonychia or edema
- No lymphadenopathy or thyromegaly
- Pulse: 78/min
- BP: 120/80 mm Hg
- Respiratory rate: 30/min
- Temperature: Normal.

SYSTEMIC EXAMINATION

Respiratory System

Inspection:

- Chest expansion on both sides is reduced symmetrically.

Palpation:
- Trachea is central in position
- Apical beat is in left 5th intercostal space, just medial to the midclavicular line, normal in character
- Vocal fremitus is normal on both sides.

Percussion:
- Percussion note is resonant over both lung fields
- Upper border of liver dullness is in right 4th intercostal space in midclavicular line
- Area of cardiac dullness is normal.

Auscultation:
- Breath sound is vesicular with prolonged expiration
- Bilateral basal end-inspiratory fine crepitations (like unfastening of Velcro) unaltered by coughing is present
- Vocal resonance is normal.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 45 years old, worker in a pillow shop, normotensive, nondiabetic, smoker, hailing from …, presented with frequent cough for ... months, which is usually non-productive, but sometimes with scanty mucoid expectoration. Cough is aggravated on exposure to dust and fume. He also complains of breathlessness. Initially, it was present during moderate to severe exertion, but for the last ... months, it is progressively increasing, becoming worse with mild exertion such as going to toilet, dressing, etc. There is no history of orthopnea or paroxysmal nocturnal dyspnea. He does not give any history of chest pain, hemoptysis, fever, joint swelling or pain, skin rash, oral ulcer. For the last ... months, he is experiencing malaise, marked loss of appetite and body weight. His bowel and bladder habits are normal. He denies any history of contact with birds at home or at work or with tuberculosis patient. He smokes about 15 sticks per day for 30 years. He used to take cough syrup, salbutamol, aminophylline, etc. for his cough. There is no family history of such illness.

On examination – general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is DPLD (likely to be IPF).

Q. What are your **differential diagnoses?**

A. As follows:
- Bilateral bronchiectasis
- Fibrosis of the lung due to other causes
- Chronic heart failure.

Q. **Why not** pulmonary edema?

A. From the history, there is no orthopnea or PND or history suggestive of any cardiac disease. On examination, there is generalized clubbing which is against pulmonary edema.

Also, in pulmonary edema, crepitations are usually fine, both present in inspiration and expiration and altered by coughing. But in case of DPLD, it is usually end inspiratory coarse crepitations, unaltered by coughing.

Q. What **history did you take** to diagnose DPLD?

A. As follows:

- Onset of the disease—acute or chronic
- History of connective tissue disease like rheumatoid arthritis, systemic sclerosis, dermatomyositis, SLE
- History of drugs
- Occupational and environmental history.

Q. What are the causes of bilateral basal crepitations?

A. As follows:
- LVF (fine crepitation, may be altered by coughing, has other evidences of LVF)
- Bilateral brochiectasis (crepitations both in inspiration and expiration, altered by coughing)
- DPLD.

Q. What are the causes of clubbing with bilateral basal crepitations?

A. As follows:
- Bilateral brochiectasis
- DPLD.

Q. What investigations should be done in IPF (or DPLD)?

A. As follows:
1. Full blood count (shows different changes in different diseases):
   - ESR may be high (polycythemia is rare)
   - Lymphopenia (in sarcoidosis)
   - Eosinophilia (in pulmonary eosinophilia and drug reactions).
   - Neutrophilia (in hypersensitivity pneumonitis).
2. X-ray chest: Initially ground glass appearance, bilateral reticulonodular shadow mainly in lower zone. Lung size may be reduced, diaphragm may be raised. In advanced stage, there may be a honeycomb appearance.
3. HRCT: Helpful in early diagnosis, even when chest X-ray is normal. Changes are usually bilateral, peripheral and mainly in the lower lobes. There are patchy subpleural reticular abnormality with minimal or no ground glass changes, honeycomb (thick walled cysts 0.5 to 2 cm in terminal and respiratory bronchioles) and traction bronchiectasis.
4. Pulmonary function tests:
   - Restrictive pattern (FVC and FEV_1 are proportionately low, and ratio is normal or high).
   - Lung volumes are reduced (may be paradoxically preserved in patient with concomitant emphysema).
   - Reduced carbon monoxide (CO) transfer.
   - Peak flow rate may be normal.
5. Arterial blood gas: Hypoxemia with normal or low P_aCO_2 (due to hyperventilation).
6. Bronchoscopy: Bronchoalveolar lavage shows increased number of cells particularly neutrophils and macrophages. There may be increased lymphocytes in sarcoidosis, extrinsic allergic alveolitis and drug induced lung disease. Transbronchial lung biopsy may be needed for confirmation.
7. Others (according to suspicion of cause):
   - CRP may be raised
   - LDH (high level indicates disease activity in DPLD)
   - For sarcoidosis: Calcium may be elevated. Urinary calcium excretion and liver biopsy may be useful. Serum ACE is an indicator of disease activity. Gallium scanning may be done
   - For autoimmune diseases: Rheumatoid factor and anti-CCP antibodies. RA test and ANA are positive in 30% cases (in low titer)
   - Hypergammaglobulinemia.

8. For confirmation, lung biopsy is the definitive investigation. It is done in selected cases if diagnosis is uncertain. Biopsy is done in the following methods:
   - Transbronchial biopsy
   - Video assisted thoracoscopic (VATS) lung biopsy
   - Open lung biopsy in some cases.

Note

Lung biopsy is not a routine investigation. Typical clinical features and high-resolution CT (HRCT) are sufficient for diagnosis. However, lung biopsy is strongly indicated in young patient.

RELATED QUESTIONS AND ANSWERS

Q. What is **DPLD**?

A. DPLD are a heterogenous group of diseases characterized by diffuse lung injury and inflammation that can progress to lung fibrosis. Previously, it was called interstitial lung disease (ILD).

Q. **Why** is it called DPLD?

A. The term DPLD is preferred than ILD, because the pathological lesion involves the alveoli along with interstitium.

Q. What are the **stages** of DPLD?

A. As follows:
- Stage of ground glass opacity
- Stage of reticulonodular shadow
- Stage of streaky fibrosis
- Stage of honeycombing.

Q. **Classify** DPLS.

A. Six groups:
1. Granulomatous DPLD (e.g sarcoidosis).
2. Granulomatous DPLD with vasculitis (e.g. Wegener's granulomatosis, Churg Strauss syndrome, microscopic vasculitis).
3. Idiopathic interstitial pneumonia (IIP):
   a. Idiopathic pulmonary fibrosis (IPF, also called usual interstitial pneumonia—UIP. It was previously called cryptogenic fibrosing alveolitis 90%)
   b. Idiopathic interstitial pneumonia other than IPF (10%)
      - Desquamated interstitial pneumonia
      - Acute interstitial pneumonia
      - Nonspecific interstitial pneumonia
      - Respiratory bronchiolitis
      - Cryptogenic organizing pneumonia (COP, also called BOOP—bronchiolitis obliterans organizing pneumonia)
      - Lymphocytic interstitial pneumonia.
4. Pulmonary autoimmune rheumatic diseases (e.g. rheumatoid arthritis, SLE).
5. Drugs (busulfan, bleomycin, methotrexate, nitrofurantoin, amiodarone).
6. Other forms of DPLD, as for example histiocytosis X (Langerhans' cell histiocytosis), Goodpasture's syndrome, idiopathic pulmonary hemosiderosis, diffuse alveolar hemorrhage, lymphangioleiomyomatosis, pulmonary alveolar proteinosis.

Q. What are the **presentations** with IPF?

A. Patient is usually elderly, uncommon < 50 years

- Cough, usually dry
- Progressive breathlessness, usually exertional
- Arthralgia, cyanosis and finger clubbing (20 to 50% cases).

Q. What is the mechanism of **end-inspiratory crepitations** in IPF?

A. In IPF, alveoli remain collapsed. During forceful inspiration, sudden opening of collapsed alveoli produces coarse crepitations.

Q. What are the **diagnostic criteria** of IPF?

A. As follows:

Major criteria:

1. Exclusion of other known causes of DPLD, such as certain drug toxicities, environmental exposures, and connective tissue diseases.
2. Abnormal pulmonary function studies that include evidence of restriction.
3. Bibasilar reticular abnormalities with minimal ground glass opacities on HRCT scans.
4. Transbronchial lung biopsy or BAL showing no features to support an alternative diagnosis.

Minor criteria:

1. Age >50 year, male, smoker.
2. Insidious onset of otherwise unexplained dyspnea on exertion.
3. Duration of illness >3 months.
4. Bibasilar, inspiratory crackles (dry or "Velcro"-type in quality).

In the immunocompetent adult, the presence of all of the major diagnostic criteria as well as at least three of the four minor criteria increases the likelihood of a correct clinical diagnosis of IPF.

Q. How will you **investigate** a case of DPLD?

A. As follows:

Q. What are the **conditions mimicking** DPLD?

A. As follows:

- Infections: Viral pneumonia, TB, fungal infection, *Mycoplasma pneumoniae*, *Pneumocystis jirovecii* and parasites (e.g. filariasis).
- Malignancy: Leukemia, lymphoma, multiple metastases, lymphatic carcinomatosis, bronchoalveolar carcinoma.

- Pulmonary edema.
- Aspiration pneumonitis.

Q. How to **treat** IPF?

A. As follows:

1 Prednisolone 0.5 mg/kg with azathioprine 2 to 3 mg/kg is recommended in:
   - Highly symptomatic
   - Rapidly progressive disease
   - Ground glass opacity on CT scan
   - Sustained > 50% fall of FVC over 3 to 6 months.

2 Antifibrotic therapy (on trial):
   - Interferon γ 1b
   - Pirfenidone
   - Sildenafil
   - Bosentan
   - Etanercept (biological agent)
   - Thalidomide
   - N- acetyl cysteine.

3 Single lung transplantation in young patient at advanced stage. Survival is 1 year in 60% cases.

Prednisolone is given for at least 2 months and then tapered to a maintenance dose of 10 to 12.5 mg daily.

Q. What is the **prognosis** of IPF?

A. Usually 3 to 5 years survival in 50% cases (65% in steroid responder and 25% in steroid non-responder).

Q. What are the **complications** of IPF?

A. As follows:

- Pulmonary hypertension and cor pulmonale.
- Respiratory failure
- Others—infection and bronchial carcinoma.

Q. What are the **differences** between IPF (UIP) and COP (BOOP)?

A. As follows:

Features	IPF (UIP)	COP (BOOP)
1. Age	Elderly (55 to 60 years), slightly more in male	Adult
2. Smoking	Associated	Not associated
3. Onset	Insidious	Abrupt
4. Constitutional symptoms (fever, fatigue and weight loss)	Unusual	Common
5. Finger clubbing	Present	Absent
6. ESR	May be normal	Markedly increased

Contd...

Contd...

7. Lung function tests	Restrictive with reduced diffusing capacity	Restrictive but concomitant obstruction in 25% cases
8. Chest X-ray	Diminished lung volume	Normal lung volume
9. ANA, RA tests	Positive in 30%	Negative
10. Biopsy	Usually not required for diagnosis	Required. It typically shows buds of connective tissue (Masson's bodies)
11. Response to corticosteroid	Poor	Good in 2/3rd patients
12. Prognosis	Poor, median survival 3 to 5 years	Good if responsive to steroid Relapse are common

Q. What is **Hamman-Rich syndrome?**

A. It is a type of acute form of IPF, occurs in a small proportion of cases.

Q. What are the **restrictive** and **obstructive** airway diseases? What are the **differences**?

A. As follows:

- Restrictive: DPLD, ankylosing spondylitis and kyphoscoliosis.
- Obstructive: Emphysema, chronic bronchitis and bronchial asthma.

The differences are:

Features	Restrictive	Obstructive
1. Both FEV_1 and FVC	Proportionately reduced	FEV_1 is markedly reduced and FVC also reduced
2. Ratio between FEV_1 and VC	Normal	Reduced
3. RV	Reduced or normal	Increased
4. TLC	Reduced	Increased
5. Ratio between RV and TLC	Normal or slightly increased	Markedly increased

CYSTIC FIBROSIS

CHIEF COMPLAINTS

- Severe cough for … days
- Breathlessness for … days
- Fever for … days.

HISTORY

History of present illness: According to the statement of the patient, she was alright … days back. Since then, she has been suffering from severe cough which is productive with moderate amount of whitish sputum, which is more in the morning after waking from sleep. She also noticed scanty amount of blood in sputum once. She is also experiencing breathlessness for … days which is not related to physical exertion. There is no history of orthopnea or paroxysmal nocturnal dyspnea. The patient also complains of fever for … days which is high grade, intermittent, not associated with chill or rigor and subsides with sweating after taking paracetamol. Her appetite, bowel and bladder habits are normal. There is no history of chest pain, headache, sore throat, skin rash. There is no history of contact with tuberculosis patient.

History of past illness: She has been suffering from recurrent respiratory infection and bronchial asthma since her childhood. She took inhaler regularly for asthma. She also had intermittent abdominal pain and loose, bulky stool.

Family history: One of her sister had similar problems with recurrent respiratory tract infection and died at the age of 18 years.

Personal history: Mention according to the patient's statement.

Socioeconomic history: Mention according to the patient's statement.

Drug history: She took paracetamol, cough syrup, and salbutamol inhaler.

GENERAL EXAMINATION

- The patient is slightly emaciated.
- There is generalized clubbing involving both toes and fingers, but no hypertrophic osteoarthropathy.
- No anemia, jaundice, cyanosis, edema, koilonychia or leukonychia.
- No thyromegaly or lymphadenopathy.
- Pulse: 84/min.
- BP: 120/70 mm Hg.
- Respiratory rate: 26/min.
- (Examination of the sputum cup: Always look at the cup at the side of the patient, if any).

SYSTEMIC EXAMINATION

Respiratory System

Inspection:

- Chest movement slightly restricted (mention where). Or, no abnormality.

Palpation:
- Trachea—Central
- Apex beat—In left 5th intercostal space 9 cm from the midsternal line
- Vocal fremitus—Slightly increased on both base
- Chest expansion—Normal.

Percussion:
- Percussion note—Normal
- Liver and cardiac dullness—In normal area.

Auscultation:
- Breath sound—Normal vesicular (may be bronchial over the involved area)
- There are multiple coarse crepitations on the base of both lungs, both in inspiration and expiration, reduced (or disappeared) after coughing
- Vocal resonance—Slightly increased (mention where).

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Ms …, 15 years old, student, normotensive, nondiabetic, nonsmoker, hailing from …, presented with severe cough for … days which is productive with moderate amount of whitish sputum, which is more in the morning after waking from sleep. She also noticed scanty amount of blood in sputum once. She is also experiencing breathlessness for … days which is not related to physical exertion. There is no history of orthopnea or paroxysmal nocturnal dyspnea. The patient also complains of fever for … days which is high grade, intermittent, not associated with chill or rigor and subsides with sweating after taking paracetamol. Her appetite, bowel and bladder habits are normal. There is no history of chest pain, headache, sore throat, skin rash. There is no history of contact with tuberculosis patient. She has been suffering from recurrent respiratory infection and bronchial asthma since her childhood. She took inhaler regularly for asthma. She also had intermittent abdominal pain and loose, bulky stool. One of her sister had similar problems with recurrent respiratory tract infection and died at the age of 18 years. She took paracetamol, cough syrup, and salbutamol inhaler.

On examination – general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is bronchiectasis, more likely due to cystic fibrosis.

Q. What is **cystic fibrosis**?

A. Cystic fibrosis is an autosomal recessive disease characterized by abnormal transport of chloride and sodium ions across an epithelium, causing thick, viscous secretions and leading to bronchopulmonary infection and pancreatic insufficiency.

There is an abnormality in the gene encoding a chloride ion channel in the nasal epithelium, lungs, salivary glands, pancreas, intestine and bile ducts.

Prevalence is 1/2,500.

Q. What are the **clinical features** of cystic fibrosis?

A. As follows:

1. Neonate: Failure to thrive, meconium ileus, rectal prolapse.
2. Children and young adult—
   - Respiratory: Cough, wheeze, recurrent infection, bronchiectasis, lung abscess, pneumothorax, lobar collapse, hemoptysis, respiratory failure, cor pulmonale, asthma, otitis media, sinusitis, nasal polyps, etc.

- Abdominal: Diabetes mellitus, steatorrhea, malabsorption, cholesterol gallstone, secondary biliary cirrhosis and portal hypertension, distal intestinal obstruction syndrome (meconium ileus equivalent syndrome). There is increased incidence of peptic ulceration and gastrointestinal malignancy.
- Others—male infertility (due to failure of development of vas deferens and epididymis), delayed puberty and skeletal maturity, arthritis, osteoporosis, vasculitis, hypertrophic pulmonary osteoarthropathy, clubbing, stress incontinence due to repeated forced cough. About 20% of female with cystic fibrosis are infertile.

Q. What is **distal intestinal obstruction syndrome** (meconium ileus equivalent syndrome)?

A. It is a form of small intestinal obstruction occurring during infancy and onwards in a patient with cystic fibrosis, resulting from a combination of steatorrhea and viscid intestinal secretions, causing fecal impaction in ascending colon or in ileocecal junction.

Q. How to **diagnose** a case of cystic fibrosis?

A. It is based on clinical history and:

- Family history of cystic fibrosis.
- Sweat test—high sweat sodium and chloride concentration over 60 mmol/L.
- Blood DNA analysis of gene defect.
- Radiological features of bronchiectasis.
- Absent vas deferens and epididymis.
- Blood immunoreactive trypsin levels (for screening purpose).

Q. What other **investigations** should be done in a patient with cystic fibrosis?

A. As follows:

- Blood—CBC, liver function tests, creatinine, electrolyte, coagulation study.
- Vitamin A, D, E levels.
- Glucose tolerance test (annually).
- Bacteriology—cough swab, sputum culture.
- X-ray chest (hyperinflation, bronchiectasis).
- Ultrasonogram of whole abdomen (fatty liver, cirrhosis, chronic pancreatitis).
- Spiromery (obstructive defect).
- Aspergillus serology or skin test.
- Fecal fat analysis.

Q. How to **treat** cystic fibrosis?

A. As follows:

1. General care:
   - Nutritional support
   - Fat soluble vitamin supplement
   - Strict glucose control
   - Smoking cessation
   - Vaccination with influenza and pneumococcal vaccines
2. For respiratory problems:
   - Regular physiotherapy (postural drainage, active cycle techniques, forced expiratory techniques, etc.).
   - Antibiotic for acute infective exacerbations (oral or IV) and prophylactically (oral flucloxacillin or nebulized colomycin or torbramycin).

- Symptomatic relief by mucolytic, bronchodilators, inhaled corticosteroid. In some patients, inhalation of recombinant DNAse or hypertonic saline may give some relief.
- Oxygen therapy, as needed.
- Pulmonary rehabilitation.

3. For advanced lung disease: Oxygen, diuretics (for cor pulmonale), non-invasive ventilation, lung or heart-lung transplantation.
4. For abdominal problems:
   - Pancreatic enzyme replacement.
   - If acute abdomen due to intestinal obstruction—nothing by mouth, IV fluid and nasogastric suction should be given. Acetylcysteine given intravenously or through the nasogastric tube has been shown to be useful in resolving bowel obstruction.
   - Ursodeoxycholic acid for impaired liver function.
   - Liver transplantation may be needed in cirrhosis.
5. Others: Treatment for osteoporosis, arthritis, sinusitis, vasculitis and infertility.
6. Genetic counseling.

Note Remember the following points:

- Diagnosis of cystic fibrosis should be suspected in any young patient who presents with chronic respiratory and chronic gastrointestinal problem.
- Gastrointestinal problems, malabsorption and diabetes mellitus in patient with cystic fibrosis is due to pancreatic insufficiency.
- Fecal elastase is used as a screening test for exocrine pancreatic dysfunction.
- *P. aeruginosa* is the most common organism, causing recurrent respiratory infection.
- Prognosis—median survival is now over 30 years.

CHAPTER 3

Cardiovascular System

Usually, few cases are selected as long case. Most are selected as short cases. Occasionally, combinations of multiple valvular lesions are selected. Prototype of a single case and also common combinations are described in this chapter.

- **Mitral Stenosis 162**
- **Mitral Regurgitation 175**
- **Mixed Mitral Stenosis with Mitral Regurgitation 181**
- **Aortic Stenosis 183**
- **Aortic Regurgitation 189**
- **Mixed Aortic Stenosis and Regurgitation 196**
- **Congestive Cardiac Failure with Valvular Lesion 199**
- **Hypertension 208**
- **Subacute Bacterial Endocarditis 217**
- **Rheumatic Fever 224**
- **Eisenmenger's Syndrome 231**
- **Tetralogy of Fallot 235**
- **Ventricular Septal Defect (VSD) 240**
- **Atrial Septal Defect (ASD) 244**
- **Patent Ductus Arteriosus (PDA) 248**
- **Coarctation of Aorta 252**
- **Hypertrophic Cardiomyopathy 257**

While taking history, remember to describe the common symptoms related to cardiac disease (see page 30). Common symptoms related to cardiac diseases are:

- Dyspnea (difficulty in breathing)
- Chest pain
- Palpitation
- Edema.

Other symptoms may occur secondarily due to the involvement of other anatomical systems of the body. Examples are as follows:

Respiratory:
- Cough (pulmonary edema)
- Hemoptysis (due to pulmonary hypertension).

Renal:
- Reduction of urine output (in CCF).

Gastrointestinal tract (GIT):
- Anorexia, nausea (in congestive cardiac failure (CCF))
- Pain abdomen (hepatomegaly in CCF, vascular occlusion due to embolism).

Neurological:
- Syncope (occurs in aortic stenosis, arrhythmia, hypotension)
- Stroke (may occur in atrial fibrillation, hypertension, SBE, mitral stenosis due to cerebral embolism).

All these symptoms should be enquired during taking the history.

Note Remember the following:

Remember, in any cardiac case, patient's complaint or presentations are almost similar. Signs are written separately in individual cases.

MITRAL STENOSIS

After mentioning the name, age, sex, occupation, etc. as in proforma (written in the beginning), proceed as follows:

CHIEF COMPLAINS

- Breathlessness for … months
- Palpitation for … months
- Cough ... months
- Weakness for … months.

HISTORY

History of present illness: According to the patient's statement, he has been fit and well. However for the … months, he has been suffering from occasional breathlessness. Initially, the patient felt breathless during moderate to severe exertion, but for the last few weeks, it has been increasing progressively. Now he feels breathless even on mild exertion. Occasionally, he experiences nocturnal breathlessness, usually at late hours of night, for which he has to get up from sleep, walk and take deep breath to be comfortable.

There is no history of breathlessness on lying flat (orthopnea).

The patient also complains of occasional palpitation with mild exertion, even while going to toilet or dressing. He also complains of cough with sputum, which is mucoid in nature, but not associated with hemoptysis. For the last … months, he feels weak and fatigued.

There is no history of chest pain, swelling of legs, syncope, loss of consciousness, hoarseness of voice or difficulty in swallowing.

History of past illness: The patient suffered from rheumatic fever in his childhood (arthritis involving the big joints which were fleeting in nature), but there was no abnormal limb movements (even if no history of rheumatic fever or chorea, mention it. History of rheumatic fever may be absent in 40% case).

Family history: Both of his parents are in good health. His two brothers and two sisters are also in good health. There is no such illness in his family.

Personal history: He is a student, nonsmoker, nonalcoholic (mention if anything significant).

Socioeconomic history: He is from a middle class family, living in a small house with good sanitation and water supply facilities.

Drug history: He was taking injection Benzylpenicillin for few years, but has now stopped. He was treated by a community physician, but cannot recall the medications.

GENERAL EXAMINATION

- Appearance: Ill looking. (If malar flush, called mitral facies, is present, mention it.)
- Built: Normal
- Nutrition: Average
- Decubitus: On choice
- Anemia: Mild
- No jaundice, cyanosis, edema, clubbing, koilonychia, leukonychia
- No lymphadenopathy or thyromegaly

- Pulse: 88/min, low volume, regular in rhythm
- BP: 100/70 mm Hg
- Temperature: 98.8ºF.

SYSTEMIC EXAMINATION

Cardiovascular System

- **Pulse:** 88/min, low volume and regular in rhythm, normal character, no radio-femoral and radio-radial delay. Condition of vessel wall is normal.
- **Neck veins**: not engorged.
- **Blood pressure:** 100/70 mm Hg.

Precordium

Inspection:

- Visible cardiac impulse in mitral area (if other impulse, mention it)
- No deformity or scar-mark (mention if there is valvotomy scar or midline scar for valve replacement).

Palpation:

- Apex beat: In left 5th intercostal space ... cm from midline, tapping in nature
- Thrill: There is apical thrill, diastolic in nature
- Palpable P_2: Absent
- Left parasternal lift: Absent
- Epigastric pulsation: Absent (if present, mention it).

Auscultation:

- First heart sound: Louder in all the areas, more prominent in mitral area
- Second heart sound: Normal in all the areas (P_2 is loud in pulmonary area, if pulmonary hypertension)
- Murmur: There is a mid diastolic murmur in mitral area, which is low pitched, localized, rough, rumbling (LLRR), best heard with the bell of stethoscope, in left lateral position with breathing hold after expiration, with presystolic accentuation
- There is also opening snap, just medial to the mitral area.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr ..., 20-year-old, a college student, nonhypertensive, nondiabetic, nonsmoker, presented with breathlessness for … months, palpitation for … months, cough for ... months and weakness for … months. Initially, he felt breathless during moderate to severe exertion, but for the last few weeks, it is progressively increasing. Now he feels breathlessness even on mild exertion. Occasionally, he experiences paroxysmal nocturnal dyspnea but no history of orthopnea. The patient also complains of occasional palpitation with mild exertion, even while going to toilet or dressing. Cough is productive, with mucoid sputum, but not associated with hemoptysis. For the last … months, he feels weak and fatigued. There is no history of chest pain, swelling of legs, syncope, loss of consciousness, hoarseness of voice or difficulty in swallowing.

In his past medical history, there is history of rheumatic fever in his childhood. All the family members are in good health and there is no history of known genetic diseases. He was taking injection Benzylpenicillin for few years, but has now stopped. He was treated by a community physician but cannot recall the medications.

On general examination (see above).

On systemic examination (see above).

My diagnosis is: Chronic rheumatic heart disease with mitral stenosis.

(If signs of pulmonary hypertension are present, then add it with the above diagnosis).

Q. What are the main **points in favor** of your diagnosis?

A. The points in favor are:
- Apex beat is tapping in nature
- Diastolic thrill in mitral area
- Loud first heart sound
- Presence of MDM in mitral area with presystolic accentuation
- Presence of opening snap.

Q. What is the likely **cause** of MS?

A. Chronic rheumatic heart disease (always the most common cause).

Q. If there is **no** history of rheumatic fever, then what would be the cause?

A. Still it is likely to be rheumatic fever, because history of rheumatic fever may be absent in 40% cases. Rheumatic fever is the commonest cause of MS, rarely it may be congenital.

Q. Is there any evidence of pulmonary hypertension (PH)?

A. No.

Q. What are the **signs** of PH?

A. As follows:
- Palpable P_2
- Prominent 'a' wave in JVP
- Left parasternal heave (indicates RVH)
- Epigastric pulsation (indicates RVH)
- Loud P_2 on auscultation
- Early diastolic murmur (Graham Steel murmur due to pulmonary regurgitation).

Q. What are your **differential diagnoses?**

A. As follows:
- Tricuspid stenosis
- Left atrial myxoma
- Others: Ball valve thrombus in left atrium, cortriatum (a rare congenital disease).

Q. Why **not** this is tricuspid stenosis?

A. In TS, MDM is prominent in left lower parasternal edge, which increases during inspiration. Also, there may be other features such as raised JVP and signs of right heart failure.

Q. Why **not** this is left atrial myxoma?

A. In left atrial myxoma, physical signs and murmur change with posture. Also, there may be history of fever, weight loss, myalgia, arthralgia, skin rash, Raynaud's phenomenon (which are absent in this case). To be confirmed, 2D echocardiography should be done.

Q. What is **myxoma** of the heart? What are the **features**? How to **investigate** and **treat**?

A. It is the common primary tumor of heart, usually benign, may be pedunculated, polypoid, gelatinous, attached by a pedicle to the atrial septum. It may be sporadic and familial. It occurs in any age (third to sixth decade), and any sex (more in female).

Sites of origin:

- Left atrium (75%), near the fossa ovalis or its margin
- Right atrium, rarely from ventricles.

Clinical features: There are 3 groups of manifestations:

1. Obstructive features: Like MS, signs vary with posture. Occasionally, there is a low-pitched sound called tumor plop. There may be syncope or vertigo.
2. Embolic features either systemic or pulmonary embolism.
3. Constitutional features: Such as fever, malaise, weakness, loss of weight, myalgia, arthralgia, clubbing, skin rash, Raynaud's phenomenon.

Investigations:

- CBC: May be anemia, leukocytosis, polycythemia, high ESR, thrombocytopenia or thrombocytosis
- Hypergammaglobulinemia
- Chest X-ray (may be similar to MS)
- Echocardiogram: 2D or transesophageal
- CT scan or MRI may be done.

Treatment: Surgical excision. Recurrence may occur.

Note Remember the following:

Other tumors of the heart are rhabdomyoma and sarcoma. All are rare.

Q. What **investigations** should be done in mitral stenosis?

A. As follows:

- X-ray chest P/A view.
- ECG: "P" is bifid (P-mitrale. May be RVH, RAH, AF, etc).
- To confirm, echocardiogram (2D or preferably color doppler).
- Cardiac catheter may be done in some cases, specially when associated with other diseases (coronary artery disease, MS with MR, pulmonary artery pressure measurement).

Q. What are the **radiological features** of mitral stenosis?

A. As follows:

- Upper lobe veins are dilated (called upper lobe diversion, which is the early feature). Normally, ratio between upper and lower lobe veins is 1:3, which is altered to 1:1.
- Straightening of left border of heart (also called **mitralization**): It is due to fullness of pulmonary conus (due to dilated pulmonary artery) and filling of pulmonary bay (due to prominent left atrial appendage due to left atrial enlargement).
- Kerley's B lines (horizontal septal lines in costophrenic angle, which indicates pulmonary hypertension).
- Double shadow in right border of heart (due to enlarged left atrium).
- Widening of carina.
- Left bronchus is horizontal (due to enlarged left atrium).
- Pulmonary edema.
- Mottling or reticulonodular shadow due to pulmonary hemosiderosis.
- Calcified shadow of mitral valve (it is best seen in fluoroscopy).

Q. What is the **barium swallow** of esophagus (right anterior oblique view) finding?

A. Indentation of the esophagus due to enlarged left atrium (it is not done now a days, because echocardiogram is more diagnostic).

Q. What are the **echocardiogram findings** in mitral stenosis?

A. As follows:

- Thick mitral valve leaflet (with restricted opening), diastolic doming of anterior mitral leaflet and restricted movement of posterior mitral leaflet.
- Reduction of valvular area (narrow): Button like or funnel shaped.
- Calcification of valves (increased echogenecity).
- Shortening of chordae tendinae.
- Enlarged left atrium.
- Reduced rate of diastolic filling of left ventricle.
- Characteristic "M" shape movement of anterior leaflet normally seen in diastole is lost and the diastolic slope (EF) is reduced.
- Thrombus may be seen.

RELATED QUESTIONS AND ANSWERS

Q. If the patient with MS suddenly becomes **unconscious**, what is the likely cause?

A. CVD (cerebral infarction), usually with right sided hemiplegia. Usually CVD occurs when there is associated atrial fibrillation (AF).

Q. What may be the **cause of CVD** in this case?

A. Cerebral embolism (involving lenticulostriate branch of the left middle cerebral artery, causing infarction of the internal capsule).

Q. Why **syncope** may occur in MS?

A. Due to reduction of cardiac output. Also, may be due to atrial fibrillation with fast ventricular rate, pulmonary hypertension, pulmonary embolism, ball valve thrombus, cerebral embolism.

Q. What is the cause of **hemoptysis** in MS?

A. Rupture of pulmonary or bronchial veins associated with pulmonary hypertension (pulmonary apoplexy). Also hemoptysis may be due to pulmonary infarction.

Q. What is **paroxysmal nocturnal dyspnea** (PND)?

A. Paroxysmal breathlessness usually at night, which awakens the patient from sleep with a feeling of suffocation and choking sensation. The patient sits, stands up or open the windows for fresh air. It is due to pulmonary edema, and indicates early LVF or left atrial failure.

Q. What are the **causes** of PND?

A. The causes are as follows:

- Venous return increases while lying down.
- Mobilization of edema fluid from extravascular to intravascular compartment in supine position.
- Low adrenergic drive at sleep.
- Heart rate increases during rapid eye movement (REM) sleep.
- Vital capacity is reduced in supine position.
- Left atrial pressure is elevated and PaO_2 is reduced during sleep.
- Abdominal contents are also pushed up giving pressure on diaphragm.

Q. What are the **causes** of mid diastolic murmur (MDM)?

A. As follows:

- Mitral stenosis
- ASD (due to increased flow through tricuspid valve)
- Tricuspid stenosis
- Left atrial myxoma
- Austin-Flint murmur in aortic regurgitation
- Carey Coomb's murmur (a soft MDM due to mitral valvulitis in acute rheumatic fever).

Q. What are the characters of **Austin-Flint murmur** in aortic regurgitation?

A. As follows:

- It is not associated with loud first heart sound or presystolic accentuation
- No diastolic thrill
- No opening snap
- Patient will have features of aortic regurgitation.

Note Remember the following:

These features are present in organic MS.

Q. What is **Lutembacher's syndrome**?

A. Combination of ASD with rheumatic MS (it occurs in 4% cases of ASD).

Q. Why the apex beat is **tapping**?

A. It is the accentuated, palpable 1st heart sound.

Q. When and why the **pre-systolic accentuation** is present?

A. It is present only if there is sinus rhythm. It is due to atrial systole, which increases the flow across the stenosed mitral valve from left atrium to left ventricle, causing accentuation or loudness of the murmur. It is absent, if there is atrial fibrillation.

Q. What is **opening snap**? What is the **mechanism**?

A. It is a short, sharp high pitched sound, heard immediately after 2nd heart sound (during diastole), produced by sudden opening of mitral valve, due to raised left atrial pressure.
Opening snap is usually found in MS. (Rarely, it may be found in TS, severe MR, etc.).

Q. What is the **significance** of opening snap?

A. As follows:

- It indicates that the valve cusp is still mobile
- It is absent when the valve is calcified
- The gap between second heart sound and opening snap indicates the severity of MS. The diminishing gap indicates severe MS
- It is always due to organic MS.

Q. How to assess the **severity** of MS (is it severe)?

A. Normal area of mitral valve is 4 to 6 cm^2, if severe it may be <1 cm^2 (tight MS).

Signs of severe MS are:

- Pulse: Low volume
- 1st heart sound: Soft
- Opening snap: Nearer to the 2nd sound
- MDM: Prolonged
- Evidence of pulmonary hypertension and pulmonary congestion.

Q. How to assess the **pliable mitral valve**?

A. Short, sharp, accentuated first sound and presence of opening snap.

Q. What is the feature of **non-pliable** mitral valve?

A. Muffled first heart sound and no opening snap.

Q. What is **mitral facies**?

A. It is the rosy coloration of cheeks, may be bluish tinge, due to dilated capillaries and venules on the cheeks. It is not pathognomonic. It may be present in pulmonary hypertension and occasionally in normal person.

Q. Why there is **pulmonary hypertension in MS**?

A. Because of:

- Passive backward transmission of raised left atrial pressure
- Reflex pulmonary artery vasoconstriction
- Organic obliterative change in pulmonary vascular bed.

Q. What are the **complications** of MS?

A. As follows:

- Atrial fibrillation.
- Pulmonary edema (left atrial failure).
- Pulmonary hypertension leading to CCF.
- Left atrial thrombus with systemic embolism—commonly cerebral (cerebral infarction with hemiplegia), also in mesenteric, renal and peripheral.
- Ball valve thrombus (which is a big thrombus) may lead to sudden death.
- Hemoptysis.
- Pulmonary congestion, embolism, infarction.
- Ortner's syndrome (enlarged left atrium gives pressure on left recurrent laryngeal nerve, causing hoarseness of voice. It is rare).
- Dysphagia due to enlarged left atrium.
- Bronchitis and recurrent bronchopulmonary infection.
- Chest pain in 10% cases (due to pulmonary hypertension).
- Long standing MS may cause interstitial lung disease (due to prolonged pulmonary edema) and hemosiderosis.
- Infective endocarditis: Very rare (common in mitral regurgitation).

Q. How to **treat** MS medically?

A. As follows:

- Restrictive activity.
- Anticoagulant to reduce the risk of embolism.
- If atrial fibrillation: Digoxin, beta blocker, rate limiting calcium antagonsist (e.g. verapamil, diltiazem).
- If there is CCF: Diuretics, digoxin.
- Infective endocarditis is very unusual in MS. So, routine prophylaxis with antibiotic is not recommended.

Q. What are the indications of anticoagulant (warfarin) in MS?

A. As follows:

- Systemic and pulmonary embolism.
- Atrial fibrillation.
- Left atrial thrombus.
- Left ventricular systolic dysfunction.

Q. What are the **indications of surgery** in MS?

A. As follows:

- Symptomatic moderate or severe MS when balloon valvuloplasty is unavailable
- Moderate or severe MS with moderate or severe MR
- Recurrent thromboembolism
- Episodes of pulmonary edema without precipitating cause
- Associated atrial fibrillation which does not respond to medical therapy
- Pulmonary hypertension or recurrent hemoptysis
- Occasionally in pregnancy, with pulmonary edema (surgery may be done in second trimester as blood volume increases significantly with increased pulmonary pressure).

Q. What **surgery** is usually done?

A. As follows:

- Valvotomy (CMC—closed mitral commissurotomy, OMC—open mitral commissurotomy)
- Valvuloplasty (percutaneous balloon mitral valvuloplasty)—Treatment of choice
- Valve replacement.

Q. What are the **criteria for valvuloplasty**?

A. As follows:

- Significant symptoms
- Pure MS
- No or trivial MR
- Valve—Mobile, no calcification
- Left atrium—No thrombus.

Q. What are the **indications of valve replacement**?

A. As follows:

- Associated MR
- If the valve is calcified and rigid
- Thrombus in left atrium despite anticoagulation.

Q. What are the **complications** of surgery?

A. As follows:

- Mitral regurgitation
- Thromboembolism
- Restenosis.

Q. What is the **contraindication** of surgery in MS?

A. Active rheumatic carditis.

Q. How to **treat MS in pregnancy**?

A. As follows:

- Bed rest
- Correction of anemia
- Correction of nutrition
- If severe, symptomatic and tight MS—Mitral valvotomy may be done (usually in middle trimester)
- All patients should go into full term and cesarean section should be done
- Advice the patient to restrict number of pregnancy (1 to 2).

Note

Symptoms of MS are usually more marked in second trimester, which is due to increase in blood volume that increases pulmonary pressure. The symptoms improve in third trimester due to decrease in blood volume.

MITRAL STENOSIS WITH CONGESTIVE CARDIAC FAILURE (CCF)

Mitral stenosis may be associated with congestive cardiac failure. In such cases, **in addition to the history mentioned in mitral stenosis**, add the following:

- In the history, patient may complain of weakness, anorexia, nausea, vomiting, swelling of legs, pain in the right hypochondrium, etc.
- In physical finding, signs of CCF should be mentioned: Engorged and pulsatile neck veins, enlarged tender liver and dependent pitting edema (For details, see CCF on page 201).

Q. How to **treat** your case?

A. As follows:

- Complete rest.
- Restriction of salt and fluid.
- If breathlessness, oxygen therapy.
- Diuretics (frusemide, bumetanide, thiazide, spironolactone).
- If pulse rate is high: Digoxin may be given.
- Vasodilator drugs may be helpful (reduce afterload). Drugs are ARB, ACE inhibitor, nitrates.
- Treatment of mitral stenosis (such as valvotomy or valvuloplasty).

MITRAL STENOSIS WITH CARDIOVASCULAR DISEASE (CVD)

Mitral stenosis may be associated with CVD (cerebral embolism). In such case, the patient usually presents with unconsciousness or may be conscious and right sided hemeplagia.

- Physical findings are upper motor neuron science on the right side of the body (hypertonia, exaggerated reflects, extensor plantar response). For details, see CVD in neurology chapter.
- Usually there is atrial fibrillation (see below).

Q. What **investigations** should be done in such case?

A. As follows:

- As in mitral stenosis
- CT scan of brain (usually shows infarction).

Q. How to **treat** such case?

A. As follows:

- Treatment of atrial fibrillation
- Antiplatelet drugs: Aspirin, clopidogrel
- Anticoagulant: Warfarin.

MITRAL STENOSIS WITH ATRIAL FIBRILLATION (AF)

Mitral stenosis may be associated with atrial fibrilation. In such case, in addition to the history and signs of MS (as mentioned above), mention the signs of AF as follows:

- Pulse 110/min, irregularly irregular (in rhythm and volume)
- Pulse deficit is present (auscultate on heart and feel the radial pulse)
- No 'a' wave in JVP
- Variable intensity of first heart sound, no opening snap
- MDM is present, but no presystolic accentuation.

Q. Why **presystolic accentuation** is absent in AF?

A. Because in AF, atria contracts in an uncoordinated and ineffective manner.

Q. What do you think the **cause in this case**?

A. Chronic rheumatic heart disease.

Q. What are the **causes of irregularly irregular pulse**?

A. As follows:
- Atrial fibrillation
- Multiple ectopics
- Others: Atrial flutter with variable block, paroxysmal atrial tachycardia with variable block.

Q. How to **differentiate** atrial fibrillation and multiple ectopics at bedside?

A. By physical exercise. With exercise, ectopics will disappear. But atrial fibrillation will be more prominent or even worse. It is confirmed by ECG.

Q. What are the **causes of atrial fibrillation**?

A. As follows:
- Chronic rheumatic heart disease with valvular lesions, commonly mitral stenosis
- Coronary artery disease (commonly acute MI)
- Thyrotoxicosis
- Hypertension
- Lone atrial fibrillation (idiopathic in 10% cases)
- Others: ASD, chronic constrictive pericarditis, acute pericarditis, cardiomyopathy, myocarditis, sick sinus syndrome, coronary bypass surgery, vulvular surgery, acute chest infection (pneumonia), thoracic surgery, electrolyte imbalance (hypokalemia, hyponatremia), alcohol, pulmonary embolism.

Note Remember the following points:
- First 5 causes should always be mentioned sequentially at the top of the list.
- Mention the causes of atrial fibrillation according to the age of the patient in that particular long case (see below).

Q. If the patient is **young**, what are the **causes** of atrial fibrillation?

A. As follows:
- Chronic rheumatic heart disease with valvular lesions, commonly mitral stenosis
- Thyrotoxicosis
- Others—atrial septal defect (ASD), acute pericarditis, myocarditis, pneumonia.

Q. If the patient is **elderly**, what are the **causes** of atrial fibrillation?

A. As follows:
- Coronary artery disease (commonly acute myocardial infarction)
- Thyrotoxicosis

- Hypertension
- Lone atrial fibrillation (idiopathic in 10% cases)
- Others: See above (unusual or less in chronic rheumatic heart disease).

Q. What are the **complications** of atrial fibrillation?

A. As follows:

- Systemic and pulmonary embolism (systemic from left atrium and pulmonary from right atrium). Annual risk is 5% (1 to 12%).
- Heart failure.

Q. What is **lone atrial fibrillation?**

A. Lone atrial fibrillation means atrial fibrillation without any cause. Genetic predisposition may be responsible.

- 50% patients with paroxysmal atrial fibrillation and 20% with persistent or permanent atrial fibrillation have no cause and heart is normal.
- Lone atrial fibrillation usually occurs below 60 years of age.
- It may be intermittent, later may become permanent.
- Prognosis: Low risk of CVD (0.5% per year). Usually lifespan is normal.

Q. What is **atrial fibrillation?**

A. It is an arrhythmia where atria beat rapidly, chaotically and ineffectively, while the ventricles respond at irregular intervals, producing irregularly irregular pulse. Any conditions causing raised atrial pressure, increased atrial muscle mass, atrial fibrosis, inflammation and infiltration of the atrium can cause atrial fibrillation.

The atria usually fire impulse at the rate of 350 to 600/minute, ventricles respond at irregular intervals usually at the rate of 100 to 140/minute. Many of the atrial impulse reach the AV node in the refractory period. So, not all are conducted.

Q. What are the **types** of atrial fibrillation?

A. Three types:

- Paroxysmal: Discrete self-limiting episodes. May be persistent if underlying disease progresses.
- Persistent: Prolonged episode that can be terminated by electrical or chemical cardioversion.
- Permanent: Sinus rhythm cannot be restored with drug or DC shock.

Q. If a patient with atrial fibrillation is **unconscious**, what is the likely cause?

A. Cerebral embolism (usually with right sided hemiplegia).

Q. How to **treat** atrial fibrillation?

A. Aim of treatment is as follows:

- Control of heart rate
- Restoration of sinus rhythm and prevention of recurrence
- Treatment of primary cause.

Treatment (according to the type):

1. Paroxysmal atrial fibrillation:
   - If asymptomatic: Does not require any treatment, follow-up the case.
   - If troublesome symptoms are present: β-blocker. Other drugs—flecainide or propafenone may be given.
   - Amiodarone is effective in prevention.
   - Low dose aspirin to prevent thromboembolism.

- If bradycardia is present (in sinoatrial disease): Permanent over drive atrial pacing (60% effective).
- In some intractable cases: Radiofrequency ablation may be required, who does not have structural heart disease (70% effective).

2. Persistent atrial fibrillation:
   - Control of heart rate: β-blocker, digoxin or calcium channel blocker (verapamil, diltiazem). Combination of digoxin and atenolol may be used.
   - To control rhythm: DC cardioversion may be done safely. It may be repeated, if relapse occurs. Concomitant use of β-blocker or amiodarone may be used to prevent recurrence.
3. Permanent atrial fibrillation:
   - Control of heart rate: Digoxin, β-blocker, calcium channel blocker (verapamil or diltiazem).
   - In some cases: Transvenous radiofrequency ablation may be done (it induces complete heart block. So, permanent pacemaker should be given. This is known as "patch and ablate strategy").

Q. What is the **role of anticoagulant** in atrial fibrillation?

A. Usually, warfarin is given who are at risk of stroke. Target INR is 2 to 3. It reduces stroke in 2/3rd cases. Aspirin reduces stroke in 1/5th cases. Anticoagulation is indicated in patient with atrial fibrillation having risk factors for thromboembolism.

Risk factors for thromboembolism in atrial fibrillation:

- Previous ischaemic stroke or TIA
- Mitral valve disease
- Age over 65 years
- Hypertension
- Diabetes mellitus
- Heart failure
- Echocardiographic evidence of left ventricular dysfunction, left atrial enlargement or mitral anular calcification.

Risk groups with thromboembolism (nonrheumatic):

- Very high: Previous stroke or TIA (12%)
- High: Age > 65 years and one other risk factor (6.5%)
- Moderate: (i) Age > 65 years, no risk factor (4%), (ii) Age < 65 years, other risk factor (4%)
- Low: Age < 65 years, no risk factor (1.2%).

Note Remember the following points:

- In lone atrial fibrillation—aspirin may be given to prevent thromboembolism.
- Age < 65 years and young with no structural heart disease—aspirin may be beneficial. No warfarin.
- Target INR following anticoagulation is 2 to 3.

Assessment of risk of thromboembolism in atrial fibrillation—**CHADS score**:

- **C**ongestive cardiac failure (1 point)
- **H**ypertension (1 point)
- **A**ge > 75 (1 point)
- **D**iabetes mellitus (1 point)
- **S**troke or transient ischemic attack (2 points).

In **CHADS** score:

- Score 0 has a stroke risk of 1.9% per year.
- Score 6 correlates with 18.2% stroke risk per year.

For **prevention**:

- The patient with score 0 should get aspirin only
- The patient with score 1 should get warfarin or aspirin
- The patient with score 2 or more should get warfarin.

MITRAL REGURGITATION

History and general examination are similar to mitral stenosis (mention if other findings are present).

Cardiovascular System

- Pulse: 88/min, normal in volume, rhythm and character
- JVP: Not engorged
- Blood pressure: 130/85 mm Hg.

Precordium

Inspection:

- Visible cardiac impulse in mitral area.

Palpation:

- Apex beat: Shifted, in the left 6th intercostal space, ... cm from midline, diffuse, thrusting in character.
- Thrill: Present in left 6th intercostal space, systolic in nature.

Auscultation:

- 1st heart sound: Soft in mitral area, normal in other areas
- 2nd sound: Normal in all the areas
- 3rd heart sound: May be present
- There is a pansystolic murmur in mitral area, which radiates to the left axilla (reduced on inspiration and more on expiration).

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Present as mentioned in the chapter mitral stenosis. Also mention the physical findings as above.

My diagnosis is chronic rheumatic heart disease with mitral regurgitation.

Q. Why your diagnosis is MR?

A. Because:

- Systolic thrill in mitral area
- First heart sound is soft
- There is a PSM radiating to the left axilla.

Q. What do you think the **cause** in this case?

A. Chronic rheumatic heart disease, mitral valve prolapse.

Q. What are your **differential diagnoses**?

A. As follows:

- Tricuspid regurgitation (TR)
- Ventricular septal defect (VSD).

Q. Why not this is TR?

A. In TR, findings are:

- Pansystolic murmur is present in the left lower parasternal area, no radiation to axilla (No systolic thrill).
- Murmur is prominent on inspiration and less on expiration.
- Raised JVP with prominent "V" wave.
- Enlarged, tender and pulsatile liver.

Q. Why not this is VSD?

A. In VSD, findings are:

- Systolic thrill in left parasternal area (fourth or fifth intercostal space).
- Pansystolic murmur in left parasternal area (fourth or fifth intercostal space), no radiation.

Q. What **investigations** should be done in MR?

A. As follows:

- X-ray chest P/A view (cardiomegaly may be found)
- ECG (LVH, LAH)
- Echocardiogram, preferably color Doppler echocardiography
- Cardiac catheterization may be needed in some cases.

Q. What is **mitral valve prolapse**? What are the **features**? How would you **treat**?

A. It is also called Barlow's syndrome or floppy mitral valve. In this condition, a mitral valve leaflet (most commonly the posterior leaflet) prolapses into the left atrium during ventricular systole. It is one of the commonest causes of MR. It may be congenital anomaly or due to degenerative myxomatous changes. It may be associated with Marfan's syndrome, Ehler-Danlos syndrome, thyrotoxicosis, rheumatic or ischemic heat disease, atrial septal defect or hypertrophic cardiomyopathy.

Mitral valve prolapse is more common in thin, young women, may be familial. It may be present in healthy women in up to 10% cases. The most common symptom is atypical chest pain, usually in left submammary region and stabbing in quality. Rarely, it may be confused with anginal pain. There may be palpitation, dyspnea, fatigue, benign arrhythmia or rarely fatal ventricular arrhythmia. Embolic stroke and TIA are rare complications. Symptoms increases with aging.

On examination, the typical features are midsystolic click followed by late systolic murmur. Later, MR may develop and there is PSM. Two-dimensional echocardiography confirms the diagnosis.

Asymptomatic patient only needs reassurance, periodic echocardiography may be done. Atypical chest pain and palpitation are treated with β-blocker. Other antiarrhythmic drugs may be needed. If there is significant MR or AF, anticoagulation is indicated to prevent thromboembolism (aspirin may be given). If MR is severe, mitral valve repair or replacement should be done. Prophylaxis for infective endocarditis in most cases is not recommended. Overall prognosis is good.

RELATED QUESTIONS AND ANSWERS

Q. What are the **causes of MR**?

A. As follows:

- Chronic rheumatic heart disease
- Mitral valve prolapse
- Papillary muscle dysfunction (due to acute myocardial infarction)
- Infective endocarditis
- Trauma or mitral valvotomy

- Connective tissue diseases (RA, SLE, Marfan's syndrome, Ehler-Danlos syndrome)
- Ankylosing spondylitis
- Cardiomyopathy
- Secondary to left ventricular dilatation (hypertension, aortic valve disease)
- Rarely by drugs (such as fenfluramine, phentermine which are used to treat obesity).

Q. What are the **causes** of acute MR?

A. As follows:
- Acute myocardial infarction (due to rupture of papillary muscle)
- Trauma or surgery (mitral valvotomy)
- Infective endocarditis (due to perforation of mitral valve leaflet or chordae)
- Acute rheumatic fever (due to mitral valvulitis)
- Spontaneous rupture of chorda tendineae or myxomatous degeneration of valve.

Q. What are the **causes of pansystolic murmur**?

A. As follows:
- Mitral regurgitation
- Tricuspid regurgitation (TR)
- VSD.

Q. Is there any MDM in MR?

A. Yes, it may be present due to increased flow of blood through mitral valve (or if associated with MS).

Q. What are the signs of **severe MR**?

A. Severe MR is suggested by the following findings:
- Large left ventricle (apex is shifted, thrusting)
- Presence of third heart sound
- Presence of mid diastolic flow murmur (due to rapid filling of the left ventricle).

Q. What are the **complications** of MR?

A. As follows:
- Acute LVF
- Infective endocarditis
- Embolism
- Arrhythmia (atrial fibrillation, ectopics)
- CCF.

Q. Where the murmur **radiates** following the rupture of chorda tendineae?

A. As follows:
- Rupture of anterior leaflet of chorda tendineae—murmur radiates to axilla and back
- Rupture of posterior leaflet of chorda tendineae—murmur radiates to cardiac base and carotid arteries.

Q. How to **treat** MR?

A. As follows:

1. In mild to moderate case:
   - Diuretic
   - Vasodilator: ACE inhibitor
   - If fast AF: Digoxin
   - Anticoagulant if associated AF or history of pulmonary embolism
   - Prophylactic penicillin to prevent endocarditis

- Follow-up every 6 months by echocardiogram.
- If the ejection fraction falls to 55% and left ventricular dilatation >60 mm, valve replacement may be considered.

2. In severe MR or in progressively worsening MR—Replacement of valve.

Q. What type of **valve** should be replaced?

A. As follows:

- In young patient: Metallic valve
- In elderly patient: Tissue valve.

Q. What are the **indications** of surgery in MR?

A. As follows:

- Symptomatic.
- Asymptomatic patient with severe MR with mild to moderate LV dysfunction (EF 30 to 60% and end systolic dimension 45 to 55 mm).
- Asymptomatic patient with normal left ventricle and atrial fibrillation or pulmonary hypertension.

Q. What are the **types** of prosthetic valve?

A. Prosthetic valves are of 2 types:

1. **Metallic valves:**
   - Starr-Edward valve (ball-cage valve)
   - Bjork-Shiley valve (tilting disc)
   - St Jude's valve (bi-leaflet, double tilting disc).
2. **Tissue valves:**
   - Carpentier-Edwards valve
   - Hancock porcine valve
   - Ionescu Shiley valve (less used).

Note Tissue valve – 2 types:

- Xenograft: Made from porcine valve or bovine pericardium. These are less durable and may require replacement after 8 to 10 years. Anticoagulation is not required unless there is AF.
- Homograft: These are cadaveric valves (aortic or pulmonary human valve), particularly useful in young patient and in the replacement of infected valves.

Q. How to **detect** that the patient has prosthetic valves?

A. It is detected in the following ways:

- Usually there is a vertical mid-sternal scar mark of thoracotomy. (It may also be due to CABG).
- In metallic valve replacement, there is metallic sound on auscultation. However, modern mechanical valve (St Jude's valve) makes softer opening and closing sound than older valves.
- In case of tissue valve prosthesis, there is no metallic sound or plopping sound. Rather, there is a click.

Q. How to **detect clinically** whether the replaced valve is mitral or arotic?

A. As follows:

1. **Mitral valve prosthesis is detected by:**
   - Site: Over the mitral valve
   - Metallic sound is present, coincides with first heart sound (sharp closing)
   - Normal second heart sound
   - Diastolic flow murmur (MDM) may be present normally
   - Sharp opening or closing sound or click that coincide with the carotid pulse.

2. Aortic valve prosthesis is detected by:
- Site: Over the aortic valve
- Metallic sound is present, coincides with second heart sound (sharp closing)
- Normal first heart sound. Ejection systolic flow murmur (ESM) may be present normally
- Sharp opening or closing sound or click that occurs shortly after the carotid pulse.

Note Remember the following:

Mostly, Starr-Edward valve is used.

Q. How to **detect**, if prosthetic valve is **leaking?**

A. As follows:
- In mitral valve prosthesis: Appearance of PSM indicates leaking (MDM may be normally present. Ball and cage valves project into the left ventricle and cause a low intensity ESM. Tissue valve and bileaflet valve can have a low intensity diastolic murmur. Consider any systolic murmur of loud intensity to be a sign of regurgitation and failure of the valve.).
- In aortic valve prosthesis: Appearance of EDM indicates leaking (ESM may be normally present as all types of valves produce a degree of outflow obstruction and thus have an ESM).

Q. What happens, if there is **dysfunction** of prosthetic valve?

A. Absence of opening and clicking or closing sounds indicates dysfunction. Unexplained heart failure may be due to dysfunction. Biological valve dysfunction is usually associated with regurgitant murmur.

Q. What are the **advantages and disadvantages** of different valves?

A. As follows:

1. In case of metallic valve:
- Advantage: Incidence of valve failure is less and more durable.
- Disadvantage: Incidence of thrombosis is usually high, requiring long-time anticoagulant therapy, even life long. There may be microangiopathic hemolytic anemia.

2. In case of tissue valve:
- Advantage: Incidence of thrombosis is less, hence long-time anticoagulant therapy is not required (short-term anticoagulant is used in postoperative period. Also, anticoagulant is required, if associated with AF). No hemolysis.
- Disadvantage: Incidence of valve failure is high due to stiffening and later tearing of valve leaflets over 10 years, and requires repeat valve replacement and is less durable. There is degeneration and calcification in advanced stage.

Q. What are the **complications** of metallic valve?

A. As follows:
- Thromboembolism
- Anticoagulation is needed which may lead to bleeding
- Microangiopathic hemolytic anemia
- Infective endocarditis.

Q. What are the **complications** of tissue valve?

A. As follows:
- Primary valve failure
- Perforation or rupture
- Degenerative changes

- Calcification
- Infective endocarditis.

Q. What are the **complications** of prosthetic valve?

A. As follows:

- Thromboembolism: More on metallic valve (common in mitral than aortic). Anticoagulant is necessary (INR should be between 3 and 4.5).
- Primary valve failure: Rare in metallic valve (common in tissue valve).
- Valve leaking.
- Dehiscence or detachment of valve from the site or valve ring resulting in paraprosthetic leak.
- Valve obstruction by thrombosis or calcification.
- Mechanical or microangiopathic hemolytic anemia (mainly in aortic valve in 10 to 20% in 10 years. Occurs due to metallic valve.).
- In tissue valve, there may be perforation, rupture, degenerative changes due to calcium deposition.
- Infective endocarditis, especially in dental procedure or catheterisation. Common organism is *Staphylococcus epidermidis*. Occasionally, treatment may be difficult, high mortality and may require to replace the valve again. If infection occurs within 60 days of valve replacement (early), it is mostly by contamination of intravenous (IV) cannula and if the infection occurs after 60 days (late), it is like other valve endocarditis.

Note Remember the following points:

- Ball and cage valve causes hemolysis more than other valve
- Tilting disc is more thrombogenic.

Q. How to **choose** a particular valve?

A. In the following way:

- In young patients, if no contraindication for anticoagulant therapy, metallic valve prosthesis is preferred.
- In elderly patient or if there is contraindication to anticoagulant therapy, tissue valve prosthesis is preferred.

Q. Which prosthesis is used in a **woman at child bearing age**?

A. Mechanical valves are now preferred for woman at child bearing age. During pregnancy, warfarin is substituted with IV unfractionated heparin in the first 6 to 12 weeks and last 2 weeks. This is associated with a low rate of warfarin embryopathy and of bleeding. However, subcutaneous heparin and low molecular weight heparin are not recommended at the present.

Recent studies have showed that women who need low doses of warfarin (5 mg or less) are at low risk for fetal warfarin embryopathy, bleeding, still birth or abortion. In these women, warfarin may be given throughout pregnancy but should be closely monitored.

Previously tissue valve was used for young woman considering the risk of anticoagulation at pregnancy. But with tissue valve, there is increased risk of early structural valve deterioration (SVD) during or shortly after the end of pregnancy. In addition, tissue valve is less durable and repeat valve replacement may be needed after about 10 years.

MIXED MITRAL STENOSIS WITH MITRAL REGURGITATION

The patient's history of present illness or presentation is same as in mitral stenosis.

GENERAL EXAMINATION

Mentions as in mitral stenosis or regurgitation (mentioned previously).

SYSTEMIC EXAMINATION

Cardiovascular system

- Pulse: 84/min, low in volume, normal rhythm and character
- JVP: Normal
- Blood pressure: 115/60 mm Hg.

Precordium

Inspection:

- Visible cardiac impulse in mitral area.

Palpation:

- Apex beat: In the left … intercostal space, … cm from midline, tapping in nature
- Thrill: Present in apical area, both systolic and diastolic.

Auscultation:

- First heart sound: Louder in all the areas
- Second heart sound: Normal in all the areas
- There is a mid-diastolic murmur in mitral area and also a pansystolic murmur in mitral area, which radiates to the left axilla.

Examination of the other systems reveals no abnormalities.

SALIENT FEATURES

Present the history and physical findings as mentioned above.

My diagnosis is: Chronic rheumatic heart disease with mitral stenosis with mitral regurgitation.

Q. What is the **predominant** lesion and why?

A. Predominant lesion is MS, because:

- Pulse: Low volume
- Apex beat: Not shifted and tapping in nature
- First heart sound is loud.

Q. What are the findings if **MR is predominant**?

A. If MR is predominant:

- Pulse: Normal/high volume
- Apex beat: Shifted and thrusting in nature

- First heart sound is soft or absent
- There may be third heart sound.

Q. What **investigations** should be done?

A. As follows:
- X-ray chest
- ECG
- Echocardiography, preferably color Doppler.

Q. What is the **cause** of mixed MS and MR?

A. Chronic rheumatic heart disease.

Q. In which lesion of MR or MS, **endocarditis** is common?

A. Endocarditis is common in MR.

Q. How will you **treat** your case?

A. As follows
- Conservative treatment: Rest, diuretic, prophylactic penicillin to prevent infective endocarditis, antiplatelet like aspirin, warfarin to prevent thromboembolism.
- In severe case: Valve replacement may be needed.

AORTIC STENOSIS

CHIEF COMPLAINTS

- Shortness of breath for … months
- Palpitation for … months
- Chest pain for … months
- Loss of consciousness ... hours.

HISTORY

History of present illness: The patient states that he was quite well … months back. Since then, he has been suffering from shortness of breath, which is more marked on moderate to severe exertion and relieved by rest. This is not associated with cough. Occasionally, he experiences nocturnal breathlessness, usually at late hours of night, which compels him to get up from sleep, walk and take deep breath to be comfortable. There is no history of breathlessness on lying flat (orthopnea).

The patient also complains of occasional palpitation and chest pain, which occur during mild to moderate exertion. The pain does not radiate and it is relieved by taking rest. The patient also experiences occasional dizziness. There are 2 episodes of loss of consciousness in the last 3 months, each episode lasted for few minutes. It was preceded by giddiness and lightheadedness, but no convulsion or urinary or fecal incontinence or tongue biting.

History of past illness: He was always in good health. There is no history of rheumatic fever or other illnesses.

Family history: All the members are in good health. No history of such illnesses in the family.

Personal history: He is a school teacher. He smokes 2 to 3 cigarettes per day for the last 5 years.

Socioeconomic history: He comes from a lower middle-class family, living in a tin shed house in a rural area with access to sanitary toilet and arsenic free tubewell water. His monthly income is about 4000 TK.

Drug history: Nothing significant.

Psychiatric history: There is no history of any psychiatric illness.

GENERAL EXAMINATION

As in other valvular diseases written above, mention as your findings.

SYSTEMIC EXAMINATION

Cardiovascular System

- Pulse: 92/min, low volume and slow rising, normal in rhythm, no radiofemoral or radioradial delay.
- JVP: Normal.
- BP: 95/80 mm Hg (low systolic, normal diastolic and narrow pulse pressure).

Note

However, slow rising pulse and low pulse pressure may not be found in elderly, due to the stiffening of the arteries.

Precordium

Inspection:

- Visible cardiac impulse in mitral area (or nothing).

Palpation:

- Apex beat—In the left … intercostal space, ... cm from midline, heaving in nature
- Systolic thrill—Present in aortic area.

Auscultation:

- First heart sound—Normal in all the areas.
- Second heart sound—A_2 is soft in all the areas, P_2 is normal (may be reversed splitting of 2nd heart sound).
- Fourth heart sound may be present (due to atrial contraction).
- There is a harsh ejection systolic murmur in aortic area, which radiates towards the neck.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, a 40-year-old school teacher, smoker, nondiabetic, non-hypertensive, presented with shortness of breath for … months, which is more marked on moderate to severe exertion and relieved by rest. This is not associated with cough, wheeze or hemoptysis. He occasionally complains of paroxysmal nocturnal dyspnea but no orthopnea. The patient also complains of occasional palpitation and chest pain, which occur during mild to moderate exertion. There is no radiation of pain and it is relieved by taking rest. The patient also experiences occasional dizziness. There are 2 episodes of loss of consciousness in the last 3 months; each episode lasted for few minutes. It was preceded by giddiness and lightheadedness, but no convulsion or urinary or fecal incontinence or tongue biting. There is no history of rheumatic fever or other illness. Other history does not reveal anything significant. No family history of such illness. He used to take diuretics, vitamins prescribed by the local physicians.

On examination, general examination: Nothing significant.

Examination of cardiovascular system: Mention as above.

Other systems revealed no abnormalities.

My diagnosis is aortic stenosis.

Q. Why is your diagnosis aortic stenosis?

A. Because:

- In the history, there is exertional dyspnea, chest pain and syncopal attack.
- On examination, there is systolic thrill in aortic area, soft aortic component of second sound (A_2) and ejection systolic murmur in aortic area that radiates to the carotid.

Q. What are your **differential diagnoses?**

A. As follows:

- Pulmonary stenosis
- Hypertrophic cardiomyopathy (HCM).

Q. **Why not** pulmonary stenosis?

A. In pulmonary stenosis, findings are:

- Systolic thrill in pulmonary area.
- Left parasternal lift and epigastric pulsation may be present (due to RVH).
- P_2 is soft, A_2 is normal (wide splitting of the second heart sound may be present).
- Ejection systolic murmur in pulmonary area, which radiates to the left side of neck (murmur is more on inspiration).
- Apex is normal (not heaving as in AS).

Q. **Why not** HCM?

A. In HCM, the findings are:

- Pulse is jerky.
- Prominent **"a"** wave in JVP.
- Double impulse at the apex (palpable 4th heart sound due to left atrial hypertrophy).
- Systolic thrill in left lower parasternal area.
- Associated pansystolic murmur due to MR.
- Family history of HCM may be present or there may be history of sudden death in family.

Note Remember the following:

In HCM, echocardiography is very helpful for diagnosis. ECG shows LVH and bizarre abnormalities like pseudoinfarction pattern, deep T inversion.

Q. What **investigations** do you suggest in AS?

A. As follows:

- X-ray chest (may be normal in early case. Enlarged left ventricle and dilated ascending aorta, calcification of valve on lateral view).
- ECG (LVH, may be LBBB, complete AV block due to calcification of ring may be found).
- Echocardiogram, preferably color Doppler echocardiography.
- Cardiac catheterization (mainly to identify associated coronary artery disease. Also to measure the gradient between left ventricle and aorta).

RELATED QUESTIONS AND ANSWERS

Q. Does the **loudness of the murmur** indicate severity?

A. No, prolongation of murmur indicates severity. Loudness of murmur may be associated with mild stenosis.

Q. What are the **causes** of aortic stenosis?

A. As follows:

- Chronic rheumatic heart disease
- Bicuspid aortic valve (common in male)
- Calcification in old age
- Congenital (in early age).

Causes of aortic stenosis according to age:

- **Infants, children, adolescents:**
  - Congenital aortic stenosis
  - Congenital subvalvular aortic stenosis
  - Congenital supravalvular aortic stenosis.
- **Young adults to middle-aged:**
  - Calcification and fibrosis of congenitally bicuspid aortic valve
  - Rheumatic aortic stenosis.
- **Middle-aged to elderly:**
  - Senile degenerative aortic stenosis
  - Calcification of bicuspid valve
  - Rheumatic aortic stenosis.

Remember the following points in elderly patient:

- Aortic stenosis (AS) is the most common form of valve disease in old age
- It is a common cause of syncope, angina and heart failure in this age group
- Low pulse pressure and slow rising pulse may not be present due to stiffening of the arteries
- Surgery can be successful in the absence of co-morbidity but operative mortality is higher. Prognosis is poor in symptomatic patients without surgery
- Biological valve is more preferable than mechanical valves. Anticoagulant is not needed.

Q. What is the role of **ETT** in AS?

A. ETT should be avoided in symptomatic patient with aortic stenosis as it may be fatal. However, it may be done in asymptomatic cases with high grade aortic stenosis. May be helpful in deciding the role of surgery.

Q. What are the **types** of aortic stenosis?

A. Three types:

- Valvular: Involving valve cusps. It is the most common type.
- Subvalvular: Narrowing of outflow tract of left ventricle.
- Rarely supravalvular: Constriction at the first part of aorta.

Q. What is the **type of pulse** in AS?

A. Plateau pulse, it is a slow rising, small volume pulse (pulsus parvus). It may be late peaking (pulsus tardus).

Q. What is aortic sclerosis? How to **differentiate** from aortic stenosis?

A. It is a degenerative condition in which there is thickening of aortic valve cusps, common in elderly. It does not produce any significant obstruction to the outflow of blood.

Features	Aortic stenosis	Aortic sclerosis
1. Pulse volume	Low volume, slow rising	Normal
2. Apex beat	Heaving	Normal
3. Thrill	Systolic	No thrill
4. A_2	Absent or soft	Normal
5. ESM and radiation	Present, radiates to the neck	Present, usually no radiation

Note Risk of aortic sclerosis:

- There may be calcification leading to AS. There are some risk factor like hyperlipidemia, diabetes mellitus, smoking, hypertension are prone to develop aortic calcification.

Q. What are the **presentations** of aortic stenosis?

A. As follows:

- Breathlessness, mainly on exertion
- Palpitation
- Anginal pain (in 50% cases with or without coronary artery disease)
- Syncope: Specially during effort (which may be due to inadequate cardiac output or reflex vasodilatation after exercise or arrhythmia), causing cerebral hypoperfusion
- Sudden death (probably due to ventricular fibrillation).

Note Remember the following points:

- Aortic stenosis may be asymptomatic if it is mild or congenital, even may be asymptomatic throughout life.
- In elderly—May be associated with complete heart block or LBBB.

Q. **Why** anginal pain occurs in AS?

A. There is left ventricular hypertrophy, so there is more oxygen demand. Also, there is reduced coronary flow due to less cardiac output (limitation of duration of diastole).

Q. What are the **signs of severe** AS?

A. Signs of severe AS are:

- Pulse is feeble or absent. Slow rising plateau pulse may be present.
- Systolic aortic thrill.
- Absent or soft A_2 (or single S_2).
- Harsh, loud, prolonged murmur with late peaking (soft and short ESM with early peaking suggest mild stenosis).
- Reversed splitting of second heart sound.
- Presence of fourth heart sound.
- Presence of heart failure or LVF (late sign).

Note Also remember the following points:

- Normal area of aortic valve is 1.5 to 2 cm^2. It is severe, if the area is < 1 cm^2 or valve mean pressure gradient is > 50 mm Hg.
- Critical aortic stenosis: If the valve area is < 0.7 cm^2 or valve pressure gradient is > 70 mm Hg.

Q. What are the **complications** of aortic stenosis?

A. As follows:

- Left ventricular failure
- Infective endocarditis (10% cases)
- Sudden death due to ventricular fibrillation
- Complete heart block (in case of calcification of aortic valve)
- Systemic embolism.

Q. What is the **prognosis** of AS in symptomatic patients?

A. If aortic valve is not replaced, the onset of angina, syncope and dyspnea has been shown to correlate with an average time to death of 5, 3 and 2 years.

Q. How to **treat** aortic stenosis?

A. As follows:

- In mild or asymptomatic cases and if valvular pressure gradient < 50 mm Hg—follow-up (periodic echocardiogram should be done). Conservative symptomatic management is given.
- If symptomatic or even single syncopal attack immediate valve replacement.
- In asymptomatic patient with severe AS and a deteriorating ECG—valve replacement is also recommended.
- If the patient is unfit for surgery, percutaneous valvuloplasty may be attempted.
- Aortic balloon valvuloplasty is useful in congenital AS. But this is of no value in old age with calcific AS (valve replacement is necessary in such cases).
- In children, elderly or pregnancy—valvotomy may be done.
- Anticoagulant is only necessary if there is associated atrial fibrillation or mechanical valve prosthesis is used.

Q. Which prosthetic valve is **preferred** in elderly patient?

A. Usually biological or tissue valve is preferred than mechanical one, as biological valve does not require anticoagulation. In younger age, mechanical valve is preferred, but anticoagulant should be given.

Q. What are the **indications of surgery**?

A. As follows:

- All symptomatic patient (such as syncope).
- If mean systolic pressure gradient is > 50 mm Hg (left ventricular systolic pressure > aorta).
- If the valve area is < 0.7 cm^2 (normal – 2.5 to 3 cm^2).
- Asymptomatic patient undergoing surgery for coronary disease, other valve, LV dysfunction, progressive decline in LVEF, marked LVH.
- Abnormal BP in response to exercise.
- VT.

Q. If the patient with AS has **bleeding** per rectum, what is the likely underlying cause?

A. Angiodysplasia of the colon (Heydis syndrome).

AORTIC REGURGITATION

CHIEF COMPLAINTS

- Palpitation for … months
- Shortness of breath for … months
- Occasional cough for … months.

HISTORY

History of present illness: The patient states that he was alright … months back. Since then, he has been suffering from occasional palpitation and shortness of breath, which usually occurs during mild to moderate exertion, relieved by taking rest. There is no history of orthopnea or paroxysmal nocturnal dyspnea. There is no diurnal variation or association with dust, fume or cold exposure. The patient also complaints of occasional dry cough, but there is no chest pain or hemoptysis. Sometimes he experiences dizziness, but no loss of consciousness.

History of past illness

Family history

Personal history

Socioeconomic history

Drug history: Mention according to the statement of the patient.

GENERAL EXAMINATION

As in other valvular diseases written before.

SYSTEMIC EXAMINATION

Cardiovascular System

- Pulse: 92/min, regular, high volume, collapsing type
- JVP: Normal
- There is dancing carotid pulse in the neck (Corrigan's sign)
- BP: 160/30 mm Hg (high systolic, low diastolic and wide pulse pressure).

Precordium

Inspection:

- Visible cardiac impulse.

Palpation:

- Apex beat: Shifted in left … intercostal space, ... cm from midline, thrusting in nature
- Thrill: Present in left parasternal area, diastolic in nature.

Auscultation:

- First heart sound: Normal in all the areas
- Second heart sound: A_2 is absent and P_2 is normal

- There is an early diastolic murmur, which is high pitched, blowing, best heard in the left lower parasternal area, with patient bending forward and breathing hold after expiration.

Note Mention if the following findings are present:

- Ejection systolic murmur (in aortic area which radiates to the neck, due to increased stroke volume and flow through the aortic valve).
- A soft mid-diastolic murmur (called Austin Flint murmur).
- Duroziez's murmur (over the femoral artery).
- Capillary pulsation (seen in the nail bed, inner side of lip, fundus during ophthalmoscopy).

Examination of other systems reveals no abnormalities.

SALIENT FEATURE

Mr …, 30-year-old, businessman, normotensive, nondiabetic, smoker, presented with occasional palpitation and shortness of breath for … months, which usually occurs during mild to moderate exertion and relieves after taking rest. There is no history of orthopnea or paroxysmal nocturnal dyspnea. There is no diurnal variation or association with dust, fume or cold exposure. The patient also complaints of occasional dry cough, but there is no chest pain or hemoptysis. Sometimes he experiences dizziness, but no loss of consciousness. There is no family history of such illness. He took some diuretics prescribed by local physicians.

General examination: Mention as above.

Examination of cardiovascular system: Mention as above.

Examination of other systems reveals no abnormalities.

My diagnosis is aortic regurgitation.

Q. Why your diagnosis is AR?

A. Because:

- Pulse is high volume and collapsing
- Dancing carotid pulse
- High systolic and low diastolic BP (wide pulse pressure)
- Presence of EDM in the left lower parasternal area.

Q. What is your differential diagnosis?

A. Pulmonary regurgitation (PR).

Q. How to differentiate AR from PR?

A. In PR, findings are:

- Early diastolic murmur in pulmonary area (called Graham Steel murmur), which is more prominent on inspiration.
- Evidence of pulmonary hypertension may be present (e.g. palpable P_2, left parasternal heave, epigastric pulsation, etc.).

Note

Pulmonary regurgitation is rare as an isolated phenomenon, usually associated with pulmonary artery dilatation due to pulmonary hypertension, secondary to other diseases (e.g. mitral stenosis).

Q. Mention **one investigation** to confirm your diagnosis.

A. Echocardiography, preferably color Doppler.

Q. What **investigations** do you suggest in this case?

A. As follows:

- X-ray chest (cardiomegaly, dilated ascending aorta, pulmonary edema)
- ECG (LVH)
- Echocardiogram, preferably color Doppler
- Cardiac catheterization
- Other investigations to find out the cause according to the clinical suspicion.

RELATED QUESTIONS AND ANSWERS

Q. Why this is called **water hammer pulse**?

A. The name originated from a Victorian toy, consisted of a sealed tube, half filled with water and half being vacuum. Inversion of the tube causes the fluid to fall rapidly without air resistance and strike the end like hammer blow.

Q. Are "high volume pulse" and "collapsing pulse" synonymous?

A. Collapsing pulse is always high volume, but all high volume pulse are not collapsing.

Q. What are the causes of **high volume pulse**?

A. As follows:

- Aortic regurgitation
- Hypertension
- Hyperdynamic circulation due to any cause (severe anemia, thyrotoxicosis, arteriovenous fistula, fever, etc.)
- PDA.

Q. What is **collapsing pulse**? What are the **causes**?

A. In collapsing pulse, there is rapid upstroke and descent of pulse, seen by raising the arm above the head. Causes are:

- AR (the most common cause)
- Hyperdynamic circulation due to any cause (see above)
- PDA
- Rupture of sinus of Valsalva
- Large arteriovenous communication.

Q. In AR, what other **signs** do you want to look for?

A. As follows:

- Quinke's sign: Capillary pulsation at the nail bed (alternate flushing and paleness of skin at the root of the nail while pressure is applied at the tip of the nail). It may be normally present and better seen with glass slide.
- de Musset's sign: Head nodding with heart beat (with each pulse).
- Duroziez's sign: Usually diastolic (may be systolic) murmur over the femoral artery on gradual compression of the vessel and ausculted proximally.
- Pistol shot: May be heard over femoral artery (Traube's sign).
- Hill's sign: High BP in legs than arms (high systolic BP, 60 mm difference) indicates severe AR.
- Mueller's sign: Pulsation in uvula with heart beat.

Note

Most of the signs are rare and unhelpful.

Q. What will you see **in the eye and mouth** in a patient with AR?

A. As follows:

- Eye: Argyll Robertson pupil (may be present in neurosyphilis), dislocated lens, irregular pupils, iridodonesis (found in Marfan's syndrome).
- Mouth: High arched palate (Marfan's syndrome).

Note

Also look for evidence of ankylosing spondylitis, rheumatoid arthritis which may cause aortic regurgitation.

Note To diagnose AR, remember the formula of 3:

- 3 pulse: Collapsing (water hammer), dancing carotid and capillary pulsation.
- 3 BP: Rise of systolic, fall of diastolic and wide pulse pressure.
- 3 murmur: Early diastolic murmur, Austin Flint murmur and ejection systolic murmur.

Q. What are the causes of **wide pulse pressure**?

A. As follows:

- AR
- PDA
- A-V fistula
- Hyperdynamic circulation (thyrotoxicosis, anemia, beriberi, pregnancy).

Q. What are the causes of **EDM**?

A. As follows:

- Aortic regurgitation
- Pulmonary regurgitation (evidence of pulmonary hypertension is present and other peripheral signs of AR are absent).

Q. Why there is **ESM** in AR?

A. Due to increased flow through aortic valve without aortic stenosis (or may be associated with AS).

Q. Why there is MDM in AR **(Austin Flint murmur)**?

A. It is due to regurgitant flow from aortic valve causing vibration of the anterior leaflet of mitral valve.

Q. Why not this **MDM** is due to mitral stenosis?

A. In MS, there should be:

- Tapping apex beat
- Loud first heart sound
- MDM associated with presystolic accentuation
- Opening snap.

Q. What are the signs of **severe AR**?

A. Signs of severe AR:

- Prolonged EDM
- A_2 absent
- Presence of left ventricular 3rd heart sound
- Presence of Austin Flint murmur
- Signs of LVF
- Signs of enlarging heart.

Q. What are the **causes of AR**?

A. As follows:

- Chronic rheumatic heart disease
- Infective endocarditis
- Syphilitic aortitis
- Bicuspid aortic valve
- Dissecting aneurysm affecting ascending aorta
- Hypertension (by aortic dilatation)
- Marfan's syndrome
- Seronegative arthritis (ankylosing spondylitis, Reiter's syndrome)
- Rheumatoid arthritis
- Cystic medial necrosis
- Congenital.

Causes of AR according to the site or abnormality:

- Due to involvement of valve:
  - Rheumatic fever
  - Infective endocarditis
  - Bicuspid aortic valve
  - Trauma
- Aortic root dilatation:
  - Marfan's syndrome
  - Dissecting aneurysm affecting ascending aorta
  - Syphilitic aortitis
  - Hypertension
  - Trauma
  - Seronegative arthritides (ankylosing spondylitis, Reiter's syndrome, psoriatic arthropathy)
  - SLE
  - Rheumatoid arthritis
  - Pseudoxanthoma elasticum
  - Osteogenesis imperfecta
  - Rare causes—appetite suppressants (like fenfluramine, phentermine).

Q. What are the **causes of acute AR**?

A. As follows:

- Acute bacterial endocarditis
- Acute rheumatic fever (due to valvulitis)
- Dissecting aneurysm affecting ascending aorta
- Trauma.

Note

In acute AR, there is soft, short, early diastolic murmur with diastolic thrill. Most patients have heart failure. Peripheral signs and cardiomegaly are absent. It should be treated by emergency surgery.

Q. What are the **complications** of AR?

A. As follows:

- Acute LVF
- Infective endocarditis
- Arrhythmia.

Q. How to **differentiate** AR of rheumatic origin and due to other causes?

A. In rheumatic origin:

- History of rheumatic fever
- Other valvular lesion: Commonly mitral
- Echocardiogram: There is thickening and shortening of cusps, fusion of commissures (If AR is due to other cause: There is dilatation of aorta or valve ring).

Q. How to **differentiate** syphilitic AR and rheumatic AR?

A. As follows:

Features	Syphilitic AR	Rheumatic AR
1. Age	>40 years	Early age
2. History of	Syphilis	Rheumatic fever
3. EDM	In aortic area (right sternal border)	In left lower parasternal area
4. Peripheral signs	Usually absent	Present
5. Lesion	Only AR, never AS	Both may be present
6. Echocardiogram	No cusp involvement	Cusp involvement
7. Aorta	Dilated, calcification may occur	No calcification

Note

Syphilis never causes AS, only AR.

Q. How to **treat** AR?

A. As follows:

1. In asymptomatic moderate to severe AR with normal LV function—long acting nifedipine.
2. In symptomatic patient with:
   - Normal LV function: Long acting nifedipine
   - LV dysfunction: Digitalis, ACE inhibitor, diuretic
   - Heart failure: Digitalis, ACE inhibitor, diuretic.
3. In severe case: Valve replacement.

Indications of surgery:

1. Symptomatic patient.
2. Asymptomatic patient with
   - LV systolic dysfunction (EF < 50%)
   - LV dilatation (LV end systolic dimension >55 mm or LV end diastolic dimension >75 mm).
   - Aortic root dilatation >50 mm.

Note

The valve should be replaced before significant left ventricular dysfunction occurs.

Q. What are the **causes** of angina in AR?

A. As follows:

- Low diastolic blood pressure compromise the coronary perfusion pressure causing angina.
- Marked LVH.

MIXED AORTIC STENOSIS AND REGURGITATION

CHIEF COMPLAINTS

- Breathlessness on exertion for … months
- Palpitation for … months
- Chest pain for … months
- Occasional dizziness for … months.

HISTORY

History of present illness: The patient states that he had been well … months back. For the last … months, he has been suffering from shortness of breath and palpitation on moderate to severe exertion. Sometimes, he experiences orthopnea and paroxysmal nocturnal dyspnea. His breathlessness is not related to dust, fume or change in weather. There is no diurnal variation.

The patient also complains of central chest pain, which is aggravated during moderate exertion and is relieved by taking rest. The pain is compressive in nature, without any radiation. Occasionally he feels dizzy. He became unconscious twice during the last … months. Each episode was preceded by giddiness and lightheadedness and persisted for few minutes. There is no history of cough, fever or swelling. His bowel and bladder habits are normal.

History of past illness

Personal history

Family history

Socioeconomic history

Drug history: Mention according to the statement of the patient.

GENERAL EXAMINATION

Mention as described in other cases, according to your finding.

SYSTEMIC EXAMINATION

Cardiovascular System

- Pulse: 98/min, low volume and slow rising, normal in rhythm, pulsus bisferiens is present (in carotid).
- JVP: Normal.
- BP: Low systolic and normal diastolic, narrow pulse pressure.

Precordium

Inspection:

- Visible cardiac impulse.

Palpation:

- Apex beat: Shifted in left … intercostal space, … cm from midline, heaving in nature.
- Systolic thrill: Present in aortic area.

Auscultation:

- First heart sound: Normal in all the areas.
- Second heart sound: A_2 is soft or absent and P_2 is normal.
- There is an ejection systolic murmur in aortic area which radiates to the neck and also there is an early diastolic murmur in the left lower parasternal area.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr…., 40-year-old, businessman, normotensive, nondiabetic, smoker, presented with shortness of breath and palpitation on moderate to severe exertion for … months. Sometimes he experiences orthopnea and paroxysmal nocturnal dyspnea. His breathlessness is not related to dust, fume or change in weather. There is no diurnal variation. The patient also complains of central chest pain, which is aggravated during moderate exertion and is relieved by taking rest. The pain is compressive in nature, without any radiation. Occasionally he feels dizzy. He became unconscious twice during the last … months. Each episode was preceded by giddiness and lightheadedness and persisted for few minutes. There is no history of cough, fever or swelling. His bowel and bladder habits are normal. He took some diuretics the name of which he cannot mention. There is no such illness in his family.

On examination, general examination—mention as above.

Examination of cardiovascular system—mention as above.

Examination of other systems reveals no abnormalities.

My diagnosis is aortic stenosis with aortic regurgitation.

Q. What is your **differential** diagnosis?

A. There is combined systolic and diastolic murmur. So this may be confused with conditions that present with continuous murmur like:

- Patent ductus arteriosus (murmur is called machinery murmur or train in a tunnel)
- Pulmonary arteriovenous fistula
- Pulmonary stenosis with pulmonary regurgitation.

Q. Could it be **purely AR** without stenosis?

A. Yes, ESM here may be due to increased flow through aortic valve without AS.

Q. What do you think the likely **cause** in this case?

A. Chronic rheumatic heart disease.

Q. Could it be due to **syphilis**?

A. No, **syphilis never causes AS.**

Q. What is the **predominant** lesion in this case and why?

A. Predominant lesion is aortic stenosis, because:

- Pulse: Low volume and slow rising.
- Blood pressure: Low systolic and normal diastolic, narrow pulse pressure.
- Apex beat is heaving.
- Systolic thrill in aortic area.
- A_2: Absent.

Note

If AS is predominant, there may be history of more anginal pain and syncopal attack.

Q. What are the findings, if **AR** is predominant?

A. If AR is predominant, there will be:

- Pulse: High volume and collapsing (water hammer type).
- Apex beat: Shifted and thrusting.
- Blood pressure: Increased systolic, fall of diastolic and wide pulse pressure.

Note

If AR is predominant, in history, palpitation will be more and there will be less anginal pain and syncopal attack.

RELATED QUESTIONS AND ANSWERS

Q. What **investigations** do you suggest?

A. As follows:

- X-ray chest
- ECG (LVH)
- Echocardiogram, preferably color Doppler
- Cardiac catheterization.

Q. How to **treat** the case?

A. As follows:

- In mild to moderate case: Follow-up.
- In severe case: Valve replacement.

CONGESTIVE CARDIAC FAILURE WITH VALVULAR LESION

CHIEF COMPLAINTS

- Breathlessness on exertion for … months
- Cough with mucoid expectoration for … months
- Palpitation for … months
- Pain in right upper abdomen for … months
- Swelling of legs for … months
- Weight loss, anorexia, weakness for … months.

HISTORY

History of present illness: According to the patient's statement, she was relatively alright … months back. Since then, she has been suffering from progressively increasing difficulty in breathing. Initially she felt breathless on moderate to severe exertion, but now it is more marked even during normal activities like going to the toilet or dressing. She also complains of cough, with expectoration of mucoid sputum, but with no hemoptysis or wheeze. The cough is not aggravated by exposure to cold, dust, fume, etc. Occasionally, she experiences nocturnal breathlessness, at late hours of night, for which she has to get up from sleep and walk to take deep breath, which makes her comfortable. There is no history of breathlessness on lying flat (orthopnea).

The patient also experiences occasional palpitation, aggravated on mild exertion and relieved by taking rest. She also noticed pain in the right upper abdomen, which aggravates on lying on right lateral position. The pain is dull aching in nature, but no radiation to any site. She also complains of gradual swelling of both legs, which is more marked during prolonged sitting or standing. The swelling used to disappear while she gets up from sleep early in the morning. She also complains of weakness, loss of appetite and loss of about one third of her body weight within the last … months.

History of past illness: There is no history of rheumatic fever or any cardiac disease. She does not give any history suggestive of COPD (to exclude cor pulmonale). There is no history of hypertension, diabetes mellitus.

Family history

Personal history

Socioeconomic history

Drug history: Mention according to the statement of the patient.

GENERAL EXAMINATION

- Appearance: Ill looking and dyspneic
- Decubitus: Propped up
- Built: Emaciated
- Nutritional status: Below average
- Anemia: Moderately anemic
- Cyanosis: Present
- Edema: Present, pitting

- No jaundice, clubbing, koilonychia, leukonychia or lymphadenopathy or thyromegaly
- Pulse: 104/min, low volume and regular in rhythm
- Blood pressure: 100/70 mm Hg
- Temperature: 97.6ºF
- Respiratory rate: 30/min.

SYSTEMIC EXAMINATION

Cardiovascular System

- Pulse: 104/min, low volume, regular in rhythm, normal in character, no radio-radial or radio-femoral delay and the condition of the vessel wall is normal. All the peripheral pulses are normal.
- Blood pressure: 100/70 mm Hg.
- JVP: Engorged … cm and pulsatile.

Precordium

Inspection:

- There is visible cardiac impulse in apical area and also visible epigastric pulsation.

Palpation:

- Apex beat is in left … intercostal space, 9 cm from midsternal line, normal in character
- Thrill: Absent
- P_2 is palpable in pulmonary area
- Left parasternal heave and epigastric pulsation are present
- (Mention other findings of vulvular lesion, if present).

Auscultation:

- Mention the heart sounds according to the vulvular lesion (all the heart sounds may be soft).
- Murmur: Mention which one is present.

Abdomen

Inspection:

- Mention according to your findings (may be all normal).

Palpation:

- Liver is enlarged … cm, from the right costal margin in mid clavicular line. It is tender, soft in consistency, margin is sharp, surface is smooth. Upper border of the liver dullness is in right 4th intercostal space in midclavicular line, no hepatic bruit or rub.
- Other findings: Mention accordingly.

Respiratory System

- May show signs of emphysema or chronic bronchitis (to exclude cor pulmonale).

Other systemic examinations reveals no abnormalities.

SALIENT FEATURE

The patient Mrs …, 38-year-old, housewife, normotensive, nondiabetic, nonsmoker, presented with progressively increasing difficulty in breathing for … months. Initially she felt breathless on moderate to severe exertion, but now it is more marked even during normal activities like going to toilet or dressing. She also complains of cough, with expectoration of mucoid sputum, but with no hemoptysis or wheeze. The cough is not aggravated by exposure to cold, dust, fume, etc. Occasionally, she experiences nocturnal breathlessness, at late hours of night, for which she has to get up from sleep and walk to take deep breath, which makes her comfortable. There is no history of breathlessness on lying flat (orthopnea).

The patient also experiences occasional palpitation, aggravated on mild exertion and relieved by taking rest. She also noticed pain in the right upper abdomen, which aggravates on lying on right lateral position. The pain is dull aching in nature, but no radiation to any site. She also complains of gradual swelling of both legs, which is more marked during prolonged sitting or standing. The swelling used to disappear while she gets up from sleep early in the morning. She also complains of weakness, loss of appetite and loss of about one third of her body weight within the last … months. There is no history of rheumatic fever or any cardiac disease. She does not give any history suggestive of COPD. There is no history of hypertension, diabetes mellitus. There is no family history of such illness. She used to take tablet frusemide and inhaler salbutamol as prescribed by local physicians.

On examination, general examination—mention as above.

Examination of cardiovascular system and abdomen—mention as above.

Other systems reveal no abnormalities.

My diagnosis is congestive cardiac failure (with … vulvular lesion – mention according to your finding).

Q. Why is it CCF?

A. Because there is engorged and pulsatile neck veins, enlarged tender liver and dependent pitting edema.

Q. What are your differential diagnoses?

A. As follows:

- Chronic cor pulmonale
- Nephrotic syndrome
- Cirrhosis of liver.

Q. What is cor pulmonale?

A. It is defined as right ventricular hypertrophy with or without failure, secondary to the diseases of lung parenchyma, pulmonary vessels or thoracic bony abnormality.

Q. Why is this not a case of cor pulmonale?

A. This is not a case of cor pulmonale, because there is no previous history of lung disease like chronic bronchitis, emphysema (COPD) or ankylosing spondolytis. Also on examination, there is no finding in chest such as kyphosis, scoliosis, barrel shaped chest or no findings in the lung suggestive of COPD.

Also, if any vulvular lesion is present (e.g. MS or MR), mention it, which is against cor pulmonale.

Q. Why not nephrotic syndrome?

A. In nephrotic syndrome, the face is swollen first, followed by abdomen and legs and ultimately generalized edema. Here facial swelling is absent. Also the engorged pulsatile neck vein and tender hepatomegaly are against NS.

Q. Why not **cirrhosis** of liver?

A. Because there are no stigmata of CLD.

Q. What **investigations** do you suggest in this case?

A. As follows:

- X-ray chest (cardiomegaly, plethoric lung fields)
- ECG
- Echocardiogram
- Others: CBC, ESR, urea, creatinine, electrolytes, serum total protein and AG ratio, lung function test (if COPD)
- BNP, ANP.

RELATED QUESTIONS AND ANSWERS

Q. What is **heart failure**?

A. It is defined as failure of the heart to maintain adequate cardiac output to meet the demand of the tissue or can do so only at the expense of an elevated filling pressure.

Q. What are the **cardinal signs** of congestive cardiac failure?

A. It actually means right heart failure. Cardinal signs of CCF are:

- Engorged and pulsatile neck veins
- Enlarged and tender liver
- Dependent pitting edema.

Note CCF may be associated with:

- Pleural effusion (commonly right sided, may be bilateral)
- Ascites
- Jaundice due to hepatic congestion (or cirrhosis, called cardiac cirrhosis).

Q. What are the **causes** of CCF?

A. As follows:

- Secondary to left sided heart failure (common cause)
- Mitral stenosis with pulmonary hypertension
- Chronic cor pulmonale due to any cause
- Pulmonary hypertension
- Pulmonary valve disease (stenosis or regurgitation)
- Tricuspid regurgitation
- Shunt anomaly (ASD, VSD), when there is reversal of shunt (Eisenmenger's syndrome)
- Cardiomyopathy
- Right ventricular myocardial infarction.

Q. What is **BNP**?

A. **B-type natriuretic peptide (BNP)** is a 32 amino acid polypeptide secreted by the left ventricle of the heart in response to excessive stretching of heart muscle cells. It is elevated in left ventricular systolic dysfunction. It may aid in the diagnosis and assess the prognosis and response to therapy in patient with heart failure. It helps to differentiate heart failure from other conditions (like bronchial asthma) that might mimic heart failure. However, BNP level may be elevated in renal failure (due to low clearance), pulmonary embolism, pulmonary hypertension, atrial fibrillation, acute myocardial

infarction, chronic hypoxia and sepsis. Originally, BNP was isolated from porcine brain and was called brain natriuretic peptide.

Q. What is the **functional classification** of cardiovascular disease status?

A. A close relationship of symptoms and exercise is the hallmark of heart disease. New York Heart Association (NYHA) functional classification of cardiovascular status is as follows:

- **Grade I:** No limitation during ordinary activity (asymptomatic).
- **Grade II:** Slight limitation during ordinary activity (symptomatic with mild activity).
- **Grade III:** Marked limitation of normal activities without symptoms at rest (symptomatic with moderate activity).
- **Grade IV:** Unable to undertake physical activity without symptoms. Symptoms may be present at rest (symptomatic at rest).

Q. How to **treat** CCF?

A. As follows:

- Complete rest.
- Restriction of fluid and salt.
- Diuretic (frusemide or bumetanide).
- Aldosterone receptor antagonist (e.g. spironolactone, eplerenone).
- Vasodilator (ACE inhibitor or ARB).
- β-blocker (especially bisoprolol 1.25 mg daily and gradually increased over 12 weeks up to 10 mg daily) may be used. It reduces the risk of arrhythmia and sudden death. β-blocker should not be initiated at a high dose since it may precipitate acute on chronic heart failure. But when given in a small incremental dose (as above), it can increase ejection fraction, improve symptoms, reduce frequency of hospitalization and reduce mortality in patient with chronic heart failure.
- Digoxin (helpful in CCF with atrial fibrillation).
- Treatment of arrhythmia (amiodarone is the drug of choice).
- Treatment of the underlying cause.
- Heart transplantation—If all above measures fail.

Q. What are the **complications of digoxin?** How to treat if toxicity of digoxin develops?

A. As follows:

1. Extracardiac:
   - Gastrointestinal: Anorexia, nausea, vomiting, diarrhea
   - Altered color vision (xanthopsia)
   - Others: Weight loss, confusion, headache, gynecomastia.
2. Cardiac:
   - Bradycardia
   - Multiple ventricular ectopics
   - Ventricular bigeminy
   - Atrial tachycardia with variable block
   - Ventricular tachycardia (bidirectional VT is mainly due to digitalis)
   - Ventricular fibrillation.

Treatment of digoxin toxicity:

- Digoxin should be stopped
- Serum electrolytes, creatinine and digoxin level should be checked.
- Correction of electrolytes, if any
- If bradycardia: IV atropine, sometimes pacing may be needed
- Correction of arrhythmia.

Q. What are the causes of **peripheral edema**?

A. As follows:

1. Pitting edema occurs in:
   - CCF
   - Hypoalbuminemia (nephrotic syndrome, protein loosing enteropathy or less protein intake, CLD)
   - Chronic venous insufficiency (varicose vein)
   - Drugs (calcium channel blockers, e.g. nifedipine, amlodipine)
   - Idiopathic (also called 'Fluid retention syndrome', common in women).
2. Non-pitting edema occurs in:
   - Myxedema.
   - Chronic lymphatic obstruction or lymphedema (e.g. filariasis, Milroy's disease).

Q. What are the causes of **lymphedema**?

A. As follows:

1. Primary:
   - Secondary to agenesis or hypoplasia
   - Hereditary (Milroy's disease)
   - Associated with Turner's syndrome, Noonan syndrome and Yellow nail syndrome.
2. Secondary:
   - Recurrent lymphangitis or cellulitis
   - Filariasis
   - Trauma
   - Tuberculosis
   - Neoplasm
   - Surgery (in the arm, it may be due to mastectomy)
   - Radiation
   - Burn.

Q. What are the causes of **bilateral** leg swelling?

A. As follows:

- Edema due to any cause (CCF, nephrotic syndrome and hypoproteinemia)
- Myxedema
- Some cases of lymphedema
- Acromegaly
- Inferior vena caval (IVC) obstruction (dilated tortuous veins in the lower limbs with upward flow)
- Iliac vein thrombosis
- Pregnancy
- Drugs (calcium channel blockers, such as nifedipine or amlodipine).

Q. What are the **causes of unilateral** leg swelling?

A. As follows:

- Lymphedema
- DVT
- Angioneurotic edema
- Ruptured Baker's cyst
- Chronic venous insufficiency.

Note

Unilateral swelling in arm may occur following mastectomy or radiation.

Q. What are the causes of **acute unilateral** leg swelling?

A. As follows:

- Deep venous thrombosis
- Ruptured Baker's cyst
- Cellulitis
- Trauma
- Angioedema.

Q. What is **high output** cardiac failure and **low output** cardiac failure? What are the **causes**?

A. As follows:

1. High output cardiac failure means "the heart fails to maintain sufficient circulation despite an increased cardiac output". Presentations are same as in low output cardiac failure except tachycardia, gallop rhythm, warm extremities with distended superficial veins. Causes are:
   - Severe anemia
   - Thyrotoxicosis
   - Arteriovenous fistula
   - Beriberi
   - Gram-negative septicemia
   - Paget's disease of the bone.
2. Low output cardiac failure means "the heart fails to maintain sufficient circulation with low cardiac output". Common causes are:
   - Ischemic heart disease
   - Multiple valvular lesion
   - Hypertension
   - Cardiomyopathy
   - Pericardial disease.

Q. What are the causes of **biventricular failure**?

A. As follows:

- Cardiomyopathy (commonly dilated cardiomyopathy)
- Myocarditis
- Ischemic heart disease (extensive myocardial infarction)
- Right sided heart failure secondary to left sided heart failure (e.g. MR, AS or AR)
- Hyperdynamic circulation (in severe anemia, thyrotoxicosis, arteriovenous shunt, beriberi)
- Myxedema (called myxedema heart)
- Multiple vulvular diseases.

Q. What are the causes of **left-sided heart failure (or pulmonary edema)**?

A. As follows:

- Systemic hypertension
- Acute myocardial infarction
- Aortic valvular disease (stenosis and regurgitation)
- Mitral regurgitation
- Cardiomyopathy
- Coarctation of aorta
- Rapid and excess infusion of fluid or blood or plasma
- Hyperdynamic circulation.

Q. What are the **cardinal features** of LVF?

A. As follows:
- Bilateral basal crepitations
- Gallop rhythm
- Pulsus alternans.

Q. How would you **manage** acute LVF (or acute pulmonary edema)?

A. As follows:
- Bed rest
- Propped up position
- High flow oxygen inhalation
- Diuretic—frusemide IV
- Morphine (if there is no contraindication)—10 to 20 mg IV slowly, if needed with antiemetic like metoclopramide or cyclizine
- ACE inhibitor
- If no response, inotropic agents like dopamine, dobutamine may be added
- Treatment of primary cause.

Q. What are the causes of **sudden** cardiac failure?

A. As follows:
- Acute myocardial infarction
- Arrhythmia (especially ventricular fibrillation)
- Circulatory overload (transfusion or infusion)
- Severe anemia
- Accelerated hypertension
- Dissecting aneurysm of aorta
- Massive pulmonary thromboembolism.

Q. What is **cardiac cachexia**?

A. Marked loss of weight or body mass that may occur in some cases of long standing moderate to severe cardiac failure is called cardiac cachexia.

It occurs commonly in patient more than 40 years with heart failure for more than 5 years. It is associated with high morbidity and mortality. Probable mechanisms are as follows:
- Malabsorption, anorexia and nausea due to intestinal venous congestion or edema, congestive hepatomegaly or toxicity of drugs (digoxin).
- Increased metabolic activity.
- TNF-α is increased, which is an important contributing factor for cachexia.
- Natriuretic peptide C is also increased.
- Poor tissue perfusion due to low cardiac output.

Q. What are the differences between **cardiac and bronchial asthma**?

A. As follows:

Features	Cardiac asthma	Bronchial asthma
1. History	Hypertension, IHD, valvular disease, family history of hypertension	History of previous attack of asthma, allergy or rhinitis, family history of asthma or allergy
2. Age	Usually elderly	Young, may be any age

Contd...

Contd...

3. Symptoms	» Dyspnea, cough with frothy sputum » Wheeze—rare » Sweating—common	» Dyspnea, cough with little mucoid sputum » Wheeze—common » Sweating—less
4. Signs	Pulse—may be pulsus alternans Blood pressure—high (if hypertensive) Heart— » Evidence of cardiomegaly (apex is shifted) » Gallop rhythm » Primary cause may be present (e.g. mitral or aortic valvular disease) Lungs— » Bilateral basal crepitation, later, extensive crepitations » No or little rhonchi	Pulse—may be pulsus paradoxus Blood pressure—normal, low in severe cases Heart— » Absent » No » No Lungs— » Plenty of rhonchi all over the lungs » No or little crepitations
5. CXR	» Perihilar opacities (bat's wing appearance) » Cardiomegaly	Relatively clear, evidence of infection may be present
6. ECG	LVH, myocardial infarction	Normal, only tachycardia may be present

HYPERTENSION

CHIEF COMPLAINTS

- Occasional headache, dizziness and giddiness for … months
- Chest pain for … months
- Sleeplessness for … months.

HISTORY

History of present illness: According to the patient's statement, he was reasonably alright … months back. Since then, he has been suffering from occasional headache, dizziness and giddiness. The headache mostly involves the occipital region and the back of the neck. It is pulsatile in nature, localized, mostly during the daytime, initiated by exertion or anxiety and relieved by sleeping. His headache is not associated with vertigo, nausea, vomiting, visual or hearing problem or facial pain. It is not preceded by any premonitoring symptoms. He also experiences occasional chest pain on moderate to severe exertion which is relieved by taking rest. There is no cough or breathlessness. For the last … months, he is experiencing sleeplessness and used to take sleeping pills. There is no history of fever, loss of consciousness, weight gain, muscular weakness, etc. His bowel and bladder habits are normal.

History of past illness

Family history

Personal history

Socioeconomic history

Drug history: Mention according to the statement of the patient.

GENERAL EXAMINATION

- Appearance: Anxious
- No anemia, cyanosis, jaundice, clubbing, edema, koilonychia, leukonychia, lymphadenopathy or thyromegaly
- Pulse: 84/min
- Blood pressure: 195/100 mm Hg
- Respiratory rate: 18/min
- Temperature: 98°F.

SYSTEMIC EXAMINATION

Cardiovascular System

- Pulse: 84/min, regular in rhythm, high volume and normal in character
- BP: 195/100 mm Hg
- JVP: Not engorged.

Precordium

Inspection:

- Visible cardiac impulse (mention if any).

Palpation:

- Apex beat is palpable, at left 5th intercostal space 8 cm from midsternal line, normal in character.
- Thrill: Absent.

Auscultation:

- All the heart sounds are normal
- There is no murmur or added sounds.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 45-year-old, businessman, smoker, nondiabetic, hailing from …, presented with occasional headache, dizziness and giddiness for … months. The headache mostly involves the occipital region and the back of the neck. It is pulsatile in nature, localized, mostly during the daytime, initiated by exertion or anxiety and relieved by sleeping. It is not associated with vertigo, nausea, vomiting, visual or hearing problem or facial pain. His headache is not preceded by any premonitoring symptoms. He also experiences occasional chest pain on moderate to severe exertion which is relieved by taking rest. There is no cough or breathlessness. For the last … months, he is experiencing sleeplessness and used to take sleeping pills. There is no history of fever, loss of consciousness, weight gain, muscular weakness, etc. His bowel and bladder habits are normal.

The patient smokes 1 pack of cigarette everyday for the last 25 years. His father is hypertensive and mother has diabetes. There is no history of renal disease in his family.

On examination, general examination—Mention as above.

Examination of cardiovascular system—Mention as above.

Other systems reveal no abnormalities.

My diagnosis is hypertension.

Q. What is the **cause of hypertension** in this patient?

A. This is most likely to be primary hypertension because there are no history or physical signs suggestive of a secondary cause.

Q. What **investigations** would you do in this patient?

A. As follows:

1. Routine:
   - Urine R/M/E: To see protein, RBC cast, pus cell, etc.
   - Blood urea, creatinine
   - Serum electrolytes
   - Fasting blood sugar
   - Serum lipid profile (total serum cholesterol, VLDL, LDL, HDL, triglyceride)
   - X-ray chest PA view
   - ECG
   - Echocardiogram.
2. Other investigation according to suspicion of cause:
   - If renal cause: Ultrasonogram of whole abdomen, IVU, CT scan of renal system, isotope renogram.
   - Cushing syndrome: Serum cortisol level, 24 hour urinary cortisol, ACTH, dexamethasone suppression test, etc.

- Pheochromocytoma: 24 hours urinary VMA, serum catecholamines
- Conn's syndrome: Plasma aldosterone and renin
- Coarctation of aorta: CT scan, aortogram.

RELATED QUESTIONS AND ANSWERS

Q. What is **hypertension**? What are the **types**?

A. Hypertension is defined as persistent rise of blood pressure above the normal range. JNC 7 recommends the following classification of blood pressure:

Type	Systolic BP (mm Hg)		Diastolic BP (mm Hg)
1. Normal	< 120	And	<80
2. Pre-hypertension	120 to 139	Or	80 to 89
3. Stage 1 hypertension	140 to 159	Or	90 to 99
4. Stage 2 hypertension	≥ 160	Or	≥ 100

According to British Hypertension Society, blood pressure is classified as follows:

Category	Systolic BP (mm Hg)	Diastolic BP (mm Hg)
Blood pressure		
Optimal	< 120 and	< 80
Normal	120 to 129 and/or	<85
High normal (equivalent to pre-hypertension)	130 to 139 and/or	85 to 89
Hypertension		
» Grade 1 (mild)	140 to 159 and/or	90 to 99
» Grade 2 (moderate)	160 to 179 and/or	100 to 109
» Grade 3 (severe)	≥ 180	≥ 110
Isolated systolic hypertension		
» Grade 1	140 to 149	< 90
» Grade 2	≥ 160	< 90

Q. When would you diagnose a patient to be **hypertensive**?

A. When systolic blood pressure is 140 or more or diastolic BP is 90 or more, the patient is diagnosed as hypertensive.

Note Remember the following points:

- A single reading is not sufficient. At least 3 readings in different times should be taken to label as hypertensive.
- BP should be measured at least 5 minutes after the patient has taken rest comfortably in sitting or supine position.
- BP should be measured at least 30 minutes after smoking or coffee ingestion.

Q. What is **white coat hypertension**?

A. When blood pressure is recorded in a hospital set up or in the physician's clinic, there may be transient rise in BP in a normal individual that gives a wrong perception of hypertension. This is called white coat hypertension. About 20% patient with apparent hypertension measured by a physician may have a normal BP, when it is recorded by automated devices at home.

Q. What is hypertensive **encephalopathy**?

A. It is characterized by very high BP with neurological abnormalities, such as severe headache, loss of consciousness, convulsion, paresthesia, transient disturbance of speech or vision, retinopathy, etc.

Q. What is hypertensive **emergency** and hypertensive **urgency**?

A. As follows:

- Hypertensive emergency or hypertensive crisis: It means severe elevation of BP (>180/120 mm Hg) with evidence of impending or progressive target organ dysfunction. It includes hypertensive encephalopathy (headache, irritability, confusion, altered mental status due to cerebrovascular spasm), hypertensive nephropathy (hematuria, proteinuria, progressive kidney dysfunction due to arteriolar necrosis and intimal hyperplasia of the interlobular arteries), intracranial hemorrhage, aortic dissection, pre-eclampsia, eclampsia, pulmonary edema, unstable angina or myocardial infarction. It needs substantial reduction of BP within 1 hour to avoid the risk of serious morbidity or death. Parenteral therapy is indicated in most hypertensive emergencies, especially if encephalopathy is present. At first BP should be reduced no more than 25% within minutes to 1 to 2 hours and then it should be gradually lowered to a target level of 160/100 mm Hg within 2 to 6 hours. Excessive reductions in pressure may precipitate coronary, cerebral or renal ischemia.
- Hypertensive urgency means severe elevation in BP without life-threatening target organ dysfunction. It is characterized by asymptomatic severe hypertension (systolic BP > 220 mm Hg or diastolic BP > 125 mm Hg), optic disk edema, progressive target organ complications and severe perioperative hypertension. Here BP must be reduced within a few hours. Parenteral drug therapy is not usually required and slow reduction of BP with relief of symptoms is the goal.

Q. What are the **causes** of hypertension?

A. As follows:

1. Primary or essential hypertension (95%).
2. Secondary (5%):
   a. Renal (commonest secondary cause):
      - Chronic glomerulonephritis
      - Chronic pyelonephritis
      - Diabetic nephropathy
      - Adult polycystic kidney disease
      - Renal artery stenosis.

   b. Endocrine:
      - Cushing's syndrome
      - Conn's syndrome (primary aldosteronism)
      - Pheochromocytoma
      - Congenital adrenal hyperplasia
      - Hyperparathyroidism
      - Primary hypothyroidism
      - Hyperthyroidism
      - Acromegaly.

c. Drugs:
- Alcohol
- Oral contraceptive pill
- Steroids
- NSAIDs
- Erythropoietin
- Sympathomimetics.

d. Others:
- Pre-eclamptia and eclampsia (toxemia of pregnancy)
- Pregnancy induced hypertension: Usually hypertension develops in the second half of pregnancy, which usually resolves after delivery (In contrast, hypertension developing in the first half of pregnancy or persisting after delivery is more likely to be essential hypertension)
- Coarctation of aorta
- Cerebral tumor.

Q. What are the **complications** of hypertension?

A. As follows:

1. Cardiovascular:
   - Ischemic heart disease
   - Acute left ventricular failure
   - Dissecting aneurysm.
2. Renal:
   - Renal failure.
3. Ocular:
   - Retinopathy.
4. Neurological:
   - CVD (intracerebral hemorrhage, sometimes infarction)
   - Subarachnoid hemorrhage
   - Hypertensive encephalopathy.

Q. What is **malignant hypertension**?

A. It is characterized by severe hypertension with diastolic BP > 130 mm Hg, associated with grade III or IV retinopathy (retinal hemorrhage or exudates and papilledema) and renal failure or encephalopathy. It is a rare complication of hypertension. There is accelerated microvascular damage with fibrinoid necrosis in the walls of small arteries and arterioles and intravascular thrombosis. This may lead to LVF and if untreated, death occurs within months.

Treatment: Slow, controlled reduction of BP over a period of 24 to 48 hours is ideal (Rapid reduction is avoided, as it reduces tissue perfusion and can cause cerebral damage including occipital blindness, may even precipitate coronary or renal insufficiency).

- Complete rest.
- Oral antihypertensive is sufficient to control the blood pressure.
- Sometimes IV or IM labetalol, IV glycerin trinitrate, IM hydralazine, IV nitroprusside may be given with careful supervision.

Q. What is **refractory hypertension?** What are the **causes?**

A. When there is no response to antihypertensive drugs, it is called refractory hypertension. The causes are:

- Poor compliance to drug therapy (the most common cause)

- Inadequate therapy
- Failure to recognize an underlying cause like renal artery stenosis or pheochromocytoma.

JNC 7 has defined **resistant hypertension** as, "the failure to reach BP control in patients who are adherent to full doses of an appropriate three drug regimen including a diuretic". The following things should be carefully excluded:

- Improper BP measurement.
- Volume overload which may be due to excess sodium intake, renal disease or inadequate diuretic therapy.
- Inadequate dose, inappropriate combination of drugs or nonadherence.
- Drug induced hypertension like NSAIDs, steroid, oral contraceptive pills, cyclosporine, tacrolimus, erythropoietin, etc.
- Other secondary causes of hypertension.
- Associated conditions like obesity, excess alcohol intake, etc.

Q. What are the **grades** of hypertensive retinopathy?

A. Four grades (Keith-Wagener-Barker classification):

- **Grade I:** Thickening of arterial wall, increase tortuosity, narrowing of arteriole and increased light reflex (silver wiring).
- **Grade II:** Grade I plus AV nipping and reduction of arterial calibre in comparison to vein (normal ratio of V:A = 3:2).
- **Grade III:** Grade II plus cotton wool exudate and flame-shaped hemorrhage.
- **Grade IV:** Grade III plus papilloedema (Grade III and IV indicate malignant hypertension).

Q. What **history** would you take in a patient with hypertension?

A. As follows:

- Age: If young, likely to be secondary cause. If elderly, likely to be primary.
- Family history: Family history of hypertension, hyperlipidemia, diabetes mellitus, obesity, etc. may be present in case of primary hypertension. In some secondary hypertension, there may be positive family history, e.g. polycystic kidney disease.
- Past medical history: Previous history of renal disease (hematuria, UTI, renal trauma, pain, pyelonephritis), toxemia of pregnancy (in female).
- Drug history: Prolong use of NSAIDs, steroids, oral contraceptive pill, etc.
- History of smoking.
- Symptoms to find out the secondary casue:
  a. Symptoms of renal disease like polyuria, frequency, hematuria, loin pain.
  b. Paroxysmal attack of headache, palpitation, flushing and sweating (pheochromocytoma).
  c. Polyuria, polydipsia, extreme muscular weakness, tingling (Conn's syndrome).
  d. Weight gain, hirsutism, striae, menstrual abnormality in female (Cushing syndrome).
  e. Claudication and cramp in lower limbs in a young patient (coarctation of aorta).
  f. Frequent attack of headache, vomiting, visual disturbance, neurological features (intracranial tumor).

Q. What physical **signs** would you look for in a patient with hypertension?

A. As follows:

- Puffy face: Renal failure.
- Central obesity with plethoric moon face, hirsutism, striae: Cushing syndrome.

- Pulse: Bradycardia suggests raised intracranial pressure, feeble pulse in lower limbs with radiofemoral delay found in coarctation of aorta.
- Blood pressure: High BP in upper limbs, but low in lower limbs suggest coarctation of aorta.
- Anemia: Suggests chronic renal failure.
- Edema: May be present in renal failure.
- Cardiovascular system: Apex may be heaving and shifted (left ventricular hypertrophy or enlargement), murmur may be present in coarctation of aorta.
- Abdomen: Bilateral renal mass in polycystic kidney disease, renal bruit in renal artery stenosis.
- Fundoscopy to see retinal change.
- Other finding according to suspicion of cause like intracranial space occupying lesion.
- Bed side urine examination for hematuria and proteinuria.

Q. Whom should you treat for hypertension? What is the target BP?

A. The following patients should be treated with drugs and lifestyle change:

- Malignant hypertension.
- All patients with a sustained (at least 2 visits) systolic BP ≥ 160 mm Hg and/or diastolic BP ≥ 100 mm Hg (grade 2 or 3 hypertension).
- Patients with systolic BP 140 to 159 mm Hg and/or diastolic BP 90 to 99 mm Hg (grade 1 hypertension) with 10 year cardiovascular (CVD) risk of at least 20% or existing CVD, target organ damage or diabetes mellitus.
- Isolated systolic hypertension (systolic BP >160 mm Hg).

In patients with grade 1 hypertension without 10 year CVD risk of at least 20% or target organ damage should get lifestyle modification and yearly reassessment. Those who have systolic BP < 140 and diastolic BP < 90 mm Hg should be reassessed in 5 years.

The target BP is ≤ 140/90 mm Hg. But in diabetes mellitus, it should be < 130/80 mm Hg and in case of proteinuria, the target is <125/75 mm Hg.

Q. How to treat hypertension?

A. As follows:

1. General measures (**non-drug treatment** of hypertension):
   - Salt restriction (< 6 g/day).
   - Smoking should be stopped.
   - Weight reduction in obese patients (BMI should be < 25 kg/m^2).
   - Dietary modification: Low fat and saturated fat and increase fruits and vegetables, also oily fish.
   - Regular exercise (at least 30 minutes dynamic exercise daily).
   - Reduction of anxiety and tension.
   - Control of diabetes mellitus.
   - Restriction of tea and coffee.
   - Restriction of alcohol intake (< 21 units/week for men and <14 units/week for women).
   - Control of other modifiable risk factors.
2. Drug treatment:
   - Diuretic: Thiazide (bendroflumethiazide or cyclopenthiazide).
   - ACE inhibitors: Enalapril, lisinopril, ramipril.
   - ARB: Losartan, valsartan, irbesartan.
   - Calcium channel blocker: Amlodipine, nifedipine, diltiazem, verapamil.
   - Beta blocker: Atenolol, metoprolol, bisoprolol.
   - Combined alpha and beta blocker: Labetalol, carvedilol.
   - Alpha blocker: Prazosin, doxazosin.

- Renin inhibitor: Aliskiren (this is a newly introduced drug).
- Others: Methyldopa (specially for pregnancy).

3. Management of primary cause, if any.

Note

Adjuvant therapy-antiplatelet (aspirin) may be added with antihypertensive drugs especially in patients over 50 years. Also statin may be added. Both of these, reduces cardiovascular risk.

TREATMENT OF HYPERTENSION IN SPECIFIC CONDITIONS

Hypertension in bronchial asthma:

- Drugs like diuretics, calcium channel blocker, ARB, ACE inhibitor (it may cause cough).
- Avoid β-blockers.

Hypertension in chronic kidney disease: (Target BP is < 130/80 mm Hg).

- ACE inhibitors and ARB may delay progression of kidney disease (if creatinine is >2.5 mmol/L, these should be avoided).
- Calcium channel blocker may be used.
- Thiazide diuretic may be replaced with loop diuretics.

Hypertension in pregnancy:

- Methyldopa or labetalol.
- Other drugs: Calcium channel blocker (nifedipin) may be used. Sometimes, β-blocker may be used but should be avoided in first trimester.
- ACE inhibitor is contraindicated.
- Diuretic is also avoided (there is risk of uteroplacental blood flow reduction).

Hypertension in diabetes mellitus:

- ACE inhibitor, ARB, calcium channel blocker may be used.
- Avoid thiazide (it aggravates diabetes).
- Avoid β-blocker in patient who is on insulin (it masks symptoms of hypoglycemia).

Hypertention in peripheral vascular disease:

- Calcium channel blocker.
- Alpha blocker may be an alternative.
- Avoid β-blocker. ACE inhibitor should be used carefully (as the patient may have renal artery stenosis also).

Hypertension in dyslipidemia:

- Alpha blocker, ACE inhibitor, ARB, calcium channel blocker.
- Avoid β-blocker and diuretic (which worsen lipid profile).

Hypertension in psoriasis:

- Calcium channel blocker.
- Avoid β-blocker, ACE inhibitor (which aggravates).

Hypertension in angina:

- Beta blocker, calcium channel blocker, nitrate.

Hypertension in elderly:

- Thiazide (it is avoided if coexistent diabetes mellitus and gout).
- Calcium channel blocker.

Q. How would you treat **hypertension in pregnancy**?

A. As follows:

- Methyldopa or labetalol.
- Calcium channel blocker like nifedipine may also be used.
- More severe hypertension or eclampsia may be treated with intravenous hydralazine, even termination of pregnancy may be required.

SUBACUTE BACTERIAL ENDOCARDITIS

CHIEF COMPLAINTS

- Fever for … months
- Chest pain and palpitation for … months
- Difficulty in breathing for … months
- Weight loss for … months.

HISTORY

History of present illness: According to the patient's statement, he was reasonably alright … months back. Since then, he has been suffering from low grade, continued fever, sometimes associated with chills and rigor, also with profuse sweating, subsides only with paracetamol, highest recorded temperature was 101°F. He also complains of central chest pain, sharp in nature without any radiation, does not aggravate by cough or movement of the chest. He also experiences occasional palpitation, associated with difficulty in breathing after mild to moderate exertion for the last … months, which are relieved by taking rest. There is no history suggestive of orthopnea or paroxysmal nocturnal dyspnea.

For the last … months, the patient also experiences malaise, generalized weakness, arthralgia, myalgia, anorexia and substantial loss of weight.

There is no history of unconsciousness, hematuria or loin pain (differentiates from embolic phenomenon). He does not give any history of dental procedures or cardiac or other surgery or instrumental procedure (catheterization, colonoscopy, cannula, etc.) or any history of intravenous drug abuse. His bowel and bladder habits are normal.

History of past illness: He has been suffering from some valvular heart disease for several years (mention, if there are other histories like cardiac surgery).

Family history

Personal history

Socioeconomic history

Drug history: Mention according to the statement of the patient.

GENERAL EXAMINATION

- Appearance: Ill looking, emaciated and toxic (there may be brownish pigmentation of face and limbs called Cafe-au-lait pigmentation).
- Moderately anemic.
- Generalized clubbing: Involving all the fingers and toes.
- There are two splinter hemorrhages in the left index finger.
- No cyanosis, jaundice, koilonychia, leukonychia, lymphadenopathy or thyromegaly.
- Pulse: 110/min.
- Blood pressure: 95/75 mm Hg.
- Respiratory rate: 28/min.
- Temperature: 100°F.
- (If present, mention the following: Osler's node, Janeway lesion, infarction at the tip of fingers or toes, petechiae on the dorsum of hands or feet or other parts.)

SYSTEMIC EXAMINATION

Cardiovascular System

- Pulse: 110/min, regular in rhythm, normal in volume and character.
- BP: 95/75 mm Hg.
- JVP: Not engorged.

Precordium

Inspection:

- Visible cardiac impulse (mention if any).

Palpation:

- Apex beat is palpable, at left 5th intercostal space 8 cm from midsternal line, normal in character.
- Thrill: Present, in … space, diastolic (or systolic) in nature.

Auscultation:

- First heart sound is soft in all the areas, 2nd heart sound is normal in all the areas.
- There is a systolic (or diastolic) murmur, in … intercostal space, with (or without) radiation (mention accordingly).
- Mention any valvular or cardiac lesion according to your finding.

Abdomen

- Spleen is just palpable.
- No other abnormality in abdominal examination.

Eye

- Roth's spot (white centered retinal hemorrhage).

Nervous System

- There is no change (but if there history of cerebral embolism, there may be signs of hemiplegia).

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 28-year-old, student, normotensive, nondiabetic, nonsmoker, presented with fever for … months, which is low grade, continued, sometimes associated with chills and rigor, also with profuse sweating, subsides only with paracetamol, highest recorded temperature was 101°F. He also complains of central chest pain, sharp in nature without any radiation, does not aggravate by cough or movement of the chest. He also experiences occasional palpitation, associated with difficulty in breathing after mild to moderate exertion for the last … months, which are relieved by taking rest. There is no history suggestive of orthopnea or paroxysmal nocturnal dyspnea. For the last … months, the patient also experiences malaise, generalized weakness, arthralgia, myalgia, anorexia and substantial loss of weight. There is no history of unconsciousness, hematuria or loin pain (differentiates from embolic phenomena). He does not give any history of dental procedures or cardiac or other surgery or instrumental procedure (catheterization, colonoscopy, cannula, etc.) or any history of intravenous

drug abuse. His bowel and bladder habits are normal. He has been suffering from some valvular heart disease for several years. There is no family history of such illness. He used to take frusemide, propranolol and vitamins prescribed by the local physicians.

On examination, general examination—mention as above.

Examination of cardiovascular system—mention as above.

Examination of other systems reveals no abnormalities.

My diagnosis is subacute bacterial endocarditis with valvular lesion (mention which one is present).

Q. Why your first diagnosis is SBE?

A. Because:

- The patient is a known case of heart disease (mention which one)
- Fever which is not responding to multiple antibiotics
- Associated features like clubbing, splinter hemorrhage, cardiac murmur, splenomegaly, Roth's spot, etc.

Q. What are your differential diagnoses?

A. As follows (any cause of PUO should be considered. Common possibilities are):

- Tuberculosis
- Kala-azar
- Malaria
- Collagen disease (SLE)
- Lymphoma.

Note Remember, in any patient with prolong fever, which is not responding to usual therapy, SBE should be considered if there are:

- History of previous cardiac lesion
- Appearance of a new murmur
- Change in the nature of a pre-existing murmur.

Q. What investigations should be done to diagnose SBE?

A. As follows:

- Hb%, TC, DC, ESR (normochromic normocytic anemia, neutrophil leukocytosis, high ESR may be present).
- Serum CRP (increased. It is more reliable than ESR in monitoring progress).
- Blood culture (both aerobic and anaerobic)—3 cultures from different sites at 1 hour apart during peak fever, taken after all aseptic measures (10 to 20 mL blood is taken each time). If possible, both aerobic and anaerobic cultures should be done. In some cases, fungal culture should also be done. 10% are culture negative.
- Echocardiography (to see vegetation, valvular lesion or congenital anomaly). Transesophageal echocardiography is more sensitive than transthoracic echocardiography. TOE is mandatory in case of doubtful case, prosthetic or pacemaker endocarditis or when an abscess is suspected. The sensitivity of transthoracic echo is about 55 to 65%, but that of transesophageal echo is more than 90%.
- Urine R/M/E (hematuria and proteinuria may be present).
- CXR P/A view (may show cardiomegaly or evidence of cardiac failure).
- ECG: May show prolong PR interval (AV block due to aortic root abscess formation) and occasionally infarction (due to emboli).
- Urea and creatinine.

RELATED QUESTIONS AND ANSWERS

Q. What are the **predisposing factors or causes** of SBE?

A. Causes or predisposing factors are as follows:

- Rheumatic valve lesion (e.g. AR, MR, etc.).
- Congenital heart disease (VSD, PDA, bicuspid aortic valve, coarctation of aorta, TOF. SBE is rare in ASD, PS, MS, AS).
- Prosthetic valve.
- Dental extraction.
- Instrumentation (catheterization, sigmoidoscopy, cystoscopy, endoscopy, cannulation).
- Cardiac surgery or cardiac catheterization.
- IV drug abuse (right sided endocarditis is more common, especially involves tricuspid valve).

Q. What are the **organisms** causing infective endocarditis?

A. As follows:

1. Subacute bacterial endocarditis:
   - *Streptococcus viridans* (*S. sanguis*, *S. mitis*)—the most common (35 to 50%)
   - *Enterococcus faecalis*, *E. faecium*
   - *S. bovis*, *S. milleri* and other streptococci
   - *S. aureus* or *epidermidis*
   - Diphtheroids
   - HACEK organism (*Haemophilus, Actinobacillus, Cardiobacterium hominis, Eikenella, Kingella*).
2. Acute bacterial endocarditis:
   - *S. aureus* (the most common)
   - *Pseudomonas*
   - *Candida*
   - *S. pneumoneae*
   - *Neisseria gonorrhoea*
3. Postoperative endocarditis:
   - *S. albus*
   - *Candida*
   - *Aspergillus*
   - All other organisms causing subacute and acute endocarditis.

Q. What are the **signs in the hand** in SBE?

A. As follows:

- Clubbing (a late sign).
- Osler's node (small painful violaceous raised nodule, 0.5 to 1.5 cm, present on the tip of the fingers, palmar aspect and tip of the toes, probably due to the product of vasculitis or septic embolism).
- Splinter hemorrage (subungual).
- Janeway lesion (large painless erythematous macules on the palm and sole).
- Patechial hemorrhage.
- Infarction due to embolism.

Q. What is **vegetation**?

A. It is a small solid mass composed of platelet, fibrin and organism, occurring at the site of endothelial damage in the valve or endocardium. It may result in embolism.

Q. What are the **differences** between acute and subacute bacterial endocarditis?

A. As follows:

Parameter	Acute bacterial endocarditis	Subacute bacterial endocarditis
1. Organism	Highly virulent	Less virulent
2. Cardiac lesion	Usually no previous cardiac lesion	Cardiac lesions are usually present
3. Presentations	Sudden onset with high temperature, chill and rigor	Insidious onset
4. Mortality	High	Low
5. Peripheral signs like Osler's node, Janeuray lesion, etc.	Absent	Present

Q. What are the **Duke criteria** for the diagnosis of infective endocarditis?

A. As follows:

Major criteria:

1. Positive blood culture:
   - Typical organism from 2 cultures or,
   - Persistently positive blood cultures defined as: Positive blood cultures obtained more than 12 hours apart or, positive culture in all three or majority of four or more blood samples with the first and last one taken over 1 hour apart or,
   - Single blood culture of *Coxiella burnetii* or positive serological test for Q fever with phase 1 IgG antibody titer of >1:800.
2. Endocardium involvement:
   - Positive echocardiogram (vegetation, abscess, new partial dehiscence of prosthetic valve) or,
   - New valvular regurgitation (worsening or change in murmur is not sufficient).

Minor criteria:

- Predisposition (cardiac lesion, IV drug abuse).
- Fever 38ºC or more.
- Vascular signs (major arterial emboli, septic arterial emboli, mycotic aneurysm, intracranial hemorrhage, Janeway lesion).
- Immunological signs (Osler's node, Roth's spot, glomerulonephritis, rheumatoid factor).
- Positive blood culture that does not meet major criteria.
- Positive echocardiogram that does not meet major criteria.

Diagnosis:

- Definite infective endocarditis: 2 major or 1 major and 3 minor or 5 minor criteria (if no major criteria is met).
- Possible infective endocarditis: 1 major and 1 minor or 3 minor criteria.

Note

It has a sensitivity of about 80%.

Q. What are the **immunological features** of SBE?

A. Osler's node, Roth's spot, glomerulonephritis and rheumatoid factor.

Q. What are the causes of **culture negative endocarditis?**

A. As follows:

- Prior antibiotic treatment (common cause).
- Fungal, yeast, anaerobic infection or Q fever (needs special culture).
- Right sided endocarditis.
- Non-infective endocarditis: Libmann Sac (non-bacterial verrucous endocarditis in SLE, which is usually associated with antiphospholipid antibody syndrome), marantic endocarditis (non-bacterial thrombotic or verrucous endocarditis found in malignancy, such as bronchial carcinoma).

Q. What are the **complications** of SBE?

A. As follows:

- Heart failure (LVF is a common cause of death).
- Valve destruction, regurgitation, obstruction.
- Aortic root abscess, may lead to prolongation of PR interval or even complete AV block.
- Systemic embolism.
- Right sided endocarditis usually involves the pulmonary valve and may cause septic pulmonary emboli, occasionally with infarction and lung abscess.
- Vasculitis.

Q. How to **treat** SBE?

A. As follows:

1. Antibiotic:
   - Ideally antibiotic should be given according to culture and sensitivity. However, treatment should be started as soon as the blood sample is sent for culture and sensitivity. In subacute cases, benzylpenicillin 1.2 g IV 4 hourly and gentamicin 1 mg/kg IV 8 hourly for 4 weeks is given. In acute cases, flucloxacillin 2 g IV 6 hourly is added to cover staphylococci. In case of penicillin allergy, a prosthetic valve or suspected methicillin-resistant *Staphylococcus aureus* (MRSA) infection, triple therapy with vancomycin, gentamicin and oral rifampicin should be considered.
   - Another regimen of empirical therapy—vancomycin 1 g 12 hourly IV with ceftriaxone 2 g every 24 hours is a good choice pending definitive diagnosis.
   - For viridans streptococci, ceftriaxone 2 g once daily IV or IM for 4 weeks is effective. In penicillin allergic patients, vancomycin 15 mg/kg IV 12 hourly for 4 weeks is given. In prosthetic valve endocarditis, penicillin for 6 weeks and gentamicin for 2 weeks should be given.
   - For HACEK organisms, ceftriaxone 2 g IV once daily for 4 weeks are given. If prosthetic valve is involved, then treatment should be given for 6 weeks.
   - Q fever endocarditis needs prolong treatment with doxycycline and rifampicin or ciprofloxacin. Even then, organisms are not always eradicated. Valve surgery is often required.
2. Other antibiotic may be given according to the suspicion of the cause.
3. Any source of infection (e.g. a tooth with an apical abscess) should be removed as soon as possible.
4. Other supportive treatment should be given accordingly.
5. Treatment of the underlying cause like valvular disease.

Q. What **preventive** measures should be taken during dental procedure?

A. Routine antibiotic prophylaxis prior to dental procedure is no longer recommended as this has not been proven to be effective. However, in few high risk cases antibiotic prophylaxis may be considered. These are:

- Prosthetic cardiac valve.
- Previous infective endocarditis.

- Congenital heart disease (CHD)—unrepaired cyanotic CHD, completely repaired CHD with prosthetic material or device or repaired CHD with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device.
- Cardiac transplantation recipient in whom cardiac valvulopathy develops.

Drugs used for prophylaxis:
- Amoxicillin 2 g 1 hour before procedure.
- If penicillin allergy—clindamycin 600 mg or cephalexin 2 gm or azithromycin or clarithromycin 500 mg 1 hour before procedure.
- If the patient is unable to take by mouth, parenteral therapy may be given with ampicillin 2 g IV or IM 30 minutes before the procedure. In case of penicillin allergy, clindamycin 600 mg IV 1 hour before procedure or cefazolin 1 g IM or IV 30 minutes before procedure.

Q. What are the **indications of cardiac surgery** in infective endocarditis?

A. Surgery (debridement of infected material and valve replacement) is indicated in following conditions:
- Progressive heart failure from valve damage
- Valvular obstruction
- Repeated embolization
- Fungal endocarditis
- Persistent bacteremia in spite of adequate antibiotic therapy
- Myocardial abscess
- Endocarditis of prosthetic valve
- Large vegetation in left sided valve.

Q. What is the **prognosis**?

A. 30% mortality with staphylococci, 14% with bowel organisms, 6% with sensitive streptococci.

Note Remember the following points:
- Infective endocarditis typically occurs at the site of pre-existing endocardial damage. However, if the organism is virulent or aggressive (e.g. *Staphylococcus aureus*), it may occur in a previously normal heart.
- *S. viridans* is the most common cause of subacute endocarditis.
- *S. aureus* is the most common cause of acute endocarditis. It originates from skin infection, abscess, vascular access sites or from intravenous drug misuse. It is highly virulent and can cause endocarditis in normal heart. It usually causes florid vegetations, rapid valve destruction and abscess formation.
- Other causes of acute endocarditis are *S. pneumoniae*, *S. pyogenes*, *S. lugdenensis*, etc.
- The most common cause of endocarditis after cardiac surgery is *S. epidermidis*.
- Prosthetic valve endocarditis—in early infection (<2 months) common organism is *Staphylococcus* (this is usually acquired at the time of surgery and has a poor prognosis). In late case (> 2 months), commonest is *Streptococcus* and is acquired hematogenously. Aortic valve prosthesis is more prone to develop endocarditis than mitral valve.
- Right sided endocarditis is common in IV drug users, also sometimes in patients receiving central venous catheter. The most common organism is *Staphylococcus aureus*. Also, other organisms like *Streptococcus pneumoniae* and fungus may be responsible. It mainly affects the tricuspid valve, rarely pulmonary valve. Prognosis is relatively better. It may cause septic pulmonary emboli, occasionally with infarction and lung abscess.
- *S. bovis* and *S. milleri* are associated with large bowel neoplasms.
- In Q fever endocarditis (by *Coxiella burnetii*) and brucellosis, usually aortic valve is involved. Both have history of contact with farm animals.
- Hepatomegaly is common in Q fever endocarditis.

RHEUMATIC FEVER

CHIEF COMPLAINTS

- Migrating polyarthritis involving bigger joints (knee, ankle, elbow) for … days
- Fever for … days
- Palpitation, chest pain … for days
- Malaise, weakness, fatigue for … days.

HISTORY

History of present illness: According to the patient's statement, she was quite fit and well … days back. Then she suffered from sore throat from which she recovered completely within a few days. After … days, she developed severe joint pain. Initially, it involved the right knee joint, but then sequentially the right ankle, left knee, left ankle and elbow joints were involved. The joints are swollen, red and very painful, even with mild movement. The smaller joints are not involved. There was no morning stiffness.

The patient also complains of fever, which is high grade, continued and reduces with antipyretic drugs. It is not associated with chill and rigor, but there is profuse sweating. She also complains of palpitation, chest pain, malaise, fatigue, weakness during her disease period. There is no history of abnormal or involuntary movement (chorea) or skin changes. Her bowel and bladder habits are normal. She denied any history of diarrhea, sexual exposure, skin rash, mouth ulcer, uveitis or any urinary complaint.

History of past illness

Family history

Personal history

Socioeconomic history

Drug history: Mention according to the patient's statement.

GENERAL EXAMINATION

- Appearance: Ill looking
- Built: Average
- Nutrition: Average
- Anemia: Mildly anemic
- No jaundice, cyanosis, clubbing, leukonychia, koilonychia, edema or dehydration
- Pulse: 110/min
- BP: 130/75 mm Hg
- Temperature: 39°C
- Respiratory rate: 24/min
- No lymphadenopathy, thyromegaly, etc.

(Mention any other sign of rheumatic fever, if present).

SYSTEMIC EXAMINATION

Cardiovascular System

- Pulse: 110/min.
- BP: 130/75 mm Hg.
- Neck vein: Not engorged.

Precordium: (findings depend on pancarditis).

Inspection:

- Visible cardiac impulse in mitral area.

Palpation:

- Mention the position of apex and other findings as present in your case.

Auscultation:

- First and second heart sounds: Normal
- No murmur is present
- No added sound.

Locomotor Examination: (Involved joint, e.g. knee joint):

Inspection:

- Swollen (parapatellar fossa are full)
- Red.

Palpation:

- Local temperature: Increased
- Tenderness: Present
- Fluctuation test: Positive
- Movement: Restricted due to pain.

Skin changes (such as subcutaneous nodule, erythema marginatum).

Alimentary system—no abnormality.

Respiratory system—no abnormality.

Nervous system (abnormal movements such as chorea).
(Mention according to your findings).

SALIENT FEATURES

Ms …, 18-year-old, student, normotensive, nondiabetic, nonsmoker, hailing from …, had suffered from sore throat for a few days about … days ago with complete recovery. After … days, she developed migrating, inflammatory, polyarthritis of large joints which sequentially involved the right knee, right ankle, left knee, left ankle and elbow joints. He felt pain even with mild movement. The small joints are not involved and there was no morning stiffness. The patient also had high grade, continued fever without chill or rigor but associated with profuse sweating. She also complains of palpitation, chest

pain, malaise, fatigue, weakness during her disease period. There is no history of abnormal or involuntary movement (chorea) or skin changes. Her bowel and bladder habits are normal. She denied any history of diarrhea, sexual exposure, skin rash, mouth ulcer, uveitis or any urinary complaint. She used to take some painkiller the name of which she could not mention. There is no family history of such illness.

On examination, general examination—mention as above.

Examination of cardiovascular system—mention as above.

Other systems reveal no abnormalities.

My diagnosis is acute rheumatic fever.

Q. What are your differential diagnoses?

A. As follows:

- Infective arthritis (viral or bacterial)
- Juvenile chronic arthritis (juvenile <16 years)
- SLE
- Seronegative arthritis (reactive arthritis, Reiter's syndrome)
- Rheumatoid arthritis.

Q. Why do you think this is a case of rheumatic fever?

A. This young patient has a history of sore throat followed by a latent period and then she developed migrating, inflammatory polyarthritis involving the large joints without any deformity. All these are in favor of acute rheumatic fever.

Q. Why not this is a case of SLE?

A. Because , in this case, arthritis is fleeting is nature involving the bigger joints that is not common in SLE. Also, other criteria of SLE like skin rash, butterfly rash, mouth ulcer, alopecia, menstrual irregularity, etc. are absent.

Q. Why not this is a case of JIA?

A. JIA occurs in young patient less than 16 years of age. The arthritis is not fleeting in nature. Also, in JIA there is usually deformity of the joints.

Q. Why not this is a case of reactive arthritis or Reiter's syndrome?

A. Reiter's syndrome is characterized by triad of iritis, arthritis and urethritis. But the patient does not have history of involvement of the eyes or urinary tract. Also, it occurs after an episode of diarrhea or urethritis which are not present here.

Q. What investigations will you do in this patient?

A. As follows:

- Hb, TC, DC, ESR (high ESR and leukocytosis)
- C-reactive protein (CRP is high)
- Antistreptolysin O (ASO) titre (may be high, in adult > 200, in children > 300)
- Throat swab culture (to find *Streptococcus* beta hemolyticus)
- Chest X-ray (cardiomegaly, pulmonary edema may be present)
- ECG
- Echocardiography (to see valve abnormality and cardiomegaly)
- Others—RA factor (to exclude rheumatoid arthritis) and ANA (to exclude SLE), if needed.

RELATED QUESTIONS AND ANSWERS

Q. What is **rheumatic fever?** What is the **mechanism or pathogenesis**?

A. Rheumatic fever is a multisystem disorder, occurring as a sequelae to pharyngitis by group A β hemolytic *Streptococcus*. It is due to autoimmune reaction between the antigen (M protein) of *Streptococcus* β hemolyticus and cardiac myosin and sarcolemal membrane protein (laminin). As a result, antibody is produced against streptococcal enzyme, causing inflammation in the endocardium, myocardium and pericardium as well as joints and skin. There is formation of "Aschoff's nodule" in heart, which is pathognomonic of rheumatic fever.

Q. What are the usual **presenting complaints** of a patient with rheumatic fever?

A. Rheumatic fever (RF) usually occurs in children and young adults. Peak incidence is 5 to 15 years. It usually recurs unless prevented. There is usually a history of sore throat by group A β hemolytic *Streptococcus* 1 to 3 weeks prior to the fever.

Features are:

- Migrating (fleeting), non-deforming polyarthritis involving the large joints (knee, ankle and elbow) and wrists with fever, which may be continuous, high grade is the presenting feature in 75% cases.
- Palpitation and chest pain (due to carditis in 50% cases).
- Skin rash (erythema marginatum), subcutaneous nodules.
- Involuntary movement (chorea in 10 to 30% cases).
- Malaise, weakness and fatigue.

Q. Which **joints** are commonly involved in acute rheumatic fever?

A. Commonly large joints like ankle, wrist, knee and elbow (usually does not involve small joints of the hands and feet, rarely involves hip joint).

Q. What are the **diagnostic criteria** of rheumatic fever?

A. It is diagnosed by revised **Jones' criteria**. Following an attack of *Streptococcus pharyngitis*, there is usually a latent period of 1 to 3 weeks.

1. Major criteria:

- Carditis
- Shifting polyarthritis
- Rheumatic chorea
- Erythema marginatum
- Subcutaneous nodule.

2. Minor criteria:

- Fever
- Arthralgia
- Previous history of rheumatic fever
- High ESR or CRP
- Leukocytosis
- First or second degree AV block in ECG.

In addition, **supportive evidence of previous streptococcal infection**, like recent streptococcal infection, history of scarlet fever, raised ASO titer (>200) or other streptococcal antibody titer (anti-DNAse or antihyaluronidase) or positive throat swab culture.

Diagnosis is made by two or more major criteria, or one major and two or more minor criteria plus supportive evidence of streptococcal infection.

Q. What are the **signs** of carditis?

A. Rheumatic fever can cause carditis involving all the layers of the heart (endocardium, myocardium and pericardium), called pancarditis.

Signs of endocarditis:

- Soft heart sounds
- Pansystolic murmur (due to MR)
- Mid diastolic murmur (Carey Coombs murmur)
- Early diastolic murmur (due to AR which is due to valvulitis with nodules on the valve).

Signs of myocarditis:

- Tachycardia
- Soft heart sounds, S_3 gallop
- Cardiomegaly
- Features of heart failure.

Signs of pericarditis:

- Pericardial rub (patient usually complains of chest pain)
- Pericardial effusion may be present.

Q. What is **'Aschoff's nodule'**?

A. It is a granulomatous nodule composed of central fibrinoid necrosis and multinucleated gaint cells, with surrounding macrophages and T-lymphocytes. It occurs throughout the heart and is common in the interstitial tissue close to the small blood vessels situated beneath the endocardium of the left ventricle. It is pathognomonic of RF.

Q. What is **erythema marginatum**?

A. It is a transient, geographical type rash with pink or red raised edges, round margin and clear center. It may coalesce into crescent or ring shaped patches. The rash blanches on pressure. It is found mostly on the trunk and proximal limbs (not in face). It occurs in about 10% cases.

Q. What is **subcutaneous nodule?**

A. These are small, mobile, firm, painless, pea-shaped nodules, felt over bony prominences, tendons or joints on the extensor surface. Occurs in 10 to 15% cases.

Q. What is **Sydenham's chorea** (St Vitus' dance)?

A. It is a neurological manifestation of acute RF, which usually occurs after 3 months of an acute attack, when almost all other signs have disappeared.

- It occurs in one-third of cases, common in children and adolescents, especially in female of 5 to 15 years of age.
- Usually associated with emotional instability, irritability, inattentiveness and confusion.

- It may occur without any feature of acute RF. Carditis is common and may be the first manifestation.
- Speech may be explosive and halting.
- ESR, ASO titre and CRP are usually normal.
- Rheumatic chorea is usually self-limiting, and recovers within few months.
- Relapse may occur only in few cases, occasionally during pregnancy (called chorea gravidarum) or in those who use oral contraceptive pill.
- Treatment—sedation (haloperidol) along with other treatment and prophylaxis of rheumatic fever.
- 25% of cases develop chronic rheumatic heart disease in course of time.

Q. What are the **signs of activity** in rheumatic fever?

A. As follows:

- Persistent fever
- Tachycardia
- High ESR
- Leukocytosis
- Evidence of carditis.

Q. How to **treat** acute RF?

A. As follows:

1. Complete bed rest (until disease activity resolves).
2. Oral phenoxymethylpenicillin 250 mg 6 hourly for 10 days or single injection of benzathine penicillin 1.2 million units, deep IM in the buttock (to eliminate the streptococcal infection). Erythromycin may be given if allergic to penicillin.
3. Analgesic (to relieve pain). Aspirin 60 mg/kg per day in divided doses. Higher dose may be required.
4. Other treatment:
   - If there is carditis or severe arthritis, corticosteroid should be given (prednisolone 1 to 2 mg/kg daily).
   - If there is chorea, diazepam (for mild case) or haloperidol (in severe case) should be given.
   - If there is erythema marginatum or subcutaneous nodules, no treatment is necessary.
5. Treatment of complications like cardiac failure, valvular lesion, heart block, arrhythmia, etc. if needed.

Q. What is the **prophylactic** treatment of RF? **How long** should it be continued?

A. Recurrence is common in patient who had carditis during initial episode. In children, 20% recurrence occurs within 5 years. Recurrence is uncommon after 5 years and in patient over 25 years of age.

To prevent recurrence, oral phenoxymethylpenicillin 250 mg 12 hourly or injection benzathine penicillin 1.2 million units deep IM in the buttock every 4 weeks should be given. In penicillin-sensitive patient, erythromycin (250 mg 12 hourly) or sulfadiazine (1 g daily) may be used.

Prophylactic drug should be continued up to 21 years of age or 5 years after the last attack (recurrence after 5 years is rare), whichever comes last. After this, antibiotic prophylaxis should be given for dental or surgical procedure. However, in high-risk streptococcal infection or if the attack occurs in the 5 years or patient lives in high area of prevalence, treatment may need to be extended. If there is documented recurrence or documented rheumatic valvular heart disease, life-long prophylaxis should be considered.

Note Remember the following points:

- Skin infection with streptococci is not associated with RF. It may be associated with acute post streptococcal glomerulonephritis.
- 2 to 3% of previously healthy person may suffer from rheumatic fever following streptococcal pharyngitis.
- Streptococcal sore throat may not be present in some cases.
- More than 50% patients of RF with carditis will develop chronic valvular disease after 10 to 20 years. All the cardiac valves may be involved, but most commonly the mitral valve is affected (90%). Also aortic valve may be involved. Involvement of the tricuspid and pulmonary valves is rare.
- In chronic rheumatic heart disease, there may not be any history of rhematic fever in 50 to 60% cases.
- Arthritis is rheumatic fever recovers completely without any residual change (**Rheumatic fever licks the joints and kills the heart**). However, a rare type of arthritis called Jaccoud's arthritis is associated with deformity of metacarpophalangeal joints after repeated attack of rheumatic fever.

Q. What is the prognosis?

A. Acute attack may last up to 3 months, but recurrence may be precipitated by streptococcal infections, pregnancy, use of oral contraceptive pill, etc. 60% patients with carditis develop chronic rheumatic heat disease. Mitral valve is most commonly involved followed by aortic valve. Tricuspid and pulmonary valves are rarely involved. Usually, regurgitation of cardiac valves develops during acute attacks, while stenosis develops years later.

Q. What are the causes of migrating polyarthritis?

A. As follows:

- Rheumatic fever
- Septicemia
- Gonococcal arthritis
- Syphilitic arthritis
- Lyme arthritis
- Hyperlipidemia (type 2)
- SLE.

Q. What is the **difference** between arthritis and arthralgia?

A. Arthralgia means subjective joint pain but no swelling. Arthritis means joint pain with swelling.

EISENMENGER'S SYNDROME

CHIEF COMPLAINTS

- Breathlessness on exertion for … months
- Fatigue, weakness, dizziness for … months
- Chest pain for … months
- Cough with occasional blood stained sputum for … months.

HISTORY

History of present illness: According to the patient's statement, she has been suffering from some heart disease since her childhood. For the last … months, she is complaining of difficulty in breathing, initially which was only during moderate to severe activity, but for the last … months, she feels breathless even on mild exertion such as going to toilet, undressing, etc. There is no history suggestive of orthopnea or paroxysmal nocturnal dyspnea. Her breathlessness is not related to dust, pollen, fumes, cold, etc. and there is no diurnal or seasonal variation. She also complains of weakness, fatigue and dizziness for … months, which are gradually increasing. Occasionally, the patient experiences chest pain during moderate to severe exertion. The pain is compressive in nature, but no radiation and it is relieved by taking rest. She is also suffering from cough which is sometimes associated with mucoid sputum and streaks of blood. There is no swelling of legs or abdominal pain.

History of past illness: The patient used to feel palpitation during moderate to severe exertion. After several investigations, she was diagnosed with some heart disease. She could not mention the name of the disease (if the patient can tell the diagnosis, mention it).

Family history

Personal history

Socioeconomic history

Drug history: Mention according to the patient's statement.

GENERAL EXAMINATION

- Appearance: Ill looking, emaciated with puffy face, suffused or red conjunctiva
- Central cyanosis: Present (involving toes, fingers, lips, tongue)
- Clubbing: Present involving both toes and fingers
- There is no anemia, leukonychia, koilonychia, jaundice and dehydration
- Pulse: 104/minute, low volume
- BP: 110/70 mm Hg
- Temperature: 37°C
- Respiratory rate: 24/min
- There is no lymphadenopathy, thyromegaly.

SYSTEMIC EXAMINATION

Cardiovascular System

- Pulse: 104/minute, low volume
- BP: 110/70 mm Hg
- JVP: Raised, with prominent "a" wave.

Precordium

Inspection:

- Visible cardiac impulse in pulmonary area.

Palpation:

- Apex beat—In the left … intercostal space, … cm from midsternal line, normal in character
- Left parasternal lift—Present
- Palpable P_2—Present
- Epigastric pulsation – present.

Auscultation:

- First heart sound—normal in all the areas
- Second heart sound—louder in all the areas, P_2 is accentuated in pulmonary area
- There is a pansystolic murmur in the left 3rd and 4th intercostal space, in left parasternal area without any radiation.

Abdomen

- Liver is palpable, 2 cm from the right costal margin in right mid clavicular line. It is slightly tender, margin is sharp, surface is smooth, soft in consistency and upper border of the liver dullness is in the right fifth intercostal space, in the midclavicular line.

Other systemic examinations reveal no abnormalities.

SALIENT FEATURES

The patient Ms …, 22-year-old, student, normotensive, nondiabetic, nonsmoker, a known case of some heart disease since childhood, presented with difficulty in breathing for last … months. Initially it was only during moderate to severe activity, but for the last … months, she feels breathless even on mild exertion such as going to toilet, undressing, etc. There is no history suggestive of orthopnea or paroxysmal nocturnal dyspnea. Her breathlessness is not related to dust, pollen, fumes, cold, etc. and there is no diurnal or seasonal variation. She also complains of weakness, fatigue and dizziness for … months, which are gradually increasing. Occasionally, the patient experiences chest pain during moderate to severe exertion. The pain is compressive in nature but no radiation and it is relieved by taking rest. She is also suffering from cough which is sometimes associated with mucoid sputum and streaks of blood. There is no swelling of legs or abdominal pain. There is no family history of such illness. She used to take some medicines but could not mention the names.

On examination, general examination—mention as above.

Examination of cardiovascular system—mention as above.

Examination of other systems reveals no abnormalities.

My diagnosis is Eisenmenger's syndrome due to VSD.

Q. What are your **differential diagnoses**?

A. As follows:

- Congestive cardiac failure
- Chronic cor pulmonale.

Q. Why not CCF?

A. In CCF, the triad of engorged and pulsatile neck vein, enlarged tender liver and dependent edema should be present. It is usually secondary to other causes like mitral stenosis or left sided heart failure, which are absent in this case.

Q. Why not this is a case of chronic cor-pulmonale?

A. Cor pulmonale is defined as enlargement of right ventricle with or without failure which may be due to causes in the lung parenchyma, pulmonary vessels or chest wall (like kyphosis, scoliosis, etc.). All of these are absent in this case.

Q. What investigations do you suggest in this case?

A. As follows:

1. X-ray chest (enlargement of central pulmonary arteries with peripheral pruning of pulmonary vessels).
2. ECG (RVH, RAH, right axis deviation).
3. Echocardiography.

RELATED QUESTIONS AND ANSWERS

Q. What are the clinical features of Eisenmenger's syndrome?

A. As follows:

- Dyspnea
- Fatigue
- Syncope
- Angina
- Hemoptysis
- Features of CCF.

On examination:

- Central cyanosis (not corrected by giving 100% oxygen. Differential cyanosis (cyanosis in toes, not in the hand) occurs in PDA.
- Clubbing (differential clubbing—clubbing in toes, not in the hand, occurs in PDA).
- Pulse—low volume.
- Prominent **"a" wave in JVP.**
- Other signs of pulmonary hypertension – palpable P2, left parasternal lift, epigastric pulsation due to RVH. Ejection click and ejection systolic murmur may be present.
- TR may occur (in such case, prominent **V wave in JVP, also there may be a pansystolic murmur in left lower parasternal area).**
- Polycythemia.
- Original murmur of VSD, ASD or PDA—decrease in intensity, even may disappear.

Q. What is Eisenmenger's syndrome?

A. Pulmonary hypertension with reversal of shunt is called Eisenmenger's syndrome.

Causes are:

- VSD
- ASD
- PDA.

In VSD, this occurs in early life, in PDA a little later than VSD, in ASD this occurs in adult life.

In these patients, persistently raised pulmonary flow (due to left to right shunt) causes increased pulmonary resistance followed by pulmonary hypertension. This increases the pressure in right ventricle, leading to reversal of shunt (from right to left side).

Q. How to **treat Eisenmenger's syndrome?**

A. Pulmonary hypertension with reversal of shunt, when due to VSD is called Eisenmenger's complex.

Q. What is the **treatment**?

A. As follows:

- Diuretic.
- Digoxin may be given in some cases.
- Venesection may be required, especially if there is polycythemia.
- Heart lung transplantation may be done (mortality rate is very high than heart transplantation alone).

Surgery of shunt is contraindicated in Eisenmenger's syndrome, as it aggravates right sided heart failure.

Q. What are the **causes of death** in Eisenmenger's syndrome?

A. As follows:

- Right heart failure
- Infective endocarditis
- Pulmonary infarction
- Cerebral thrombosis or abscess
- Arrhythmias.

Note Remember the following points:

- If a patient has cyanosis with evidences of pulmonary hypertension, the more likely diagnosis is Eisenmenger's syndrome.
- If a patient with VSD develops Eisenmenger's syndrome, there is appearance of cyanosis, clubbing and evidences of pulmonary hypertension. However, pansystolic murmur of VSD may disappear, because of equalization of pressure between right and left ventricles.
- Patient with Eisenmenger's syndrome is at particular risk from abrupt changes in afterload that exacerbate right to left shunting (e.g. during anesthesia and also in pregnancy).

TETRALOGY OF FALLOT

CHIEF COMPLAINTS

- Breathlessness for … months
- Bluish discoloration of the lips and fingers during exertion for … months
- Weakness for … months
- Palpitation for … months
- Chest pain for … months
- Cough for … months.

HISTORY

History of present illness: According to the patient's statement, she has been suffering from breathlessness since her childhood. Her breathlessness was less marked in earlier stage, only felt during moderate to severe activity. But for the last few months, it is progressively increasing, even during mild exertion. There is no seasonal variation of breathlessness and it is not associated with exposure to dust, pollen or fume. There is no history suggestive of paroxysmal nocturnal dyspnea or orthopnea. The patient also noticed bluish discoloration of skin, finger nail, toes and lips for the last … months, which is more marked during exercise and less by taking squatting position. She also experiences diffuse chest pain, usually following any activity or after eating, which radiates to left shoulder and subsides after taking rest. She also complains of palpitation, weakness and occasional dry cough. Her bowel and bladder habits are normal. Her mother mentioned that the patient used to become bluish and breathless while feeding or crying during the first few years of life.

History of past illness

Family history

Personal history

Socioeconomic history

Drug history: Mention according to the patient's statement.

GENERAL EXAMINATION

- The patient is emaciated and short in stature
- Dyspneic
- Central cyanosis (involving tongue, lips, fingers and toes) is present
- There is generalized clubbing (involving all fingers and toes)
- Pulse: 112/min, low volume, regular in rhythm and normal character
- BP: 100/60 mm Hg
- Temperature: 98ºF
- Respiratory rate: 28/min
- No anemia, leukonychia, koilonychia, edema, jaundice, lymphadenopathy or thyromegaly.

SYSTEMIC EXAMINATION

Cardiovascular System

- Pulse: 112/min, low volume, regular in rhythm and normal character
- BP: 100/60 mm Hg
- JVP: Prominent "a" wave

Precordium

Inspection:

- Visible cardiac impulse in apical and epigastric region.

Palpation:

- Apex beat—palpable in the left … intercostal space, … cm from midline, normal in character
- Left parasternal lift and epigastric pulsation—present
- Systolic thrill—present in pulmonary area.

Auscultation:

- First heart sound—normal in all the areas
- Second heart sound—P_2 is soft (or absent) in pulmonary area, A_2 is normal
- There is a harsh ejection systolic murmur in the pulmonary area, which radiates to the neck, more on inspiration.

Examination of other systems reveals normal findings.

SALIENT FEATURES

The patient Ms …, 12-year-old, student, normotensive, nondiabetic, nonsmoker, presented with breathlessness since her childhood. Her breathlessness was less marked in earlier stage, only felt during moderate to severe activity. But for the last few months, it is progressively increasing, even during mild exertion. There is no seasonal variation to this breathlessness and it is not associated with exposure to dust, pollen or fume. There is no history suggestive of paroxysmal nocturnal dyspnea or orthopnea. The patient also noticed bluish discoloration of skin, finger nail, toes and lips for the last … months, which is more marked during exercise and less by taking squatting position. She also experiences diffuse chest pain, usually following any activity or after eating, which radiates to left shoulder and subsides after taking rest. She also complains of palpitation, weakness and occasional dry cough. Her bowel and bladder habits are normal. Her mother mentioned that the patient used to become bluish and breathless while feeding or crying during the first few years of life. There is no history of such illness in her family.

On examination, general examination—mention as above.

Examination of cardiovascular system—mention as above.

Examination of other systems reveals no abnormalities.

My diagnosis is tetralogy of Fallot:

Q. Mention some **cyanotic congenital heart disease**.

A. As follows:
- Tricuspid atresia
- Transposition of great vessels
- Pulmonary atresia
- Ebstein's anomaly.

Q. What **investigations** are done in TOF?

A. As follows:
- Chest X-ray- shows boot-shaped heart, pulmonary conus is concave (small pulmonary artery), right ventricle enlarged (prominent elevated apex), oligemic lung, right-sided aortic arch in 25% cases.
- 2D echocardiography and color Doppler (diagnostic—it shows that the aorta is not continuous with the anterior ventricular septum).
- Other investigations: ECG (RVH), cardiac catheterization in some cases.

RELATED QUESTIONS AND ANSWERS

Q. What **is tetralogy of Fallot**?

A. It is a cyanotic congenital heart disease consisting of:
- Right ventricular hypertrophy.
- VSD (perimembranous, usually large, subaortic).
- Right ventricular outflow obstruction—this may be subvalvular (infundibular), valvular or supravalvular. The most common obstruction is subvalvular, either alone (50%) or in combination with pulmonary stenosis (25%).
- Overriding and dextro-position of aorta (aortic origin—2/3rd from left ventricle and 1/3rd from right ventricle).

Q. What are the **cardinal features** of TOF?

A. As follows:
- Child with growth retardation
- Clubbing
- Cyanosis
- Pulmonary ejection systolic murmur
- History of cyanotic spells during exercise (relieved by squatting).

Q. How the patient usually **presents**?

A. As follows:
- Young children usually present with cyanotic spell (Fallot's spell) during exertion, feeding or crying. They may become apneic and unconscious.
- In older children, Fallot's spells are uncommon but cyanosis becomes increasingly apparent with clubbing and polycythemia. There may be Fallot's sign.
- Shortness of breath on exertion, easy fatiguability.
- Growth retardation.
- Syncope, seizure, cerebrovascular events or even sudden death.

Q. Why **syncope** occurs in TOF?

A. During exercise, there is increased pulmonary resistance and reduced systemic vascular resistance. So, there is increased right to left shunt and admixture of blood of right and left ventricles. As a result, there is reduced cerebral oxygenation, causing syncope.

Q. Why there is **cyanosis** in TOF?

A. Because of the overriding of aorta, there is admixture of blood of right and left ventricles. Cyanosis is absent in newborn or acyanotic Fallot's.

Q. When is cyanosis **aggravated** and Why?

A. Cyanosis is aggravated during exercise and is called cyanotic spell or Fallot's spell. It is also aggravated during feeding or crying. Cyanosis is reduced by squatting. Child may be apneic and unconscious. Syncope, seizure, cerebrovascular accident (CVA) or sudden death may occur. Fallot's spell is uncommon in older children. Cyanotic spell is due to increased obstruction, as a result of increased sympathetic stimulation that occurs during exercise, feeding and crying.

Q. How **squatting** relieves cyanosis?

A. In squatting position, abdominal aorta and femoral artery are compressed. So, there is increased arterial resistance, which increases the pressure in the left ventricle, leading to diminished right to left shunt through VSD and increased flow through pulmonary artery. This reduces admixture of blood from right and left ventricles and relieves cyanosis.

Q. What are the **complications** of tetralogy of Fallot?

A. As follows:

- Infective endocarditis (common)
- Paradoxical emboli
- Cerebral abscess (10% cases)
- Polycythemia (due to hypoxemia, and may lead to cerebrovascular accident and myocardial infarction)
- Coagulation abnormality.

Q. How to **assess the severity** of TOF?

A. As follows:

- Mild case—loud and prolonged murmur
- Severe case—murmur reduced or absent.

Q. What is **pentalogy** of Fallot?

A. When TOF is associated with ASD.

Q. What is **triology** of Fallot?

A. ASD with PS with RVH.

Q. Why there is **no murmur** of VSD in TOF?

A. Because VSD is large and there is equal pressure in right and left ventricles.

Q. What is **acyanotic Fallot**?

A. When the TOF is associated with infundibular pulmonary stenosis. Outflow obstruction is mild and there is no cyanosis.

Q. How to **treat** TOF?

A. As follows:

- Surgical correction is the definitive treatment, ideally should be done prior to 5 years of age. Surgical relieve of pulmonary stenosis and closure of VSD is done.
- If pulmonary artery is hypoplastic or anatomy is unfavorable, then temporarily palliative surgery called Blalock-Taussig shunt is performed. Corrective surgery is done later on.
- Prophylactic antibiotic to prevent infective endocarditis.

Q. What is **Blalock-Taussig shunt**?

A. Blalock-Taussig shunt is the anastomosis between left subclavian artery with left pulmonary artery. This improves pulmonary blood flow and pulmonary artery development, and may facilitate definitive surgery later on.

Q. How to **treat during cyanotic spell**?

A. As follows:

- Knee-chest position of child
- High concentration of O_2
- Injection morphine or diamorphine (it relaxes right ventricular outflow obstruction)
- β-blocker may be used
- If medical therapy fails, emergency surgical shunt may be considered.

Q. What is the **prognosis** of TOF?

A. Prognosis is good after surgery, especially if operation is done in childhood. Re-stenosis, recurrence of septal defect and rhythm disorder may occur after surgery. So, regular follow-up is required in every case.

VENTRICULAR SEPTAL DEFECT (VSD)

CHIEF COMPLAINTS

- Breathlessness for … years
- Palpitation for … years.

HISTORY

History of present illness: According to the patient, she was alright … months back. Since then, she has been suffering from occasional breathlessness, more during moderate to severe exertion and relieved by taking rest. There is no history of nocturnal breathlessness or orthopnea. There is no diurnal variation of breathlessness and it is not associated with exposure to dust or cold. The patient also complains of occasional palpitation, usually with moderate to severe activity, relieved with taking rest. She does not complain of cough or hemoptysis. There is no history of chest pain, swelling of legs and syncope.

History of past illness

Family history

Personal history

Socioeconomic history

Drug history: Mention according to the statement of the patient.

GENERAL EXAMINATION

- Built: Slightly emaciated
- Anemia: Mild
- No jaundice, edema, clubbing, koilonychia, leukonychia
- No lymphadenopathy or thyromegaly
- Pulse: 84/min
- BP: 110/65 mm Hg
- Temperature: 98.8ºF.

SYSTEMIC EXAMINATION

Cardiovascular System

- Pulse: 84/minute, low volume, regular in rhythm and normal in character
- BP: 110/65 mm Hg
- JVP: Not raised.

Precordium

Inspection:

- Visible cardiac impulse in left parasternal area.

Palpation:

- Apex beat—in left ... intercostal space, ... cm from midsternal line, diffuse, thrusting in nature
- Systolic thrill is present in left parasternal area (4th or 5th intercostal area).

Auscultation:

- First and second heart sounds—normal in all the areas.
- There is a harsh pansystolic murmur in left parasternal area in 4th or 5th intercostal space (may be MDM due to increased flow through mitral valve).
- Third heart sound may be present.

Examination of other systems reveals normal findings.

SALIENT FEATURES

The patient …, 16-year-old, student, hailing from …, presented with occasional breathlessness, more during moderate to severe exertion and relieved by taking rest. There is no history of nocturnal breathlessness or orthopnea. There is no diurnal variation of breathlessness and it is not associated with exposure to dust or cold. The patient also complains of occasional palpitation, usually with moderate to severe activity, relieved with taking rest. She does not complain of cough or hemoptysis. There is no history of chest pain, swelling of legs and syncope. There is no such illness in her family. She used to take some medicine the name of which she cannot mention.

On examination, general examination—mention as above.

Examination of cardiovascular system—mention as above.

Other systems reveal no abnormalities.

My diagnosis is ventricular septal defect.

Q. Why your diagnosis is VSD?

A. Because of presence of systolic thrill and pansystolic murmur in the left lower parasternal area.

Q. What are your **differential diagnoses**?

A. As follows:

- Mitral regurgitation (MR)
- Tricuspid regurgitation (TR).

Q. Why not this is a case of MR?

A. In MR findings are:

- First heart sound is soft
- Pansystolic murmur in mitral area, which radiates towards the left axilla.

Q. Why not this is a case of TR?

A. In TR, findings are:

- JVP may be raised. There may be giant **V wave, oscillating up to the ear lobule.**
- First heart sound is soft in tricuspid area.
- There is a pansystolic murmur in left lower parasternal area with no radiation and the murmur is louder with inspiration.
- Also there may be enlarged, tender, pulsatile liver.

Q. Mention **one single investigation** to confirm your diagnosis.

A. Color Doppler echocardiogram.

Q. What **investigations** do you suggest in your case?

A. As follows:
- ECG (LVH, biventricular hypertrophy)
- X-ray chest (cardiomegaly, large pulmonary conus, large hilar arteries, plethoric lung fields)
- Echocardiography, preferably color Doppler
- Cardiac catheterization may be necessary in some cases
- CMR (cardiac magnetic resonance angiography) may be helpful.

RELATED QUESTIONS AND ANSWERS

Q. What are the **causes** of VSD?

A. As follows:
- Commonly congenital (VSD is the most common congenital heart disease)
- Acquired—rupture of interventricular septum after acute MI, rarely trauma.

Q. What is the **site** of VSD?

A. Common site is the perimembranous part of intraventricular septum (in 90% cases).

Q. Does the presentation vary with the **size of VSD**?

A. VSD may be of three types according to the size. These are:
- **Small VSD (maladie de Roger):** It is asymptomatic and usually closes spontaneously. But, there is a future risk of development of aortic regurgitation or endocarditis even after spontaneous closure. The systolic murmur is loud and prolonged.
- **Moderate VSD:** The patient presents with fatigue and dyspnea. Heart is usually enlarged with a prominent apex beat. There is often a palpable systolic thrill and a loud "tearing" pansystolic murmur at the left lower sternal edge.
- **Large VSD:** The murmur is soft. It may lead to pulmonary hypertension and Eisenmenger's complex may result.

Q. What are the **complications** of VSD?

A. As follows:
- Infective endocarditis (more common in small VSD)
- Pulmonary hypertension with reversal of shunt (Eisenmenger's syndrome)
- Heart failure.

Note

When Eisenmenger's syndrome develops, there is cyanosis, clubbing and evidence of pulmonary hypertension. Pansystolic murmur may disappear, because of equalization of pressure in right and left ventricle.

Q. What are the **causes** of plethoric lung field?

A. As follows:
- ASD
- VSD
- PDA.

(Also in congestive cardiac failure).

Q. How to **treat** VSD?

A. As follows:

- If small: Surgery is not needed; only follow-up should be done. Spontaneous closure may occur in infants if it is in the muscular part. Prophylactic penicillin for SBE may be given.
- Moderate to large: Surgical correction is needed if pulmonary to systemic flow ratio >1.5:1. Percutaneous transcatheter closure may be done.
- When Eisenmenger's syndrome develops: Surgery is contraindicated, as it aggravates right sided heart failure. Then following treatments are given:
  - Diuretic
  - Digoxin in some cases
  - Venesection, especially if there is polycythemia
  - Heart lung transplantation may be done. Mortality rate is very high than heart transplantation alone.

Note

VSD may be associated with Turner's syndrome, Down's syndrome or maternal rubella during pregnancy.

Q. Can VSD be closed **spontaneously?**

A. If small VSD, spontaneous closer may occur.

ATRIAL SEPTAL DEFECT (ASD)

CHIEF COMPLAINTS

- Weakness for ... months
- Palpitation for ... months
- Breathlessness for … months.

HISTORY

History of present illness: The patient states that she was alright … months back. Since then, she has been suffering from weakness and palpitation which are more marked on moderate to severe exertion and relieved by taking rest. She also experiences occasional breathlessness precipitated by moderate to severe exertion. However, there is no diurnal variation of this breathlessness and it is not associated with exposure to dust or fume. There is no chest pain or cough. She denies any history of swelling of legs, fever, fainting or loss of consciousness. Her appetite, bowel and bladder habits are normal.

History of past illness

Family history

Personal history

Socioeconomic history

Drug history: Mention according to the statement of the patient.

GENERAL EXAMINATION

- Appearance and built: Normal
- Anemia: Moderate
- No jaundice, edema, clubbing, koilonychia, leukonychia
- No lymphadenopathy or thyromegaly
- Pulse: 96/min
- Blood pressure: 100/65 mm Hg
- Temperature: 98.8ºF.

SYSTEMIC EXAMINATION

Cardiovascular System

- Pulse: 96/min, regular, low volume
- BP: 100/65 mm Hg
- JVP: Not raised.

Precordium

Inspection:

- Nothing significant.

Palpation:

- Apex beat—in left ... intercostal space, ... cm from midline, normal in character
- Thrill—absent.

Auscultation:

- First heart sound—normal in all the areas
- Wide and fixed splitting of 2nd heart sound
- An ejection systolic murmur is present in the left 2nd and 3rd intercostal space
- There is also a high pitched MDM in tricuspid area.

Examination of other systems reveals normal findings.

SALIENT FEATURES

Ms …, 28-year-old, service holder, normotensive, nondiabetic, nonsmoker, hailing from …, presented with generalized weakness and palpitation for … months, which are more marked on moderate to severe exertion and relieved by taking rest. She also experiences occasional breathlessness precipitated by moderate to severe exertion. However, there is no diurnal variation of this breathlessness and it is not associated with exposure to dust or fume. There is no chest pain or cough. She denies any history of swelling of legs, fever, fainting or loss of consciousness. Her appetite, bowel and bladder habits are normal. There is no history of such illness or other illness in her family. She used to take some vitamins only.

On examination, general examination—mention as above.

Examination of cardiovascular system—mention as above.

Other systems reveal no abnormalities.

My diagnosis is atrial septal defect.

Q. What are your **differential diagnoses**?

A. As follows:

- Pulmonary stenosis
- VSD.

Q. Why not this is a case of pulmonary stenosis?

A. In pulmonary stenosis, the findings are:

- Soft or absent P_2
- Thrill present in pulmonary area
- Wide and fixed splitting of 2nd heart sound is absent
- ESM may radiate to the neck.

Q. Why not this is a case of VSD?

A. In VSD, the findings are:

- Systolic thrill in the left lower parasternal area
- Pansystolic murmur in the left lower parasternal area.

Q. What **investigations** do you suggest in ASD?

A. As follows:

- X-ray chest—cardiomegaly (right ventricle and right atrium are enlarged, also small left artium and normal aorta), large pulmonary conus, large hilar arteries and plethoric lung fields (lung fields become oligemic, when pulmonary hypertension develops).

- ECG.
- 2D echocardiography and color Doppler (transesophageal echocardiography is better).
- Cardiac catheterization in some cases (fluoroscopy shows hilar dance).
- MRI (or CMR) may be helpful.

RELATED QUESTIONS AND ANSWERS

Q. What is **wide and fixed splitting** of 2nd sound and why wide and fixed splitting?

A. Wide and fixed splitting means it is remaining same in inspiration and expiration.
- Wide—because of delay in right ventricular ejection, which is due to increased stroke volume.
- Fixed—because of equalization of pressure between left and right atrium, so no change of 2nd heart sound with respiration (normally, there is wide splitting during inspiration due to delay of closure of pulmonary valve).

Q. What are the **murmurs** in ASD?

A. Two murmurs:
- ESM—due to increased flow through pulmonary valve.
- MDM—due to increased flow through tricuspid valve.

(No murmur due to ASD, because of equal pressure between left and right atrium).

Q. What are the **types** of ASD?

A. Two types:
- Ostium primum (15% cases)—results from atrioventricular defect in septum and there is involvement of AV valve, so there may be MR or TR.
- Ostium secundum (75% cases)—defect mainly at the fossa ovalis in the atrial mid septum (it should not be confused with patent foramen ovale, which is a normal variant, not a true septal defect. PFO is usually asymptomatic, but may be associated with paradoxical emboli and increased incidence of embolic stroke. PFO may be treated with angiographic closure using transcatheter clamshell device to prevent thromboembolism).

(ASD is common in female, M:F = 1:2. Ostium primum may occur in Down's syndrome).

Q. What is the **ECG finding** in ASD?

A. ECG shows:
- In primum type—RBBB with left axis deviation.
- In secundum type—RBBB with right axis deviation.

Q. What are the **complications** of ASD?

A. As follows:
- Pulmonary hypertension with reversal of shunt (Eisenmenger's syndrome).
- Arrhythmia—atrial fibrillation (the most common).
- Embolism (pulmonary and systemic) and brain abscess.

Q. What are the findings when there is **reversal of shunt**?

A. As follows:
- Both murmurs are reduced in intensity
- P_2 is loud
- Systolic ejection sound is accentuated
- Other features of pulmonary hypertension are found.

Q. What is **Lutembacher's** syndrome?

A. ASD with an acquired rheumatic mitral stenosis.

Q. How to **treat** ASD?

A. As follows:

- Small ASD—Surgery is not needed, only follow-up should be done (the patient usually lives a normal life).
- Moderate to large—Surgical closure should be done, if pulmonary flow to systemic flow is 2:1 or more.
- Angiographic closure is possible with transcatheter clamshell device.
- If Eisenmenger's syndrome develops—surgical closer is contraindicated (For other treatment, see in Eisenmenger's syndrome).

PATENT DUCTUS ARTERIOSUS (PDA)

CHIEF COMPLAINTS

- Breathlessness for … months
- Palpitation for ... months
- Weakness and loss of appetite for ... months.

HISTORY

History of present illness: The patient was quite well ... months back. Since then, he has been suffering from occasional breathlessness, more during moderate to severe exertion and relieved by taking rest. There is no history of PND or orthopnea. There is no seasonal variation and it is not related to intake of any food or exposure to dust, fume, pollen, etc. The patient also complains of occasional palpitation, usually with moderate to severe activity or during anxiety. He also experiences weakness and loss of appetite. His bowel and bladder habits are normal. He does not complain of cough, hemoptysis, chest pain or fever.

History of past illness

Family history

Personal history

Socioeconomic history

Drug history: Mention according to the statement of the patient.

GENERAL EXAMINATION

- Appearance: Normal
- Anemia: Mild
- No jaundice, edema, clubbing, koilonychia, leukonychia
- No lymphadenopathy or thyromegaly
- Pulse: 88/min
- BP: 120/60 mm Hg
- Temperature: 98.8ºF.

SYSTEMIC EXAMINATION

Cardiovascular System

- Pulse: 88/minute, high volume (bounding), regular in rhythm, no radio-femoral or radio-radial delay
- BP: 120/60 mm Hg
- JVP: Not raised.

Precordium

Inspection:

- Visible cardiac impulse in apical area and another impulse in pulmonary area.

Palpation:

- Apex beat—in left ... intercostal space, ... cm from midline, thrusting or heaving in nature
- Systolic thrill—present in pulmonary area (may be diastolic also)
- Pulmonary arterial pulsation may be felt.

Auscultation:

- First and second heart sounds—normal in all the areas (may be reverse splitting of 2nd heart sound, if large shunt).
- There is a continuous murmur in left 2nd and 3rd intercostal space, more prominent in systole (murmur is prominent on expiration, may be heard posteriorly), radiates to the neck.
- There may be MDM (due to increased flow).

Examination of other systems reveals normal findings.

SALIENT FEATURES

The patient, ..., 16-year-old, student, hailing from ..., presented with occasional breathlessness for … months which is more during moderate to severe exertion and relieved by taking rest. There is no history of PND or orthopnea. There is no seasonal variation and it is not related to intake of any food or exposure to dust, fume, pollen, etc. The patient also complains of occasional palpitation, usually with moderate to severe activity or during anxiety. He also experiences weakness and loss of appetite. His bowel and bladder habits are normal. He does not complain of cough, hemoptysis, chest pain or fever. There is no family history of such illness. He used to take some medicines but could not mention the names.

On examination, general examination—mention as above.

Examination of cardiovascular system—mention as above.

Other systems reveal no abnormalities.

My diagnosis is patent ductus arteriosus.

Q. What are your **differential diagnoses**?

A. The typical continuous murmur is highly suggestive of PDA. However, any cause of continuous murmur should be excluded such as:

- Arteriovenous fistula (coronary, pulmonary or systemic)
- Venous hum
- Rupture of sinus of Valsalva to the right ventricle or atrium.

Q. What is **venous hum?**

A. It is a continuous murmur, due to kinking and partial obstruction of one of the large veins in the neck. It is found in the neck above the clavicle and upper part of chest, more on the right side of sternum. The hum can be obliterated by pressure on the neck or lying down or altering the position of neck (as there is reduction of venous obstruction). It is accentuated by sitting with head extended and turned to the side opposite to that auscultated. Venous hum has no clinical significance, commonly present in children, should not be confused with any pathology.

Q. What **investigations** do you suggest in PDA?

A. As follows:

- ECG: It may be normal. There may be LVH, but RVH occurs in Eisenmenger's syndrome.
- X-ray chest: Cardiomegaly (left ventricle and left atrium are enlarged, large aorta), large pulmonary conus, large hilar arteries, plethoric lung fields.

- 2D echocardiography and color Doppler echocardiography.
- MRI or CMR (cardiac magnetic resonance angiography) may be helpful.
- Cardiac catheterization may be necessary in some cases.

RELATED QUESTIONS AND ANSWERS

Q. What is the **murmur** in PDA?

A. Continuous murmur (machinery murmur like train in a tunnel), with late systolic accentuation.

Q. What are the **causes** of continuous murmur?

A. As follows:
- PDA
- Arteriovenous fistula (coronary, pulmonary or systemic)
- Aortopulmonary fistula (may be congenital or Blalock-Taussig shunt)
- Venous hum
- Rupture of sinus of Valsalva to the right ventricle or atrium.

Q. What are the **causes** of PDA?

A. Common in female, M:F = 1:3. Probable etiological factors are:
- Maternal rubella in the first trimester
- Birth at high altitude with continuous prenatal hypoxia
- Prematurity.

Note

During fetal life, ductus arteriosus connects pulmonary artery at its bifurcation to the descending aorta just below the origin of left subclavian artery and permits blood flow from pulmonary artery to aorta. After birth, within hours or days, it closes spontaneously and remains as ligamentum arteriosum.

In PDA, it allows blood to flow from aorta to pulmonary artery. Up to 50% of left ventricular output may enter into pulmonary artery, because pressure in aorta is higher.

Q. What are the **findings** in reversal of shunt?

A. As follows:
- Cyanosis and clubbing in lower limb, absent in upper limb (called differential cyanosis and differential clubbing).
- Murmur—quiet or absent or systolic only (diastolic disappears).
- Evidence of pulmonary hypertension.

Q. What are the **complications** of PDA?

A. As follows:
- Pulmonary hypertension with reversal of shunt (Eisenmenger's syndrome)
- CCF
- Infective endocarditis
- Arrhythmia (atrial fibrillation)
- Duct may rupture or calcify.

Q. How to **treat** PDA?

A. As follows:
- Majority of PDA are small and can be closed at cardiac catheterization by using implantable occlusive device.

- In large PDA, surgical closure should be done as early as possible.
- Prophylaxis for infective endocarditis.
- In neonate (1 to 3 weeks old), indomethacin (0.2 mg/kg IV) or ibuprofen may be given to constrict and close PDA by inhibiting prostaglandin E synthesis (prior to birth, the duct is kept patent by the effect of circulating prostaglandin). It is not helpful in older children.
- If Eisenmenger's syndrome develops, surgery is contraindicated (see Eisenmenger's syndrome).

Prognosis: If untreated, 1/3rd individuals die from heart failure, pulmonary hypertension or endocarditis by the age of 40 and 2/3rd by the age of 60.

COARCTATION OF AORTA

CHIEF COMPLAINTS

- Frequent headache, dizziness and giddiness for … years
- Cramps in the legs for … years
- Palpitation for … years.

HISTORY

History of present illness: The patient was well and fit ... months back. Since then, he has been suffering from frequent headache, dizziness and giddiness. Headache is diffuse, more marked over the forehead, throbbing in nature, not associated with nausea or vomiting and relieved by taking high dose paracetamol or after sleep. He also complains of cramping in both lower limbs for the same duration during physical activity or walking, which is relieved by taking rest or massaging. The patient also experiences occasional palpitation, even with mild exertion and subsides with rest. There is no history of loss of consciousness, chest pain, cough or any bleeding manifestations.

History of past illness

Family history

Personal history

Socioeconomic history

Drug history: Mention according to the statement of the patient.

GENERAL EXAMINATION

- Appearance: Normal
- Anemia: Mild
- No jaundice, edema, clubbing, koilonychia, leukonychia
- No lymphadenopathy or thyromegaly
- Pulse: 80/min
- BP: 160/90 mm Hg in both arms. In the lower limbs, it could not be recorded. (Usually large sphygmomanometer calf is required to detect pressure in the lower limb)
- Temperature: 98.8ºF.

SYSTEMIC EXAMINATION

Cardiovascular System

- Pulse: 80/minute, normal in rhythm, high volume in upper limb, femoral pulse is very feeble. There is radio-femoral delay, but no radio-radial delay.
- BP: 160/90 mm Hg in both arms. In the lower limbs it could not be recorded.
- JVP: Not raised.
- Carotid pulse: High volume and vigorous.
- There is visible suprasternal, right carotid pulse and supraclavicular pulsation.

Precordium

Inspection:

- Visible cardiac impulse
- Visible dilated tortuous artery around the scapula, anterior axilla and over the left sternal border (collateral vessels are best seen by sitting and bending forward, with arm hanging by the side).

Palpation:

- Apex beat—in left ... intercostal space, heaving in nature
- (There may be thrill over the collateral vessels).

Auscultation:

- Both first and second heart sounds – normal
- Murmur—systolic murmur audible in, ... intercostal space close to the sternum and better heard in 4th intercostal space posteriorly (site of coarctation). May be ejection click, ESM in aortic area and EDM (bicuspid aortic valve or dilatation of aortic valve due to aneurysm, causing AR).

Examination of other systems reveals normal findings.

SALIENT FEATURES

The patient, Mr ..., 26-year-old, student, nonsmoker, nondiabetic presented with frequent headache, dizziness and giddiness for … years. Headache is diffuse, more marked over the forehead, throbbing in nature, not associated with nausea or vomiting and relieved by taking high dose paracetamol or after sleep. He also complains of cramping in both lower limbs for the same duration during physical activity or walking which is relieved by taking rest or massaging. The patient also experiences occasional palpitation, even with mild exertion and subsides with rest. There is no history of loss of consciousness, chest pain, cough or any bleeding manifestations. There is no family history of such illness. He used to take some vitamins only.

On examination, general examination—mention as above.

Examination of cardiovascular system—mention as above.

Other systems reveal no abnormalities.

My diagnosis is hypertension due to coarctation of aorta.

Q. Why is it a case of coarctation of aorta?

A. Because radial pulse is high volume, femoral pulse is feeble and there is radio-femoral delay. Also, the BP is very high in upper limbs and very low in lower limbs.

Q. What investigations do you suggest in coarctation of aorta?

A. As follows:

1. X-ray chest P/A view:
   - Poorly developed aortic knuckle (or elongated aortic knuckle), cardiomegaly, post-stenotic dilatation of aorta.
   - Rib notching, mostly at the middle part posteriorly, due to enlargement of intercostal arteries from 3rd rib downwards (1st and 2nd ribs are not affected, because intercostal arteries here arise from subclavian artery above the constriction).
   - Figure of **3** (constriction at coarctation, prestenotic and poststenotic dilatation).

2. ECG (LVH).
3. Others: CT scan and CMR (cardiac magnetic resonance angiography) are ideal for confirming the diagnosis. Echocardiogram and aortography may also be done.

RELATED QUESTIONS AND ANSWERS

Q. Why murmur in coarctation of aorta?

A. Usually due to increased flow through collateral vessels, also may be due to associated congenital bicuspid aortic valve.

Q. What are the types of coarctation of aorta?

A. 2 types:
- Post-ductal (adult type): Commonly below the origin of left subclavian artery, where ductus arteriosus joins the aorta.
- Pre-ductal (infantile type, 2%): Above the origin of left subclavian artery. So, left radial pulse is weak and rib notching on right side. Without other communication, patients do not survive. It may be associated with PDA.

Q. What type of hypertension develops and why?

A. Usually systolic hypertension, diastolic may be normal. Causes of hypertension are:
- Mechanical
- Renin angiotensin mechanism (due to coarctation, there is less blood flow to kidney)
- Resetting of baroreceptors.

Note

Collateral vessels are formed involving periscapular, internal mammary and intercostal arteries.

Q. What is reverse coarctation?

A. When pulse is absent in upper limb, but present in lower limb, it is called reverse coarctation. It occurs in Takayasu's disease.

Q. What are the complications of coarctation of aorta?

A. As follows :
- Hypertension and its complication (LVF, CVA)
- Infective endocarditis
- Rupture at the coarctation site
- Dissecting aneurysm
- Aneurysm of aorta
- Subarachnoid hemorrhage (rupture of Berry aneurysm of circle of Willis).

Q. What are the causes of death in coarctation of aorta?

A. As follows:
- Acute left ventricular failure
- Dissecting aneurysm or aorta
- Subarachnoid hemorrhage (due to rupture of aneurysm of circle of Willis)
- Cerebral hemorrhage.

Associations in coarctation of aorta:
- Bicuspid aortic valve (in 50% cases)

- VSD
- PDA
- Aneurysm of circle of Willis (5 to 10% cases)
- In female, Turner's syndrome
- Occasionally, Marfan's syndrome.

Note Remember the following points:

- Coarctation of aorta is twice more common in male than female
- It is 7% of all congenital heart diseases
- Even if there is hypertension, renal involvement is unusual and the fundal changes are also unusual.

Q. What are the causes of coarctation?

A. As follows:

- Congenital (the most common).
- Rarely, may be acquired in trauma, Takayasu's disease.

Q. What are the presentations of coarctation of aorta?

A. As follows:

- May be asymptomatic
- Symptoms such as headache, nose bleeding, claudication of lower limbs and cold legs (due to poor blood flow in lower limbs).

Q. What are the sites of collaterals?

A. Severe narrowing of the aorta encourages the formation of collateral arterial circulation involving the pericapsular, internal mammary and intercostals arteries, may result in localized bruit.

Q. What are the causes of unilateral rib notching?

A. As follows:

- Coarctation of aorta (before the origin of left subclavian artery)
- Blalock-Taussig shunt (iatrogenic, done in Fallot's tetralogy)
- Subclavian artery obstruction
- Neurofibromatosis
- Congenital.

Q. What are the causes of bilateral rib notching?

A. Usual causes are:

- Coarctation of aorta (after the origin of left subclavian artery)
- Neurofibromatosis
- Congenital.

Q. What are the causes of rib notching?

A. As follows:

1. Arterial cause:
   - Coarctation of aorta
   - Subclavian artery obstruction.
2. Venous causes:
   - SVC obstruction (rare)
   - IVC obstruction (rare).

3. Neurological cause:
   - Neurofibromatosis
   - Enlarged nerve (as in amyloidosis, congenital hypertrophic polyneuropathy).
4. Others:
   - Congenital
   - Blalock-Taussig shunt (iatrogenic).

Q. What is the **treatment** of coarctation of aorta?

A. As follows:

- Coarctation of aorta should be treated surgically as early as possible, preferably before 5 years of age. Surgical resection and end-to-end anastomosis is usually done. If coarctation is extensive, then prosthetic vascular graft may be done (if surgery is done during adolescence or adulthood, hypertension may persist in up to 70% cases, because of irreversible changes in arterioles or renal damage. If done in early childhood, hypertension usually resolves completely.)
- Balloon angioplasty may be helpful. It is particularly effective after restenosis.

Prognosis after surgery:

- If surgical correction is done in childhood, there is 25-year survival in 83%. If surgery is delayed until adulthood, 25-year survival rate drops to 75%. Without surgery, only 25% live up to 50 years of age, while cardiac failure occurs in 2/3rd of surviving patients over 40.
- In few cases, there is restenosis as the child grows. This can be treated by balloon angioplasty.
- If operation is delayed, patient may have persistent hypertension, because of irreversible changes in the arterioles.
- May develop paradoxical hypertension, due to baroreceptor induced increased sympathetic activity (detected by increased serum and urinary catecholamines).
- Coexistent bicuspid aortic valve, which occurs in over 50% of cases, may lead to progressive aortic stenosis or regurgitation, and also requires long-term follow-up.

HYPERTROPHIC CARDIOMYOPATHY

CHIEF COMPLAINTS

- Shortness of breath on exertion for … months
- Palpitation for … months
- Chest pain for … months.

HISTORY

History of present illness: The patient was quite well … months back. Since then, he has been suffering from shortness of breath, palpitation and chest pain on moderate to severe exertion and relieved by rest. The pain is central, compressive in nature but there is no radiation. There is no history of dizziness, loss of consciousness, vertigo, cough, paroxysmal nocturnal dyspnea, orthopnea. His bowel and bladder habits are normal.

History of past illness: There is no history of rheumatic fever or other illnesses.

Family history: One of his brother suddenly died at the age of 30. All other members are in good health.

Personal history

Socioeconomic history

Drug history

Psychiatric history: Mention according to the patient's history.

GENERAL EXAMINATION

As in other valvular diseases, mention according to your findings.

SYSTEMIC EXAMINATION

Cardiovascular System

- Pulse: 88/min, normal volume, normal in rhythm, no radiofemoral or radioradial delay
- Carotid pulse: Jerky
- JVP: Normal
- BP: 95/80 mm Hg (low systolic, normal diastolic and narrow pulse pressure).

Precordium

Inspection:

- No abnormality.

Palpation:

- Apex beat—in the left … intercostal space ... cm from midline, heaving in nature (may be double apical impulse).
- A systolic thrill may be palpable at apex from severe mitral regurgitation or at the lower left sternal border from outflow tract obstruction.

Auscultation:

- First and second heart sounds—normal in all the areas.
- Fourth heart sound may be present (due to atrial contraction).
- There is a harsh ejection systolic murmur at the left lower sternal border (increasing during standing and Valsalva maneuver and decreases during squatting or sustained hand grip). There may be pansystolic murmur at the apex due to mitral regurgitation.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, a 28-year-old cultivator, smoker, nondiabetic, non-hypertensive, presented with shortness of breath, palpitation and chest pain on moderate to severe exertion and relieved by rest for the last … months. The pain is central, compressive in nature but there is no radiation. There is no history of dizziness, loss of consciousness, vertigo, cough, paroxysmal nocturnal dyspnea, orthopnea. His bowel and bladder habits are normal. There is no history of rheumatic fever or other illnesses. One of his brothers suddenly died at the age of 30 without any history of previous illness. All other members are in good health.

On examination, general examination—nothing significant.

Examination of cardiovascular system—mention as above.

Other systems revealed no abnormalities.

With these findings, I have some **differential diagnoses:**

- Mitral regurgitation
- Aortic stenosis
- Hypertrophic cardiomyopathy.

Q. Why not pulmonary stenosis?

A. In pulmonary stenosis, findings are:

- Systolic thrill in pulmonary area.
- Left parasternal lift and epigastric pulsation may be present (due to RVH).
- P_2 is soft, A_2 is normal (wide splitting of the second heart sound may be present).
- Ejection systolic murmur in pulmonary area, which radiates to the left side of neck (murmur is more on inspiration).
- Apex is normal (not heaving as in AS).

Q. Why not AS?

A. In AS, the findings are:

- Pulse is low volume and slow rising.
- BP shows low systolic, normal diastolic and narrow pulse pressure.
- Systolic thrill in aortic area.
- Second heart sound shows soft A_2 in all the areas, P_2 is normal, may be reversed splitting of 2nd heart sound.
- There is a harsh ejection systolic murmur in aortic area which radiates towards the neck.

Q. What investigations should be done?

A. As follows:

- X-ray chest (may be normal)
- ECG (may be LVH, infarct, deep T-bizarre pattern)

- Echocardiogram (diagnostic)
- Cardiac MR
- Genetic analysis.

RELATED QUESTIONS AND ANSWERS

Q. What is **cardiomyopathy?** What are the **types**?

A. Cardiomyopathies are a group of disease that primarily affect the heart muscle and not due to the result of congenital, acquired valvular, hypertension, coronary arterial or pericardial abnormalities.

It is of 3 types:
- Dilated cardiomyopathy (ischemic)
- Hypertrophic cardiomyopathy
- Restrictive cardiomyopathy.

Q. What is **hypertrophic cardiomyopathy** (HCM)?

A. Hypertrophic cardiomyopathy (HCM) is a disease of the heart muscle characterized by hypertrophy of cardiac muscle with misalignment of the cardiac fibers. Hypertrophy may be generalized or localized to the interventricular septum (asymmetrical septal hypertrophy) or other regions (apical hypertrophic cardiomyopathy).

Note Remember the following points:
- It is a common type of cardiomyopathy. Prevalence is 1:500 to 1:1000, inherited as autosomal dominant.
- About half of the patients have a positive family history. First degree relatives should be screened.
- Previously it was called hypertrophic obstructive cardiomyopathy (HOCM), but left ventricular outflow obstruction is found only in 1/3rd patients.

Q. What are the **types** of HCM?

A. As follows:
- Asymmetrical septal hypertrophy (70%)
- Basal septal hypeatrophy (15 to 20%)
- Concentric (8 to 10%)
- Apical or lateral wall (< 2%).

Q. What are the **presentations** of HCM?

A. As follows:
- Angina on effort
- Dyspnea on effort
- Presyncope or syncope on effort
- Sudden death.

Q. How to **treat** HCM?

A. As follows:

1. Specific measures:
   - β-blocker, rate limiting calcium channel blocker (verapamil, diltiazem) and disopyramide for symptomatic relief and prevention of syncope.
   - Amiodarone may be helpful in arrhythmia.

- In some patients with significant left ventricular outflow obstruction and symptoms, dual chamber pacing may be needed.
- Outflow tract obstruction can be improved by partial surgical resection (myectomy) or by iatrogenic infarction of the basal septum (septal ablation), by a catheter delivered alcohol solution.
- ICD should be considered in patient with clinical risk factors for sudden death.
- Cardiac transplantation may be needed in CHF not responding to treatment.
- Infective endocarditis prophylaxis may be needed.

2. Advice:
   - Vigorous exercise and dehydration should be avoided.

Q. What are the **risk factors** for sudden death in HCM?

A. As follows:
- A history of previous cardiac arrest or sustained VT
- Recurrent syncope
- An adverse genotype and/or family history of sudden cardiac death (< 50 years old)
- Failure of blood pressure to rise during exercise (no change or hypotension)
- Non-sustained VT on 24 hour Holter monitoring
- Marked increase in left ventricular wall thickness (> 30 mm on echocardiography)
- Delayed gadolinium enhancement on cardiac MRI.

Q. What drugs should be **avoided**?

A. As follows:
- Digoxin
- Vasodilators
- Diuretics
- Nitrates
- Dihydropyridine calcium channel blockers
- Alcohol (may cause vasodilatation).

Q. What is the effect of HCM in **pregnancy**? What **precautions** should be taken?

A. HCM is not a contraindication to pregnancy. The patient usually tolerates pregnancy well if not severely symptomatic prior to conception. There is no evidence that pregnancy increases the risk of sudden cardiac death (SCD). Following precautions should be taken:
- Prenatal counseling regarding risk of disease in offspring
- The patient should have regular follow-up in well-equipped center with expertise in high-risk pregnancies and cardiac disease
- β-blockers or calcium blockers should be continued.

CHAPTER 4

Gastroenterology

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CHRONIC DUODENAL ULCER

CHIEF COMPLAINTS

- Pain in the epigastric region for … months
- Heart burn, nausea and belching for … months.

HISTORY

History of present illness: The patient states that he was quite well … months back. Since then, he has been suffering from frequent pain in the epigastric region. The pain is burning or dull aching in nature, more marked in empty stomach, like hunger pain. It is relieved by taking food or antacid. Sometimes, the pain appears at the late hours of night, awakening the patient from sleep, relieved by taking food or antacid. The patient also complains of occasional nausea and belching for … months. There is no history of vomiting, hematemesis, melena, anorexia, weight loss or weakness. His bowel and bladder habits are normal.

History of past illness: Nothing significant.

Family history: His parents are alive and in good health. His wife and two children are good health. There is no history of similar illness in his family.

Personal history: He is a government service holder. He smokes about 20 to 30 sticks of cigarettes per day for the last 25 years. There is no history of taking alcohol.

Socioeconomic history: He comes from a middle class family and lives in a brick built house with good sanitation and water supply.

Drug history: He occasionally takes antacids, ranitidine and omeprazole for his illness. However, there is no history of taking any NSAIDs or steroid.

GENERAL EXAMINATION

- The patient appears to be in good health
- No anemia, jaundice, clubbing, cyanosis, koilonychia, leukonychia or oedema
- No lymphadenopathy or thyromegaly
- Pulse: 80/min
- BP: 120/80 mm Hg.

SYSTEMIC EXAMINATION

Gastrointestinal System

Lips, gums, teeth, tongue and oral cavity—normal.

Abdomen:

Inspection: Normal

Palpation:

- Tenderness in epigastric region, no palpable mass
- Liver: Not palpable
- Spleen: Not palpable

- Kidneys: Not ballotable
- No lump or mass.
- Genetalia: Normal.

Percussion:

- Percussion note is tympanitic
- No shifting dullness.

Auscultation:

- Bowel sounds—normal.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, a 42-year-old, serviceman, normotensive, nondiabetic, smoker, used to take 20 to 30 sticks per day, hailing from …, presented with frequent pain in the epigastric region for ... months. The pain is burning or dull aching in nature, more marked in empty stomach, like hunger pain. It is relieved by taking food or antacid. Sometimes, the pain appears at the late hours of night, awakening the patient from sleep, relieved by taking food or antacid. The patient also complains of occasional nausea and belching for … months. There is no history of vomiting, hematemesis, melena, anorexia, weight loss or weakness. His bowel and bladder habits are normal. He occasionally takes antacids, ranitidine and omeprazole for his illness. However, there is no history of taking NSAID or steroid. There is no similar illness in his family.

On examination—general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is chronic duodenal ulcer.

Q. What are your **differential diagnoses**?

A. As follows:

- Chronic cholecystitis
- Chronic pancreatitis
- Non-ulcer dyspepsia
- Gastroesophageal reflux disease
- Irritable bowel syndrome.

Q. How to **confirm** your diagnosis?

A. Endoscopy of upper GIT.

Q. What **investigations** do you suggest?

A. As follows:

- Endoscopy of the upper GIT.
- If the patient refuses endoscopy or cannot be done due to poor general condition, recent MI or unstable angina—barium meal X-ray of stomach and duodenum should be done.
- USG of the whole abdomen to exclude other causes.
- Screening for *Helicobacter pylori* (see below).
- To exclude other causes—stool microscopy for ova, trophozoites, occult blood test.

RELATED QUESTIONS AND ANSWERS

Q. What are the **sites** of peptic ulcer disease?

A. As follows:

- First part of duodenum

- Around lesser curvature of stomach
- Lower end f oesophagus
- In gastrojejunostomy stoma
- Rarely, in Meckel's diverticulum.

Q. What is the **etiology or risk factors** for PUD?

A. As follows:

- *H. pylori* infection
- Drugs—aspirin or other NSAIDs, steroid, KCl, bisphosphonate
- Smoking
- Others—acid hypersecretory disorder (e.g. Zollinger Elison syndrome), hyperparathyroidism, Crohn's disease, sarcoidosis, myeloproliferative disorder.

Q. What is ***Helicobacter pylori***?

A. *H. pylori* is a spiral shaped Gram negative multiple, flagellete bacterium. It is slowly growing and produces urease. It colonizes in the mucosal layer of the gastric antrum, also found in duodenum only in areas of gastric metaplasia. Its prevalence is high in developing countries (80 to 90%) and low in developed countries (20 to 50%).

Mode of transmission: It spreads from person to person by feco-oral or oro-oral, either by kissing or ingestion of contaminated vomit. Infection is acquired in childhood, persist for life unless treated. Majority of the infected case remain healthy and asymptomatic, only few develop clinical disease, especially in smokers.

Q. How *H. pylori* causes PUD?

A. It is associated with 90% duodenal ulcers and 70% gastric ulcers. After infection, *H. pylori* causes the following:

1. Antral gastritis: Usual effect of *H. pylori* infection, commonly asymptomatic but may cause dyspepsia. After antral gastritis, excess gastrin release from antral G cells, which causes hypergastrinemia that increases acid output.
2. Duodenal ulcer (DU): *H. pylori* increases acid secretion due to excess gastrin secretion and also increased parietal cell mass. *H. pylori* induced gastritis causes depletion of somatostatin from D cells, which leads to loss of negative feedback on gastrin secretion, resulting in excess acid secretion. In addition, duodenal bicarbonate secretion is decreased by *H. pylori* inflammation. There is also gastric metaplasia in which *H. pylori* colonizes, causing local release of cytokines that cause further damage.
3. Gastric ulcer (GU): It is associated with gastritis affecting the body and antrum of the stomach. This leads to gastric atrophy, parietal cell loss and reduced acid production (hypochlorhydria). Reduction of gastric mucosal resistance due to cytokine production by the infection or due to alteration in gastric mucosa causes gastric ulcer. However, most of the gastric ulcers are probably due to combination of *H. pylori* infection, NSAIDs and smoking.

Q. How to **diagnose** *H. pylori* infection?

A. As follows:

1. Non invasive tests:
   - Serology—anti *H. pylori* antibody (IgG), 90% sensitive, 83% specific.
   - ^{13}C urea breath test—measurement of $^{13}CO_2$ in the breath after ingestion of ^{13}C urea it is 97% sensitive and 96% specific. False negative result may occur if the patient is taking PPI. This test can be done by using a rapid release tablet (positive in 15 minutes).

- Fecal antigen test—97.6% sensitive, 96% specific. This test is useful in the diagnosis and for monitoring the efficacy of eradication. The patient should stop taking PPI for one week before the test, but can continue H_2 blocker.

2. Invasive tests (antral biopsy by endoscopy) –
   - Rapid urease tests, e.g. CLO, Pyloritek (its specificity is 95% and sensitivity is 85%).
   - Histology (modified Giemsa stain of gastric biopsy specimen)—*H. pylori* can be detected from the gastric mucosa.
   - Microbiological culture (biopsy material in a special media)—it is slow, less sensitive.

Q. What are the **indications** of *H. pylori* eradication?

A. As follows:

- All patients with proven gastric or duodenal ulcer
- *H. pylori* positive dyspepsia
- MALToma
- Atrophic gastritis
- After gastric cancer resection
- First degree relatives of patients with gastric cancer.
- *H. pylori* infection should be sought for and treatment in unexplained iron deficiency anemia, ITP.

Note Remember the following:

In asymptomatic case with *H. pylori* infection, there is controversy. Treatment may be considered with the hope that symptoms will be reduced, and also, to prevent gastric cancer.

Q. How to **treat *H. pylori*** infection?

A. As follows:

1. First-line therapy: The following combination is given for **7 days**.
   - Omeprazole 20 mg 12 hourly PLUS
   - Clarithromycin 500 mg 12 hourly PLUS
   - Amoxicillin 1 g 12 hourly or Metronidazole 400 mg 12 hourly.
2. Second-line therapy: Given if there is failure of first line therapy. The following combination is given for **14 days**—
   - PPI 20 to 40 mg 12 hourly PLUS
   - Bismuth citrate 120 mg 6 hourly PLUS
   - Metronidazole 400 mg 8 hourly PLUS
   - Tetracycline 500 mg 6 hourly.

Note Remember the following points:

- None of the drugs is effective alone. So, 2 powerful antibiotics and powerful acid suppressive drugs are given.
- Success rate is 90%.
- Reinfection is uncommon in developed countries (1%), but it is more in developing countries.
- Sequential therapy is used in areas where the resistance is high.

Q. What are **complications** of chronic duodenal ulcer?

A. As follows:

- Acute—bleeding (leading to hematemesis and melena), perforation
- Chronic—gastric outlet obstruction (pyloric stenosis), hourglass contracture, tea-pot diformity. (Carcinoma stomach occur in gastric ulcer, never in duodenal ulcer).

Q. How will you **manage** a case of chronic duodenal ulcer?

A. As follows:

Aims of management:

- To relieve symptoms
- To induce healing
- To prevent recurrence
- To prevent future complication.

Treatment:

1. *H. pylori* eradication (see above).
2. General measures:
   - Avoid smoking, aspirin and NSAIDs (moderate alcohol is not harmful).
   - No special dietary advice.
3. Other treatments like antacid, H_2 antagonist, PPIs, chelates, complex salts (sucralfate), prostaglandin analogs may be given for short-term therapy.
4. Maintenance treatment may be needed in some cases.
5. Surgical treatment: Less needed nowadays. Indications are:
   - Emergency:
     - Perforation
     - Hemorrhage
   - Elective:
     - Complications, such as pyloric stenosis
     - Recurrent ulcer following gastric surgery.

Gastrojejunostomy with vagotomy is usually done. Sometimes partial gastrectomy may be done.

Q. How to **manage peptic ulcer bleeding?**

A. The patient should be assessed and managed simultaneously in the following way:

1. IV access should be established. Resuscitation is done by IV normal saline (crystalloid) or colloid solution.
2. Initial clinical assessment:
   - To check circulatory status—see pulse and BP, urine output, other features of shock like cold clammy extremities. CVP should be monitored in patient with severe bleeding, particularly if the patient has cardiac disease.
   - Other systems—cardiorespiratory, cerebrovascular or renal diseases should be assessed.
   - Evidence of liver disease should be sought.
3. Blood tests:
   - Blood grouping and cross matching
   - Full blood count
   - Urea and electrolytes
   - Liver function tests
   - Prothrombin time.
4. Blood transfusion should be given when the hemoglobin is less than 10 g/dL or the patient is in shock. CVP is monitored and fluid replacement should be adjusted accordingly.
5. Oxygen should be given to all patients in shock (pallor, cold nose, systolic BP < 100 mm Hg, pulse > 100/min).
6. Intravenous PPI therapy (omeprazole 80 mg followed by infusion 8 mg/h for 72 hours). Followed by oral therapy according to improvement. H_2 receptor antagonists are of no value.

7. Endoscopy of upper GIT should be performed after resuscitation. When applicable, patient may be treated with heater probe, injection of dilute adrenaline or by metallic clips to stop bleeding.
8. Pulse, BP and urine output should be monitored hourly.
9. Surgical management—urgent surgery is indicated when:
   - Endoscopic management fails to stop active bleeding
   - Rebleeding occurs on one occasion in an elderly or frail patient, or twice in younger fit patient.

Remember the following:

- If the patient is suffering from chronic peptic ulcer, eradication therapy for *H. pylori* should be started as early as possible.
- PPI should be continued for 4 weeks to ensure healing.

Q. What are the **predictors for adverse prognosis** in upper GIT bleeding?

A. The following factors affect the risk of rebleeding and death:

- Age more than 60 years
- Presence of other diseases like cardiac failure, IHD, renal disease like CRF, and malignancy
- Clinical signs of chronic liver disease
- Presentation of patient with shock (pallor, cold extremities, systolic BP < 100 mm Hg, pulse > 100/min)
- Ulcer with active bleeding or stigmata of recent bleeding at endoscopy (i.e. a spurting artery, active oozing, fresh or organized blood clot or black spots).

Note Remember the following:

- Scoring systems may be used to assess the risk of rebleeding or death. Rockall score, which is based on clinical and endoscopic findings (as above). Another system called Blatchfort score uses the level of plasma urea, hemoglobin and clinical markers but not endoscopic finding.
- Rebleeding (fresh hematemesis or melena associated with shock or a fall of Hb > 2 g/dL over 24 hours) is associated with a 10 fold rise in mortality.
- Varices and cancer have the worst prognosis.

Q. What are the **complications of surgical management** of PUD (gastric resection or vagotomy)?

A. As follows:

1. Recurrent ulcer (check for *H. pylori* and also rule out Zollinger-Ellison syndrome).
2. Dumping syndrome: This occurs following gastrectomy or gastrojejunostomy.
   - Early dumping syndrome: It occurs 15 to 30 minutes after a meal, especially after taking sweet food. Rapid gastric emptying of food into the jejunum causes rapid fluid shift from plasma into the lumen, resulting in reduction of blood volume. The patient complains of nausea, abdominal distension associated with flushing, palpitation, faintness, sweating, tachycardia and hypotension. This is usually mild and patients adapt themselves. Reassurance is sufficient.
   - The late dumping syndrome: It occurs 2 to 3 hours after meal which is due to hypoglycemia. The patient complains of sweating, light-headedness, palpitations and occasional syncope. In such case, the patient should avoid taking large meals with high carbohydrate content. Instead, they should take small amounts of food at frequent intervals. Anticholinergic agents or subcutaneous octreotide may be given.
3. Bile reflux gastritis.

4. Diarrhea, mostly after vagotomy.
5. Nutritional:
   - Iron deficiency anemia, due to poor absorption
   - Vitamin B_{12} deficiency anemia, due to lack of intrinsic factor
   - Folic acid deficiency, due to poor intake and absorption of food
   - Osteomalacia and osteoporosis, due to vitamin D and calcium deficiency respectively
   - Weight loss, due to less intake of food or malabsorption.
6. Carcinoma stomach after partial gastrectomy.

Q. What is **non-ulcer dyspepsia?**

A. It is defined as "chronic dyspepsia characterized by pain or upper abdominal discomfort without any organic cause". The cause is unknown, but probably due to spectrum of mucosal motility and psychiatric disorder. The patient is usually young (< 40 years), women are twice more affected.

Symptoms are pain or upper abdominal discomfort, early satiety, fullness, bloating and nausea after a meal. Symptoms are more in the morning. There is no weight loss. Features like IBS may be present. Sometimes, these two conditions may exist together. The patient may look anxious. Symptoms may be disproportionate to clinical well being. Abdomen may be inappropriately tender on palpation.

Diagnosis is often apparent from history. No investigation is needed if the patient is less than 50 years. For older patients or those with alarming symptoms, endoscopy should be done to exclude other disease. In young female, pregnancy should be excluded. Other investigations include USG of whole abdomen (to exclude hepatobiliary or pancreatic disease), liver function test, CBC, OBT, colonoscopy, CT abdomen when appropriate.

Treatment:

- In majority of cases, explanation, reassurance and lifestyle change
- Restriction of fat, coffee, alcohol
- Cigarette smoking must be stopped
- Drug treatment—antacids, prokinetic drugs (metoclopramide, domperidone) if nausea, vomiting or bloating is prominent, H_2 blockers if night pain or heartburn is prominent. PPI may be given as well. Low dose amitriptyline may be helpful.
- *H. pylori* eradication regimen may be given. It is helpful in some case, but the role is controversial.
- Psychotherapy may be given.

Q. What are the **functional disorders** of GIT?

A. It may be in the esophagus, small gut or large gut.

1. Functional esophageal disorder:
   - Heartburn
   - Chest pain
   - Dysphagia
   - Globus.
2. Functional gastroduodenal disorder:
   - Non-ulcer dyspepsia
   - Nausea and vomiting disorder
   - Rumination syndrome (persistent effortless regurgitation of recently swallowed food into the mouth with subsequent remastication and reswallowing)
   - Belching disorder.

3. Functional bowel disorder:
   - Irritable bowel syndrome
   - Functional bloating
   - Functional constipation
   - Functional diarrhea
   - Unspecified functional bowel disorder.
4. Functional abdominal pain syndrome.
5. Functional gall bladder and sphincter of Oddi disorder.

CHRONIC DUODENAL ULCER WITH PYLORIC STENOSIS

CHIEF COMPLAINTS

- Nausea, abdominal discomfort and vomiting for … months
- Weight loss for … months
- Constipation for … months.

HISTORY

History of present illness: According to the patient's statement, he has been suffering form chronic duodenal ulcer for … years. But for the last … months, his abdominal pain has subsided and he has been suffering from nausea, abdominal discomfort after taking food and repeated vomiting. Vomiting is painless, projectile, large in volume, contains previous day's food, but there is no blood or bile. The patient admits occasional self-induced vomiting, which relieves his abdominal discomfort. He also complains of weakness, constipation and substantial loss of weight for the last … months. There is no history of hematemesis or melena.

History of past illness: He was suffering from peptic ulcer disease for 15 years.

Family history: There is no such illness in his family.

Personal history: He is a farmer, used to take food irregularly. He smokes 20 sticks a day for the last 10 years but non alcoholic.

Socioeconomic history: He is from lower socioeconomic condition and lives in a remote rural area.

Drug history: He used to take antacid, omeprazole and ranitidine frequently for PUD.

GENERAL EXAMINATION

- Ill looking, emaciated and dehydrated
- Moderately anemic
- No jaundice, cynosis, clubbing, koilonychia, leukonychia or edema
- Lymphadenopathy or thyromegaly absent
- Pulse: 100/min
- BP: 100/70 mm Hg
- Temperature: 98ºF
- Respiratory rate: 16/min.

SYSTEMIC EXAMINATION

Gastrointestinal System

Lips, gums, teeth, tongue and oral cavity—mention according to the finding.

Abdomen:

Inspection:

- Abdomen is distended, mostly in upper part
- Visible peristalsis—present, from left to right.

Palpation:
- No rigidity or tenderness
- Liver—not palpable
- Spleen—not palpable
- Kidneys—not ballotable
- Succussion splash—present

Percussion: No abnormality detected (may be tympanitic).
Auscultation: Bowel sound is increased.

Examination of the other systems reveals no abnormalities.

SALIENT FEATURES

Mr … 48-year-old, farmer, normotensive, nondiabetic, smoker, hailing from …, has been suffering form chronic duodenal ulcer for … years. But for the last … months, his abdominal pain has subsided and he has been suffering from nausea, abdominal discomfort after taking food and repeated vomiting. Vomiting is painless, projectile, large in volume, contains previous day's food, but there is no blood or bile. The patient admits occasional self-induced vomiting, which relieves his abdominal discomfort. He also complains of weakness constipation and substantial loss of weight for the last … months. There is no history of hematemesis or melena. He was suffering from peptic ulcer disease for 15 years. There is no such illness in his family. He used to take food irregularly. He smokes 20 sticks a day for the last 10 years but non alcoholic. He is from lower socioeconomic condition and lives in a remote rural area. He used to take antacid, omeprazole and ranitidine frequently for PUD.

On examination—general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is chronic duodenal ulcer with gastric outlet obstruction (pyloric stenosis).

Q. What are the **causes** of GOO?

A. As follows:
- Chronic duodenal ulcer
- Carcinoma of pylorus
- Adult hypertrophic pyloric stenosis (rare)
- Others—Crohn's disease, compression by pancreatic carcinoma.

Q. What are your **differential diagnoses**?

A. As follows:
- Gastric outlet obstruction due to carcinoma of stomach (or rarely, gastric lymphoma).
- Gastric outlet obstruction due to adult hypertrophic pyloric stenosis.

Q. **Why not** this is a case of carcinoma of the stomach?

A. Because there is long history of duodenal ulcer, and now at present there is loss of pain and also periodicity. Also in carcinoma of stomach, there is marked loss of weight and survival is also short.

Q. How to **confirm** your diagnosis?

A. Endoscopy of the upper GIT, barium meal X-ray of the stomach and duodenum may be done.

Q. What **investigations** do you suggest?

A. As follows:
- CBC with ESR

- Serum electrolytes
- Blood urea, serum creatinine
- Endoscopy of the upper GIT with biopsy (if needed)
- Barium meal X-ray of the stomach and duodenum
- USG of the whole abdomen to exclude other causes.

RELATED QUESTIONS AND ANSWERS

Q. What are the **features of gastric outlet obstruction** (or pyloric stenosis)?

A. As follows:
- History of peptic ulcer
- Loss of pain and periodicity
- Anorexia, nausea and vomiting (profuse and projectile, occasionally self induced). Vomitus contains previous day's food. Patient feels better after vomiting
- Food habit: The patient eats breakfast, a little lunch and little or nothing at dinner
- Abdominal distension, weight loss and constipation
- Succussion splash present 4 hours or more after the last meal or drink
- Visible gastric peristalsis.

Q. What are the **electrolyte abnormalities** in pyloric stenosis?

A. As follows:
- Sodium and chloride—low
- Potassium—low
- Bicarbonate—high (metabolic alkalosis)
- Urea—high.

Q. Why is **potassium low**?

A. Due to:
- Repeated vomiting (less potassium is lost).
- Metabolic alkalosis due to vomiting, which causes potassium to enter into the cells.
- Secondary aldosteronism which causes renal K^+ excretion.
- Hyponatremia and metabolic alkalosis results in renal reabsorption of sodium and hydrogen in exchange of excretion of potassium (loss of potassium by kidney is much more than by vomiting).

Note

When serum potassium level is very low, the kidney starts to excrete hydrogen in exchange of sodium leading to aciduria despite metabolic alkalosis. This is called paradoxical aciduria.

Q. How will you **manage** the case?

A. As follows:
- Resuscitation of the patient. Correction of dehydration and electrolyte imbalance (normal saline 3 to 4 L and potassium).
- Nasogastric aspiration may be given.
- Surgery—partial gastrectomy or gastrojejunostomy with vagotomy followed by PPI to prevent stomal ulceration.
- Endoscopic dilatation may be done.

CARCINOMA OF THE STOMACH

CHIEF COMPLAINTS

- Upper abdominal pain, loss of appetite, discomfort, nausea and vomiting for … months
- Weakness and weight loss for … months.

HISTORY

History of present illness: According to the statement of the patient, he was alright … months back. Since then, he has been suffering from upper abdominal pain, loss of appetite, abdominal discomfort, nausea and vomiting. The pain is dull aching in nature, constant, aggravated by taking food and does not radiate to any site. It occasionally reduces after taking antacid. He also complains of occasional vomiting, which occurs after taking food, the vomitus contains the food materials but no blood or bile. There is no history of induced or projectile vomiting. The patient also complains of weakness, marked loss of appetite and significant weight loss for the last … months. There is no history of melena, cough or evening rise of temperature. His bowel and bladder habits are normal.

History of past illness

Family history

Personal history

Socioeconomic history

Drug history: Mention according to the patient's statement.

GENERAL EXAMINATION

- Ill looking and grossly emaciated
- Moderately anemic
- No jaundice, cyanosis, clubbing, koilonychia, leukonychia or edema
- No lymphadenopathy or no thyromegaly
- Pulse: 120/min
- BP: 90/70 mm Hg
- Temprature: 97ºF
- Respiration: 20/min.

SYSTEMIC EXAMINATION

Gastrointestinal System

Lips, gums, teeth, tongue and oral cavity—mention according to the finding.

Abdomen:

Inspection: No abnormality detected (may be visible mass in epigastrium or distension of upper abdomen).

Palpation:

- There is an ill-defined mass in the epigastric region, 2 × 3 cm, margin irregular, nontender, firm in consistency, surface slightly irregular, mobile from side to side.

- Liver—not palpable.
- Spleen—not palpable.
- Kidneys—not ballotable.
- Succussion splash—absent.

Percussion: No abnormality detected.
Auscultation: No abnormality detected.

Examination of the other systems reveals no abnormalities.

SALIENT FEATURES

Mr … 64-year-old, businessman, non-hypertensive, nondiabetic, smoker, hailing from …, presented with upper abdominal pain, loss of appetite, abdominal discomfort, nausea and vomiting. The pain is dull aching in nature, constant, aggravated by taking food and does not radiate to any site. It occasionally reduces after taking antacid. He also complains of occasional vomiting, which occurs after taking food, the vomitus contains the food materials but no blood or bile. There is no history of induced or projectile vomiting. The patient also complains of weakness, marked loss of appetite and significant weight loss for the last … months. There is no history of melena, cough or evening rise of temperature. His bowel and bladder habits are normal.

There is no history of such illness in his family. He used to smoke about 20 sticks of cigarettes for the last 40 years but not alcohol.

For his symptoms, local doctor prescribed tablet ranitidine and antacid, but his symptoms did not improve.

On examination—general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is gastric outlet obstruction due to carcinoma of the stomach.

Q. What are your **differential diagnoses?**

A. As follows:
- Gastric outlet obstruction due to chronic duodenal ulcer with pyloric stenosis.
- Gastric lymphoma.

Q. **Why not** this is chronic duodenal ulcer?

A. There is no history of long standing duodenal ulcer, and also there is marked anorexia, rapid loss of weight and also there is a mass in the epigastric region.

Q. **What else** have you seen in association of the epigastric mass?

A. Enlargement of left supraclavicular lymph node (Virchow's gland), called Troisier's sign.

Q. How to **confirm** your diagnosis?

A. Endoscopy of upper GIT with biopsy.

Q. What other **investigations** do you suggest in this case?

A. As follows:
- Hb%, TC, DC, ESR.
- USG of whole abdomen (to see the origin of the mass like liver, stomach, transverse colon, pancreas or secondary in the liver from carcinoma of stomach).
- Barium meal (filling defect, irregular ulcer, in infiltrating type—stomach looks like tube).
- Stool for occult blood test.
- To see recurrence—CEA may be done.

RELATED QUESTIONS AND ANSWERS

Q. What are the **presentations** of carcinoma of stomach?

A. As follows:

- Any patient above 40 years of age presenting with "**3 A**" (Anemia, Anorexia, Asthenia).
- Vomiting (if tumor in the pyloric end).
- Pain in the epigastrium.
- Dysphagia (if tumor in the cardiac end).
- Hematemesis and melena.
- Mass in the epigastrium.
- Only unexplained features of anemia.
- Features of metastasis:
  - Hepatomegaly
  - Virchow's gland
  - Hard nodule around umbilicus (Sister Mary Joseph's nodule)
  - Ovarian involvement (Krukenberg's tumor)
  - Pre-rectal pouch—a shelf-like mass (Blumer's shelf).
- Paraneoplastic syndrome (acanthosis nigricans, dermatomyositis, thrombophlebitis migrans).

Q. What are the **types** of carcinoma of stomach?

A. As follows:

1. Macroscopic—4 types:
   - Polypoid
   - Ulcerative
   - Fungating or cauliflower
   - Diffuse infiltrative—linitus plastica (rare).
2. Microscopic:
   - Adenocarcinoma (95%): 2 types :
     - Intestinal (better prognosis)
     - Diffuse (bad prognosis).
   - Others:
     - Squamous cell carcinoma
     - Non-Hodgkin's lymphoma
     - Leiomyosarcoma.

Q. What are the **causes** or predisposing factors for carcinoma of stomach?

A. Causes are unknown. Predisposing factors are:

1. Diet:
   - Preservatives in diet such as nitrates. It is converted to nitrosamines, which is carcinogenic. Nitrate is converted by the nitrite reducing bacteria which colonize in achlorhydric stomach.
   - Excess spicy, salted and pickled food.
   - Diet lacking fresh fruits and vegetables as well as vitamin C and A may be contributing factors.
2. Smoking.
3. Alcohol.
4. Gastric surgery (partial gastrectomy, gastrojejunostomy). Carcinoma is due to intestinal metaplasia and chronic gastritis, probably due to untreated *H. pylori* infection also.
5. Infection with *Helicobacter pylori* that cause chronic gastritis, that eventually leads to atrophic gastritis and intestinal metaplasia, which is premalignant. This organism may be responsible in

60 to 70% case, mostly associated with achlorhydria. Chronic inflammation with generation of reactive oxygen species and depletion of antioxidant ascorbic acid are also important.

6. Others—pernicious anemia, familial adenomatous polyposis, Menetriere's disease, blood group-A, first degree relative.

Q. What are the **sites** of carcinoma stomach?

A. As follows:

- Antrum—50%
- Body of the stomach (greater curvature)—20 to 30%
- Cardiac end of stomach—20%.

In the western population, proximal gastric tumors are becoming more common than those arising in the body or distal stomach.

Q. What is the **benign tumor** of stomach?

A. Leiomyoma.

Q. How to **treat** a case of carcinoma stomach?

A. As follows:

1. Surgery is the only curative treatment. 5 year survival is 90% if surgery is done in early gastric cancer, but only 10% if done in advanced cases.
2. Perioperative chemotherapy—ECF (epirubicin, cisplatin and fluorouracil) has improved 5 year survival in operable gastric and lower esophageal adenocarcinoma.
3. Chemotherapy- not much helpful. **FAM** (combination of 5-Fluorouracil + adriamycin + mitomycin C) may be tried.
4. Palliative:
   - Radiotherapy—very little role.
   - Endoscopic laser ablation of tumor tissue may be done if surgery is not possible.
   - Endoscopic dilatation or insertion of expandable metallic stents may be used for relief of dysphagia or vomiting.

Q. What is **early gastric cancer**?

A. When carcinoma is confined to mucosa or submucosa regardless of lymph node involvement, it is called early gastric cancer. It is associated with 5 years survival of about 90%. Many may survive 5 years even without treatment. It may be cured by endoscopic mucosal resection or endoscopic submucosal dissection.

Q. What is **linitus plastica**?

A. It means diffuse submucosal infiltration of schirrous carcinoma. Stomach becomes a rigid tube. Other causes of linitus plastica include lymphoma, sarcoidosis, secondary syphilis and gastric lymphoma.

Gastric Lymphoma

It is the second most common neoplasm of stomach. Among the GIT lymphoma, 60% occur in the stomach. 95% is low grade non-Hodgkin's B-cell type. Gastric lymphoma may be:

- Primary—arise from mucosa associated lymphoid tissue (MALT).
- Secondary to lymph node involvement in other parts of the body.

Primary gastric lymphoma may be due to *Helicobacter pylori* infection. 85% are low grade and 40% are high grade when associated with *H. pylori* infection. Chronic antigenic stimulation result in monoclonal lymphoproliferation that may cause low grade MALT lymphoma.

Symptoms: Similar to that of gastric cancer. Patients with primary gastric lymphoma have stomach pain, ulcers or other localized symptoms but systemic complaints such as fatigue or fever are rare.

Diagnosis: By endoscopy and biopsy. At endoscopy, the tumour usually appears as a polypoid or ulcerating mass.

Treatment:

- **Primary type:** Treatment with anti-*Helicobacter* therapy may regress the tumor. If no response, other therapy for lymphoma should be given (radiotherapy or chemotherapy).
- **Secondary type:** Usual therapy for lymphoma (chemotherapy, radiotherapy).

Prognosis: Varies according to the type. Features predicting a favorable prognosis are stage I or II disease, small resectable tumor or tumor with low grade histology, and age below 60 years.

CARCINOMA HEAD OF THE PANCREAS

CHIEF COMPLAINTS

- Pain in epigastric region for … months
- Loss of appetite and weight loss for … months
- Yellow discoloration of the skin, eyes and urine for the last … days
- Severe generalized itching for … days.

HISTORY

History of present illness: According to the statement of the patient, she was alright … months back. Since then, she has been suffering from pain in epigastric region, which is deep seated, dull aching in nature, radiates to the back and is aggravated by taking food. Pain is more marked while lying flat, and slightly reduced on bending forward. She also complains of gradual loss of appetite and marked weight loss for … months. The patient also noticed yellow discoloration of skin, eyes and urine for last … days, which is progressively increasing. Jaundice is not preceded by any prodromal symptoms like anorexia, nausea, vomiting, etc. For the last … days, she is also experiencing severe generalized itching and occasional diarrhea. The stool was initially yellowish, but for the last … days, it is clay or muddy, or whitish colored and voluminous. There is no history of vomiting, hematemesis, melena, fever or cough.

History of past illness

Family history

Personal history

Socioeconomic history

Drug history: Mention according to the patient's statement.

GENERAL EXAMINATION

- The patient is extremely ill looking and grossly emaciated, also pigmented
- Severely anemic and also severely icteric
- Scratch mark present on different parts of the body
- No cyanosis, clubbing, koilonychia, leukonychia or edema
- No lymphadenopathy or no thyromegaly
- Pulse: 108/min
- BP: 90/65 mm Hg
- Temperature: 97ºF
- Respiration: 20/min.

SYSTEMIC EXAMINATION

Gastrointestinal System

Lips, gums, teeth, tongue and oral cavity—mention according to the finding.

Abdomen:

Inspection: No abnormality detected.
Palpation:
- There is an ill-defined mass in the epigastric region, 2 × 3 cm in size, margin is irregular, nontender, hard in consistency, surface is irregular, not freely mobile.
- Liver—not palpable.
- Spleen—not palpable.
- Kidneys—not ballotable.
- Succusion splash—absent.

Percussion: No abnormality detected.
Auscultation: No abnormality detected.

Examination of the other systems reveals no abnormalities.

SALIENT FEATURES

Mrs … 65-year-old, housewife, normotensive, nondiabetic, non-smoker, hailing from …, presented with pain in epigastric region for … months, which is deep seated, dull aching in nature, radiates to the back and is aggravated by taking food. Pain is more marked while lying flat, and slightly reduced on bending forward. She also complains of gradual loss of appetite and marked weight loss for … months. The patient also noticed yellow discoloration of skin, eyes and urine for last … days, which is progressively increasing. Jaundice is not preceded by any prodromal symptoms like anorexia, nausea, vomiting, etc. For the last … days, she is also experiencing severe generalized itching and occasional diarrhea. The stool was initially yellowish, but for the last … days, it is clay or muddy, or whitish coloured and voluminous. There is no history of vomiting, hematemesis, melena, fever or cough. She used to take some drugs prescribed by local physicians, the name of which she cannot mention. There is no family history of such illness.

On examination—general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is obstructive jaundice probably due to carcinoma head of the pancreas.

Q. What are your **differential diagnoses?**

A. Obstructive jaundice due to:
- Carcinoma of the ampulla of Vater
- Periampullary carcinoma
- Cholangiocarcinoma
- Stricture of common bile duct or sclerosing cholangitis.

Q. Suggest **one single investigation** in this case.

A. Ultrasonogram of upper abdomen.

Q. What **other investigations** do you suggest?

A. As follows:
- Liver function test (bilirubin, SGPT, alkaline phosphatase, prothrombin time, etc. Alkaline phosphatase is usually very high)
- Barium meal X-ray with C-loop (it will show widening of the C-loop)
- CT scan of abdomen
- MRI scan and endoscopic ultrasound are helpful in some cases

- CT or ultrasound guided FNAC—may be done but not in potentially operable case. It may spread the malignancy to the peritoneum
- Blood glucose
- Tumor markers especially CA 19-9 is highly sensitive (80%) but false positive result may be found
- ERCP (to see obstruction, irregularity or distortion of pancreatic duct. Also, helpful to insert stent in obstructive jaundice)
- MRCP may be done
- Sometimes, laparoscopy and laparoscopic USG (in very small lesion).

RELATED QUESTIONS AND ANSWERS

Q. What are the causes of **epigastric mass**?

A. As follows:
- Carcinoma of stomach
- Carcinoma of the head of the pancreas
- Hepatic mass (hepatoma, secondary, liver abscess, hydatid cyst)
- Carcinoma of transverse colon
- Gall bladder mass—such as carcinoma
- Mucocele or empyema of the gallbladder
- Pseudocyst of pancreas
- Epigastric hernia.

Q. What are the **causes** of carcinoma head of pancreas?

A. Actual causes are unknown. Some factors are responsible:
- Age, above 70 years
- Male, predominant (twice more than female)
- Chronic pancreatitis
- Alcohol
- Smoking
- Environmental factors, such as petroleum product and naphthylamine
- Genetic in 5 to 10% cases. There may be hereditary pancreatitis, multiple endocrine neoplasia (MEN) and hereditary non-polyposis colon cancer (HNPCC).

Q. What are the **types** of carcinoma of pancreas and what are the **sites?**

A. Usually adenocarcinoma (90%), which arises from the epithelium of pancreatic duct. Sites are as follows:
- 60% in head
- 25% in body
- 15% in tail.

Q. What are the **presentation**s of carcinoma of the pancreas?

A. As follows:
- Painless obstructive jaundice, with palpable gallbladder—in case of carcinoma of head of pancreas.
- Carcinoma involving the body and tail – usually presents with pain in the epigastrium, deep seated, dull aching, radiates to the back, more on lying flat, feels better with bending forward (pain is due to involvement of celiac plexus)
- Loss of weight, anorexia, nausea
- Mass in upper abdomen (in 20% cases)

- Others—diabetes mellitus, acute pancreatitis
- Rare features are—thrombophlebitis migrans (arm vein is more involved than leg vein), venous thrombosis, portal hypertension and marantic endocarditis.

Note

Courvoisier's law: In a jaundiced patient with palpable gallbladder, the cause is unlikely to be gallstones, rather it is due to carcinoma head of pancreas and extrinsic pressure in bile duct. (Reverse of the law—Obstructive jaundice without palpable gallbladder is unlikely to be due to carcinoma head of pancreas and extrinsic pressure in common bile duct.)

Q. How to **treat** carcinoma head of pancreas?

A. As follows:

1. In early stage, surgical resection (Whipple's operation is performed. In this operation, pancreas, duodenum, draining lymph node and part of mesentery are removed). About 5-year survival is 20% after surgery. Survival is improved with adjuvant chemotherapy (5-FU).
2. Other treatment (usually palliative):
   - Endoscopic insertion of stent to relieve intractable itching.
   - For pain—analgesic, injection of alcohol in celiac plexus (USG guided or endoscopic USG guided).
   - Chemotherapy—5FU, adriamycin and cisplatin may be tried. Combination of 5FU plus gemcitabine may help to improve the survival in advanced disease.
   - Radiotherapy is not much helpful.

Q. What is the **prognosis?**

A. Prognosis is bad, mean survival is < 6 months. Usual 5 year survival is 2 to 5%. Following Whipples' operation, 5 year survival is 5 to 14% (may be up to 20%). If adjuvant chemotherapy is given with 5-fluorouracil, then 5 year survival becomes 21 to 29%. Prognosis is better if tumor size < 3 cm, no lymph node involvement, negative resection of margin at surgery, ampulary or islet cell tumors.

INFLAMMATORY BOWEL DISEASE

CHIEF COMPLAINTS

- Frequent loose motion with mucus for … months
- Abdominal pain for … months
- Recurrent mouth ulcer for … months
- Weight loss and loss of appetite … months.

HISTORY

History of present illness: According to the statement of the patient, she was alright … months back. Since then, she has been suffering from occasional loose motion, 4 to 6 times daily, often mixed with mucus, but not blood. It is not related to any food or drug. She also complains of sense of incomplete evacuation of bowel and occasional abdominal pain. The pain is mostly around the umbilicus, colicky in nature, mild to moderate in intensity, radiates to the back, persists for minutes to few hours, not related to food intake and sometimes relieved by defecation. For the last ... months, she noticed recurrent painful mouth ulcer. She also complains of loss of appetite and significant weight loss during this period. There is no history of any perianal pain, joint pain, eye-problem, fever, cough, any skin rash, ulceration or nodules or contact with tuberculosis patient.

History of past illness: She suffered from similar illness several times over the last 2 years and was hospitalized once.

Family history

Personal history

Socioeconomic history

Drug history: Mention according to the patient's statement.

GENERAL EXAMINATION

- The patient is emaciated and ill looking
- Moderately anemic
- There are generalized clubbing involving fingers and toes
- No jaundice, cyanosis, koilonychia, leukonychia and edema
- No lymphadenopathy or no thyromegaly
- Pulse: 88/min
- BP: 120/75 mm Hg
- Temperature: 98ºF
- Respiratory rate: 18/min.

SYSTEMIC EXAMINATION

Gastrointestinal System

Lips, gums, teeth—normal. There is one ulcer in the inner part of the right side of the cheek (aphthous ulcer). Lips (may be) swollen.
Tongue—pale.

Abdomen

Inspection: No abnormality detected (there may be visible peristalsis, that moves from above downwards, multiple fistula, scar mark, ileostomy bag, etc.)

Palpation:
- Liver—not palpable.
- Spleen—not palpable.
- Kidneys—not ballotable.
- Succusion splash—absent.

Percussion: No abnormality detected.

Auscultation: No abnormality detected.

Per-rectal examination:
- Inspection—a fistula is noted on the 3o' clock position of the anus.
- Digital Rectal Examination—no abnormality detected.

Examination of the other systems reveals no abnormalities.

SALIENT FEATURES

Mrs …, 46-years-old, housewife, normotensive, nondiabetic, nonsmoker, hailing from …, presented with occasional loose motion, 4 to 6 times daily for … months. It is often mixed with mucus, but not blood. It is not related to any food or drug. She also complains of sense of incomplete evacuation of bowel and occasional abdominal pain. The pain is mostly around the umbilicus, colicky in nature, mild to moderate in intensity, radiates to the back, persists for minutes to few hours, not related to food intake and sometimes relieved by defecation. For the last ... months, she noticed recurrent painful mouth ulcer. She also complains of loss of appetite and significant weight loss during this period. There is no history of any perianal pain, joint pain, eye-problem, fever, cough, any skin rash, ulceration or nodules or contact with tuberculosis patient. She suffered from similar illness several times over the last 2 years and was hospitalized once. She used to take pain killers, ranitidine and omeprazole. One of his maternal uncle suffered from similar illness.

On examination—general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is IBD, more likely to be Crohn's disease.

Q. What are your **differential diagnoses?**

A. As follows:
- Ileocecal tuberculosis
- Lymphoma
- Ulcerative colitis
- IBS
- Chronic pancreatitis.

Q. What are the **sites** of Crohn's disease?

A. Any part of gastrointestinal tract, from mouth to anus, may be involved, but commonly terminal ileum is involved (hence, it was previously called regional ileitis). In order of frequency, ileum and right side of colon, colon alone, terminal ileum alone, ileum and jejunum. Lesion is transmural (all layers are involved). The disease can involve a small area of the gut, or multiple areas with relatively normal bowel in between them, called "skip lesion".

Q. What **investigations** should be done in Crohn's disease?

A. As follows:

- CBC (anemia is usually normocytic, may be megaloblastic due to vitamin B_{12} deficiency)
- ESR and CRP (both high)
- Total protein and A/G ratio (low albumin)
- Liver function tests (may be abnormal)
- Blood for C/S (if septicemia is suspected)
- Stool for R/E and C/S (to exclude infective cause like *Salmonella, Shigella, Campylobacter, E. coli, Clostridium difficile*)
- USG of whole abdomen
- Barium follow through or small bowel enema (detects ileal disease, there may be narrowing of the affected segment, called string sign, which is pathognomonic of Crohn's disease)
- Barium enema
- Colonoscopy (in colonic Crohn's disease) with ileoscopy and biopsy
- Enteroscopy
- Capsule endoscopy (in assessing small bowel disease)
- CT scan or MRI of abdomen.

RELATED QUESTIONS AND ANSWERS

Q. What is **Crohn's disease**? What are the **presentations**?

A. Crohn's disease is a chronic inflammatory disease of unknown etiology involving any part of gastrointestinal tract, commonly the terminal ileum. It is slightly common in female, M:F = 1:1.2, more in young (mean age is 26 years). Common presentations are as follows:

- Frequent diarrhea
- Abdominal pain (colicky)
- Weight loss
- Failure to thrive in children
- Other systemic features are malaise, lethargy, low grade fever, anorexia, nausea, vomiting
- Extra-intestinal manifestations (see below)
- Sometimes, it may present with acute emergency like acute appendicitis. If laparotomy is done, terminal ileum looks edematous and red
- Sometimes, the patient may present with recurrent aphthous ulceration of mouth, mass in right iliac fossa (due to inflamed loops of bowel matted together or abscess), anal fissures or perianal abscess.

Q. What are the **extra-intestinal manifestations** of Crohn's disease?

A. As follows:

- Eyes—conjunctivitis, episcleritis, uveitis or iritis.
- Mouth—aphthous ulcer and thickened lip.
- Skin—erythema nodosum, pyoderma gangrenosum or fistula in abdominal wall.
- Bones and joints—acute peripheral arthritis (occurs in 15 to 20%, related to active disease, treatment of Crohn's disease improves the condition. In severe case, even colectomy improves arthritis). Sometimes, ankylosing spondylitis or sacroiliitis and clubbing may also occur.
- Perianal region—perianal fistula, skin tag and abscess.
- Liver or hepatobiliary—fatty liver, pericholangitis, sclerosing cholangitis (common in ulcerative colitis), autoimmune hepatitis, cirrhosis of liver, granuloma, liver abscess or portal pyemia, gall stone and cholangiocarcinoma.

- Kidney—nephrolithiasis (oxalate stone), hydronephrosis and pyelonephritis.
- Others—amyloidosis and venous thrombosis.

Q. What are the **complications** of Crohn's disease?

A. As follows:
- Intestinal obstruction
- Enteric fistula to bladder or vagina
- Abscess formation
- Perianal disease (fissure, skin tag, fistula, perianal abscess, hemorrhoid)
- Carcinoma (rare, may occur if Crohn's disease involves the colon)
- Toxic dilatation of the colon (more common in ulcerative colitis)
- Malabsorption syndrome.

Q. What are the **causes** of Crohn's disease?

A. Actual causes unknown. Probable factors are:
- Genetic and familial
- Diet—high sugar and fat, but low residue diet
- Smoking
- Probable association with mycobacteria and measles virus (not proved)
- Abnormal immunological response.

Note Remember the following points:
- Appendicectomy is protective of ulcerative colitis, but may increase the risk of Crohn's disease or may result in more aggressive disease.
- Oral contraceptive pill increases the risk of Crohn's disease.

Q. What is the **relation of smoking** in IBD?

A. In smokers, the incidence of Crohn's disease is high. But there is increased risk of ulcerative colitis in nonsmoker or ex-smokers.

Q. How to assess the **activity** of Crohn's disease?

A. Signs of activity are:

1. Clinical:
   - Eye signs—episcleritis, conjunctivitis and iritis
   - Mouth—aphthous ulcer
   - Skin—erythema nodosum and pyoderma gangrenosum
   - Arthralgia of large joints
   - Fatty liver or liver abscess or portal pyemia
   - Mesenteric or portal vein thrombosis
   - Venous thrombosis (in other veins).
2. Morphology—by radiological or endoscopy
3. Laboratory:
   - Low albumin (due to protein losing enteropathy)
   - High ESR
   - High C-reactive protein (CRP).
4. Scanning with white cell labelled with ^{111}Indium or ^{99m}Tc to locate active site.

Q. What are the types of **arthritis** in Crohn's disease?

A. Peripheral arthropathy is common, which may be of two types:

- Type 1, Pauciarticular—usually acute, self limiting, < 10 weeks duration, occur with IBD relapses, usually associated with other extra-intestinal features of IBD. Indicates active disease.
- Type 2, Polyarticular—last longer (months to years), not related to IBD activity, usually associated with uveitis.

Other types are—ankylosing spondylitis, arthralgia, inflammatory back pain. These are not related to IBD disease activity.

Q. How to **treat** Crohn's disease?

A. Induction of remission in active disease and maintenance of remission.

1. Induction of remission:
   a. General measures:
      - Diet, with high protein, low fat and milk free. If needed, enteral or parenteral feeding.
      - For anemia—supplement of iron, B12, folic acid and zinc. Erythropoietin may be given.
      - Symptomatic treatment for diarrhea (loperamide, codeine phosphate or cophenotrope). In long standing diarrhea, cholestyramine may be helpful.

   b. Drugs:
      - Prednisolone—40 to 60 mg/day. Budenoside may be used in moderately active disease.
      - Combination of prednisolone and azathioprine or 6 mercaptopurine (6MP) may be used.
      - For perianal disease, metronidazole (400 mg bd for 14 days) plus ciprofloxacin may be given. 6MP or azathioprine may be used in chronic case. Infliximab and adalimumab are effective in healing fistula and perianal disease.
      - In active and moderate to severe total Crohn's colitis or ileocolitis, treatment is like active ulcerative colitis, as follows:
        - Oral and per-rectal aminosalicylate plus per-rectal steroid should be given.
        - Oral prednisolone is indicated for more active disease or when aminosalicylate is ineffective.
        - In more severe colitis or in patient who fails to maximum oral therapy, patient should be hospitalized and treated as follows:
          - IV fluid and nutritional support.
          - IV methylprednisolone or hydrocortisone 100 mg 6 hourly.
          - Topical and oral aminosalicylates are also used.
          - If the patient does not respond to steroid therapy, then IV cyclosporine or infliximab may be given. Otherwise urgent surgery should be done.
2. Maintenance of remission:
   - Smoking must be stopped.
   - Aminosalicylate may be given, but has minimal efficacy.
   - Thiopurines (azathioprine or 6-MP) is given in patient who relapses more than once a year.
   - If it fails, weekly MTX should be given.
   - In aggressive disease, combination of immuosuppressive and anti TNF therapy should be given.
3. In resistant cases (to steroid or immunosuppressive) or failure of above therapy, the following treatment may be given:
   - Methotrexate
   - IV cyclosporine
   - Anti-TNF antibody, e.g. infliximab may be given in infusion 4 to 8 weekly, in three occasions. Aslo, adalimumab may be used. Relapse usually occurs after 12 weeks. So, MTX or azathioprine or 6-MP should be added to maintain remission (etanercept is ineffective).

Infliximab helps in healing fistula and perianal disease. These agents are contraindicated in presence of infection including tuberculosis. Allergic reaction may occur.

4. Surgical management: Surgery should be avoided if possible and only minimum resection should be done, as the disease is multicentric and recurrence is almost inevitable. Indications of surgery are:
   - Failure of medical therapy, intractable disease or fulminant disease.
   - Complications like toxic megacolon, obstruction, perforation, massive hemorrhage, refractory fistula and abscess, etc., which are not responding to medical treatment.
   - Extra-intestinal complications like severe arthritis or pyoderma gangrenosum, not responding to medical treatment.
   - Failure to grow in children despite medical treatment.
   - Suspicion of malignancy or severe dysplasia.

Recurrence is common after surgery. If second surgery is needed, azathioprine or 6MP should be added to prevent recurrence. There is no strong benefit, if it is given after first surgery.

Note Remember the following:

Prednisolone has no role to prevent recurrence.

Q. What are the **differential diagnoses** of Crohn's disease?

A. As follows:

1. Infectious conditions:
   - Bacterial—salmonella, shigella, ETEC, campylobacter, pseudomembranous colitis, Chlamydia proctitis, gonococcal proctitis.
   - Viral—herpes simplex proctitis, HIV, CMV.
   - Parasitic—amebiasis, strongyloidiasis, isospora.
2. Non infectious:
   - Acute appendicitis
   - Diverticulitis
   - Ischemic colitis
   - Radiation proctitis
   - Behcet's disease
   - Carcinoma of colon
   - Drugs—NSAIDs.

Q. What are the **causes of fistula** in abdominal wall?

A. As follows:

- Crohn's disease.
- Ileocecal tuberculosis.
- Actinomycosis.
- Disseminated malignancy.
- Trauma.

Q. What are the **differences** between ulcerative colitis and Crohn's disease?

A. As follows:

Features	Crohn's disease	Ulcerative colitis
1. Site	Mouth to anus, commonly ileum and right side of colon	Large gut, commonly rectum
2. Nature	Transmural (all layers of gut wall are involved)	Mucosa
3. Type	Patchy and discontinuous, skip lesions are present	Continuous or confluent
4. Crypt abscess	Less	Common
5. Fistula, perianal or ischiorectal abscess and skin tag	Common	Uncommon
6. Others	Deep ulcers with fissure. Mucosa in between them looks like cobblestone	Pseudopolyps (hypertrophy of mucosa)
7. Colon cancer	Less	Common
8. Microscopy - » Granuloma » Goblet cells » Cells	» In 50 to 60% cases, non-caseating granuloma present » Slight loss or normal » Chronic inflammatory cells with lymphoid hyperplasia	» Absent » Loss or depleted and distorted » Acute and chronic inflammatory cells in lamina propria and crypts
9. Smoking	Common in smoker	Common is nonsmoker and ex-smoker

Brief Discussion on Ulcerative Colitis

Q. What is **ulcerative colitis?**

A. It is a type of inflammatory bowel disease that involves usually the large gut, specially rectum, mainly involving the mucosa, characterized by frequent attack of bloody diarrhea.

Q. What is the **site** of involvement in ulcerative colitis?

A. Large gut commonly the rectum, which is invariably involved in 95% cases. Occasionally, terminal ileum may be involved called backwash ileitis.

Q. What is a **pseudopolyp**?

A. These are formed by swollen residual mucosa in between the areas of ulceration.

Q. What are the **types** of ulcerative colitis?

A. According to the site of involvement:

- Proctitis (when the disease is limited to rectum).
- Distal colitis (when sigmoid and descending colon are involved).
- Pancolitis or total colitis (when the whole colon is involved).

According to severity, it is divided into two types:

Points	Mild	Severe
1. Number of diarrhea	<4	>6
2. Blood in stool	Slight or no	Profuse, fresh blood
3. Pulse	<90/minute	>90/minute
4. Temperature	Normal	>37.5°C
5. Hemoglobin	Normal	<10 g%
6. ESR	Normal or <30 mm	>30 mm
7. Serum albumin	>35 g/L	<35 g/L
8. Stool volume	<200 g/day	>400 g/day
9. X-ray of abdomen	Normal	Dilated bowel with mucosal island
10. Sigmoidoscopy	Normal or granular mucosa	Blood in lumen or ulceration

Note Remember the following:

There may be a moderate type, the features for which are between mild and severe types.

Q. What are the **complications** of ulcerative colitis?

A. The complications are intestinal and extraintestinal:

1. Intestinal:
   - Perforation of colon
   - Toxic megacolon
   - Severe hemorrhage
   - Malignant change.
2. Extraintestinal—the features are similar to that for Crohn's disease (see in page 195).

Q. What is **toxic megacolon**?

A. Huge dilatation of colon with severe colitis associated with fever, tachycardia, shock and cessation of diarrhea. There is free passage of bacterial toxin through the diseased mucosa into the portal circulation. It usually occurs in the first attack of ulcerative colitis. The patient is toxic and abdomen is distended, commonly involve transverse colon. In plain X-ray, if transverse colon is > 6 cm, colonic perforation with peritonitis may occur. Barium enema is contraindicated. CT scan may be done.

Causes of toxic megacolon:

- Ulcerative colitis (common cause).
- Rarely, Crohn's disease.
- Other causes are ischemic colitis and pseudomembranous colitis.

Plain X-ray abdomen should be taken daily.

Q. How to **treat** toxic megacolon?

A. As follows:

- Nothing by mouth
- Intravenous fluid and correction of electrolytes
- Blood transfusion, if Hb <10 g%
- Hydrocortisone 100 to 200 mg 6-hourly IV or methylprednisolone IV
- Antibiotic, if infection
- Nutritional support
- If no response within 5 to 7 days, or if the condition deteriorates, surgery should be done.

Q. How to suspect **malignancy** in ulcerative colitis?

A. Extensive ulcerative colitis of more than 10 years duration is at a high risk of colorectal cancer (5% after 20 years, 12% after 25 years, 20% after 30 years). Dysplastic changes in colonic biopsy may be the early features.

Q. How will you **investigate** a case of ulcerative colitis?

A. Same as Crohn's disease.

- Barium enema—in early stage, mucosal irregularity, pseudopolyp, stricture, etc. may be seen. In chronic case, there is shortening and narrowing of the bowel with loss of haustration.
- Sigmoidoscopy—uniform continuous involvement of the mucosa, loss of mucosal vascularity, diffuse erythema, multiple ulcers, blood, mucus or pus, also there may be pseudopolyp.

Q. How to **treat** ulcerative colitis?

A. Object of treatment is—control of active disease and maintenance of remission.

Control of active disease

1. Active proctitis.
   - Oral aminosalicylate (mesalazine) plus mesalazine enema or suppository.
   - Rectal steroid (10% hydrocortisone foam or prednisolone 20 mg enema or foam) may be used.
   - If no response, then oral prednisolone 40 mg daily is administered.
2. Active left-sided or extensive proctocolitis.
   - In a mild case, oral aminosalicylate (mesalazine) plus mesalazine enema or suppository and rectal steroid.
   - In moderate to severe case, oral prednisolone 40 mg daily.
3. In severe ulcerative colitis, the patient should be hospitalised.
   - Intravenous methylprednisolone 60 mg or hydrocortisone 100 mg 6 hourly **plus** oral and topical aminosalicylate.
   - Intravenous antibiotic, if necessary.
   - General measures—intravenous fluid, blood transfusion and nutrition.
   - If no response—IV cyclosporine or infliximab may be given.
   - In patient with colonic dilatation >6 cm, or if the clinical condition deteriorates or who do not respond after 7 to 10 days with maximum conservative therapy, urgent surgery (colectomy) may be needed.
   - After recovery, oral prednisolone should be given. Once remission, it should be tapered 5 to 10 mg weekly.

Following features indicate failure of medical therapy:

- Persistent fever
- Tachycardia
- Falling hemoglobin
- Rising WBC
- Falling potassium
- Falling albumin.

Persistently raised stool volume >500 g/day with loose bloody stool:

- In such cases, surgery is indicated.

Maintenance of remission:

After recovery, oral aminosalicylate either mesalazine or balsalazide is given to prevent relapse. In chronic cases with frequent relapse or who require steroid in high dose, azathioprine (1.5 to 2 mg/kg) may be given. Cyclosporine may also help.

Note

Prednisolone is used only in active disease, it has no role to prevent relapse. 5-aminosalicylates administered are either mesalazine or olsalazine or balsalazide. Oral and enema forms are available.

Q. How to treat ulcerative colitis in **pregnancy**?

A. Pregnancy is not affected in ulcerative colitis. However, exacerbation may occur in puerperium, sometimes in first trimester of pregnancy. Drug treatment with corticosteroid, aminosalicylate or azathioprine can be continued during pregnancy.

Q. What **surgery** is done?

A. Proctocolectomy with ileostomy or proctectomy with ileoanal anastomosis is the surgical procedure done.

Indications of surgery:

1. Emergency surgery should be done in:
   - Fulminating acute active colitis, if failure of medical treatment
   - Toxic megacolon, if medical treatment fails
   - Perforation
   - Hemorrhage.
2. In chronic cases, elective surgery is done. Indications are
   - Less or no response to medical therapy
   - Frequent relapse inspite of adequate medical treatment
   - High dose steroid requirement
   - Non-compliance with drugs
   - Colonic dysplasia and suspicion of malignancy.

ILEOCECAL TUBERCULOSIS

CHIEF COMPLAINTS

- Occasional loose motion for the last … month
- Recurrent abdominal pain for … months
- Fever for … months
- Severe weakness and lethargy for … months
- Weight loss and loss of appetite for … months.

HISTORY

History of present illness: According to the statement of the patient, he was alright … months back. Since then, he has been suffering from occasional loose motion, about 5 to 6 times a day, not related to any food or drugs. Stool is moderate in amount, not mixed with fresh or altered blood. The patient also experiences recurrent colicky abdominal pain mostly around the umbilicus and also right side of the abdomen, but no radiation. It is not related to food, but relieved after defecation. He also complains of low grade continued fever for … months, with occasional peaks during evening, also associated with occasional night sweating. For the last ... months, the patient also complains of severe weakness, lethargy, loss of appetite and weight loss for the same duration. There is no history of cough, bladder abnormality or sweating.

History of past illness

Family history

Personal history

Socioeconomic history

Drug history: Mention according to the patient's statement.

GENERAL EXAMINATION

- The patient is ill-looking and emaciated (also looks depressed)
- Moderately anemic
- No jaundice, cyanosis, clubbing, koilonychia, leukonychia or edema
- No lymphadenopathy or no thyromegaly
- Pulse: 96/min
- BP: 120/65 mm Hg
- Temperature: 101ºF
- Respiratory rate: 18/min.

SYSTEMIC EXAMINATION

Gastrointestinal System

Lips, gums, teeth, and oral cavity—normal.
Tongue—pale.

Abdomen

Inspection: No abnormality detected.

Palpation:
- Tenderness in lower abdomen, more in right iliac fossa.
- There is a small mass in the right iliac fossa, 2X2 cm in size, firm, non-terder, movable from side to side, free from overlying skin and underlying structures.
- Liver—not palpable.
- Spleen—not palpable.
- Kidneys—not ballotable.
- Succusion splash—absent.

Percussion: No abnormality detected.
Auscultation: No abnormality detected.

Examination of the other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 36-year-old, farmer, normotensive, nondiabetic, nonsmoker, hailing from …, presented with occasional loose motion, about 5 to 6 times a day for ... months. It is not related to any food or drugs. Stool is moderate in amount, not mixed with fresh or altered blood. The patient also experiences recurrent colicky abdominal pain mostly around the umbilicus and also right side of the abdomen, but no radiation. It is not related to food, but relieved after defecation. He also complains of low grade continued fever for … months, with occasional peaks during evening, also associated with occasional night sweating. For the last ... months, the patient also complains of severe weakness, lethargy, loss of appetite and weight loss for the same duration. There is no history of cough, bladder abnormality or sweating. He used to take paracetamol, vitamins, antacid, ranitidine, etc. prescribed by local physicians. There is no history of such illness in his family.

On examination – general examination (mention as above).

Systemic examination (mention as above).

With the above history and physical findings, I have some differential diagnoses
- Ileocecal tuberculosis
- Crohn's disease
- Lymphoma
- Carcinoma of cecum (in elderly).

Q. What are the **causes** of mass in right iliac fossa?

A. As follows:

1. If the patient is young:
   - Appendicular lump (tender)
   - Ileocecal tuberculosis
   - Crohn's disease
   - Lymphoma
   - Ameboma (less common nowadays, because of wide use of metronidazole)
   - Others—actinomycosis, Yersinia, tubo-ovarian mass in female, pelvic kidney.
2. If the patient is elderly or middle aged:
   - Appendicular lump (tender)
   - Ileocecal TB
   - Carcinoma of cecum (hard, irregular and nontender)
   - Lymphoma
   - Others—as above.

Note Remember the following:

If there is scar mark in lumbar area, diagnosis is transplanted kidney.

Q. Mention one **single investigation** which will be helpful for the diagnosis.

A. Ultrasonogram of whole abdomen.

Q. What **investigations** do you suggest?

A. As follows:

- CBC with ESR
- Ultrasonogram of whole abdomen
- X-ray chest (shows TB in 50%)
- MT
- Colonoscopy with ileoscopy
- Barium follow through with spot film in ileocecal region
- CT scan of abdomen
- Laparoscopy to see tubercle in peritoneum and biopsy.

RELATED QUESTIONS AND ANSWERS

Q. What are the **causes** of ileocecal tuberculosis? (What is the **pathogenesis**?)

A. It is caused by reactivation of primary disease by *Mycobacterium tuberculosis*. May be secondary to pulmonary TB (by swallowing of sputum). Sometimes, primary TB due to Mycobacterium bovis (rare nowadays). After involvement of mucosa and submucosa, intense inflammation with necrosis occurs in the bowel wall and lymphatic. Caseation is often found.

Q. What is the **type of lesion** and **type of ulcer** in ileocecal tuberculosis?

A. Types of lesion—ulcerative, hypertrophic or mixed. Ulcer is transverse (in typhoid and Crohn's disease, the ulcer is longitudinal).

Q. What are the **presentations** of ileocecal TB?

A. History of pulmonary TB may be present. Other features are:

- Abdominal pain is the commonest (usually in right iliac fossa, occasionally generalized), colicky in nature.
- Features of intestinal obstruction (acute or subacute), or peritonitis or ascites.
- Diarrhea or malabsorption syndrome.
- Mass in right iliac fossa.
- Others are fever, malaise, loss of weight and fistula formation.

Q. What are the **complications** of ileocecal tuberculosis?

A. As follows:

- Intestinal obstruction
- Fistula (entero-enteric or entero-cutaneous)
- Malabsorption
- Perforation (rare).

Q. How to **treat** ileocecal TB?

A. As follows:

- Standard anti-TB chemotherapy (using four drugs) for one year.
  Occasionally, surgery (if intestinal obstruction or fistula).

CARCINOMA OF COLON

CHIEF COMPLAINTS

- Pain in left lower abdomen for … months
- Constipation for … months
- Occasional bleeding per rectum for … days
- Weight loss for … months.

HISTORY

History of present illness: According to the patient, he was reasonably well … months ago. Since then, he has been suffering from occasional pain in the left lower abdomen. The pain is colicky, localized, associated with constipation and relieved by bowel movement. It has no relation to food or empty stomach. He denies any history of vomiting, hematemesis or melena. Stool is semisolid or sometimes hard in consistency and very often mixed with fresh blood. The patient also complains of marked loss of appetite and significant weight loss over the last … months. There is no history of fever, excessive sweating, polyuria or diarrhea.

History of past illness

Family history

Personal history

Socioeconomic history

Drug history: Mention according to the patient's statement.

GENERAL EXAMINATION

- The patient is ill-looking and emaciated
- Moderately anemic
- No jaundice, cyanosis, clubbing, koilonychia, leukonychia or edema
- No lymphadenopathy or thyromegaly
- Pulse: 100/min
- BP: 110/70 mm Hg
- Temperature: 98ºF
- Respiratory rate: 18/min.

SYSTEMIC EXAMINATION

Gastrointestinal System

Lips, gums, teeth, and oral cavity—normal.
Tongue—pale.

Abdomen

Inspection: No abnormality detected.
Palpation:

- There is a mass in left iliac fossa, 3 × 4 cm, non-tender, firm in consistency, surface is irregular, margin is irregular and it is immobile.

- Liver—enlarged, ... cm from the costal margin in right midclavicular line. Margin is round, surface is irregular and nodular, nontender, hard in consistency. Upper border of liver dullness in ... intercostal space in right midclavicular line. There is no hepatic bruit.
- Spleen—not palpable.
- Kidneys—not ballotable.
- Succusion splash—absent.

Percussion: No abnormality detected.
Auscultation: No abnormality detected.

Digital rectal examination (DRE): No abnormality.
Examination of the other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 70-year-old, retired policeman, normotensive, nondiabetic, nonsmoker, hailing from …, presented with occasional pain in the left lower abdomen for … months. The pain is colicky, localized, associated with constipation and relieved by bowel movement. It has no relation to food or empty stomach. He denies any history of vomiting, hematemesis or melena. Stool is semisolid or sometimes hard in consistency and very often mixed with fresh blood. The patient also complains of marked loss of appetite and significant weight loss over the last … months. There is no history of fever, excessive sweating, polyuria or diarrhea. There is no such illness in his family. He used to take some vitamins and pain killers.

On examination—general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is carcinoma colon with hepatic metastasis.

Q. What is your **differential diagnosis?**

A. As follows:
- Lymphoma.

Q. What **investigations** do you suggest in colorectal carcinoma?

A. As follows:
- USG of whole abdomen (to see the mass, metastases, lymph node involvement).
- Sigmoidoscopy or colonoscopy and biopsy (gold standard).
- CT colonography.
- CT scan of whole abdomen.
- Endoanal ultrasound or pelvic MRI (used for staging of rectal cancer).
- PET scan is useful for detecting occult metastases and for evaluation of suspicious lesions found on CT or MRI.
- Barium enema (double contrast)—may be helpful to see the mass, but CT colonography is more preferable.
- Others—complete blood count, stool for occult blood, CEA (to see recurrence), X-ray chest.
- FNAC (CT guided or USG guided).
- Sometimes, laparotomy may be needed.

Q. What are the **causes** of mass in left iliac fossa?

A. Mention according to the age of the patient:

If the patient is young, the causes are:
- Thick colon (in irritable bowel syndrome).

- Fecal mass (mass indented and moulded by pressure).
- Occasionally, normal colon may be palpable (mainly in lean and thin person).
- Carcinoma of colon (rare).
- Diverticulitis.
- Tubo-ovarian mass in female.
- Pelvic kidney.
- (If laparotomy scar is present, the diagnosis is transplanted kidney. Examine for AV fistula and anemia).

If the patient is elderly the causes are

- Carcinoma of colon (descending or sigmoid colon).
- Diverticulitis (tender, mobile mass).
- Fecal mass.
- (If laparotomy scar is present, the diagnosis is transplanted kidney. Examine for AV fistula and anemia).

Note Remember the following:

- Carcinoma may be in the cecum, transverse colon, etc. In this case, there may be mass in the right iliac fossa.

RELATED QUESTION OF COLORECTAL CARCINOMA

Q. What are the **sites** of colorectal carcinoma?

A. As follows:

- Rectum (20%)
- Rectosigmoid (10%)
- Sigmoid colon (25%)
- Cecum and ascending colon (25%)
- Transverse colon (15%)
- Descending colon (5%).

Q. What is the **most common site** of carcinoma of colon?

A. Rectosigmoid (65% cases) is the most common site.

Q. What are the **types** of carcinoma of colon?

A. As follows:

1. Macroscopically:
   - Polypoid and fungating
   - Annular and constricting.
2. Microscopically: Adenocarcinoma.

Q. What are the **causes** or **predisposing factors** for carcinoma of colon?

A. The causes are unknown. Predisposing factors are as follows:

3. Dietary factors:
   - Excess consumption of red meat, saturated animal fat.
   - Less dietary fibers.
   - Less intake of vegetables and fruits (high vegetables and fruits may be preventive for carcinoma).
   - Excess and prolonged sugar consumption.

4. Non-dietary factors:
   - Increasing age.
   - Genetic factors such as benign adenomatous polyp or familial adenomatous polyposis.
   - Hereditary non-polyposis colonic cancer.
   - Family history of colon cancer.
   - Long-standing extensive ulcerative colitis or Crohn's colitis, especially if associated with primary sclerosing cholangitis.
   - Personal history of breast cancer.
   - Ureterosigmoidostomy.
   - Acromegaly.
   - Pelvic radiotherapy.
   - Alcohol (weak association)
   - Smoking (relative risk 1.5 to 3.0).
   - Obesity and sedentary lifestyle.
   - Cholecystectomy.
   - Type 2 diabetes (hyperinsulinemia).

Factors which decrease risk of colorectal carcinoma:

- Diet—Increased fiber, fruits, vegetable, garlic, milk.
- Exercise (colon only).
- Drugs—Aspirin or other NSAIDs, calcium, folic acid, omega 3 fatty acids, combined estrogen and progesterone hormone replacement therapy.

Q. What are the **features** of carcinoma of colon?

A. The features of carcinoma of colon depend on the site (may be asymptomatic)

- If on the left side, there may be bleeding per rectum, alteration of bowel habit, mass in left iliac fossa.
- If on the right side, there may be alteration of bowel habit, intestinal obstruction, mass in right iliac fossa.

Note Remember the following:

Any patient over 35 to 40 years of age presenting with new large bowel symptoms should be investigated. Alarming symptoms are change in bowel habit, rectal bleeding, anorexia and weight loss, fecal incontinence, tenesmus and passing mucus per rectum.

Q. How **screening and prevention** are done in carcinoma of colon?

A. Screening is done as follows:

- Any person >50 years of age, stool is tested for the presence of occult blood.
- Colonoscopy (gold standard).
- Flexible sigmoidoscopy is an alternative to colonoscopy.
- CT colonoscopy may be used in screening program.
- Screening for high risk patients by molecular genetic analysis (very promising, but not widely available).

Prevention:

- Chemoprevention by using aspirin, calcium, folic acid. Cox 2 inhibitor may have some role to play in prevention.
- Secondary prevention to detect early and precancer stage. It is done by screening.

Note Remember the following:

- Colorectal carcinoma is common in the western world, less among Asians
- Second common cause of death.

Q. How the colorectal carcinoma **spreads**?

A. As follows:

- Local infiltration through bowel wall
- By lymphatics
- By blood
- Transcoelomic.

Q. How to **treat** colorectal carcinoma?

A. Depends upon the stages of the cancer

1. Curative:
   - Surgical resection of the tumor with removal of pericolic lymph nodes.
   - Adjuvant postoperative chemotherapy (with 5 fluorouracil and folinic acid).
   - Radiotherapy is not much helpful. Preoperative radiotherapy may be given to large fixed rectal cancer to make it resectable. Postoperative radiotherapy may be required in some cases.
   - In some cases with metastatic disease, monoclonal antibody like bevacizumab or cituximab either alone or with chemotherapeutic agents, such as irinotecan may be used.
2. Palliative:
   - Palliative chemotherapy with 5FU may improve survival. If this fails, second line drug such as irinotecan may be given.
   - Endoscopic laser therapy or insertion of an expandable metal stent can be used to relieve obstruction.

READ THE FOLLOWING

Q. What are the causes of **epigastric mass**?

A. Mention according to the age of the patient.

If the patient is middle aged or elderly, the causes are:

1. Mass in left lobe of liver (hepatoma, secondaries and hydatid cyst).
2. Carcinoma of stomach.
3. Lymphoma of stomach.
4. Carcinoma of head of the pancreas.
5. Others:
   - Tender mass (liver abscess)
   - Soft and cystic mass (pancreatic pseudocyst)
   - Mass in transverse colon (carcinoma)
   - Pulsating mass (aneurysm of abdominal aorta)
   - Epigastric hernia.

If the patient is young, causes are:

- Lymphoma of stomach
- Mass in left lobe of liver (hydatid cyst and hepatoma. If tender mass, it may be liver abscess)
- Epigastric hernia
- Pancreatic pseudocyst.

Q. What are the causes of mass in **right iliac fossa**?

A. Tell the causes according to the age of the patient.

If the patient is young:

1. Appendicular lump (tender)
2. Ileocecal TB
3. Crohn's disease
4. Lymphoma
5. Ameboma (less common nowadays, because of wide use of metronidazole)
6. Others:
   - Actinomycosis, Yersinia infection
   - Tubo-ovarian mass in female
   - Pelvic kidney.

If the patient is elderly or middle aged:

- Appendicular lump (tender)
- Ileocecal TB
- Carcinoma of cecum (it is hard, irregular and non-tender)
- Lymphoma
- Others may be as above.

Note Remember the following:

If there is scar mark in lumbar area, diagnosis is transplanted kidney.

Q. What are the causes of **unilateral renal mass?**

A. As follows:

- Renal cell carcinoma (in elderly) or Wilms' tumor (in children)
- Unilateral hydronephrosis or pyonephrosis
- Hypertrophied single kidney (if nephrectomy of other kidney or congenital absence of one kidney).
- Renal cyst
- Polycystic kidney with single palpable kidney (due to asymmetrical enlargement).

Note Remember the following:

Right kidney may be normally palpable.

Q. What are the causes of **bilateral renal mass**?

A. As follows:

- Polycystic kidney disease
- Bilateral hydronephrosis
- Diabetic nephropathy in early stage
- Amyloidosis
- Rarely, bilateral renal cell carcinoma.

Q. What are the causes of mass in **right hypochondrium?**

A. As follows:

- Mass in liver (hepatoma, secondaries and hydatid cyst)
- Gall bladder mass (carcinoma, mucocele or empyema of gallbladder)
- Mass in right side of colon (malignancy)
- Carcinoma head of pancreas.

Q. What are the causes of mass in **central abdomen** (other than epigastric mass)**?**

A. According to the age and sex, the causes are as follows:

If the patient is young or early aged, the causes are:

- Lymphoma
- Tuberculosis (tabes mesentericus or lymphadenitis)
- Hydatid cyst
- Mesenteric cyst
- In female, ovarian cyst, pregnancy
- Distended urinary bladder (urinary retention).

If the patient is elderly or middle aged, the causes are:

- Intra-abdominal malignancy
- TB (tabes mesentericus or lymphadenitis)
- Lymphoma
- Metastatic lymphadenitis
- Hydatid cyst
- Mesenteric cyst
- Retro-peritoneal growth (sarcoma)
- Distended urinary bladder (urinary retention).

CHAPTER 5

Hepatobiliary System

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OBSTRUCTIVE JAUNDICE

CHIEF COMPLAINTS

- Yellow discoloration of urine and eyes for … months
- Itching of whole body for … months
- Anorexia and weight loss for … months

HISTORY

History of present illness: The patient states that he was completely alright about … months back. Since then, he noticed yellow discoloration of his urine, eyes and whole body, which is gradually increasing. Initially jaundice is not associated with any nausea, loss of appetite or vomiting (which are prodrome of acute viral hepatitis). His stool is clay colored, voluminous, associated with mucus but no blood. He also complains of generalized itching that is more marked during the night and interferes with sleeping. For the last … months, the patient also complains of anorexia and marked loss of weight, about 10 kg. He does not complain of fever or abdominal pain or swelling of the body and leg.

History of past illness: There is no previous history jaundice, injection, infusion or blood transfusion, dental extraction, sharing of needles, colicky abdominal pain or abdominal surgery.

Personal history: He is a clerk, nonsmoker, nonalcoholic.

Family history: Nothing significant.

Drug and treatment history: Mention according to the patient's statement.

GENERAL EXAMINATION

- Ill looking
- Deeply jaundiced and mildly anemic
- No cyanosis, clubbing, koilonychia, leukonychia or edema
- No lymphadenopathy or thyromegaly
- There are multiple scratch marks all over the body, more marked over the extensor surfaces of upper and lower limbs
- No stigmata of chronic liver disease
- Bony tenderness—absent
- Flapping tremor—absent.

SYSTEMIC EXAMINATION

Gastrointestinal System

- Lips, gums, teeth normal
- Tongue and oral cavity—yellowish.

Abdomen

Inspection: Normal.

Palpation:

- Liver is palpable, 10 cm from the right costal margin in the mid-clavicular line, margin is sharp, surface is smooth, firm in consistency and nontender. Upper border of the liver dullness is in the right 4th intercostal space, in midclavicular line. There is no bruit.
- Spleen—not palpable.
- Kidneys—not ballotable.
- Testes—normal.

Percussion: Normal.

Auscultation: No abnormality detected.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 44 years old, a clerk, normotensive, nondiabetic, nonsmoker, nonalcoholic, hailing from …, presented with yellow discoloration of his urine, eyes and whole body, which is gradually increasing. Initailly jaundice is not associated with any nausea, loss of appetite or vomiting (which are prodrome of acute viral hepatitis). His stool is clay colored, voluminous, associated with mucous but no blood. He also complains of generalized itching, which is more marked during the night and interferes with sleeping. For the last … months, the patient also complains of anorexia and marked loss of weight, about 10 kg. He does not complain of fever or abdominal pain or swelling of the body and leg.

There is no previous history jaundice, injection, infusion or blood transfusion, dental extraction, sharing of needles, colicky abdominal pain or abdominal surgery. There is no history of intravenous drug abuse. There is no family history of similar illness. He used to take ranitidine and painkillers.

On examination – general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is obstructive jaundice which may be due to:

- Carcinoma head of the pancreas
- Stone in the common bile duct
- Periampullary carcinoma
- Cholangiocarcinoma.

Q. Mention one **single** investigation that is helpful for your diagnosis.

A. Ultrasonography of abdomen.

Q. **Why** it is obstructive jaundice?

A. Because:

- The stool is pale or clay colored with steatorrhea
- Generalized itching with scratch mark
- Deep and progressively increasing jaundice.

Q. Can these features occur in viral hepatitis?

A. Obstructive features may occur in viral hepatitis due to intrahepatic cholestasis, which recovers completely after acute stage is over.

Q. What other **investigations** do you suggest?

A. As follows:

- CBC.

- Liver function tests—Serum bilirubin, SGPT, alkaline phosphatase (very high), γ glutamyl transferase (very high), prothrombin time, serum total protein and A : G ratio.
- CA 19–9 (high in carcinoma of pancreas).
- USG of hepatobiliary system and pancreas.
- Viral markers (HBsAg, Anti-HBc IgG, HBeAg, Anti-HCV).
- CT scan or MRI of upper abdomen.
- MRCP or ERCP.

Q. What are the **features** of obstructive jaundice?

A. As follows:

1. Early features:
   - Deep jaundice, dark yellow skin, deep yellow or mustard oil like urine.
   - Pale or clay colored stool.
   - Generalized itching with scratch mark.
   - Palpable gallbladder may be present (obstruction due to carcinoma of the head of the pancreas).
   - Deep seated abdominal pain due to stone in the common bile duct (choledocholithiasis), pancreatitis, choledochal cyst, sometimes due to carcinoma head of the pancreas.
2. Late features:
   - Malabsorption leading to weight loss, steatorrhea, osteomalacia due to vitamin D deficiency, bleeding disorder due to vitamin K deficiency, night blindness due to vitamin A deficiency (all are due to lack of bile salts).
   - Xanthoma, xanthelasma may be present.
   - There may be cholangitis due to secondary infection. Features of cholangitis are jaundice, right upper quadrant pain and fever (Charcot's triad).

Q. Why there is **bleeding tendency** in obstructive jaundice?

A. Due to vitamin K deficiency, which is due to lack of bile salts. So, vitamin K dependent factors such as factor II, VII, IX, X will be deficient, leading to bleeding. Prothrombin time will be prolonged. In such case, vitamin K therapy is helpful, should be given parenterally.

Q. What are the features of **hepatocellular jaundice?**

A. As follows:

- Prodromal syndrome like anorexia, nausea and vomiting
- Orange yellow tinge of the bulbar conjunctiva
- Yellowish urine
- High colored stool (may become pale if there is intrahepatic cholestasis. Pruritus is present)
- Tender hepatomegaly
- Disproportionate rise in the aminotransferases compared to the alkaline phosphatase
- There may be bleeding manifestations as a result of hepatocellular failure.

Q. What are the features of **hemolytic jaundice?**

A. As follows:

- Triad of jaundice, anemia and splenomegaly. Jaundice is usually mild, serum bilirubin is usually < 6 mg/dL. Bilirubin is predominantly of unconjugated variety (SGPT, SGOP, gamma GT, alkaline phosphatase, all are normal).
- Liver may be mildly enlarged, not tender.
- Pale lemon complexion.
- If hemolysis is due to hemoglobinopathy, the jaundice is persistent for a long time. There may be Mongoloid faces (frontal and parietal bossing, prominent malar bones), short stature, leg ulcer.
- Acholuric urine.

- High colored stool due to excess amount of stercobilinogen and stercobilin.
- Reticulocytosis in peripheral blood.

Q. What are the causes of **mass in right hypochondrium?**

A. As follows:
- Hepatic mass, such as hepatocellar carcinoma, secondaries and hydatid cyst.
- Gall bladder mass such as carcinoma, mucocele or empyema of gallbladder.
- Mass in right side of colon, such as carcinoma of the ascending colon, also in hepatic flexure.
- Carcinoma of the head of the pancreas.

RELATED QUESTIONS AND ANSWERS

Q. What are the **causes** of obstructive jaundice?

A. Obstruction usually occurs in common bile duct. The causes may be in the lumen, in the wall and outside the wall of CBD.

1. Causes in the lumen:
   - Stone in CBD (choledocholithiasis)
   - Worms (ascariasis).
2. Causes in the wall:
   - Sclerosing cholangitis
   - Cholangiocarcinoma
   - Periampulary carcinoma
   - Stricture (may be following surgery, trauma).
3. Causes outside the wall:
   - Carcinoma head of the pancreas
   - Lymphoma
   - Enlargement of the lymph node in porta hepatis.

Q. What are the **intrahepatic causes** of cholestatic (obstructive) jaundice?

A. As follows:
- Primary biliary cirrhosis
- Primary sclerosing cholangitis
- Viral hepatitis (especially HEV)
- Drugs and alcohol
- Autoimmune hepatitis
- Cystic fibrosis
- Postoperative
- Benign recurrent intrahepatic cholestasis
- Pregnancy.

Q. What are the causes of **fluctuating jaundice?**

A. As follows:
- Choledocholithiasis
- Choledochal cyst
- Sometimes in primary sclerosing cholangitis
- Hemolytic jaundice
- Wilson disease
- Gilbert's syndrome
- Benign recurrent intrahepatic cholestasis (BRIC)
- Recurrent pancreatitis.

Q. What are the causes of **progressive jaundice?**

A. As follows:

- Carcinoma of the head of the pancreas
- Cholangiocarcinoma
- Primary biliary cirrhosis
- Primary sclerosing cholangitis.

Q. What are the causes of **palpable gallbladder with jaundice?**

A. As follows:

- Carcinoma of head of pancreas
- Carcinoma of ampulla of Vater
- Stone in common bile duct
- Pressure from outside on bile duct (lymphoma and secondaries)
- Cholangiocarcinoma
- Sclerosing cholangitis.

Q. What are the causes of **palpable gallbladder without jaundice?**

A. As follows:

- Mucocele
- Empyema
- Occasionally, carcinoma of the gallbladder.

Q. Could it be **gall stone** with palpable gallbladder?

A. Unlikely (but gallbladder is palpable, if the stone is in common bile duct).

Uncommon but possible if there is double impaction, i.e. one stone in cystic duct and one stone in distal CBD.

Q. What is **Courvoisier's law?**

A. It is as follows:

- In a jaundiced patient with palpable gallbladder, the cause is unlikely to be gallstones, rather it is due to carcinoma head of pancreas and extrinsic pressure in bile duct.

Reverse of the law:

- Obstructive jaundice without palpable gallbladder is unlikely to be carcinoma head of pancreas and extrinsic pressure in common bile duct.

Q. Why gallbladder is **not palpable** in gallstone disease?

A. Gallstone is associated with chronic cholecystitis and gallbladder is fibrosed, which is unable to enlarge.

Q. What are the **congenital nonhemolytic hyperbilirubinemia?**

A. As follows:

1. Gilbert's syndrome (unconjugated hyperbilirubinemia)
2. Crigler-Najjar syndrome (unconjugated hyperbilirubinemia)
3. Dubin-Johnson syndrome (conjugated hyperbilirubinaemia)
4. Rotor's syndrome (conjugated hyperbilirubinemia).

Gilbert's syndrome:

- It is inherited as autosomal dominant. There is reduction of glucuronyl transferase and abnormality in uptake of bilirubin.
- Mild jaundice, especially with fasting.
- No treatment is necessary, only reassurance is sufficient.

Crigler-Najjar syndrome

- There are two types:
- Type I is inherited as autosomal recessive. There is absence of glucuronyl transferase, the patient dies in neonatal period due to kernicterus.
- Type II is inherited as autosomal dominant. There is reduction of glucuronyl transferase. The patient usually survives up to adulthood. Treatment is by phenobarbitone, ultraviolet light or liver transplantation.

Dubin-Johnson syndrome:

- It is inherited as autosomal recessive. There is defect in excretion of bilirubin.
- Usually mild disease.
- Liver is black due to deposition of lipofuscin and melanin.
- Urinary coproporphyrin I is increased.
- No treatment is necessary.

Rotor's syndrome:

- It is inherited as autosomal recessive. There is defect in uptake and conjugation bilirubin in the liver.
- Mild disease.
- Urinary total coproporphyrin is increased.
- No treatment is necessary.

ACUTE VIRAL HEPATITIS

CHIEF COMPLAINTS

- Loss of appetite, nausea and vomiting for … days
- Yellow coloration of urine and eyes for … days.
- Pain and discomfort in the upper abdomen for the same duration
- General weakness for … days

HISTORY

History of present illness: The patient states that, she was alright about … days back. Since then, she has been suffering from malaise, loss of appetite, nausea and vomiting. The vomitus is bile-stained with some food residue, but no blood. She also noticed gradually increasing yellow coloration of her urine and eyes for the same duration. Her stool is yellowish and not voluminous and not clay colored. There is no history of itching. The patient also complains of pain and discomfort in the right upper abdomen. It is not related to food and there is no radiation to the shoulder. She also complains of general weakness for the same duration. There is no history of fever, skin rash, contact with jaundice patient, intake of drugs, injection, infusion, blood transfusion or IV drug abuse, travel history or sexual exposure.

History of past illness: Mention according to the patient's statement.

Personal history: Mention according to the patient's statement.

Family history: There is no history of such illness in her family.

Drug and treatment history: She is on oral contraceptives, but takes no other medicine related to her symptoms.

Menstrual history: It is regular. Her LMP was 10 days ago.

GENERAL EXAMINATION

- The patient is ill looking
- There is moderate jaundice
- No cyanosis, clubbing, koilonychia, leukonychia or edema, spider angioma or palmar erythema Flapping tremor is absent
- No lymphadenopathy or thyromegaly
- No skin rash
- Pulse—68/min
- BP—110/70 mm Hg
- Respirator`y rates—20/min
- Temperature—100°F.

SYSTEMIC EXAMINATION

Gastrointestinal System

- Lips, gums, teeth—normal
- Under surface of tongue and oral cavity—yellowish.

Abdomen

Inspection: No abnormality detected.

Palpation:

- Liver is palpable, 3 cm from the right costal margin in the mid-clavicular line, margin is sharp, surface is smooth, soft in consistency, and tender. Upper border of liver dullness is in the right 5th intercostal space along the midclavicular line. There is no hepatic bruit.
- Spleen is not palpable.
- Kidneys are not ballotable.
- Ascitis is absent as evidenced by absent shifting dullness and fluid thrill.

Percussion: No abnormality detected.

Auscultation: No abnormality detected.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mrs. …, 33 years old, housewife, normotensive, nondiabetic, nonsmoker, nonalcoholic, hailing from …, presented with malaise, loss of appetite, nausea and vomiting for … days. The vomitus is bile stained with some food residue, but no blood. She also noticed gradually increasing yellow coloration of her urine and eyes for the same duration. Her stool is yellowish and not voluminous and not clay colored. There is no history of itching. The patient also complains of pain and discomfort in the right upper abdomen. It is not related to food and there is no radiation to the shoulder. She also complains of general weakness for the same duration. There is no history of fever, skin rash, contact with jaundice patient, intake of drugs, injection, infusion, blood transfusion or I/V drug abuse, travel history or sexual exposure. There is no history of such illness in her family. She is on oral contraceptives, but takes no other medicine related to her symptoms. Her LMP was 10 days ago.

On examination – general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is acute viral hepatitis

Q. What are your **differential diagnoses?**

A. As follows:

- Obstructive jaundice
- Hemolytic jaundice
- Weil's disease.

Q. Why is this not **obstructive jaundice?**

A. Because, there is no feature of obstructive jaundice, such as – no itching, scratch mark or shiny nails and no clay colored stool. Also in obstructive jaundice, there is deep jaundice, dark yellow skin and deep yellow or mustard oil like urine, which are not present in this case.

Q. Why not **hemolytic jaundice?**

A. Because, in case of hemolytic anemia, usually there are triad of anemia, jaundice and splenomegaly. Also, there is long history of jaundice, but no anorexia, nausea or vomiting. If hemolytic jaundice is due to hemoglobinopathy, there may be bony changes like frontal and parietal bosing, prominent malar bones (Mongoloid facies).

Q. What **investigations** do you suggest in acute viral hepatitis?

A. As follows:

1. CBC (there may be leukopenia, with relative lymphocytosis).
2. Liver function tests:
   - Serum bilirubin—high.
   - SGPT—high.
   - SGOT – may be high (SGOT is more raised in drug-induced hepatitis).
   - Alkaline phosphatase may be high (rarely more than twice the upper limit. In cholestatic hepatitis, alkaline phosphatase may be very high).
   - Prothrombin time – prolonged in severe hepatitis.
3. Viral markers:
   - Virus A (anti-HAV, IgM indicates acute infection).
   - Virus B (HBsAg, HBeAg, anti-HBc). In acute infection, HBsAg may be cleared rapidly; anti-HBc IgM is diagnostic.
   - Virus E (anti-HEV, IgM indicates acute infection), anti-HCV.
4. USG of hepatobiliary system.
5. Others—Blood sugar, urine R/E.

Note Remember the following points:

- HBsAg appears in the blood 6 weeks to 3 months after acute infection, then disappears.
- HBeAg rises early and declines rapidly.
- Anti-HBc is the first antibody to appear and high titers of IgM anti-HBc suggest acute infection and continuing viral replication. It persists for many months.
- Anti-HBsAg appears late and indicates immunity.
- Anti-HBe appears after anti-HBc. Its appearance indicates decreased infectivity.

Q. What are the **markers** of HBV infection?

A. As follows:

- HBsAg (it may persist for few days, but usually 3 to 4 weeks, can persist up to 5 months. But if it persists > 6 months, indicates chronic infection).
- HBeAg (indicates active replication. If it persists for > 6 month, indicates chronic infection).
- Anti-HBc (IgM type indicates acute infection).
- HBV DNA (by PCR).

Q. What are the **markers** of B virus replication?

A. HBeAg, HBV-DNA.

RELATED QUESTIONS AND ANSWERS

Q. What are the causes of **acute hepatitis?**

A. As follows:

- Acute viral hepatitis (see below).
- Drugs – paracetamol, alcohol.
- Nonviral infection—Toxoplasma gondii, Leptospira icterohaemorrhagiae, Coxiella burnetii (Q fever).
- Others—pregnancy, Wilson's disease, poisons (amanita phyllodes mashroom, aflatoxin, carbon tetrachloride).

Q. What are the causes of **chronic hepatitis?**

A. As follows:

- Virus—HBV, HCV, combined HBV and HDV
- Autoimmune
- Drugs—methyldopa, isoniazid, ketoconazole, nitrofurantoin
- Alcohol
- Hereditary—Wilson's disease, hemochromatosis, α_1 antitrypsin deficiency
- Inflammatory bowel disease (Ulcerative colitis).

Q. What are the **viruses** causing hepatitis?

A. As follows:

- Hepatitis A, B, C, D and E virus.
- Other viruses are Epstein-Barr virus, CMV, herpes simplex virus and yellow fever virus.

Note Remember the following:

D virus is a RNA-defective virus, can infect only with B virus or can superinfect in those who are HBV carriers. Only B virus is DNA type, and all others are RNA type.

Q. What **history** should be taken in acute viral hepatitis?

A. As follows:

1. Anorexia, nausea and vomiting.
2. Pain (usually in right hypochondrium).
3. High-colored urine, yellow eye and body.
4. Later on (due to intrahepatic cholestasis), there may be itching, pale stool.
5. History specific for HBV:
   - Injection or infusion of blood and blood products, any fluid
   - Injection of contaminated needle or sharing of syringe by others or parenteral drug abusers
   - Acupuncture or tattooing
   - Sexual contact with infected person
   - Homosexuality
   - Organ transplantation
   - Chronic hemodialysis
   - Travel to other parts
   - Newborn in infected mother with HBV.

Note Remember the following:

Clinical features and pathological features are same in all viruses causing hepatitis. They differ in their tendency to cause acute and chronic infections. HBV and HCV may cause chronic hepatitis. HDV can cause chronic infection with HBV. HAV and HEV are not associated with chronic infection.

Q. What are the **complications** of acute viral hepatitis?

A. As follows:

- Acute fulminating hepatic failure (by B and sometimes with E viral infection in pregnancy. It is rare by HAV).
- Relapsing hepatitis. It may be clinically evident (5 to 15%) or, more commonly, only biochemically detectable. It settles spontaneously.
- Cholestatic hepatitis mostly by HAV, may persist for 7 to 20 weeks.

- Post-hepatitis syndrome: It is seen in anxious patient who complain of malaise, anorexia, nausea, vomiting, right hypochondrial pain or discomfort in the absence of clinical or biochemical evidence of liver disease. Reassurance is necessary.
- Chronic liver disease (due to B and C virus), which may lead to cirrhosis of liver and ultimately to hepatoma.
- Others: Aplastic anemia (usually reversible), rarely Coomb's positive hemolytic anemia, polyarteritis nodosa, Henoch-Schönlein purpura, glomerulonephritis and collagen vascular disease.

Q. How would you **treat** a patient with acute viral hepatitis?

A. As follows:
- Bed rest
- Normal diet
- Supportive and symptomatic
- Avoid sedative, opium and alcohol.

> **Note Remember the following:**
>
> Bed rest and extra dietary measures are unhelpful.

Q. What is the **prognosis** of acute viral hepatitis?

A. It depends on the type of the virus:

1. HAV:
   - Good, recovery in 3 to 6 weeks
   - Rarely (0.1%) develop acute liver failure
   - Mortality in young adult is 0.1% from acute fulminating hepatic failure. Mortality increases with age.
2. HBV:
   - In 90 to 95% cases, full recovery occurs within 6 months.
   - 5 to 10% develop chronic infection which usually continues for life. Many may remain as inactive HBV infection. In some cases, cirrhosis of the liver and hepatoma may develop after many years. Cirrhosis usually develops in 5 to 20% cases in 5 to 20 years. This proportion is higher in those with HBeAg positive.
   - < 1% may develop fulminating hepatic failure.
   - Infection from mother to child during pregnancy leads to chronic infection in child in 90% case and recovery is rare.
   - Chronic infection is also common in Down's syndrome and HIV infection.
3. HCV:
   - Rarely causes acute infection
   - Commonly it causes chronic hepatitis.
4. Combined HBV and HDV infection can cause more aggressive disease.
5. HEV:
   - Similar to HAV
   - Can cause acute liver failure with high mortality in pregnancy.

Features of Different Virus Causing Hepatitis

Hepatitis A virus (HAV):

- It is a picorna group of enterovirus (RNA virus).

- Highly infectious, spread by feco-oral route.
- Infection is common in children, mostly remain asymptomatic.
- Infection is common in overcrowding and poor sanitation.
- No chronic carrier.

Hepatitis B virus (HBV):

- It is a hepadna group of DNA virus.
- Humans are the only source of infection.
- Mode of infection:
  - Vertical transmission from mother to child in the perinatal period is the commonest mode of infection worldwide (90% cases). It is not transmitted by breastfeeding.
  - Horizontal transmission by injection, transfusion, sexual exposure, etc. occurs only in 10% cases. Virus can be found in semen and saliva. In children, it may be transmitted by minor abrasion, close contact with other children, etc. But it usually does not spread in feco-oral route.
- Features of acute infection are same as in any viral infection. But certain extra features may be present such as serum sickness like illness characterized by skin rash (urticaria or maculopapular rash), polyarthritis affecting small joints, fever, extrahepatic immune complex mediated arteritis or glomerulonephritis.
- There is no definite role of antiviral drug in acute infection. But antiviral drugs may be needed in chronic HBV infection (see below).
- Neonates born of hepatitis B infected mother should be immunized at birth and immunoglobulin is given. HBV serology should be checked at 12 months of age.

Q. How to **treat** chronic HBV infection?

A. As follows:

1. In chronic hepatitis B infection, no drug is available to eradicate the infection completely (that is render the patient HBsAg negative). However, drug treatment is given to:
   - Make HBeAg seroconversion
   - Reduction of HBV-DNA
   - Normalization of liver function tests.
2. Indication of drug treatment are—patient with high viral load, HBeAg positive, high ALT and histological evidence of inflammation and fibrosis should be treated.
   - The patient with positive HBeAg, HBsAg and HBV-DNA > 20000 IU/mL, with ALT > 2 times of normal – should be treated. Liver biopsy is not essential in this group.
   - Similar patient with HBV-DNA > 20000 IU/mL, but with ALT < 2 times of normal – should not be treated as efficacy is less. If liver biopsy shows inflammation, then the patient may be treated.
   - The patient with negative HBeAg with HBV-DNA > 20,000 IU/mL – should also be treated.
   - The patient with compensated cirrhosis with HBV-DNA > 2,000 IU/ml or patient with compensated cirrhosis with HBV-DNA < 2,000 IU/mL, but high ALT – should be treated.
   - The patient with decompensated cirrhosis can be treated, but liver transplantation may be required.
3. Drugs:
   - Oral—lamivudine, adefovir, entecavir, telbivudine, tenofovir.
   - Injectable—interferon α, emtricitabine.
4. Current treatment:
   - In HBeAg positive cases, pegylated interferon or tenofovir or entecavir may be used. Interferon is used for 1 year. Oral antiviral drugs are given for a long time.

5. Liver transplantation in HBV—Previously it was thought that liver transplantation is contraindicated in the presence of HBV infection as it recurred in the graft. However, the use of post-liver transplant prophylaxis with lamivudin and hepatitis B immunoglobulin, has reduced the reinfection rate in up to 10% and 5 year survival up to 80%. So, transplantation may be considered.

Q. How to **treat** a patient with incidental finding of positive HBsAg?

A. Incidental HBsAg positive patient should have investigations such as HBeAg, anti-HBe, HBV-DNA and SGPT. Most of this type of patient remain asymptomatic as chronic HBV healthy carrier. In many cases, there is no active liver disease, normal or slightly raised transaminase and the patient is not highly infective, do not develop progressive liver disease although some patients develop reactive hepatitis. There is an annual spontaneous clearance rate of HBsAg of 1 to 2%.

No treatment is necessary. Only regular follow-up and reassurance is needed. Indications of treatment are as above.

Hepatitis D virus (HDV):

- It is called an RNA defective virus, which does not have any independent existence. It requires HBV infection for replication.
- Source and mode of transmission is like HBV.
- Management of HBV effectively cures HDV.

Hepatitis C virus (HCV):

- It is an RNA flavivirus.
- Acute infection is rare. About 80% of the individual exposed to this virus is chronically infected and spontaneous viral clearance is rare. This virus can cause cirrhosis in 20 to 40 years in 20% cases. May lead to hepatoma in cirrhotic patient, risk is 2 to 5% per year.
- Mode of transmission is by transfusion of blood and blood products.
- There are 6 genotypes of this virus (genotype 1 to 6).
- Treatment is by pegylated α interferon given weekly subcutaneously plus oral ribavirin. Genotype 1 needs 12 months treatment.
- Liver transplantation should be considered when complication of cirrhosis occurs such as resistant ascites. However, C infection recurs in the transplanted liver. Up to 15% patient will develop cirrhosis in the grafted liver in 5 years.

Hepatitis E virus (HEV):

- It is an RNA virus.
- Spread via feco-oral route, mostly a self-limiting disease, does not cause chronic liver disease.
- Only serious during pregnancy, may cause acute liver failure which has a high mortality.

Brief Discussion on Weil's Disease (Leptospirosis)

Organism and animal hosts:

- Leptospira icterohaemorrhagiae of rat
- Leptospira pomona of pig
- Leptospira canicola of dog
- Leptospira hardjo of cattle.

Q. What is **Weil's disease?** What is it's mode of infection, clinical features, investigation and treatment?

A. It is a leptospiral disease caused by leptospira icterohaemorrhagiae characterized by high fever, jaundice, hemorrhage and renal impairment.

Mode of infection: Spread is typically by contact with infected rat urine.

Incubation period: 7 to 14 days.

Clinical features: There are 2 phases –

1. Leptospiremic or bacteremic phase: This phase lasts for one week. Organisms may be found in blood and CSF. Characterized by:
   - High fever with chill
   - Anorexia, nausea, vomiting
   - Headache, myalgia (mainly calf and back)
   - Conjunctival suffusion (blood shot eyes)
   - Skin rash (maculopapular, purpura, bruise, etc.)
   - Lymphadenopathy
   - Jaundice, hepatosplenomegaly
   - In severe case, renal impairment (caused by impaired renal perfusion and acute tubular necrosis, manifested as oliguria or anuria) and hemorrhage (epistaxis, hematemesis, melena, etc.) may occur. There may be liver failure, myocarditis, pulmonary hemorrhage, encephalitis, aseptic meningitis may occur. There may be cardiac failure, hemolytic anemia, thrombocytopenia
   - Relative bradycardia, neck rigidity may be found.
2. Immunological phase: There is development of antibody, leptospira disappears from blood. It lasts for 2 to 5 days. Features are usually mild, but meningism or aseptic meningitis and iridocyclitis may occur. Majority recover uneventfully.

Note Remember the following:

Any patient with high fever, jaundice, bleeding manifestations and renal involvement, Weil's disease is a strong possibility.

Investigations:

- CBC—usually polymorphoneuclear leucocytosis, thrombocytopenia in severe case.
- Blood culture (Fletchur's media)—positive in 1st week of illness (within 4 days of illness).
- Urine R/E—proteinuria, hematuria, RBC cast.
- Urine culture for leptospira in second week.
- LFT—high bilirubin, SGPT and prothrombin time.
- Serum CPK—high.
- Serological test—MAT (microscopic agglutination test) positive at the end of 1st week. ELISA, immunofluorescence technique, etc. may be done.
- CSF study—abnormal in 90% cases.
- PCR—leptospira DNA by PCR in blood can be detected in early symptomatic disease and also in urine from 8th day of illness, may remain for months thereafter.

Treatment:

1. Antibiotic:
   - IV benzyl penicillin (1.5 million units 6 hourly for 1 week) or ampicillin (1g 6 hourly for 1 week). Ceftriaxone (1 g daily for 1 week) is as effective as penicillin.

- Doxycycline (100 mg 12 hourly for 1 week) or ampicillin (750 mg 6 hourly for 1 week) when started within 4 days of onset of symptoms.

2. In renal failure and jaundice:
   - Fluid and electrolyte balance must be maintained
   - Dialysis may be needed
   - Exchange transfusion may be needed in severe hyperbilirubinemia.
3. If anemia and thrombocytopenia—blood transfusion may be needed.

Prophylaxis: Doxycycline 200 mg weekly may have a role.

CHRONIC LIVER DISEASE (CIRRHOSIS OF LIVER)

CHIEF COMPLAINTS

- Swelling of abdomen for … months
- Abdominal discomfort and a sense of heaviness for … months
- Scanty micturition for … months
- Weakness, malaise, loss of appetite for … months.

HISTORY

History of present illness: The patient states that he was reasonably well about … months back. Since then, he has been suffering from gradual swelling of his abdomen which has increased progressively over the last few days. It is not associated with abdominal pain, but there is discomfort and sense of heaviness. He also complains of scanty micturition, generalized weakness, malaise and loss of appetite for … months. There is no history of hematemesis, melena or loss of consciousness. The patient does not give any history of fever, shortness of breath or cough, puffiness of the face, joint pain, skin rash, pigmentation etc. His bowel habit and sleep pattern are normal.

History of past illness: He suffered from jaundice … year back that lasted for about … months and then subsided. At that time, he took some herbal medications. There is no history of any injection, infusion, blood transfusion, IV drug abuse or sharing of needles.

Personal history

Family history

Drug and treatment history: Mention according to the statement of the patient.

GENERAL EXAMINATION

- The patient is ill looking and emaciated.
- Hepatic facies characterized by – pinched face, sunken eyes, hollowed temporal fossa, pinched up nose, malar prominence, muddy complexion of the skin, shallow and dry face with icteric conjunctiva (mention, if present).
- Mildly icteric and mildly anemic.
- Generalized pigmentation is present. There are few ecchymoses in upper limbs.
- Pitting pedal edema—present.
- Multiple spider angiomas are present over the upper part of chest and back.
- There is generalized clubbing, leukonychia (fingers and toes) and palmar erythema.
- Gynecomastia present.
- No koilonychia or cyanosis.
- No lymphadenopathy or thyromegaly.
- Dupuytren's contracture and flapping tremor are absent.
- Pulse—88/min.
- BP—110/75 mm Hg.
- Temperature—99°F.
- Respiratory rate—18/min.

SYSTEMIC EXAMINATION

Gastrointestinal System

- Lips, gums, teeth, tongue and oral cavity—normal.

Abdomen

Inspection:

- The abdomen is distended, flanks are full
- Umbilicus—everted
- Visible superficial veins with normal flow (away from umbilicus)
- There is no visible peristalsis, no scar mark.

Palpation:

- Liver—not palpable.
- Spleen is palpable, 4 cm from the left costal margin in anterior axillary line towards the right iliac fossa. The surface is smooth, firm in consistency, nontender.
- Kidneys—not ballotable.
- Testes—both testes are atrophied.
- Fluid thrill—present.

Percussion: Shifting dullness present.
Auscultation: No abnormality detected.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr. …, 45 years old, businessman, normotensive, nondiabetic, nonsmoker, nonalcoholic, hailing from …, presented with gradual swelling of abdomen for … months which has increased progressively over the last few days. It is not associated with abdominal pain, but there is discomfort and sense of heaviness. He also complains of scanty micturition, generalized weakness, malaise and loss of appetite for … months. There is no history of hematemesis, melena or loss of consciousness. The patient does not give any history of fever, shortness of breath or cough, puffiness of the face, joint pain, skin rash, pigmentation, etc. His bowel habit and sleep pattern are normal.

In the past medical history, he suffered from jaundice … year back that lasted for about … months and then subsided. At that time, he took some herbal medications. There is no history of any injection, infusion, blood transfusion, I/V drug abuse or sharing of needles. There is no family history of such illness. He was treated with frusemide, vitamins, antacids, etc.

On examination – general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is cirrhosis of the liver with portal hypertension

Q. Why portal hypertension?

A. Because, the patient has:

- Splenomegaly
- Ascites.

Note Other features of portal hypertension are (mention if asked):

- Collateral circulation, esophageal varices, hemorrhoid, venous hum (between xiphisternum and umbilicus, called Cruveilhier Baumgarten syndrome).
- Portosystemic encephalopathy.
- Endoscopy shows esophageal varices.

Q. What are the other **possible causes** of ascites in this case?

A. As follows:

- Intra-abdominal malignancy with peritoneal metastasis
- Lymphoma
- Tuberculous peritonitis
- Chronic constrictive peritonitis
- Nephrotic syndrome.

Q. What **investigations** should be done in this case?

A. As follows:

1. LFT (total protein with A/G ratio, and prothrombin time are the two most important tests for CLD. Others are serum bilirubin, SGPT and alkaline phosphatase).
2. USG of whole abdomen (in cirrhosis, liver may be small, shrunken, coarse and high echogenic texture, splenomegaly, ascites and dilated portal vein).
3. Viral markers for HBV (HBsAg, HBeAg, anti-HBc) and for HCV (anti-HCV).
4. Proctoscopy (to test for hemorrhoid).
5. Endoscopy (to see esophageal varices).
6. CT scan of hepatobiliary system may be performed.
7. Liver biopsy under USG control (confirmatory).
8. If CLD is due to other cause, investigation should be done accordingly, such as:
   - If hemochromatosis is suspected serum iron, TIBC and ferritin.
   - If PBC is suspected anti-mitochondrial antibody and other auto-antibodies.
   - In younger age, if Wilson's disease is suspected—serum copper, ceruloplasmin and urinary copper.
   - If α_1 antitrypsin deficiency—serum α_1 antitrypsin (which is sometimes associated with liver disease and also pulmonary emphysema, particularly in smokers).
9. Test for ascitic fluid (cytology, biochemistry, SAAG).
10. Other routine investigations:
    - CBC, ESR
    - Serum urea and creatinine, electrolytes, blood sugar.

Q. What investigations are done to see the **severity** of liver disease?

A. As follows:

- Serum albumin—if < 28 g/L, outlook is poor.
- Prothrombin time—prolong PT indicates severe liver disease.
- Serum electrolytes—low sodium indicates severe liver disease due to a defect in free water clearance.
- Serum creatinine—high creatinine > 130 μmol/L is a marker of worse prognosis.

RELATED QUESTIONS AND ANSWERS

Q. What is chronic liver disease (**CLD**) and **chronic liver failure?**

A. As follows:

- CLD is defined as liver disease for 6 months or longer.
- Chronic liver failure means functional capacity of liver cannot be maintained, and is characterized by encephalopathy and/or ascites. When chronic liver failure occurs, it is called decompensated liver disease.

Q. What is **cirrhosis** of liver? What are the **types?**

A. Cirrhosis of liver is a chronic diffuse liver disease characterized by destruction of liver cells with fibrosis, distortion of normal liver architecture and nodular regeneration due to proliferation of surviving hepatocytes. Three types of cirrhosis are:

- Micronodular—regenerative nodule is usually small, 1 mm size, involving every lobule, also called Laennec's cirrhosis and is common in alcoholics.
- Macronodular—large nodules, common in post-necrotic cirrhosis, found in HBV.
- Rarely, mixed type (micronodular and macronodular).

Q. What are the **causes** of cirrhosis of liver?

A. As follows:

- Chronic viral hepatitis (B or C or B and D).
- Chronic alcoholism.
- Nonalcoholic fatty liver disease (NAFLD).
- Immunological (autoimmune liver disease and primary sclerosing cholangitis).
- Biliary (PBC, secondary biliary cirrhosis and cystic fibrosis).
- Genetic (hemochromatosis, Wilson's disease and α_1-antitrypsin deficiency).
- Budd-Chiari syndrome.
- Drugs—methotrexate.
- Idiopathic or cryptogenic.

Q. What are the **commonest causes** of cirrhosis of liver?

A. Viral infection (B and C), alcohol, nonalcoholic fatty liver disease. In young patient with cirrhosis, Wilson's disease may be an important cause.

Q. What are the **stigmata** of CLD or cirrhosis?

A. As follows:

1. In hands:
   - Palmar erythema (liver palm)
   - Dupuytren's contracture
   - Leukonychia
   - Clubbing
   - Flapping tremor
   - Others—scratch mark, spider angioma, xanthoma, pigmentation, jaundice and cyanosis.
2. In face:
   - Parotid enlargement (bilateral)
   - Xanthelasma
   - Spider angioma (also in neck, arm, forearm, hand and any part above the nipple line)
   - Pigmentation
   - Hepatic facies

- Jaundice
- Cyanosis.

3. In chest and abdomen:
   - Gynecomastia (also spider angioma)
   - Less hair in chest or body, scanty axillary (also pubic hair)
   - Engorged veins in chest and also abdomen (due to portal hypertension)
   - In abdomen—splenomegaly, ascites, engorged veins and Caput Medusae
   - Testis—small and atrophied.
4. Others:
   - Generalized pigmentation (any CLD can cause pigmentation, but commonly in hemochromatosis and primary biliary cirrhosis)
   - Purpura and ecchymosis.

Note The following findings are common in alcoholic cirrhosis:

- Bilateral parotid enlargement
- Florid spider angioma
- Dupuytren's contracture
- Gynecomastia
- Testicular atrophy with loss of body hair.

Q. What specific findings will you see in CLD or cirrhosis of liver in a young patient?

A. As follows:

- The eyes should be examined to see KF ring for Wilson's disease.
- In lung, signs of emphysema may be present in case of α_1-antitrypsin deficiency.

Q. What are the signs of portal hypertension?

A. As follows:

- Splenomegaly (single definite sign, mild in adult but marked splenomegaly in childhood and adolescent). Hypersplenism is common (there may be pancytopenia).
- Ascites.
- Collateral circulation, esophageal varices, hemorrhoid, venous hum (between xiphisternum and umbilicus called Cruveilhier Baumgarten syndrome).
- Portosystemic encephalopathy.
- Endoscopy shows esophageal varices.

Note Remember the following points:

- Normal portal pressure is 2 to 5 mm Hg. If it is > 12 mm Hg, then sign and symptoms, also complications may develop.
- Portal vein is formed by fusion of superior mesenteric vein and splenic vein.
- In adults, cirrhosis of liver is the common cause of portal hypertension.
- In children, extrahepatic portal vein obstruction is the common cause.

Q. What are the signs of decompensated cirrhosis?

A. As follows:

- Ascites
- Increasing jaundice
- Hepatic encephalopathy
- Portal hypertension with variceal bleeding
- Worsening liver function (prolonged PT and low albumin).

Q. What are the **complications** of cirrhosis of liver?

A. As follows:

- Portal hypertension with rupture of esophageal varices (causing hematemesis and melena).
- Portosystemic encephalopathy (hepatic precoma) and hepatic coma
- Hepatorenal syndrome
- Hepatopulmonary syndrome
- Hepatoma
- Spontaneous bacterial peritonitis (SBP).

Q. What are the **bad prognostic signs** of CLD?

A. As follows:

1. Clinical:
   - Increasing jaundice
   - Ascites
   - Portosystemic encephalopathy.
2. Laboratory:
   - Increasing bilirubin
   - Sodium < 120 mmol/L (not due to diuretic)
   - Falling plasma albumin < 30 g/L
   - Prothrombin time – prolonged.

Note Remember the following:

Child-Pugh score can be used to see prognosis.

Child-Pugh classification of prognosis in cirrhosis

Score	1	2	3
Encephalopathy	None	Mild	Marked
Bilirubin (μmol/L) » PBC or sclerosing cholangitis » Other causes of cirrhosis	 <68 <34	 68 to 170 34 to 50	 >170 >50
Albumin (g/L)	>35	28 to 35	<28
Prothrombin time (seconds prolonged)	<4	4 to 6	>6
Ascites	None	Mild	Marked

Add the individual scores: <7 = Child's A, 7 to 9 = Child's B, >9 = Child's C

Child-Pugh grade	Survival (%)			Hepatic deaths (%)
	1 year	5 years	10 years	
A	82	45	25	43
B	62	20	7	72
C	42	20	0	85

Q. What is spontaneous bacterial peritonitis (SBP)?

A. It means infection of ascitic fluid in a patient with cirrhosis of liver, in the absence of any apparently primary source of infection. SBP may develop in 8% cases (may be as high as 20 to 30%). It is usually by single organism (monomicrobial). Source of infection cannot be determined usually (so it is named as spontaneous). It is suspected in any patient with ascites who clinically deteriorates.

Causes of SBP: The infective organism gain access to the peritoneum by hematogenous route or mesenteric lymphatics. Most organisms are enteric origin, mainly *Escherichia coli, Klebsiella*, *Haemophilus*, *Enterococcus*, other enteric Gram-negative organisms, rarely *Pneumococcus* and *Streptococcus*. Anaerobic bacteria are not usually associated with SBP.

Clinical features: In a patient with cirrhosis and ascites, may present with sudden abdominal pain, rebound tenderness, absent bowel sounds and fever. There may be increasing ascites, not responding to diuretic. Abdominal signs may be mild or absent in one-third patients. In these patients, hepatic encephalopathy and fever are the main features.

Ascitic fluid in SBP shows the following:

- Fluid looks cloudy (exudative is with high protein and low sugar).
- Neutrophil counts of fluid > 250/mm^3.
- Ascitic fluid culture in blood culture bottles gives the highest yield of organisms. C/S may be negative.

Treatment of SBP: Pending the result of culture, if neutrophil in ascitic fluid is high, treatment should be started immediately as follows:

- Broad-spectrum antibiotics – cefotaxime 2 g 8 to 12 hourly for at least 5 days.
- Ceftriaxone plus amoxyclav is an alternative.
- Intravenous albumin may reduce mortality.

Prognosis and prevention of SBP: Mortality is 10 to 15%. SBP is an indication for referral to liver transplantation center. Recurrence is common in 70% case within one year. This can be prevented by norfloxacin 400 mg daily or ciprofloxacin 500 mg once or twice daily or co-trimoxazole (1 double strength tablet, 5 days/week). In any patient with acute variceal bleeding, risk of bacterial peritonitis may be reduced by giving injection ceftriaxone 1 g daily or oral norfloxacin. Also, patient with high risk group in cirrhosis (low albumin, increased PT, low ascitic fluid albumin), norfloxacin may be used to prevent bacterial peritonitis.

Note

Occasionally, there may be secondary bacterial infection other than SBP. To differentiate from SBP, the following features in ascitic fluid may suggest secondary bacterial infection -

- Neutrophil > 10,000 (very high).
- Total protein – very high (> 1 g/dL is against SBP, highly suggestive of secondary bacterial infection).
- Glucose < 50 mg%.
- Ascitic LDH > serum LDH.
- Presence of multiple organisms in culture.

Q. What is hepatorenal syndrome?

A. If a patient with cirrhosis and ascites develops renal failure, it is called hepatorenal syndrome. It occurs in 10% cases and is of two types:

- Type 1 hepatorenal syndrome is characterized by progressive oliguria and rapid rise in serum creatinine. There is no proteinuria, urine sodium excretion is low, < 10 mmol/day and urine/plasma osmolality ratio is > 1.5. Prognosis is poor, without treatment median survival is < 1 month.
- Type 2 hepatorenal syndrome occurs with refractory ascites, characterized by moderate and stable increase of serum creatinine. Prognosis is better.

Mechanism of hepatorenal syndrome: Initially there is vasodilatation possibly due to nitric oxide, leading to hypotension. As a result, there is high plasma renin, aldosterone, norepinephrine and vasopressin, leading to vasoconstriction of the renal vasculature. This causes increased preglomerular vascular resistance. There is reduced GFR and also sodium and water retention.

Other mediators like eicosanoids may also be involved.

Renal failure is functional and tubular function is intact. Hepatorenal syndrome may be precipitated by excess diuretic therapy, NSAIDs, diarrhea or paracentesis and infection especially spontaneous bacterial peritonitis.

Treatment:

- Diuretic should be stopped.
- Hypovolemia should be corrected, preferably with albumin.
- Terlipressin or noradrenaline with intravenous albumin may be used.
- Liver transplantation is the best option.

Q. What is **hepatopulmonary syndrome?**

A. Hepatopulmonary syndrome is defined as hypoxemia occurring in patient with advanced liver disease. PaO_2 is < 9.3 κPa or 70 mm Hg. It is due to intrapulmonary vascular dilatation with no evidence of primary pulmonary disease. Hypoxia is due to intrapulmonary arteriovenous communication.

The patient has features of cirrhosis with clubbing, spider angioma and cyanosis. Most patients have no respiratory symptoms. But with more severe disease, the patient is dyspnoic on standing. There is a characteristic reduction of arterial oxygen saturation on standing.

Transthoracic echo shows intrapulmonary shunting (which is probably due to nitric oxide over production) and arterial gas analysis shows low oxygen saturation. HRCT may be helpful for detecting dilated pulmonary vessels.

Liver transplantation is indicated in hepatopulmonary syndrome. Features improve after liver transplantation.

Q. What is **portopulmonary hypertension?**

A. It is defined as pulmonary hypertension and cirrhosis of the liver with portal hypertension. There is normal pulmonary artery wedge pressure. It occurs in 1 to 2% cases of cirrhosis. It is caused by vasoconstriction and obliteration of the pulmonary arterial system due to circulating vasoconstrictors particularly endothelin 1. This leads to breathlessness and fatigue. It may respond to medical therapy.

Severe pulmonary hypertension is a contraindication for liver transplantation.

Read the following Topics in Relation to CLD

Portosystemic anastomosis (between portal and systemic veins). Sites are:

1. At the lower end of oesophagus—esophageal tributaries of left gastric vein (portal) communicate with esophageal tributaries of hemiazygos veins (systemic).
2. At the lower end of rectum and anal canal—superior rectal vein (portal) communicates with middle and inferior rectal veins (systemic).

3. Anterior abdominal wall (around the umbilicus):
   - Paraumbilical vein (portal) communicates with systemic veins in epigastric, lateral thoracic, intercostal and lumbar veins.
   - Paraumbilical vein (portal) communicates with diaphragmatic veins (systemic) by a number of small veins, called accessory portal system of Sappey.
4. At bare area of liver—portal radicles of liver communicates with diaphragmatic veins (systemic).
5. At retroperitoneal site—the splenic and colic veins (portal) communicate with left renal veins and other tributaries of IVC by small veins, called veins of Retzius.
6. At the fissure for ligamentum venosum, rarely, persistent ductus venosus establishes direct porto-caval anastomosis (in fetal life, left branch of portal vein at the porta hepatis communicates with IVC via ductus venosus. After birth, ductus venosus is fibrosed to form ligamentum venosum).

Spider angioma

It consists of central arteriole from which numerous capillaries radiate, looks like spider legs. Size varies from pinhead to 1 to 2 mm (sometimes 1 to 2 cm). These are found along the area of SVC, commonly in neck, face, chest and dorsum of hand and above the nipple lines, cause of which is not known. It blanches on pressure, may pulsate if large. Better seen with glass slide or pinhead.

Causes of spider angioma:
1. Physiological:
   - Rarely present in normal people (2%), one to two in number, common in children. If > 2 in number, it is usually pathological, especially in male than female.
   - Pregnancy (usually in the third trimester, disappears after 2 months of delivery).
2. Pathological:
   - CLD, commonly in alcoholic cirrhosis (disappears with improvement of liver function, appearance of new spider indicates deterioration of liver function).
   - Viral hepatitis (transient).
   - Estrogen therapy and estrogen-containing oral contraceptive pill.
   - Rarely, in rheumatoid arthritis, thyrotoxicosis.

Mechanism of spider angioma:
- Due to hyperdynamic circulation
- Excess estrogen level (due to reduced metabolism by the liver).

Differential diagnoses of spider angioma:
- Purpura (spontaneous bleeding into skin and mucous membrane, does not blanch on pressure and there is progressive color change)
- Hereditary hemorrhagic telangiectasia
- Campbell de Morgan spots
- Venous stars.

Venous stars

These are 2 to 3 cm lesions that occur on dorsum of foot, leg, back and lower chest. Caused by elevated venous pressure and are usually found overlying the main tributary of large veins. Do not blanch on pressure and blood flow is from periphery to the center of lesion (opposite to spider angioma).

Palmar erythema (liver palm)

Redness in thenar and hypothenar eminence and pulp of fingers. Blanches on pressure. With glass slide, flushes synchronously with pulse. Causes of palmar erythema:

1. Physiological:
   - Normal people, may be familial
   - Pregnancy.
2. Pathological:
   - CLD (commonly alcoholic cirrhosis)
   - Thyrotoxicosis
   - Polycythemia
   - Prolonged rheumatoid arthritis
   - Chronic leukemia
   - Febrile illness.

Mechanism of palmar erythema in CLD:
- Hyperdynamic circulation
- Probably, high estrogen (controversial).

Q. Why **itching** in liver disease?

A. Common in primary biliary cirrhosis and obstructive jaundice. Actual cause is unknown, probably due to upregulation of opioid receptors and increased levels of endogenous opioids.

Q. What are the **vitamin K-dependent** coagulation factors?

A. Factors II, VII, IX and X (which are produced by liver).

Q. In which liver disease, vitamin K therapy is **helpful?**

A. Usually in obstructive jaundice, as bile salt is necessary for absorption of vitamin K. Less or not helpful in parenchymal liver disease, as vitamin K is not used or less used by the diseased liver.

Note Remember the following:

PT depends on factors I, II, V, VII and X. In CLD, the PT is prolonged, when these factors fall below 30%.

Flapping tremor (asterixis)

It is characterized by irregular, flexion-extension movement of wrist and MCP joints, abduction-adduction of fingers, produced by dorsiflexion of wrist and spreading of the fingers. It is called flapping, because of resemblance to a bird flapping its wings. It is demonstrated by asking the patient to stretch out arms in front, separate the fingers, dorsiflexion of wrist with fixed forearm by the examiner's hand.

If it is present, there is:
- Jerky, irregular, flexion-extension of wrist and MCP joint (looks like goodbye).
- Accompanied by lateral movement of fingers or abduction-adduction of fingers.

Features of flapping tremor:
- It is absent at rest, produced by intentional movement, maximum at sustained posture.
- Usually bilateral, and not necessarily synchronous on each side.
- Disappears during coma.
- Occasionally arms, face, neck, tongue, jaw and eyelids are involved.

Causes of flapping tremor:
- Hepatic encephalopathy (the commonest cause)
- Severe cardiac failure
- Respiratory failure

- Renal failure
- Other causes (rare)—cerebrovascular accident (CVA), drug toxicity (phenytoin and barbiturate), acute focal parietal or thalamic lesion (vascular) and hypoglycemia.

Mechanism of flapping tremor in CLD:

- It is due to impaired inflow of joint position sense and other afferent informations to the brainstem reticular formation, resulting in rhythmical lapse of postural muscle tone.

Q. What is **fetor hepaticus?**

A. It is a bad smell (slightly fecal) of breath, like that of dead mouse, due to methylmercaptan, exhaled in breath. It is derived from amino acid methionine, which is not deaminated by the diseased liver. Methylmercaptan is of intestinal origin (reduced by defecation or use of antibiotics). Presence of fetor hepaticus indicates severe hepatocellular failure with collateral circulation.

Q. What are the **causes of bad breath (halitosis)?**

A. As follows:

- Hepatic precoma (called fetor hepaticus, like dead mouse).
- Diabetic ketoacidosis (sweetish due to ketone body).
- Uremia (fishy ammoniacal).
- Lung abscess with anaerobic infection (may be foetid).
- Others—faulty oral hygiene and alcoholism.

Dupuytren's contracture

It is characterized by thickening, fibrosis and shortening of superficial palmar fascia, causing flexion contracture of fingers. The ring and little fingers are commonly affected and also other fingers are affected. Inability to extend the fingers fully is associated with puckering of the skin and presence of palpable nodules. Usually painless, bilateral, age related, 5 times common in male than in female, often familial with dominant inheritance. It may affect the sole of foot also. It is slowly progressive and fasciotomy is seldom necessary.

Causes are:

- Cirrhosis of liver (commonly alcoholic)
- Alcoholism (itself, not by cirrhosis)
- Prolonged antiepileptic drug (phenytoin)
- Manual worker (gardener) and chronic vibration injury
- Traumatic
- Familial (as autosomal dominant, associated with Garrod's patch on dorsum of hand)
- Diabetes mellitus (diabetic cheiroarthropathy, confuses with systemic sclerosis)
- Peyronie's disease
- Idiopathic (in many cases).

Q. What is **diabetic cheiroarthropathy?**

A. It is a complication of long-standing diabetes mellitus, in which skin of the dorsum of fingers is tight, waxy, shiny and depigmented with joint stiffness and flexion deformities of many fingers. Usually painless, limitation of joint movement may be present, sometimes painful. There is inability to extend the MCP or IP (interphalangeal) joint of at least one finger bilaterally. This can be better detected by prayer sign. Occasionally, affects the wrist and shoulders. Cause of cheiroarthropathy is unknown. There is probably cross-linking and thickening of collagen. It occurs in any type of diabetes mellitus. It is confused with systemic sclerosis. There is no specific treatment.

Portosystemic Encephalopathy (PSE) or Hepatic Precoma

Definition: Portosystemic encephalopathy is a state of neuropsychiatric syndrome due to biochemical disturbance of brain function, caused by chronic liver disease. It may progress from confusion to coma. Liver failure and portosystemic shunting are two important factors for PSE. It is reversible, does not cause marked pathological change in brain and may have cerebral edema in advanced stage.

Mechanism of PSE: It is due to the nitrogenous substances of gut origin that enters into the brain. Normally, these substances are metabolized by healthy liver. In diseased liver, these are not metabolized and enters into the brain through portosystemic shunt.

The PSE can occur in portal hypertension with cirrhosis, also after surgery like portocaval or TIPS shunt.

Nitrogenous substances are:

- Ammonia (produced by intestinal bacteria, which breakdown protein).
- Gamma aminobutyric acid (GABA).
- Amino acid, mercaptan, fatty acids and octopamine, which act as false neurotransmitters.

Factors precipitating PSE (by increasing the availability of nitrogenous substance):

- High dietary protein
- Gastrointestinal bleeding
- Constipation
- Drugs (sedative, antidepressants and diuretics)
- Infection including spontaneous bacterial peritonitis
- Fluid and electrolyte imbalance (hypokalemia)
- Trauma
- Surgery (shunt surgery, TIPSS or other surgery)
- Paracentesis (> 3 to 5 L)
- Development of hepatocellular carcinoma.

Clinical features of PSE (remember the mnemonic DPIST-F)

- **D: Disturbance** of consciousness (confusion, disorientation, drowsiness, delirium, stupor and later coma).
- **D: Disorder** of sleep (hypersomnia, inversion of sleep and more sleep in daytime).
- **P: Personality** change (childish behavior, abnormal behavior, apathy, irritability).
- **I: Intellectual** deterioration, from simple mathematical calculation to organic mental function. Earliest is constructional apraxia (see below).
- **S: Speech** disturbance (slow, slurred, monotonous and dysphasia) and sleep inversion (daytime sleeping).
- **T: Tremor** (flapping tremor).
- **F: Fetor** hepaticus (sweet musty odor in breath).

Other features are convulsion, exaggerated reflex, extensor plantar response and clonus. Rarely, chronic hepatic encephalopathy may be associated with cerebellar dysfunction, Parkinsonism, spastic paraplegia and dementia.

Q. What are the **differential diagnoses** of PSE?

A. As follows:

- Intracranial bleeding (subdural, extradural hematoma)
- Drug or alcohol intoxication

- Delirium tremens (alcohol withdrawal)
- Hypoglycemia
- Wernicke's encephalopathy
- Primary psychiatric disorder
- Wilson's disease
- Postictal state.

Q. How to **diagnose** PSE in early stage?

A. By EEG, which shows diffuse slowing in frequency of normal α range (8 to 13 Hz) to δ range (1.5 to 3 Hz). However, diagnosis is mostly clinical.

Q. How to **treat** PSE?

A. As follows:

- Possible precipitating factors should be identified and avoided (drugs, constipation, electrolyte imbalance, bleeding).
- **No** sedative and **no** diuretic. No protein restriction is recommended.
- Nutrition—glucose (300 to 400 g/day) orally. If the patient cannot take by mouth, then IV should be given.
- Lactulose—15 to 30 mL 8 hourly (bowel should move at least twice daily). If the patient is unable to take lactulose by mouth, it can be given per rectally (300 mg lactulose in 700 mL saline or sorbitol as retention enema). Lactitol is an alternative to lactulose.
- Low bowel wash (if no response to lactulose, then enema).
- Gut sterilizer—metronidazole (200 mg 8 hourly) or neomycin 1 to 4 g, 4 to 6 hourly (it is ototoxic, less or not used). Rifaximin 400 mg TDS orally is more preferable (not absorbed).
- Correction of electrolyte imbalance (especially hypokalemia).
- Control of infection by antibiotic.
- It is suggested that eradication of *H. pylori* which is ammonia producing may help (not proved).
- Chronic or refractory hepatic encephalopathy is an indication for liver transplantation.
- Other treatment—Zinc deficiency should be corrected, if present.
- If the patient is agitated – oxazepam (10 to 30 mg) may be given by mouth.
- Other therapy includes flumazenil, a benzodiazepine receptor antagonist (may help in some cases).

Q. What is the **mode of action** of lactulose?

A. Lactulose is a non-absorbable disaccharide, reaches the colon intact and is metabolized by colonic bacteria to lactic acid. It acts in the following way:

- Osmotic laxative.
- Lactic acid reduces pH of colonic contents, inhibits ammonia-producing colonic bacteria and reduces ammonia absorption by converting NH_3 to NH_4, which is not absorbed.
- Promotes incorporation of nitrogen into bacteria.

Q. What is **fulminating hepatic failure?**

A. It is a clinical syndrome of encephalopathy characterized by confusion, stupor and coma, resulting from sudden severe impairment of hepatic function, occurring within 8 weeks of onset in the absence of pre-existing liver disease. It is also called acute liver failure. It may be hyperacute (< 7 days), acute (within 8 to 28 days) or subacute (29 days to 12 weeks), between the onset of jaundice and encephalopathy.

The two **commonest causes** are viral hepatitis (commonly B and E, and rarely A) and paracetamol toxicity. Other causes are acute fatty liver in pregnancy, Wilson's disease, following shock and rarely extensive malignancy of liver.

Clinical features are similar to PSE.
Treatment is also similar to PSE. Liver transplantation may be considered.

Q. What is **constructional apraxia?** How to **test** for it?

A. Constructional apraxia means inability to perform a known act in the absence of any motor or sensory disturbance. It is tested in the following way (patient will be unable to do):

- Ask the patient to draw a star.
- Writing disturbance (unable to write or disturbance of writing).
- Ask the patient to make triangle with three match sticks or ask to lighten the cigarette by match stick.
- Reitan's trail making test (it is the ability to join or connect the numbers serially with a pen in a certain fixed time). It becomes prolonged in PSE.

Brief Discussion about Ascites

Q. What are the **causes** of abdominal distension?

A. Fluid, fat, flatus, feces and fetus (5F).

Q. How to **confirm** ascites clinically?

A. By eliciting shifting dullness, also fluid thrill (which is present in tense ascites).

Q. What is **ascites?** How much **fluid** is required to detect ascites?

A. It is the pathological accumulation of free fluid in peritoneal cavity. Usually, 2 liters fluid is necessary to detect clinically (at least 1 liter is necessary, even in thin person). Pleural effusion may be present in 10% cases with ascites, usually on the right side, mostly small, occasionally massive and unusual on left side.

Note Remember the following:

Normally, little amount of fluid is present in peritoneal cavity. In a female, up to 20 mL may be present, which varies with menstruation.

Q. What are the **causes** of ascites?

A. As follows:

1. Liver diseases: Cirrhosis of liver with portal hypertension, hepatoma with secondary inperitoneum, Budd-Chiari syndrome.
2. Abdominal causes: Intra-abdominal malignancy with peritoneal metastasis (such as carcinoma of kidney, stomach, colon and ovary).
3. Peritoneal causes: Peritonitis (tuberculous or pyogenic) and secondaries in the peritoneum.
4. Cardiovascular: Chronic constrictive pericarditis (early ascites) and CCF (ascites occurs later).
5. HypoproteinemiaL: Nephrotic syndrome, malnutrition and malabsorption.
6. Others:
   - Collagen disease (SLE and polyarteritis nodosa)
   - Lymphoma and leukemia
   - Meig's syndrome (ovarian fibroma, ascites and right-sided pleural effusion)
   - Acute pancreatitis
   - Myxedema
   - Chylous ascites.

Common causes of ascites:

- Cirrhosis of liver with portal hypertension (commonest cause, in 80% cases).
- Intra-abdominal malignancy with peritoneal metastasis (usually ovarian and gastrointestinal tract malignancy).
- Tuberculous peritonitis.

Ascites may be exudative or transudative:

1. Transudative causes (protein < 25 g/L):
   - Cirrhosis of liver with portal hypertension
   - Nephrotic syndrome
   - CCF
   - Meig's syndrome
   - Other causes of hypoproteinemia (malnutrition and malabsorption).
2. Exudative causes (protein > 25 g/L):
   - Peritonitis (TB and pyogenic)
   - Malignancy
   - Collagen disease
   - Myxedema
   - Budd-Chiari syndrome
   - Others are acute pancreatitis and chylous ascites.

Causes of hepatomegaly with ascites:

- Hepatoma with secondary in the peritoneum
- Chronic constrictive pericarditis
- Lymphoma
- Budd-chiari syndrome
- Alcoholic hepatitis
- Secondary in the liver with peritoneal carcinomatosis (disseminated malignancy).

Causes of splenomegaly with ascites:

- Cirrhosis of liver with portal hypertension
- Collagen disease (SLE)
- Lymphoma
- Leukemia
- Disseminated TB.

Causes of hemorrhagic ascites:

- Traumatic
- Malignancy
- Ruptured ectopic pregnancy
- Acute hemorrhagic pancreatitis
- Rupture of spleen
- Any cause of bleeding disorder
- Excess anticoagulant
- Occasionally, tuberculous peritonitis.

Causes of straw colored ascites:

- Tuberculous peritonitis
- Occasionally, cirrhosis of liver.

Causes of cloudy ascites:

- Pyogenic infection
- SBP.

Causes of chylous ascites (milky color, high triglyceride and Sudan staining of ascitic fluid shows fat cells):

- Trauma
- Filariasis
- Tuberculosis
- Malignancy.

Q. If the patient has cirrhosis and ascites, what does it indicate?

A. Decompensated cirrhosis with portal hypertension (a bad prognostic sign).

Q. What is the character of ascitic fluid in CLD?

A. Usually clear, may be straw or light green colored and transudative.

Q. What is the single best investigation to detect ascites?

A. Ultrasonography.

Q. What investigations are done in ascites?

A. As follows (according to suspicion of cause):

1. If CLD is suspected, LFT should be done (see CLD).
2. CBC (high ESR in TB and leuocytosis in pyogenic infection).
3. Chest X-ray (TB, cardiomegaly and chronic constrictive pericarditis).
4. USG of abdomen (to see liver, para-aortic lymph nodes, neoplasm and ovary in female).
5. Ascitic fluid tap for the following tests:
   - Naked eye examination (straw colored, blood-stained, serous and chylous).
   - Gram staining and C/S (in pyogenic infection).
   - Cytology (neutrophil > 250 cells/mm^3 or WBC > 500 cells/mm^3 in SBP, high lymphocyte in tuberculous peritonitis).
   - Biochemistry for protein and sugar shows high protein in exudative and low protein in transudative. Simultaneous serum albumin to see **serum ascitic albumin gradient** (see below).
   - If tuberculous peritonitis is suspected—ascitic fluid for ADA, AFB and mycobacterial C/S, PCR.
   - Exfoliative cytology (to see malignant cells).
6. Other tests (according to suspicion of causes).
   - For tuberculous peritonitis—MT.
   - Urine for proteinuria and serum total protein (nephrotic syndrome).
   - Ascitic fluid amylase in acute pancreatitis (> 1000 is highly suggestive).
7. CT scan or MRI (if any growth or mass suspected).
8. Laparoscopy and biopsy.

Serum Ascites Albumin Gradient (SAAG)

It is the difference of albumin between serum and ascitic fluid (calculated by serum albumin minus ascitic albumin, from samples taken at the same time). This gradient correlates directly with portal pressure. It is the single test to differentiate ascites due to portal hypertension from non-portal hypertension.

- If the gradient is > 1.1 g/dL, it indicates CLD with portal hypertension.
- If < 1, no portal hypertension (ascites is likely to be causes other than portal hypertension). It is 97% accurate.

Note Remember the following:

Ascites protein < 25 g/L and SAAG > 1.1 g/dL is usually suggestive of portal hypertension.

Q. What is the **mechanism of ascites** in cirrhosis of liver?

A. It is mainly due to renal reabsorption of sodium and water. Multiple factors are involved, such as:

1. Splanchnic vasodilatation is the main factor for ascites in cirrhosis of liver. This is mediated by vasodilator (mainly nitric oxide), that are released when the portal hypertension causes shunting of blood into the systemic circulation. Due to splanchnic vasodilatation, systemic arterial pressure falls, which leads to activation of renin-angiotensin mechanism with secondary aldosteronism, increased sympathetic activity, increased atrial natriuretic peptide secretion and altered activity of kallikrein-kinin system. All these produce salt and water retention.
2. Other factors are:
   - Combination of splanchnic vasodilatation and portal hypertension alters intestinal capillary permeability, leading to accumulation of fluid in peritoneal cavity.
   - Portal hypertension also increases local hydrostatic pressure and causes increased hepatic lymph production, which accumulates into the peritoneal cavity.
   - Low albumin causes low plasma osmotic pressure, which causes extravasation of fluid.
   - Failure to metabolize vasopressin by the liver, that causes further retention of fluid.

Q. How to **treat** ascites in cirrhosis of liver?

A. As follows:

1. Bedrest. It improves renal flow (in horizontal position) and increases diuresis.
2. Sodium and water restriction:
   - Sodium 88 mmol/day (no added salt), in severe case 40 mmol/day.
   - Water 0.5 to 1 L/day (fluid restriction is not necessary, unless sodium is <125 mmol/L).
   - Avoid salt containing and salt retaining diets and drugs (NSAIDs, steroid).
3. Monitor weight, abdominal girth and urinary output daily. Weight loss should be 0.5 to 1 kg/day (fluid loss should not be more than 1 liter daily).
4. Measure serum electrolyte and creatinine.
5. Few patients will respond to the above therapy.
6. If no response in 4 days with above therapy – diuretic should be given. Aldosterone antagonist such as spironolactone 100 to 400 mg/day is given. If no response, frusemide 40 mg daily is added. If still no response with spironolactone 400 mg plus frusemide 160 mg daily, it is considered as refractory ascites. Prolong use of spironolactone can cause painful gynecomastia and hyperkalemia. Eplerenone 25 mg once daily may be a suitable alternative (does not cause gynecomastia).
7. If no response or refractory ascites
   - Ensure that patient is not taking any salt or salt containing diet or drugs.
   - If serum protein (mainly albumin) is low, diuretics may not respond. Then IV salt-poor albumin followed by IV frusemide may be given. Occasionally IV dextran may be tried.
8. Paracentesis:
   - It is indicated if there is huge ascites with cardiorespiratory embarrassment or resistant ascites.
   - 3 to 5 L of fluid can be removed. It is safe provided circulation is maintained (no fear of hepatic encephalopathy, thought previously). Paracentesis is followed by IV albumin (6 to 8 g/L of

ascetic fluid removed, usually 100 mL of 20% human albumin solution for every 3 liter of ascitic fluid drained). Another plasma expander, such as dextran (8 g/L of ascitic fluid removed) or hemaccel (125 mL/L of ascitic fluid removed) may be used.

9. Other modes of treatment (in resistant ascites)
   - LeVeen shunt (peritoneovenous): A catheter is used with one-way valve to communicate between peritoneal cavity and internal jugular vein, which allows ascitic fluid to pass directly into the systemic circulation (rarely done now a days). Its main complications are infection, SVC thrombosis, pulmonary edema, bleeding from esophageal varices and DIC.
   - TIPSS (transjugular intrahepatic portosystemic stent shunt): A stent is placed between portal vein and hepatic vein in liver to make portosystemic shunt. It is carried out under radiological control via internal jugular vein. TIPSS is mainly used to reduce portal pressure and also variceal bleeding. Also, it is helpful to relieve resistant ascites, but does not prolong life. Following its use, frequency of paracentesis and diuretic dose is reduced. It can be done provided reasonable liver function without encephalopathy and minimal disturbance of renal function (TIPSS is ineffective with intrinsic renal disease). Hepatic encephalopathy may occur following TIPSS. This can be managed by reducing the shunt diameter.
   - Portosystemic shunt surgery: Portocaval or splenorenal shunt. Rarely done now a days. May cause encephalopathy.
10. Liver transplantation may be considered, if all measures fail.

Q. Will you **prefer** paracentesis or TIPSS in refractory ascites?

A. TIPSS is preferable than repeated paracentesis, as large volume of fluid and protein are lost in paracentesis. Moreover, TIPSS can improve survival also.

Q. If a patient of CLD with ascites complains of fever and abdominal pain, what is the likely **diagnosis?**

A. Spontaneous bacterial peritonitis (other causes of fever in CLD with ascites are secondary infection, hepatoma and excess pyrogen accumulation).

Q. What are the **complications** of ascites in CLD?

A. SBP and hepatorenal syndrome.

Q. If patient with CLD **deteriorates**, what are the possibilities?

A. As follows:
- Spontaneous bacterial peritonitis.
- Hepatocellular carcinoma.

LIVER ABSCESS

CHIEF COMPLAINTS

- Fever for … days
- Pain in the right upper abdomen for … days
- Loss of appetite, weight loss and malaise for … days.

HISTORY

History of present illness: According to the statement of the patient, he was reasonably well … days back. Since then, he has been suffering from continued high grade fever, highest recorded temperature is 104ºF. Fever is associated with chill and rigor, subsides only after taking paracetamol. He also complains of pain in the right upper abdomen for … days, which is dull aching in nature, radiates to right shoulder, more marked on lying in right lateral position and gradually increasing in severity. The patient also complains of marked weight loss, loss of appetite and malaise. His bowel and bladder habits are normal. There is no complaint of cough or hemoptysis.

He gives no recent history of cholangitis, appendicitis or abdominal trauma.

History of past illness: Nothing significant.

Family history: Nothing contributory.

Personal history: He is nonsmoker, nonalcoholic but chews betel leaves and nuts. He is a truck driver by occupation.

Drug history: He was treated with some antibiotics (mention the names or if not known, then tell that the patient cannot mention the names) and paracetamol without significant relief.

History of allergy: Nothing significant.

GENERAL EXAMINATION

- Ill looking, toxic and slightly emaciated
- Complexion is muddy
- No anemia, jaundice, cyanosis, edema, clubbing, koilonychia or leukonychia
- No lymphadenopathy or thyromegaly
- Pulse—110/min
- BP—110/75 mm Hg
- Respiratory rate—28/min
- Temperature—103°F.

SYSTEMIC EXAMINATION

Gastrointestinal System

- Lips, gums, teeth, tongue and oral cavity—normal.

Abdomen

Inspection:

- The abdomen is scaphoid in shape.
- Movement with respiration is restricted in the upper part of abdomen in right side.
- There is fullness of the intercostal spaces in right lower chest (also edema in right lower part of the chest with punch tenderness on the same site).

Palpation:

- There is tenderness over the right upper quadrant of the abdomen.
- Liver is palpable, … cm from the right costal margin in the mid-clavicular line, extremely tender, with a smooth surface and a sharp margin, soft in consistency. Upper border of the liver dullness is in the right 5th intercostal space and it is tender on percussion. There is no hepatic bruit.
- Spleen—not palpable.
- Kidneys—not ballotable.

Percussion:

- The percussion note is tympanic, ascites is absent.

Auscultation:

- Bowel sound—normal.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 42 years old, a truck driver, normotensive, nondiabetic, nonsmoker, nonalcoholic, hailing from …, presented with high grade continued fever, highest recorded 104ºF, for … days. Fever is associated with chill and rigor, subsides only after taking paracetamol. He also complains of pain in the right upper abdomen for … days, which is dull aching in nature, radiates to right shoulder, more marked on lying in right lateral position and gradually increasing in severity. The patient also complains of marked weight loss, loss of appetite and malaise. His bowel and bladder habits are normal. There is no complaint of cough or hemoptysis. He gives no recent history of cholangitis, appendicitis or abdominal trauma. He was treated with some antibiotics and paracetamol without significant relief. All the members in his family are in good health.

On examination – general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is liver abscess (probably pyogenic)

Q. What are your **differential diagnoses?**

A. As follows:

- Hepatocellular carcinoma
- Acute viral hepatitis
- Congestive cardiac failure
- Acute cholecystitis
- Acute cholangiohepatitis.

Q. Why not **viral hepatitis?**

A. As there is history of high fever with chill and rigor, enlarged tender liver which is associated with fullness of the intercostal spaces and edema in right lower part of the chest with punch tenderness. Also there is no jaundice and absence of prodromal symptoms of viral hepatitis like anorexia, nausea, vomiting, etc.

Q. Why not **congestive cardiac failure?**

A. In CCF, there should be triad of engorged and pulsatile neck veins, dependent edema and enlarged tender liver.

Q. Mention **one single investigation** for the diagnosis.

A. Ultrasonogram of hepatobiliary system.

Q. What **investigations** do you suggest in liver abscess?

A. As follows:

1. Full blood count (leukocytosis in pyogenic liver abscess).
2. LFT (usually high alkaline phosphatase, bilirubin is high in 25% cases. Aminotransferases are usually normal, may be slightly high).
3. Serum albumin (low), a fetoprotein.
4. Chest X-ray (PA view) shows raised right dome of diaphragm, small right-sided pleural effusion or collapse of right lung.
5. Blood for C/S (in pyogenic, positive in 30% cases. In some series, 50 to 80% cases may be positive).
6. Ultrasonogram of the upper abdomen.
7. CT scan (shows multiple bull's eye appearance) or MRI of the upper abdomen may be done.
8. If needed, USG-guided aspiration of pus for C/S (in pyogenic), and amoebae is rarely found in pus.
9. For amebic liver abscess:
   - Immunofluorescent antibody test (positive in 95%)
   - Indirect hemagglutination test (positive in 95%)
   - Complement fixation test
   - ELISA.

Q. What are the **types** of liver abscess?

A. Two types:

- Pyogenic liver abscess
- Amoebic liver abscess.

Q. What are the **causes of pyogenic** liver abscess? What are the **causal organisms?**

A. As follows:

- Ascending cholangitis in biliary obstruction (common bile duct) by stone, stricture and neoplasm, or spreads from empyema of gallbladder.
- Hematogenous:
  - Portal pyemia (mesenteric infection) from intra-abdominal sepsis, suppurative appendicitis and perforation.
  - Septicemia or bacteremia (along the hepatic artery).
- Direct extension from peripheral abscess.
- Trauma.
- Infection of liver tumor or cyst.

Causal organisms are *Escherichia coli*, *Streptococcus milleri*, *Streptococcus faecalis* or other *Streptococcus* species, *Staphylococcus aureus*, *Proteus vulgaris*, anaerobic organisms or bacteroids (from large bowel). Often the infection is mixed.

Q. How does the patient usually **present?**

A. As follows:

Pyogenic liver abscess:

- Fever, may be high with chill and rigor, malaise, anorexia and weight loss
- Abdominal pain, mainly in right upper abdomen, may radiate to right shoulder
- Pleuritic right lower chest pain (may be small pleural effusion, pleural rub)
- Jaundice is usually mild, may be severe in multiple abscesses causing biliary obstruction
- Sometimes, only pyrexia of unknown origin (PUO) may be present.

Note Remember the following:

Single abscess is common in right lobe, multiple abscesses are due to infection secondary to biliary obstruction. Immunocompromised patients are likely to develop liver abscess. Complications include rupture, secondary infection and septicemia.

Amebic liver abscess (common in right lobe, usually single):

- History of diarrhea or intestinal disease (absent in 50% cases)
- Fever (low grade) and pain
- Toxicity is absent.

Note Remember the following:

Amebic liver abscess is usually large, single and located in right lobe. Multiple abscesses may occur in advanced disease.

Q. What is the **character of pus** in amebic liver abscess?

A. Chocolate or anchovy sauce color.

Q. How to **treat liver abscess?**

A. As follows:

1. Pyogenic liver abscess:
   - Antibiotic (amoxicillin plus gentamicin) **plus** metronidazole. Cefoperazone (1 to 2 g IV 12 hourly) with metronidazole (500 mg every 6 hours) is an alternative. To be continued for 2 to 3 weeks, sometimes up to 6 weeks.
   - If larger (>5 cm) liver abscess or not responding to antibiotic therapy, then USG-guided aspiration should be done.
   - Surgical drainage is rarely needed. Even more rarely hepatic resection may be indicated for chronic persistent abscess or pseudotumor.
   - Treatment of the underlying cause like biliary obstruction.
2. Amoebic liver abscess:
   - Metronidazole 800 mg 8 hourly for 10 days or secnidazole 2 g daily for 5 days or tinidazole or ornidazole 2 g daily for 3 days.
   - Nitazoxanide 500 mg 12 hourly for 3 days.
   - Diloxanide furoate 500 mg 8 hourly for 10 days or paromomycin should be given for intestinal infection. This is given after the treatment of amoebic liver abscess.
   - USG guided aspiration should be done if abscess size is large (>5 cm), no response to medical therapy or threaten to burst.

Note Remember the following points:

- Mixed infections may be found in many cases. Hence, antibiotic plus anti-amoebic drugs may be needed.
- Abscess may rupture into pleural cavity, pericardial sac or peritoneal cavity. In such cases, immediate aspiration or surgical drainage is needed.

Q. What are the **differences** between pyogenic and amebic liver abscess?

A. As follows:

Points	Pyogenic	Amebic
1. Organism	*E. coli* and others	*E. histolytica*
2. History	Cholangitis, septicemia	Amebiasis
3. Symptoms	High fever with chill and rigor	Fever mild to moderate, no chill and rigor
4. Neutrophil leukocytosis	Common	Less
5. Ultrasonography	Multiple lesion	Usually single
6. Aspiration	Frank pus	Chocolate and anchovy sauce
7. Prognosis	More fatal (mortality 16%)	Less fatal (<1%)

PRIMARY BILIARY CIRRHOSIS

CHIEF COMPLAINTS

- Itching of the whole body for … months
- Distension of abdomen for … months
- Yellow coloration of eyes … months
- Scanty micturition for … months
- Weakness, nausea and loss of appetite for … months.

HISTORY

History of present illness: The patient states that she was reasonably well about … months back. Since then, she has been suffering from severe, generalized itching which is present throughout the day and night. It is not related to any food or any allergen. The patient also noticed gradual abdominal distention, which is progressively increasing over the last few days. It is not associated with any abdominal pain, but there is discomfort and sense of heaviness in the abdomen. She also complains of yellowish coloration of her eyes and high colored urine, which is gradually increasing. For the last … months, she has also noticed frequent passage of voluminous, pale colored, foul smelling stool, which is not mixed with blood or mucus. The patient is also experiencing loss of appetite, generalized weakness, nausea and occasional vomiting, gradual darkening of her skin and scanty micturition for … months. There is no history of hematemesis, melena, backache or bodyache or loss of consciousness.

History of past illness: There is no history of any injection, infusion, blood transfusion, IV drug abuse or sharing of needles.

Personal history: Mention according to the statement of the patient.

Family history: Nothing significant.

Menstrual history: She has amenorrhea for the last 3 years.

Drug and treatment history: Mention according to the statement of the patient.

GENERAL EXAMINATION

- Ill looking, emaciated and hyperpigmented.
- Moderately icteric, mildly anemic.
- Xanthelasma is present around both eyes (xanthomatous deposit may also be present in elbow, knee, buttock, hand crease and tendocalcaneus).
- There are multiple scratch marks.
- Spider angiomas are present on both front and back of upper chest.
- Generalized clubbing, leukonychia and palmer erythema are present.
- No koilonychia, cyanosis, lymphadenopathy or thyromegaly.
- Dupuytren's contracture and flapping tremor are absent.
- Pulse—88/min.
- BP—120/65 mm Hg.
- Temperature—97°F.
- Respiratory rate—18/min.

SYSTEMIC EXAMINATION

Gastrointestinal System

- Lips, gums, teeth, tongue and oral cavity—normal, but yellowish.

Abdomen

Inspection:

- The abdomen is distended, flanks are full, skin is hyperpigmented
- Umbilicus is everted
- Superficial veins are visible with normal flow (away from umbilicus).

Palpation:

- Liver is palpable, … cm from right costal margin in the mid-clavicular line, non-tender, soft in consistency, with smooth surface and sharp margin. There is no hepatic bruit.
- Spleen is palpable, … cm from the costal margin in left anterior axillary line, towards the right iliac fossa, surface is smooth, consistency is firm, nontender.
- Kidneys—not ballotable.
- Fluid thrill—present.

Percussion: Shifting dullness is present.

Auscultation: Normal.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mrs. …, 49 years old, housewife, normotensive, nondiabetic, nonsmoker, hailing from …, presented with severe, generalized itching for … months. It is present throughout the day and night and not related to any food or any allergen. The patient also noticed gradual abdominal distention, which is progressively increasing over the last few days. It is not associated with any abdominal pain, but there is discomfort and sense of heaviness in the abdomen. She also complains of yellowish coloration of her eyes and high colored urine, which is gradually increasing. For the last … months, she has also noticed frequent passage of voluminous, pale colored, foul smelling stool, which is not mixed with blood or mucus. The patient is also experiencing loss of appetite, generalized weakness, nausea and occasional vomiting, gradual darkening of her skin and scanty micturition for … months. There is no history of hematemesis, melena, backache or bodyache or loss of consciousness. She does not have any history of injection, infusion, blood transfusion, IV drug abuse or sharing of needles. There is no history of such illness in her family. She is amenorrhoic for the last 3 years. She was treated with frusemide, antacids, vitamins, etc. by local physicians.

On examination – general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is primary biliary cirrhosis with portal hypertension.

Q. What are your **differential diagnoses?**

A. As follows:

- Hemochromatosis
- Cirrhosis of the liver due to HBV or HCV infection.

Q. Why it is **PBC?**

A. Because, in this middle-aged lady, there is history of itching, jaundice, steatorrhea, ascites, pigmentation, xanthelasma, scratch marks and hepatosplenomegaly. All are suggestive of PBC.

Q. Why not this is a case of cirrhosis of liver?

A. In cirrhosis, usually there is no itching and liver is usually not enlarged (rather small and shrunken).

Q. Why not hemochromatosis?

A. Because it is not common in female, usually there is no itching, steatorrhea, xanthelasma, scratch mark, etc. in hemochromatosis.

Q. What **investigations** are done in PBC?

A. As follows:

- LFT (alkaline phosphatase is very high, may be the only finding. Aminotransferases may be elevated, but not more than 5 times of the upper limit. γ GT is also high. Serum total protein and albumin is reduced. There is marked rise of 5-nucleotidases activity).
- USG (hepatomegaly with cirrhotic change, splenomegaly and ascites).
- Anti-mitochondrial antibody is positive in 95% cases (M2 is specific). Other antibodies such as anti-smooth muscle antibody (35%) and antinuclear antibody (25%) may be present.
- Liver biopsy (There is infiltration of lymphocytes and plasma cells in portal tract, destruction of small bile duct with ductal proliferation, piecemeal necrosis and cirrhosis. Granuloma may be present in 40% cases).
- ERCP or MRCP (to rule out extrahepatic biliary obstruction in doubtful cases).
- Others—serum cholesterol (high) and serum immunoglobulin (IgM) is very high.

RELATED QUESTIONS AND ANSWERS

Q. What is **primary biliary cirrhosis?** What are the **causes?**

A. PBC is a chronic, progressive, cholestatic liver disease characterized by granulomatous destruction of interlobular bile ducts, inflammatory damage with fibrosis spreading from portal tract to liver parenchyma and eventual cirrhosis.

Causes: Actual cause is unknown. It is probably an autoimmune disease occurring in a genetically predisposed person, triggered by environmental factors like infections by retrovirus, bacteria including *E. coli* and mycobacteria. None are proved.

Q. What is **secondary biliary cirrhosis?**

A. When cirrhosis develops due to prolonged obstruction of the large biliary ducts. Causes are stone, strictures and sclerosing cholangitis.

Q. How the patient with PBC usually **presents?**

A. PBC is common in middle-aged (40 to 60 years of age) females. Common presentations are:

- May be asymptomatic. Incidental finding like isolated hepatomegaly on routine examination. High alkaline phosphatase in LFT.
- Pruritus may be the early feature, may precede jaundice by many months or years.
- Jaundice (usually with pruritus).
- Abdominal pain or discomfort.
- Malabsorption (steatorrhea).
- Malaise, weakness, loss of weight, hyperpigmentation.
- Others are hepatic osteodystrophy (characterized by bony pain or fracture due to osteoporosis or osteomalacia from malabsorption).

Q. Why itching in PBC?

A. Actual cause of itching is unknown, but probably it is due to upregulation of opioid receptors and increased level of endogenous opioids. This is why opioid antagonist (naltrexone) is used to control itching in PBC.

Q. What are the diseases associated with PBC?

A. PBC is an autoimmune disease, may be associated with other auto-immune diseases, such as:

- Sjogren syndrome
- Thyroid disease (hypothyroidism should be considered especially with fatigue)
- Systemic sclerosis
- Rheumatoid arthritis
- Renal tubular acidosis
- Dermatomyositis
- Addison's disease
- Membranous glomerulonephritis
- Fibrosing alveolitis.

Note Remember the following:

There is high incidence of celiac disease in PBC. It should be excluded when a patient presents with features of malabsorption.

Q. What is anti-mitochondrial antibody (AMA)?

A. It is an antibody directed against mitochondrial pyruvate dehydrogenase complex (PDC) of mitochondrial enzymes. There are 4 types of antigens (M_2, M_4, M_8 and M_9) of which M_2 is specific for PBC. Five M_2 specific antigens have been further identified, of which E_2 component of the pyruvate dehydrogenase complex is the major M_2 autoantigen.

AMA is present in 95% cases of PBC, detected by ELISA (>1:160). It may be positive in auto-immune hepatitis (20%). It is not related to severity and prognosis.

Q. What is the best indicator for prognosis in PBC?

A. Serum bilirubin (if >100 µmol/L, liver transplantation is indicated).

Q. What are the causes of granuloma in liver?

A. As follows:

- PBC
- Tuberculosis
- Sarcoidosis
- Brucellosis
- Parasitic (strongyloidiasis)
- Schistosomiasis
- Drug (phenylbutazone).

Q. How to treat this patient?

A. As follows:

- Urso-deoxycholic acid 10 to 15 mg/kg. (It improves bile flow, replaces toxic hydrophobic bile acid in the bile acid pool, reduces apoptosis of the biliary epithelium. It also improves LFT, slows down histological progress).

- For pruritus, cholestyramine is given, 4 to 16 g/day orally, usually with orange juice. Main dose (8 g) is given before and after breakfast (as duodenal bile acid secretion is more). Alternatively, rifampicin 300 mg/day or naltrexone (opioid antagonist) 25 mg/day up to 300 mg/day may be given. Naloxone is an alternative. In intractable itching, plasmapheresis or liver support device (molecular absorbent recirculating system—MARS) may be considered. Liver transplantation may be indicated in intractable pruritus.
- Vitamins A, D, K and calcium supplement, alfacalcidol (1 mg/day orally).
- If osteoporosis—Bisphosphonate (such as risedronate may be used).
- Liver transplantation should be considered in liver failure. Five years survival is over 80% but recurrence of PBC after transplantation occurs in one-third of cases at 10 years.

Note Remember the following points:

- Colchicine 0.6 mg orally twice daily and methotrexate 15 mg/weekly may be helpful in improving symptoms in some cases.
- Steroid improves biochemical and histological disease, but aggravates osteoporosis and other side effects and should not be used.
- Azathioprine, penicillamine and cyclosporine have no beneficial role.
- In asymptomatic patient, follow-up should be done.

Q. What are the **indications of liver transplantation** in PBC?

A. As follows:

- Advanced liver disease (increasing jaundice with serum bilirubin >100 μmol/L).
- Intractable pruritus.

Q. How **cholestyramine** works?

A. It is a chelating agent, acts by binding pruritogens in intestine and increase excretion in stool. It is ineffective in complete biliary obstruction.

Q. What is the **prognosis** of PBC?

A. As follows:

- Asymptomatic patients or patients presenting with pruritus—survive for more than 20 years.
- Once symptoms like jaundice develops, average survival is around 5 years (may be 7 to 10 years).

Q. What is the risk of **hepatobiliary malignancy** in PBC?

A. It is increased in PBC. Risk factors for malignancy are older age, male sex, prior blood transfusion and signs of cirrhosis and portal hypertension.

HEPATOMA

CHIEF COMPLAINTS

- Upper abdominal discomfort and feeling of a mass for … days
- Loss of appetite, weakness and weight loss for … days
- Distension of abdomen for … days.

HISTORY

History of present illness: According to the patient's statement, he was reasonably alright … days back. Since then, he is complaining of upper abdominal discomfort and occasional dull pain for … days. The pain is not associated with food intake or there is no radiation. This patient is also experiencing a mass in the upper abdomen which is painless but slowly increasing in size. For the last … days, he is also complaining of marked loss of appetite, marked loss of weight and extreme weakness, gradual distension of abdomen, and scanty micturition. His bowel habit is normal. There is no history of fever, vomiting, cough, etc.

History of past illness: The patient has suffered from jaundice 5 years back.

Personal history: He smokes about 20 sticks per day for 25 years but, not an alcoholic. He was an intravenous drug abuser 15 years ago and used to share needles with others. There is no history of exposure.

Family history: He is married and has 2 sons and a daughter. There is no history of such illness in his family.

Drug and treatment history: For his present illness, he was treated by his local physician by frusemide, vitamins, ranitidine, etc. but no improvement.

GENERAL EXAMINATION

- The patient is ill looking and emaciated
- Mildly icteric and mildly anemic
- Clubbing, leukonychia (fingers and toes) and palmar erythema are present, no edema
- There are few spider angioma over the chest and back
- No koilonychia, cyanosis, lymphadenopathy or thyromegaly
- Dupuytren's contracture and flapping tremor are absent
- Pulse—96/min
- BP—110/55 mm Hg
- Temperature—98°F
- Respiratory rate—18/min.

SYSTEMIC EXAMINATION

Gastrointestinal System

- Lips, gums, teeth, tongue and oral cavity—normal.

Abdomen

Inspection:

- The abdomen is distended, flanks are full
- Umbilicus is everted
- Superficial veins are visible with normal flow (away from umbilicus).

Palpation:

- Liver is palpable, … cm from right costal margin in the mid-clavicular line, non-tender, hard in consistency, surface is nodular and irregular, margin is irregular. There is a hard nodular mass measuring 3 × 3 cm on the right lobe. Hepatic bruit is audible over the mass
- Spleen is not palpable
- Kidneys are not ballotable
- Fluid thrill—absent.

Percussion: Shifting dullness—absent.

Auscultation: Normal.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 55 years, laborer, normotensive, nondiabetic, smoker, nonalcoholic, hailing from …, presented with upper abdominal discomfort and occasional dull pain for … days. The pain is not associated with food intake or there is no radiation. This patient is also experiencing a mass in the upper abdomen which is painless but slowly increasing in size. For the last … days, is also complaining of marked loss of appetite, marked loss of weight, extreme weakness, gradual distension of abdomen and scanty micturition. His bowel habit is normal. There is no history of fever, vomiting, cough, etc.

The patient mentioned that he had suffered from jaundice 5 years back. He smokes about 20 sticks per day for 25 years. He is not an alcoholic. He was an intravenous drug abuser 15 years ago and used to share needles with others. There is no history of exposure. He is married and has 2 sons and a daughter. There is no history of such illness in his family. For his present illness, he was treated by his local physician by frusemide, vitamins, ranitidine, etc. but no improvement.

On examination – general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is hepatocellular carcinoma (hepatoma).

Q. What are your **differential diagnoses?**

A. As follows:

- Secondary deposit in liver
- Hydatid cyst
- Polycystic liver
- Macronodular cirrhosis.

Q. **Why** is this hepatoma?

A. Because the liver is hard, irregular, nodular, non-tender and there is hepatic bruit.

Q. Why not secondary deposit?

A. In secondary, there may be history of a primary carcinoma. The nodules are multiple and small. There may be umbilication, but no hepatic bruit.

Q. What **investigations** are done to diagnose hepatoma?

A. As follows:

1. USG (shows filling defects in 90% of cases).
2. α-fetoprotein—high (60%), normal (one-third). Levels increase with the size of tumor.
3. Others:
   - CT or MRI.
   - Carcinoembryonic antigen (high in secondaries).
   - Plain X-ray of abdomen to see calcification in liver (sunburst calcification).
4. Liver biopsy under USG control. (This is confirmatory, but avoided in patient eligible for transplantation or surgical resection, because of small risk of tumor seeding along the needle tract).
5. Viral markers (HBV and HCV).

Note Remember the following:

Metabolic abnormalities in hepatoma are polycythemia, hypercalcemia, hypoglycemia and porphyria cutanea tarda.

Q. What are the **screening tests** to detect hepatoma in cirrhosis of liver?

A. USG and α-fetoprotein. Ultrasonography, every 3 to 6 months in high-risk group (in B and C infection, alcoholic cirrhosis and hemochromatosis).

RELATED QUESTIONS AND ANSWERS

Q. How to **differentiate** between primary carcinoma (hepatoma) and secondary carcinoma?

A. As follows:

Primary	Secondary
1. History of hepatitis B and C infection or cirrhosis of liver	History of primary carcinoma (GIT, bronchus, breast, thyroid and kidney). No primary source in 50% cases
2. Nodule usually single, may be more	Usually multiple nodules
3. No umbilication over the nodule	There is umbilication (due to necrosis)
4. Bruit present (due to increased vascularity)	No bruit (because of the necrotic lesion)
5. Rub may be present	Rub is more common
6. Investigations: » α-fetoprotein increased » Alkaline phosphatase slightly increased » Carcinoembryonic antigen is normal	Investigations: » α-fetoprotein usually not high » Alkaline phosphatase very high » Carcinoembryonic antigen is high

Q. How to **suspect** that hepatoma has developed in cirrhosis of liver?

A. In the following way:

- Rapid deterioration of general condition

- Pain in right hypochondrium
- Increasing ascites, not responding to usual therapy
- Enlarging liver with appearance of nodule (hard and irregular)
- Presence of bruit
- Biochemically increase α-fetoprotein.

Q. What are the **causes** of hepatoma?

A. As follows:

- Chronic hepatitis B infections. HCC is four times common in those with HBeAg positive, then those with HBsAg alone. 75 to 90% are associated with cirrhosis of liver.
- Chronic hepatitis C infections. Risk of HCC is higher in HCV than HBV. Almost always associated with cirrhosis.
- Cirrhosis of liver—in alcoholic cirrhosis, nonalcoholic steatohepatitis (NASH), hemochromatosis, Wilson's disease, α_1-antitrypsin deficiency and primary biliary cirrhosis. Macronodular variant is more prone to develop hepatoma.
- Aflatoxin produced by a fungus Aspergillus flavus (from contaminated ground nut grain, stored in tropical condition).
- Chronic arsenicosis.
- Chlonorsis sinensis (a parasitic infection).
- Prolonged androgen therapy, anabolic steroid and oral contraceptive pill (estrogen) may cause hepatoma (usually adenoma, rarely hepatoma).
- Smoking (rare).

Q. What are the other **primary** tumors of liver?

A. Rarely, fibrolamellar hepatocellular carcinoma, common in young adults, affecting equally in male and female, in the absence of hepatitis B and cirrhosis. The tumor is large at presentation, α-fetoprotein is normal. This tumor is treated by surgical resection.

Other primary tumor include hemangioendothelial sarcoma, cholangiocarcinoma, hepatoblastoma, leiomyosarcoma, fibrosarcoma.

Q. What are the **benign tumors** of liver?

A. As follows:

- Hemangioma is the commonest. Rarely, causes symptom. No treatment is required.
- Adenoma, more in females, caused by estrogen containing oral contraceptives, androgen and anabolic steroid. Surgical resection, if pressure symptoms, also if pregnancy is desired (as size is increased in pregnancy).
- Focal nodular hyperplasia.
- Fibroma.
- Leiomyoma.

Q. Why **secondary carcinoma** is more common in the liver?

A. Because, relatively blood flow in liver is more, double blood supply (by portal vein and hepatic artery).

Q. How to **treat** hepatoma?

A. As follows:

- Surgical resection, in non-cirrhotic patient. Recurrence in 50% at 5 years.
- In cirrhotic patient, resection may be done with small tumor and good liver function.
- Liver transplantation (5-year survival is 70% with single tumor < 5 cm, or three tumors < 3 cm). Hepatitis B and C may recur in transplanted liver.

- Percutaneous injection of ethanol, if tumor size is 3 cm or less, 80% cure rate. Recurrence is 50% at 3 years. Repeated injection may be given. It causes tumor necrosis.
- Transcatheter radiofrequency ablation using a single electrode inserted into the tumor under radiological guidance.
- Transcatheter hepatic arterial embolization (transarterial chemoembolization, TACE) by Gelfoam and doxorubicin. TACE is contraindicated in decompensated cirrhosis and multifocal HCC.
- Chemotherapy—doxorubicin may be effective in 30% cases. IV sorafenib, a multikinase inhibitor, is under phase III trial.

Q. What is **α-fetoprotein?** What are the **causes** of high α-fetoprotein?

A. It is a normal component of plasma protein, produced by the fetal liver older than 6 weeks and reaches maximum concentration at 12 to 16 weeks of fetal life. It falls few weeks after birth. Reappearance in blood in adult life is pathognomonic. Causes of high α-fetoprotein:

1. Hepatoma is the commonest, may be very high, > 500 ng/mL in patients with liver disease is highly suggestive. Level increases with size, may be normal in small size.
2. Others:
   - Chronic active hepatitis (indicates hepatocellular regeneration).
   - Acute viral hepatitis (indicates hepatocellular regeneration).
   - Acute hepatic necrosis following paracetamol toxicity.
   - Embryonic tumours of the ovary and testis.
   - Embryonic hepatoblastoma.
   - Rarely, in other malignancy, such as carcinoma of stomach, pancreas, bile duct and gall bladder (usually with large metastasis in liver).
   - During pregnancy (in serum and amniotic fluid), high level indicates neural tube defect (meningomyelocele or anencephaly).

Causes of hepatic bruit:

- Hepatoma is the commonest cause (due to increased vascularity)
- Acute alcoholic hepatitis
- AV fistula in liver (due to trauma or iatrogenic during liver biopsy)
- Hemangioma.

Causes of hepatic rub

- Secondary deposit in the liver
- Trauma
- Infarction in liver
- Perihepatitis in pelvic inflammatory disease (gonococcal or chlamydial in females, called Fitz–Hugh–Curtis syndrome).

Fitz-Hugh-Curtis Syndrome

Fitz-Hugh-Curtis syndrome is caused by *Chlamydia* or *Gonococcus* infection, which tracks up the right paracolic gutter to cause perihepatitis, secondarily from endocervical or urethral infection. It is characterized by fever, pain in the right hypochondrium with radiation to right shoulder, tender hepatomegaly, hepatic rub and small right pleural effusion.

Chlamydia infection is asymptomatic in 80% cases.

Investigation: Endocervical swab for microscopy and special culture, direct fluorescent antibody for *Chlamydia*, ELISA and PCR may be performed.

Treatment: Tetracycline or doxycycline or erythromycin or azithromycin are used for *Chlamydia* infection.

SECONDARIES IN THE LIVER

CHIEF COMPLAINTS

- Loss of appetite, weakness and weight loss for … days
- Pain in upper abdomen for … days.

HISTORY

History of present illness: According to the patient's statement, he was reasonably alright … days back. Since then, he is complaining of gradual loss of appetite and weakness. He has lost about 5 kg body weight in … days. For the last … days, he is suffering from pain in upper abdomen which is dull aching in nature, not related to food intake or bowel movement and without any radiation. He feels occasional nausea, but there is no vomiting. He did not notice any mass in the abdomen. There is no history of fever, cough, chest pain, shortness of breath. His bowel and bladder habits are normal.

History of past illness

Personal history

Family history

Drug and treatment history: Mention according to the patient's statement.

GENERAL EXAMINATION

- The patient is ill looking and emaciated
- Moderately anemic, but not icteric
- No clubbing, koilonychia, leukonychia, cyanosis or edema
- There is no lymphadenopathy or thyromegaly
- Pulse—108/min
- BP—105/55 mm Hg
- Temperature—97°F
- Respiratory rate—20/min.

SYSTEMIC EXAMINATION

Gastrointestinal System

- Lips, gums, teeth, tongue and oral cavity—normal.

Abdomen

Inspection: Right upper abdomen is distended.

Palpation:

- Liver is palpable … cm from the right costal margin in the midclavicular line, nontender, hard in consistency, surface is nodular and irregular, margin is irregular. Hepatic bruit is absent. Upper margin in the ------ space.
- Spleen is not palpable.
- Kidneys are not ballotable.
- Fluid thrill—absent.

Percussion: Shifting dullness is absent.
Auscultation: Normal.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 65 years, farmer, normotensive, non-diabetic, smoker, non-alcoholic, hailing from …, presented with gradual loss of appetite and weakness for … days. He has lost about 5 kg body weight in … days. For the last … days, he is suffering from pain in upper abdomen which is dull aching in nature, not related to food intake or bowel movement and without any radiation. He feels occasional nausea, but there is no vomiting. He did not notice any mass in the abdomen. There is no history of fever, cough, chest pain, shortness of breath. His bowel and bladder habits are normal. There is no history of such illness in his family. He used to take antacids, vitamins and painkillers.

On examination – general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is secondaries in the liver.

Q. What are your **differential diagnoses?**

A. As follows:
- Hepatoma
- Hydatid cyst
- Polycystic disease of liver.

Q. **Why** is it secondary and not primary?

A. Because there are multiple hard nodules of variable size and shape. There is no bruit. If primary, there is usually a single hard nodule, occasionally with hepatic bruit.

Q. What are the **primary sources?**

A. In male, common primary sources are carcinoma of the stomach, lung and colon. In female, common sources are carcinoma of breast, colon, stomach and uterus. Less common sources for both sexes are carcinoma of the pancreas, gallbladder, carcinoid tumor.

Q. Which tumor is more **common** in liver?

A. Secondaries in the liver is more common (90%), primary hepatic tumor is less common.

Q. How to **diagnose**?

A. As follows:
- Ultrasonogram of the whole abdomen.
- CT or MRI of the abdomen may be done.
- Liver function tests—usually alkaline phosphatase is high.
- Other investigation to find out the primary source according to the history of the patient. For example X-ray chest P/A view, endoscopy of upper GIT, colonoscopy, etc.
- FNAC or USG guided liver biopsy may be done in some cases.

Q. How to **treat** the case?

A. As follows:
- Treatment of the primary cause if possible.
- If solitary metastasis, surgery may be possible (as in colorectal carcinoma).

- If surgery is not possible, radiofrequency ablation of the metastasis may be tried.
- Majority requires palliative treatment.

Q. What is the **prognosis**?

A. Most patients survive less than 6 months. Prognosis is relatively better in colorectal carcinoma with metastasis in the liver.

HEMOCHROMATOSIS

CHIEF COMPLAINTS

- Swelling of abdomen with discomfort for … months
- Swelling of both legs for … months
- Breathlessness on exertion for … months
- Weakness, malaise, loss of appetite for … months
- Generalized pigmentation for … months.

HISTORY

History of present illness: The patient states that he was reasonably well about … months back. Since then, he has noticed gradual swelling of his abdomen, which is increasing progressively over the last few days. It is not associated with any abdominal pain, but the patient feels discomfort and sense of heaviness. He also complains of gradually increasing swelling of his both legs and scanty micturition for the last … months. The patient is experiencing difficulty in breathing after exertion such as walking for some distance or going upstairs for the last … months, and it is progressively becoming worse day by day. There is no history of paroxysmal nocturnal dyspnea or orthopnea. For the last … months, the patient also complains of generalized weakness, malaise, loss of appetite, loss of libido and joint pain involving both the knees. He noticed generalized pigmentation all over his body for … months. He denies any history of cough, puffiness of the face, skin rash, hematemesis, melena, palpitation, chest pain or loss of consciousness, etc. His bowel habit and sleep pattern is normal.

History of past illness: There is no previous history of jaundice or breathlessness.

Personal history: He does not smoke or drink alcohol. There is no history of intravenous drug abuse, sharing of needle or extramarital sexual relationship.

Family history: His father and one uncle also had such illness.

Drug and treatment history: There is no history of any injection, infusion or blood transfusion.

GENERAL EXAMINATION

- Ill looking and emaciated with generalized pigmentation
- Mildly icteric and mildly anemic
- Pitting edema is present
- Multiple spider angiomas are present over the upper part of chest and back
- There is leukonychia (involving fingers and toes) and palmar erythema (in both hands)
- No clubbing, koilonychias or cyanosis
- No lymphadenopathy or thyromegaly
- Dupuytren's contracture and flapping tremor are absent
- Body hair diminished in chest, axillary and pubic region
- Pulse—88/min
- BP—110/75 mm Hg sitting and 95/60 mm standing
- Temperature—99°F
- Respiratory rate—18/min.

SYSTEMIC EXAMINATION

Gastrointestinal System

- Tongue, oral mucosa, hard palate—pigmented.

Abdomen

Inspection:

- The abdomen is distended, flanks are full
- Umbilicus—everted
- Visible superficial veins with normal flow (away from umbilicus)
- There is no visible peristalsis, no scar mark.

Palpation:

- Liver—enlarged, … cm from right costal margin in right midclavicular line, firm in consistency, nontender, with smooth surface and no hepatic bruit.
- Spleen is palpable, 4 cm from the left costal margin in the anterior axillary line towards the right iliac fossa, surface is smooth, firm in consistency, nontender.
- Kidneys—not ballotable.
- Testes—both are atrophied.
- Fluid thrill—present.

Percussion: Shifting dullness is present.
Auscultation: No abnormality detected.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 49 years, businessman, normotensive, nondiabetic, nonsmoker, hailing from …, presented with gradual swelling of abdomen for … months, which is increasing progressively over the last few days. It is not associated with any abdominal pain, but the patient feels discomfort and sense of heaviness. He also complains of gradually increasing swelling of his both legs and scanty micturition for the last … months. The patient is experiencing difficulty in breathing after exertion such as walking for some distance or going upstairs for the last … months, and it is progressively becoming worse day by day. There is no history of paroxysmal nocturnal dyspnea or orthopnea. For the last … months, the patient also complains of generalized weakness, malaise, loss of appetite, loss of libido and joint pain involving both the knees. He noticed generalized pigmentation all over his body for … months. He denies any history of cough, puffiness of the face, skin rash, hematemesis, melena, palpitation, chest pain or loss of consciousness, etc. His bowel habit and sleep pattern is normal. There is no previous history of jaundice or breathlessness. He does not smoke or drink alcohol. There is no history of intravenous drug abuse, sharing of needle or extramarital sexual relationship. There is no history of any injection, infusion or blood transfusion. His father and one uncle also had such illness.

On examination – general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is decompansated cirrhosis of liver with portal hypertension due to hemochromatosis.

Q. What are your **differential diagnoses?**

A. As follows:

- Decompansated cirrhosis of liver due to HBV or HCV infection or metabolic cause.
- Primary biliary cirrhosis.
- Hepatocellular carcinoma due to cirrhosis of liver.

Q. **Why** it is hemochromatosis?

A. Because there are features of CLD, generalized pigmentation, arthralgia and testicular atrophy.

Q. **Why not** PBC?

A. PBC is more common in female and there is long standing generalized itching, xanthelasma, xanthoma, etc.

Q. What is the **size of liver** in cirrhosis?

A. Small.

Q. What are the cause of **hepatomegaly with cirrhosis?**

A. Hemochromatosis, primary biliary cirrhosis and alcoholic cirrhosis (early stage).

Q. What **investigations** should be done in hemochromatosis?

A. As follows:

1. CBC
2. Liver function tests
3. Iron profile:
   - Serum iron (increased)
   - Total iron binding capacity (>70% is saturated)
   - Serum ferritin (increased, > 600 μg/L)
4. CT scan or MRI of hepatobiliary system (increased density of liver due to iron deposits). MRI has high specificity for iron overload, but less sensitivity
5. Hepatic iron index (HII): Shows quantification of liver iron, HII > 1.9 suggests genetic hemochromatosis
6. Liver biopsy (shows iron deposition, hepatic fibrosis, cirrhosis). Liver biopsy to measure the iron stores is a definitive test
7. Others: Blood sugar, ECG, X-ray chest, echocardiogram, X-ray of the involved joint (shows chondrocalcinosis).

RELATED QUESTIONS AND ANSWERS

Q. What are the causes of **hemochromatosis**?

A. As follows:

1. Primary: Hereditary disorder, inherited as autosomal recessive.
2. Secondary:
   - Hemolytic anemia
     - β thalassemia
     - Sideroblastic anemia
     - Chronic hemolytic anemias.
   - Exogenous iron overload:
     - Repeated blood transfusion (transfusion siderosis)
     - Repeated iron injection
     - Prolonged oral iron.

- Chronic liver diseases:
  - Hepatitis C
  - Porphyria cutanea tarda
  - Alcoholic cirrhosis (in advanced stage).

Q. What is primary hemochromatosis?

A. This is a hereditary disorder, inherited as autosomal recessive, characterized by excess deposition of iron in various organs, leading to fibrosis and functional organ failure. It is associated with HLA-B3, B7 and B14. It is more in male, less in female. However, in female it becomes more in postmenopausal case.

Note Remember the following:

Normal body iron is 3 to 4 grams. In hemochromatosis, it may be 20 to 60 gram. Mainly iron is deposited in liver and pancreatic islets, also in endocrine glands (pituitary, adrenal), heart and skin.

Q. Why hemochromatosis is less in female?

A. Females are protected by iron loss in menstruation and pregnancy.

Q. What is the mechanism (pathogenesis) of primary hemochromatosis?

A. In hemochromatosis, mucosal absorption of iron is more and inappropriate to the body needs. Ultimately progressive accumulation of iron causes elevation of plasma iron, increase saturation of transferrin and high-level of ferritin, which is deposited in different organs of the body.

Q. What are the common features of hemochromatosis?

A. Usually it occurs in male above 40 years. Common features are:

- Liver involvement—hepatomegaly, CLD (about 30% may develop HCC).
- Skin pigmentation (leaden gray skin pigmentation due to melanin deposition).
- Diabetes mellitus.
- Cardiac dysfunction (dilated cardiomyopathy, CCF, arrhythmia).
- Arthritis and chondrocalcinosis.
- Hypogonadism (due to testicular atrophy).

Q. What type of diabetes occurs in hemochromatosis?

A. This is called "bronze diabetes" due to the bronze coloration of the skin.

Q. What are the common causes of pigmentation?

A. As follows:

- Addison's disease
- Hemochromatosis
- Kala-azar
- Arsenicosis
- Drugs—amiodarone, busulfan, bleomycin, phenothiazine, phenytoin, psoralen
- Systemic sclerosis
- Alkaptonuria
- Nelson's syndrome
- Chronic debilitationg illness (malignancy, CLD, CRF).

Q. What are the causes of raised ferritin level?

A. As follows:

- Hemochromatosis
- Alcoholic liver disease

- Hepatitis C infection
- Non-alcoholic steatohepatitis
- As an acute phase reactant in inflammatory and neoplastic conditions
- Adult Still's disease.

Q. How do you **treat** hemochromatosis?

A. As follows:

- Weekly or twice weekly venesection of 500 mL blood (200 to 250 mg of iron is removed) until the serum ferritin is normal. It may take 2 years of more. The aim is to reduce ferritin to <50 µg/L. Thereafter, venesection is continued as required to keep the serum ferritin normal (usually 3 to 4 venesections per year is needed). Following venesection, most of the symptoms improve or disappear, except testicular atrophy, diabetes mellitus and chondrocalcinosis. Joint pain may even worsen.
- Chelation therapy with desferrioxamine (40 to 80 mg/kg/day subcutaneously) may be given. It removes 10 to 20 mg of iron per day. It is mainly used if the patient cannot tolerate venesection, specially those with cardiac disease or severe anemia.
- Symptomatic treatment of cirrhosis, diabetes mellitus (usually by insulin), CCF and cardiac arrhythmia.
- Alcohol must be avoided.
- Supplemental vitamin C must be avoided as pharmacological doses can accelerate iron mobilization to a level that saturates circulating transferrin, resulting in an increase in pro-oxidant and free radical activity.
- First degree family members should be screened.

Note Remember the following:

In primary hemochromatosis, iron is deposited in hepatocytes, whereas in secondary iron overload, iron accumulates in Kupffer cells.

Q. What is the **cause of death** of hemochromatosis?

A. Death is usually due to cardiac failure (30%), hepatocellular failure or portal hypertension (25%) and HCC (30%).

Q. What is the **risk of HCC** in hemochromatosis?

A. HCC usually occurs as a late sequelae in patient who is cirrhotic at presentation. It does not occur if the disease is treated in the pre-cirrhotic stage. In presence of cirrhosis, venesection reduces but does not abolish the risk of HCC.

Q. What is the **prognosis**?

A. If it is diagnosed and treated in pre-cirrhotic stage, life expectancy is normal. Even in cirrhotic patients, there is a good prognosis compaired to other causes of cirrhosis. Three-fourth cases survive 5 years after the diagnosis.

BUDD-CHIARI SYNDROME

CHIEF COMPLAINTS

- Pain and distension of abdomen for … days
- Yellow coloration of the sclera for … days
- Anorexia, nausea and vomiting for … days
- Scanty micturition for … days.

HISTORY

History of present illness: According to the patient, she was reasonably well … days back. Since then, she has been suffering from continuous dull aching pain in upper abdomen which is not associated with food intake. It is more marked on lying on the right side and there is no radiation of pain. She also noticed distension of her abdomen for the same duration, which is gradually increasing, associated with scanty micturition. For last … days, her sclera and urine have turned yellow which is associated with occasional nausea and vomiting. Vomitus contains food material and bile, but no blood. There is no fever, cough, chest pain, hematemesis or melena. Her bowel habit is normal.

History of past illness: There is no past history of jaundice.

Personal history: She is married and has 2 daughters. She is a nonsmoker and nonalcoholic. There is no history of intravenous drug abuse.

Family history: There is no history of similar illness in her family.

Drug and treatment history: She used to take oral contraceptive pills regularly for last 10 years. There is no history of blood transfusion.

GENERAL EXAMINATION

- Ill looking
- Mildly anemic and moderately icteric
- No clubbing, koilonychia, leukonychia, cyanosis or edema
- No lymphadenopathy or thyromegaly
- No stigmata of chronic liver disease
- Pulse—82/min
- BP—110/65 mm Hg
- Temperature—98.6°F
- Respiratory rate—18/min.

SYSTEMIC EXAMINATION

Gastrointestinal System

- Lips, gums, teeth, tongue and oral cavity—normal, but yellowish.

Abdomen

Inspection:

- The abdomen is distended, flanks are full.
- Umbilicus is everted
- Superficial veins are visible with normal flow (away from umbilicus).

Palpation:

- Liver is palpable, … cm from right costal margin in the mid-clavicular line, tender, soft in consistency, with smooth surface and sharp margin. There is no hepatic bruit
- Spleen is not palpable
- Kidneys—not ballotable
- Fluid thrill—present.

Percussion: Shifting dullness is present.
Auscultation: Normal.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mrs …, 40 years, housewife, normotensive, nondiabetic, nonsmoker, hailing from …, presented with continuous dull aching pain in upper abdomen for … days, which is not associated with food intake. It is more marked on lying on the right side and there is no radiation of pain. She also noticed distension of her abdomen for the same duration which is gradually increasing, associated with scanty micturition. For last … days, her sclera and urine have turned yellow which is associated with occasional nausea and vomiting. Vomitus contains food material and bile, but no blood. There is no fever, cough, chest pain, hematemesis or melena. Her bowel habit is normal. There is no past history of jaundice. There is no history of intravenous drug abuse or blood transfusion. She used to take oral contraceptive pills regularly for last 10 years. There is no history of similar illness in her family.

On examination – general examination (mention as above).

Systemic examination (mention as above).

The patient has moderate jaundice, tender hepatomegaly with ascites. The probable diagnoses are:

- Hepatoma with secondaries in the peritoneum
- Secondaries in the liver and peritoneum
- Acute cholangiohepatitis
- Chronic constrictive pericarditis
- Budd-Chiari syndrome.

Q. What are the causes of **enlarged tender liver?**

A. As follows:

- Acute viral hepatitis
- Liver abscess
- Congestive cardiac failure
- Chronic constrictive pericarditis
- Budd-Chiari syndrome

- Hepatoma
- Acute cholangiohepatitis.

Q. What **investigations** are done in Budd-Chiari syndrome?

A. As follows:

1. CBC, ESR, platelet.
2. Liver function tests (serum bilirubin, SGPT, alkaline phosphatase, prothrombin time, serum total protein, A : G ratio).
3. Ultrasonography of whole abdomen, specially doppler ultrasonography (pulsed doppler sonography or a color doppler). It may reveal obliteration of the hepatic veins and reversed flow or associated thrombosis in portal vein.
4. CT or MRI of abdomen:
   - Hepatic vein occlusion with diffuse abnormal parenchyma on contrast-enhancement, which spares the caudate lobe (because of its independent blood supply and venous drainage).
   - There may be compression of the inferior vena cava.
   - Caudate lobe may be enlarged.
5. Venography: Needed if CT and MRI fail to show the hepatic venous anatomy.
6. Aspiration of ascitic fluid: Shows high protein content (above 25 g/L, exudative) in the early stages, but often falls later.
7. Liver biopsy: Shows centrilobular congestion (zone 3), hemorrhage, fibrosis and cirrhosis depending on the duration of illness.
8. Other tests to find out the cause, e.g. coagulation screening (anti-thrombin III, protein S, protein C).

RELATED QUESTIONS AND ANSWERS

Q. What is **Budd-chiari syndrome?**

A. It is a syndrome characterized by obstruction to the venous outflow of the liver due to the occlusion of the hepatic vein and sometimes IVC. This syndrome comprises hepatomegaly, abdominal pain, ascites and hepatic histology showing zone 3 sinusoidal distension and pulling.

Site of obstruction—usually in hepatic vein at any site from the efferent vein of the acinus to the entry of inferior vena cava to right atrium. This type of syndrome may be produced by constrictive pericarditis or right-sided heart failure.

Q. What are the **causes** of Budd-chiari syndrome?

A. The causes are:

1. Hematological disorder that causes thrombosis. It may be due to hypercoagulability states like:
   - Polycythemia rubra vera
   - Paroxysmal nocturnal hemoglobinuria
   - Deficiency of antithrombin III, protein C and protein S
   - Pregnancy and oral contraceptive pill
   - Antiphospholipid syndrome
   - Leukemia.
2. Compression of the hepatic vein due to:
   - Carcinoma of liver, kidney or adrenal gland
   - Posterior abdominal wall sarcoma
   - Hepatic infections (like hydatid cyst)
   - Congenital venous webs
   - Inferior vena caval obstruction.

3. Others: Radiotherapy, trauma to the liver, Behcet's syndrome.
4. Unknown in 1/3rd to half of the cases.

Q. What is the pathogenesis?

A. Initially, there is centrilobular venous dilatation and congestion, then centrilobular fibrosis, eventually cirrhosis occurs in those who survive long time.

Q. What are the usual presentations of Budd-chiari syndrome?

A. As follows:

- In acute form, there is rapid development of upper abdominal pain, nausea, vomiting, tender hepatomegaly with marked ascites.
- In chronic form or if there is gradual occlusion, there may be gross ascites with upper abdominal discomfort, mild jaundice, splenomegaly.

On examination:

- Hepatomegaly, often tender
- Peripheral edema is present, if there is IVC obstruction
- Those who survive acute events may present with cirrhosis and portal hypertension.

Q. What are your differential diagnoses of Budd-chiari syndrome?

A. As follows:

- Inferior vena caval obstruction
- Right-sided cardiac failure
- Chronic constrictive pericarditis CCF.

Q. How to treat?

A. As follows:

1. Treatment of predisposing conditions or underlying disorders. For example, if thrombosis is suspected, then treatment with streptokinase followed by heparin and oral anticoagulation should be considered.
2. The following may be considered to relieve obstruction:
   - Short hepatic venous strictures can be treated with angioplasty.
   - More extensive hepatic vein occlusion may be treated with insertion of a covered TIPSS followed by anticoagulation.
   - Side to side portocaval or splenorenal anastomosis may be done if there is no caval obstruction. Surgical shunts are less commonly performed, if TIPSS is available.
   - Congenital webs should be resected surgically.
   - IVC stenosis may be dilated.
3. Ascites is initially treated medically.
4. Liver transplantation is the treatment of choice for chronic Budd-Chiari syndrome and for the fulminant form, followed by life-long anticoagulantion. Progressive liver failure is an indication for liver transplantation and life-long anticoagulation.

Q. What is the prognosis?

A. Prognosis depends on the cause. It is poor without liver transplantation or shunting, particularly following an acute presentation with liver failure, but some patients can survive for several years. Following liver transplantation, 1 and 10 years survival is 85% and 69% respectively. This compares with 5- and 10-year survival of 87% and 37% following surgical shunting.

CHAPTER 6

Nephrology

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NEPHROTIC SYNDROME

CHIEF COMPLAINTS

- Swelling of the whole body for … months.
- Scanty micturition for … months.
- Generalized weakness and loss of appetite for … months.

HISTORY

History of present illness: According to the patient's statement, he was alright … months back. Since then, he has been suffering from generalized swelling of the whole body. Initially, he noticed swelling around the eyes and face, followed by arms, abdomen and then legs. He also complains of scanty micturition, but there is no history of burning, hematuria or pain. For the ... months, he is experiencing generalized weakness and loss of appetite. There is no history of sore throat, skin infection, breathlessness, cough, chest pain, bowel abnormality, cold intolerance and jaundice. He did not give any history of skin rash, joint pain or oral ulcers (to exclude collagen disease), or weight loss. There is no history of taking any herbal medicine and nephrotoxic drugs.

History of past illness: Nothing significant.

Family history: Mention according to the patient's statement.

Personal history: He is a student of secondary class, non-smoker.

Socioeconomic history: He comes from a middle class family, lives in a brick built house with good sanitation and water supply.

Drug history: He took frusemide tablets and some antibiotics as prescribed by the local physician.

GENERAL EXAMINATION

- The patient is grossly edematous, the face is puffy with baggy eyelids
- Pitting edema is present
- Mildly anemic
- No clubbing, jaundice, cyanosis, koilonychia, but leukonychia involving all the nails of fingers and toes is present
- No lymphadenopathy or thyromegaly
- Pulse—90/min regular in rhythms
- BP—110/75 mm Hg.

SYSTEMIC EXAMINATION

Gastrointestinal System

Lips, gum, tongue, oral cavity—normal.

Abdomen

1. Inspection:
   - There is generalized distension of abdomen

- Umbilicus is everted
- Scrotum and penis are grossly swollen.

2. Palpation:
   - No organomegaly
   - Kidneys are not ballotable
   - Fluid thrill—present
   - There is no tenderness over the renal angle
   - Genitalia—scrotum and penis are swollen
3. Percussion: Shifting dullness present. There is gross ascites as suggested by presence of shifting dullness and fluid thrill.
4. Auscultation: No abnormality.

Cardiovascular System

There is no abnormality.

Respiratory System

There is no abnormality.

> **Note**
>
> There may be bilateral pleural effusion. If present, mention the signs of pleural effusion.

Examination of the other systems reveals no abnormalities.

Bedside urine for protein +++, sugar nil.

SALIENT FEATURES

Mr. …, 17 years old, student, normotensive, non-diabetic, non-smoker, hailing from …, presented with generalized swelling of the whole body for … months. Initially, he noticed swelling around the eyes and face, followed by arms, abdomen and then legs. He also complains of scanty micturition, but there is no history of burning, hematuria or pain. For the ... months, he is experiencing weakness and loss of appetite. There is no history of sore throat, breathlessness, cough, chest pain, bowel abnormality or cold intolerance and jaundice. He did not give any history of skin rash, joint pain or oral ulcers, or weight loss. For this illness he took frusemide tablets and some antibiotics as prescribed by the local physician. There is no history of taking any herbal medicine and nephrotoxic drugs. There is no family history of such illness.

On Examination—

General examination (mention as above).

Systemic examination (mention as above).

Urine shows gross proteinuria.

My diagnosis is nephrotic syndrome.

(The patient may have bilateral pleural effusion or pericardial effusion. These are often missed while telling the diagnosis).

Q. What are your **differential diagnoses?**

A. As follows:

- Acute glomerulonephritis
- Congestive cardiac failure
- Cirrhosis of the liver
- Hypoproteinemia due to malnutrition or malabsorption.

Q. Why **not** acute glomerulonephritis?

A. Because, in AGN, there will be history of sore throat or skin lesion, no gross or generalized swelling. Also, there may be hypertension and hematuria. Proteinuria is usually mild, urine is smoky.

Q. Why **not** congestive cardiac failure?

A. Because, the signs of CCF are engorged pulsatile neck vein, enlarged tender liver and dependent edema, which are absent in this patient. Usually, there is no generalized edema and no gross proteinuria in CCF.

Q. Why **not** cirrhosis of liver?

A. Because in this patient there are no stigmata or signs of cirrhosis, or CLD. In cirrhosis usually there is only ascites but no generalized edema. Also, in cirrhosis, there is no generalized edema and no gross proteinuria.

Q. What **history** you have taken in NS?

A. As follows:

- Diabetes mellitus
- Malignancy (lymphoma, leukemia)
- Drugs, e.g. captopril, NSAIDs, penicillamine, gold
- Skin rash, arthritis, arthralgia, alopecia (SLE)
- History of other diseases like malaria, leprosy, syphilis, HBV, HCV, amyloidosis, vasculitis
- Family history of sickle cell disease, Alport syndrome, nail patella syndrome.

Q. What **investigations** should be done in nephritic syndrome?

A. As follows:

1. Urine R/E—Shows gross proteinuria. Red cells and red cell casts are absent (also, look for urine sugar to exclude diabetic nephropathy).
2. 24 hours urinary total protein (more than 3.5 g/ 24 h is suggestive of nephritic syndrome).
3. Serum total protein, serum albumin and A:G ratio (hypoalbuminemia).
4. Serum lipid profile (high cholesterol and high TG may be present).
5. Blood sugar, blood urea, serum creatinine, serum electrolytes should be done.
6. USG of the whole abdomen to look for renal pathology.
7. To find out causes:
   - Blood sugar (to exclude diabetic nephropathy).
   - Chest X-ray (to exclude bronchial carcinoma, lymphoma. Also, to see bilateral pleural effusion, pericardial effusion).
   - ANA, Anti-dsDNA (if the history is suggestive of SLE)
   - P-ANCA and c-ANCA (if the history is suggestive of vasculitis)
   - HBsAg and anti HCV screening
   - Complement C3 and C4
   - Renal biopsy (to see the type of GN, whether minimal, membranous or membranoproliferative —this will guide for diagnosis, therapy and prognosis).

RELATED QUESTIONS AND ANSWERS

Q. What is **nephrotic syndrome**? What are the **causes**?

A. Nephrotic syndrome is characterized by generalized edema, massive proteinuria and hypoalbuminemia (with or without hyperlipidemia). Causes are:

1. Primary renal disease—all types of glomerulonephritis (80%):
   - Minimal change glomerular disease (the most common in children)
   - Membranous GN (the most common in adult)
   - Mesangiocapillary and proliferative gomerulonephritis
   - Focal and segmental glomerulosclerosis
   - IgA nephropathy.
2. Secondary to other disease:
   - Diabetic nephropathy
   - Collagen disease, mainly SLE, also rheumatoid arthritis (by amyloidosis)
   - Amyloidosis
   - Drugs—penicillamine (common), captopril, gold, mercury
   - Neoplastic—carcinoma (bronchial carcinoma), lymphoma
   - Infection—malaria (quartan malaria), bacterial endocarditis, HBV, HCV, HIV, secondary syphilis, leprosy
   - Allergies—bee stings, snake bite, anti-snake venom, pollens.

Q. What is the **most common cause** of nephrotic syndrome in children and adult?

A. Most common cause in children is minimal change glomerulonephritis, and the most common cause in adult is membranous glomerulonephritis.

Q. What are the **lipid abnormalities** in NS? What are the **mechanisms**?

A. Lipid abnormalities are:

- Hypercholesterolemia and hypertriglyceridemia
- High LDL, VLDL and IDL
- There is no change or low HDL.

The mechanisms are:

- Increased synthesis of lipoproteins by the liver, secondary to hypoalbuminemia
- Reduced clearance of triglyceride bearing lipoprotein (chylomicron and VLDL) in direct response to albuminuria.

As a result, there is high rate of atherosclerosis.

Q. What is the mechanism of **proteinuria**?

A. There is increased permeability of the glomerular capillary wall due to –

1. Reduction of fixed negatively charged protein molecules in glomerular capillary wall which repel negatively charged protein molecules, allows proteins to pass through the pores
2. Damage to the glomerular basement membrane that leads to increase in the size and number of pores, allowing passage of larger molecules.

Q. Why **edema** in NS?

A. Previously it was thought that reduction of albumin causes low plasma oncotic pressure, which causes to edema. But recent view is oncotic pressure is not changed in NS, edema is due to sodium retention in the extracellular compartment. Also, there is change in molecular barrier, which causes edema.

Q. What is the **blood pressure** in NS?

A. Usually blood pressure is normal, even low. If there is hypertension, usually it is secondary to underlying disease like SLE with renal involvement, polyarteritis nodosa, diabetic nephropathy or terminal stage of nephrotic syndrome.

Q. How to **treat nephrotic syndrome**?

A. As follows:

1. Fluid restriction—depending on previous day's output and patient's edema status (average - 500 mL to 1000 mL/day).
2. Salt restriction.
3. High protein diet (2g/kg/day). In severe case, intravenous salt poor albumin may be given to diuretic resistant patients and those with oliguria and uremia in the absence of severe glomerular damage, e.g. in minimal change nephropathy. It helps in diuresis. Protein intake should be restricted in patient with impaired renal function.
4. Diuretics—loop diuretics (frusemide, bumetanide). If needed, potassium sparing diuretics (spironolactone) should be added.
5. ACE inhibitors and/or angiotensin II receptor antagonists are used in all types of GN (for their antiproteinuric properties. These drugs reduce proteinuria by lowering glomerular capillary filtration pressure).
6. In case of minimal change disease:
   - Prednisolone 60 mg/m^2 body surface area (maximum 80 mg/day) is given for 4 to 6 weeks, followed by 40 mg/m^2 every other day for a further 4 to 6 weeks. More than 95% responds (in children). Alternately, prednisolone 1mg/kg/day up to response (urine protein free) or 3 months followed by tapering the dose in next 3 months.
   - If there is relapse after withdrawal of steroid, it should be given again with gradual withdrawal. Some patients may require low dose maintenance dose (5 to 10 mg/day) for 3 to 6 months.
   - If there is frequent relapse or need high dose steroid or incomplete response to steroid—cyclophosphamide (2.0 mg/kg/day for 8 to 12 weeks) and mycophenolate mofetil with low dose steroid should be given.
7. In membranous glomerulopathy, the following treatment may be given:
   - Inj. methylprednisolone 500 mg to 1000 mg IV for 3 days, followed by oral prednisolone 0.5 mg/kg/day for 27 days in 1st, 3rd and 5th months and Tab. cyclophosphamide 2 mg/kg/day or chlorambucil 0.2 mg/kg/day for 30 days in 2nd, 4th and 6th months.
   - Chlorambucil (0.2 mg/kg/day in months 2, 4 and 6 alternating with oral prednisolone 0.4 mg/kg/day in months 1, 3 and 5) or cyclophosphamide (1.5 to 2.5 mg/kg/day for 6 to 12 months with 1 mg/kg/day of oral prednisolone on alternate days for the first 2 months) are equally effective. However, this treatment is reserved for patients with severe or prolonged nephrosis (proteinuria > 6 gm/day for > 6 months) or renal insufficiency and hypertension.
   - Cyclosporine and mycophenolate mofetil with oral steroid may be used.
   - Anti CD20 antibodies (rituximab) have been shown to improve renal function, reduce proteinuria and increase the serum albumin.
   - Oral high dose corticosteroid and azathioprine are ineffective.
8. Focal and segmental glomerulosclerosis:
   - Symptomatic and supportive treatment.
   - Steroid is effective in 40% cases. Tablet prednisolone 1 mg /kg /day for 3 months then tapered. Total duration of treatment at least about 6 months to 1 year. Most cases progress to renal failure.
   - If no response—MMF 1 to 2 g/day or ciclosporine 5 to 6 mg/kg/ day for 3 months, and maintenances up to 15 months.
   - Tacrolimus 0.05 mg/kg/day may be tried (occasionally effective).
   - Renal transplantation can be done in renal failure, but may relapse after transplantation.

9. Mesangiocapillary or membrano-proliferative GN:
   - Only symptomatic and supportive treatment.
   - No specific treatment.
   - Aspirin may be given.
10. Treatment of complication:
   - If infection—antibiotic is given. Pneumococcal vaccine is recommended.
   - Venous thrombosis—to prevent, prolong bedrest should be avoided. Prophylactic heparin if immobile (enoxaparin may be given), followed by oral anticoagulant.
   - For hyperlipidemia—statin may be added.
11. Treatment of underlying cause, if any.

Q. What is the **prognosis** in NS?

A. It depends on the type of NS.

- Prognosis of minimal change disease in children is excellent. Remission and relapse may occur (common in children and less in adult). CKD does not occur.
- In membranous nephropathy, one-third may remit spontaneously, one-third remain in nephrotic syndrome and one-third shows progressive loss of renal function.
- In FSGS and mesangiocapillary GN—prognosis is bad.
- IgA nephropathy—course of the disease is indolent. ESRD occurs in 20 years.

Q. What are the **complications** of nephrotic syndrome?

A. As follows:

- Hypercoagulability leading to venous thrombosis (especially renal vein thrombosis, also DVT) and pulmonary embolism.
- Infection such as pneumococcal infection (may cause peritonitis and septicemia), cellulitis, streptococcal infection, etc. due to loss of immunoglobulin (IgG deficiency) complements.
- Hyperlipidemia leading to atherosclerosis.
- Oliguric renal failure.
- May cause bilateral pleural effusion, pericardial effusion.
- Loss of thyroxin binding globulin, that causes low FT3 and FT4 which leads to hypothyroidism.
- Loss of transferrin and iron, resulting in iron deficiency anemia.
- Loss of vitamin D binding protein, leading to osteomalacia.

Q. What are the **mechanisms of renal vein thrombosis** in nephrotic syndrome?

A. Mechanisms are as follows:

1. In nephrotic syndrome, there is hypercoagulable state due to:
   - Loss of inhibitors of coagulation in urine, such as antithrombin III, protein C and S, and also loss of fibrinolytic factor (plasminogen).
   - Increase synthesis of clotting factors—factor V, VIII and fibrinogen.
   - Other factors—thrombocytosis and over diuresis resulting in dehydration, reduced renal blood flow and increased viscosity, prolonged bed ridden.
2. Also, there is hyperlipidemia, commonly high LDL, VLDL, cholesterol and triglyceride. So, there is more atherosclerosis.

These predispose to increased venous thrombosis that occurs specially in renal vein.

Note Remember the following:

- In nephrotic syndrome, if there is loin pain, hematuria and deterioration of renal function, it is highly suggestive of renal vein thrombosis. It is more common in membranous nephropaty, mesangiocapillary glomerulonephritis and amyloidosis.
- To diagnose renal vein thrombosis, Doppler ultrasound, CT-Scan or MRI, sometimes renal angiogram (venous phase) may be done.
- Treatment—anticoagulant heparin for 5 to 7 days, then warfarin for 3 to 6 months.

BRIEF DISCUSSION OF DIFFERENT GLOMERULONEPHRITIS

Membranous Glomerulopathy

- It is a common cause of NS in adult, predominantly in males
- It is mostly idiopathic
- May be secondary to—SLE, bronchial carcinoma, drugs (penicillamine), heavy metals like mercury, HBV, HCV
- Renal vein thrombosis is a common complication
- Renal biopsy shows thickening of glomerular basement membrane, increased matrix deposition and glomerulosclerosis
- There is granular subepithelial IgG deposit
- May progress to CKD
- Response to steroid and other cytotoxic drugs is less.

Minimal Change Nephropathy

- Common in children, particularly male, but may occur in all ages, associated with atopy
- On light microscopy, there is no abnormality
- No immune deposit
- On electron microscopy, there is fusion of podocyte foot process
- Progress to renal failure is rare
- Good response to steroid and cytotoxic drugs.

Focal Segmental Glomerulosclerosis

- Segmental scar in glomeruli, no acute inflammation, podocyte foot process fusion may be found. There is C3 and IgM deposition in the affected portions of glomerulus
- Cause is unknown, but may be related to HIV, heroin misuse, morbid obesity, reflux nephropathy, also secondary to any other GN
- Mostly present as idiopathic NS, may progress to renal failure, often resistant to steroid therapy and recurs after renal transplantation
- There is massive proteinuria (usually non selective), hematuria, hypertension and renal impairment.

POST-STREPTOCOCCAL GLOMERULONEPHRITIS (PSGN)

CHIEF COMPLAINTS

- Swelling and puffiness of the face for … day.
- Scanty micturition for … day.
- Generalized weakness, loss of appetite for … day.

HISTORY

History of present illness: According to the patient's statement, she was suffering from pain in the throat with dry cough 3 weeks back from which there was complete recovery. For the last 2 days, she has noticed swelling and puffiness of the face, which is more marked in the morning after waking from sleep. She also complains of scanty micturition, which is slightly smoky and high colored, but no frank blood. The patient also complains of weakness and loss of appetite for the same duration. There is no history of difficulty in breathing, convulsion or unconsciousness or loin pain. She does not give any history of skin infection, arthritis or arthralgia.

History of past illness

Family history

Personal history

Socioeconomic history

Drug history

(Mention according to the patient's statement).

GENERAL EXAMINATION

- Ill looking with puffy face and baggy eyelids
- Mildly anemic
- No edema
- No clubbing, jaundice, cyanosis, leukonychia or koilonychia
- No lymphadenopathy or thyromegaly
- Pulse—110/min
- BP—150/95 mm Hg.

Note Remember the following:

If any skin lesion suggestive of scabies or any skin infection is present, mention it. Diagnosis is then post-streptococcal glomerulonephritis.

SYSTEMIC EXAMINATION

Gastrointestinal System

Mouth, lip, oral cavity—all normal.

Abdomen

1. **Inspection:** No abnormality detected.
2. **Palpation:**
   - No organomegaly
   - Kidneys are not ballotable
   - Fluid thrill—absent
   - There is no tenderness over the renal angle.
3. **Percussion:** Shifting dullness absent.
4. **Auscultation:** No renal bruit.

Cardiovascular System

Heart sounds are normal, no bilateral basal crepitations.

Examination of the other systems reveals no abnormalities.

Examination of urine: Urine is high colored, smoky. There is mild proteinuria.

SALIENT FEATURES

Ms …, 13 years old, student, normotensive, nondiabetic, hailing from …, was suffering from pain in the throat with dry cough 3 weeks back from which there was complete recovery. For the last 2 days, she has noticed swelling and puffiness of the face, which is more marked in the morning after waking from sleep. She also complains of scanty micturition, which is slightly smoky and high colored, but no frank blood. The patient also complains of weakness and loss of appetite for the same duration. There is no history of difficulty in breathing, convulsion or unconsciousness or loin pain. She does not give history of any skin infection, arthritis or arthralgia.

On examination—

General examination (mention as above).
Systemic examination (mention as above).

My diagnosis is acute glomerulonephritis (most likely post-streptococcal).

Q. What is your **differential diagnosis?**

A. Nephrotic syndrome.

Q. **Why** not nephrotic syndrome?

A. Because in nephrotic syndrome, there will be generalized edema, massive proteinuria which are absent in this case. (Serum protein will show hypoalbuminemia). In this case, there is acute onset of facial puffiness followed by scanty smoky urine, absence of generalized edema, presence of hypertension. These are against NS.

Q. **Why** not acute renal failure?

A. Because there is no anorexia, nausea or vomiting. Also, previous history of sore throat followed by scanty micturition is in favor of AGN.

Q. What **investigations** do you suggest in AGN?

A. As follows:

1. Urine R/E: Urine looks smoky. It shows mild to moderate proteinuria, RBC, RBC cast and granular cast (RBC cast is suggestive of AGN)

2. 24 hours urinary total protein (increases, but less than 3 g/L) and volume is less
3. Blood urea, serum creatinine and serum electrolytes
4. CBC (leukocytosis may be present)
5. ASO titer (may be high in post-streptococcal glomerulonephritis)
6. Throat swab for C/S to find streptococcal infection
7. USG of the whole abdomen (to look for renal pathology)
8. CXR (cardiomegaly or pulmonary edema if LVF)
9. Other investigation according to suspicion of causes:
   - ANA, Anti-dsDNA, C3, C4 (if the history is suggestive of SLE)
   - P-ANCA, C-ANCA (if the history is suggestive of vasculitis)
   - HbsAg, Anti-HCV
   - Renal biopsy may be done in some cases.

Q. What are the different **urinary casts** present in different diseases?

A. As follows:
- RBC cast—AGN
- WBC cast—Pyelonephritis
- Granular cast—GN
- Hyaline cast—Normal finding.

RELATED QUESTIONS AND ANSWERS

Q. What is **AGN**? What are the **causes**?

A. AGN is the inflammation in kidney characterized by hematuria, hypertension, edema (periorbital, leg or sacral) and oliguria. Urine shows proteinuria and red cell cast.

Causes are:
- Infection—post-streptococcal commonest. Other infections include infective endocarditis, infectious mononucleosis, HBV, HCV, etc.
- Non-infectious—SLE, Henoch-Schonlein purpura, cryoglobulinemia, etc.
- Primary glomerular disease—diffuse proliferative GN, IgA nephropathy, membranous GN, focal segmental GN.
- Shunt nephritis.

Q. Why there is **hypertension** in AGN?

A. There is salt and water retention secondary to oliguria. Also, there is secondary hyperaldosteronism.

Q. What are the causes of **glomerulonephritis with low complement?**

A. As follows:
- Post-streptococcal glomerulonephritis
- Lupus nephritis
- Infective endocarditis
- Cryoglobulinemia
- Mesangiocapillary glomerulonephritis (90% in type II and 70% in type I)

Q. What are the **complications** of AGN?

A. As follows:
- Acute renal failure
- Hypertension and its complications, such as acute LVF, CVD, hypertensive encephalopathy
- Fluid and electrolyte imbalance

- Nephrotic syndrome
- May lead to chronic glomerulonephritis.

Q. How to **treat**?

A. As follows:

- Rest
- Fluid restriction (total intake 500 to 1000 mL/day)
- Salt restriction
- Protein restriction, if urea and creatinine are high
- Diuretics (frusemide)—to relief edema. If renal function impairment, dose of diuretics is single and high. But if renal function is normal, then divided and low dose
- If hypertension is present, it should be treated accordingly
- Antibiotic—penicillin (crystalline penicillin or phenoxymethyl penicillin) or erythromycin for 7 to 10 days, especially in post-streptococcal glomerulonephritis.
- Management of complication like pulmonary edema, hypertensive encephalopathy, ARF (dialysis may be required).
- If recovery is slow, corticosteroid may be given.

Post-streptococcal glomerulonephritis (PSGN):

- It is a common cause of acute nephritic illness. Caused by group A beta hemolytic streptococcus of nephritogenic type. But can occur following other infection. Common in children than adult. There is a latent period of about 10 days (1 to 3 weeks) after a throat infection or longer after skin infection (such as infected scabies, impetigo, furunculosis), suggesting an immune mechanism. Even streptococcal otitis media or cellulitis can lead to PSGN.
- It is common with poor personal hygiene, over crowding and skin infection like scabies.
- The patient presents with periorbital edema, hypertension, reduced urinary volume. There is reduction of GFR, proteinuria, hematuria, etc. Urine is red or smoky.
- There is low C_3 and C_4 and evidence of streptococcal infection (high ASO, culture of throat swab).
- Prognosis is usually good in children. A small number of adults develop hypertension and/or renal failure later in life.

Characteristics of AGN in adult:

- Usually no preceding history of infection like sore throat, skin infection, etc.
- Edema is not marked
- Hypertension may or may not be present.

READ THE FOLLOWING TOPICS IN RELATION TO AGN

Causes of puffy face:

- Renal cause—nephrotic syndrome, acute glomerulonephritis
- Myxedema
- Cushing's syndrome
- SVC obstruction
- Angioneurotic edema
- Hypoproteinemia
- Congestive cardiac failure in advanced stage
- Alcoholism
- Acromegaly.

Characteristics of edema in different disease:

- Nephrotic syndrome—edema is generalized. It starts in face, and then involves whole body. May be ascites, bilateral pleural effusion, pericardial effusion, etc. due to hypoalbuminemia.
- Congestive cardiac failure—edema starts in leg (dependent edema). In severe, advanced case, there may be ascites, swelling of face.
- Cirrhosis of liver—first there is ascites, then may be edema in leg.
- Malnutrition or hypoproteinemia—edema of the feet and face, later may be ascites or even generalized.

Causes of red urine:

- Hematuria
- Hemoglobinuria
- Myoglobinuria
- Ingestion of beet root, senna, some dyes used to color sweets
- Drugs—rifampicin, clofazimine, phenindione, purgative like phenolphthaline.

Causes of black urine (fresh urine is normal, but when kept for hours, it turns dark):

- Acute intermittent porphyria
- Alkaptonuria.

Causes of painless hematuria:

- Glomerulonephritis, commonly IgA nephropathy
- Renal tuberculosis
- Tumors of urinary system (renal cell carcinoma, papilloma of the urinary bladder, etc.)
- Bleeding disorder
- Anticoagulant or antiplatelet drug therapy
- Bilharziasis (schistosomiasis)
- Interstitial nephritis.

Cause of painful hematuria:

- Renal infection
- Renal calculi
- Trauma
- Polycystic kidney disease (clot colic)
- Loin pain hematuria syndrome
- Hemorrhagic cystitis due to cyclophosphamide.

Few common definitions:

- **Anuria—**it is defined as failure to pass urine more than 50 mL in 24 hours
- **Oliguria—**failure to pass less than 400 mL of urine in 24 hours
- **Nocturia—**need to get up during the night to pass urine
- **Polyuria—**passing of large volume of urine more than 3 L in 24 hours
- **Frequency of micturition—**repeated scanty urination.

POLYCYSTIC KIDNEY DISEASE

CHIEF COMPLAINTS

- Heaviness and mass in abdomen for … months
- Frequency of micturition for … months
- Occasional pain in both loins for … months.

HISTORY

History present illness: The patient states that she was alright … months back. Since then, she has been experiencing heaviness in the abdomen. It is persistent, not related to any food. Also she feels mass on both sides of the abdomen for the same duration. It is associated with pain in both loins, which is dull aching in nature and does not radiate to any site. The patient also complains of frequency of micturition for … months. It is more marked at night, associated with profuse amount of urine, but no burning or pain. There is no history of hematuria, headache, visual disturbance, unconsciousness, nausea, vomiting or anorexia.

History of past illness: The patient is hypertensive for the last … months. She had recurrent UTI few months back.

Family history: Her mother and one brother also have kidney disease, but does not know the specific type of disease.

Personal history: Mention according to the patient's statement.
Socioeconomic history: Mention according to the patient's statement.
Drug history: She took some antibiotics for her recurrent UTI and is taking atenolol for her hypertension.

GENERAL EXAMINATION

- The patient looks healthy
- No edema, clubbing, jaundice, cyanosis, leukonychia or koilonychia
- No lymphadenopathy or thyromegaly
- Pulse—80/min
- BP—130/85 mm Hg with drug.

SYSTEMIC EXAMINATION

Gastrointestinal System

Lips, gums, teeth, tongue and oral cavity—normal.

Abdomen

1. **Inspection:** Abdomen appears distended, flanks are full.
2. **Palpation:**
   - The kidneys are enlarged and ballotable. The right one is slightly larger than the left which are non-tender and firm with irregular surface, moves with respiration above downward and get above the swelling is possible.

- Fluid thrill—absent.
- Both the renal angles are slightly tender.

3. **Percussion:**
   - Shifting dullness—absent
   - Colonic resonance over the mass is present.
4. **Auscultation—**no renal bruit.

Examination of the other systems reveals no abnormalities.

SALIENT FEATURES

Mrs …, 45 years old, housewife, hypertensive, non-diabetic, hailing from …, presented with heaviness in the abdomen for … months. It is persistent, not related to any food. Also she feels mass on both sides of the abdomen for the same duration. It is associated with pain in both loins, which is dull aching in nature and does not radiate to any site. The patient also complains of frequency of micturition for … months. It is more marked at night, associated with profuse amount of urine, but no burning or pain. There is no history of hematuria, headache, visual disturbance, unconsciousness, nausea, vomiting or anorexia. She had recurrent UTI few months back. Her mother and brother also have some kidney disease. She took some antibiotics for her recurrent UTI and is on atenolol for her hypertension.

On Examination—
General examination (mention as above).
Systemic examination (mention as above).

My diagnosis is hypertension with bilateral renal mass, which may be due to polycystic kidney disease.

Q. What is your **differential diagnosis?**

A. Bilateral hydronephrosis with hypertension.

Q. Mention **one** single investigation for your diagnosis.

A. Ultra sonogram of whole abdomen.

Q. What **investigations** should be done in PKD?

A. As follows:
- Ultrasonography (always mention as the first investigation)
- Urine for R/E and C/S
- Full blood count (polycythemia may be found)
- Renal functions—urea, creatinine, serum electrolytes (some patients may be salt looser)
- High resolution CT-Scan or MRI of KUB
- IVU or retrograde pyelography
- Family screening.

Q. What are the **USG criteria** for diagnosis of PKD?

A. USG criteria are:
- Person below 30 years—presence of at least 2 renal cysts (unilateral/bilateral)
- Person between 30 to 59 years—presence of at least 2 renal cysts in each kidney
- Persons 60 years and above—at least 4 cyst in each kidney.

Q. What are the **findings in IVU** in polycystic kidney disease?

A. IVU shows:
- Enlargement of both the kidneys
- Stretching, distortion and elongation of pelvicalyceal system (giving rise to spidery appearance).

RELATED QUESTIONS AND ANSWERS

Q. What is **polycystic kidney disease (PKD)?**

A. It is an inherited cystic disease of the kidney. There are two types:
- Adult PKD (APKD): It is inherited as autosomal dominant, common type, males and females are equally affected. Gene on chromosome 16 (PKD1) and 4 (PKD2).
- Infantile PKD (IPKD): It is inherited as autosomal recessive, rare, associated with cyst in other organs and hepatic fibrosis and fatal in first year due to hepatic or renal failure. Gene on chromosome 6.

Q. What are the **presentations** of adult PKD?

A. As follows:
- May be asymptomatic (renal mass detected on routine examination)
- Discomfort, pain or heaviness in the loin
- Recurrent painful hematuria (due to rupture of cyst in renal pelvis or infection)
- Recurrent UTI
- Acute loin pain or renal colic
- Features of hypertension (usually after 20 years of age) and its complications
- Features of renal failure
- CVA (usually subarachnoid hemorrhage, due to rupture of berry aneurysm. Sometimes, may be cerebral hemorrhage as a complication of hypertension).

Q. What are the **other features** of PKD?

A. As follows:
- Cystic liver—30%, but hepatic dysfunction is rare. There may be cyst in spleen, ovary and pancreas
- Berry aneurysm in circle of Willis—10% (may rupture causing subarachnoid hemorrhage)
- Polycythemia (due to increased erythropoietin secretion)
- Renal stone—10% cases (usually calcium oxalate, urate)
- Renal neoplasm—rarely.

Q. What are the **causes of acute pain** in PKD?

A. Pain is due to:
- Acute hemorrhage in the cyst
- Infection in the cyst
- Renal stone
- Renal cell carcinoma rarely.

Q. If the patient with polycystic kidney disease is **unconscious**, what is likely diagnosis?

A. Subarachnoid hemorrhage due to rupture of berry aneurysm.

Other causes may be:
- Cerebral hemorrhage as a complication of hypertension
- Hyponatremia (salt losing nephropathy).

Q. What are the **causes of death** in PKD?

A. Death may be due to:
- Chronic renal failure (in one third cases)
- Intracerebral hemorrhage (SAH)
- Myocardial infarction.

Q. How to **manage** the patient of PKD?

A. As follows:
- Control of hypertension
- Control of urinary tract infection
- Plenty of fluid
- Salt (there may be salt looser in some cases)
- For renal pain or if large cyst, ultrasonic guided aspiration or laparoscopic cystectomy may be done
- Treatment of renal failure. Dialysis and even renal transplantation may be done
- Genetic counseling
- Family screening—USG of the abdomen should be done in all members of the family over 20 years of age to detect cysts.
- MR angiography to detect berry aneurysm may be considered in some cases, where other members having history of subarachnoid hemorrhage.

Note Remember the following points:
- Polycystic kidney disease is always bilateral (may be unilateral, if other kidney is absent)
- Polycystic kidney disease is a misnomer, cyst occurs in many other organs (liver, spleen)
- More common in sickle cell disease, cystic fibrosis, Huntington's disease
- May be associated with mitral valve prolapse (25%), causing mitral regurgitation, and aortic regurgitation (rarely severe)
- Colonic diverticula may occur
- Abdominal wall hernia
- Polycystic kidney disease is not premalignant
- Hypertension is present in 75% cases
- Usually there is polycythemia due to high erythropoietin level.There may be anemia if there is chronic renal failure (however, hemoglobin level is higher than expected for the degree of renal failure).

Q. What are the causes of **unilateral renal mass?**

A. As follows:
- Renal cell carcinoma
- Hydronephrosis or pyonephrosis
- Renal abscess
- Solitary kidney (due to hypertrophy) in lean and thin person.

Q. What are the causes of **bilateral** renal mass**?**

A. As follows:
- Polycystic kidney disease
- Bilateral hydronephrosis
- Amyloidosis
- Diabetic nephropathy in early stage
- Bilateral renal cell carcinoma (rare)
- Lymphoma (rare).

Q. What are the **cystic diseases** of kidney?

A. As follows:

- Simple cyst, usually congenital
- Acquired cyst, after dialysis (in chronic renal failure)
- Polycystic kidney disease
- **Medullary sponge kidney:** Cause is unknown, but not genetic. Cyst is confined to the papillary collecting ducts. Age 40 to 60 years, prognosis is good. Usually no hypertension or no renal failure.
- **Medullary cystic disease:** Small cysts in cortical area or corticomedullary junction. Renal failure is common, hypertension may occur. The patients usually have polyuria and increased thirst and are salt loser.

READ THE FOLLOWING TOPICS

Types of hematuria:

- **Initial Hematuria:** Presence of blood at the beginning of micturition. It is usually due to penile urethral cause.
- **Terminal hematuria:** Presence of blood at the end of micturition. It is usually due to bladder neck or prostatic urethral cause.
- **Total hematuria:** Presence of blood throughout micturition. It is usually due to bladder or urinary tract disease (such as renal cell carcinoma, papilloma of urinary bladder, UTI, renal stone) or blood dyscrasia or excess anticoagulant.

Urinary incontinence: It means when urine leaks involuntarily. It is of 4 types:

- **Stress incontinence:** Leakage of urine with activity such as coughing, sneezing, lifting any object, exercise. Found in women after child birth and in man after prostate operation.
- **Urge incontinence:** Uncontrolled leakage of urine preceded by strong urge to void urine. It is due to UTI, enlargement of prostate, stone in urinary bladder.
- **Overflow incontinence:** This occurs when the bladder is chronically over distended. Found in benign prostatic enlargement, pelvic surgery leading to pelvic nerve damage.
- **Continual incontinence:** Patient voids urine at any time, at any position due to loss of sphincter efficacy. Found in vesico-vaginal fistula, uretero-vaginal fistula.

Causes of red/dark urine:

- Hematuria (red)
- Hemoglobinuria (dark)
- Myoglobinuria (in rhabdomyolysis)
- Food dye (beet root)
- Drugs—rifampicin (orange), L-dopa (dark on standing), phenophthalein (pink), senna (orange)
- Acute intermittent porphyria (urine becomes dark on standing)
- Alkaptonuria (urine becomes black on standing).

Q. How to **differentiate** between hematuria and hemoglobinuria?

A. As follows:

Points	Hematuria	Hemoglobinuria
1. Urine	Red	Dark
2. Microscopy	RBC present	RBC absent

CHRONIC KIDNEY DISEASE (CKD, DIABETIC NEPHROPATHY)

CHIEF COMPLAINTS

- Weakness and loss of appetite for … months
- Nausea and occasional vomiting for … months
- Scanty micturition for … days
- Swelling and puffiness of the face for … days.

HISTORY

History of present illness: According to the patient's statement, she was alright … years back. At that time, she was diagnosed as diabetes mellitus incidentally. It was treated with insulin for few months, then oral hypoglycemic drugs. About 5 years back, the patient noticed swelling of both lower limbs. After evaluation, it was treated with frusemide. For the last 3 years, she has been suffering from weakness, loss of appetite, nausea and occasional vomiting. Weakness is progressively increasing. Vomitus contains food material but no blood or bile. The patient also noticed swelling of the face and legs which is associated with scanty micturition during daytime and frequently at night, which disturbs her sleep. For the last … months, she noticed gradual swelling of whole body and puffiness of the face, which is more marked after getting up from sleep in the morning. There is marked weight loss over the last … months. Occasionally, she experiences palpitation and breathlessness on exertion. For these complaints, she consulted with a nephrologist who advied immediate hospitalization for further management. Her bowel habit is normal. There is no history of fever, abdominal pain, loin pain, itching, joint pain, skin rash or hematuria.

History of past illness: She is nonhypertensive. She gives history of recurrent UTI for the last ... months. For this, she was treated with several antibiotics by local physicians.

Family history: There is no history of such illness in her family.
Personal history: Mention according to the patient's statement.
Socioeconomic history: Mention according to the patient's statement.
Drug history: She did not take any drug that may be responsible for such illness.

GENERAL EXAMINATION

- The patient is ill looking and pale, with puffy face and baggy eyelids
- Moderately anemic
- Pitting edema—present
- There is leukonychia (or half and half nail—proximal brown, distal whitish) involving all the fingers and toes
- No clubbing, jaundice, cyanosis or koilonychia
- No lymphadenopathy or thyromegaly
- Skin—multiple scratch marks are present, also there is pigmentation
- Pulse—110/min
- BP—160/95 mm Hg.

(If any fistula for dialysis, comment on it).

SYSTEMIC EXAMINATION

Gastrointestinal System

Lip, teeth, oral cavity, tongue—normal but tongue is pale.

Abdomen

- **Inspection:** No abnormality detected
- **Palpation:**
  - No organomegaly
  - Kidneys are not ballotable
  - Fluid thrill—absent
  - There is no tenderness over the renal angle
- **Percussion:** Shifting dullness absent
- **Auscultation:** No renal bruit.

Nervous System:

- **Higher psychic functions**—normal
- **Cranial nerves**—normal
- **Motor function**—normal
- **Sensory function**—normal
- **Fundoscopy**—diabetic retinopathy grade II.

(However, in motor function, there may be muscular weakness, diminished reflexes, planter equivocal. All are related to neuropathy. Also, in sensory function—there may be reduction of pain, touch, temperature in the legs and hands, due to peripheral neuropathy. So, mention according to your findings.)

Bedside urine examination: Sugar present, protein +++.

Examination of the other systems reveals no abnormalities.

SALIENT FEATURES

Mrs. …, 60 years old, housewife, normotensive, nonsmoker, hailing from …, was diagnosed as diabetes mellitus … years back. It was treated with insulin for few months, then oral hypoglycemic drugs. About 5 years back, the patient noticed swelling of both lower limbs. After evaluation, it was treated with frusemide. For the last 3 years, she has been suffering from weakness, loss of appetite, nausea and occasional vomiting. Weakness is progressively increasing. Vomitus contains food material but no blood or bile. The patient also noticed swelling of the face and legs, which is associated with scanty micturition during daytime and frequently at night, which disturbs her sleep. For the last … months, she noticed gradual swelling of whole body and puffiness of the face, which is more marked after getting up from sleep in the morning. There is marked weight loss over the last … months. Occasionally, she experiences palpitation and breathlessness on exertion. For these complaints, she consulted with a nephrologist who advised immediate hospitalization for further management. Her bowel habit is normal. There is no history of fever, abdominal pain, loin pain, itching, joint pain, skin rash or hematuria.

She gives history of recurrent UTI for the last ... months, for which she was treated with several antibiotics by local physicians. There is no history of such illness in her family. She did not take any drug that may be responsible for such illness.

On Examination—
General examination (mention as above).
Systemic examination (mention as above).

My diagnosis is chronic kidney disease (CKD) due to diabetic nephropathy.

Q. What investigations do you suggest in CKD?

A. As follows:
- Urine R/E (to see pus cell, RBC or WBC cast, glycosuria, proteinuria, etc.)
- CBC with PBF (shows normocytic, normochromic anemia)
- Renal function tests (blood urea and serum creatinine are elevated)
- Creatinine clearance
- Serum electrolytes
- Serum calcium (low) and phosphate (high)
- Serum uric acid (may be high)
- Plain X-ray abdomen (calcification, renal stone, kidney size may be seen)
- USG of the whole abdomen (shows shrunken kidneys. Kidneys may be large in diabetic glomerulosclerosis, amyloidosis, PKD and bilateral hydronephrosis)
- CT scan of abdomen
- IVU (rarely needed)
- Isotope renogram
- Renal biopsy (may be needed in some cases)
- Other investigation according to suspicion of cause (ANA and anti ds-DNA for SLE, screening for hepatitis B and C, HIV, etc.).

RELATED QUESTIONS AND ANSWERS

Q. What is **CKD** and what is **ESRD**?

A. As follows:
- CKD is the irreversible deterioration of renal function, classically developing over a period of years
- End stage renal disease or failure (ESRD) is a stage when renal replacement therapy is compulsory either dialysis or renal transplantation, without which death is likely.

Q. What is **acute renal failure?** What are the **causes?**

A. Sudden deterioration in renal function, occurring within weeks or months (<3 months), biochemically detected by high urea and creatinine level. This is usually reversible.

Causes of ARF:

1. Prerenal:
   - Fluid loss due to diarrhea, vomiting, dehydration, etc
   - Blood loss due to hemorrhage.
   - Plasma loss in burn
   - Hypotension due to myocardial infarction, shock, vasodilator drugs, heart failure
   - Rhabdomyolysis
   - Hemolytic uremic syndrome
   - Hepatorenal syndrome
   - Renal artery occlusion or stenosis
   - Disease affecting arterioles.

(Under perfusion to the kidney initially causes rapidly reversible changes. Subsequently, acute tubular necrosis or other changes cause long lasting but usually temporary intrinsic renal failure.)

2. Renal (intrinsic renal disease):
   - Acute tubular necrosis or toxic or septic renal failure (85%)
   - RPGN, due to:
     a. Primary GN, e.g. MCGN, IgA nephropathy
     b. Systemic disease such as SLE, rheumatoid arthritis, systemic sclerosis, multiple myeloma, vasculitis
   - Tubulo-interstitial disease (10%) due to drugs (NSAIDs, ciprofloxacin, allopurinol, sulfonamide, cyclosporine).
3. Post renal:
   - Urethral—phimosis, paraphimosis, stricture, stone, blood clot, slaughed papilla.
   - Bladder neck—prostatic hypertrophy, malignancy, stone.
   - Bilateral ureteric—calculus, following surgery, pelvic tumor, uterine prolapse, retroperitoneal fibrosis (due to radiation, methysergide, idiopathic).

Q. What are the **causes** of CKD?

A. As follows:
- Glomerular diseases (30 to 40%), e.g. IgA nephropathy, MCGN
- Diabetes mellitus (20 to 40%)
- Hypertension (5 to 20%)
- Obstructive uropathy
- Chronic pyelonephritis
- Tubulointerstitial diseases (5 to 10%)
- Systemic inflammatory diseases (5 to 10%), e.g. SLE, vasculitis
- Renal artery stenosis (5%)
- Congenital and inherited (5%), e.g. polycystic kidney disease, Alport's syndrome
- Unknown (5 to 20%).

Q. What are the **clinical manifestations** of CKD?

A. As follows:
1. May be asymptomatic, until GFR falls below 30 mL/min/1.73 m^2 of body surface area. High urea and creatinine may be found on routine investigation, sometimes there may be hypertension, anemia, proteinuria on routine urine examination.
2. General features—early features may be nocturia, polyuria, anorexia, nausea, vomiting, diarrhea, weakness, malaise, insomnia, breathlessness on exertion, paresthesia, bone pain, edema, amenorrhea in woman, sexual dysfunction in man.
3. In ESRF—general features are more severe, and CNS symptoms may be more. Features like hiccup, pruritus, deep respiration (Kussmaul's respiration), muscular twitching, fit, drowsiness, even coma may occur.
4. Other features may be present, which may occur due to involvement of different systems of the body (see below).

Q. What are the different **features** due to involvement of different systems of the body?

A. CKD can involve any system of the body, symptoms and signs may develop according to the involvement:
1. Bone diseases (renal osteodystrophy):
   - Osteomalacia (or ricket called renal ricket)
   - Osteoporosis
   - Osteosclerosis (in vertebral body, giving rise to Rugger Jersey spine)
   - Osteitis fibrosa cystica.

2. Skin disease:
   - Pruritus—due to retention of nitrogenous waste products, hypercalcemia, hyperphosphatemia, hyperparathyroidism and iron deficiency. Patient on dialysis, inadequate dialysis may have pruritus due to unknown mechanism
   - Dry skin
   - Eczematous lesions, particularly near arteriovenous fistula
   - Ecchymosis in advanced disease due to increased bleeding tendency
   - Porphyria cutanea tarda (PCT) due to decreased hepatic uroporphyrinogen decarboxylase and decreased clearance of porphyrins in urine or by dialysis
   - Pseudoporphyria (features like PCT but without enzyme deficiency).
3. Gastrointestinal—anorexia, nausea, vomiting. Also there may be decreased gastric emptying, increased risk of reflux esophagitis, peptic ulceration, acute pancreatitis and constipation.
4. Metabolic abnormalities:
   - Hyponatremia, hyperkalemia or sometimes hypokalemia
   - Metabolic acidosis (due to increased tissue catabolism and retention of organic acids)
   - Hyperuricemia and gout
   - Hypocalcemia, hyperphosphatemia
   - Lipid abnormalities (hypercholesterolemia, hypertriglyceridemia).
5. Endocrine abnormalities:
   - Secondary hyperparathyroidism, may be tertiary
   - Prolonged half-life of insulin, due to reduced tubular metabolism of insulin. Also, insulin requirement in a diabetic patient decreases. But in advanced CKD, there may be end organ resistance to insulin, leading to impaired glucose tolerance
   - Hyperprolactinemia (presents with galactorrhea in men as well as women, loss of libido and sexual dysfunction in both sexes).
   - Others—increased LH, decreased serum testosterone (erectile dysfunction, decreased spermatogenesis), oligomenorrhea or amenorrhea (in female), impaired growth in children, abnormal thyroid hormone levels (hypothyroid feature), partly because of altered protein binding.
6. Muscle dysfunction:
   - Generalized myopathy (due to the combination of poor nutrition, vitamin D deficiency, electrolyte abnormalities, hyperparathyroidism)
   - Muscle cramps
   - Restless leg syndrome.
7. Nervous system:
   - Peripheral nervous system:
     i. Polyneuropathy—both motor and sensory. Improves or resolve with dialysis
     ii. Median nerve compression in the carpal tunnel due to β 2 microglobulin related amyloidosis
     iii. Restless leg syndrome.
   - Central nervous system:
     i. Clouding of consciousness, convulsion, coma
     ii. Asterixis (flapping tremor)
     iii. Tremor
     iv. Myoclonus
     v. Dialysis disequlibrium syndrome
     vi. Dialysis dementia
     vii. Psychiatric problems—(anxiety, depression, phobia, psychosis)
     viii. CVD secondary to hypertension.

- Autonomic dysfunction:
  i. Postural hypotension
  ii. Fixed heart rate
  iii. Urinary retention or incontinence
  iv. Constipation
  v. Impotence
  vi. Pupillary constriction
  vii. Gustatory sweating
  viii. Anhydrosis.

8. Calciphylaxis (calcific uremic arteriolopathy)—rare but life threatening
9. Cardiovascular:
   - Hypertension
   - Cardiac failure
   - Pericarditis, pericardial effusion or tamponade, chronic constrictive pericarditis
   - Uremic cardiomyopathy
   - Increased atherosclerosis
   - Left ventricular hypertrophy is common in ESRF, even arrhythmia leading to death may occur
   - Systolic dysfunction due to myocardial fibrosis, abnormal myocyte function due to uremia, calcium overload and hyperparathyroidism, carnitine and selenium deficiency
   - Coronary artery calcification.
10. Respiratory—pulmonary edema (uremic lung) due to fluid overload
11. Malignancy—incidence is increased in CKD (RCC)
12. Nephrogenic systemic fibrosis—seen in patients with moderate to severe CKD, particularly those on dialysis. There is skin involvement with plaques, papules and nodules. The affected skin becomes thick, firm and assume a peau d'orange appearance. There is also muscle stiffness, joint contracture and fibrosis of lungs, pleura, diaphragm, myocardium, pericardium and dura mater. Probably Gadolinium containing contrast agent is responsible for this.

Q. What are the **stages** of CKD?

A. As follows:

Stage	Description	GFR (mL/min/1.73 m^2)
1	Kidney damage with normal or ↑ GFR	≥ 90
2	Kidney damage with mild ↓ GFR	60 to 89
3	Moderate ↓ GFR A&B	30 to 59 (**A:** 45 to 59, **B:** 30 to 44)
4	Severe ↓ GFR	15 to 29
5	Kidney failure	< 15 (or dialysis)

Q. What are the **causes of anemia** in CKD?

A. Anemia is common in CKD, correlates with the severity of renal failure. It is usually normocytic and normochromic. The mechanisms are:

- Erythropoietin deficiency (most significant)
- Diminished erythropoiesis due to toxic effects of uremia on bone marrow suppression. Also by PTH, ACE inhibitor
- Reduced dietary intake and absorption of hematinics (iron, vitamin B12, folic acid)
- Increased red cell destruction (may also be during hemodialysis due to mechanical, oxidant and thermal damage)

- Increased blood loss due to capillary fragility, poor platelet function, occult gastrointestinal bleeding and blood loss during hemodialysis
- Erythropoietin alpha therapy may cause anemia (by pure red cell aplasia).

Note Remember the following:

- Anemia is less severe or absent in polycystic kidney disease, as erythropoietin is relatively more in this case
- In CKD, the patient can tolerate mild to moderate anemia, because there is more release of oxygen from hemoglobin. The mechanisms are—in CKD patient, there is acidosis and high 2, 3 DPG level in RBC, which shifts the oxygen dissociation curve to the right and more oxygen is released from hemoglobin. So, the patient doesn't require blood transfusion in mild to moderate anemia. Target hemoglobin is 11 to 12.5 g/dL.
- Anemia becomes obvious in stage B CKD.

Q. What is **renal osteodystrophy**?

A. This is a group of metabolic bone disease secondary to chronic renal failure and comprises the following:

- Osteomalacia (or ricket, called renal ricket)
- Osteoporosis
- Osteosclerosis (in vertebral body, giving rise to Rugger jersey spine)
- Osteitis fibrosa cystica.

Note Remember the following:

There may be adynamic bone disease in which bone formation and resorption are both depressed. Cause is unknown, may cause spontaneous fracture. There may be hypercalcemia, normal alkaline phosphatase, PTH is low, dual X-ray absorptiometry shows osteopenia. No proven treatment.

Q. What are the **mechanisms** of renal osteodystrophy?

A. As follows:

- Osteomalacia is secondary to deficiency of 1, 25-dihydroxycholecalciferol as kidney is unable to convert 25 hydroxycholecalciferol to 1,25 dihydroxycholecalciferol, due to deficiency of 1 α-hydroxylase enzyme
- Osteoporosis, though its mechanism is unknown, may be due to secondary hyperparathyroidism and hypocalcemia, also probably due to malnutrition
- Osteosclerosis—due to hyperparathyroidism which causes increased bone density, particularly seen in the spine in which there is bands of sclerosis in the margin and porotic bone in between, giving rise to Rugger jersey spine
- Osteitis fibrosa cystica—due to secondary hyperparathyroidism.

Q. How to **treat** renal osteodystrophy?

A. As follows:

- Treatment of renal failure
- Calcium supplement
- 1-α hydroxylated synthetic analog of vitamin D (active vitamin D).

Q. How to **treat CKD**?

A. As follows:

1. General measures:
   - Fluid restriction

- Salt restriction
- Protein restriction (0.5 g/kg body weight/day). However, this is controversial. Severe protein restriction is avoided. Excess consumption of protein should be avoided
- Smoking should be stopped
- Social and psychological support.

2. Symptomatic and supportive:
   a. Hypertension: Good control of blood pressure delays renal deterioration. Target control of BP is 130/80 mm Hg (if UTP < 1g/day) and 125/75 mm Hg (if UTP > 1g/day)
      - ACE inhibitor, increased to maximum dose
      - ARB is added, if goal is not achieved (in case of type 2 DM, treatment should be started with ARB)
      - Diuretic to prevent hyperkalemia and to help control BP. High and single dose is preferable
      - Calcium channel blocker (verapamil or diltiazem), added if goal is not achieved.
   b. Statins for dyslipidemia
   c. Hyperkalemia:
      - Dietary restriction of potassium intake (fruits like banana, orange, coconut, etc)
      - Drugs causing potassium retention should be stopped. (e.g. ACEI, ARB, spironolactone, ciclosporin)
      - Injection 10% calcium gluconate 10 cc over 5 minutes, may be repeated (it is cardio-protective, provides protection for 2 hours)
      - Glucose and insulin (50 mL of 50% glucose I/V + injection insulin 10 units), may be repeated
      - Correction of acidosis (if pH < 6.9, Inj. sodi-bi-carb 7.5% I/V, 50 to 100 mL daily for 3 days)
      - Occasionally, ion exchange resins may be needed (calcium resonium powder 15 g in 1 cup water to be taken orally. If the patient is unconscious, it may be given as enema, which is more effective then oral route)
      - If all fails or hyperkalemia is severe, hemodialysis or peritoneal dialysis may be needed.
   d. Acidosis:
      - Sodium bicarbonate (1.26%, IV) or calcium carbonate (upto 3 g/day). Bicarbonate should be maintained above 22 mmol/L.
   e. Calcium and phosphate control and suppression of PTH:
      - Hypocalcemia should be treated with calcitriol or alpha-calcidol and calcium supplementation. Serum calcium should be monitored frequently to avoid hypercalcemia.
      - For hyperphosphatemia—dietary restriction of phosphate containing food (milk, cheese, eggs) and phosphate binding drugs like calcium carbonate, aluminium hydroxide and lanthanum carbonate may be used with food to prevent phosphate absorption. Polymer based phosphate binders may be used.
   f. Anemia:
      - Synthetic (recombinant) human erythropoietin (EPO). Side effects are hypertension and thrombosis (may occur in arteriovenous fistula, used for hemodialysis)
      - If there is no response after 300 IU/kg weekly, or a fall in hemoglobin after a satisfactory response, then erythropoietin is likely to be ineffective, which may be due to iron deficiency, bleeding, infection, malignancy, formation of anti-EPO antibody or aluminum overload that occur in dialysis. These should be searched and treated. If iron is needed, it should be given intravenously.
      - Blood transfusion may be given in severe anemia. Risk of blood transfusion in CKD patient—fluid overload, potassium overload, increased chance of graft rejection after kidney transplant, so blood transfusion is better to be avoided. In severe anemia, BT should be given during hemodyalisis.

g. Male erectile dysfunction:
   - Testosterone deficiency should be corrected
   - Phosphodiesterase inhibitors like sildenafil may be used.

3. Definitive treatment of CKD – renal replacement therapy may be given, such as:
   - Hemodialysis
   - Hemofiltraiton
   - Peritoneal dialysis
   - Renal transplantation.
4. Treatment of primary cause, if any:
   - Diabetis melitus—insulin
   - Hypertension—antihypertensive
   - APKD—sirolimus decreases the cyst size
   - Removal of obstruction in obstructive uropathy.

Q. What are the **reversible factors** in CKD?

A. As follows:
- Hypertension
- Reduced renal perfusion, such as—renal artery stenosis, hypotension due to drug treatment, sodium and water depletion, poor cardiac function
- Urinary tract infection
- Urinary tract obstruction
- Other systemic infections that causes increased catabolism and urea production
- Nephrotoxic drugs.

Q. What are the indications of **urgent dialysis**?

A. As follows:
- Severe hyperkalemia
- Pulmonary edema or severe fluid overload
- Severe metabolic acidosis
- Uremic pericarditis
- Uremic encephalopathy
- Toxicity with a dialyzable poison (methanol, barbiturate, etc.)
- Recurrent vomiting due to uremia.

Q. What are the **indications** of renal replacement therapy?

A. As follows:
- Serum creatinine > 600 to 800 µmol/L (7 to 9 mg/dL), or e.GFR< 8 to 10
- Hyperkalemia (plasma potassium > 6 mmol/L despite medical treatment)
- Metabolic acidosis (H^+ > 56 nmol/L, pH < 7.25), HCO_3< 10 mmol/L
- Fluid overload and pulmonary edema
- Uremic pericarditis or encephalopathy
- Sepsis (tentative evidence for mediator removal), CRRT (continuous renal replacement therapy).

READ THE FOLLOWING TOPICS

Hemodialysis

Complications:

- Hypotension during dialysis due to fluid removal and hypovolemia. There may be chest pain and leg cramps

- Cardiac arrhythmia due to potassium and acid base shift
- Hemorrhage due to anticoagulation. Also, venous needle disconnection may lead to hemorrhage
- Anaphylactic reaction
- Sepsis, usually involving vascular access devices
- Pulmonary edema due to fluid overload
- Hemolytic reactions
- Air embolism
- Hard water syndrome
- Dialysis disequilibrium due to rapid correction of uremia.

Contraindication of HD:

- CCF with low EF%
- Generalized atherosclerosis with poor vascular access for AVF.

(They are the ideal candidate for peritoneal dialysis).

Peritoneal Dialysis

Complications:

- Peritonitis due to infection
- Infection around the catheter site
- Constipation
- Massive pleural effusion (dialysate leak through a diaphragmatic defect into the thoracic cavity). Dialysate may leak into the scrotum down through a patent processus vaginalis
- Failure of peritoneal membrane function due to long-term CAPD
- Sclerosing peritonitis (potentially fatal).

Contraindications:

- Previous peritonitis causing peritoneal adhesions
- Presence of a stoma (e.g. colostomy)
- Active intra-abdominal sepsis (absolute contraindication)
- Abdominal hernia
- Co-morbidities like coronary artery disease, congestive cardiac failure.

Q. What are the **complications** of long-term dialysis?

A. As follows:

- Cardiovascular disease
- Sepsis (leading cause of death in long term dialysis patient)
- Dialysis associated ascites
- Dialysis amyloidosis
- Dialysis associated arthropathy.

Renal transplantation is the treatment of choice for ESRD.

Q. What are the **contraindications** of renal transplantation?

A. As follows:

1. Absolute:
   - Active malignancy – a period of at least 2 years of complete remission recommended for most tumors

- Active vasculitis or recent anti GBM disease
- Severe heart disease or any severe co-morbid condition
- Severe occlusive aorto-iliac vascular disease.

2. Relative:
   - Age—while practice varies, transplants are not routinely offered to very young children (< 1 year) or older people (>75 years)
   - High risk of disease recurrence in the transplant kidney
   - Disease of the lower urinary tract—in patients with impaired bladder function, stricture urethra (ileal conduit may be considered.)
   - Significant co-morbidity.

Q. What drugs are used to **prevent rejection**?

A. Usually a combination of:
- Cyclosporine or tacrolimus
- Azathioprine or mycophenolate mofetil/ sirulimus or evanolimus
- Prednisolone.

Q. What are the **complications** after renal transplantation?

A. As follows:
- Acute rejection
- Chronic rejection
- Infection—CMV, pneumocystis jiroveci, oral candidiasis, polioma virus. Bacterial infection is common in first few months
- Complication of immunosuppressive drugs including steroid
- Acute tubular necrosis (ATN)—it is the most common cause of cadaveric graft dysfunction (40 to 50%). It is associated with a worse long-term outcome and predisposes to rejection.
- Technical failures—occlusion or stenosis of the arterial anastomosis, occlusion of the venous anastomosis and urinary leaks
- Post transplantation lymphoproliferative disorder—EBV associated malignancies (such as lymphoma) are common in patients who received biological agents and in children
- Chronic allograft nephropathy—most common cause of late graft failure
- Malignancy—skin tumor (including basal and squamous cell carcinoma), renal, cervical and vaginal
- Hypertension
- Atherosclerosis
- Recurrence of renal disease.

Complication of Renal transplantation (Remember the formula— 'TROPICAL'):
- **T**–Thrombosis of graft kidney artery and vein
- **R**–Rejection of graft kidney
- **O**–Obstruction of graft ureter with perinephric hematoma, seroma, urinoma, or lymphocele
- **P**–Primary disease recurrence. The most common recurrence is MCGN type II (80 to 100%)
- **I**–Infection which may be bacterial (any, TB), Viral (CMV, chicken pox, polioma virus), fungal, (*Cryptococcuus neoformans*), Parasite (*Pneumocystis Jiroveci*, ispspora cycloporium , microspora, Giardia)
- **C**–ciclosporine toxicity and other imunosupressive drugs toxicities
- **A**–Acute tubular necrosis
- **L**–Leakage of graft ureter due to error or ischemia.

Q. What is **acute rejection**?

A. Acute rejection characterized by rising of creatinine, fever, loin pain, hypertension, swelling of the graft. Urine shows protein, lymphocyte, and renal tubular cells. Occurs in 10 to 30% cases within 6 months. Graft biopsy shows immune cell infiltrate and tubular damage.

Treatment—high dose methylprednisolone, resistant cases may require antithymocyte globulin or ALG or OKT3 may be used.

Q. What is **chronic rejection**?

A. It occurs usually after 6 months. The patient presents with gradual rise of creatinine and proteinuria. Graft biopsy shows vascular change, fibrosis and tubular atrophy. It is not responsive to increased immunosuppression.

HYPERTENSION WITH CKD

CHIEF COMPLAINTS

- Frequency of micturition for … months
- Excessive thirst, weakness and palpitation for … months
- Anorexia, nausea and occasional vomiting for … months.

HISTORY

History of present illness: The patient was alright about … years back. Then she noticed swelling of the face and legs, associated with scanty micturition, increased thirst, palpitation and weakness for which she consulted with local doctor. After evaluation, she was diagnosed as a case of kidney disease and referred to nephrologist. She was hospitalized and thorough investigation was done including renal biopsy from left kidney. While she was in the hospital, treatment with prednisolone and ranitidine were given, continued for 6 months. With this treatment, the patient was feeling better. 2 years later, she again developed same type of illness. Her weakness is increasing, which is associated with severe loss of appetite followed by occasional vomiting. She denies any history of fever, abdominal pain, loin pain or burning during micturition. With this problem , she was admitted in the hospital.

After evaluation, she was found having severe renal failure, hypertension, severe anemia. Emergency dialysis was given along with blood transfusion. Subsequently an arterio-venous fistula was made in the left forearm. Now patient is on regular hemodialysis 3 session per week.

History of past illness: There is no history of diabetes mellitus or hypertension or any infection prior to her present illness.

Family history: There is no such illness in the family.

Personal history: Mention according to the patient's statement.

Socioeconomic history: Mention according to the patient's statement.

Drug history: She did not take any drug that may be responsible for such illness.

GENERAL EXAMINATION

- Ill looking, puffy face and depressed looking
- Moderately anemic
- Edema—present, pitting
- Nail—half and half nail, no clubbing
- No jaundice, cyanosis
- No lymphadenopathy or thyromegaly
- Pulse—110/min
- BP—200/110 mm Hg
- Skin—dry, there are multiple scratch mark.

SYSTEMIC EXAMINATION

Gastrointestinal System

Lip, gum, tongue, oral cavity—looks pale.

Abdomen

1. **Inspection:** No abnormality detected.
2. **Palpation:**
   - No organomegaly
   - Kidneys are not ballotable
   - Fluid thrill—absent
   - There is no tenderness over the renal angle.
3. **Percussion:** Shifting dullness is absent.
4. **Auscultation:** No renal bruit.

Nervous System

All findings like HPF, motor, sensory, etc. are normal. Fundoscopy shows - Bilateral papilloedema present.

Examination of the other systems reveals no abnormalities.

Bedside urine for protein: (++) or (+++)

SALIENT FEATURES

Mrs … 40 years old, housewife, nondiabetic, nonsmoker, hailing from …was hospitalized with frequency of micturition, excessive thirst, weakness and palpitation ,anorexia, nausea and occasional vomiting for … months.

The patient was alright about … years back. Then she noticed swelling of the face and legs, associated with scanty micturition, increased thirst, palpitation and weakness for which she consulted with local doctor. After evaluation, she was diagnosed as a case of kidney disease and referred to nephrologist. She was hospitalized and thorough investigation was done including renal biopsy from left kidney. While she was in the hospital, treatment with prednisolone and ranitidine were given, continued for 6 months. With this treatment, the patient was feeling better. About 2 years later, she again developed same type of illness. Her weakness is increasing, which is associated with severe loss of appetite followed by occasional vomiting. She denies any history of fever, abdominal pain, loin pain or burning during micturition. With this problem, she was admitted in the hospital.

After evaluation, she was found having severe renal failure, hypertension, severe anemia. Emergency dialysis was given along with blood transfusion. Subsequently an arterio-venous fistula was made in the left forearm. Now patient is on regular hemodialysis 3 sessions per week.

On Examination—
General examination (mention as above).
Systemic examination (mention as above).

My diagnosis is hypertension with CKD (stage v) on maintenance hemodialysis.

Q. What is your **differential** diagnosis?
A. Chronic pyelonephritis.

Q. What **investigations** should be done in this case?
A. As follows:
1. Urine analysis:
   - Low and fixed specific gravity (around 1.010)

- Albuminuria may be present. RBC, WBC
- Granular casts may be present.

2. CBC and PBF examination (shows normocytic, normochromic anemia)
3. Renal function tests (blood urea and serum creatinine are high)
4. Creatinine clearance (important to assess the severity of renal failure)
5. Serum electrolytes, calcium and phosphate (shows hypocalcemia, hyperphosphatemia, hyperkalemia and reduced bicarbonate level).
6. Serum uric acid (may be high).
7. Plain X-ray abdomen (shows the presence of any obstructive uropathy, may also show the kidney size).
8. USG of the whole abdomen (typically shows bilateral contracted kidney. Kidneys may be enlarge or normal in size in diabetic glomerulosclerosis, amyloidosis, polycystic kidney diseases, bilateral hydronephrosis and myeloma kidney).
9. CT scan of abdomen.

Q. What are the **types** of glomerulonephritis?

A. It may be primary or secondary:

1. **Primary:**
   - Minimal change
   - Membranous
   - Proliferative:
     a. Post-streptococcal (and after other infection)
     b. Mesangiocapillary
     c. Crescentic
     d. Mesangial proliferative
   - IgA nephropathy
   - Focal segmental glomerulosclerosis. (FSGS).
2. **Secondary to systemic disease:**
   - Systemic lupus erythromatosis (SLE)
   - Wegener's granulomatosis
   - Polyarteritis nodosa (PAN)
   - Goodpasture's syndrome
   - Honoch-Schonlein purpura
   - Infective endocarditis
   - Cryoglobulinemia with or without hepatitis C
   - Multiple myeloma.

Q. What is the **treatment** of CGN?

A. If any cause is identified, it should be treated. Other treatment as in CRF.

BRIEF NOTES ABOUT BERGER'S IGA NEPHROPATHY

Definition: It is a type of immune complex mediated focal and segmental proliferative glomerulonephritis with mesangial deposition of IgA. In some cases, IgG, IgM, C_3 may be deposited in mesangium. It is the most common form of glomerulonephritis.

Presentation: It is common in children and young adults. Males are 2 to 3 times more affected than female. Most patients usually present with recurrent microscopic or even gross hematuria. It may follow a viral respiratory or GIT infection or flu like illness. Hematuria is universal, proteinuria is usual and hypertension is common, 5% may develop nephrotic syndrome. In some cases, progressive

loss of renal function, leading to end stage renal failure (20%) in 20 years. IgA nephropathy may be associated with hepatic cirrhosis, celiac disease, HIV and CMV infection.

It may be confused with Henoch-Schonlein purpura (HSP). IgA nephropathy causes only kidney. HSP causes systemic disease involving skin, gut, kidney and joints.

Investigations:

- Serum IgA—high in upto 50% (serum complements are usually normal)
- Immune complex estimation
- Kidney biopsy shows focal proliferative glomerulonephritis with diffuse mesangial IgA deposit. In some cases, IgG, IgM, C_3 may be deposited in mesangium
- Skin biopsy often shows granular deposit of IgA in dermal capillaries of affected patients
- Other investigations—renal function tests, ultrasonogram of renal system

Treatment:

- Episodic attack resolves spontaneously
- Patient with proteinuria over 1 to 3 g/day, mild glomerular change and good renal function should be treated with steroid
- In progressive renal disease, prednisolone plus cyclophosphamide for 3 months, then prednisolone plus azathioprine
- Combination of ACE inhibitor and ARB should be given to all cases with or without hypertension or proteinuria
- Other treatment like fish oil may be beneficial
- Tonsillectomy may be helpful, if recurrent tonsillitis
- If the patient develops ends stage renal failure, kidney transplantation is an excellent option. Recurrence of the disease may occur in 30% cases in 5 to 10 years in post-transplant.

Prognosis: Complete remission is uncommon. Prognosis is usually good, renal failure is uncommon. Bad prognostic factors are:

- Proteinuria > 1 g/day
- Others—hypertension, persistent microscopic hematuria and proteinuria, glomerulosclerosis and abnormal kidney function.

Q. What are the diseases **associated** with IgA deposit in kidney?

A. As follows:

- IgA nephropathy
- Henoch-Schonlein purpura
- Chronic liver disease
- Malignancy like bronchial carcinoma
- Seronegative spondyloarthropathy
- Coeliac disease
- Mycosis fungoides
- Psoriasis.

BRIEF NOTES ABOUT GOODPASTURE'S SYNDROME

Definition: Goodpasture's syndrome is a clinical syndrome of glomerulonephritis and pulmonary hemorrhage, mediated by anti-GBM antibody.

Clinical presentations: Goodpasture's syndrome is 6 times more in males, age 20 to 40 years. Females are affected more, if it occurs after the age of 60. Onset is preceded by upper respiratory

tract infection. Patient presents with cough, hemoptysis and glomerulonephritis or renal failure. In one-third cases, only glomerulonephritis is present, no lung injury. Lung hemorrhage is more in smokers. Systemic features like fever, malaise, arthritis, headache, weight loss are not common, but may occur. Hypertension is usually not a feature. Chest pain and pleurisy are also rare.

Differential diagnoses: In young patient with renal and lung involvement, the most common cause is Goodpasture's syndrome. Other causes are:

- Microscopic polyangitis (MPA)
- Wegener's granulomatosis
- SLE
- In elderly, bronchial carcinoma with metastasis in the kidney or membranous glomerulonephritis may occur.

Investigations:

- CBC and ESR
- Chest X-ray (shows lung infiltrate due to hemorrhage)
- P-ANCA (positive in 30%) and C-ANCA
- ANA is negative and complements are normal
- Anti-GBM antibody is positive in 90% cases (usually IgG, occasionally IgA or IgM)
- Lung function test (shows increased CO transfer due to pulmonary hemorrhage and restrictive lung disease may occur in advanced stage. Associated influenza A_2 virus may be found).
- In sputum, hemosiderin-laden macrophage may be present.
- Kidney biopsy (it shows proliferative or crescentic glomerulonephritis. Immunofluorescence shows anti-GBM antibody deposition in a linear pattern).

Treatment:

- Plasmapheresis plus methylprednisolone (1 to 2 g/day for 3 days), followed by oral prednisolone (1 mg/kg/day)
- Cyclophosphamide 2 to 3 mg/kg/day or IV 0.5 to 1 g/m^2 surface area, every month may be given
- Dialysis may be needed in renal failure
- Sometimes, kidney transplantation may be considered. Recurrence may occur in transplantated kidney.

LUPUS NEPHRITIS

CHIEF COMPLAINTS

- Pain in different large and small joints for.... months
- Swelling of lower limbs and scrotum for.... month.

HISTORY

History of present illness: Mr … a young man of 28 was admitted in the hospital on … with the complaints of pain in different large and small joints for .... months, swelling of lower limbs and scrotum for 1 month.

According to statement of patient, he was alright .... months back. Since then, he has been suffering from pain and swelling of both knee joints, subsequently involving the ankle, elbow and small joints of limbs. Pain is more with activity and reduces with rest. He also noticed morning stiffness, usually persist 2 to 3 hours, reduces with some exercise.

For the last .... month, the patient noticed swelling of both lower limbs and scrotum, which is gradually increasing. There is also passage of scanty reddish urine. He consulted with a local physician, who prescribed tablet frusemide and ciprofloxacin, but no improvement. His swelling both lower limbs was increasing and after a week, the patient was admitted in the hospital. 2 days after admission, the patient is complaining of high fever with chills and rigor, associated with right loin pain, which is dull ache in nature, no radiation.

On enquiry, there is no history of purulent urethral discharge, bloody dysentery, skin rash and mouth ulcer.

History of past illness: The patient suffered from occasional low grade fever, pain in multiple joints for few months back.

Family history: All the family member are in good health, there is no such illness in the family.

Personal history: He is married and has a kid, non smoker, non alcoholic.

Socioeconomic history: He comes from a middle class family, lives in a brick built house with good sanitation and water supply.

Drug history: He took frusemide tablets and some antibiotics as prescribed by the local physician.

GENERAL EXAMINATION

- The patient is ill looking, edematous and pale
- Pitting edema is present
- Mildly anemic
- No clubbing, jaundice, cyanosis, koilonychia but leukonychia involving all the nails of fingers and toes is present
- No lymphadenopathy or thyromegaly
- Pulse—80/min regular in rhythms
- BP—90/75 mm Hg
- Temperature—103ºF.

SYSTEMIC EXAMINATION

Gastrointestinal System

Lips, gum, tongue, oral cavity—normal. There is one small ulcer on inner side of mouth.

Abdomen

1. **Inspection:**
   - Generalized distension of abdomen, umbilicus is everted
   - Scrotum is grossly swollen
2. **Palpation:**
   - No organomegaly
   - Kidneys are not ballotable
   - Fluid thrill—present
   - Tenderness is present over the renal angle
3. **Percussion:** Shifting dullness present
4. **Auscultation:** No abnormality.

Examination of the other systems reveals no abnormalities.

Bedside urine: protein+, sugar nil.

SALIENT FEATURES

Mr … a young man of 28 was admitted in the hospital on … with the complaints of pain in different large and small joints for .... months, swelling of lower limbs and scrotum for 1 month.

According to statement of patient, he was alright .... months back. Since then, he has been suffering from pain and swelling of both knee joints, subsequently involving the ankle, elbow and small joints of limbs. Pain is more with activity and reduces with rest. He also noticed morning stiffness, usually persist 2 to 3 hours, reduces with some exercise.

For the last .... month, the patient noticed swelling of both lower limbs and scrotum, which is gradually increasing. There is also passage of scanty reddish urine. He consulted with a local physician, who prescribed tablet frusemide and ciprofloxacin, but no improvement. His swelling both lower limbs was increasing and after a week, the patient was admitted in the hospital. About 2 days after admission, the patient is complaining of high fever with chills and rigor, associated with right loin pain, which is dull ache in nature, no radiation.

On enquiry, there is no history of purulent urethral discharge, bloody dysentery, skin rash and mouth ulcer.

In his past medical history, the patient suffered from occasional low grade fever, pain in multiple joints for few months back.

There is no family history of such illness. He used to take vitamins prescribed by local doctors.

On Examination—

General examination (mention as above).
Systemic examination (mention as above).
Urine shows gross proteinuria.

My diagnosis is Glomerulonephritis, which may be due to SLE, rheumatoid arthritis.

Q. Why it is **SLE** ?

A. As there is history of polyarthritis, mouth ulcer.

For details of renal lupus (see rheumatology chapter)

Q. What **investigations** should be done in this case?

A. As follows:

1. CBC and ESR
2. Urine R/M/E (albuminuria, granular casts may be present)
3. Renal function test (blood urea and creatinine)
4. Creatinine clearance (important to assess the severity of renal failure)
5. Serum electrolytes, calcium and phosphate
6. Serum uric acid (may be high)
7. ANA and anti-ds DNA, C_3 and C_4
8. Others:
   - Plain X-ray abdomen
   - USG of the whole abdomen
   - CT scan of abdomen (in some case)
   - Transcutaneous renal biopsy.

Q. What is the **typical renal problem** in SLE?

A. Proliferative glomerulonephritis, which is characterized by hematuria, proteinuria and casts on routine urine microscope.

Renal involvement in SLE occurs in 30% case. Of these, 25% will develop end stage renal failure within 10 years. All patients of SLE should have regular screening of urine for blood and protein. Asymptomatic patient with proteinuria may be the early stage and treatment may prevent the progression of renal impairment. Renal vein thrombosis may occur in antiphospholipid syndrome.

Treatment:

- Depends on clinical presentation and type. Definitive histological diagnosis is essential.
- Type I—no treatment, only follow up.
- Type II—usually benign. Some patients may need treatment.
- Type III, IV and V—immunosuppressive therapy with steroid and cyclophosphamide or mycophenolate mofetil are used for induction. Then azathioprine and mycophenolate mofetil are used for maintenance.
- Rituximab (anti CD-20) may be used in some patient.
- Symptomatic treatment for hypertension and edema.

PUO IN HEMODIALYSIS PATIENT

CHIEF COMPLAINTS

- Fever for -----months
- Weakness and loss of appetite for … months
- Nausea and occasional vomiting for … months
- Swelling and puffiness of the face for … days.

HISTORY

History of present illness: Mrs … 40 years house wife, known case of diabetes mellitus for 10 years was diagnosed as case of CKD, and on regular hemodialysis. For the last … months, she has been suffering from fever, which is low grade continued, highest recorded temperature is 101°F. Fever is not associated with chill and rigor, subside only with paracetamol. She also complains of weakness, loss of appetite, nausea and occasional vomiting. Her bowel habit is normal. There is no history of joint pain, skin rash, cough or oral ulcer.

History of past illness: She is non-hypertensive, but diabetic for … years and used to take insulin.

Family history: There is no history of such illness in her family.

Personal history: Mention according to the patient's statement.

Socioeconomic history: Mention according to the patient's statement.

Drug history: She was treated with ceftriaxone, ceftazidime and vancomycin but no response.

GENERAL EXAMINATION

- The patient is ill looking, emaciated and pale
- Moderately anemic
- Pitting edema—present
- Skin is rough with some scratch mark in different parts of the body
- There is leukonychia (or half and half nail)
- No clubbing, jaundice, cyanosis or koilonychia
- No lymphadenopathy or thyromegaly
- Pulse—110/min
- BP—110/65 mm Hg (mention postural drop if present)
- Fistula for dialysis in the right hand.

SYSTEMIC EXAMINATION

Gastrointestinal System

Lip, gum, tongue, oral cavity—looks pale.

Abdomen

1. **Inspection:** No abnormality detected.
2. **Palpation:**
   - No organomegaly

- Kidneys are not ballotable
- Fluid thrill—absent
- There is no tenderness over the renal angle.

3. **Percussion:** Shifting dullness absent
4. **Auscultation:** No renal bruit.

CVS: Mention position of apex, carotid bruit.

Nervous System

Examined the sensory system, dorsal column lesion, reflexes (ankle jerk) and fundoscopy (diabetic retinopathy, hypertensive retinopathy).

Bedside urine examination: Sugar present, protein+++.

Daily urine output 500 mL/day

SALIENT FEATURES

Mrs … 40 years house wife, known case of diabetes mellitus for 10 years was diagnosed as case of CKD, and on regular hemodialysis. For the last … months, she has been suffering from fever, which is low grade continued, highest recorded temperature is 101°F. Fever is not associated with chill and rigor, subside only with paracetamol. She also complains of weakness, loss of appetite, nausea and occasional vomiting. Her bowel habit is normal. There is no history of joint pain, skin rash, cough or oral ulcer. There is no history of such illness in her family. She was treated ceftriaxone, ceftazidime and vancomycin but no response.

On Examination—
General examination (mention as above).
Systemic examination (mention as above).

My diagnosis is PUO with CKD on hemodialysis.

Q. What **investigations** do you suggest fever in CKD on hemodialysis?

A. As follows:
- Urine R/E and C/S
- CBC and PBF
- Blood for C/S
- CXR P/A view
- MT
- USG of the whole abdomen
- Echocardiography
- Anti-CMV antibody
- ANA and anti ds-DNA for SLE, screening for hepatitis B and C, HIV
- P-ANCA, C-ANCA
- Other investigations according to suspicion of cause—anti-toxoplasma antibody, anti-brucella antibody, antifungal antibody (for aspergiloma, histoplasma).

Q. What are the **causes** of fever in such case?

A. As follows:
- Tuberculosis
- Viral infection (commonly CMV)

- Collagen disease (SLE)
- Vasculitis (microscoic polyartaritis, Wegners granulomatosis).

Q. How will you treat a **tuberculosis patient with CKD**?

A. Rifampicin, INH and pyrazinamide are given in the usual dose. Only ethambutol 7.5 mg/kg body weight is given.

Q. How to **treat Tuberculosis in hemodialysis** patient**?**

A. Treatment is as above, but on the day of dialysis, anti-tubercular drug should be given after the dialysis.

Q. How to **treat CMV** infection?

A. IV Gancyclovir is used in the following dose:

- Induction: 5 mg/kg every 12 hourly for 14 to 21 days.
- Maintenance: 5 mg/kg once daily for 7 days per week or 6 mg/kg once daily for 5 days per week. Dose to be given by IV infusion.
- In patients with renal impairment getting dialysis: 1.25 mg/kg for induction and 0.625 mg/kg for maintenance, to be given post-dialysis on days when dialysis is performed.

CrCl (mL/min)	Dosage Recommendation	
	Induction	Maintenance
» ≥70	5 mg/kg every 12 hours	5 mg/kg every 24 hours
» 50 to 69	2.5 mg/kg every 12 hours	2.5 mg/kg every 24 hours
» 25 to 49	2.5 mg/kg every 24 hours	1.25 mg/kg every 24 hours
» 10 to 24	1.25 mg/kg every 24 hours	0.625 mg/kg every 24 hours

CHAPTER 7

Rheumatology

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SYSTEMIC LUPUS ERYTHEMATOSUS

CHIEF COMPLAINTS

- Pain in multiple joints for … months
- Skin rash for … months
- Fever for … months
- Weight and hair loss for … months
- Oral ulcer for … months.

HISTORY

History of present illness: According to the statement of the patient, she was reasonably well … months back. Since then, she has been suffering from pain in multiple small and large joints of both upper and lower limbs, predominantly lower limbs, mostly involving the hands, wrists, knees, ankles and small joints of feet. The pain persists throughout day and night, more marked in the morning, associated with morning stiffness, and not relieved by rest, but reduces with pain-killers. She also noticed skin rashes on the face, arms and legs for the last … months that are aggravated on exposure to sunlight. The patient also complains of low grade continued fever for the last … months, highest recorded temperature is 100ºF. Fever is not associated with chills and rigors, subsides by taking paracetamol. There is no history of night sweats. The patient also complains of marked loss of weight and weakness. She noticed some loss of scalp hair and painless mouth ulcer. There is no history of spontaneous abortion, bleeding, venous thrombosis, convulsion, unconsciousness, dryness of the mouth or eyes, pain in abdomen, dysuria, edema, Raynaud's phenomenon, gangrene or cough. Her bowel and bladder habits are normal.

History of past illness: Nothing significant.

Drug history: There is no history of taking OCP or other drugs.

Family history: There is no similar illness in her family. Her parents and two sisters are in good health.

Personal history: Mention according to the patient's statement.

Socioeconomic history: Mention according to the patient's statement.

Menstrual history: The patient complains of occasional irregular menstruation, sometimes associated with menorrhagia.

GENERAL EXAMINATION

- Ill looking and emaciated.
- Alopecia is present on the scalp.
- Butterfly rash is present on the face over the cheek, nasal bridge, sparing the nasolabial folds that are fixed, erythematous, some are flat, some are raised. Also, maculopapular skin rashes are present on the dorsum of the hands and legs, some of these are pigmented and scaly.
- Oral ulcer present on inner side of lips and cheeks, some are coated with whitish discharge and has irregular margin.
- Moderately anemic.
- No jaundice, cyanosis, clubbing, koilonychia, leukonychia or edema.

- No lymphadenopathy or thyromegaly.
- Pulse: 88/min.
- BP: 90/40 mm Hg.
- Temperature: 99^0 F.

Musculoskeletal system:

- Both knee and ankle joints are slightly swollen and tender
- Wrist, MCP and IP joints of both hands—slightly swollen and tender, but no deformity.

Gastrointestinal system: No abnormality detected (liver and spleen may be palpable, mention if any).

Eyes: No abnormality detected.

Respiratory system: No abnormality detected.

Cardiovascular system: No abnormality detected.

Nervous system: No abnormality detected.

Bedside urine examination: Normal (or proteinuria, mention if present).

SALIENT FEATURES

Ms. …, 33 years, housewife, normotensive, nondiabetic, nonsmoker, hailing from …, presented with pain in multiple small and large joints of both upper and lower limbs for … months. The pain involves predominantly lower limbs, mostly the hands, wrists, knees, ankles and small joints of feet. The pain persists throughout day and night, more marked in the morning, associated with morning stiffness, and not relieved by rest, but reduces with pain-killers. She also noticed skin rashes on the face, arms and legs for the last … months that are aggravated on exposure to sunlight. The patient also complains of low grade continued fever for the last … months, highest recorded temperature is 100ºF. Fever is not associated with chills and rigors, subsides by taking paracetamol. There is no history of night sweats. The patient also complains of marked loss of weight and weakness. She noticed some loss of scalp hair and painless mouth ulcer. There is no history of spontaneous abortion, bleeding, venous thrombosis, convulsion, unconsciousness, dryness of the mouth or eyes, pain abdomen, dysuria, edema, Raynaud's phenomenon, gangrene or cough. Her bowel and bladder habits are normal. She complains of occasional irregular menstruation, sometimes associated with menorrhagia. There is no history of taking OCP or other drugs. There is no similar illness in her family. She was treated by local physicians by multiple drugs the name of that she could not mention.

On examination, general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is systemic lupus erythematosus.

Q. What are your **differential diagnoses?**

A. As follows:

- Dermatomyositis
- Mixed connective tissue disease (MCTD)
- Sarcoidosis
- Rheumatoid arthritis.

Q. Why not **rheumatoid arthritis?**

A. Because in this case, there are multiple skin rash and butterfly rash and there is no deformity of the involved joints.

Q. What **investigations** should be done in SLE?

A. As follows:

1. CBC (anemia, leukopenia, thrombocytopenia, lymphopenia and high ESR)
2. Urine (proteinuria, hematuria, and RBC or granular cast). If proteinuria is present, 24 hours urinary protein should be done
3. CRP (It is normal. If CRP is increased, it indicates infection)
4. Antinuclear antibody (ANA) (positive in 95% cases. It is the most sensitive screening test)
5. Anti-double-stranded DNA (positive in 30% to 50% of the cases. It is highly specific for SLE)
6. Anti-Sm (Smith) antibody (positive in 10% to 25% cases)
7. Complements (C3 and C4 are low in active disease)
8. Immunoglobulin (high titer of IgM and IgG)
9. Serum anti-phospholipid antibody
10. Others (these indicate presence of antiphospholipid antibody):
    - Venereal disease research laboratory (VDRL) (false positive)
    - Platelet (low)
    - Prothrombin time (prolonged)
    - Activated partial thromboplastin time (APTT) (prolonged, not corrected by addition of normal plasma)
11. Skin biopsy (from normal skin and skin lesion for histopathology and DIF):
    - Normal skin biopsy—immunofluorescence test shows deposition of immune complex at dermoepidermal junction (lupus band). Biopsy specimen of normal skin for DIF should be sent in normal saline soaked gauge (not in formalin, as the protein is denatured by formalin). For histopathology, biopsy specimen is taken in formalin
12. If renal involvement—24 hours urinary protein, serum urea and creatinine, creatinine clearance rate (CCR), renal biopsy
13. If CNS involvement—EEG, CT or MRI.

Q. What are the **antibodies** found in SLE?

A. As follows:

- ANA
- Anti-double-standard DNA
- Anti-Smith (more specific in SLE)
- Anti-Ro/La (responsible for congenital heart block in neonate)
- Antiphospholipid antibody/lupus anticoagulant (may cause repeated abortion, thrombocytopenia)
- Anti-histone (found in drug induced SLE)
- Anti-C_{1q} (it has prognostic significance in lupus nephritis).

Q. What are the **causes** of positive **ANA**?

A. As follows:

- SLE
- Sjogren syndrome
- Systemic sclerosis
- Dermatomyositis
- Polymyositis
- MCTD
- Autoimmune hepatitis
- Others—rheumatoid arthritis, autoimmune thyroid disease, vasculitis.

RELATED QUESTIONS AND ANSWERS

Q. What is SLE?

A. It is an autoimmune chronic multisystem disease characterized by production of multiple autoantibodies, immune complexes and widespread immune mediated organ damage.

Q. From where is the name SLE derived?

A. Lupus means wolf. SLE is named because of the erosive nature of the condition that looks like the damage caused by hungry wolf's bite.

Q. What are the manifestations of SLE?

A. SLE is more in females, F:M = 9:1, age in second and third decades. Sex ratio is equal in children and elderly. It involves any organ of the body.

1. General features:
- Fever
- Arthralgia, arthritis (non-erosive), myalgia
- Fatigue, tiredness, weakness, malaise
- Weight loss
- Skin manifestation (80%)—malar rash, discoid rash, photosensitivity, ulcer, vasculitic lesions on the finger tips and around the nail folds, livedo reticularis. (In discoid lupus, only skin is involved)
- Scarring alopecia. Lupus hair (short broken hair above the forehead).

2. Heart (involved in 25%):
- Pericarditis, pericardial effusion and myocarditis
- Rarely, non-infective endocarditis called Libman-Sacks endocarditis (common in anti-phospholipid syndrome). Mitral regurgitation may occur
- There is increased frequency of IHD and stroke in patients with SLE.

3. Vascular: Raynaud's phenomenon, vasculitis, arterial and venous thrombosis (in anti-phospholipid syndrome) and atherosclerosis.

4. Lungs (involved in up to 50% cases):
- Pleurisy, pleural effusion (may be bilateral) and pneumonitis
- Atelectasis and shrinking lung with elevation of diaphragm (shrinking lung syndrome)
- Pulmonary fibrosis (rare, found in overlap syndrome)
- Increased risk of thromboembolism
- Intrapulmonary hemorrhage with vasculitis (rare but dangerous).

5. Eyes:
- Episcleritis, scleritis, conjunctivitis and optic neuritis (blindness is uncommon)
- Secondary Sjögren's syndrome (dry eye and dry mouth) in 15% cases
- Retinal vasculitis can cause infarct (fundoscopy shows white, hard exudate called cytoid body).

6. Gastrointestinal tract (GIT) (rarely involved):
- Mouth ulcer (usually painless, but may be painful if secondary infection)
- Mesenteric vasculitis (causing small bowel infarction or perforation)
- Ascites
- Others—nausea, vomiting, diarrhea, abdominal pain, mild hepatosplenomegaly.

7. Hematological:
- Anemia (normocytic normochromic) and Coombs' positive autoimmune hemolytic anemia
- Thrombocytopenia (often confused with ITP), leukopenia, neutropenia and lymphopenia.

8. Central nervous system (CNS):
- Fatigue, headache, poor concentration

- Visual hallucination
- Chorea
- Epilepsy
- Migraine
- Cerebrovascular disease (CVD)
- Organic psychosis
- Paralysis
- Depression
- Transverse myelitis
- Lymphocytic meningitis
- Cerebellar ataxia
- Cranial nerve palsy
- Peripheral neuropathy.

9. Kidneys:
- Glomerulonephritis (commonly proliferative, may be mesangial, focal or diffuse, and membranous)
- Nephrotic syndrome
- Renal vein thrombosis.

10. Others—lymphadenopathy, infertility, abortion, menorrhagia.

Q. What are the features of **renal involvement** in SLE?

A. Renal involvement occurs in 1/3rd of SLE, of these 25% develop end stage renal failure within 10 years. Lupus nephritis is classified histologically by WHO.

Type	Histology	Clinical features
Type I	**Minimal** mesangial lupus nephritis (LN), normal on light microscopy	Asymptomatic
Type II	**Mesangial** proliferative LN with mesangial hypercellularity and matrix expansion	Mild renal disease
Type III	**Focal** LN (involving < 50% glomeruli) Subepithelial deposits seen	Hematuria and proteinuria
Type IV	**Diffuse** LN (involving ≥ 50% glomeruli) There are segmental and global lesions as well as active and chronic lesions. Subendothelial deposits are present	Progression to nephrotic syndrome, hypertension and renal insufficiency. It is the most common and most severe form of LN
Type V	**Membranous** LN, occurs in 10 to 20% patients. Can occur in combination with type III and IV	Heavy proteinuria (NS), hematuria, hypertension. Good prognosis
Type VI	Advanced **sclerosing** LN. It causes sclerosis of > 90% glomeruli	Progressive renal failure, severe form

Treatment of LN:

- Type I—no treatment
- Type II—benign. But sometimes, steroid may be needed

- Type III, IV and V—immunosuppressive therapy with steroid and cyclophosphamide or mycophenolate mofetil are used for induction. Then azathioprine and mycophenolate mofetil are used for maintenance
- Rituximab (anti CD-20) may be used in some patient
- Symptomatic treatment for hypertension and edema.

Note Remember the following:

- Focal glomerulonephritis respond well to treatment with prednisolone 40 to 60 mg/day.
- Diffuse and membranous lesions do not respond well to steroid only. Pulse therapy with methylprednisolone for 3 days followed by maintenance with prednisolone is necessary. Sometimes azathioprine 2 to 3 mg/kg body weight or cyclophosphamide 100 to 150 mg daily with prednisolone may be given.
- Pulse therapy—IV cyclophosphamide is more effective than pulse methylprednisolone alone. Also, combination therapy is sometimes more effective. Continuing IV treatment, quarterly for one year, after renal remission decreases the risk of renal flare.
- Prognosis is better in type I, II and V.

Q. How to **diagnose renal involvement** in SLE?

A. The patient may present with nephrotic syndrome or acute nephritic illness or renal failure. Renal involvement is diagnosed by:

1. Urine for routine microscopie examination (R/M/E):
- Proteinuria (+++), hematuria, and granular or RBC cast
- UTP (24 hours urinary total protein) > 0.5 g

2. Blood:
- Urea and creatinine (high)
- Creatinine clearance rate (CCR)—low.

3. Renal biopsy.

Q. What are the **diagnostic criteria** of SLE?

A. The diagnostic criteria are (11 criteria):

1. Malar rash (fixed erythema, flat or raised, sparing the nasolabial folds)
2. Discoid rash (erythematous raised patches with adherent keratotic scarring and follicular plugging)
3. Photosensitivity
4. Oral ulcer (oral or nasopharyngeal ulcer that may be painless)
5. Arthritis (non-erosive, involving two or more peripheral joints)
6. Serositis:
   - Pleuritis (pleuritic pain, rub or pleural effusion)
   - Pericarditis (pericardial rub, ECG evidence or pericardial effusion)
7. Renal involvement:
   - Persistent proteinuria > 0.5 g per day, or
   - Greater than 3+ (if total urinary protein is not performed), or
   - Cellular casts (red cell, granular or tubular).
8. Neurological disorder seizure or psychosis in the absence of offending drug or metabolic derangement (uremia, ketoacidosis and electrolyte imbalance).
9. Hematological disorders:
   - Hemolytic anemia or
   - Leukopenia (< 4,000/cmm in two or more occasions) or
   - Lymphopenia (< 1,000/cmm in two or more occasions) or

- Thrombocytopenia (< 100,000/cmm in two or more occasions), in the absence of offending drug.

10. Immunological disorders:
    - Anti-DNA antibody in abnormal titer or
    - Anti-Sm antibody (antibody to Sm nuclear antigen) or
    - Positive anti-phospholipid antibody
    - False-positive serological tests for syphilis (positive for at least 6 months and confirmed by treponema pallidum immobilization or fluorescent treponemal antibody absorption test).
11. **ANA** positive (in the absence of drugs causing lupus syndrome).

Note Remember the following

Presence of **four or more** criteria at a time or sequential appearance is diagnostic. Positive anti-double-stranded DNA and anti-Sm (Smith) antibodies are diagnostic of SLE.

Q. What is the **type of arthritis** in SLE?

A. Usually non-erosive and non-deforming. Rarely, deformity may occur similar to RA called Jaccoud's arthritis. Aseptic necrosis of head of femur may occur.

Q. What is the cause of **avascular necrosis** of head of femur in SLE?

A. It is because of

- Vasculitis in SLE
- Prolonged use of steroid therapy (actual cause of necrosis because of steroid is unknown. Probably steroid causes hypertrophy of lipocytes that compresses blood vessels, leading to ischemic necrosis of bone).

Q. What is the cause of **backache** in SLE?

A. Avascular necrosis (that is because of vasculitis and steroid therapy).

Q. What are the differential diagnoses of **butterfly rash**?

A. As follows:

- Systemic lupus erythematosus (SLE) or discoid lupus erythematosus (DLE)
- Dermatomyositis
- Mixed connective tissue disease (MCTD)
- Sarcoidosis
- Drug rash
- Acne rosacea (characterized by red patch with telangiectasia on the face with papules and pustules, that are absent in SLE)
- Lepromatous leprosy
- Post-kala-azar dermal leishmaniasis (PKDL).

Q. What are the **atypical features** of SLE?

A. As follows:

- Raynaud's phenomenon
- Chorea
- Repeated abortion
- Epilepsy or cerebrovascular accident (CVA) in young age
- Psychiatric disorder.

Q. What are the **types** of SLE?

A. As follows:

A. According to presence of **American Rheumatism Association (ARA) criteria:**

- Possible SLE—when 2 criteria are present
- Probable SLE—when 3 criteria are present
- Definite SLE—when 4 or more criteria are present
- Classic SLE—when many criteria are present.

B. According to the **severity:**

1. **Mild:**
   - Fever
   - Arthralgia or arthritis
   - Rash, headache
   - Mild pericarditis or mild pericardial effusion
   - Mild pleural effusion.
2. **Severe:**
   - Massive pleural effusion
   - Massive pericardial effusion
   - Renal involvement
   - CNS involvement
   - Acute vasculitis
   - Myocarditis
   - Lupus pneumonitis
   - Hemolytic anemia
   - Thrombocytopenic purpura.

Q. What is **'disseminated lupus erythematosus' (DLE)?**

A. It is a variant of SLE in which the disease is mainly limited to skin, characterized by photosensitivity, discoid rash, erythema, scaling, follicular plugging and telangiectasia. M:F = 1:2 (in SLE, the ratio is 1:9). SLE may occur in 5% cases (more in children). ANA is positive (30% cases), anti-double-stranded DNA is negative and complements are normal.

Treatment of DLE:

- Hydroxychloroquine—200 to 400 mg/day
- In severe cases, prednisolone
- Use of sunscreen and topical steroid may help.

Q. What is **SCLE (subacute cutaneous lupus erythematosus)?**

A. It consists of scaly red patch or circular, flat, red lesions (confused with psoriasis), highly photosensitive. Most patients have anti-Ro (SSA).

Q. What are the **drugs causing SLE?**

A. As follows:

- Hydralazine (slow acetylator)—the most common cause (90%)
- Procainamide (rapid acetylator)
- Anticonvulsant (carbamazepine and phenytoin)
- Phenothiazine
- Isoniazid (INH)
- Oral contraceptive pill
- ACE inhibitor

- Penicillamine
- Methyldopa
- Minocycline.

Features of drug induced SLE**:**

- Sex ratio—equal
- Renal and neurological involvements are absent. Lung involvement is common
- ANA is usually positive, but anti-ds DNA is negative
- Complements are normal
- Anti-histone antibody is positive in 95% cases (characteristic, but not specific)
- Drugs causing SLE-like syndrome usually do not aggravate primary SLE
- Clinical features and laboratory abnormalities revert to normal, when the offending drugs are withdrawn.

Treatment:

- Withdrawal of drugs
- Occasionally a short course of steroid is necessary.

Q. What is the relation of **pregnancy with SLE?**

A. Pregnancy is not contraindicated. Fertility is usually normal except in severe disease. Repeated abortion (due to the presence of anti-phospholipid antibody), still birth and intrauterine growth retardation may occur.

The disease should be in remission and pregnancy should be avoided if there is neurological, renal and cardiac abnormality. Relapse may occur in the first trimester and in puerperium.

If the mother has "**anti-Ro antibody"** (SSA), there may be congenital complete heart block of the baby, due to transplacental transfer of antibody. With anti Ro or anti La antibodies in mother, there is 2% risk of giving birth to a baby with neonatal lupus syndrome. This is characterized by skin rash, hepatitis and fetal heart block.

Treatment of SLE during pregnancy: Prednisolone should be continued (avoid dexamethasone and betamethasone that are broken by placental enzymes).

Q. What are the causes of **abdominal pain in SLE?**

A. As follows:

- Mesenteric vasculitis or perforation of gut
- Peptic ulcer as a complication of steroid
- Perisplenitis or splenic infarction
- Pancreatitis.

Q. How to **treat** SLE?

A. As follows:

1. General measures:
   - Explanation and education regarding the nature of the disease
   - Reassurance
   - Psychological support
   - Avoidance of UV light exposure, use of sun blocks
   - Cardiovascular risk factors like hypertension and hyperlipidemia should be controlled. Smoking should be stopped.

2. Drug therapy:
   - Mild cases—NSAID (if fever, arthralgia and headache)

- Chloroquine or hydroxychloroquine—effective in cutaneous lesion, arthritis, arthralgia and serositis without organ involvement
- Rash, synovitis or pleuropericarditis—short course steroid
- Severe and active disease—steroid should be given
- Acute life-threatening SLE affecting kidney, CNS or CVS, hemolytic anemia, thrombotic thrombocytopenia—high dose steroid and immunosuppressive drug. Pulse methylprednisolone (500 mg to 1 g IV) daily for 3 to 5 days. Cyclophosphamide (2 mg/kg IV) may be given 2 to 3 weekly on 6 to 8 occasions.
- In renal involvement—mycophenolate mofetil may be used instead of cyclophosphamide
- In thrombocytopenia not responding to immunosuppressive therapy, danazol may be used.

Steroid (prednisolone):

Indications:

- In mild disease, not responding to chloroquine and NSAID
- Severe and active disease with involvement of organ (heart, kidney, CNS and hematological abnormality).

Dose:

- Without major organ involvement—0.25 to 0.5 mg/kg/day
- Major organ involvement—1 to 1.5 mg/kg/day.

Dose schedule of steroid (one suggested regimen):

- Initially, full dose (45.0 to 60.0 mg daily) for 4 to 8 weeks, then-
- Reduce 10.0 mg weekly till 30.0 mg, then-
- 25.0 mg/day for 1 week, then-
- 20.0 mg/day for 1 week, then-
- 15.0 mg for 1 month, then-
- Reduce 2.5 mg every 2 weekly as follows:
  - First day 15.0 mg, second day 12.5 mg for 2 weeks, then-
  - First day 15.0 mg, second day 10.0 mg for 2 weeks, and so on.
  - This is continued until 2nd day regimen is completed, then-
- 15.0 mg on alternate day (continue and follow-up).

When the disease activity (both clinically and biochemically) disappears, steroid should be reduced slowly over months and can be withdrawn (may be needed to continue for 2 to 3 years. For lupus nephritis, treatment is usually given for 5 years).

Methylprednisolone:

Indication: Severe SLE, when there is carditis, renal and cerebral involvement, poor general condition.

Dose: 500 mg to 1gm mixed with 200 mL 5% DA IV daily for 3 to 5 days, followed by prednisolone 1mg/kg for 6 to 10 weeks, then gradual tapering.

Cyclophosphamide:

Indications:

- Renal lupus (classes III, IV and V)
- Severe renal disease as evidenced by (UTP > 1 g, raised serum creatinine and decreased creatinine clearance)
- CNS involvement.

Dose:

- 0.5 to 1 g/m^2 of body surface area. It is given monthly as a pulse therapy IV with 500 mL fluid (every month for six cycles, then every 3 months for another six cycles or till the disease is inactive for 1 to 2 years). Then hydroxychloroquine or azathioprine can be started.
- Alternately, cyclophosphamide 250 mg/m^2 of body surface may be given every 15 days for 12 doses, followed by prednisolone as maintenance therapy.
- Oral cyclophosphamide can be given.
- After 12 weeks of cyclophosphamide, oral azathioprine (2 to 2.5 mg/kg daily) may be given.
- Advantages of azathioprine—no gonadal toxicity and no adverse effect on pregnancy.
- Cyclophosphamide can cause hemorrhagic cystitis, gonadal toxicity, amenorrhea, sterility, premature menopause and sometimes, leukemia. Moreover, it can not be continued in pregnancy.
- Cyclophosphamide is usually given with high dose prednisolone.

(Periodic blood count should be done initially 2 weekly, then monthly.)

Q. What is the **mechanism of hemorrhagic cystitis?** How to **prevent** this?

A. Cyclophosphamide can cause hemorrhagic cystitis (more by oral route). It is due to production of **acrolein**, a metabolite from cyclophosphamide that is highly toxic to the mucosa of the urinary bladder.

This can be prevented by:

- Plenty of fluid (3 to 4 L)
- Using mesna (0, 4 and 8 hours of therapy)
- Advise the patient to micturate frequently.

Prognosis in SLE:

- 10-year survival rate is 90%, but this is lower if vital organs are involved (heart, kidney, lung, CNS).
- Mortality shows bimodal pattern. In early age, death is usually because of infection (mostly opportunistic), renal or cerebral disease. In later age, accelerated atherosclerosis is common, incidence of myocardial infarction is 5 times more than in general population (so, risk factor for atherosclerosis should be avoided, such as avoid smoking, control hypertension, obesity, hyperlipidemia, etc.).
- In the long-term, some patients may develop cancers, especially lymphoma.
- Rarely, there may be deforming arthritis, chronic progressive destruction of joints and osteoarthrosis.

Q. What is **anti-phospholipid syndrome**?

A. Anti-phospholipid syndrome is characterized by the presence of anti-phospholipid antibody, associated with recurrent arterial or venous thrombosis, recurrent fetal loss or thrombocytopenia. Some patients with anti-phospholipid antibody may not get anti-phospholipid syndrome. It is positive in SLE and may be found in many other cases. But may be positive without any cause, called primary anti-phospholipid syndrome.

Two types of anti-phospholipid antibody:

- Anti-cardiolipin antibody—may be IgG or IgM. IgG is more pathogenic
- Lupus anticoagulant—it interferes with phospholipid dependent coagulation tests.

In some patients, only one of these is positive and in others, both are positive.

Presence of anti-phospholipid antibody is associated with:

- Thrombosis, venous or arterial.17% of stroke < 45 years of age is thought to be due to anti-phospholipid antibody
- Recurrent abortion or intrauterine growth retardation
- Hematological—thrombocytopenia and autoimmune hemolytic anemia
- Neurological—epilepsy, TIA, stroke, migraine and chorea
- Heart—sterile endocarditis (Libman-Sacks)
- Renal involvement with proteinuria and lupus nephritis (membranous)
- Skin-ulceration, livedo reticularis, gangrene and necrosis of digit.

It is of 2 types:

1. Primary—it causes thromboembolism without features of SLE.
2. Secondary—causes are:
   - Rheumatological—SLE, DLE, RA, systemic sclerosis, Sjögren's syndrome, psoriatic arthropathy, dermatomyositis
   - Vasculitis—Behcet's syndrome, temporal arteritis, Takayasu's arteritis
   - Malignancy—solid tumors, such as bronchial carcinoma, hypernephroma, prostatic carcinoma, thymoma, esophagial carcinoma
   - Hematological disease—leukemia, lymphoma, myelofibrosis, polycythemia, myeloma, monoclonal gammopathy
   - Infections—HIV, infectious mononucleosis, rubella, parvovirus, hepatitis, TB, leprosy, infective endocarditis, klebsiella, syphilis
   - Drug induced—procainamide, phenothiazine
   - Miscellaneous—diabetes mellitus, dialysis patient.

In < 1% cases of antiphospholipid syndrome, a severe type called catastrophic antiphospholipid syndrome may occur. In such case, there may be diffuse thrombosis, thrombotic microangiopathy and multiorgan failure. It is treated with intravenous heparin, high dose steroid and intravenous immune globulin and plasmapheresis.

Investigations:

1. Serum anti-phospholipid antibody (anti-cardiolipin and lupus anticoagulant)
2. Indirect tests for anti-phospholipid antibody (anti coagulant):
   - Thrombocytopenia
   - False positive VDRL
   - Prolonged prothrombin time
   - Prolonged APTT that is not corrected by addition of normal plasma.

Treatment anti-phospholipid syndrome:

- With thrombosis—warfarin should be continued for life long.
- Without history of thrombosis, but with antiphospholipid antibody only, aspirin or clopidogrel may be given. Rarely, warfarin may be needed.
- In pregnancy—low dose aspirin and subcutaneous heparin should be started early in gestation. This reduces the chance of miscarriage, but pre-eclampsia and poor fetal growth remains common.

RHEUMATOID ARTHRITIS

CHIEF COMPLAINTS

- Pain and swelling in multiple joints of both hands and feet for … months
- Fever, anorexia and weight loss for … months.

HISTORY

History of present illness: According to the statement of the patient, she was alright … months back. Since then, she has been suffering from pain and swelling involving small joints of both hands and feet. Initially pain was mild, but gradually it has become severe and incapacitating. The pain is associated with morning stiffness that persists for about two hours and is relieved by activity or exercise. She also complains of continued low grade fever, substantial weight loss, malaise and anorexia for the last … months. There is no history of mouth ulcer, skin rash, photosensitivity, eye problems, breathlessness, cough, chest pain or alopecia. Her bowel and bladder habits are normal.

History of past illness: Mention according to the patient's statement.

Family history: All the family members are in good health. No such illness in the family.

Personal history: Mention according to the patient's statement.

Drug and treatment history: He used to take painkiller, such as indomethacin, diclofenac, but no disease modifying drugs.

Menstrual history: Mention according to the patient's statement.

Socioeconomic history: Mention according to the patient's statement.

GENERAL EXAMINATION

- The patient looks ill and anxious
- Moderately anemic
- No jaundice, cyanosis, clubbing, koilonychia, leukonychia or edema
- No lymphadenopathy or thyromegaly
- There is no nail fold infarct or skin rash or vasculitis
- Pulse—88/min
- BP—110/80 mm Hg
- Temperature—99^0 F.

SYSTEMIC EXAMINATION

Musculoskeletal System

Examination of hands:

1. **Inspection:**
   - Wrist joints are swollen. PIP joints of both hands are spindle shaped. There is swan neck deformity in right little and ring fingers, Z deformity in right thumb and ulnar deviation of the right hand. There is mild flexion deformity of fingers on right hand as evident by prayer sign.
   - There is wasting of thenar and hypothenar muscles with dorsal guttering in both hands. There is no atrophy, ulcer, infarction, gangrene or rash.

- Movement is restricted in both wrists and fingers of both hands with slightly impaired functional activity.

2. **Palpation:**
   - All the joints of both hands are tender
   - Synovial thickening is present in both wrists
   - There is a rheumatoid nodule in the extensor surface of the right forearm.

Examination of feet:

- All the metatarsophalangeal joints and interphalangeal joints are swollen and deformed in both feet
- Lateral deviation with dorsal subluxation of toes
- Plantar subluxation of the metatarsal head
- Hallus valgus deformity
- Feet are flat with plantar erythema.

Examination of other joints:

- Both the knee joints are swollen and tender. There is no Baker cyst or popliteal cyst
- Elbow joints—swollen, tender with some flexion deformity.

Examination of eyes:

- No redness, no nodule.

Examination of respiratory system:

- Normal (No bilateral basal crepitations).

Examination of CVS:

- No abnormality detected.

Examination of the nervous system:

- No evidence of peripheral neuropathy, carpal tunnel or tarsal tunnel syndrome.

Examination of abdomen:

- There is no splenomegaly (to exclude Felty's syndrome).

SALIENT FEATURES

Mrs …, 55 years, housewife, normotensive, nondiabetic, hailing from …, presented with pain and swelling involving small joints of both hands and feet for ... months. Initially pain was mild, but gradually it has become severe and incapacitating. The pain is associated with morning stiffness that persists for about two hours and is relieved by activity or exercise. She also complains of continued low grade fever, substantial weight loss, malaise and anorexia for the last … months. There is no history of mouth ulcer, skin rash, photosensitivity, eye problems, breathlessness, cough, chest pain or alopecia. Her bowel and bladder habits are normal. All the family members are in good health. No such illness in the family. She used to take painkiller, such as indomethacin, diclofenac, but no disease modifying drugs.

On examination, on general examination (mention as above).

On systemic examination (mention as above. Always never forget to mention the extra-articular features).

My diagnosis is rheumatoid arthritis.

Q. What is your **differential diagnosis?**

A. Systemic lupus erythematosus (SLE), mixed connective tissue disease (MCTD), and seronegative arthritis (SNA) (However, if the history and physical findings are typical of Rheumatoid arthritis, no differential diagnosis).

Q. **Could it be** seronegative arthritis or ankylosing spondylitis?

A. No, as is seronegative arthritis there is usually asymmetrical involvement of the bigger joints. But in this case, there is bilateral symmetrical involvement of small peripheral joints associated with morning stiffness that persists more than 1 hour.

Q. Which joint is **spared** in RA?

A. Distal interphalangeal joint (may be involved in secondary osteoarthrosis).

RELATED QUESTIONS AND ANSWERS

Q. **What** is RA?

A. It is 13
r menopause, sex ratio is almost equal.

Q. What are the mechanisms of **wasting of muscles** in RA?

A. Multiple factors are responsible—disuse, vasculitis, polyneuropathy, mononeuritis multiplex and entrapment neuropathy.

Q. What is **boutonniere deformity**? What is the **mechanism?**

A. Fixed flexion of PIP joint and extension of DIP joint. Because of chronic synovitis of PIP joint, there is rupture of central slip of extensor tendon, allowing to protrude the joint between two lateral slips of extensor tendon.

Q. Why it is called **boutonniere** or **button-hole?**

A. Because of rupture of central slip of extensor tendon, it looks like the gap of button hole.

Q. What is **swan neck deformity**? What are the **mechanisms?**

A. Fixed flexion of DIP joint and extension of PIP joint (reverse of boutonniere).
Mechanism—because of chronic synovitis:

- Rupture or stretching of extensor tendon on dorsum of DIP joint
- Secondary to stretching of volar plate at PIP joint
- Shortening of intrinsic muscles of hands that exert tension of dorsal tendon sheath leading to hyperextension of PIP joint.

Q. Why **Z-deformity** of thumb?

A. Because of chronic synovitis, there is hyperextension of IP joints and fixed flexion and subluxation of metacarpophalangeal (MCP) joints of thumb.

Q. Why **radial deviation?**

A. Weakness of extensor carpi ulnaris leads to radial deviation at wrist as the carpal bone rotates.

Q. Why **ulnar deviation?**

A. It occurs in response to radial deviation to keep the tendons to the phalanges in normal line to the radius.

Q. What is rheumatoid nodule? Where is it found?

A. These are painless, firm, subcutaneous nodule, invariably associated with positive rheumatoid factor. It is present in 20 to 30% cases of rheumatoid arthritis.

Sites: Pressure points, such as elbow, extensor surface of forearm and hands (fingers), scapula, scalp, sacrum, shin, Achilles tendon, toes, sclera, pleura, lungs and pericardium.

Significance of rheumatoid nodule:
- It is one of the diagnostic criteria
- Associated with high titer of rheumatoid factor (positive RA test)
- Associated with active and aggressive RA
- A bad prognostic sign.

Histologically 3 zones:
- Central zone of necrotic material including collagen fibril, noncollagen filament and cellular debris
- Mid zone of palisading macrophages
- Outer zone of granulation tissue.

Nodules may ulcerate and become infected. Treatment with methotrexate may increase the number of rheumatoid nodule in some patients.

Nodules resolve when the disease is under control. If it causes problem, it may be removed surgically or by local injection of corticosteroid.

Note Remember the following:

Rheumatoid nodules may be confused with tophi of gout, xanthomata, olecranon bursa in elbow, sarcoid nodule or neurofibroma.

Q. What is Baker's cyst?

A. Cyst on the back of knee joint, communicates with the joints but fluid is prevented from returning to the joint by a valve-like mechanism. May rupture during knee flexion and fluid enters into the calf. After rupture, severe pain, swelling and tenderness in the calf. It is confused with DVT.

Diagnosis: USG of knee joint. Sometimes, CT scan or MRI and arthrogram may be done.

Treatment after rupture of Baker's cyst:
- Relief of pain by NSAID
- Elevation of the limb, rest and observation
- Antibiotic, if necessary
- Intra-articular injection—methylprednisolone or triamcinolone may be given
- Surgical toileting and removal of cyst, if necessary.

Q. What are the causes of Baker's cyst?

A. Commonly in RA. Also in osteoarthrosis and rarely congenital.

Q. What are the diagnostic criteria of rheumatoid arthritis?

A. ARA (American Rheumatism Association criteria):
1. Morning stiffness (> 1 hour)
2. Arthritis of three or more joint areas
3. Arthritis of hand joints and wrist
4. Symmetrical arthritis
5. Rheumatoid nodule

6. Positive RA factor
7. Typical radiological changes (erosion or periarticular osteopenia).

The duration should be 6 weeks or more. There are 14 joint areas in the body for diagnosis of RA. They are—elbow, wrist, PIP, MCP, knee, ankle, MTP of both sides (7 × 2 = 14).

Note Remember the following:

When four or more criteria are present, there is 93% sensitivity and 90% specificity.

Q. What are the **extra-articular** manifestations of RA?

A. As follows:

1. Eye:
- Episcleritis
- Scleritis
- Scleromalacia
- Scleromalacia perforans
- Keratoconjunctivitis sicca.

2. Respiratory:
- Pleurisy
- Pleural effusion (may be bilateral)
- Fibrosing alveolitis
- Nodules in the lungs (in Caplan's syndrome)
- Bronchiolitis.

3. Cardiac:
- Pericarditis (30%)
- Pericardial effusion (rare)
- Chronic constrictive pericarditis (rare)
- Rarely myocarditis, endocarditis, conduction defect, heart block, dysrhythmia, cardiomyopathy, aortic regurgitation, coronary vasculitis, coronary artery occlusion and granulomatous aortitis.

4. Vasculitis:
- Digital arteritis and nail fold infarct
- Ulcers
- Raynaud's phenomenon
- Visceral arteritis
- Mononeuritis multiplex
- Pyoderma gangrenosum.

5. Neurological:
- Entrapment neuropathy (compression of nerves by hypertrophic synovium), commonly carpal tunnel syndrome (compression of median nerve) and tarsal tunnel syndrome (compression of posterior tibial nerve)
- Peripheral neuropathy
- Mononeuritis multiplex
- Cervical cord compression (due to atlanto-axial subluxation)
- Progressive cervical myelopathy.

6. Hematological:
- Anemia (usually normocytic normochromic, occasionally macrocytic because of folate deficiency or associated with pernicious anemia and microcytic hypochromic because of bleeding from NSAID)

- Thrombocytosis
- Eosinophilia
- Pancytopenia (because of hypersplenism in Felty's syndrome).

7. Musculoskeletal:
- Muscle wasting
- Tenosynovitis
- Bursitis
- Osteoporosis.

8. Others:
- Lymphadenopathy
- Splenomegaly
- Nodules causing sinus or fistula
- General features (fatigue, fever, weakness, loss of weight, susceptibility to infection)
- Amyloidosis.

Note Remember the following:

Persistent inflammatory process in rheumatoid arthritis may cause large B cell lymphoma.

Q. What is **rheumatoid factor?**

A. Rheumatoid factor is an antibody, directed against Fc portion of IgG. It may be IgM or IgG type. Rheumatoid factor is positive in 75% cases, but 100% positive in RA with extra-articular manifestations. It is detected by latex slide test (RA test is more sensitive, but less specific, and is used for screening) and Rose Waaler test (RW test, the sheep cell agglutination test, is less sensitive, but more specific). Other causes of positive rheumatoid factor are:
- Collagen diseases—Sjögren's syndrome (90%), SLE (30%), systemic sclerosis, dermatomyositis, fibrosing alveolitis and mixed essential cryoglobulinemia
- Infections—infectious mononucleosis, infective endocarditis, tuberculosis, leprosy, kala-azar, hepatitis B, syphilis, malaria, filariasis and schistosomiasis
- Liver disease—PBC (50%)
- Sarcoidosis
- Temporarily after vaccination and blood transfusion
- Over 65 years (20% in normal population).

High titer of rheumatoid factor indicates:
- Severe erosive disease
- More extra-articular manifestations
- Poor prognosis
- Associated with rheumatoid nodule, vasculitis and Felty's syndrome.

Q. What are the **presentations** of RA?

A. As follows:
- Chronic persistent—common (65 to 70%)
- Remitting type (5 to 10%)
- Rapidly progressive (5%)
- Palindromic type (5%).

Pattern of onset:
- Monoarticular (20%)

- Oligoarticular (45%)
- Polyarticular (35%).

Mode of onset:
- Insidious (70%)
- Acute (15%)
- Systemic (10%)
- Palindromic (5%).

Site of onset:
- Small joints (32%)
- Medium size joints (16%)
- Large joints (29%)
- Combined (26%).

Q. What is **malignant** RA?

A. Severe and progressive RA associated with severe extra-articular manifestations, systemic features and vasculitis.

Q. What is **palindromic** RA?

A. Recurrent acute episode of monoarthritis lasting 24 to 48 hours. Knee and finger joints are most commonly affected, but any peripheral joint may be involved. Fever may occur, but no other systemic features. It may be confused with acute gouty arthritis and atypical onset of rheumatoid arthritis. There may be many attacks without any permanent articular damage. However, one-third to half cases may develop typical RA. This can be treated with NSAID during pain. Hydroxychloroquine may be used in preventing recurrent attack.

Q. What is **Caplan's syndrome**?

A. Rheumatoid lung nodules with pneumoconiosis is called Caplan's syndrome. Common in coal-workers pneumoconiosis, may occur in any pneumoconiosis. Nodules are rounded, 0.5 to 2.5 cm, present at periphery of the lung. These may rupture causing pneumothorax or may cavitate and cause hemoptysis. It may be confused with tuberculosis or neoplasm.

Q. What is **Felty's syndrome**?

A. Rheumatoid arthritis with splenomegaly and neutropenia is called Felty's syndrome. There may be hypersplenism (anemia, leukopenia and thrombocytopenia). It occurs in long standing, seropositive, deforming, but inactive arthritis, in < 1% of the cases. Female is more affected than male, age 50 to 70 years. Leg ulcers or sepsis are complications due to neutropenia. Splenectomy may be necessary for hypersplenism. It is associated with high titer of rheumatoid factor, subcutaneous nodules and other manifestations of systemic rheumatoid disease.

Q. What are the **mechanisms of anemia** in rheumatoid arthritis?

A. Multiple factors are responsible:
- Anemia of chronic disorder
- Megaloblastic anemia (because of either folate deficiency or vitamin B_{12} deficiency, if associated with pernicious anemia)
- Hypersplenism (in Felty's syndrome)
- Hemolytic anemia (Coombs' test may be positive)
- GIT bleeding (due to NSAID or vasculitis causing iron deficiency anemia)
- Marrow suppression (gold and penicillamine—though less or no use now a days).

Q. What are the **investigations** done in RA?

A. As follows:

- FBC (ESR is high, pancytopenia may occur in Felty's syndrome)
- RA test and RW test
- Anti-CCP antibody (cyclic citrullinated peptide)
- X-ray of hands and other involved joints, chest X-ray to see fibrosis, pleural effusion, nodule, cardiomegaly
- Others—CRP (high) and urine analysis (proteinuria, may occur in amyloidosis).

Q. What are the **ARA criteria for disease activity** in RA?

A. As follows:

1. Number of tender joints
2. Number of swollen joints
3. Patient's global assessment
4. Physician global assessment
5. VAS—(visual analog scale for pain)
6. Duration of morning stiffness
7. ESR or CRP.
8. Functional assessment health status (HAQ—health assessment questionnaire).

Q. What precaution is necessary before **general anesthesia or upper GI endoscopy**?

A. X-ray of the cervical spine should be taken to rule out atlanto-axial subluxation. (Otherwise during anesthesia, cervical cord compression may lead to sudden death).

Q. If the patient develops **nephrotic syndrome** (or proteinuria in urine examination), what is the likely cause?

A. Renal amyloidosis.

Q. What is **anti-CCP antibody**? What is its **significance?**

A. It is the antibody to cyclic citrullinated peptide (CCP). It binds to peptides in which the amino acid arginine is converted to citrulline by peptidyl arginine deaminase, an enzyme abundant in inflamed synovium.

Anti-CCP antibody is highly specific in RA (95%), present in 70% patients with rheumatoid arthritis. Unlike rheumatoid factor, it is not positive in other autoimmune diseases. It is helpful for early diagnosis and is also a predictor of an aggressive disease. In patient with undifferentiated arthritis, anti-CCP antibody is helpful for early diagnosis of RA. It may be detected in asymptomatic patient several years before the development of RA.

Q. How to **treat** RA?

A. As follows:

- Relief of symptoms by rest and NSAID. Also intra-articular injection, splinting, hydrotherapy, etc. may relieve symptoms.
- Suppression of activity and progression of disease by disease modifying anti-rheumatic drug (DMARD).
- Other measures—physiotherapy, orthopedic measures. Synovectomy of the wrist or finger tendon sheaths of the hands may be required for pain relief or to prevent tendon rupture when medical interventions have failed. Osteotomy, arthrodesis or arthroplasty may be needed later.
- Patient's education is important.

Q. What are the **surgical** treatments in RA?

A. As follows:

- Synovectomy of wrist or finger tendon sheath (for pain relief or tendon rupture)
- In advanced or severe cases—arthrodesis, arthroplasty and osteotomy may be done in selected cases.

Q. What are the **criteria for remission** of RA?

A. As follows:

- No joint pain
- No fatigue
- No joint tenderness
- Morning stiffness less than 15 minutes
- No soft tissue swelling
- ESR less than 30 mm in 1st hour.

At least 5 criteria must be present for at least 2 consecutive months.

Q. What are the **bad or poor** prognostic factors of RA?

A. As follows:

1. Clinical:
   - Insidious rather than explosive onset
   - Early development of rheumatoid nodule
   - Extra-articular manifestations
   - Severe functional impairment
   - One year active disease without remission
   - Increasing number of peripheral joints involvement
   - Level of disability at the onset
   - Female sex.
2. Blood tests:
   - High titers of anti-CCP antibodies and RA test
   - High CRP
   - Normochromic normocytic anemia.
3. X-rays:
   - Early erosive damage (Note: Ultrasound and MRI can show cartilage and bone damage prior to conventional X-rays).

Q. What **DMARDs** are used?

A. As follows:

- First choices are sulfasalazine and methotrexate.
- Other drugs—chloroquine, hydroxychloroquine, leflunomide, azathioprine, and cyclosporine (gold and penicillamine are not used any more).
- Anti-TNF alpha and IL-1, also rituximab are more effective than other DMARD in preventing joint erosions. If disease activity persists despite an adequate trial of two DMARDs, anti-TNF therapy should be considered.

The DMARD should be started from the beginning, may take 4 to 12 weeks for response. If no effect in 6 to 12 weeks, combination with methotrexate and sulfasalazine may be given. Prednisolone 7.5 to 10 mg may be added with DMARD to give symptomatic relief.

Brief Note About DMARDs

Sulfasalazine:

1. When taken by mouth, it is broken to sulfapyridine and 5-aminosalicylic acid (ASA). Sulfapyridine is effective in RA (ASA is effective in inflammatory bowel disease). It acts probably by inhibiting cyclo-oxygenase and other enzymes responsible for synthesis of prostaglandin.
2. Dose—start with low dose, increase the dose every weekly.
   - Initially, 250 mg (½ tablet) BID for 1 week,
   - Then 500 mg (1 tablet) BID for 1 week,
   - Then 1,000 mg (2 tablets) BID to be continued (maximum dose 2 to 3 g daily).
3. Side effects—GIT upset (anorexia, nausea, vomiting, diarrhea), skin rash, Stevens Johnson syndrome, reversible sterility in males, blood dyscrasias (agranulocytosis, megaloblastic anemia and hemolytic anemia).
4. Periodic check up—FBC, liver function test (SGPT) and renal function tests (creatinine), every 1 to 3 months.

Methotrexate:

- Very effective DMARD. May take 4 to 6 weeks to act.
- Dose—7.5 to 10 mg, in a fixed day weekly (up to 25 mg). Folic acid 5 mg/day should be given on the next day (folinic acid is more preferable).
- Side effects—Anorexia, nausea, vomiting (prevented by using anti-emetic before starting the drug). Rarely, may cause bone marrow depression. Prolong use may cause hepatic fibrosis and DPLD.
- Periodic check up—CBC, liver function tests (SGPT) and renal function test (creatinine) should be done.
- Mechanism of action—competitively inhibits dihydrofolate reductase that interferes with DNA synthesis and cell division.

Chloroquine:

- It is a weak with slow DMARD effect.
- Dose—250 mg daily as a single dose.
- Side effects—Anorexia, nausea, vomiting, skin rash. Prolonged use may cause neuromyopathy and ocular toxicity. In eye, corneal microdeposit (reversible after drug withdrawal), retinopathy (may cause blindness), bull's eye macula and optic neuritis.
- Periodic examination of eye is essential. To reduce ocular toxicity, the drug can be given for 10 months in a year.

Hydroxychloroquine:

- Dose—200 to 400 mg daily
- Used alone in mild disease or as an adjuvant with other DMARD
- Retinopathy is the serious complication, but this is rare before 6 years of treatment.

Leflunomide:

- It can be used if methotrexate fails to respond. Also can be used together with methotrexate.
- Dose—100 mg daily for 3 days, then 10 to 20 mg daily.
- Side effects—Skin rash, diarrhea, reversible alopecia, hepatotoxicity, carcinogenic and teratogenic. It needs a washout of 2 years before conception (3 months in man and 2 years in female), so avoid in women who want to be pregnant.
- Periodic blood checkup is mandatory.

Biological agents:

These agents block specific immune factors responsible for RA. Drugs are—anti-TNF α and IL-1 receptor antagonist. These are highly expensive, used only when there is failure of 2 DMARDs.

Anti-TNF α:

1. It is more effective, rapid onset of action, greater clinical efficacy and sustained benefit than standard DMARD.
2. Anti-TNF drugs are:
   - Infliximab (given in infusion every 1 to 2 months)
   - Etanercept (given SC every 2 weeks)
   - Adalimumab (given SC every 2 weeks).
3. Common side effects: Hypersensitivity reaction, headache, hypotension. Reactivation of latent tuberculosis may occur. Sometimes lymphoma may occur.

Anti-interleukin (IL-1) receptor antagonist:

- Anakinra may be used in RA when anti-TNF α is unsuccessful (less effective than anti-TNF). It is used in combination with methotrexate.

Anti-interleukin 6 (IL-6) receptor:

- Tocilizumab: It is a humanized monoclonal antibody against IL-6 receptor. It acts similar to those of TNF blockade. It is used for treatment of moderate to severe active rheumatoid arthritis in adult patient, alone or in combination with methotrexate and/or other DMARDs. Dose—8 mg/kg as IV infusion, once in every 4 weeks.

Rituximab:

- It is an antibody directed against the CD-20 receptor, expressed on B lymphocytes.
- It produces significant improvement in RA positive patients. May be used alone or in combination with steroid or methotrexate.
- It is given by 2 IV infusions (1 g each) 2 weeks apart.

Q. What is **Sjögren's syndrome**? How will you **confirm** it?

A. It is an autoimmune disorder characterized by dryness of eye (keratoconjunctivitis sicca) and dryness of mouth (xerostomia) with nonerosive arthritis. Fibrosis and atrophy of the salivary glands occur. There is infiltration of lymphocytes and plasma cells in lacrimal and salivary glands. It is of 2 types:

- Primary—not associated with collagen disease (sicca syndrome)
- Secondary—associated with collagen disease (commonly RA).

Presentation of primary Sjogren's syndrome—common in females, F:M = 9:1, 40 to 50 years.

- Dryness of mouth and eyes
- Arthralgia and non-progressive arthritis
- Raynaud's phenomenon
- Dysphagia
- In lung—pulmonary diffusion defect and fibrosis
- Renal (renal tubular acidosis, nephrogenic diabetes insipidus)
- Vasculitis
- Others (fever, weakness, lymphadenopathy and neuropathy, fit, depression)
- Lymphoma—increased incidence of non-Hodgkin's B cell lymphoma. (It is associated with 40-fold risk).

- May be associated with other autoimmune disease, such as thyroid disease, myasthenia gravis, PBC, autoimmune hepatitis.

Investigations:

1. CBC (high ESR)
2. Schirmer test (a strip of filter paper is placed inside of lower eyelid. In normal people, at least 6 mm is wet in 5 minutes. In Sjögren's syndrome < 5 mm)
3. Biopsy of lip or salivary gland (lymphocytic and plasma cell infiltration)
4. Rose Bengal staining of eyes shows punctate or filamentary keratitis
5. Antibody test:
   - RA test (positive in 90%)
   - ANA (positive in 60 to 70%)
   - Anti-Ro (SS-A, positive in 70%. It can cross placenta causing congenital complete heart block)
   - Anti-La (SS-B).

Treatment:

- Artificial tear (hypromellose), contact lens, oral hygiene, artificial saliva, oral gel and chewing gum
- Stimulation of saliva flow by sugar free chewing gum or lozenges may be helpful
- Oral candidiasis should be promptly treated
- Vaginal dryness is treated with lubricants, such as K-Y jelly
- Hydroxychloroquine (2 to 3 mg/kg daily, may improve the flow of tear)
- Treat the primary cause
- Extraglandular and MSK manifestations may respond to steroid. Immunosuppressive drugs can be added.

Q. What are the **differences** between rheumatic fever and RA?

A. As follows:

Points	Rheumatic fever	RA
1. Age	5 to 15 years	20 to 40 years
2. Cause	Sequelae of immune response to *Streptococcus* β-hemolyticus sore throat	Autoimmune
3. Joints	Large	Peripheral small joints
4. Type of arthritis	Fleeting	Bilateral, symmetrical
5. Diagnosed by	Two major or one major and two minor criteria plus signs of previous *Streptococcus* infection	Four of seven criteria
6. Morning stiffness	Absent	Present
7. RA test	Negative	Positive
8. SC nodule	Present	Rheumatoid nodule
9. Erythema marginatum	Present	Absent
10. Joint deformity	Absent	Present
11. Cardiac involvement	Common	Less

Contd...

Contd...

12. Chronic constrictive pericarditis	Never	May cause
13. Chorea	May be present	Absent
14. Treatment	Prophylactic penicillin	DMARD
15. Sequelae	Rheumatic valvular lesion. It licks the joints, kills the heart.	Not so

DERMATOMYOSITIS

CHIEF COMPLAINTS

- Weakness and generalized muscular pain for … months
- Skin rash for … months
- Joint pain involving multiple joints for … months.

HISTORY

History of present illness: According to the statement of the patient, she was reasonably well … months back. Since then, she has been complaining of weakness, along with generalized muscle pain. Weakness is more marked during standing up from sitting position and raising both arms above head, especially while combing her hair. There is no diurnal variation of weakness. For last … months, she noticed reddish, scaly, non-itching skin rashes over her face, trunk, leg and hands that do not increase on exposure to sunlight. She also experiences joint pain involving the ankle, knee, wrist and small hand joints. Pain is aggravated by activity, slightly relieved by rest, but is not associated joint swelling or morning stiffness. She gives no history of fever, oral ulcer or respiratory symptoms. Her bowel and bladder habits are normal.

History of past illness: Mention according to the patient's statement.

Family history: No such illness in the family.

Personal history: Mention according to the patient's statement.

Drug and treatment history: Mention according to the patient's statement.

Menstrual history: Mention according to the patient's statement.

Socioeconomic history: Mention according to the patient's statement.

GENERAL EXAMINATION

- The patient looks ill and anxious
- Face is puffy with periorbital edema and heliotrope rash over both upper eyelids
- Skin shows maculopapular, scaly, erythematous rash on the cheeks in a butterfly distribution, on forehead, dorsum of hands, upper arms, shoulders and on chest
- Telangiectasia present on face and hands
- Mildly anemic
- No jaundice, cyanosis, clubbing, koilonychia, leukonychia or edema
- No lymphadenopathy or thyromegaly
- Pulse—84/min
- BP—120/70 mm Hg
- Temperature—98.6^0 F.

Note Remember the following:

Erythematous rash may be present on the neck and upper chest (in the shape of V—called **V** sign), or on the shoulders (Shawl sign).

SYSTEMIC EXAMINATION

Musculoskeletal System

1. **Hands:**
   - Maculopapular, scaly, erythematous rash on the dorsum of the hands. There are rashes with flat topped macules over the knuckles (Gottron's sign). Finger shows periungual erythema, ragged cuticles and hemorrhage.
   - Telangiectasia (dilated nailfold capillary) seen.
2. **Joints:** Swollen, tender with contracture deformity
3. **Muscles:**
   - Proximal myopathy is present both in the upper and lower limbs
   - Muscles are tender.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mrs …, 45 years, housewife, normotensive, nondiabetic, nonsmoker, hailing from …, presented with weakness and generalized muscle pain for … months. Weakness is more marked during standing up from sitting position and raising both arms above head, especially while combing her hair. There is no diurnal variation of weakness. For last … months, she noticed reddish, scaly, non-itching skin rashes over her face, trunk, leg and hands that do not increase on exposure to sunlight. She also experiences joint pain involving the ankle, knee, wrist and small hand joints. Pain is aggravated by activity, slightly relieved by rest, but is not associated joint swelling or morning stiffness. She gives no history of fever, oral ulcer, respiratory symptoms. Her bowel and bladder habits are normal. No such illness in the family. She was treated with painkillers and vitamins by local physicians.

On examination, general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is dermatomyositis.

Q. What are the **differences** of skin rash in dermatomyositis and SLE?

A. Rash in dermatomyositis usually involves knuckles, spares the phalanges. In SLE, it involves the phalanges, spares the knuckles.

Q. What are the **differential diagnoses**?

A. As follows:
- Systemic lupus erythematosus
- Mixed connective tissue disease (MCTD)
- Systemic sclerosis
- Sarcoidosis
- Polymyalgia rheumatica.

Q. Why not this is **polymyalgia rheumatica?**

A. Usually in polymyalgia rheumatica, there is no skin rash. About 30 to 50% cases are associated with temporal arteritis. CPK and other enzymes are typically normal that are high in dermatomyositis.

Q. What **investigations** should be done in dermatomyositis?

A. As follows:

1. FBC (ESR is high, but may be normal even in active disease)

2. Muscle enzymes:
   - Creatine phosphokinase (CPK) is very high (the most sensitive test)
   - Other enzymes—serum aldolase, SGOT, SGPT and LDH (may be high)
3. Electromyography—abnormal almost in every case, normal in 10%
4. Muscle biopsy shows the following findings:
   - Necrosis, swelling, vacuolation, disruption and fragmentation of muscles
   - Infiltration of lymphocyte, plasma cells, eosinophils and macrophages
   - Fibrosis
   - Perivascular inflammatory cells infiltration and thickening of vessel wall
5. Other tests:
   - To exclude malignancy (chest X-ray, USG, CT scan, MRI, PET scan, mammogram, gastrointestinal tract imaging)
   - Other X-rays (limbs or hands) to see soft tissue calcification. It is common in childhood dermatomyositis
   - RA test and ANF (positive in 50% cases)
   - Anti-Jo-1 antibody is more specific. Positive in 30% cases of dermatomyositis and 50% cases of polymyositis (if anti-Jo-1 antibody is present, respiratory muscles involvement may occur)
   - MRI of muscles—to detect abnormal muscles (helpful to take biopsy)
   - Urine for myoglobin in acute cases.

Measurement of CPK is important for the following reasons:

- Very high in dermatomyositis
- Indicates active disease
- To see therapeutic response (reduces after therapy).

Occasionally, CPK may be normal in dermatomyositis:

- If dermatomyositis is associated with internal malignancy
- Due to long standing disease with atrophy of muscles
- Due to the presence of inhibitors in blood.

Causes of high CPK:

- Exercise
- Intramuscular injection
- Muscle trauma or road traffic accident
- Convulsion
- Alcoholism
- Dermatomyositis or polymyositis
- Acute myocardial infarction (CPK-MB)
- Myopathy
- Rhabdomyolysis
- Chronic liver disease (CLD)
- Drugs—statins, busulfan, narcotics, colchicine and chloroquine.

Isoenzymes of CPK:

- MM (mainly in skeletal muscle)
- MB (mainly in cardiac muscle)
- BB (in brain).

Q. What are the **EMG findings** in dermatomyositis?

A. As follows:

- Spontaneous fibrillation (at rest)
- Small amplitude, short duration and polyphasic action potential (after voluntary activity)
- Salvos of repetitive potential on mechanical stimulation of the nerve.

RELATED QUESTIONS AND ANSWERS

Q. What is **polymyositis** or **dermatomyositis**?

A. Polymyositis is the nonsuppurative, noninfective inflammation of skeletal muscle of unknown cause, characterized by necrosis, fibrosis and regeneration of muscles. When associated with **skin rash**, it is called dermatomyositis.

Q. How do you **classify** dermatomyositis or polymyositis?

A. Five types:

1. Adult polymyositis
2. Adult dermatomyositis
3. Dermatomyositis or polymyositis associated with malignancies
4. Childhood dermatomyositis or polymyositis
5. Dermatomyositis or polymyositis associated with other autoimmune rheumatic disease (ARD, e.g. SLE, rheumatoid arthritis, SSc).

Q. What are the **causes** of dermatomyositis?

A. Actual cause unknown. Probable factors are:

- Autoimmune mechanism (presence of anti-Jo-1 antibody and lymphocyte infiltration in muscle).
- Viral (coxsackie B, rubella and influenza have been suggested).
- Associated with malignancy (the most common cause is bronchial carcinoma in male and ovarian carcinoma in female). Dermatomyositis can precede any malignancy of lungs, ovary, breast, stomach.
- Drugs causing polymyositis—penicillamine and zidovudine.

Q. If the patient is **elderly,** what disease should be excluded?

A. Malignancy (bronchial carcinoma, also carcinoma of the breast, GIT and ovary).

Q. What are the **presentations** of dermatomyositis?

A. Common in female, F:M = 2:1, peak incidence is in fifth and sixth decades.

- Muscular weakness, mainly involving the proximal muscles (shoulder and pelvic girdle).
- Skin rash—typically affects upper eyelids with erythema called "Heliotrope rash" (photosensitive, erythematous and scaly). Flat, red rash on face and upper trunk, erythematous rash of knuckles with raised violaceous scaly eruption (Gottron's sign). Erythematous rash also may occur in knee, elbow, malleoli, neck and anterior chest (often a V sign) or back and shoulder (shawl sign).
- Pharyngeal, laryngeal and respiratory muscles involvement may cause dysphagia, dysphonia and respiratory failure.
- Others—arthralgia, arthritis, myalgia and Raynaud's phenomenon.

Note Remember the following points:

- In some patients, only skin rash may be present without muscle involvement called **dermatomyositis sine myositis**
- Ocular involvement is rare
- Malignancy is more in dermatomyositis, less in polymyositis
- The patient may present with acute renal failure because of myoglobinuria secondary to rhabdomyolysis.

Q. How do you **test for proximal myopathy**?

A. As follows:

In the upper limb:

- Ask the patient to raise the arms above the head (patient is unable to do so)
- Ask the patient to sit, keep the arm on side at 90° and press against resistance
- The patient may complain of difficulty in combing, climbing upstairs, rising from the chair.

In the lower limb:

- With the patient lying flat, press the knee and ask the patient to raise the foot against resistance
- Ask the patient to squat, now ask him to stand up (patient is unable to do so).

Q. What are the **causes of proximal myopathy**?

A. Causes are:

- Myopathy (limb girdle, fascioscapulohumeral), except myotonic dystrophy
- Dermatomyositis or polymyositis
- Myasthenia gravis
- Myasthenic myopathic syndrome (Eaton-Lambert syndrome)
- Thyrotoxicosis, also in hypothyroidism
- Cushing's syndrome
- Osteomalacia
- Diabetic amyotrophy
- Hyperparathyroidism
- Drugs—lovastatin, chloroquine, colchicine (all are associated with high CPK). Steroid can cause proximal myopathy (it is not associated with high CPK).

Q. What are the **causes of painful muscle?**

A. Causes are:

- Physiological—after exercise
- Polymyositis
- Polymyalgia rheumatica
- Fibromyalgia syndrome
- Viral infection
- Chronic alcoholism
- Following convulsion
- Functional
- Associated with rheumatological disease.

Q. What are the causes of **acute or sudden muscular weakness?**

A. As follows:

- Gullain Barre syndrome
- Hypokalemia and hyperkalemia
- Familial periodic paralysis
- Thyrotoxic periodic paralysis
- Functional (HCR).

Q. What will be the **deep tendon reflex** in dermatomyositis?

A. Usually intact.

Q. What is the **pathognomonic sign** in dermatomyositis?

A. Heliotrope rash.

Q. What is **heliotrope rash**?

A. It is a violaceous, purple or lilac colored rash, present usually over the upper eyelids. It may also be present on the cheeks, nasal bridge and knuckles. Presence of heliotrope rash is highly suggestive of dermatomyositis. It is derived from the name of the shrub Heliotropium, which has fragmented, purple flowers. It is common in childhood dermatomyositis, also occurs in adults.

Q. What is **Gottron's sign**?

A. It is scaly, purple-red, raised, flat-topped, and vasculitic patches over the extensor surface of joints and knuckles of hands. It may be found on the elbow and knee.

Q. How to **treat** dermatomyositis or polymyositis?

A. As follows:

- Prednisolone 0.5 to 1 mg/kg daily to induce remission. Continued for at least 1 month after myositis is clinically and enzymatically inactive. Then taper the dose slowly. Maintenance dose is 5 to 7.5 mg daily. May be required to continue for months, even years.
- If severe respiratory or pharyngeal weakness—methylprednisolone 1 g daily for 3 days.
- If no response to steroid—methotrexate or azathioprine may be given.
- If methotrexate and azathioprine fail—cyclosporine or cyclophosphamide or mycophenolate mofetil may be tried.
- High-dose IV immunoglobulin may help in some cases.
- Treatment of underlying malignancy may improve the condition.
- Physiotherapy.

Q. What is the **prognosis?**

A. As follows:

- 5 years survival rate in treated patient is > 95%, 10 years survival is 84%.
- Worse prognosis if severe in presentation, delay of treatment, severe dysphagia or respiratory difficulty, older patient and if underlying malignancy.
- Dermatomyositis responds better than polymyositis. So, better prognosis.

Q. What is **Eaton-Lambert syndrome?**

A. It is a paraneoplastic syndrome characterized by proximal muscle weakness and wasting because of defective acetylcholine release at the neuromuscular junction. It commonly involves the lower limb, but may involve any muscle.

Causes:

- There is defect in **acetylcholine** release at the neuromuscular junction that is thought to be due to an auto-antibody against prejunctional voltage gated calcium channel on the motor nerve terminal. Small cell carcinoma of the lung may trigger the auto-antibody reaction.
- It is commonly because of small cell carcinoma of the lung, may be associated with or may precede the manifestations of carcinoma.

Features:

- Proximal weakness, commonly in the lower limbs but any muscle can be involved. Ptosis and diplopia may occur in 70% cases.
- Reflexes are absent or diminished.
- Muscle power may be increased and tendon reflexes may return after repeated activity or sustained contraction of the relevant muscle (reverse of myasthenia gravis).
- Patients may have autonomic dysfunction (dry mouth, constipation, impotence).

Note Long-standing

Abnormality of reflex, muscle power and autonomic disturbance are absent in myasthenia gravis.

Investigations:

- EMG shows progressive incremental response (reverse of myasthenia gravis, where there is decremental response).
- Antibody to P/Q type voltage gated calcium channel (anti VGLC)—found in 90% cases.

Treatment:

- 3, 4 diaminopyridine may be given
- IV immunoglobulin may be helpful
- Pyridostigmine may give symptomatic relief
- Plasmapheresis
- Treatment of the primary cause.

ANKYLOSING SPONDYLITIS

CHIEF COMPLAINTS

- Low back pain for … months.

HISTORY

History of present illness: According to the patient's statement, he was reasonably well … months back. Since then, he has been suffering from low back pain, worse in the morning after waking from sleep that improves with physical activity or exercise. Sometimes, it is worse while sleeping at night. He also feels difficulty in bending forward, backward or to either sides for pain. He does not complain of pain in any other joints. There is no history of pain in the eye, fever, mouth ulcer, palpitation, cough, chest pain, rash, urinary or bowel abnormality.

History of past illness: Nothing significant. There is no history of diarrhea (to exclude IBD), skin problem (to exclude psoriatic arthritis).

Family history: He has 2 brothers and 1 sister. No one in his family is suffering from such illness. No family history of psoriasis or inflammatory bowel disease.

Personal history: Mention according to the patient's statement.

Socio economic history: Mention according to the patient's statement.

Treatment History: He used to take some painkillers during his illness.

GENERAL EXAMINATION

- The patient is slightly emaciated
- Eye—slightly red
- No skin or nail change (to exclude psoriatic arthritis)
- No anemia, jaundice, cyanosis, clubbing, koilonychia, leukonychia or edema
- No lymphadenopathy or thyromegaly
- Pulse—90/minutes
- BP—120/80 mm Hg.

SYSTEMIC EXAMINATION

Locomotor System

- There is loss of lumbar lordosis, thoracic kyphosis and compensatory hyperextension of neck (in advanced stage, **question mark "?"** or stooped posture).
- The patient is unable to look up and unable to turn to any side without movement of whole body.
- There is restricted movement of spine in all directions (forward, lateral and backward bending).
- SLR is positive.
- The patient is unable to make contact between the occiput and the wall, when standing with heel and back against the wall (ask the patient to stand along the side of the wall with heel and back against the wall, now measure occiput to wall distance. Gap indicates limitation of thoracic and cervical spine).
- Sacroiliitis is present.
- Achilles tendinitis and plantar fasciitis are present.
- Right knee joint is mildly tender and swollen with slight reduction of movement.
- Schober's test is positive.

Respiratory System

- Chest expansion is restricted
- Respiration—abdominal
- Few crepitations over both apical zones (indicates apical fibrosis).

Cardiovascular System

Precordium:
1. Inspection – No abnormality
2. Palpation – No abnormality
3. Auscultation:
   - First heart sound—normal
   - Second heart sound—aortic component is soft
   - There is early diastolic murmur in left lower parasternal area (due to AR).

Abdomen

- Abdomen—looks protruded
- No hepatosplenomegaly
- Kidney—Not ballotable.

Examination of other system reveals no abnormalities.

SALIENT FEATURES

Mr …, 35 years, service holder, normotensive, nondiabetic, nonsmoker, hailing from …, presented with low back pain for ... months that is worse in the morning after waking from sleep that improves with physical activity or exercise. Sometimes, it is worse while sleeping at night. He also feels difficulty in bending forward, backward or to either sides for pain. He does not complain of pain in any other joints. There is no history of pain in the eye, fever, mouth ulcer, palpitation, cough, chest pain, rash, urinary or bowel abnormality. No one in his family was suffering from such illness. No family history of psoriasis or inflammatory bowel disease. He was treated with painkillers by local physicians.

On examination – general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is ankylosing spondylitis.

Q. What are your **differential** diagnoses?

A. Any cause of spondyloarthropathy may be considered as differential diagnosis.
- Reiter's syndrome or reactive arthritis
- Enteropathic arthritis (Crohn's disease and ulcerative colitis)
- Psoriatic arthritis
- Juvenile chronic arthritis (if the patient is less than 16 years old).

Q. What are the **investigations** done in ankylosing spondylitis?

A. As follows:
1. X-ray of SI joints and spine (lumbosacral, dorsal and cervical)

2. MRI of lumbosacral spine may be done in some cases
3. CBC (ESR may be high)
4. CRP (may be high)
5. Rheumatoid factor (negative)
6. HLA-B27 (measured in blood lymphocytes) is positive in 90% of the cases
7. Others according to cause (barium enema and follow through for inflammatory bowel disease).

Note Remember the following:

HLA-B27 is neither necessary not sufficient for diagnosis of AS. However, presence of HLA-B27 increases the probability of AS. In typical AS with absence of HLA-B27, there is probability of IBD.

X-ray shows:

- Sacroiliitis—often the first abnormality, beginning in the lower synovial parts of the joints with irregularity and loss of cortical margins, widening of the joint space and subsequently sclerosis, narrowing and fusion.
- In thoracolumbar spine—squaring of vertebrae due to erosion. Bridging syndesmophytes formation at the outermost fibers of the annulus, results in **bamboo spine appearance.** There may be ossification of anterior longitudinal ligament or interspinous ligament and facet joint fusion.

RELATED QUESTIONS AND ANSWERS

Q. What is **ankylosing spondylitis**? What are the usual **presentations**?

A. It is a chronic inflammatory seronegative arthritis characterized by progressive stiffening and fusion of axial skeleton.

Common in young adult, second and third decade, M:F = 3:1. The patient presents with low back pain with morning stiffness, worse in the morning and with inactivity, pain improves after exercise. Peripheral arthritis occurs in 10% cases.

Q. What is the **nature of arthritis** in ankylosing spondylitis?

A. Inflammatory.

Q. What are the **extra-articular manifestations** of ankylosing spondylitis?

A. As follows:

1. Eyes: Anterior uveitis (iritis) 25%, conjunctivitis 20% (the patient may present with painful red eye and photophobia).
2. Heart:
   - AR (4%, due to aortitis), mitral regurgitation
   - Conduction defect, such as first-degree block, left bundle branch block (LBBB) and atrioventricular block (AV block)
   - Pericarditis.
3. Chest and lungs:
   - Chest pain (pleuritic) and reduced chest expansion (costovertebral joint involvement)
   - Apical upper lobe pulmonary fibrosis, cavitation and later on, aspergilloma may occur
   - Pulmonary hypertension and cor pulmonale.
4. Prostatitis (80%), usually asymptomatic.
5. Neurological: Cauda equina syndrome (there is weakness of lower limb, loss of sphincter and rectal control with saddle sensory loss).
6. Others: Plantar fasciitis, Achilles' tendinitis, amyloidosis and osteoporosis.

Q. What are the **diagnostic criteria** for AS?

A. The presence of 3 of following 4 indices in adults < 50 years with chronic back pain indicates AS:
- Morning stiffness > 30 minutes
- Improvement of back pain with exercise but not rest
- Awakening because of back pain during second half of the night only
- Alternating buttock pain.

Alternately Modified New York Criteria (1984) is used:
- Low back pain at least 3 months duration increased by exercise relieved by rest
- Limitation of lumbar spine movement in at least 2 planes
- Decreased chest expansion less than normal
- Bilateral sacroiliitis grade 2 to 4
- Unilateral sacroiliitis grade 3 to 4.

Definite AS—sacroiliitis with any clinical criteria.

Note Remember the following :

MRI is more sensitive than X-ray.

Q. What is the cause of **chest pain** in ankylosing spondylitis?

A. Chest pain is due to costochondral junction involvement.

Q. What are the **types** of ankylosing spondylitis?

A. Two types:
- Primary- without any other association
- Secondary- when associated with other seronegative arthritis.

Q. What are the other **causes of sacroiliitis**?

A. Any cause of spondylo-arthropathy.

Q. What is **spondylo-arthropathy** or **spondarthritis**?

A. It is a group of inflammatory arthritis characterized by:
1. Seronegative rheumatoid factor (RA test is negative)
2. Sacroiliitis and inflammatory spondylitis
3. Asymmetrical inflammatory oligoarthritis (lower > upper limbs, bigger joints are involved)
4. Inflammatory enthesitis
5. Absence of nodules and other extra-articular features of rheumatoid arthritis
6. Typical overlapping extra-articular features:
   - Mucosal inflammation (such as conjunctivitis, buccal ulceration, urethritis, prostatitis, bowel ulceration)
   - Pustular skin lesions and nail dystrophy
   - Anterior uveitis
   - Aortic root fibrosis (AR, conduction defects)
   - Erythema nodosum
7. Familial association (high in HLA-B27).

Q. What are the **diseases** in spondylo-arthropathy?

A. As follows:
- Ankylosing spondylitis
- Reiter's syndrome or reactive arthritis

- Enteropathic arthritis (in Crohn's disease and ulcerative colitis)
- Psoriatic arthritis.

Q. What is **enthesopathy**?

A. Inflammation at the ligamentous attachment with erosion of adjacent bone. Healing of such lesion at the junction of intervertebral disk and vertebral bodies causes new bone formation, called syndesmophyte (**hallmark** of ankylosing spondylitis).

Q. What is the **natural history** of ankylosing spondylitis?

A. Up to 40% may develop severe spinal restriction, 20% may have significant disability. Early peripheral joint disease, especially hip joint involvement indicates poor prognosis.

Q. How would you perform **genetic counseling** with this patient?

A. If the patient is HLA-B27 positive, there is 30% chance for the siblings to develop ankylosing spondylitis.

Q. How **Schober's test** is performed?

A. As follows:

- Mark the points in midline 10 cm above and 5 cm below a line joining the 'Dimple of Venus' on the sacral promontory (the line passes along the L_5 spinous process between the posterior superior iliac spines).
- Ask the patient to bend forward as far as possible.
- Now measure the distance between upper and lower markings.

Normally, it increases by > 5 cm below 50 years of age. If it is < 5 cm, it indicates limitation of mobility of spine.

Modified Schober's test: Only the upper marking is taken that is sufficient for the test, as the lower part is remaining fixed. It is called modified Schober's test.

Q. How to **differentiate** between mechanical and inflammatory arthritis?

A. As follows:

Features	Mechanical arthritis	Inflammatory arthritis
1. Age	Any, 15~90 yrs	Below 40 yrs
2. Onset	Acute	Insidious, > 3 months
3. Family history	No	Usually positive
4. Exercise	Worse	Improved
5. Rest	Better	Worse
6. Morning stiffness	No	Positive
7. Sleep disturbance	No	Yes
8. Neurological signs	May be present	No
9. Range of movement	Asymmetrical	Symmetrical
10. Straight leg raise (SLR)	Positive	Normal

Q. How to **differentiate** aortic regurgitation of rheumatic heart disease and of ankylosing spondylitis?

A. From history and echocardiogram:

- In rheumatic heart disease, echocardiogram shows the involvement of valve cusps (shortening, thickening and fusion).
- In ankylosing spondylitis, echocardiogram shows involvement of aorta or aortic root dilatation due to aortitis.

Q. What are the **differences between** syndesmophyte and osteophyte?

A. As follows -

Syndesmophyte	Osteophyte
1. Secondary to inflammatory disease	1. Degenerative
2. Due to endochondral calcification of the annulus fibrosus	2. New bone at the corners of the vertebra
3. It grows longitudinally (above or below) causing bridging of adjacent vertebra	3. It grows horizontally outwards
4. Hallmark of ankylosing spondylitis	4. Hallmark of osteoarthrosis

Q. What are the **causes of death** in ankylosing spondylitis?

A. Causes are:

- Amyloidosis
- Spinal fracture, especially in cervical spine leading to quadriplegia.

Q. How to **treat** ankylosing spondylitis?

A. As follows:

- Exercise is the mainstay. The patient must remain active. Swimming is the best activity
- Prolong sitting or inactivity should be avoided
- NSAID to relieve pain
- Physiotherapy
- DMARDs—sulfasalazine or methotrexate (MTX) are helpful in peripheral arthritis, but have no effect on axial disease
- In patient with persistent active inflammation, anti-TNF drug therapy may be helpful for both spinal and peripheral arthritis
- Local steroid injection may be given for persistent plantar fasciitis, other enthesopathies and peripheral arthritis
- Oral steroid may be needed for acute uveitis
- Orthopedic measures—may be needed for severe hip, knee or shoulder restriction.

Q. What is the **prognosis**?

A. With appropriate treatment, the prognosis is usually excellent and there is minimum disability unless the hip joints are involved. Around 80% patients remain fully employed.

Note Remember the following points:

- Disease is mild in women. Peripheral arthritis is more in women. Spinal arthritis is less
- May be severe, when it affects in early age, also worse prognosis
- Hip joint involvement is more in teen age
- In the past, radiotherapy was given that is not used nowadays, because there is 10-fold increase incidence of leukemia (AML).

Radiographycally, AS may confused with Alkaptonuria, DISH, lumbar spondylosis and Osteitis condensans ilii.

- In alkaptonuria, calcification looks like AS. But there is calcification of intervertebral disk in Alkaptonuria, never in AS.
- Diffuse idiopathic skeletal hyperostosis (DISH)—florid new bone formation along the anterolateral aspects of at least four contiguous vertebral bodies. In DISH, calcification gives the appearance of **flowing wax** on the anterior body of vertebrae. Sacroiliac and apophyseal joints are normal in DISH. It occurs in middle age and elderly, usually asymptomatic.
- In lumbar spondylosis, there is disk space narrowing and marginal sclerosis.
- In osteitis condensans ilii, there is sclerosis on the iliac site of sacroiliac joints, confuses with sacroilütis. It is a postpartum radiographic finding.

SYSTEMIC SCLEROSIS

CHIEF COMPLAINTS

- Thickening and tightness of skin for … months
- Pain and swelling of multiple joints for … months
- Difficulty in deglutition for … months.

HISTORY

History of present illness: According to the statement of the patient, she was reasonably well … months back. Since then, she noticed gradual thickening and tightening of the skin on the dorsum of her hands that causes difficulty in movement of fingers and wrist joints. After a few months, she noticed the same changes involving her face causing difficulty in opening her mouth. On enquiry, she admitted that her fingers change color and sequentially become pale, blue and red, on exposure to cold water or weather. She also complains of pain and swelling of multiple joints including both knee joints, wrist joints and small joints of hand for last … months. It is not associated with morning stiffness and improves on rest. The patient also complains of occasional heartburn, difficulty in deglutition, loss of appetite and significant loss of body weight for... months. There is no history of fever, shortness of breath, cough, pain abdomen, oral ulcer, skin rash or dryness of eyes or mouth. Her bowel and bladder habits are normal.

History of past illness

Family history: There is no such illness in the family

Personal history

Drug and treatment history

Menstrual history

Socioeconomic history: Mention according to the patient's statement.

GENERAL EXAMINATION

- The patient ill looking and emaciated.
- The face is smooth, shiny, tight, and immobile with hypopigmented and pigmented areas (salt and pepper appearance). There is loss of wrinkling of forehead. The nose is pinched up and tapered (beaking of nose, bird beak face). There is puckering of skin around the lips with a small orifice of mouth (microstomia). The patient has difficulty in opening the mouth. Multiple telangiectasias are noted (mention the location)
- The skin of both hands is smooth, shiny, tight, thick and edematous with pigmented and hypopigmented area. The skin of legs, chest and other parts of the body is normal.
- Mildly anemic.
- No jaundice, cyanosis, clubbing, koilonychia, leukonychia or edema.
- No lymphadenopathy or thyromegaly.
- Pulse—84/min.
- BP—120/75 mm Hg.
- Temperature—98.6^0 F.

SYSTEMIC EXAMINATION

Musculoskeletal System

1. **Hands:**
   - The skin of both hands is smooth, shiny, tight, thick and edematous with pigmented and hypopigmented area
   - Interphalangeal (IP) and metacarpophalangeal joints of both hands are swollen with flexon contracture
   - There is sclerodactyly (tapering of fingers) and infarction (or ulcer or gangrene) at the tip of the fingers and atrophy of pulp
   - Telangiectasia at the base of nails
   - (Also, look for resorption, beaking of the nails called pseudoclubbing due to resorption, and amputation of finger. Also mention if hard nodule or calcinosis seen over any finger).
2. **Joints:** Both knee joints and both wrists are swollen and tender.
3. **Muscles:** Generalized wasting is present.

Examination of other systems reveals no abnormalityies.

SALIENT FEATURES

Mrs …, 41 years, housewife, normotensive, nondiabetic, nonsmoker, hailing from …, presented with gradual thickening and tightening of the skin on the dorsum of her hands for … months that causes difficulty in movement of fingers and wrist joints. After a few months, she noticed the same changes involving her face causing difficulty in opening her mouth. On enquiry, she admitted that her fingers change color and sequentially become pale, blue and red, on exposure to cold water or weather. She also complains of pain and swelling of multiple joints including both knee joints, wrist joints and small joints of hand for last … months. It is not associated with morning stiffness and improves on rest. The patient also complains of occasional heartburn, difficulty in deglutition, loss of appetite and significant loss of body weight for ... month**.** There is no history of fever, shortness of breath, cough, pain abdomen, oral ulcer, skin rash or dryness of eyes or mouths. Her bowel and bladder habits are normal. There is no family history of such illness. She was treated with different creams and ointments, the name of that she could not mention.

On examination, general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is systemic sclerosis.

Q. In this case, what **specific questions** did you ask?

A. I have asked the following questions:

- Whether any change of color in her finger on exposure to cold? (Raynaud's phenomenon)
- If yes, what colors are they? (Pallor, cyanosis and redness).
- Is there any difficulty in swallowing?
- Is there any difficulty in breathing?
- Is there any bowel abnormality? (occasional diarrhea or constipation.)

Q. If patient complains of **difficulty in deglutition**, what is the likely cause?

A. CREST syndrome.

Q. What is **CREST** or **CRST** syndrome? What questions should be asked in CREST syndrome?

A. It is a syndrome characterized by:

- **C: C**alcinosis
- **R: R**aynaud's phenomenon
- **E: E**sophageal involvement (dysphagia)
- **S: S**clerodactyly
- **T: T**elangiectasia.

Ask about Raynaud's phenomenon and dysphagia. CREST syndrome is also called limited cutaneous systemic sclerosis, with a better prognosis. Anti-centromere antibody is present in serum in 70% to 80% cases (if diffuse deposition of calcium in subcutaneous tissue with presence of acrosclerosis, it is called Thibierge-Weissenbach syndrome).

RELATED QUESTIONS AND ANSWERS

Q. What is **systemic sclerosis**? What are the **presentations**?

A. It is a connective tissue disease characterized by fibrosis and degenerative changes in skin, vasculature and internal organs. Common in female (F:M = 4:1), age 30 to 50 years. Usual presentations are:

- Raynaud's phenomenon—90 to 97% cases. May proceed by months or years before other symptoms.
- Tightening and thickening of the skin of hands and other parts of the body, arthralgia and arthritis (nonerosive inflammatory), heartburn (reflux esophagitis due to hiatus hernia), dysphagia, odynophagia, occasional diarrhea and constipation (blind-loop syndrome) and shortness of breath (DPLD).

Two types of systemic sclerosis:

- Diffuse cutaneous systemic sclerosis (DCSS, 30%)—skin involvement of trunk and extremities above the knee and elbow. Initially, skin is edematous, thick and tight. Raynaud's phenomenon may occur just before or with skin symptoms. DPLD and renal involvement are more in DCSS, who have topoisomerase 1 antibody.
- Limited cutaneous systemic sclerosis (LCSS, 70%)—skin involvement only at the extremities. Hands, feet or forearm may be involved. Raynaud's phenomenon may occur before skin change. Face may be involved. CREST is a localized type of systemic sclerosis. Pulmonary hypertension is more common in limited disease.

Other varieties (localized):

- Scleroderma sine scleroderma—involves internal organ without skin lesion
- Morphea—localized, well demarcated, indurated or plaque with central hypopigmentation and tethering of skin, usually in extremities and face
- Linear—if skin involvement is in a linear pattern, usually in lower limbs.

Pathology or pathogenesis in systemic sclerosis:

- Vascular change—widespread vascular damage in arteries, arterioles and capillaries. There is intimal proliferation, vessel wall inflammation, and endothelial damage with release of cytokines and endothelin-I, the later cause vasoconstriction. Also, platelet activation.
- Fibrotic change—fibroblast synthesize collagen I and III, fibronectin, glycosaminoglycans, producing fibrosis in dermis and internal organs.

- Humoral immunity—increased during T-lymphocyte and complement activation, autoimmunity and autoantibody production to nuclear antigen.

Histological findings of skin biopsy in systemic sclerosis:

- Thinning or absence of epidermis
- Excess collagen and fibrosis of dermis, loss of appendages in dermis, perivascular infiltration of chronic inflammatory cells (lymphocytes and plasma cells) and intimal proliferation and obliteration of blood vessels.

Q. What **investigations** would you do in systemic sclerosis?

A. Diagnosis is usually clinical. The following investigations may be done:

1. Complete blood count (ESR is high, but CRP is usually normal unless there is severe organ involvement or coexisting infection).
2. Serology:
   - RA test (positive in 20% to 30% cases)
   - ANA (positive in 70% cases)
   - Anti-topoisomerase 1 or anti-Scl-70 (positive in 30% in diffuse type)
   - Anti-centromere antibody (positive 60% in CREST and 10% in diffuse systemic sclerosis) with a speckled nucleolar pattern.
3. Skin biopsy for histopathology.
4. Others:
   - Urine R/E (may be proteinuria)
   - X-ray of the hands (deposition of calcium around the fingers, erosion, resorption of phalanges and disorganization of joints)
   - Chest X-ray (DPLD and honeycomb lung)
   - CT scan of the chest (to detect DPLD)
   - Lung function tests (restrictive lung disease)
   - Barium swallow (dysmotility or reduction of peristalsis, narrowing and dilatation. Hiatus hernia may be present, detected by barium swallow X-ray in Trendelenburg position)
   - Barium follow through
   - Motility study may be done
   - Electrocardiogram (ECG)
   - IgG level (raised).

Q. What are the **changes** in the different systems of the body?

A. As follows:

1. Skin changes:
   - Hands—initially non-pitting edema of fingers and flexor tendon sheaths. Then skin becomes shiny, thick and tight, distal skin creases disappear. There is erythema and tortuous dilatation of capillary loops in nail fold bed.
   - Face and neck—thinning of lips, furrowing, microstomia.
   - Skin in other parts of the body (thick, tight, hyper or hypopigmented and vitiligo).
   - Skin of the chest is tight and thick.
   - Skin score is calculated by Rodnan total skin score.
2. Raynaud's phenomenon: It may lead to critical tissue ischemia, skin ulceration over pressure areas, infarction and pulp atrophy at finger tips.
3. Joints and muscles: Arthralgia, morning stiffness, flexor tenosynovitis, flexion contracture or deformity. Proximal or distal muscle weakness and wasting.
4. Gastrointestinal:

- Esophagus—50% involvement. Dysphagia and odynophagia may be because of reflux esophagitis, sliding hiatus hernia, constriction or secondary achalasia, and dysmotility or reduction of peristalsis. Esophageal manometry shows abnormal and reduced peristalsis in 90%.
- Stomach—early satiety, gastric outlet obstruction and recurrent occult upper gastrointestinal tract bleeding causing "**watermelon stomach**" (antral vascular ectasia in 20% cases).
- Intestine—hypomotility, bloating, distension, intestinal obstruction or pseudo-obstruction, blind-loop syndrome, diarrhea and wide-mouth diverticula in colon. Rarely, a serious disorder called **pneumatosis cystoides intestinalis,** in which there is radiolucent cyst or streaks in the wall of small intestine due to air in the intestinal wall can occur. The patient presents with severe abdominal pain. It is detected by plain X-ray abdomen.

5. Liver: Primary biliary cirrhosis (PBC) may be associated.
6. Respiratory:
   - DPLD, pulmonary hypertension and cor pulmonale. Pulmonary hypertension may occur without parenchymal lung disease due to pulmonary vessel involvement. It is six times more common in limited type than diffuse type.
   - Others—pneumonitis, rarely pleural effusion and alveolar cell carcinoma.
7. Heart—Dysrhythmia, conduction defect, heart failure, cardiomyopathy, myocardial fibrosis and pericardial effusion.
8. Kidneys (20% involvement):
   - Renal failure in advanced stage (often fatal)
   - Malignant hypertension (difficult to control, may respond to angiotensin-converting enzyme inhibitors).
9. Endocrine:
   - Hypothyroidism (due to thyroid gland fibrosis)
   - Impotence.
10. Neurologic:
    - Entrapment neuropathy
    - Facial nerve palsy
    - Autonomic dysfunction.

Q. How to **manage** systemic sclerosis?

A. There is no specific therapy.

1. General management for Raynaud's phenomenon:
- Exposure to cold should be avoided (by the use of gloves or mittens), lubricants should be used (to avoid dryness).
- Smoking should be stopped, regular exercise and massage of skin, cleanliness of digital ulcer.
- Drugs to be avoided (beta-blocker, ergotamine, oral contraceptive and sympathomimetic).
- Antiplatelet (aspirin) may be given.
- Calcium antagonist (diltiazem and nifedipine), ACE inhibitor, angiotensin II receptor blocker (valsartan) may be effective.
- If no response or in severe case, prostacyclin analog epoprostenol infusion intermittently.
- If still no response, then surgery (digital sympathectomy and microsurgical revascularization), lumbar sympathectomy, thoracic sympathectomy under video assisted thoracic surgery. If needed, amputation of fingers or toes.
- Antibiotic may be needed, if there is infection on ulcerated skin lesions. Higher doses should be given since tissue penetration is poor in scleroderma.

2. For arthritis—Non-steroidal anti-inflammatory drugs (NSAIDs).

3. Steroid and cytotoxic drugs may be used, if myositis or alveolitis.

4. Other drugs that have shown no proven benefit, but may be tried are:
   - Penicillamine—reduces cross-linking of collagen (acts as anti-fibrotic)
   - Methotrexate (given in a weekly dose of 7.5 to 15 mg)
   - Cyclosporin or interferon-γ. Recombinant human relaxin therapy (subcutaneously).
5. Other therapy: According to the involvement of the organ.
   - Physiotherapy
   - If DPLD—cyclophosphamide or azathioprine combined with low dose steroid
   - Hypertension—ACE inhibitor may be given
   - Pulmonary hypertension—oral vasodilator, warfarin and oxygen. In advanced case, prostacyclin therapy (inhaled, subcutaneous or intravenous) or oral endothelin receptor antagonist (bosentan, sitaxsentan) should be given
   - Right heart failure—symptomatic treatment with diuretic, digoxin, etc. Heart lung or single lung transplantation in selected cases
   - For reflux esophagitis—proton pump inhibitor and prokinetic drugs
   - For blind-loop syndrome—broad spectrum antibiotic is useful
   - If renal involvement—ACE inhibitor may be helpful
   - Myositis—corticosteroid and cytotoxic drugs may be needed.

Q. What is the role of **steroid**?

A. Steroid has little or no role in the treatment of scleroderma. It can be given in low doses (10 mg/day) with cyclophosphamide if the patient has associated DPLD or myositis.

Prognosis of systemic sclerosis**:** Depends on type, age, sex, involvement of internal organ and extent of skin involvement.

Bad prognostic factors are:
- Diffuse cutaneous systemic sclerosis
- Elderly patient
- Male sex
- Involvement of internal organs (especially kidney, lung and heart). Proteinuria, high ESR, low gas transfer of carbon monoxide and pulmonary hypertension.

Limited cutaneous systemic sclerosis (CRST or CREST):
- Prognosis is relatively better
- Usually mild
- 70% show 10-year survival
- Pulmonary hypertension may develop later on.

Diffuse type:
- 70% show 5-year survival
- Death due to cardiac, renal and pulmonary involvement.

Q. What are the **differential diagnoses** of systemic sclerosis or thickened skin?

A. Scleroderma-like thickening of skin, secondary to some other diseases is called **pseudo-scleroderma.** The causes are:
- Scleroderma
- Scleromyxedema
- Eosinophilic fasciitis or eosinophilic myalgia syndrome
- Amyloidosis
- Graft-versus-host disease (GVHD)
- Diabetic cheiroarthropathy
- Acromegaly

- Porphyria cutanea tarda
- Carcinoid syndrome
- Toxic oil syndrome
- Chemically induced (pentazocine, bleomycin and vinyl chloride).

Scleroedema: It is a disease characterized by painless, edematous induration of face, scalp, neck, trunk and upper part of the extremities. There is no involvement of the hands and feet. Common in children, may be associated with streptococcal infection, usually self-limiting, resolves in 6 to 12 months.

Mixed connective tissue disease (MCTD):

When localized systemic sclerosis coexisting with SLE, polymyositis and rheumatoid arthritis, it is called MCTD. This overlap syndrome is associated with high titer of anti-RNP.

The patient usually presents with Raynaud's phenomenon, myalgia and swollen finger. Later, features, such as sclerodactyly, calcinosis, cutaneous telangiectasia develop. Skin rash of SLE or dermatomyositis, pulmonary fibrosis, pulmonary hypertension, Sjogren's syndrome, may develop later. Prognosis is good.

Treatment: Good response to steroid.

JUVENILE IDIOPATHIC ARTHRITIS (JIA)

CHIEF COMPLAINTS

- Pain and swelling of multiple joints for … months
- Weight loss for … months
- Fever and anorexia for … months.

HISTORY

History of present illness: According to the statement of the patient, he was alright … months back. Since then, he has been suffering from pain and swelling of multiple joints, including the right knee, right ankle, small joints of both hands and both wrist joints. The pain was initially mild, associated with morning stiffness that persists for 2 hours, worse after taking rest and improves with exercise. It is gradually more severe, associated with swelling of the joints. For the last ... days, pain is so severe that it interferes with his daily activities. He also complains of continued low grade fever, substantial weight loss, malaise and anorexia for the last … months. There is no history of mouth ulcer, skin rash, photosensitivity, eye problems, breathlessness, cough, chest pain or alopecia.

History of past illness

Family history: All the family members are of good health. No such illness in the family.

Personal history

Drug and treatment history

Menstrual history

Socioeconomic history: Mention according to the patient's statement.

GENERAL EXAMINATION

- The patient looks anxious and emaciated
- Moderately anemic
- Skin is normal, no rash
- No jaundice, cyanosis, clubbing, koilonychia, leukonychia or edema
- No lymphadenopathy or thyromegaly
- Pulse—88/min
- BP—110/80 mm Hg
- Temperature—99° F.

SYSTEMIC EXAMINATION

Musculoskeletal System

Examination of hands:

1. **Inspection:**
   - There is wasting of thenar and hypothenar muscles. No atrophy, ulcer, infarction, gangrene or rash.
   - Wrist joints are swollen. PIP joints of both hands are spindle shaped. There is mild flexion deformity of fingers on right hand.
   - Movement is restricted in the right wrist and fingers with slightly impaired functional activity.

2. Palpation:
- The joints of both hands are tender
- Synovial thickening is present in right wrist.

Examination of right knee joint:
- The right knee joint is swollen, more marked above the patella
- Skin is red and shiny
- Local temperature is raised and the joint is tender
- There is restricted movement on right knee.

Examination of other joints:
- Right ankle is swollen and tender.

Examination of eyes:
- No redness, no nodule.

Examination of respiratory system:
- Normal.

Examination of CVS:
- No abnormality detected.

Examination of the nervous system:
- No evidence of peripheral neuropathy, carpal tunnel or tarsal tunnel syndrome.

Examination of abdomen:
- There is no organomegaly.

SALIENT FEATURES

Mr …, 15 years, student, normotensive, nondiabetic, hailing from …, presented with pain and swelling of multiple joints, including the right knee, right ankle, small joints of both hands and both wrist joints for ... months. The pain was initially mild, associated with morning stiffness that persists for 2 hours, worse after taking rest and improves with exercise. It is gradually more severe, associated with swelling of the joints. For the last ... days, pain is so severe that it interferes with his daily activities. He also complains of continued low grade fever, substantial weight loss, malaise and anorexia for the last … months. There is no history of mouth ulcer, skin rash, photosensitivity, eye problems, breathlessness, cough, chest pain or alopecia. There is no such illness in the family. He used to take painkiller tablet frequently.

On examination, on general examination (mention as above).

On systemic examination (mention as above. Always never forget to mention the extra-articular features).

My diagnosis is JIA.

Q. What are your **differential diagnoses?**

A. As follows:
- Rheumatic fever
- Seronegative arthritis

- SLE
- Viral arthritis
- Acute leukemia.

Q. Could it be **rheumatic fever**?

A. Unlikely, because in rheumatic fever, there is no deformity of joints and wasting of muscles. Moreover, rheumatic fever is diagnosed by major and minor criteria (rheumatic fever licks the joints and kills the heart).

Q. What **investigations** should be done in JIA?

A. As follows:
- Complete blood count (leukocytosis in Still's disease, may be lymphocytosis, thrombocytosis and high ESR)
- CRP (high)
- RA test (usually negative, positive in 10% cases)
- ANA, Anti-ds DNA if SLE is suspected
- X-ray of the joint involved
- Other investigations—to exclude other diseases (according to history).

RELATED QUESTION AND ANSWERS

Q. What is **JIA?**

A. It may be defined as onset of arthritis before 16 years of age and persisting for more than 3 months.

Q. Why there is **wasting** of muscles in JIA?

A. Disuse and release of cytokines (interleukin 1, 6 and TNF).

Q. What are the **causes of acute arthritis in children**?

A. As follows:
- Rheumatic fever
- JIA
- Infections (bacterial and viral)
- Acute leukemia
- Henoch-Schonlein purpura.
- Hemophilic arthritis
- Reactive arthritis
- Others are sickle cell disease, psoriatic arthritis, SLE, osteomyelitis and hypermobility syndrome.

Q. What are the **types** of JIA?

A. As follows:

1. Systemic onset (**Still's disease**)—10% to 15% cases.

2. Oligoarthritis (pauciarticular)—It is of 2 types:
   - Oligoarthritis (persistent)—common (50% to 60%), four or less joints are affected, mainly knee, ankles and wrists, in asymmetrical pattern. Common in girls, 3 years of age. Uveitis may occur. Relatively good prognosis.
   - Oligoarthritis (extended)—occurs in 25% cases, arthritis of many joints may develop after 6 months. This can be very destructive.

3. Polyarticular JIA—involvement of more than four joints, 30% to 40% cases of JIA. It is of 2 types.
   - RA test is positive—affects girl above 8 years. Small joints of hands, wrist, ankle, feet, etc. are involved, later larger joints are involved. Can be very destructive.

- RA test is negative—affects more in girls < 12 years, but may be in any age. Joints involvement like RA positive type, but cervical spine, temporomandibular joint and elbows may be involved. ANA may be positive with chronic uveitis.

4. Other types of juvenile arthritis:
- Enthesitis-related JIA
- Psoriatic arthritis
- Unclassified.

Q. What are the **features** of systemic onset JIA (Still's disease)?

A. As follows:
- Arthritis—involving knee, wrist and ankle. Other joints may be involved.
- High fever—intermittent type, may be continuous.
- Skin rash—appears with fever and disappears when fever subsides. These are macular or maculo-papular, Salmon pink color rashes (**Salmon rash**).
- Extra-articular features—hepatosplenomegaly and lymphadenopathy (common). There may be pericardial effusion, pleural effusion and disseminated intravascular coagulation (DIC).
- In chronic cases—micrognathia (small mandible), fusion of cervical spine and retardation of growth.

Q. How to **treat** JIA?

A. As follows:

1. To relieve pain: NSAID

2. General measures:
- Rest during pain and passive movement of the limb to prevent contracture
- Physiotherapy
- Explanation and reassurance to the parents, also to the patient

3. In severe cases—Steroid, preferably alternate days. Pulse methylprednisolone may be given, followed by methotrexate (steroid may cause early fusion of epiphysis resulting in short stature. Even 3 mg prednisolone daily may cause this effect.)

4. Disease modifying drugs should be given in all cases:
- Methotrexate—5 mg weekly (increase the dose gradually)
- Sulfasalazine—30 to 50 mg/kg, effective in enthesitis related JIA
- Others—IV immunoglobulin, cyclosporin and cytotoxic drugs (cyclophosphamide, chlorambucil and azathioprine) may be tried
- If methotrexate fails—anti-TNF may be given (helpful in all cases, except in systemic onset type, where results are variable). Etanercept may be used

5. Orthopedic surgery, if needed.

Note Remember the following:

If aspirin is used for fever or arthritis, associated with viral infection like influenza below 12 years of age, it may cause Reye's syndrome. So, it should be avoided.

ADULT STILL'S DISEASE

It is a disease of unknown cause characterized by high fever, seronegative arthritis, skin rash and polyserositis. Usually, it is diagnosed by exclusion of other diseases. Commonly occurs in young adults between 16 and 35 years of age, rarely after 60 years.

Diagnostic criteria of Adult Still's disease:

Each of the 4 criteria:

- Quotidian fever, more than 39°C
- Arthralgia or arthritis (knee, wrist and ankle)
- Rheumatoid factor is negative
- ANF is negative.

Plus 2 of the following:

- Leukocytosis > 15 × 10^9/L (usually very high, may be > 40,000)
- Evanescent macular or maculopapular rash, Salmon colored, non-pruritic (common in chest and abdomen)
- Serositis (pleurisy or pericarditis)
- Hepatomegaly
- Splenomegaly
- Lymphadenopathy (usually cervical, may be generalized).

High fever with chill and sweating is very common. Initially arthritis may be mild.
Other features—abdominal pain, myalgia and sore throat.

Investigations:

- CBC (low hemoglobin, high ESR and leukocytosis)
- CRP (is high)
- RA and ANF (are negative)
- Serum ferritin is very high (> 10,000)
- Fibrinogen level (high)
- AST and ALT (high).

Treatment:

- NSAID (high dose aspirin—1 g 8 hourly). Other NSAIDs—indomethacin, ibuprofen may be helpful. NSAID may be effective in 50% cases.
- If no response—high dose prednisolone (60 to 100 mg/day). When the fever subsides, reduce the dose slowly. Steroid is necessary in 50% cases.
- Other drugs—chloroquine, hydroxychloroquine, methotrexate, sulfasalazine, azathioprine and cyclophosphamide may be tried.
- In chronic case, anti-TNF, such as Enbrel (etanercept) or anakinra (interleukin-1 receptor agonist) may be considered.

Note Remember the following:

Recurrent episode occurs in one-third cases.

HEMOPHILIC ARTHRITIS

CHIEF COMPLAINTS

- Recurrent pain and swelling of both knee joints for … years
- Prolonged bleeding following any injury for … years
- Weight loss for … months.

HISTORY

History of present illness: According to the statement of the patient, he was alright … years back. Since then, he has been suffering from recurrent pain and swelling of both knee joints. Initially, only the right knee was involved, persisted for 3 to 4 weeks. After 3 months, both knee joints were involved and the attack persisted for 2 months. Each episode is preceded by mild to moderate physical exertion like playing in the field or trauma. Pain is very severe, aggravates even on slight movement of the joint and improves on rest or hot compression. There is also difficulty in walking, but no history of morning stiffness. Other joints were never involved. The patient agreed that there is prolong bleeding following any minor injury since his childhood. For the last ... months, he is also suffering from fatigue and weakness and has lost some weight. There is no history of fever, gum bleeding or any other bleeding manifestation, skin rash, photosensitivity or bowel or bladder abnormality.

History of past illness: There is prolonged bleeding following any cut injury.
Personal history: Mention according to the patient's statement.
Drug and treatment history: Mention according to the patient's statement.
Family history: One of his maternal uncles has similar disorder since his childhood. He has one brother and one sister. None of them has such illness.
Socioeconomic history: Mention according to the patient's statement.

GENERAL EXAMINATION

- The patient looks anxious
- Moderately anemic
- Skin is normal. There is no rash
- No jaundice, cyanosis, clubbing, koilonychia, leukonychia or edema
- No lymphadenopathy or thyromegaly
- No bony tenderness
- Pulse—88/min
- BP—110/80 mm Hg
- Temperature—97^0 F.

SYSTEMIC EXAMINATION

Musculoskeletal System

Knee joints:

1. **Inspection:**
   - Both knee joints are swollen, erythematous and deformed, right one more than the left
   - Muscle wasting is present around both knee joints, more over the right knee
   - There are few ecchymosis of various sizes over the right thigh.

2. **Palpation:**
   - Both knee joints are warm and tender
   - Patellar tap is positive
   - Movement is restricted.

Other joints: No abnormality.

Gastrointestinal System

- No gum hypertrophy
- There is no organomegaly.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Master …, 12 years, student, normotensive, nondiabetic, hailing from …, presented with recurrent pain and swelling of both knee joints for … years. Initially, only the right knee was involved, persisted for 3 to 4 weeks. After 3 months, both knee joints were involved and the attack persisted for 2 months. Each episode is preceded by mild to moderate physical exertion like playing in the field or trauma. Pain is very severe, aggravates even on slight movement of the joint and improves on rest or hot compression. There is also difficulty in walking, but no history of morning stiffness. Other joints were never involved. The patient agreed that there is prolong bleeding following any minor injury since his childhood. For the last ... months, he is also suffering from fatigue and weakness and has lost some weight. There is no history of fever, gum bleeding or any other bleeding manifestation, skin rash, photosensitivity or bowel or bladder abnormality. He has history of prolong bleeding following circumcision. One of his maternal uncles has similar disorder since his childhood.

On examination, on general examination (mention as above).

On systemic examination (mention as above).

With this history and physical findings, I have some differential diagnoses:
- Hemophilic arthritis (due to hemophilia A)
- Christmas disease with arthritis.

Q. What are the other possible **diagnoses**?

A. As follows:
- Juvenile idiopathic arthritis (JIA)
- Acute leukemia.

Q. **Why** not JIA?

A. There is history of persistent bleeding following any injury that is against JIA.

Q. Can it be **rheumatic fever**?

A. No. Because rheumatic fever is diagnosed by major and minor criteria that are not present in this case. Also there is persistent bleeding and deformity of joints that are against rheumatic fever.

Q. Which **joints are commonly involved** in hemophilic arthritis?

A. Commonly knee, elbow, ankle and hip joints are involved.
- In infants—hip joint is commonly involved
- In older children—knee joint is commonly involved.

Q. What is the **cause of joint deformity** in hemophilia?

A. It is due to secondary osteoarthrosis and wasting of the muscles around the joint.

Q. What are the **causes of hemarthrosis?**

A. As follows:
- Trauma
- Hemophilia
- Christmas disease
- Von Willebrand disease
- Sickle cell disease
- Excess anticoagulant
- Rarely, malignancy.

RELATED QUESTIONS AND ANSWERS

Q. What are the **presentations of hemophilic arthritis**?

A. Hemarthrosis occurs when plasma level of factor VIII: C is < 1%. Arthritis may be spontaneous without trauma or may follow even minor trauma.
- Initially—tingling, abnormal sensation, stiffness and instability of the joint.
- Later on—the joint is red, hot, swollen and painful.

Repeated hemarthrosis may cause:
- Synovium hypertrophy
- Fibrotic change in synovium
- Destruction of cartilage
- Reduction of joint space
- Subchondral cyst formation
- Bone shows erosion, marginal sclerosis, osteophyte formation and ankylosis of joint.

Q. What are the **radiological signs** in hemophilic arthritis?

A. As follows:
- Initially—joint space is increased and widening of intercondylar notch occurs (in knee joint, indicates long standing hemorrhage).
- Later on- reduction of joint space, periarticular osteopenia, marginal sclerosis, subchondral cyst formation, secondary osteoarthrosis (with osteophyte) and ankylosis of joint.

Q. What are the **causes of widening of intercondylar notch**?

A. As follows:
- Hemophilia
- Christmas disease
- Long standing effusion in knee joint.

Q. How to **treat** hemophilic arthritis?

A. As follows:
- Complete rest, elevation of the affected limb and immobilization by splinting.
- Analgesic may be given (paracetamol or acetaminophen or codeine). Aspirin or other NSAIDs are contraindicated (as they interfere with platelet function and may cause excess bleeding).
- Factor VIII transfusion—20 to 30 IU/kg. Repeated after 12 hours and also after 24 and 36 hours (higher dose is required, if treatment is delayed).

- Once acute stage is over, the patient should be mobilized and physiotherapy should be started (isometric exercise, followed by active movement, hydrotherapy).
- Arthrocentesis (aspiration from joint) is rarely necessary.

Brief Discussion About Hemophilia

Q. What is **hemophilia**?

A. It is an X-linked inherited disorder because of deficiency of factor VIII or anti-hemophilic factor, characterized by prolonged bleeding. Usually female is the carrier and male is the sufferer. There is high rate of new mutations, in 30%, there is no family history.

Q. What are the **types** of hemophilia?

A. Normal factor VIII level is 50 to 150 IU/dL. According to severity, it is of 3 types:

- Mild—Factor VIII is > 5 IU/dL (bleeding occurs following major injury or surgery)
- Moderate—Factor VIII is 1 to 5 IU/dL (bleeding occurs following minor injury or surgery)
- Severe—Factor VIII is <1 IU/dL (spontaneous bleeding into the joints, muscles).

Q. What is the **pedigree** of hemophilia?

A. As follows:

1. If father is affected:
   - All daughters are carriers
   - All sons are normal.
2. If mother is carrier:
   - 50% daughters are carriers
   - 50% sons are sufferers.

Note Remember the following points:

- In female carrier—1 son is affected, 1 son in normal, 1 daughter is carrier and 1 daughter is normal.
- In a female carrier, factor VIII is < 50% normal, because of randomized inactivation of one X-chromosome.

Q. Can a **female** be the **sufferer** in hemophilia?

A. Yes, rarely a female can suffer, because of the following reasons:

- If her mother is a carrier and father is a sufferer of hemophilia
- Turner's syndrome (45 XO)
- According to lyoniation theory, there is randomized inactivation of one X chromosome in the developing fetus. Then the number of affected X chromosome may be predominant. Female may be affected, if normal X chromosome is disproportionately inactivated.

Q. How does a patient with hemophilia usually **present**?

A. Depends on whether factor VIII deficiency is mild, moderate or severe.

- Prolonged and persistent bleeding after trauma or injury, tooth extraction
- Sometimes, spontaneous bleeding may occur in severe cases
- Bleeding into the large joints and muscles (psoas and calf muscle) is also common.

Q. What is the common site of **muscular bleeding?**

A. Commonly in calf muscles and psoas.

Q. What happens if the patient has **bleeding into the psoas** muscle?

A. As follows:

- Severe pain in lower abdomen
- Paresthesia in thigh and weakness of quadriceps, due to compression of femoral nerve.

Q. What **investigations** are done in hemophilia?

A. As follows:

- FBC, platelet (usually normal)
- Bleeding time (normal)
- Prothrombin time (normal)
- Clotting time (prolonged)
- APTT (prolonged)
- Factor VIII: C assay (deficient or absent)
- vWF (normal)
- Serum fibrinogen (normal)
- X-ray of involved joint (in hemophilic arthritis).

Note Remember the following:

APTT is prolonged, which is corrected by addition of normal plasma. If not corrected after the addition of normal plasma, more likely there is antibody formation or the presence of anti-phospholipid antibody.

Q. Is **antenatal diagnosis** possible?

A. Yes. Antenatal diagnosis may be done by molecular analysis of fetal tissue obtained by chorionic villus biopsy at 11 to 12 weeks of pregnancy.

Q. How will you **manage hemophilia**?

A. As follows:

1. Management of bleeding episode:
   - Factor VIII concentrate is given by intravenous infusion, twice daily as its half-life is 12 hours and the blood level should be maintained for 3 to 5 days.
   - For minor bleeding, factor VIII level should be raised to 20 to 30 IU/dL. However, desmopressin 0.3 μg/kg 12 hourly infusion over 20 minutes may be given that raise factor VIII.
   - For severe bleeding, factor VIII level should be raised to at least 50 IU/dL. Treatment to be continued for a period of 1 week or more.
   - For major surgery—factor VIII level should be raised to 100 IU/dL preoperatively and maintained above 50 IU/dL until healing. Continuous infusion may be needed. Treatment to be continued for 7 to 10 days.
2. If factor VIII is not available—cryoprecipitate, fresh frozen plasma or fresh blood can be given.
3. To prevent recurrent bleeding into joints and subsequent joint damage—factor VIII infusions should be given regularly thrice a week starting from early childhood (around 2 years of age).
4. Synthetic vasopressin (desmopressin, an analog of vasopressin) is given intravenous, subcutaneous or intranasally. It produces 3 to 5 fold rise in factor VIII:C and is very useful in patient with a baseline level of factor VIII >10 IU/dL. It prevents the complications associated with blood products. It is useful for treating bleeding episodes in mild hemophilia and as prophylaxis before minor surgery, ineffective in severe hemophilia. It is also given for vWD, but not in Christmas disease.

Note Remember the following points:

- 1 unit/kg factor VIII will raise blood level by 2%. So, the dose of factor VIII is calculated as follows:

  FVIII dose = Desired factor VIII level – FVIII baseline level × body weight (kg) × 0.5 unit/kg.
- Previously, factor VIII was prepared from plasma. It is now prepared by recombinant DNA technology (so, there is less risk of transfusion transmitted infection, but more expensive).
- Advice to the patient—trauma should be avoided and precaution should be taken before tooth extraction and surgery. The patient should carry a special medical card in which details of the disease and its treatment must be recorded.

Q. What are the **complications** of hemophilia?

A. As follows:

1. Due to repeated hemorrhage:
   - Arthropathy due to repeated bleeding in joint (e.g. knee, elbow)
   - Atrophy or wasting of muscles secondary to hematoma in muscle
   - Mononeuropathy due to pressure by hematoma
   - Death may occur due to intracerebral hemorrhage.
2. Due to therapy:
   - Infections—Hepatitis A, B, C, D. Also, HIV
   - Factor VIII antibody (up to 30% patients with severe hemophilia).

Note Remember the following points:

- Risk of viral transmission is eliminated because of prior screening of donors
- Infectious agents that can cause Crutzfeldt Jakob disease, may be transmitted by blood and blood products
- All patients should receive vaccination for HAV and HBV
- Use of recombinant factor VIII effectively eliminated transfusion transmitted infection.

Q. If **factor VIII antibody** develops, how can it be suspected and treated?

A. It is suspected if no response to factor VIII in therapeutic dose. APTT is prolonged. In normal hemophilia, APTT is corrected by addition of normal plasma in 1:1 ratio. But if factor VIII antibody develops, APTT is not corrected with normal plasma in this ratio. This case is very difficult to treat. Following options are available:

- High dose and frequent infusion of factor VIII may be given
- Changing the species, such as porcine factor VIII may be used
- Factor IX may be used. It helps bypassing the inhibitors
- Recombinant factor VIIa—helps bypassing the inhibitors.
- Factor eight inhibitor bypassing activity (FEIBA, an activated concentrate of factors II, IX and X), or, prothrombin complex concentrate (PCC) that contains factor VII, IX and X may be used.
- Sometimes, immunosuppressive therapy, such as steroid, azathioprine or cytotoxic drugs may be given
- In long-term, management is to eradicate inhibitory antibody. This can be done by using immune tolerance induction (ITI). Recently, anti-CD20 monoclonal antibody (rituximab) as coadjuvant is promising.

Q. What are the **causes of death**?

A. As follows:

- Bleeding, mainly intracerebral
- HIV related
- Hepatitis due to HCV.

CHRISTMAS DISEASE

It is also called hemophilia B. It is because of deficiency of factor IX. Features are like hemophilia A. It is treated with factor IX concentrate, half-life is 24 hours. Prophylaxis is given twice a week. Desmopressin is ineffective.

CHAPTER 8

Neurology

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PARKINSONISM

CHIEF COMPLAINTS

- Tremor of the whole body for … months
- Stiffness and difficulty in walking for … months
- Weakness and generalized body ache for … months.

HISTORY

History of present illness: According to the statement of the patient, he was reasonably well … months back. Since then, he has been experiencing tremor of the body. Initially, the tremor was present at the right hand, followed by the left hand, tongue, head and rest of the body. It is present during rest and reduces during any voluntary activity. His wife mentioned that the tremor is absent during sleep. Recently, for … months, the patient feels increasing weakness and stiffness of the whole body, difficulty in walking, performing daily activities like combing, eating, writing, etc. He also complains of generalized persistent bodyache, which is not related to any activity or rest. His bowel and bladder habits are normal. There is no history of head injury, fever, headache, unconsciousness, convulsion or intake of any offending drug.

History of past illness: Nothing significant.

Family history: There is no similar illness in the family.

Personal history: He is a service holder, nonsmoker, nonalcoholic, there is no history of drug abuse.

Drug and treatment history: He gives no history of taking any offending drug related to his illness (e.g. antipsychotics).

GENERAL EXAMINATION

- Titubation of head
- The face is mask-like, expressionless and apathetic (less wrinkling of forehead)
- There is less blinking of the eyes, with staring look (frequency of spontaneous blinking is reduced, called serpentine stare)
- Blepharoclonus (tremor of eyelids, when eyes are gently closed)
- Dribbling of saliva
- No anemia, jaundice, cyanosis, edema, thyromegaly, lymphadenopathy
- Pulse: 72/min
- BP: 125/75 mm Hg
- Temperature: 98.6° F.

SYSTEMIC EXAMINATION

Nervous System

1. Higher psychic (cerebral) functions:
   - The patient is conscious, cooperative and alert
   - Intelligence and memory—intact
   - He looks depressed

- Speech—slow initiation, husky, slurred, indistinct, lacking intonation, low volume and monotonous (or mutism). Palilalia is present (repetition of the end of a word).
- Orientation to time, place, person—intact.

2. Cranial nerves including fundoscopy: Intact.

3. Motor system:
- Muscle tone—lead pipe (better seen in elbow) and cog wheel (better seen in wrist) rigidity are present
- Muscle power—normal
- Reflex—normal (however may be difficult to elicit because of rigidity)
- Plantar response—flexor (may be difficult to elicit)
- Coordination—could not be tested (because of rigidity)
- Gait—flexed and stooped attitude on standing. He has difficulty in starting to walk (freezing). Steps are short, shuffling with paucity of movement, less swinging of the arms, flexed attitude and inability to turn rapidly (fractionated turn).

4. Involuntary movement:
- Resting tremor is present in all the extremities, specially on thumb and fingers (pill-rolling). It disappears or reduces with activity or holding something, or on complete relaxation (better term—"tremor in the position of repose". Ask the patient to keep the arm rested in semiprone position).
- There is titubation of the head.

5. Other findings:
- Glabellar tap (Myerson's sign)—present (repetitive tapping on the forehead above the bridge of the nose, two per second, produces a sustained blink response. In normal person, blinking will stop after three to five blinks. This sign is unreliable).
- There is slow initiation of movement (hypokinesia)—the patient may be unable to perform the act or can do slowly or progressive reduction of amplitude of each movement. Ask the patient to perform the following:
  - Fastening of button
  - Drinking of water from a glass
  - Touching tips of all the fingers with thumb successively or count the number like 1 to 5.
  - Performing rapid fine finger movements like piano playing (it becomes indistinct, slurred and tremulous)
  - Performing two different simultaneous motor acts.
- Handwriting (there is micrographia, handwriting becomes small, tremulous and cramped).

6. Sensory functions: Intact.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 55 years old, service holder, normotensive, nondiabetic, smoker, hailing from …, presented with tremor of the body for … months. Initially, the tremor was present at the right hand, followed by the left hand, tongue, head and rest of the body. It is present during rest and reduces during any voluntary activity. His wife mentioned that the tremor is absent during sleep. Recently, for … months, the patient feels increasing weakness and stiffness of the whole body, difficulty in walking, performing daily activities like combing, eating, writing, etc. He also complains of generalized persistent body ache, which is not related to any activity or rest. His bowel and bladder habits are normal. There is no history of head injury, fever, headache, unconsciousness, convulsion or intake of any offending

drug. There is no similar illness in the family. He was a previous smoker but has stopped smoking about 6 months ago. He gives no history of drug abuse. He gives no history of taking any offending drug related to his illness (e.g. antipsychotics). There is no family history of such illness. He was treated with vitamins by local physicians.

On Examination

General examination (mention as above)

Systemic examination (mention as above).

My diagnosis is Parkinson's disease (paralysis agitans).

Q. What specific **past history** have you taken in this patient?

A. As follows

- History of head injury (punch drunk syndrome)
- Drugs (phenothiazine, butyrophenone, metochlopramide, tetrabenazine, α methyldopa, lithium, valproic acid, fluxetine)
- Any history of fever, convulsion, headache, coma (postencephalitic)
- Jaundice, CLD (in Wilson's disease, occur in early age).
- Any history of headache, vomiting, convulsion (cerebral tumor).

Q. What **investigations** should be done in Parkinsonism?

A. Diagnosis is usually clinical. Investigations are done for specific cases or to exclude other diseases:

1. CT scan or MRI (may be done if pyramidal, cerebellar and autonomic involvement or doubtful diagnosis).
2. In patient < 50 years, screening for Wilson's disease:
   - Serum ceruloplasmin (low)
   - Serum copper (high serum free copper)
   - 24 hours urinary copper (high). Following penicillamine therapy, 24 hours urinary copper > 25 mmol (confirmatory)
   - Liver function tests may be done
   - Liver biopsy with quantitative measurement of copper (less done).

RELATED QUESTIONS AND ANSWERS

Q. What are the **diagnostic criteria** for Parkinsonism?

A. **Triad** of **T**remor at rest (4 to 6 Hz), **R**igidity and **H**ypokinesia (remember the formula **TRH**. According to Brain Bank criteria, postural instability is another criteria).

Q. What is **Parkinsonism?**

A. It is a syndrome consisting of tremor, rigidity, bradykinesia and loss of postural reflexes.

Q. What is **Parkinson's disease?**

A. Parkinson's disease (paralysis agitans) is the primary or idiopathic Parkinsonism. It is a neurodegenerative disorder due to involvement of the basal ganglia, characterized by slowness of movement, rigidity, tremor and loss of postural reflex.

Q. What is **Parkinsonian plus?**

A. It is characterized by features of Parkinsonism with other degenerative disease like progressive supranuclear palsy (Steele-Richardson-Olszeweski syndrome), olivo-ponto-cerebellar degeneration, nigrostriatal degeneration, primary autonomic failure (Shy-Drager syndrome).

Q. Describe the **tremor** in Parkinsonism.

A. Tremor is involuntary, coarse (4 to 6 Hz), present at rest, disappears or reduces during voluntary activity and sleep, and increases with emotion or anxiety. Initially, the tremor is characterized by pill-rolling movement between thumb and index finger, flexion and extension of fingers, abduction and adduction of thumb and pronation and supination of forearm. Later, tremor may affect arms, legs, feet, jaw and tongue. Tremor is absent in one-third cases at presentation and throughout its course in some cases.

Commonly, the patient presents with unilateral resting tremor in hand.

Q. What are the types of **rigidity** in Parkinsonism?

A. Two types:

- Lead pipe—uniform rigidity in flexors and extensors of limbs (better seen in elbow or knee).
- Cog wheel—rigidity is interrupted by tremor (better seen in wrist joint). It is due to exaggerated stretch reflex interrupted by tremor.

Note Remember the following:

Rigidity of the examining limb is increased, with simultaneous active movement of the opposite limb (one type of reinforcement).

Q. What is the difference between **rigidity and spasticity**?

A. As follows:

- Rigidity means increased muscle tone affecting opposing muscle groups equally, which is present throughout the range of passive movement. It may be "lead-pipe" rigidity (uniform and smooth) or "cog-wheel" (intermittent, due to tremor). It is found in extrapyramidal lesion.
- Spasticity (clasp-knife) means increase tone in muscles, which is maximal at the beginning of movement and suddenly decreases as passive movement is continued. It occurs mainly in flexor muscles of the upper limb and extensor muscles of the lower limb (antigravity muscles). It is seen in upper motor neuron lesion.

Q. What are the features of **hysterical rigidity**?

A. In hysterical rigidity, muscle tone increases more and more with increasing maneurve of the affected limb. The more the limbs are moved or examined, the more rigid it gets.

Q. What is **dyskinesia or akinesia**? Describe **dyskinesia or hypokinesia** in Parkinsonism.

A. Dyskinesia is the difficulty in initiating motor activity or poverty or slowing of movement (bradykinesia). In Parkinsonism, it may be:

- Difficulty in initiating movement
- Slowness of movement (bradykinesia). The patient is slow and ineffective in attempt to deliver a quick hard blow, he cannot complete a rapid ballistic movement
- Poverty of movement
- Alternative movement progressively impeded, finally blocked completely
- Difficulty in executing two motor acts simultaneously
- Bradykinesia reflected also by slowness in chewing, limited capacity to make postural adjustment.

Q. Describe the typical **gait** in Parkinsonism.

A. Festinate gait, characterized by:

- Rapid small shuffling step (festination) in order to avoid falling. The patient hardly raises the foot from the ground
- The patient seems to catch up with his own center of gravity (flexed attitude)

- There is less swinging of the arms during walking
- The patient has difficulty in stopping himself
- He has difficulty in rapid turning (fractionated gait) and turns en block
- Obstacles cause the patient to freeze in place.

Q. What are the other **abnormal gaits** in Parkinsonism?

A. As follows (these tests should not be done at the bedside):

- Propulsion—if the patient is pushed from behind, he is unable to stop himself and may fall forward.
- Retropulsion—if the patient is pushed from front, he is unable to stop himself and may fall backward.
- Kinesia paradoxica—the patient is unable to initiate a movement, but once started, can complete the whole act (may run down the stairs, but cannot stop at the bottom) or the patient is unable to initiate a movement, but during emotion or fear (e.g. fire in the house), can perform the movement (even run out from the house).

Q. What are the **reflexes** and **plantar response** in Parkinsonism?

A. All the reflexes and plantar responses are normal. May be difficult to elicit, because of rigidity. Plantar is flexor. It may be extensor if associated with the following disorders -

1. Postencephalitic parkinsonism.
2. Other diseases (called atypical parkinsonian syndrome):
   - Shy-Drager syndrome
   - Steele-Richardson-Olszewski syndrome (progressive supranuclear palsy)
   - Olivopontocerebellar atrophy (OPCA)
   - Corticobasal degeneration (CBD).

Q. What is the **pathological change** in Parkinsonism?

A. In idiopathic Parkinsonism, there is progressive degeneration of the pigmented dopaminergic neurons of substantia nigra and formation of eosinophilic cytoplasmic inclusions in neurons (Lewy bodies, which is the pathological hallmark). Hence, there is deficiency of dopamine (and melanin) with relative increase in cholinergic transmission (imbalance between dopamine and acetylcholine).

Q. What are the **causes** of Parkinsonism?

A. Unknown, multiple factors are responsible:

1. Paralysis agitans (idiopathic, also called Parkinson's disease). It usually occurs in middle aged or elderly
2. Postencephalitic (encephalitis lethargica and Japanese B encephalitis)
3. Drugs: Phenothiazines (chlorpromazine, prochlorperazine), butyrophenones (haloperidol), metoclopramide, sulpiride, cisapride, tetrabenazine and methyldopa
4. Neurosyphilis
5. Poisoning—carbon monoxide, manganese and MPTP (methyl phenyl tetrahydropyridine) may occur in drug addicts
6. Herbicide (paraquat, may be related to MPTP)
7. Trauma (punch-drunk syndrome and repeated head injury)
8. Genetic (Wilson's disease and Huntington's disease)
9. Cerebral tumor (involving basal ganglia)
10. Parkinsonian plus (when associated with features or pathology of othe disease):
    - Shy-Drager syndrome.
    - Steele-Richardson-Olszewski syndrome (progressive supranuclear palsy, characterized by inability of the movement of eye vertically or laterally and dementia)
    - Olivopontocerebellar degeneration

11. Creutzfeldt-Jakob disease
12. Hypoparathyroidism
13. Normal pressure hydrocephalus (triad of urinary incontinence, gait apraxia and dementia)
14. Atherosclerotic Parkinsonism (stepwise progressive broad-based gait and pyramidal signs).

Q. What are the **causes** of Parkinsonism according to **age**?

A. As follows:

1. In elderly, the causes are:
   - Idiopathic or paralytic agitans (the most common cause)
   - Drugs
   - Others—postencephalitic Parkinsonism, neurosyphilis, trauma, cerebral tumor.
2. In young, the causes are:
   - Postencephalitic Parkinsonism
   - Drugs
   - Wilson's disease.

Q. How to **differentiate** between post-encephalitic Parkinsonism and paralytic agitans?

A. As follows:

Criteria	Postencephalitic	Paralytic agitans
1. Age	Any, commonly young	Elderly or late middle age
2. Onset	Sudden	Insidious
3. Previous history	Encephalitis, fever and headache	No particular history
4. Complaints	Mainly rigidity, also impaired higher functions, excess salivation (autonomic features), little or no tremor	Mainly tremor
5. Symmetry	Fairly symmetrical rigidity and hypokinesia	Asymmetrical
6. Eye signs:		
– Oculogyric crisis	Present	Absent
– Ophthalmoplegia	Present	Absent
– Pupil	Abnormal (dilated, irregular)	No abnormality
7. Neurological features:		
– Dystonia, dementia, chorea, hemiparesis	Present	Absent
– Rigidity	Usually lead pipe (due to absence of tremor)	Usually cogwheel
– Tendon reflexes	Brisk	Normal
– Plantar response	Extensor	Flexor
8. Levodopa	Less sensitive	Sensitive
9. Prognosis	Not good	Slowly progressive
10. Lewy body	Absent	Present

Q. What is **oculogyric crisis**?

A. It is an involuntary, sustained upward and outward deviation of the eyes. Causes are:

- Postencephalitic Parkinsonism
- Drugs (commonly phenothiazines)
- Petit mal epilepsy.

Q. What are the **differences** between essential tremor and Parkinsonian tremor?

A. As follows:

Features	Essential tremor	Parkinsonian tremor
1. Stimulus	Occurs with action	Occurs with rest
2. Family H/O tremor	Yes	No
3. Body parts involved	Hands, head	Hands, legs, rarely head
4. Distribution at onset	Bilateral and symmetric	Unilateral and asymmetric
5. Sensitivity to alcohol	Yes	No
6. Course	Stable and slowly progressive	Progressive

Q. What is the **mental status** in a patient with Parkinsonism?

A. As follows:

- Initially, intellect and memory are normal. There may be slowness of thought and memory retrieval (bradyphrenia) and subtle personality changes
- Depression occurs in one-third of the patients
- Global dementia (20%) and psychosis
- Drug treatment may precipitate acute confusion.

Q. What are the **treatment modalities** in Parkinsonism?

A. As follows:

- Treatment of the cause and withdrawal of offending drugs, if any
- Symptomatic treatment of tremor, rigidity and bradykinesia
- Physiotherapy and speech therapy
- Surgical treatment
- Occupational therapy and rehabilitation.

Q. What is the **treatment** of Parkinson's disease?

A. Drug treatment is usually not started in mild case, because of untoward side effects. It should be started when there is significant disability and when the symptoms begin to interfere with work and social life or falling becomes a threat. Combination of levodopa and dopa decarboxylase inhibitor is the treatment of choice. Available combinations are:

- Levodopa and carbidopa (co-careldopa 110 or 275 mg)
- Levodopa and benserazide (co-beneldopa 62.5 mg).

Treatment should be started with lowest possible dose and gradually increased as needed.

- Tremor and rigidity may be controlled by anticholinergic drugs.

General measures:

- Physiotherapy and speech therapy
- Occupational therapy and rehabilitation.

Other measures:

- Cognitive impairment and psychiatric symptoms may be helped by rivastigmine (a selective

serotonin reuptake inhibitory—SSRI are drugs of choice for depression. These drugs may aggravate Parkinsonian symptoms. Trazodone is helpful in treating depression and insomnia).

- For psychosis, confusion or hallucination—atypical antipsychotic can be given.

Q. What is the **role of surgery** in Parkinsonism?

A. Surgery is rarely done because medical treatment is available. Options are:

- Stereotactic thalamotomy (ventrolateral nucleus of thalamus) or pallidotomy for tremor contralateral to the side of the body affected
- Deep brain stimulation—high frequency thalamic stimulation may be helpful in suppressing tremor. Also, chronic bilateral stimulation of subthalamic nuclei or globus pallidus may be beneficial
- Foetal midbrain or adrenal tissue implantation in basal ganglia (not much beneficial).

Q. What are **stages** of Parkinsonism?

A. As follows:

- Stage I—Unilateral involvement (hemiplegic Parkinsonism)
- Stage II—Bilateral involvement, but no postural abnormality
- Stage III—Bilateral involvement with mild postural abnormality
- Stage IV—Stage 3 plus severe postural abnormality requiring substantial help
- Stage V—Severe, fully developed disease. The patient is restricted to bed and wheelchair.

A BRIEF NOTE ON DRUGS USED IN PARKINSONISM

Levodopa:

- It crosses blood brain barrier and is decarboxylated into dopamine.
- It is given with peripheral decarboxylase inhibitor (e.g. carbidopa, benserazide in 4:1 ratio) to reduce its peripheral metabolism.
- Dose—50 mg 12 or 8 hourly and increased as needed upto 1000 mg/day.
- In the elderly, L-dopa is the first line of treatment as it has the best therapeutic index.
- Levodopa is contraindicated in psychosis, narrow angle glaucoma and malignant melanoma or PUD (as it may exacerbate these diseases).
- It should not be given in a patient taking MAO-A inhibitor or within 2 weeks of withdrawal, because of hypertensive crisis (cheese effect).
- Side effects—nausea, vomiting, postural hypotension, orofacial dyskinesia, limb and axial dystonia, occasionally depression, hallucination and delusion.
- After 3 to 5 years of levodopa therapy, there may be fluctuating response to levodopa in about one-third to one half of the patients. These include:
  i. **End of dose deterioration** (wearing off effect): Due to progression of the disease and loss of capacity to store dopamine, duration of action of a dose of levodopa becomes progressively shorter. As a result, the patient complains of freezing and rigidity before the next dose of levodopa. This may be managed by dividing levodopa into smaller, but for frequent doses or by using slow-release preparations or adding dopamine agonist or adding amantadine.
  ii. **On-off phenomenon**: After prolonged use, the drug may become less effective. There is sudden, unpredictable change in response, in which periods of severe Parkinsonism (freezing and immobility—the off period), alternate with periods of dopamine induced dyskinesias, agitation, chorea and dystonic movements (the on period). Adjust L-dopa dose or interdose interval or add COMT inhibitor or add dopamine agonist.

Anticholinergics:

- Trihexyphenidyl, benzhexol, orphenadrine, benztropine, phenoxene, biperiden, cycrimine, procyclidine, etc
- Useful in controlling tremor and rigidity, not helpful for bradykinesia
- Adverse effect—urinary retention, worsening of glaucoma, confusion, dry mouth, constipation
- Should be avoided in elderly patient
- Contraindicated in prostatic hyperplasia, narrow angle glaucoma, obstructive gastrointestinal disease.

Dopamine receptor agonists:

- These may be ergot derivatives (bromocriptine, pergolide, lisuride) or non-ergot (ropinirole, pramipexole)
- Bromocriptine, cabergoline, lisuride, pergolide, ropinirole, pramipexole, etc. are given orally. Rotigotine can be administered as a transdermal patch. These are alternative or addition to levodopa therapy
- Side effects are anorexia, nausea, vomiting, hallucination, confusion, orthostatic hypotension, excessive or abrupt sleepiness, leg edema.

MAO-B inhibitor:

- Selegiline is a MAO-B inhibitor and used as an adjuvant to levodopa therapy, it prevents the breakdown of dopamine. Dose is 5 to 10 mg in the morning. Recent evidences show that it can slow down degeneration in substantia nigra and is recommended to be used in all patients from early stages of the disease. Tyramine rich food should be avoided when these are used, because of the possibility of hypertensive crisis (cheese reaction)
- Rasagiline, a selective MAO-B inhibitor, 1 mg daily in the morning, may be used as an adjuvant therapy in patient with response fluctuation to levodopa.

Catechol-O-methyltransferase (COMT) inhibitors:

- Tolcapone and entacapone are COMT inhibitors, used with levodopa.
- These enhance the benefits of levodopa by reducing the conversion of levodopa to 3-O-methyldopa, which competes with levodopa for an active carrier mechanism. This increases the availability of levodopa in brain. They are useful in patient with fluctuating response to levodopa.

Amantadine:

- Potentiates endogenous dopamine (presynaptic agonist) and has mild antiparkinsonian effect
- Dose—100 mg 8 or 12 hourly
- Useful early in the disease or in conjunction with levodopa replacement
- Side effects—postural hypotension, confusion, peripheral edema, livedo reticularis, seizure, CCF, hallucination, insomnia, prostatic outlet obstruction.

Q. What are the **extra-pyramidal effects** of different antipsychotic drugs?

A. Phenothiazine, butyrophenones, metoclopramide, etc. can produce multiple abnormal movements. These may be:

- Parkinsonism (tremor is less and responds to anticholinergic drugs than L-dopa)
- Dystonia (commonly by prochlorperazine and metoclopramide)
- Akathisia (it is the uncontrolled restlessness with repetitive and irresistible need to move)
- Tardive dyskinesia—characterized by orofacial dyskinesia including lip smacking, chewing,

pouting and grimacing. It is usually due to use of phenothiazines and butyrophenones for at least 6 months. May be worse or may persist after the withdrawal of drug. Tetrabenazine may help

❖ Chorea.

Q. What are the **types** of dyskinesia or movement disorder?

A. As follows:

1. Hypokinetic—PD, PD plus
2. Hyperkinetic:
   a. Rhythmic: Tremor
   b. Non-rhythmic:
      - Chorea (lesion in caudate nucleus)
      - Athetosis (lesion in putamen)
      - Hemiballismus (lesion in subthalamic nucleus)
      - Myoclonus (lesion in multiple areas of brain)
      - Dystonia (site of lesion unknown)
      - Tics (site of lesion unknown).

MOTOR NEURON DISEASE

CHIEF COMPLAINTS

- Weakness and inability to walk for … months
- Weight loss and wasting of the limbs for … months
- Occasional twitching of the muscles of the limbs for … months.

HISTORY

History of present illness: According to the statement of the patient, he was alright … months back. Since then, he has been suffering from generalized weakness, which is progressively increasing and for the last few weeks, he is unable to walk without the help of others. The patient also complains of weight loss which is not associated with excessive sweating, polyuria, excessive thirst, cough or diarrhea. For the last … months, he noticed progressive wasting of the lower limbs initially, followed by muscles of the hands and forearms. The patient also experienced occasional spontaneous twitching movement of different parts of the body associated with muscle cramps. His bowel and bladder habits are normal. He denies any history of difficulty in deglutition, nasal regurgitation. There is no loss of sensation in any part of the body.

History of past illness

Socioeconomic history

Family history

Drug and treatment history: Mention according to the patient's statement.

GENERAL EXAMINATION

- The patient is emaciated and ill looking
- No anemia, jaundice, cyanosis, clubbing, koilonychia, leukonychia or edema
- No lymphadenopathy or thyromegaly
- Pulse: 90/min
- BP: 150/80 mm Hg.

SYSTEMIC EXAMINATION

Nervous System

1. Higher psychic functions: Normal (or there may be emotional lability)
2. Cranial nerves: Intact
3. Motor system:
   - There is wasting of all muscles of lower limbs, both hands and forearm
   - Muscle tone—increased in both lower limbs, normal in the upper limbs
   - Muscle power is diminished in both lower limbs (grade 4/5), also in upper limbs (grade 3/5). All the small muscles of hands are weak
   - Reflexes:

Jerks	Biceps	Triceps	Supinator	Knee	Ankle	Plantar
Right	Diminished	Diminished	Diminished	Exaggerated	Exaggerated	Extensor
Left	Diminished	Diminished	Diminished	Exaggerated	Exaggerated	Extensor

- There is patellar and ankle clonus (mention, if any)
- Coordination is impaired due to weakness of the muscle.

4. Involuntary movement: Multiple fasciculations in both thigh muscles and few in upper limb muscles
5. Sensory: Intact
6. Gait: Spastic gait.

Examination of the other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 45 years old, businessman, normotensive, nondiabetic, nonsmoker, hailing from …, presented with generalized weakness for … months, which is progressively increasing and for the last few weeks, he is unable to walk without the help of others. He also complains of weight loss which is not associated with excessive sweating, polyuria, excessive thirst, cough or diarrhea. For the last … months, he noticed progressive wasting of the lower limbs initially, followed by muscles of the hands and forearms. The patient also experienced occasional spontaneous twitching movement of different parts of the body associated with muscle cramps. His bowel and bladder habits are normal. He denies any history of difficulty in deglutition, nasal regurgitation. There is no loss of sensation in any part of the body. He was treated with multiple vitamins by local physicians. There is no history of such illness in his family.

On Examination
General examination (mention as above).
Systemic examination (mention as above).

My diagnosis is motor neuron disease (MND), more likely amyotrophic lateral sclerosis.

Q. Why it is MND?

A. Because, there is wasting of muscles, no sensory loss, but exaggerated reflex. Also, fasiculations are present.

Note Remember, if any patient presents with:

- Wasting (and weakness) of muscles
- But exaggerated reflex
- No sensory loss (but fasciculation is present).

Diagnosis should be motor neuron disease, until proved otherwise.

Q. Why amytrophic lateral sclerosis?

A. Because, there is lower motor neuron lesion in the upper limb and upper motor neuron lesion in the lower limb (combined UMN and LMN lesion indicates amyotrophic lateral sclerosis. Amyotrophy means muscle atrophy and lateral sclerosis means lesion in lateral corticospinal tract).

Q. Mention one common differential diagnosis to be excluded in such case.

A. Cervical cord compression involving C5 and C6 may present with lower motor neuron lesion in the upper limb and upper motor neuron lesion in the lower limb. In such case, MRI of cervical spine should be done.

Q. What are the **differential diagnoses?**

A. As follows:

1. Diabetes mellitus
2. Syphilitic amyotrophy or syphilitic cervical pachymeningitis
3. Paraneoplastic syndrome (commonly due to bronchial carcinoma)
4. Sarcoidosis
5. Spinal diseases:
   - Cervical cord compression
   - CASMA (chronic asymmetrical spinal muscular atrophy)
   - Old poliomyelitis (confuses with progressive muscular atrophy)
   - Spinal muscular atrophy of juvenile onset type 3 (onset in childhood, mild form, affects mostly proximal muscles)
   - Motor neuropathy due to any cause (confuses with progressive muscular atrophy).

Q. Could it be **syringomyelia**?

A. Unlikely, as in syringomyelia there is dissociated sensory loss.

Q. What **investigations** should be done in this case?

A. No specific test, diagnosis is usually clinical. Investigations are done to exclude other diseases:

- Blood sugar (to exclude diabetic amyotrophy)
- VDRL or TPHA (to exclude neurosyphilis)
- Chest X-ray (to exclude bronchial carcinoma)
- X-ray of the cervical spine
- Ultrasonogram of whole abdomen (to see any neoplasm)
- EMG (to confirm fasciculation and denervation)
- NCV (normal motor and sensory conduction)
- Lumbar puncture and CSF study (no abnormality, only slightly raised protein)
- CT or MRI (brain and spinal cord).

Note There are certain '*No's* in MND:

- No sphincter disturbance (rarely involved in late case)
- No sensory involvement
- No loss of awareness till death
- No dementia
- No ocular involvement
- No cerebellar or extrapyramidal lesion
- No abnormality of CSF usually.

RELATED QUESTIONS AND ANSWERS

Q. What is **MND?** What are the **causes** of MND?

A. It is a progressive disease of unknown cause, characterized by the degeneration of motor neurons in the spinal cord, cranial nerve nuclei and pyramidal neurons in the motor cortex.

The MND is common in middle aged and elderly, rare before 30 years of age. Male commonly affected than female (pseudobulbar palsy is more in female). There is no remission, and the disease is fatal within 3 to 5 years. Young patients and those with bulbar symptoms show rapid progression.

Causes are unknown, possible factors are:
- Familial—5 to 10% of the cases, may be inherited as autosomal dominant
- May follow viral infection, trauma, exposure to toxin and electric shock
- Glutamate toxicity has been implicated as a factor in amyotrophic lateral sclerosis (ALS).

Q. What is the **pathology** of MND?

A. Degeneration of Betz cells, pyramidal tract, cranial nerve nuclei and anterior horn cells. Both UMN and LMN may be involved, but no sensory involvement.

Q. What are the **types** of MND?

A. According to the site of lesion:

1. Spinal cord lesion:
   - Progressive muscular atrophy (PMA)—LMN lesion
   - Amyotrophic lateral sclerosis (ALS)—combined UMN and LMN (LMN lesion in upper limbs and UMN lesion in lower limbs)
   - Primary lateral sclerosis (PLS)—pure UMN lesion (rare).
2. Cerebral lesion:
   - Progressive bulbar palsy—medullary lesion.
   - Pseudobulbar palsy—cortical lesion.

According to type of lesion:

1. Pure UMN lesion—PLS, pseudobulbar palsy
2. Pure LMN lesion—PMA, bulbar palsy
3. Mixed lesion—ALS.

FEATURES AND DIAGNOSIS OF INDIVIDUAL MND

Progressive muscular atrophy:

- Weakness, wasting and fasciculation of distal limb muscles, usually starting in small muscles of one or both hands
- Tendon reflexes are lost (due to involvement of anterior horn cell).

Amyotrophic lateral sclerosis:

- Weakness, wasting, fasciculation and loss of all reflexes (LMN lesion) in upper limb **plus** spastic weakness with exaggerated reflexes and extensor plantar response in lower limb (UMN lesion). In advanced stage, there may be generalized hyperreflexia.
- Bulbar and pseudobulbar palsy may follow eventually.

Primary lateral sclerosis:

- Only UMN lesion (upper limb and lower limb)
- Progressive tetraparesis with terminal pseudobulbar palsy occur.

Progressive bulbar palsy:

- Presents with **3 "D"s—d**ysarthria, **d**ysphonia and **d**ysphagia. There is nasal regurgitation, dribbling of saliva
- Speech is nasal, indistinct and slurred
- Tongue—wasted, wrinkled and fasciculating
- There is palatal palsy.

- Gag reflex is absent
- Site of lesion: Nucleus of lower cranial nerves in medulla (IX, X, XI and XII). Lesion is bilateral and LMN type.
- Common causes:
  - Motor neuron disease
  - Guillain-Barré syndrome
  - Syringobulbia
  - Brainstem infarction
  - Poliomyelitis
  - Neurosyphilis
  - Neurosarcoid.

Pseudobulbar palsy:

- This is more common in women
- Speech: Nasal, slurred, indistinct and high pitched (so called **Donald Duck** or **hot potato** dysarthria due to tight immobile tongue)
- Tongue: Small and tight, spastic, unable to protrude, but no wasting or fasciculation
- Jaw jerk is exaggerated
- Palatal movement is absent
- Gag reflex is present
- The patient is emotionally labile (crying and laughing)
- Site of lesion: Bilateral UMN lesion (supranuclear) involving the pyramidal tract (supranuclear lesion of lower cranial nerves: IX, X, XI, XII)
- Causes:
  - Bilateral repeated CVA involving internal capsule (multi-infarct dementia)
  - Demyelinating disease (multiple sclerosis)
  - Motor neuron disease.

Q. What are the **differences** between bulbar and pseudobulbar palsy?

A. As follows:

Criteria	Bulbar palsy	Pseudobulbar palsy
1. Type of lesion	LMN	UMN
2. Site of lesion	Medulla	Bilateral, internal capsule
3. Speech	Nasal	Slow, slurred and indistinct
4. Nasal regurgitation	Present	Absent
5. Tongue	Wasted, fasciculation	Small, stiff or spastic
6. Jaw jerk	Absent	Brisk
7. Emotion	Normal	Labile

Q. How to **treat** MND?

A. As follows:

1. No curative treatment
2. Supportive treatment:
   - Physical rehabilitation
   - Psychological support

- Occupational rehabilitation
- Nutritional care—change the form and texture of the food, high calorie food supplement, enteral feeding, PEG (percutaneous endoscopic gastrostomy)
- Speech and communication therapy
- Respiratory therapy—NIPPV
- Home and hospice care, end of life palliative care.

3. Symptomatic treatment:
   - Fatigue—pyridostigmine, amantadine
   - Depression—SSRI, venlafaxine, amantadine
   - Emotional lability—same
   - Cramps—quinine sulfate, vitamin E, clonazepam
   - Fasciculation—carbamazepine
   - Spasticity—baclofen, tizanidine
   - Sialorrhoea—hyoscyamine sulfate, scopolamine patch
   - Joint pain—analgesic, such as NSAIDs
   - Insomnia—zolpidem tartrate
   - Respiratory failure—bronchodilators.
4. Neuroprotective agents: Riluzole, IGF-1, ASO, vitamin E, Coenzyme Q-10, neuroprotective factors. Riluzole is a glutamate antagonist, may retard progression and prolong the survival.

Q. What is the **prognosis** of MND?

A. The MND is a progressive disorder and remission is unknown. It is usually fatal within 3 to 5 years. Younger patient with early bulbar syndrome tend to show a more rapid course. Prognosis is relatively better in progressive lateral sclerosis and progressive muscular atrophy.

Cause of death—bronchopneumonia, respiratory failure and complication of immobility.

Q. What are the causes of **wasting of the small muscles of the hand**?

A. As follows:

- MND
- Syringomyelia
- Charcot Marie Tooth disease
- Cervical spondylosis
- Cervical rib
- Pancoast's tumor
- Following arthritis
- Peripheral nerve lesion (peripheral neuropathy or combined ulnar and medial nerve lesion)
- Myopathy (dystrophia myotonica).

Q. What is the **difference** between fasciculation and fibrillation of muscle?

A. As follows:

- Fasciculation—contraction of groups of muscles. It is visible.
- Fibrillation—contraction of single muscle fibre or unit. It is not visible. Diagnosed by EMG.

Q. What is **fasciculation?** What are the **causes**? What is the **mechanism**?

A. Random spontaneous twitching of a group of muscle fibers or a motor unit that produce movement of the overlying skin or mucous membrane or digits. Fasciculation may be coarse or fine, usually present at rest, but not during voluntary movement. It is usually spontaneous, may be elicited by tapping with finger or hammer over the muscle (this procedure is controversial, as it is not accepted by some neurologists, because it should be spontaneous). If fasciculation is present with weakness and wasting, it indicates LMN lesion.

Mechanism of fasciculation:

It is due to spontaneous firing of surviving axons that strive to innervate the muscle fibers, which have lost their nerve supply.

Causes of fasciculation:

1. Neurogenic:
   - MND
   - Charcot-Marie-Tooth disease
   - Spinal muscular atrophy
   - Radiculopathy (cervical spondylosis, cervical rib)
   - Syringomyelia
   - Peripheral neuropathy
   - CJD
   - Acute stage of poliomyelitis (rarely in old polio)
   - Syphilitic amyotrophy
   - Neuralgic amyotrophy.
2. Metabolic:
   - Tetany
   - Thyrotoxic myopathy
   - Anticholinergic drugs
   - OPC poisoning.
3. Normal:
   - Benign fasciculations (in anxiety or tension. It is usually found around the shoulder joint)
   - After exercise in fit adults
   - After tensilon test
   - Muscle cramps.

Q. What are the **neurological non-metastatic syndromes** of malignancy?

A. As follows:

- Motor neuron disease
- Sensory neuropathy
- Mononeuritis multiplex
- Cranial polyneuropathy
- Eaton-Lambert syndrome
- Spastic paraparesis
- Cerebellar syndrome
- Dementia and encephalopathy
- Progressive multifocal leukoencephalopathy.

Cause of neurological non-metastatic syndromes is unknown. It may precede the clinical manifestation of malignancy. Usually, it is associated with small cell carcinoma of the lung and lymphoma.

Neuromuscular paraneoplastic syndrome (according to the site of lesion):

- **Brain:** Progressive cerebellar degeneration, dementia, myoclonus-opsoclonus
- **Brainstem:** Limbic encephalitis
- **Cranial nerves:** optic neuritis, retinal degeneration or retinopathy
- **Spinal cord:** Myelitis, MND like picture

- **Peripheral nerves:** Subacute and chronic sensorimotor neuropathy, subacute motor neuropathy, pure sensory neuropathy, autonomic neuropathy, GBS like syndrome, brachial neuritis.
- **Neuromuscular:** Lambert Eaton myasthenic syndrome.
- **Muscular:** Dystonia/myotonia, acute necrotising myopathy, stiff-person syndrome, cachexic myopathy, carcinoid myopathy.

Importance of neuromuscular PNS:

- Symptoms may appear quite ahead before the presentation of occult malignancy
- Symptoms may be so severe that may lead to death of the patient
- Symptoms may be confused with metastatic disease of the tumor
- At least three-fourth of the PNS is irreversible and fatal
- Accompanied by various antibodies that may help in the diagnosis of the condition.

MULTIPLE SCLEROSIS

CHIEF COMPLAINTS

- Weakness for … months
- Inability to walk for … months
- Weight loss for … months
- Incontinence of urine and constipation for … months.

HISTORY

History of present illness: According to the statement of the patient, she was alright … months back. Since then, she has been suffering from generalized weakness which is deteriorating progressively. For last … months, she is so weak that she cannot walk even for a short distance without the help of others. The patient also complains of substantial weight loss for the last … months. It is not associated with excessive sweating, polyuria, excessive thirst, cough or diarrhea. For the last … months, he also complains of urinary incontinence during both day and night, which is not associated with pain, burning sensation, frequency of micturition or hematuria. She also complains of constipation, but there is no history of blurring of vision, vertigo, convulsion or facial pain. She denies any history of fever, headache or trauma.

History of past illness: She had a similar attack 1 year back that improved after taking some drugs prescribed by local doctors, the name of which she cannot mention.

Socioeconomic history: High (or upper middle) class.

Family history

Personal history

Drug and treatment history: Mention according to the patient's statement.

GENERAL EXAMINATION

- The patient looks ill, apathetic and emaciated
- No anemia, jaundice, cyanosis, clubbing, koilonychia, leukonychia or edema
- No lymphadenopathy or thyromegaly
- Pulse: 74/min
- BP: 115/70 mm Hg.

Nervous System

1. Higher cerebral functions: Normal. Speech is dysarthric and scanning.
2. Cranial nerves:
   - First—intact
   - Fundoscopic findings—temporal pallor of the optic disc in the right eye, left eye is normal
   - Third, fourth and sixth—there is nystagmus in right eye on lateral movement and failure of adduction of left eye (internuclear ophthalmoplegia). Diplopia may be present (mention if any)
   - Rest of the cranial nerves are normal.

3. **Motor system:**
   - Muscle power is diminished, grade 4/5 in the lower limbs, normal in the upper limbs
   - Muscle tone is increased in lower limbs
   - Reflexes:

Jerks	Biceps	Triceps	Supinator	Knee	Ankle	Plantar
Right	Normal	Normal	Normal	Exaggerated	Exaggerated	Extensor
Left	Normal	Normal	Normal	Exaggerated	Exaggerated	Extensor

   - Patellar and ankle clonus—present in both lower limbs
   - Abdominal reflex—lost
   - Coordination—impaired in both lower limbs (due to weakness)
   - Gait—reeling or drunken gait.
4. **Sensory system:**
   - Loss of vibration, position sense and two point discrimination in the right lower limb
   - Other modalities of sensation are normal.
5. **Involuntary movement:** Absent.

Examination of the other systems reveals no abnormalities.

SALIENT FEATURES

Mrs …, 52 years old, housewife, normotensive, nondiabetic, nonsmoker, hailing from …, presented with generalized weakness for … months, which is deteriorating progressively. For last … months, she is so weak that she cannot walk even for a short distance without the help of others. The patient also complains of substantial weight loss for the last … months. It is not associated with excessive sweating, polyuria, excessive thirst, cough or diarrhea. For the last … months, the patient also complains of urinary incontinence during both day and night, which is not associated with pain, burning sensation, frequency of micturition or hematuria. She also complains of constipation, but there is no history of blurring of vision, vertigo, convulsion or facial pain. She denies any history of fever, headache or trauma. She had a similar attack one year back that improved after taking some drugs prescribed by local doctors, the name of which she cannot mention. There is no history of such illness in her family. She was treated with vitamins by local physicians.

On examination
General examination (mention as above).
Systemic examination (mention as above).

My diagnosis is demyelinating disease (multiple sclerosis).

Q. Why is it multiple sclerosis?

A. From history, she has history of recurrent neurological deficits involving both lower limbs along with incontinence and constipation. On examination, there are scanning speech, internuclear ophthalmoplegia, nystagmus, upper motor neuron lesion in lower limbs, cerebellar gait, ataxia, and temporal pallor of the optic disc in the right eye.

Q. Why not spinal cord compression?

A. Because onset over days or weeks, no radicular pain, no history of trauma or vertebral collapse. There is no upper level of sensory loss.

Also internuclear ophthalmoplegia, nystagmus, cerebellar sign's and optic neuritis are against spinal cord compression.

Q. What are the **differential diagnoses?**

A. As follows:

- Spinal cord compression
- Subacute combined degeneration of spinal cord (SCD)
- Neurosyphilis
- Adrenoleukodystrophy
- Recurrent attack of myelitis (see below).

Q. What are the causes of **recurrent attack of myelitis?**

A. As follows:

- Central nervous system sarcoidosis (neurosarcoid)
- Systemic lupus erythematosus (SLE)
- Antiphospholipid antibody syndrome
- Behcet's syndrome
- Sjogren syndrome
- Mixed connective tissue disease
- Spinal AVM
- Dural and cord vascular fistula.

Q. What **investigations** should be done in multiple sclerosis?

A. As follows:

1. MRI of brain and spinal cord—investigation of choice (positive in 95% cases). MRI shows multiple plaques, hyperintense in T_2W and FLAIR, mainly in the periventricular region, corpus callosum, cerebellar peduncles, juxtracortical posterior fossa, brainstem and subpial region of spinal cord. CT scan is not sensitive.
2. Lumbar puncture and CSF study—there is slight increase in lymphocyte, increase in total protein (in 40% cases), and oligoclonal band (in 70 to 90% cases, mainly IgG on electrophoresis).
3. Evoked potential—mainly VEP (visual evoked potential, usually delayed, if there is optic nerve involvement).
4. To exclude other conditions:
   - Chest X-ray (to exclude bronchial carcinoma)
   - X-ray of spine (to exclude cord compression)
   - Serum angiotensin converting enzyme (to exclude sarcoidosis)
   - Serum B_{12} (to exclude subacute combined degeneration of spinal cord)
   - ANA (to exclude SLE)
   - Antiphospholipid antibodies.

RELATED QUESTIONS AND ANSWERS

Q. What is **MS?** What is the **natural history** of the disease?

A. It is a chronic, inflammatory demyelinatig disorder of CNS characterized by multiple plaques of demyelination within the brain and spinal cord, gliosis and varying degree of inflammation. Usually there is relative preservation of axons.

Natural history is extremely variable—may be acute, subacute, insidious, relapsing and remitting, chronic progressive, spontaneous recovery, rapidly progressive and secondarily progressive.

It is also called disseminated sclerosis, as the plaques are **disseminated both in time and space.** Presence of two neurological lesions in anatomically unrelated sites or at different times indicates multiple sclerosis.

Q. What are the **causes** of MS?

A. Unknown, the following factors may be associated:

- Environmental factors—more in temperate zone, and rare in tropical country. Greater among rural than urban dwellers
- More frequent in the higher socioeconomic group
- Genetic—ten times more in first degree relative
- Immunological—there is increase in activated T-lymphocyte in CSF, increase in immunoglobulin in CNS and increase in antibody to some virus (measles)
- Diet—more in those who eat animal fat
- HLA association—DR_2, DR_3, B_7, A_3

Q. What are the **presentations** of MS?

A. Twice more common in females. Age of onset is 20 to 45 years. Before puberty and after 60 years, it is rare. The patient usually presents with:

- Weakness of one or more limbs
- Optic neuritis (the patient complains of blurring of vision)
- Features of spastic paraplegia (confused with spinal cord compression)
- Features of cerebellar signs (ataxia and tremor, etc.)
- Features of brainstem dysfunction (vertigo, diplopia, nystagmus, facial numbness or weakness, dysarthria, dysphagia and pyramidal signs in limbs)
- Bladder dysfunction (incontinence, dribbling and hesitancy)
- Sensory disturbance—tingling of the extremities and light banding sensation around the trunk or limbs (due to posterior column involvement)
- Others (rarely)—epilepsy, trigeminal neuralgia, facial palsy (may be recurrent), 6th nerve palsy, tonic spasm or brief spasm of limbs, dementia, neuropsychiatric dysfunction, depression
- Euphoria despite disability.

Common mode of onset:

1. Optic neuritis (25%)
2. Transverse myelitis (like spinal cord compression)
3. Cerebellar ataxia
4. Various brainstem syndromes—vertigo, facial pain or numbness, dysarthria, diplopia.

To remember the signs and symptoms of MS, remember the mnemonic—**WATSON.**

- **W** – **W**eakness
- **A** – **A**taxia (cerebellar)
- **T** – **T**remor (cerebellar)
- **S** – **S**peech (scanning)
- **O** – **O**ptic neuritis
- **N** – **N**ystagmus.

Q. Which **reflex** is lost early?

A. Abdominal reflex.

Q. What is **triad of Steinberg?**

A. Urinary incontinence, impotence and constipation.

Q. What are the **clinical courses (or types)** of MS?

A. As follows:

- Relapsing and remitting MS (80 to 90%): The patient suffers from episodes of acute worsening with recovery and remains stable between relapses.
- Primary progressive MS (10 to 20%): Gradual neurological deterioration from the onset. It usually begins after 40 years (late onset).
- Secondary progressive MS: Some cases of relapsing and remitting course show gradual neurological deterioration. There may be superimposed acute relapses.
- Fulminating MS (< 10%).

Q. What are **sites of involvement** in MS?

A. As follows:
- Optic nerve
- Brainstem and its cerebellar connection
- Spinal cord (posterior column and corticospinal tract)
- Cerebral white matter particularly periventricular region.

Q. What are the **prognostic factors** in MS?

A. As follows:

1. Good prognostic factors:
   - Early age of onset
   - Relapsing and remitting form of disease
   - Visual or sensory symptoms alone at presentation
   - Minimum neurological impairment 5 years after onset
   - More benign course in women than in men
   - Little residual disability 5 years after onset.
2. Poor prognostic factors:
   - Old age > 40 years
   - Frequent relapse in first 2 years
   - Short interval between first 2 relapses
   - Pyramidal, brainstem and cerebellar symptoms
   - Primary progressive disease
   - Poor recovery from relapse
   - MRI shows many lesions.

Q. What are the **features** of end-stage MS?

A. In end-stage disease, the patient is severely disabled with spastic paraplegia, tetraplegia, ataxia, optic atrophy with blindness, nystagmus, pseudobulbar palsy, urinary incontinence, brainstem dysfunction and dementia.

Q. What is **Uhthoff's** phenomenon?

A. Exaggeration of symptoms after raised body temperature or hot bath is called Uhthoff's phenomenon. The patient feels extreme weakness or transient blurring of vision (minutes) after hot bath. It is due to the slowing of central conduction by increased body temperature.

Q. What happens during **pregnancy** in multiple sclerosis?

A. Mild protective effect may be seen during pregnancy. However, exaggeration may occur in puerperium.

Note Remember the following points in multiple sclerosis:

- Common in women, 20 to 40 years of age (rare before puberty and after 60 years, F: M = 2:1)
- It is called disseminated sclerosis, as it is **disseminated in time and place**
- Presence of two neurological lesions in anatomically unrelated sites or at different times indicates MS
- Patient may complain of blurring or loss of vision. Using fundoscopy nothing is seen (if "doctor sees nothing, patient sees nothing" this is due to retrobulbar neuritis)
- Peripheral nervous system is spared, only CNS involvement
- Causes of death are renal failure and bronchopneumonia.

Q. How to **treat** MS?

A. As follows:

1. During acute attack:

- Intravenous (IV) methylprednisolone—1 g for 3 days or oral 500 mg for 5 days. It shortens the duration of relapse but does not affect the long-term outcome. It is followed by oral prednisolone 40 mg daily for 10 days, then 20 mg for 2 days, then 10 mg for 2 days
- Or, high dose prednisolone—40 to 60 mg daily for 10 days, then taper over 2 days (it has no role for long-term use for prevention)
- Plasmapheresis is sometimes helpful in patient with severe relapse and unresponsive to corticosteroid.

2. To prevent relapse (disease-modifying drugs may be given):

- Immunosuppressive drug—azathioprine may be helpful (cyclophosphamide sometimes helpful in aggressive disease, not recommended for widespread use). Mitoxantrone may be helpful
- Subcutaneous or intramuscular β interferon (1a or 1b) reduces the number of relapse (30%)
- Glatiramer acetate has similar effect. It has immunomodulatory effect
- Monoclonal antibody to beta-integrins (natalizumab), or to lymphocyte epitopes (campath-1H), or alemtuzumab may be helpful in severely affected patient
- IV immunoglobulin may be helpful in aggressive cases.

3. Other supportive treatment for complication and disability:

- For incontinence—intermittent self catheterization, drugs like oxybutynin, tolterodine, etc.
- Urgency or frequency – intermittent self catheterization is advised if post-micturition residual urine is > 100 mL. If < 100 mL, then oxybutynin or tolterodine may be given
- For spasticity—physiotherapy and drugs like baclofen (oral or intrathecal), tizanidine, benzodiazepine or dantrolene may be used. Local intramuscular injection of botulinum toxin or chemical neuronectomy are other options. Cannabis extracts and synthetic cannabinoids are also used
- For dysesthesia—carbamazepine, gabapentin, phenytoin or amitriptyline may be helpful
- For ataxia—INH or clonazepam
- For fatigue—amantadine, modafinil or amitriptyline
- For impotence—sildenafil may be used
- Control of infection
- Prevention of pressure sore
- Rehabilitation.

Q. What is the **role of steroid** in MS?

A. In MS with optic neuritis, high dose intravenous mythylprednisolone for 3 days followed by short course of prednisone may be given. It reduces the rate of relapse of MS over 2 years.

Q. What is the **role of exercise** in MS?

A. The patient should be active during remission and avoid excessive physical exercise during relapses.

Q. What is **Lhermitte's sign**?

A. When the neck is flexed, there is tingling or electric shock like sensation or funny sensation, which passes down in the upper limb, trunk and perhaps lower limbs called Lhermitte's sign (also called barber's chair sign). It indicates the disease is near the dorsal column nuclei of higher cervical cord (indicates cervical cord compression). Causes are:

- MS (the most common cause, especially in acute exacerbation)
- Cervical spondylosis
- Cervical cord compression (by tumor)
- Subacute combined degeneration
- Radiation myelopathy
- Cervical spondylotic myelopathy.

Note

A similar sensation provoked by neck extension may occur, called **reverse Lhermitte's sign**. It strongly suggests cervical spondylosis.

Q. What is the **role of MRI**?

A. The MRI is the single most investigation to confirm the diagnosis of MS, positive in 80% cases. It shows hyperintense focal periventricular white matter lesions in T_2 weighted images. Although these are typical, but not pathognomonic and may be found in small infarcts, disseminated metastases, moya-moya disease and inflammatory diseases.

MRI in MS is helpful for the following:

1. Reveals asymptomatic plaques in cerebrum, brainstem, optic nerves and spinal cord.
2. MS plaques are hyperintence on T_2W and even more strikingly obvious on fluid attenuated inversion recovery (FLAIR).
3. On T_2W, several asymmetrical, well demarcated lesions immediately adjacent to ventricular surface (periventricular lesion) usually denotes MS. Especially diagnostic are oval or linear regions of demyelination oriented perpendicularly to the ventricular surface. When viewed on sagittal images, they extend outward from corpus callosum in fimbriated pattern termed "Dawson fingers".
4. Another characteristic pattern is C shaped partial ring of enhancement created by rounded lesion interrupted by gyrus.
5. Lesions that have undergone some degree of cavitation are hypointense on T_1W termed "black holes".
6. Serial MRI can demonstrate progress of disease, e.g. increasing number of lesion.
7. MRI changes assume maximum diagnostic significance when they are consistent with the clinical findings.

Q. What are the **other demyelinating disorders**?

A. As follows:

- ADEM
- Leukodystrophies
- Tuberous sclerosis (patchy demyelination)
- Devic's disease (acute necrotising myelitis with optic neuritis)

- Schilder's disease (diffuse cerebral sclerosis. There may be cortical blindness, if occipital cortex is involved, cerebral deafness, quadriplegia, hemiplegia, dementia, pseudobulbar palsy.
- Tuberous sclerosis (patchy demyelination).

Q. What are the **causes** of bilateral upper motor neuron lesion involving the lower limbs?

A. As follows:

- Spinal cord compression
- MS
- MND (amyotrophic lateral sclerosis)
- Hereditary spastic paraplegia
- Transverse myeliltis
- Subacute combined degeneration
- Friedrich's ataxia
- Bilateral cerebral infarction
- Cervical myelopathy.

CEREBROVASCULAR DISEASE (CVD OR CVA)

CHIEF COMPLAINTS

- Weakness of right side of the body for … days
- Difficulty in speech and swallowing for … days
- Urinary incontinence for … days.

HISTORY

History of present illness: According to the statement of the attendant, the patient was reasonably well … days back. Suddenly in the early morning, while going to the toilet, he felt weakness of the right side of the body, initially in the upper limb, then the right lower limb, followed by fall to the ground. Since then, he is unable to move his right side of the body and cannot walk. The patient is also unable to speak and has difficulty in swallowing, which is more marked for liquid food. There is also urinary incontinence for the same duration but no bowel abnormality. There is no history of fever, loss of consciousness, convulsion, trauma to the head, nausea, vomiting and double vision.

History of past illness: He is hypertensive for 15 years and diabetic for 4 years. There is no history of any cardiac abnormality.

Family history: His father died of heart attack but his mother is alive in good health. His elder brother is also hypertensive.

Personal history: He is a smoker for the last 35 years, used to take 30 sticks/day.

Socioeconomic history: Mention accordingly.

Drug and treatment history: He used to take atenolol 50 mg/day and his diabetes is controlled by dietary modification.

GENERAL EXAMINATION

- The patient looks ill and anxious
- No anemia, jaundice, cyanosis, clubbing, koilonychia, leukonychia, edema
- No lymphadenopathy or thyromegaly
- Pulse: 85/min
- BP: 160/110 mm Hg
- Respiratory rate: 20/min
- Urinary catheter in situ.

SYSTEMIC EXAMINATION

Nervous System

1. **Higher cerebral functions:** The patient is conscious, but unable to speak fluently. Speech is slightly slurred.
2. **Cranial nerves:**

- 7th cranial nerve shows upper motor neuron lesion on the right side
- Rest of the cranial nerves are intact

3. **Motor system**:
   - Muscle tone is increased in the right upper and lower limbs
   - Muscle power: diminished in right upper and lower limbs, grade 4/5 in the lower limb and 3/5 in the upper limb.
   - Reflexes:

Jerks	Biceps	Triceps	Supinator	Knee	Ankle	Plantar
Right	Exaggerated	Exaggerated	Exaggerated	Exaggerated	Exaggerated	Extensor
Left	Normal	Normal	Normal	Normal	Normal	Flexor

   - There is patellar and ankle clonus on the right side
   - Coordination—impaired on the right lower limb
   - Gait—hemiplegic gait (during walking, the patient's right toes strike the ground and in an attempt to overcome this, the right leg is swung outwards at the hip, called circumduction).
4. **Involuntary movements:** Absent
5. **Sensory system:** Intact
6. **Fundoscopy:** Normal.

Cardiovascular System

- Pulse—85/min, regular
- BP—160/110 mm Hg
- JVP—normal
- Precordium—no abnormality

Examination of other systems—no abnormality detected.

SALIENT FEATURES

Mr. …, 62 years old, businessman, hypertensive, diabetic, smoker, hailing from …, presented with sudden weakness of the right side of the body … days ago, initially involving the right upper limb, then the right lower limb, followed by fall to the ground. Since then, he is unable to move his right side of the body and cannot walk. The patient is also unable to speak and has difficulty in swallowing, which is more marked for liquid food. There is also urinary incontinence for the same duration but no bowel abnormality. There is no history of fever, loss of consciousness, convulsion, trauma to the head, nausea, vomiting and double vision.

He is hypertensive for 15 years and diabetic for 4 years. There is no history of any cardiac abnormality. He is a smoker for the last 35 years, used to take 30 sticks/day. His father died of heart attack but his mother is alive in good health. His elder brother is also hypertensive. There is no family history of similar illness. He used to take atenolol 50 mg/day and his diabetes is controlled by dietary modification.

On Examination

General examination (mention as above)

Systemic examination (mention as above).

My diagnosis is hypertension with diabetes mellitus with CVD with right sided hemiplegia.

Q. What **type** of CVD is this?

A. Most likely, this is cerebral infarction (ischemic stroke) due to cerebral thrombosis.

Q. **Why** is it cerebral thrombosis?

A. Because, onset is slow. There is no history of vomiting, unconsciousness or convulsion.

Q. **Why not** cerebral embolism?

A. In cerebral embolism, onset is sudden (seconds to minutes), called stormy onset.

Q. **Why not** cerebral hemorrhage?

A. In cerebral hemorrhage, onset is sudden (seconds to minutes) and usually associated with loss of consciousness, vomiting or convulsion.

Q. **Why not** subarachnoid hemorrhage?

A. In subarachnoid hemorrhage, the patient is usually young. There is history of sudden severe headache mostly in the occipital region followed by vomiting and loss of consciousness. Features of meningeal irritation, like neck rigidity and Kernig's sign, are usually present. Fundoscopy shows subhyaloid hemorrhage (boot shaped concave).

Q. What is the likely **site of lesion** in your case?

A. Left internal capsule due to involvement of lenticulostriate branch of middle cerebral artery.

Q. What you have examined **in the heart?**

A. Any arrhythmia like atrial fibrillation. Also any valvular lesion, e.g. MS.

Q. Have you **examined the neck?** Why?

A. Yes. I have seen carotid bruit (thrombus from carotid may be dislodged and cause cerebral thrombosis).

Q. What **investigations** do you suggest?

A. As follows:

1. CT scan of the head (first investigation to be done)
2. Complete blood count with ESR
3. Blood sugar
4. Blood urea and serum creatinine
5. Serum lipid profile
6. Serum electrolyte
7. Chest X-ray P/A view
8. ECG
9. Source of the event:
   - Doppler study of extracranial/intracranial vessels
   - Echocardiography—transthoracic or transesophageal
   - MRA or CTA of the cerebral vessels
   - DSA of the cerebral vessels (Gold standard to find out AVM or aneurysm).
10. Other tests according to suspicion of cause:
    - For collagen vascular disease—ANA, anti-dsDNA, anti-cardiolipin and anti-phospholipid antibody
    - pANCA, cANCA
    - Coagulation screening, serum antithrombin III, protein C and protein S level
    - Others—red cell mass (PRV), chromatographic test in serum and urinary level of homocysteine or methionine (homocystinuria), TPHA and VDRL (syphilis).

RELATED QUESTIONS AND ANSWERS

Q. What is **stroke?** What are the **types** of stroke?

A. Stroke may be defined as sudden development of focal neurological deficit due to nontraumatic vascular cause, lasting more than 24 hours. It is of following types:

- Transient ischemic attack (TIA)—sudden neurological dysfunction due to cerebral ischemia lasting less than 24 hours and the patient recovers completely within 24 hours
- Stroke in evolution—the symptoms worsen gradually or in a step wise pattern over hours or days and the neurological deficit persists for more than 24 hours
- Completed stroke—clinical signs of neurological deficit are persistent
- Reversible ischemic neurological deficit (RIND)—neurodeficit persists for more than 24 hours, but recovers totally within 3 weeks
- Partial non-progressive stroke (PNS)—neurodeficit persists for more than 3 weeks, but is either partial or ends up with minimal residual deficit.

Q. What are the diseases included in **CVA?**

A. As follows:

- Cerebral hemorrhage
- Cerebral thrombosis
- Cerebral embolism
- Subarachnoid hemorrhage
- Hypertensive encephalopathy
- Cerebellar hemorrhage
- Cerebellar infarction.

Q. How to **treat** CVD?

A. As follows:

1. General measures:
   - Oropharyngeal suction
   - IV channel
   - Nasogastric tube feeding
   - Maintenance of nutritional status
   - Regular change of posture (2 hourly)
   - Care of bowel
   - Care of bladder (catheterization)
   - Care of mouth (to prevent fungal infection)
   - Care of eyes (tear naturale or taping of the affected eye shut).
2. Control of risk factors or cause, if any. For example:
   - Control of hypertension
   - Control of diabetes mellitus
   - Control of hyperlipidemia
   - Other treatment according to the cause.
3. If cerebral edema: Dexamethasone or mannitol.
4. Specific treatment according to the type of stroke (after CT scan):
   - Cerebral infarction—antiplatelet drugs (e.g. aspirin, clopidogrel). Cerebral vasodilator like vinpocetine should be given. If atrial fibrillation, heparin followed by warfarin should be considered
   - Cerebral hemorrhage—for massive hemorrhage, neurosurgical intervention may be required. Other treatment is symptomatic and supportive
   - Subarachnoid hemorrhage—nimodipine can be given, neurosurgical intervention is essential.

5. To reduce morbidity and improve quality of life:
   - Physiotherapy
   - Speech therapy
   - Occupational therapy.

Treatment of hypertension in stroke:

1. If the patient is known hypertensive—continue the antihypertensive if the BP is normal or high.
2. If the patient is not known to be hypertensive and BP is mildly or moderately high, then observe the patient and monitor BP for 7 to 10 days. If after this period BP is still high, then antihypertensive agents should be considered.
3. If the patient is not known to be hypertensive, antihypertensive drug should be started if:
   - There is evidence of target organ damage—such as hypertensive retinopathy or evidence of enlargement of heart.
   - BP is severe—>220/110 mm Hg
   - Co-morbidity—myocardial infarction, cardiac failure.
4. In CVD, following antihypertensive may be given:
   - ACEI or ARB
   - Calcium channel blocker
   - Beta blocker
   - Diuretics.

Q. What is the **prognosis** of CVA?

A. Prognosis depends on the type of lesion, site, extent of involvement and associated primary risk factors.

- Mortality rate is higher in intracerebral hemorrhage than embolic stroke
- In cerebral infarction, immediate prognosis is better, long-term prognosis depends upon extent of damage
- In cerebral hemorrhage, immediate prognosis is worse. In hemorrhagic stroke, 25% die within first 2 years, 10% die within first month. However, prognosis is better in the long run, when the hematoma resolves
- One-third of patients return to independent mobility, one-third becomes disabled requiring institutionalized care.

Q. What are the **complications** of acute stroke?

A. As follows:

- Raised intracranial pressure
- Hydrocephalus
- Aspiration pneumonia
- Convulsion
- Pressure sores
- DVT
- Pulmonary embolism
- Electrolyte imbalance
- Painful shoulder
- Urinary infection
- Constipation
- Depression and anxiety
- Alteration of sleep wake cycle.

Q. What are the causes of CVD in a **young patient?**

A. As follows:

- Mitral stenosis with atrial fibrillation (cerebral embolism from cardiac source)
- Other cardiac cause—PFO, VSD, TOF
- Antiphospholipid syndrome
- SLE
- Hematological disease—sickle cell anemia, polycythemia rubra vera, inherited deficiency of naturally occurring anti-coagulant (protein C, protein S, antithrombin III, factor V Leiden). In all these conditions, there is increased tendency of thrombosis.
- Vasculitis. Behcet's disease
- Vascular malformation—AVM, berry aneurysm causing SAH
- Arterial dissection
- In female—oral contraceptive pill, eclampsia
- Homocystinuria
- Syphilis
- Premature atherosclerosis may occur in familial hyperlipidemia
- Rarely, migraine may cause cerebral infarction
- Drugs like amphetamine, cocaine.

Q. What **investigations** should be done in a young patient with stroke?

A. See as above. For young patient, specific investigations are as follows:

- Chest X-ray, ECG and echocardiography (to exclude cardiac problem like MS with AF, other cardiac problem like PFO, TOF)
- CBC, ESR—(it will also exclude polycythemia rubra vera)
- Serum lipid profile—(in juvenile hyperlipidemia)
- For collagen vascular disease—ANA, anti-ds DNA, anti-cardiolipin and anti-phospholipid antibody
- Coagulation screening, serum antithrombin III, protein C and protein S level
- Others—red cell mass (PRV), chromatographic test in serum and urinary level of homocysteine or methionine (homocystinuria), TPHA and VDRL (syphilis).

Q. What are the **risk factors** for stroke?

A. Risk factors are variable for ischemic stroke and hemorrhagic stroke:

Risk factors for ischemic stroke:

1. Non-modifiable:
   - Age
   - Gender
   - Ethnicity or race
   - Genetics
   - Family history.
2. Modifiable:
   - Hypertension
   - Smoking
   - Lifestyle
   - Diabetes mellitus
   - Obesity
   - Heart disease (atrial fibrillation, ischemic heart disease, cardiomyopathy, etc.)
   - Dyslipidemia
   - Oral contraceptive pill

- Alcohol
- Previous history of stroke or TIA
- Carotid vessel atherosclerosis
- Atheromatous aortic arch
- Diseases like homocystinuria, hyperfibrinogenemia, deficiency of protein C, S and antithrombin III, polycythemia rubra vera, antiphospholipid syndrome, thrombotic thrombocytopenic purpura, sickle cell anemia, protein V Leiden syndrome, vasculitis (like poly arteritis nodosa, Wegener's granulomatosis, Takayasu's arteritis), migraine
- Abuse of cocaine, use of COX 2 inhibitor (slightly increased incidence of stroke).

Risk factors for hemorrhagic stroke:

- Hypertension
- AVM
- Aneurysm
- Amyloid angiopathy
- Cavernous angioma
- Anticogulant therapy
- Hypercoagulable disorder
- Drugs—cocaine, amphetamine
- Vasculitis—SLE, PAN, isolated CNS vasculitis
- Septicemia
- Moya-moya disease
- Hemorrhage into brain tumor.

Q. What are the causes of **recurrent hemiplegia**?

A. As follows –

1. CVD:
   - Atrial fibrillation
   - Hyperviscosity syndrome
   - Homocystinuria
   - Amyloidosis
   - Deficiency of protein C, S or antithrombin III
   - Polycythemia rubra vera
   - Antiphospholipid syndrome
   - Poly arteritis nodosa
   - Wegener's granulomatosis
   - Takayasu's arteritis.
2. Other causes:
   - Multiple sclerosis
   - Hemiplegic migraine
   - Epilepsy (Todd's palsy)
   - Hysteric hemiplegia.

Q. How to **prevent** stroke?

A. As follows:

- Risk factors like hypertension, diabetes mellitus, obesity, etc. should be identified and controlled
- Smoking and alcohol should be stopped
- Antiplatelet drug, e.g. aspirin
- Lifestyle modification—regular physical exercise, dietary modification

- Statin should be given to all patients
- If there is atrial fibrillation—treatment of primary cause and anticoagulation
- Treatment of primary cause.

Q. What is the **role of oral contraceptive pill** in stroke?

A. Low dose estrogen containing oral contraceptive pills do not increase the risk of stroke in healthy women, but can cause stroke if associated with other risk factors.

A BRIEF DISCUSSION ON DIFFERENT TYPES OF CVD

A. Cerebral thrombosis:

- The most common cause of CVA in middle aged or elderly (85%)
- The most common site is internal capsule and commonest vessel involvement is middle cerebral artery
- Risk factor—atherosclerosis, systemic hypertension, diabetes mellitus, polycythemia rubra vera, collagen vascular disease, dyslipidemia, smoking, obesity, oral contraceptive pill, alcohol, obesity, carotid artery occlusion
- Onset is insidious with stepwise progression. Commonly occurs during sleep or soon after waking
- Loss of consciousness is rare, but there may be headache, convulsion
- Neurological deficit depends on the site of lesion (see below)
- Shifting hemiplegia is absent (no migration of hemiplegic site)
- Carotid bruit with diminished pulsation may be present.

B. Cerebral embolism:

- Onset—very acute or stormy (develops quickly in seconds), during exertion or activity, no warning sign of TIA
- Site—left sided vascular lesion is common as left common carotid artery arises directly from the aorta. Left middle cerebral artery is commonly involved
- There is usually a source of embolus or vulvular heart disease with atrial fibrillation
- Neurological features may be increased due to associated vasospasm. Sometimes, features may be diminished or disappear due to dislodgement of the embolus. Shifting hemiplegia may occur
- Recovery—may be rapid
- Cause—atherosclerosis, mitral stenosis with atrial fibrillation, infective endocarditis, paradoxical embolism, myocardial infarction.

C. Cerebral hemorrhage:

- Usually occurs in elderly, cause of CVD is 15%
- Site—near internal capsule in basal ganglia. Other site—pons, thalamus, cerebellum and cerebral white matter
- Common vessel involved is the lenticulostriate branch of the middle cerebral artery
- Onset—usually sudden. There may be mental stress or strain
- Causes—almost all are hypertensive. Ruptured intracerebral aneurysm, blood dyscrasia, vascular anomaly like arteriovenous malformation, hemorrhage in a cerebral neoplasm
- The patient usually presents with severe headache, vomiting, convulsion, followed by unconsciousness
- On examination—conjugate deviation of eyes, Cheyne-Stokes breathing, features of raised

intracranial pressure, urinary retention. If pontine hemorrhage—pin point pupil, pyrexia and paralysis (3P). Other features depend on the site of hemorrhage
- Early recovery is unusual.

D. Subarachnoid hemorrhage:

- Common in young adults (apoplexy of the young), 5 to 10% stroke are due to subarachnoid hemorrhage. Sometimes in elderly, it is due to rupture of atherosclerotic aneurysm
- Cause—rupture of congenital berry aneurysm (commonest cause, in 80% cases). Common site—posterior communicating artery, anterior communicating artery or middle cerebral artery. Other causes are—head injury, leaking from arteriovenous malformation, rupture of cerebral angioma, rupture of mycotic aneurysm from infective endocarditis, blood dyscrasia, idiopathic in some cases. Any cause of cerebral hemorrhage can also cause
- Features—severe headache, usually in the occipital region, like struck by the hammer or thunderclap. There may be vomiting, convulsion, rapid loss of consciousness
- Neck rigidity and Kernig's sign are present. Fundoscopy shows subhyaloid hemorrhage with upward concavity (boot shaped)
- There may be paralysis of 3rd, 4th and 6th cranial nerves or monoplegia or hemiplegia due to pressure effect of berry aneurysm or vascular spasm
- Lumbar puncture and CSF study shows raised CSF pressure, which is frankly hemorrhagic. Xanthochromia is seen later on. CT scan is diagnostic. CT angiogram may be done
- Treatment—control of hypertension, nimodipine, surgical treatment.

E. Carotid hemiplegia:

- Occur in middle age or elderly
- Patients are often hypertensive and atherosclerotic
- History of TIA is commonly found
- There may be history of jaw claudication
- There may be kinking of the carotid artery, inequality of the pulse volume in two carotids or a bruit may be heard at the site of the block
- Ipsilateral visual disturbances (amaurosis fugax, means transient monocular blindness) and contralateral sensory motor deficit may be present.

Features of CVD according to site of involvement of different parts of brain:

1. Cortical:
   - Usually monoplegia
   - If lesion is extensive, contralateral hemiplegia may occur
   - Speech disturbance may be present, if lesion involves the dominant hemisphere
   - Jacksonian convulsions and headache may occur
   - There may be cortical type of sensory loss, e.g. astereognosis.
2. Subcortical:
   - Usually monoplegia
   - May be contralateral hemiplegia
   - Speech disturbance may be present
   - There may be loss of postural sensibility, tactile localization and discrimination of the affected limbs due to involvement of thalamocortical fibers.
3. Internal capsule:
   - Contralateral hemiplegia

- Hemianesthesia due to damage of the sensory fibers, homonymous hemianopia due to damage of visual fibers, both of which lie posterior to the pyramidal tract in internal capsule.
- Global aphasia in left sided lesion
- Seventh cranial nerve palsy on the side of palsy, UMN type.

4. Brainstem:
   - Symptoms are—vertigo, nausea, vomiting
   - Crossed hemiplegia, brainstem syndrome, pupilary abnormality, cerebellar involvement, gaze paralysis, Horner's syndrome
   - If pons is involved—there is deep coma, pin point pupil, hyperpyrexia, decerebrate or decortical rigidity, absence of lateral eye movement on head turning
   - If involvement of midbrain and medulla—there is loss of consciousness, quadriplegia, Cheyne-Stokes breathing, decerebrate rigidity.

BRAINSTEM SYNDROME

1. Weber syndrome: Ipsilateral paralysis of 3rd cranial nerve (LMN type) with contralateral hemiplegia (crossed hemiplegia). Paralysis of upward gaze is usually present. Lesion is at midbrain.
2. Millard-Gubler syndrome: Paralysis of 6th cranial nerve (LMN type) with or without 7th cranial nerve palsy (LMN type) with contralateral hemiplegia (crossed hemiplegia). Lesion is at pons.
3. Lateral medullary syndrome (posterior inferior cerebellar artery thrombosis, also called Wallenberg's syndrome): Patient presents with acute vertigo, nausea, vomiting and diplopia, cerebellar and other signs. Features depend on the precise structures damaged and may include:
   - **Ipsilateral:**
     i. Trigeminal lesion—diminished pain and temperature (due to the involvement of descending tract and nucleus of trigeminal nerve)
     ii. Cerebellar sign (due to the involvement of cerebellum and its connection)
     iii. Horner's syndrome (due to the involvement of descending sympathetic tract)
     iv. Palatal paralysis and diminished gag reflex (there may be hoarseness and dysphagia due to vocal cord paralysis due to IXth and Xth nerve lesion)
     v. Diplopia (VIth nerve involvement).
   - **Contralateral:**
     i. Loss of pain and temperature due to spinothalamic tract involvement (in the trunk, limbs, may be in face). It is called dissociated sensory loss.
   - When there is isolated occlusion of PICA, pyramidal pathways escape and there is no hemiplegia. However, in majority of the cases, there is vertebral artery involvement and pyramidal signs (hemiplegia) are present.
4. Medial medullary syndrome:
   - It is due to occlusion of lower basilar artery or verterbral artery or one of its medial branches. It is characterized by contralateral hemiplegia which spares the face, contralateral loss of vibration and joint position sense, ipsilateral paralysis and wasting of tongue.

Note Remember the following points:

- Damage to brainstem reticular activating system leads to coma
- Upper brainstem infarction (ventral pons) leads to the locked-in syndrome
- Pseudobulbar palsy may occur after lower brainstem infarction (medullary infarction, bilateral cerebral infarction).

Differences between different types of CVD:

Points	Cerebral hemorrhage	Cerebral thrombosis	Cerebral embolism
1. Age	Elderly	Middle age	Young
2. Sex	Male	Both male and female	More in female
3. Onset	Sudden	Slowly	More sudden (stormy)
4. Precipitating factor	During excitement, exertion	During sleep	During exertion
5. Features: » Headache » Vomiting » Convulsion » Unconsciousness » Neck stiffness » Blood pressure » Pulse » Shifting hemiplegia » Cheyne-Stokes breathing » Heart » Conjugate deviation of eyes	Features: » Severe » Common » Absent » Common » May be present » High » Low » Never » Usually present » Evidence of LVH » Usually present	Features: » Less » Less » Common » Variable » Absent » May be high » Normal » Never » Usually absent » Usually normal » Rare	Features: » Absent » Less » Rare » Rare » Absent » Normal » Irregular due to AF » May be present » Usually absent » AF or MS » Rare
6. Investigations: » CSF » CT scan	Investigations: » Hemorrhagic » Hematoma	Investigations: » Clear » Infarction	Investigations: » Clear » Infarction
7. Prognosis	Poor prognosis	Good prognosis	Good prognosis, recurrence is common

Q. What are the **causes of coma** or unconsciousness?

A. As follows—(remember the mnemonic **AEIOU DAMH**)

- **A**poplexy—cerebral hemorrhage, subarachnoid hemorrhage, etc.
- **E**pilepsy
- **I**nfection (e.g. encephalitis, meningitis, cerebral malaria, severe septicemia).
- **O**pium poisoning
- **U**remia (renal failure)
- **D**iabetes mellitus (ketoacidosis, hypoglycemia, lactic acidosis, HONC)
- **A**lcohol
- **M**etabolic—metabolic acidosis
- **H**ypoglycemia, hypoxemia, hypertensive encephalopathy, hepatic coma, hypothyroidism (myxedema coma), hyponatremia, hypothermia, hyperpyrexia, head injury.

Q. What is **funny turn**? What are the **causes**?

A. Funny turn means disturbance of consciousness which may be even transient. Causes are:

- Epilepsy
- Syncope
- Simple faints
- Cough syncope
- Effort syncope
- Micturition syncope.

- Carotid sinus syncope
- Cardiac dysrhythmias
- Autonomic failure
- Basilar migraine
- Non-epileptic attacks (pseudoseizure)
- Hyperventilation
- Breath holding
- Panic attack
- Choking attack
- Apneic episode
- TIA
- Drop attack
- Tonic attack
- Hydrocephalic attack
- Hypoglycemia
- Hypocalcemia
- Severe vertigo
- Cataplexy, narcolepsy, sleep paralysis
- Night terror in children
- Paroxysmal dyskinesia
- Carcinoid syndrome, scombroid poisoning
- Pheochromocytoma
- Drug reaction (e.g. oculogyric crisis).

Q. What is **drop attack**?

A. It is characterized by sudden, unpredictable weakness of lower limbs with falling to the ground without any warning signs, dizziness or loss of consciousness. It is common in middle aged women. It is due to sudden change in lower limb tone, presumably of brainstem origin, rather than thromboembolism.

Q. What is **coma vigil**?

A. It is a state of impaired consciousness with muttering. The unconsciousness is not such as to amount coma. It is observed in infectious fever such as typhoid, dengue or pneumonia.

FRIEDREICH'S ATAXIA

CHIEF COMPLAINTS

- Weakness of the lower limbs and difficulty in walking for … years
- Wasting of the muscles of the leg and foot for … years
- Tingling, numbness of the foot for … years

HISTORY

History of present illness: According to the statement of the patient, he was reasonably well … years back. Since then, he has been suffering from weakness of both lower limbs. His weakness is progressively increasing, which has become more severe and he is unable to walk without the help of others. He also experiences progressive wasting of the muscles of lower limbs, initially in the foot followed by the leg. The patient also complains of tingling and numbness in both lower limbs. There is no history of head or spine trauma, fever, headache, convulsion, loss of consciousness or incontinence of urine. His bowel and bladder habits are normal.

History of past illness: He suffered from repeated attacks of respiratory infection and occasional fever over the past few years.

Family history: There is no history of similar illness in the family members.

Socioeconomic history: Mention according to the statement of the patient.

Drug and treatment history: For these symptoms, he took some vitamins.

Personal history: He is a nonsmoker and nonalcoholic.

GENERAL EXAMINATION

- The patient is short, ill-looking and anxious
- There is pes cavus with cocking of toes, kyphoscoliosis and high arched palate
- Mildly anemic
- No jaundice, cyanosis, clubbing, koilonychia, leukonychia or edema
- No thyromegaly or lymphadenopathy
- Pulse: 88/min
- BP: 110/80 mm Hg
- Respiratory rate: 24/min
- Temperature: 97ºF.

SYSTEM EXAMINATION

Nervous System

1. **Higher cerebral functions:**
   - Speech—scanning (or staccato speech)
   - No other abnormality.
2. **Cranial nerves**: Optic atrophy, reduced hearing. Other cranial nerves are normal.
3. **Motor system:**
   - There is wasting of muscles of both legs
   - Muscle tone—diminished in both the lower limbs

- Muscle power—normal in upper limb and diminished in the lower limbs
- Reflexes:

Jerks	Biceps	Triceps	Supinator	Knee	Ankle	Plantar
Right	Normal	Normal	Normal	Absent	Absent	Extensor
Left	Normal	Normal	Normal	Absent	Absent	Extensor

- Coordination—could not be done due to muscle weakness
- Rombergism—positive
- Gait—ataxic gait (cerebellar)
- Involuntary movement—absent.

4. **Sensory system:** vibration, position sense and two point discrimination are impaired in both the lower limbs. Other modalities of sensation are normal.
5. **Cerebellar signs:**
   - Speech—scanning
   - Horizontal nystagmus in both eyes, more in right side than left
   - Finger nose test—dysmetria, past-pointing
   - Co-ordination—could not be done due to muscle weakness
   - Gait—ataxic gait (cerebellar)
   - Dysdiadochokinesia—absent (or present)
   - Action tremor—absent (both action and intention tremor may be present)
   - Titubation—absent.

Cardiovascular System

- Pulse—88/min, regular
- BP—110/80 mm Hg
- Precordium—no abnormalities detected.

Examination of other systems reveals no other abnormalities.

SALIENT FEATURES

Mr …, 20 years old, student, normotensive, nondiabetic, nonsmoker, nonalcoholic, hailing from …, presented with weakness of both lower limbs for … years. His weakness is progressively increasing, which has become more severe and he is unable to walk without the help of others. He also experiences progressive wasting of the muscles of lower limbs, initially in the foot followed by the leg. The patient also complains of tingling and numbness in both lower limbs. There is no history of head or spine trauma, fever, headache, convulsion, loss of consciousness or incontinence of urine. His bower and bladder habits are normal. He suffered from repeated attacks of respiratory infection and occasional fever over the past few years. There is no history of similar illness in the family members. For his illness, he took some vitamins.

On Examination

General examination (mention as above)

Systemic examination (mention as above).

My diagnosis is Friedreich's ataxia.

Q. What are your **differential diagnoses?**

A. As follows:

- Multiple sclerosis
- Tabes dorsalis
- Spinocerebellar degeneration.

Q. What **investigations** should be done in Freidreich's ataxia?

A. As follows:
- CBC, ESR
- Blood sugar (high in 10%)
- Chest X-ray (cardiomegaly)
- ECG (arrhythmia)
- MRI of brain and spinal cord (shows atrophy of cerebellum and spinal cord)
- NCS (shows conduction velocity in motor fibers is normal or mildly reduced, but sensory action potentials are small or absent).

RELATED QUESTIONS AND ANSWERS

Q. What is **Friedreich's ataxia**? What are the **features**?

A. It is the most common type of hereditary ataxia, inherited as autosomal recessive trait, and in some cases inherited as autosomal dominant.

Features of Friedreich's ataxia are:
- Cause—unknown. Mutation of FRDA gene in chromosome 9. The mutation is abnormal expansion of trinucleotide repeat within a gene that code for protein 'Frataxin', whose function is to prevent intramitochodrial iron overloading
- Family history—may be present
- Usual onset—young, < 15 years (8 to 16 years)
- Presentations—progressive difficulty in walking (truncal ataxia and ataxia of lower limbs), weakness of lower limbs and dysarthria
- Signs are:
  - Cerebellar signs (dysarthria, nystagmus, intention tremor, ataxic gait, etc.)
  - Posterior column—absent vibration and position sense, positive Rhombergism
  - Corticospinal tract sign—plantar extensor, weakness
  - Peripheral nerve—absent reflexes in lower limb, wasting of muscles.
- Diabetes mellitus (common)
- Associated with kyphoscoliosis, pes cavus, cocking of toes, optic atrophy, spina bifida and hypertrophic cardiomyopathy (may cause sudden death), hearing loss
- Normal mentation (may have mild dementia)
- Prognosis—usually progresses slowly, death occurs before 40 years of age (usually 20 years after the onset of symptoms due to cardiac and respiratory complications)
- Become chair—bound 9 to 15 years after onset of symptoms. May be static and survive up to 60 years.

Q. What are the **sites** of lesion in Friedreich's ataxia?

A. As follows (there is progressive degeneration):
- Cerebellar lesion
- Spinocerebellar tract
- Posterior column lesion (loss of vibration and position sense) and dorsal root ganglia lesion
- Degeneration of peripheral sensory fibers
- Corticospinal tract lesion (lateral column lesion)
- Eye (primary optic atrophy).

Q. Why **absent tendon reflex**, but **extensor** plantar response?

A. Because of combination of pyramidal lesion, dorsal column and dorsal root lesion. Also, there is involvement of the peripheral sensory fibers that leads to sensory disturbance in the limbs and depressed tendon reflex.

Q. What are the causes of **pes cavus?**

A. As follows:

- Congenital
- Friedreich's ataxia
- Charcot-Marie-Tooth disease
- Hereditary motor and sensory neuropathy
- Spinocerebellar degeneration
- Peripheral neuropathy in childhood
- Old poliomyelitis (usually unilateral).

Q. What are the causes of **combined** cerebellar, pyramidal and dorsal column signs?

A. As follows:

- Multiple sclerosis
- Friedreich's ataxia
- Spinocerebellar degeneration
- Syphilitic meningomyelitis
- Arnold-Chiari malformation.

Note Remember the following points:

In young patient with pes cavus **plus** combination of cerebellar lesion (bilateral), UMN lesion (extensor plantar) and posterior column lesion (loss of vibration and position senses), is highly suggestive of Friedreich's ataxia.

Q. What are the different **types** of hereditary ataxias?

A. It may be of different types, with different patterns of inheritance:

1. Autosomal recessive:
   - Friedreich's ataxia
   - Ataxia telangiectasia
   - Ataxia with vitamin E deficiency.
2. Autosomal dominant:
   - Spinocerebellar ataxia type 1-28
   - Episodic ataxia
   - DRPLA (Dentatorubropallidoluysian atrophy).
3. X-linked:
   - FXTAS (Fragile X-associated tremor/ataxia syndrome).
4. Mitochondrial:
   - MELAS (Mitochondrial encephalomyopathy, lactic acidosis and stroke)
   - MERRF (Myoclonic epilepsy with ragged red tibers)
   - KSS (Kearns-Sayre syndrome).

PERIPHERAL NEUROPATHY

CHIEF COMPLAINTS

- Progressive weakness of the lower limbs for … months
- Heaviness and wasting of the lower limbs for the … months
- Pins and needles in the hands and feet for the … months.

HISTORY

History of present illness: According to the statement of the patient, he was reasonably well … months back. Since then, he has been suffering from progressive weakness of the lower limbs. Initially, the weakness was present in both feet. Then gradually it involved the legs and thighs. The severity has increased over the last few weeks. The patient now finds it difficult to walk and also feels a sense of heaviness in the lower limbs. He also noticed wasting of the muscles of the lower limbs. For the last … months, he also experiences pins and needles like sensation in the hands and feet. It is more marked at night and is progressively becoming severe leading to marked sleep disturbance. He cannot even keep the bed sheet on his legs. There is no history of any infection, joint pain or skin rash. His bowel and bladder habits are normal. He is a known diabetic for last 15 years and is on oral drugs.

History of past illness: Mention according to the patient's statement.

Personal history: He is a smoker for the last 20 years, used to take 20 cigarettes daily but not alcoholic.

Socioeconomic history: He is a government service holder and comes from a middle class family.

Drug and treatment history: He takes tablet Glipizide 5 mg twice daily for diabetes mellitus and multivitamin.

GENERAL EXAMINATION

- The patient is obese and anxious
- Mildly anemic
- No jaundice, clubbing, koilonychia, leukonychia or edema
- No lymphadenopathy or thyromegaly
- Pulse: 88/min
- BP: 150/85 mm Hg in lying position, 140/80 mm Hg in standing position
- Temperature: Normal
- Respiratory rate: Normal.

SYSTEMIC EXAMINATION

Nervous System

1. **Higher cerebral functions:** Normal.
2. **Cranial nerves:** Intact, Fundoscopy—may be retinopathy.
3. **Motor system:**

- Muscle tone: Diminished in both the lower limbs, normal in upper limbs
- Muscle power: Diminished, grade 3/5 in the lower limbs, normal in upper limbs
- There is wasting of all the groups of muscle in the feet, legs and thighs
- Reflexes:

Jerks	Biceps	Triceps	Supinator	Knee	Ankle	Plantar
Right	Normal	Normal	Normal	Diminished	Absent	Equivocal
Left	Normal	Normal	Normal	Diminished	Absent	Equivocal

- Coordination: Impaired in the lower limbs
- Rombergism: Positive
- Gait: High stepping gait
- Involuntary movements: Absent.

4. **Sensory system:**
   - Both superficial and deep sensation—impaired upto mid thigh
   - Vibration and position sense—absent in both the lower limbs.

Examination of the other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 52 years old, Government service holder, diabetic for 15 years, normotensive, smoker, nonalcoholic, hailing from …, presented with progressive weakness of the lower limbs for … months. Initially, the weakness was present in both feet. Then gradually it involved the legs and thighs. The severity has increased over the last few weeks. The patient now finds it difficult to walk and also feels a sense of heaviness in the lower limbs. He also noticed wasting of the muscles of the lower limbs. For the last … months, he also experiences pins and needles-like sensation in the hands and feet. It is more marked at night and is progressively becoming severe leading to marked sleep disturbance. He cannot even keep the bedsheet on his legs. There is no history of any infection, joint pain or skin rash. His bowel and bladder habits are normal. He is not vegetarian. He smokes about 20 cigarettes a day for the last 20 years. He gives no history of intake of drugs that may cause these symptoms. He takes Tab. Glipizide 5 mg twice daily for diabetes mellitus and multivitamin. There is no family history of such illness.

On Examination

General examination (mention as above)

Systemic examination (mention as above).

My diagnosis is diabetes mellitus with peripheral neuropathy.

Q. Could it be **MND**?

A. No. In MND, there is no sensory loss.

Q. What **investigations** should be done in polyneuropathy?

A. As follows:

- CBC, PBF (if macrocytosis is present, it indicates subacute combined degeneration due to vitamin B_{12} deficiency)
- Blood sugar
- Chest X-ray (to exclude bronchial carcinoma)
- Serum B_{12} and folate assay

- Renal (serum urea and creatinine) and hepatic function tests—if needed
- Bone marrow (if suspicion of B_{12} deficiency)
- Other investigations according to suspicion of causes (ANA and RA test)
- Nerve conduction studies (axonal or demyelinating).

RELATED QUESTIONS AND ANSWERS

Q. What are the **causes** of peripheral neuropathy?

A. As follows (mention the causes according to the age of the patient):
- Diabetes mellitus
- Nutritional deficiency (B_1, B_6, B_{12}, folic acid, pantothenic acid and vitamin E).
- Paraneoplastic sensory neuropathy (in bronchial carcinoma, lymphoma and multiple myeloma)
- Drugs (isoniazid, vincristine, phenytoin, amiodarone, statin, cisplatin, dapsone, nitrofurantoin)
- Alcoholism
- Guillain-Barré syndrome
- Infections (leprosy, HIV, typhoid and diphtheria)
- Collagen disease (SLE, polyarteritis nodosa and rheumatoid arthritis)
- Others—chronic renal failure (CRF), chronic inflammatory demyelinating polyneuropathy (CIDP)
- Idiopathic (in many cases).

Note Common causes of neuropathy:
- Diabetes mellitus
- Leprosy
- Alcohol
- Guillain-Barré syndrome
- Chronic renal failure
- Drugs like INH, vincristine
- Deficiency—vitamin B_{12}, B_1, nicotinic acid, B_6.

Q. Which part is **first involved** in peripheral neuropathy? Why?

A. Usually distal part of the limbs is commonly involved, because longer the nerve fiber earlier is the involvement. Since the nerve fibers supplying the distal parts of the limbs are longer, they are first affected.

Q. What are the causes of **painful neuropathy?**

A. As follows:
- Diabetes mellitus
- Nutritional (deficiency of vitamins B_1 and B_{12})
- Alcohol
- GBS
- Vasculitis
- Connective tissue disease
- HIV
- Uremic neuropathy
- Paraneoplastic sensory neuropathy
- Porphyria
- Arsenic or thallium poisoning.

Treatment: Tricyclic antidepressant, phenytoin, carbamazepine and topical capsaicin.

Q. What are the causes of **predominantly sensory neuropathy?**

A. As follows:
- Diabetes mellitus
- Leprosy
- Deficiency of vitamins B_1, B_6 and B_{12}
- Chronic renal failure
- Paraneoplastic neuropathy (in bronchial carcinoma)
- Drugs (INH, vincristine)
- Hereditary sensory neuropathy
- HIV
- Multiple myeloma.

Q. What are the causes of **predominantly motor neuropathy?**

A. As follows:
- Guillain-Barré syndrome, CIDP
- Charcot-Marie-Tooth disease
- Acute intermittent porphyria
- Chronic lead poisoning
- Diabetic amyotrophy
- Diphtheria
- Paraneoplastic syndrome
- POEMS (**P**eripheral neuropathy, **O**rganomegaly, **E**ndocrinopathy, **M**-protein, **S**kin changes).

Q. What are the **mechanisms** of neuropathy?

A. As follows:
- Demyelination
- Axonal degeneration
- Wallerian degeneration (after section of nerve, axonal and myelin sheath degeneration)
- Compression (called entrapment neuropathy) and there is segmental degeneration at the site of compression
- Infarction of nerve—microinfarction of nerve due to arteritis of vessels supplying the nerve (found in diabetes mellitus and polyarteritis nodosa)
- Infiltration in nerve (found in leprosy, sarcoidosis and malignancy).

Q. What are the causes of **demyelination** and **axonal degeneration?**

A. As follows:

1. Causes of demyelination:
  - Guillain-Barré syndrome
  - Hereditary sensory motor neuropathy
  - Diphtheria
  - Diabetes mellitus.

2. Causes of axonal degeneration:
  - Toxic neuropathy (alcohol and drugs)
  - Diabetes mellitus
  - Paraneoplastic syndrome
  - IgG paraproteinemia
  - Hereditary
  - Vitamin deficiency.

Q. How to **differentiate** between demyelination and axonal degeneration?

A. By NCS and electromyography (EMG):

- In demyelination, there is slowing of nerve conduction, amplitude of nerve action potential (CMAP) is normal
- In axonal degeneration, the conduction velocity is normal as axonal continuity is maintained in surviving fibers, amplitude of CMAP is reduced. Using needle EMG, denervation on the affected muscles may be demonstrated.

Q. What is **mononeuritis multiplex** and what are the **causes** of it?

A. Involvement of multiple peripheral nerve or cranial nerve by a single disease is called mononeuritis multiplex. It is due to involvement of vasa nervorum or malignant infiltration of nerves. Causes are:

- Diabetes mellitus
- Leprosy
- Rheumatoid arthritis
- Vasculitis (SLE, polyarteritis nodosa)
- Amyloidosis
- Malignancy (carcinomatous neuropathy)
- Sarcoidosis
- HIV infection
- Wegener's granulomatosis
- Acromegaly
- Paraproteinemia
- Lyme disease
- Idiopathic multifocal motor neuropathy.

Q. What are the causes of **acute mononeuritis multiplex?**

A. As follows (usually vascular):

- Polyarteritis nodosa
- Diabetes mellitus
- Collagen disease (SLE, RA).

Q. What are the **types of neuropathy in DM?**

A. As follows:

- Commonly sensory neuropathy
- Mixed motor and sensory neuropathy
- Asymmetrical motor neuropathy (diabetic amyotrophy)
- Autonomic neuropathy
- Mononeuropathy
- Mononeuritis multiplex.

It may be symmetrical or asymetrical:

1. **Symmetrical***:*
   - Distal symmetrical primary sensory polyneuropathy
   - Subacute or chronic proximal symmetrical motor neuropathy
   - Autonomic neuropathy.
2. **Asymmetrical***:*
   - Diabetic amyotrophy
   - Cranial mononeuropathy or mononeuritis multiplex
   - Mononeuropathy involving trunks or limbs
   - Entrapment neuropathy.

Q. What is the **mechanism** of neuropathy in DM?

A. As follows:
- Axonal degeneration
- Patchy or segmental demyelination
- Involvement of intraneural capillaries.

Q. What is the **pathogenesis** of diabetic neuropathy?

A. As follows:
1. Metabolic theory: Increased neuronal concentration of glucose results in increased conversion of glucose to sorbitol. The resultant increase in diacylglycerol, protein kinase C and Na-K ATPase activity causes neuronal loss and demyelination.
2. Vascular theory: Increased aldose reductase activity causes decreased NO that results in reduced blood flow in vasa nervorum.
3. Altered metabolism of fatty acid.
4. Nutritional: Reduced concentration of nerve growth factor, vascular endothelial growth factor and erythropoetin.
5. Oxidative stress.

Q. What are the **causes of thickening of nerves?**

A. As follows:
- Leprosy
- Neurofibroma
- Amyloidosis
- Acromegaly
- Sarcoidosis
- Charcot-Marie-Tooth disease (hereditary motor and sensory neuropathy)
- Repeated friction or trauma
- Refsum disease
- Dejerine-Sottas disease (hypertrophic peripheral neuropathy).

Q. What are the causes of **autonomic neuropathy**?

A. As follows:
- Diabetes mellitus (commonest cause)
- Guillain-Barré syndrome
- Amyloidosis
- Toxin (vincristine)
- Paraneoplastic syndrome
- Porphyria
- AIDS
- Shy-Drager syndrome
- Riley-Day syndrome (familial dysautonomia)
- Hereditary sensory and autonomic neuropathy.

Q. How to **test autonomic function**?

A. As follows:
1. Simple reflex test (common in practice):
   - Heart rate responses to Valsalva maneuver (15 seconds) on R-R interval of ECG—ratio of longest to shortest R-R interval is normally 1.21 or more. If 1.20 or less, it is abnormal.
   - Heart rate responses to deep breathing (6 breaths over 1 minute)—maximum-minimum heart rate of 15 or more is normal, 11 to 14 is borderline and 10 or less is abnormal.

- Heart rate responses to standing after lying—ratio of R-R interval of 30th to 15th beats—if 1.04 or more it is normal, 1.01 to 1.03 is borderline and 1.00 or less is abnormal.
- Blood pressure response to standing—systolic BP fall (mm Hg) 10 or less is normal, 11 to 29 is borderline and 30 or more is abnormal.

2. Special tests:
   - Heart rate and blood pressure response to sustained hand grip
   - Heart rate variability using power spectral analysis of ECG monitoring
   - Heart rate and blood pressure variability using time (domain analysis of ambulatory monitoring)
   - MIBG (met-iodobenzylguanidine) scan of the heart.

Q. What is the **prognosis** of autonomic neuropathy in diabetes mellitus?

A. Development of autonomic neuropathy in diabetic mellitus is less clearly related with poor glycemic control than somatic neuropathy. Improved control of diabetes rarely improves the symptoms. Within 10 years of development of symptoms of autonomic neuropathy, 30 to 50% die from sudden cardiorespiratory arrest, cause of which is unknown. Patients with postural hypotension (a drop of systolic pressure > 30 mm Hg on standing from supine) have highest mortality.

GUILLAIN-BARRÉ SYNDROME

CHIEF COMPLAINTS

- Weakness of both lower limbs for … days
- Difficulty in walking for … days.

HISTORY

History of present illness: According to the statement of the patient, she was reasonably well … days back. Then she suffered from mild fever, cough and sore throat from which she recovered in 4 days. Adult 10 days later, she experiences weakness of both lower limbs. Initially at both feet, then sequentially involving the legs and the thighs. For … days, her weakness is gradually increasing and she feels difficulty in walking. For the last … days, she is completely bedridden and unable move her limbs, and experiences a sense of heaviness. Her bowel and bladder habits are normal. She does not have any breathing difficulty, nasal regurgitation or difficulty in swallowing. There is no history of trauma, operation, vaccination or previous episode of such illness.

History of past illness: Nothing significant.

Drug and treatment history: Nothing significant.

Personal history: She is married and has two sons. She is a nonsmoker.

Socioeconomic history: She comes from a lower middle class family.

Family history: Nothing significant.

GENERAL EXAMINATION

- The patient is bedridden, looks ill and anxious
- Mildly anemic
- No jaundice, cyanosis, clubbing, koilonychia, leukonychia or edema
- No lymphadenopathy or thyromegaly
- Pulse: 88/min
- BP: 110/75 mm Hg
- Temperature: Normal
- Respiration: Normal.

SYSTEMIC EXAMINATION

Nervous System

1. **Higher cerebral functions**: Normal.
2. **Cranial nerves** including fundoscopy: Intact.
3. **Motor system:**
   - Muscle tone—diminished in both lower limbs
   - Muscle power is grade 1/5 in lower limbs and normal in the upper limbs
   - Wasting—Absent
   - Reflexes:

Jerks	Biceps	Triceps	Supinator	Knee	Ankle	Plantar
Right	Normal	Normal	Normal	Absent	Absent	Equivocal
Left	Normal	Normal	Normal	Absent	Absent	Equivocal

- Coordination—normal in upper limbs, could not be elicited in lower limbs
- Rombergism—could not be tested
- Gait—The patient is unable to walk.
- Involuntary movement—absent

4. **Sensory system**: No abnormality detected.

Examination of the other systems reveals no abnormalities.

SALIENT FEATURES

Mrs …, 42 years old, housewife, normotensive, nondiabetic, nonsmoker, hailing from …, presented mild fever, cough and sore throat from which she recovered in 4 days. About 10 days later, she experiences weakness of both lower limbs. Initially at both feet, then sequentially involving the legs and the thighs. For … days, her weakness is gradually increasing and she feels difficulty in walking. For the last … days, she is completely bedridden and unable move her limbs, and experiences a sense of heaviness. Her bowel and bladder habits are normal. She does not have any breathing difficulty, nasal regurgitation or difficulty in swallowing. There is no history of trauma, operation, vaccination or previous episode of such illness. There is no family history of such illness. She was treated with vitamins by local doctors.

On examination
General examination (mention as above)
Systemic examination (mention as above).

My diagnosis is flaccid paraplegia, more likely due to Guillain-Barré Syndrome.

Q. What are the **causes** of flaccid paraplegia?

A. As follows:
- Guillain-Barré syndrome
- Motor neuropathy due to any cause
- Tabes dorsalis
- Freidreich's ataxia
- Progressive muscular atrophy (one type of MND)
- Acute inflammatory demyelinating polyradiculopathy (AIDP)
- HCR.

Q. What **investigations** do you suggest in GBS?

A. As follows:
- CSF analysis—typical finding is 'albuminocytological dissociation' (albumin may be very high, > 1000 mg %, lymphocytes are slightly raised or normal, < 20/mm^3. If lymphocyte is > 50, GBS is unlikely. CSF protein may be normal in first 10 days)
- Frequent monitoring of respiratory function tests (FVC, FEV_1, PEFR)
- Arterial blood gas analysis (as respiratory failure may occur at any time)
- Nerve conduction study (it shows slow conduction or conduction block. Demyelinating neuropathy, usually found after 1 week)

- Investigation to identify CMV, mycoplasma or campylobacter should be done
- Serum electrolyte.

Note

Triad of acute symmetrical ascending paralysis of limbs, areflexia and albumino: cytological dissociation in CSF is highly suggestive of GBS.

RELATED QUESTIONS AND ANSWERS

Q. What is **GBS**?

A. It is a postinfective demyelinating neuropathy of unknown cause, usually 1 to 3 weeks after respiratory infection, diarrhea and occasionally after vaccination or surgery. There is demyelination of peripheral nerve or spinal root, which is immunologically mediated. This may follow after infection with cytomegalovirus or mycoplasma or *Campylobacter jejuni*. GBS is monophasic and does not recur.

Q. What is the **cause** of GBS? What is the **mechanism**?

A. The GBS develops 1 to 3 weeks after respiratory infection or diarrhea (mainly by campylobacter) in 70% cases. Triggering factors may be *Campylobacter jejuni*, CMV, mycoplasma, herpes zoster, HIV, EBV infection.

There are 2 mechanisms:
1. Demyelinating (acute inflammatory demyelinating neuropathy, AIDP)
2. Axonal, which may be:
   - Motor (acute motor axonal neuropathy, AMAN)
   - Sensorimotor (acute motor and sensory axonal neuropathy, AMSAN).

There is predominantly cell-mediated inflammatory response to the myelin protein of spinal roots, peripheral and extra-axial cranial nerves. It is probably triggered by some infecting microorganisms. There is release of inflammatory cytokines that blocks nerve conduction and is followed by a complement mediated destruction of the myelin sheath and the associated axon.

It is a monophasic disease and does not recur.

Q. How does the patient of GBS usually **present?**

A. As follows:
- History of upper respiratory tract infection (URTI) or gastroenteritis (viral or bacterial)
- After 1 to 3 weeks, weakness of lower limbs that ascends over several weeks (ascending paralysis). It may advance quickly, affecting all the limbs at once and can lead to paralysis (quadriplegia)
- Respiratory paralysis in 20% case. Progressive respiratory involvement and paralysis is the main problem
- Paresthesia and pain in back and limbs may occur
- Facial and bulbar weakness
- Autonomic dysfunction—change of blood pressure, tachycardia, increased sweating, dysrhythmia may occur.

Q. What are the clinical **findings** in GBS?

A. As follows:
- Flaccid paralysis involving lower limbs and may involve all 4 limbs
- Loss of all reflexes
- Bilateral facial palsy (in 50% cases, unilateral in 25% cases)
- Sensory loss—minimum or absent
- Sphincter involvement (rare).

Note Remember the following points:

- Diffuse weakness with loss of all reflexes—a very striking finding in GBS
- GBS may be associated with Hodgkin's lymphoma
- Papilledema may develop
- May develop SIADH.

Diagnostic criteria for GBS:
Features required:

- Progressive weakness of both legs and arm
- Areflexia.

Features supportive:

- Progression over days, 4 weeks
- Relative symmetry
- Mild sensory symptoms or signs
- Cranial nerve involvement (bi-facial palsy)
- Recovery begins after 2 to 4 weeks
- Autonomic dysfunction
- Absence of fever
- Increased CSF protein with cell count <10/μL
- NCS—nerve conduction slowing or block.

Q. What are the variants of GBS?

1. **Regional:**
   - Fisher syndrome of ophthalmoplegia, ataxia and areflexia
   - Cervico-brachial-pharyngeal, often with ptosis
   - Oculopharyngeal weakness
   - Predominant paraparesis
   - Bilateral facial or abducens weakness with distal paresthesias
   - Ophthalmoplegia with GQ1b autoantibodies.
2. **Functional:**
   - Generalized ataxia without dysarthria or nystagmus
   - Pure sensory
   - Pure motor
   - Pandysautonomia
   - Axonal (AMAN).

Q. What are the **causes of motor neuropathy**?

A. As follows:

- Guillain-Barré syndrome
- Acute intermittent porphyria
- Diphtheria
- Diabetic amyotrophy
- Charcot-Marie-Tooth disease
- Chronic lead poisoning
- Paraneoplastic syndrome.

Q. How to **treat** GBS?

A. As follows:

- Ideally the patient should be treated in ICU and respiratory function should be monitored regularly (vital capacity and arterial blood gases). The patient may require artificial ventilation
- High dose intravenous gamma globulin should be given to all patients (it reduces the duration and severity). Dose is 400 mg/kg/day for 5 days. It is helpful, if given within 14 days. It may precipitate angina or myocardial infarction. In congenital IgA deficiency, it may cause allergic reaction
- Plasma exchange, if given within 14 days is equally effective in reducing the severity and duration of GBS
- Steroid has no proven value (may worsen). Methylprednisolone with immunoglobulin has no proven benefit
- Plasmapharesis may be required
- Physiotherapy is the mainstay of therapy
- Prevention of pressure sore and venous thrombosis
- Other symptomatic treatment.

Indication of ventilation:

- Impending respiratory failure—tachypnea, decrease in arterial O_2 tension < 85 mm Hg, FVC <20 mL/kg, maximum inspiratoy pressure <30 cm H_2O, maximum expiratory pressure <40 cm H_2O.
- FVC < 1.5 L
- PaO_2 < 10 κPa
- $PaCO_2$ > 6 κPa
- Rapid progression of disease
- Bulbar dysfunction
- Bilateral facial palsy
- Autonomic involvement.

Q. What are the **indications** of IV Ig in GBS?

- Incipient respiratory failure
- Patient unable to walk
- Oropharyngeal weakness
- Autonomic dysfunction
- Rapid progression of disease
- Ideally IV Ig should be given within 2 weeks of onset of disease.

Q. What are the **side effects** of IV Ig?

- Renal failure
- Proteinurea
- Nephrotic syndrome
- Aseptic meningitis
- Stroke
- Myocardial infarction
- CCF
- Anaphylaxis in IgA deficiency.

Q. What are the **adverse effects** of plasmapheresis?

A. As follows:

- The need for large bore venous axis
- Pneumothorax

- Infection
- Hemorrhage
- Hypotension
- Hypoprothrombinemia
- Cardiac arrhythmia
- Electrolyte imbalance.

Q. What are the **dangerous complications** of GBS **(cause of death)?**

A. As follows:
- Respiratory muscle paralysis. The patient may develop respiratory failure within hours
- Bulbar palsy (dysphagia, nasal regurgitation)
- Cardiac conduction block
- Cardiac arrythmia.

Q. What is the **prognosis** of GBS?

A. As follows:
- 80% recovery, may take several months (3 to 6 months). If axons have been damaged, the regeneration may require 6 to 18 months or longer
- 10% residual disability
- 3 to 5% die (in some study upto 10% death).

Adverse prognostic factors:
- Preceding GI infection
- > 60 years of age
- The most severe or rapidly evolving form of the disease (maximum disability within 7 days)
- Descending paralysis
- Bulbar weakness
- Autonomic dysfunction
- Asymmetrical weakness
- Very high CSF protein
- Evidence of widespread axonal damage
- Those requiring early and prolonged mechanical ventilatory assistance.

Good prognostic factors:
- Symmetrical involvement
- Slowly progressive
- Facial nerve involvement
- Young age
- Preceding hostory of respiratory infection
- Demyelinating disease
- No respiratory involvement
- Ascending paralysis
- Early treatment
- Early recovery.

Q. What is **Miller-Fisher syndrome?**

A. It is a variant of GBS characterized by triad of ophthalmoplegia, ataxia and areflexia. It is a rare disease. Antibodies to ganglioside GQ1b may be found.

CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY

CHIEF COMPLAINTS

- Numbness and paresthesia of both upper and lower limbs for … years
- Weakness and wasting of both lower and upper limb for … years.

HISTORY

History of present illness: According to the statement of the patient, he was reasonably well … years back. Since then, he noticed progressive numbness and paresthesia of both upper and lower limbs. It first started in the right lower limb and gradually involved the left lower limb and upper limbs in an ascending manner. He is also complaining of weakness and wasting of both upper and lower limbs which is of gradual onset. Initially it was progressively increasing, but for last … months, it is static. He does not give any history of headache, vomiting, neck pain. His bowel and bladder habits are normal.

History of past illness

Drug and treatment history

Personal history

Socioeconomic history

Family history: Mention according to the patient's statement.

GENERAL EXAMINATION

- The patient is bedridden, looks ill and anxious
- Mildly anemic
- No jaundice, cyanosis, clubbing, koilonychia, leukonychia or edema
- No lymphadenopathy or thyromegaly
- Pulse: 72/min
- BP: 110/70 mm Hg
- Temperature: Normal
- Respiration: Normal.

SYSTEMIC EXAMINATION

Nervous System

1. **Higher psychic functions:** Normal.
2. **Cranial nerves:** Intact.
3. **Motor system:**
   - Muscle tone—diminished in all four limbs
   - Muscle power—is grade 2/5 in all four limbs
   - Wasting—present
   - Reflexes:

Jerks	Biceps	Triceps	Supinator	Knee	Ankle	Plantar
Right	Absent	Absent	Absent	Absent	Absent	Equivocal
Left	Absent	Absent	Absent	Absent	Absent	Equivocal

- Coordination—could not be tested (because of muscular weakness)
- Rombergism—could not be tested (because of muscular weakness)
- Gait—the patient is unable to walk
- Involuntary movement—absent.

4. **Cerebellar functions:** Intact.
5. **Sensory system:**
   - Superficial and deep sensations are impaired
   - Vibration and position sense—absent.
6. **Fundoscopy:** Normal.

Examination of the other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 48 years old, school teacher, normotensive, nondiabetic, nonsmoker, hailing from …, presented with numbness and paresthesia of both upper and lower limbs for … years. which first started in right lower limb and gradually ascending, then left lower limbs and upper limbs which is progressive in nature. He is also complaining of weakness and wasting of both upper and lower limbs which is of gradual onset. Initially it was progressively increasing, but for last … months it is static. He does not give any history of headache, vomiting, neck pain. His bowel and bladder habits are normal. There is no family history of such illness. He was treated with vitamins.

On examination
General examination (mention as above)
Systemic examination (mention as above).

My diagnosis is chronic inflammatory demyelinating polyneuropathy (CIDP).

Q. What are your **differential** diagnoses?

A. As follows:
- GBS
- Electrolyte imbalance (hypokalemia or hyperkalemia)
- Acute transverse myelitis.

RELATED QUESTIONS AND ANSWERS

Q. What is **CIDP**?

A. It is an autoimmune demyelinating disease of peripheral nerves characterized by weakness and sensory loss in limbs, peripheral nerve enlargement and high CSF protein. It affects young adults.

Q. What are the **presentations** of CIDP?

A. As follows:
- Common in young adult, males slightly more affected than female
- Onset is usually gradual, but sometimes subacute
- Features are like GBS
- Relapsing and remitting or progressive generalized neuropathy
- Sensory, motor or autonomic nerves can be involved, but the signs are predominantly motor. Some patients may present with pure sensory ataxia
- There may be external ophthalmoplegia in some cases
- A variant causes only motor involvement (multifocal motor neuropathy, MMN).

Q. What is the **difference** between CIDP and GBS?

A. CIDP is clinically similar to GBS except that it has a relapsing or steadily progressive course over months or years and that autonomic dysfunction is generally less common. It is less common than GBS. CIDP responds to steroid, while GBS does not.

Q. How to **diagnose**?

A. As follows:

- CSF examination (high protein, acellular)
- NCV of peripheral nerves—GBS like feature (marked slowing of motor and sensory conduction, and focal conduction block). Signs of partial denervation may be found due to secondary axonal degeneration
- MRI (plaques resembling multiple sclerosis are found in brain and spinal cord in some cases)
- Nerve biopsy (shows segmental demyelination).

DIAGNOSTIC CRITERIA OF CIDP

1. **Mandatory clinical criteria:**
   - Progressive or relapsing muscle weakness for 2 months or longer
   - Symmetrical proximal and distal weakness in upper or lower extremities
   - Hyporeflexia or areflexia.
2. **Mandatory laboratory criteria**:
   - Nerve conduction studies with features of demyelination motor nerve conduction <70% of lower limit of normal
   - Cereborspinal fluid protein level >45 mg/dL, cell count <10/μL.
   - Sural nerve biopsy with features of demyelination and re-myelination including myelinated fibre loss and perivascular inflammation.
3. **Mandatory exclusion criteria:**
   - Evidence of relevant systemic disease or toxic exposure
   - Family history of neuropathy
   - Nerve biopsy findings incompatible with diagnosis.

Q. How to **treat**?

A. Treatment of CIDP depends on severity of disease:

1. **Mild deficit**—follow-up only, there may be spontaneous recovery:
2. **Functionally significant deficit:**
   - Prednisolone 60 to 80 mg daily for 2 to 3 months or until response occurs. If no response in 3 months, then higher dose may be tried. After response, steroid is gradually tapered, but low dose steroid may be needed to continue for a long time.
   - Intravenous immunoglobulin (0.4 g/kg/day for 5 days)—usually used as an initial treatment with steroid
   - Plasma exchange—2 to 3 treatment per week for 6 weeks may be done
   - Others—if the above treatment fails, then immunosuppressive agents like azathioprine, methotrexate, cyclosporine or cyclophosphamide may be given
   - Multifocal motor neuropathy (MMN) is best treated by IV Ig.
3. **Severe disease, non-ambulatory:** Plasma exchange 2 to 3/week for 6 weeks and prednisone 60 to 80 mg/day.

Q. What is the **prognosis**?

A. Progress is variable. With drug therapy, most CIDP cases run a mild course over many years. There is occasional spontaneous recovery with time, but the disorder frequently follows progressive course leading to severe functional disability.

MYASTHENIA GRAVIS

CHIEF COMPLAINTS

- Weakness after activity for … months
- Difficulty in speaking, chewing and swallowing for … months
- Drooping of the upper eyelids after activity for … months.

HISTORY

History of present illness: According to the statement of the patient, she was reasonably well … months back. Since then, she noticed extreme weakness following activity or exercise. These symptoms are usually more marked towards the end of the day. She also noticed difficulty in chewing, swallowing, speaking and drooping of the upper eyelid following activity for … months. There is no history of any abnormality of sensation, fever, weight loss, tremor or involuntary movements, skin rash, joint pain or swelling. Her bowel and bladder habits are normal. She is normontensive and nondiabetic.

History of past illness: Mention according to the patient's statement.

Drug and treatment history: There is no history of taking any offending drug (e.g. D-penicillamine, etc.).

Personal history: Mention according to the patient's statement.

Socioeconomic history: Mention according to the patient's statement.

Family history: Mention according to the patient's statement.

GENERAL EXAMINATION

- Ill looking and anxious
- Bilateral partial ptosis: Present
- Mildly anemic
- No jaundice, cyanosis, clubbing, koilonychia, leukonychia or edema
- No lymphadenopathy or thyromegaly
- Pulse: 76/min
- BP: 120/80 mm Hg
- Temperature: Normal
- Respiration: Normal.

SYSTEMIC EXAMINATION

Nervous System

1. **Higher cerebral functions:** Normal
2. **Cranial nerves including fundoscopy:** Normal
3. **Motor system:**
   - Muscle tone—normal
   - Muscle power—grade 4/5 in all four limbs.
   - Fatigability test (Ceiling test)—There is worsening of ptosis after sustaining upward gaze. Weakness of extraocular muscles of both sides (there may be double vision)

- Counting test—When the patient is asked to count 1 to 100, voice becoming low and ill distinct.
- Ice on eyes test
- Reflexes:

Jerks	Biceps	Triceps	Supinator	Knee	Ankle	Plantar
Right	Normal	Normal	Normal	Normal	Normal	Flexor
Left	Normal	Normal	Normal	Normal	Normal	Flexor

- Coordination—normal
- Rombergism—normal
- Gait—normal
- Involuntary movement—absent.

4. **Cerebellar function:** Intact
5. **Sensory system:** Intact.

Examination of the other systems reveals no abnormalities.

SALIENT FEATURES

Mrs …, 40 years old, housewife, normotensive, nondiabetic, nonsmoker, hailing from …, presented with extreme weakness following activity or exercise for … months. These symptoms are usually more marked towards the end of the day. She also noticed difficulty in chewing, swallowing, speaking and drooping of the upper eyelid following activity for … months. There is no history of any abnormality of sensation, fever, weight loss, tremor or involuntary movements, skin rash, joint pain or swelling. Her bowel and bladder habits are normal. There is no history of taking D-penicillamine, ciprofloxacin, etc. There is no family history of such illness.

On examination

General examination (mention as above)

Systemic examination (mention as above).

My diagnosis is myasthenia gravis.

Q. What are your **differential diagnoses?**

A. As follows:

- Eaton Lambert syndrome
- Drug induced myasthenia
- Polymyositis
- Hypokalemic periodic paralysis.

Q. What **investigations** should be done in myasthenia gravis?

A. As follows:

- Complete blood count and ESR
- Chest X-ray (to exclude bronchial carcinoma)
- CXR right lateral view and CT scan of chest (to exclude thymoma)
- Edrophonium (Tensilon) test
- Vital capacity
- Serum acetylcholine receptor antibody (anti-AChR antibody, found in 80 to 90% patients with generalized myasthenia gravis. In pure ocular MG, this is present in 50%).

- Serum anti-MuSK antibody (antibody against muscle specific receptor tyrosine kinase, present with predominantly bulbar, facial and neck muscle involvement). It is positive in anti-AChR antibody negative patient and in pure ocular MG
- RNS—(progressive decremental response to repetitive nerve stimulation at 5 to 10 Hz)
- Single fiber EMG—evidence of neuromuscular blockade in the form of jitter and blocking of motor action potentials
- To see other associations—thyroid function test, antithyroid antibody, antiskeletal muscle antibody (suggest presence of thymoma), ANA, rheumatoid factor, serum CPK, antibody against intrinsic factor.

Q. What is **Tensilon test**?

A. 2 mg edrophonium is injected initially to see any untoward side effect. If no side effect, another 8 mg is given after half a minute. Improvement in muscle power occurs within 30 seconds and persists for up to 2 to 3 minutes. Sensitivity is 80%. Occasionally, there may be bronchospasm and syncope. Resuscitation facilities must be available. Atropine should be kept ready.

Q. What is the finding in **repeated nerve stimulation test (RNS)**?

A. It shows more than >10% decrement at 3 Hz.

RELATED QUESTIONS AND ANSWERS

Q. What is **myasthenia gravis?**

A. Myasthenia gravis is an autoimmune disease of skeletal muscle due to antibody against post-synaptic nicotinic acetylcholine receptor (AChR), characterized by fluctuating weakness specially ocular, facial, neck and bulbar muscles following activity. This antibody blocks neuromuscular transmission by depletion of post-synaptic receptors.

Below the age of 50 years, it is more common in women and associated with other autoimmune disease and thymic hyperplasia. Over 50 years, it is common in men and associated with thymic atrophy or thymic tumor.

Q. What is the **pathology** in MG?

A. Myasthenia gravis is caused by IgG antibodies against acetylcholine receptor protein. Immune complex of anti-AChR IgG and complement are deposited in the post-junctional membrane of the neuromuscular junction, which block neuromuscular transmission and initiate a complement mediated inflammatory response, which reduces the number of acetylcholine receptors and damages the end plate.

Thymic hyperplasia occurs in 70% myasthenic patient below the age of 40 years. In 10 to 15% cases, thymoma is present, incidence increases with age. Antibodies to striated muscles can be found in these patients.

Young patients without thymoma have an increased association with HLA-B8 and DR3.

Q. Which **muscles are commonly involved** in MG?

A. Muscle groups involved in order are—extraocular, bulbar (swallowing or chewing), face, neck, limb girdle and trunk. Cardiac muscle is not affected.

Q. Name one **drug** which can cause myasthenia gravis.

A. Penicillamine, (IFN-α also).

Q. What is **ice on eyes test?**

A. Ice cube is placed on patient's eyes and wait for 2 minutes or upto maximum tolerability. Ptosis is improved.

This test is highly specific and sensitivite in myasthenic diplopia.

Q. What are the **features** of myasthenia gravis? What **bedside tests** are done in MG?

A. Increasing muscular fatigue or weakness following activity. Following bedside test can be done:

- Ask the patient to count from 1 to 50—voice deteriorates and becomes nasal
- Ask to look straight or at the ceiling—ptosis will occur
- Ask the patient to close the eye tightly—after some time eyelids separate (peek) to show white sclera. This is called peek sign.

Note Remember the following:

Reflexes are normal.

Q. What is **myasthenic crisis**?

A. It is the exacerbation of symptoms of myasthenia gravis. May be severe and require artificial ventilation in 10% cases. The patient with bulbar and respiratory involvement are prone to respiratory infection. It may occur in patients who are getting no or inadequate treatment, due to low dose or following development of drug resistance. Precipitating factors are exertion, extremes of temperature, respiratory infection and surgery. The patient should be closely monitored for pulmonary function and should be treated in ICU. Treatment includes:

- Respiratory assistance and pulmonary physiotherapy
- Stop all cholinesterase inhibitors
- Plasmapheresis or IV immunoglobulin
- Antibiotic, if there is infection.

Q. What is **cholinergic crisis**?

A. Overdose of anticholinesterase drugs may cause cholinergic crisis, which is due to depolarization block of motor end plates. Features of cholinergic crisis are muscle fasciculation, paralysis, pallor, sweating, excessive salivation, lacrimation, bronchial secretion, small pupil (meiosis), abdominal colic, diarrhea, urinary incontinence, etc.

There may be respiratory insufficiency, confusion and collapse. Infection, diarrhea, aminoglycoside, penicillamine, steroid, etc may precipitate the crisis. Edrophonium should be avoided in these patients.

Q. How to **differentiate** between myasthenic crisis and cholinergic crisis?

A. The clinical features are as above. In both cases, patient complains of weakness.

- But muscarinic features are present only in cholinergic crisis, but absent in myasthenic crisis.
- Pupil in constricted or small in cholinergic crisis, but normal in myasthenic crisis.
- In myasthenic crisis—edrophonium causes quick improvement.

Q. How to **treat** MG?

A. As follows:

1. Symptomatic: Anticholinesterase drugs, e.g. pyridostigmine 60 mg tablet (4 to 16 tablets in divided doses up to five times a day). Duration of action is 3 to 4 hours. It prolongs the action of acetylcholine by inhibiting the action of acetylcholinesterase (side effects—overdose can cause cholinergic crisis characterized by severe muscle weakness. Muscarinic side effects like excessive salivation, lacrimation, bronchial secretion, abdominal pain, diarrhea, miosis, urinary incontinence, etc. Oral atropine 0.5 mg helps to reduce this.
2. Definitive:
   - Thymectomy—for all patients with thymoma and thymic hyperplasia.
   - Plasmapheresis—given in severe myasthenia or myasthenic crisis or preoperative preparation. A course of 5 exchanges, each of 3 to 4 liters fluid is given over a period of 2 weeks.

- Intravenous immunoglobulin: It is an alternative to plasma exchange in short-term treatment of severe myasthenia. Usual dose is 0.4 g/kg daily for 5 days. Improvement occurs in 70% cases. Side effects are headache and fluid overload, flu-like symptoms and anaphylaxis with IgA deficiency.
- Steroid: Initially there may be marked exacerbation of myasthenic symptoms and treatment should be initiated in hospital. To minimize the side effect, low dose prednisolone initially 5 mg/day, increase 5 mg/week up to 1 mg/kg. Continued for 1 to 3 months, then gradually modified to an alternate day regimen over the course of additional 1 to 3 months. On remission, reduce the dose (may take months). About 70% patients improve with steroid. Azathioprine may be added (2.5 mg/kg daily) or weekly methotrexate may be given. Sometimes, IV methylprednisolone may be tried.
- Other immunosuppressive agents, e.g. azathioprine (2.5 mg/kg daily), mycophenolate mofetil may be given.

Q. What are the **exacerbating factors** of MG?

A. Exercise, infection, emotion, change of climate, pregnancy, magnesium enema, drugs (aminoglycosides, penicillamine, propranolol, morphine, barbiturates, procanamide, quinidine, ciprofloxacin, quinine, antiarrhythmic drugs).

Q. What is the **role of thymectomy**?

A. Thymectomy should be performed in any antibody positive patient under 45 years with symptoms not confined to extraocular muscles, unless the disease has been established for more than 7 years. If thymoma is present, thymectomy is necessary to prevent tumor spread. If there is no thymoma, thymectomy is still beneficial in 60% patients and some patients go into drug free remission. However, the improvement is noticed 1 to 10 years after surgery.

Q. What is the **prognosis** after thymectomy?

A. Thymectomy improves prognosis, more so in women than men with positive AChR antibodies, even in patients without a thymoma.

Cases positive for anti-MuSK antibodies—do not improve following thymectomy. For these patients, plasmapheresis is the choice of treatment.

Q. What **drugs** should be avoided in MG?

A. Aminoglycoside, penicillamine, ciprofloxacin, quinine, antiarrhythmic drugs.

Q. What diseases are **associated** with MG?

A. Since MG is an autoimmune disease, it may be associated with other autoimmune diseases like thyrotoxicosis, hypothyroidism, diabetes mellitus, dermatomyositis, rheumatoid arthritis, SLE, Sjogren's disease, pernicious anemia, sarcoidosis, pemphigus, etc.

Q. What is **Eaton-Lambert syndrome (LEMS)**?

A. It is a paraneoplastic syndrome characterized by proximal muscle weakness, wasting and easy fatigability. It commonly involves the lower limbs, but may involve any muscle. Bulbar symptoms are rare (unlike MG).

Cause: There is defect in acetylcholine release at the neuromuscular junction, thought to be due to an autoantibody against P/Q type voltage gated calcium channel (VGCC—present in 90% case) on the motor nerve terminal. It is commonly due to small cell carcinoma of lung. May be associated with or may precede 1 to 2 years before the manifestations of carcinoma.

Features of LEMS:

- There are diminished or absent tendon reflexes (cardinal sign), appears immediately after sustained contraction of relevant muscle
- There is transient improvement in muscle strength and deep tendon reflexes following brief exercise. Muscle power increases after repeated activity (reverse of myasthenia gravis).

Investigation: EMG is diagnostic. There is progressive incremental response following repeated stimulation (reverse of myasthenia gravis, where there is progressive decremental response).

Treatment:

- Prednisolone plus azathioprine may be helpful
- Occasionally plasmapheresis
- 3, 4 diaminopyridine (DAP) is given
- Guanidine hydrochloride may help
- IV immunoglobulin
- No response to anticholinesterase drug. However anticholinesterase (pyridostigmine or neostigmine) either alone or in combination with guanidine hydrochloride shows variable response
- Treatment of primary cause (e.g. bronchial carcinoma).

Q. What are the **differences** between Eaton-Lambert syndrome and myasthenia gravis?

A. As follows:

Topic	Eaton-Lambert syndrome	Myasthenia gravis
1. Onset	From limbs	With ptosis
2. Course	Limbs to eyes	Eyes to limbs
3. Association	Malignancy, commonly small cell carcinoma of lung	Thymoma
4. Outcome of exercise	Improvement	Aggravate
5. RNS (EMG)	Incremental	Decremental
6. AChR antibody	Absent	Present

SPASTIC PARAPLEGIA (CORD COMPRESSION)

CHIEF COMPLAINTS

- Weakness of both lower limbs and difficulty in walking for … months
- Inability to void urine for … months
- Low back pain for … months
- Tingling and numbness of both lower limbs for … months.

HISTORY

History of present illness: According to the statement of the patient, he was reasonably well … months ago. Since then, he has been suffering from weakness of both lower limbs, which is gradually increasing and now he is unable to move his lower limbs and is unable to walk without the help of others. He also complains of difficulty in micturition and urinary incontinence for the last … days. The patient also complains of low back pain for … months, which is increased with even minor activities and on movement. For the last … months, he also experiences tingling and numbness on both lower limbs, more on right than left. There is no history of trauma, fever, weight loss, cough, burning in micturition or pain in other areas. His bowel habit is normal. Other systemic enquiry revealed no complaints.

History of past illness: He has no such events earlier, no visual compliants, and no history of vaccination.

Family history: There is no history of similar illness in his family.

Drug and treatment history

Personal history

Socioeconomic history: Mention according to the patient's statement.

GENERAL EXAMINATION

- Ill looking, anxious and bedridden
- Mildly anemic
- No jaundice, cyanosis, clubbing, koilonychia, leukonychia or edema
- No lymphadenopathy or thyromegaly
- Urinary catheter in situ
- Pulse: 72/min
- BP: 120/70 mm Hg
- Temperature: Normal
- Respiration: Normal.

SYSTEMIC EXAMINATION

Nervous System

1. **Higher cerebral functions:** Normal
2. **Cranial nerves including fundoscopy:** Intact
3. **Motor system:**
   - Muscle tone—increased in both lower limbs, normal in both upper limbs

- Muscle power—diminished (grade 0/5) in both lower limbs, normal in both upper limbs.
- Wasting—absent
- Reflexes:

Jerks	Biceps	Triceps	Supinator	Knee	Ankle	Plantar
Right	Normal	Normal	Normal	Exaggerated	Exaggerated	Extensor
Left	Normal	Normal	Normal	Exaggerated	Exaggerated	Extensor

- Coordination—normal in upper limbs, heel-shin test could not be done due to weakness
- Rombergism—could not be evaluated
- Gait—could not be evaluated
- Involuntary movement—absent

4. **Cerebellar functions:** Intact
5. **Sensory system:** Sensory perception of all modalities is impaired below 10th thoracic dermatome and intact above it. There is some paresthesia along the T_{10} dermatome.

Examination of the other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 40 years old, businessman, normotensive, nondiabetic, nonsmoker, hailing from …, has been suffering from weakness of both lower limbs, which is gradually increasing and now he is unable to move his lower limbs and is unable to walk without the help of others. He also complains of difficulty in micturition and urinary incontinence for the last … days. The patient also complains of low back pain for … months, which is increased with even minor activities and on movement. For the last … months, he also experiences tingling and numbness on both lower limbs, more on right than left. There is no history of trauma, fever, weight loss, cough, burning in micturition or pain in other areas. His bowel habit is normal. There is no history of such illness in his family.

On examination

General examination (mention as above)

Systemic examination (mention as above).

My diagnosis is spastic paraplegia, more likely due to cord compression.

Q. Why is it spinal cord compression?

A. Because, there are:

- UMN sign (spastic paraplegia) in both lower limbs
- Sensory loss below 10th thoracic segment
- Patient has radicular pain (low back pain)
- Pain and sensory symptom precedes weakness and urinary incontinence.

Q. What is the site of your lesion?

A. At the level of 10th thoracic spinal cord segment, 7th thoracic vertebra (to find the site, see below).

Q. What are your differential diagnoses?

A. As follows:

- Demyelinating disease (Multiple sclerosis, ADEM)
- Herniated intervertebral disc
- Tumor
- Subacute combined degeneration (SCD).

Q. Why not **MND?**

A. Because, in MND there will be:
- No sensory loss (very important sign)
- No pain
- No sphincteric disturbance
- Fasciculation is present
- Age (usually above 40 years).

Q. Could it be due to **SCD**?

A. Unlikely, as in SCD there will be:
- No pain
- No sphincteric disturbance
- Peripheral neuropathy
- Posterior column lesion (loss of vibration and position sense)
- Knee and ankle jerk absent (knee jerk may be brisk, plantar may be extensor)
- Romberg's sign is positive
- Others—anemia and smooth shiny tongue with atrophy of papilla, dementia.

Q. Could it be due to **Friedreich's ataxia?**

A. Unlikely, as in Friedreich's ataxia:
- Occurs in early age, before 25 years
- Pes cavus and kyphosis
- Loss of knee and ankle jerk, plantar is extensor
- Signs of cerebellar lesion
- Signs of posterior column lesion (loss of vibration and position sense)
- Other findings—optic atrophy, high arched palate, deafness and cardiomyopathy.

Q. What do you think the **causes of cord compression** in this case?

A. The causes may be:
- Tuberculosis of spine (Pott's disease)
- Lymphoma
- Abscess (paravertebral)
- Neoplastic lesions, such as meningioma, neurofibroma, glioma, metastasis.

Q. What **investigations** should be done in spastic paraplegia?

A. As follows:
- X-ray of lumbodorsal spine (anteroposterior and lateral view)
- MRI of dorsal spine
- Lumbar puncture and cerebrospinal fluid (CSF) study
- Other test according to cause (e.g. tuberculosis and myeloma)
- Myelogram (not done nowadays, as CT or MRI is most preferable).

RELATED QUESTIONS AND ANSWERS

Q. What are the **symptoms** of spinal cord compression?

A. As follows:
1. Pain—localized over the spine or in a root distribution, may be aggravated by coughing, sneezing or straining.
2. Sensory—paresthesia, numbness or cold sensations, especially in the lower limbs, which spread proximally often to a level on the trunk.

3. Motor—weakness, heaviness or stiffness of the limbs, most commonly the legs.
4. Sphincter—retention followed by urinary incontinence.

Q. What are the **cardinal signs** of spinal cord compression?

A. As follows:
- UMN sign (spastic paraplegia) below the level of compression and LMN sign at the level of compression
- Segmental sensory loss (sensory loss up to a particular segmental level).

Other features of spinal cord compression:
- Sphincter disturbance—common (urinary retention and loss of bladder control)
- Root pain—frequent at the site of compression
- Pain radiates in a band around the chest (thoracic compression).

Q. What are the causes of **spastic paraplegia**?

A. As follows (remember the age and also sensory loss):
- Spinal cord compression due to any cause (see below)
- Demyelinating disease (MS), ADEM
- MND (middle aged or elderly)—amyotrophic lateral sclerosis, primary lateral sclerosis
- Friedreich's ataxia (early age)
- Hereditary spastic paraplegia
- Subacute combined degeneration (SCD)
- Transverse myelitis
- Tropical spastic paraplegia
- HIV myelopathy
- Sarcoidosis
- SLE.

Q. What are the **most common causes** of spastic paraplegia?

A. As follows (**7 T**):
- **T**rauma
- **T**uberculosis (Pott's disease)
- **T**umor (meningioma, neurofibroma, lymphoma, leukemia, myeloma, glioma)
- **T**ransverse myelitis
- **T**abes dorsalis
- **T**welve (B_{12} deficiency)
- **T**hrombosis.

Q. What are the causes of **spinal cord compression** according to the site of lesion?

A. As follows:

1. Vertebral lesion (extradural, 80%):
   - Trauma
   - Intervertebral disc prolapse
   - Tuberculosis of spine (Pott's disease)
   - Lymphoma
   - Secondary deposit (elderly)
   - Multiple myeloma (elderly)
   - Abscess (paravertebral)
   - Extramedullary hemotopoiesis in β thalassemia major.

2. Meningeal lesion (intradural, extramedullary, 15%):
   - Meningioma
   - Neurofibroma
   - Ependymoma
   - Secondary deposit (elderly)
   - Lymphoma
   - Leukemia
   - Epidural abscess.
3. Spinal cord lesion (intradural, intramedullary, 5%):
   - Glioma
   - Ependymoma
   - Metastasis
   - Syringomyelia
   - Hematomyelia.

Q. What are the causes of spastic paraplegia due to **cerebral lesion**?

A. As follows:
- Parasagittal meningioma (usually falx meningioma)
- Thrombosis of superior longitudinal sinus
- Thrombosis of unpaired anterior cerebral artery
- Multiple cerebral infarction
- Hydrocephalus
- Trauma
- In children, cerebral palsy (cerebral diplegia).

Q. What are the **features** of cerebral lesion causing paraplegia?

A. As follows:
- There is bladder disturbance (urinary retention)
- Cortical type of sensory loss
- Other features—headache, vomiting, convulsion, Jacksonian fit.

Note Remember the following:

Lower limbs and micturition center are represented in the paracentral lobule. Hence lesion in this area produces paraplegia and bladder dysfunction

Q. What are the **non-compressive causes** of spastic paraparesis or paraplegia?

A. As follows:
- MND (e.g. amyotrophic lateral sclerosis)
- Subacute combined degeneration
- Transverse myelitis
- Multiple sclerosis
- Friedreich's ataxia
- Lathyrism
- Syringomyelia
- Vascular disease of the cord
- Hereditary spastic paraplegia
- Tropical spastic paraplegia
- Post-vaccination

- Syphilitic amyotrophy
- Non-metastatic manifestation of malignancy
- Radiation myelopathy
- Functional.

According to the type of lesion:

1. Demyelinating:
   - MS
   - ADEM.
2. Inflammatory:
   - Sarcoidosis
   - Postviral
   - Post-vaccinal.
3. Infective:
   - HIV
   - Herpes zoster
   - Herpes simplex
   - Syphilis.
4. Degenerative:
   - MND (Motor nuron disease)
   - FSP (Familial spastie paraplegia)
   - SCD (Spinocerebellar degeneration)
   - FA (Friedrelen's ataxia).
5. Vascular:
   - Anterior spinal artery occlusion
   - Intramedullary hemorrhage
   - Spinal AVM.
6. Toxic:
   - Lathyrism
   - Radiation.

Q. What are the **causes of paraplegia of sudden onset?**

A. As follows:

- Trauma (to vertebral column)
- Collapse of vertebra due to any cause
- Acute transverse myelitis
- Multiple sclerosis
- Anterior spinal artery thrombosis
- Post-vaccination myelitis
- Dissecting aneurysm
- Hematomyelia (due to arteriovenous malformation or angioma).

Q. What is **paraplegia in flexion** and **paraplegia in extension**?

A. Paraplegia in extension and paraplegia in flexion follows severe injury to the spinal cord.

- Paraplegia in extension: It indicates an increase in the extensor muscle tone leading to an extension attitude of the lower limbs (hip and knee extended, feet plantar flexed), due to involvement of pyramidal tracts as a result of partial transection of spinal cord, but the extrapyramidal tracts (specially vestibulospinal tracts) are intact. It may change to paraplegia in flexion if the damage to the spinal cord becomes more extensive and the vestibulospinal tracts are destroyed.

- Paraplegia in flexion: Here lower limbs take a flexion attitude (the limbs are involuntarily flexed in hips and knees, feet are dorsiflexed). It is due to complete transection of spinal cord. Here both pyramidal and extrapyramidal tracts are affected.

Differences between Paraplegia in extension and Paraplegia in flexion:

	Paraplegia in extension	Paraplegia in flexion
1. Cause	Pyramidal lesion	Pyramidal and extrapyramidal
2. Hypertonia	More in extensors	More in flexors
3. Position of lower limbs	Extended	Flexed
4. Deep reflexes	Exaggerated	Less exaggerated
5. Clonus	Present	Absent
6. Mass reflex	Absent	May be present
7. Bladder	Precipitancy	Automatic bladder

Q. What is **mass reflex?**

A. Following stimulation of skin of the lower limbs or lower abdominal wall, there is reflex flexion of the lower trunk muscles and the lower limbs, evacuation of the bladder, bowel and semen and sweating, called mass reflex. This reflex indicates severe spinal cord lesion.

Q. What are the causes of **absent ankle jerk**, but **extensor plantar** response?

A. As follows:

- Subacute combined degeneration of the spinal cord
- Friedreich's ataxia
- Taboparesis
- Diabetes mellitus (DM) with cervical myelopathy
- Multiple sclerosis.

Q. How to **find out** the sensory level in spinal cord compression?

A. In the following ways:

Vertebral level	Spinal cord segment
1. Cervical vertebrae	Add 1
2. Upper thoracic vertebrae (T1 to T6)	Add 2
3. Mid thoracic vertebrae (T7 to T9)	Add 3
4. 10th thoracic vertebra	Lumbar 1 and 2
5. 11th thoracic vertebra	Lumbar 3 and 4
6. 12th thoracic vertebra	Lumbar 5
7. First lumbar vertebra	Sacral and coccygeal cord segments

Q. What are the **findings** of spinal cord compression at different levels of spinal cord?

A. As follows:

- **Lesion above C_5**—UMN lesion in both upper and lower limbs with loss of sensation in all four limbs.
- **Lesion at C_5**—LMN lesion in proximal muscles of upper limbs (rhomboid, deltoid, biceps, brachioradialis) with segmental loss of sensation and UMN lesion in rest of the upper limbs and in lower limbs. Biceps reflex is lost and triceps jerk is exaggerated.
- **Lesion at C_8**—LMN lesion and wasting of the intrinsic muscles of the hand and UMN lesion in lower limbs. There is segmental loss of sensation.
- **Lesion in thoracic cord**—Spastic paraplegia with segmental sensory loss. (Loss of upper abdominal reflexes at T_7 and T_8. Loss of lower abdominal reflexes and upward displacement of the umbilicus at T_{10} and T_{11}).
- **Lesion at L_1**—UMN lesion in lower limbs and cremasteric reflex is lost (normal abdominal reflex).
- **Lesion at L_4**—LMN lesion and wasting of quadriceps, loss of knee jerk but hyperreflexia of ankle jerk and extensor plantar response.
- **Lesion in L_5 and S_1**—LMN weakness of knee flexion and hip extension (S_1) and abduction (L_5) and calf and foot muscles. Knee jerk is present, but no ankle jerk or plantar response. Anal reflex is present.
- **Lesion in S_3 and S_4**—No anal reflex, saddle sensory loss, normal lower limbs.

Note Remember to diagnose the cause of spastic paraplegia:

- If spastic paraplegia with sensory loss with a definite upper limit—diagnosis is **spinal cord compression**
- If plantar response is extensor, sensory loss in glove and stocking pattern, loss of vibration and position sense—diagnosis is **SCD**
- If presence of cerebellar signs—diagnosis is **MS** or **Friedreich's ataxia**
- In young patient with pes cavus, dorsal column lesion and cerebellar signs—diagnosis is **Friedreich's ataxia**
- If spastic paraplegia, but no sensory loss—diagnosis is **MND** (amyotrophic lateral sclerosis, also LMN lesion in upper limb).

Q. What are the causes of **flaccid paraplegia**?

A. As follows:

1. With bowel bladder involvement:
   - Spinal shock
   - Cauda equina syndrome.
2. Without bowel bladder involvement:
   - MND
   - Neuropathy—GBS and any other motor neuropathy involving the lower limb, AIDP
   - Periodic paralysis due to hyperkalemia or hypokalemia
   - Guillain-Barré syndrome (GBS)
   - Motor neuropathy due to any cause (such as acute intermittent porphyria, Charcot-Marie-Tooth disease, chronic lead poisoing, paraneoplastic syndrome)
   - Progressive muscular atrophy (MND)
   - Acute inflammatory demyelinating polyradiculopathy (AIPD)
   - Tabes dorsalis
   - Friedreich's ataxia
   - UMN lesion in shock stage

- Peripheral neuropathy involving both lower limbs
- Hysterical conversion reaction (HCR).

Note Remember the following:

Common causes of flaccid paraplegia are GBS and peripheral neuropathy.

Q. What are the causes of **hypotonia**?

A. As follows:

- LMN lesion due to any cause
- UMN lesion in shock stage
- Cerebellar lesion (knee jerk may be pendular)
- Dorsal column lesion (e.g. tabes dorsalis)
- Polyneuropathy
- Chorea (it is the only extrapyramidal lesion with hypotonia)
- Hypokalemia or hyperkalemia
- Down's syndrome
- Drugs like hypnotics, sedatives, muscle relaxants, anesthetics.

Q. What are the causes of **hypertonia**?

A. As follows:

- UMN lesion (spastic, may be clasp knife)
- Extrapyramidal lesion (lead pipe or cogwheel rigidity), except chorea
- HCR (rigidity continue to increase with more and more passive movement)
- Others—tetanus, strychnine poisoning, tetany, catatonic states
- Myotonia during the contraction phase
- Decerebrate rigidity (there is marked contraction of all extensor muscles in the body).

Q. What is the **difference** between rigidity and spasticity?

A. As follows:

- Spasticity means increased resistance during the initial part of passive movement, followed by lessening of the resistance. It may be clasp-knife type where the initial resistance is followed by sudden loss of resistance. It is due to pyramidal lesions. Spasticity is better felt with attempting extension of upper limbs and flexion of lower limbs. It is associated with other signs of UMN lesion. It involves only the anti-gravity muscles (extensors of the upper limbs and flexors of the lower limbs).
- Rigidity means sustained resistance during passive movement. It may be lead pipe in which resistance is uniform throughout the passive movement (better seen in elbow and knee) or cog wheel in which continuous resistance is interrupted by tremor (better seen in the wrist joint). Rigidity is found in extrapyramidal lesion. It involves all groups of muscles.

TRANSVERSE MYELITIS

CHIEF COMPLAINTS

- Sudden inability to walk for … days
- Inability to void urine for … days.

HISTORY

History of present illness: According to the statement of the patient, he was reasonably well one week ago. Since then, he has been suffering from low grade continued fever, which is not associated with chill and rigor and does not subside with sweating. For the last 3 days, suddenly he felt weakness in both of his lower limbs and was unable to walk. After that, he is completely bedridden and is unable to void urine and also unable to pass stool. He also complains of moderate pain along the lower part of his chest. There is no history of trauma, generalized bodyache or vaccination. There is no complaint regarding his upper limbs. Other systemic enquiry revealed normal.

History of past illness

Drug and treatment history

Personal history

Socioeconomic history

Family history: Mention according to the patient's statement.

GENERAL EXAMINATION

- The patient is ill looking, anxious and bed ridden
- Mildly anemic
- No jaundice, cyanosis, clubbing, koilonychia, leukonychia or edema
- No lymphadenopathy or thyromegaly
- Urinary catheter in situ
- Pulse: 72/min
- BP: 120/70 mm Hg
- Temperature: Normal
- Respiration: Normal.

SYSTEMIC EXAMINATION

Nervous System

1. **Higher cerebral functions:** Intact
2. **Cranial nerves including fundoscopy**: Intact
3. **Motor system:**
   - Muscle tone—increased in both lower limbs, normal in both upper limbs
   - Muscle power—diminished (grade 0/5) in both lower limbs, normal in both upper limbs
   - Wasting—absent
   - Reflexes:

Jerks	Biceps	Triceps	Supinator	Knee	Ankle	Plantar
Right	Normal	Normal	Normal	Exaggerated	Exaggerated	Extensor
Left	Normal	Normal	Normal	Exaggerated	Exaggerated	Extensor

- Coordination—normal
- Rombergism—could not be evaluated
- Gait—could not be evaluated
- Involuntary movement—absent

4. **Cerebellar function:** Intact
5. **Sensory system:** Sensory perception of all modalities is impaired below 10th thoracic dermatome and intact above it. There is some paresthesia along T_{10} dermatome.

Examination of the other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 40 years old, businessman, normotensive, nondiabetic, nonsmoker, hailing from …, presented with low grade continued fever for 1 week. The fever is not associated with chill and rigor and does not subside with sweating. For the last 3 days, suddenly he felt weakness in both of his lower limbs and became unable to walk. Thereafter, he is completely bedridden and is unable to void urine and also unable to pass stool. He also complains of moderate pain along the lower part of his chest. There is no history of weight lifting, low back pain, trauma, generalized body ache or vaccination. There is no complaint regarding his upper limbs. Other systemic enquiry revealed normal.

There is no history of such illness in his family. He was treated by a local physician who referred him for immediate hospitalization.

On examination
General examination (mention as above)
Systemic examination (mention as above).

My diagnosis is spastic paraplegia, more likely due to acute transverse myelitis.

Q. What are your **differential diagnoses?**

A. As follows:
- Multiple sclerosis
- Subacute combined degeneration of spinal cord
- Trauma (to vertebral column)
- Collapse of vertebra due to any cause (metastasis, osteoporosis, TB)
- Anterior spinal artery thrombosis
- Post-vaccination myelitis
- Hematomyelia.

Q. Why is it **transverse myelitis**?

A. Because:
- Previous history of fever
- Followed by acute onset of spastic paraplegia
- Sensory loss in both lower limbs with sharp upper margin
- Involvement of bladder function
- No history of trauma, vascular incident, etc.

Q. What **investigations** should be done?

A. As follows:

- CBC (leukocytosis in systemic inflammation and infection)
- X-ray of the dorsolumbar spine (to exclude other cause)
- CSF study (protein high, lymphocyte high)
- CT scan and MRI of brain and spinal cord, depending upon site of leison.

RELATED QUESTIONS AND ANSWERS

Q. What is **transverse myelitis (TM)?**

A. It is the acute inflammatory, demyelinating disorder of the spinal cord causing paraparesis or paraplegia, or sometimes quadriplegia. It is usually secondary to viral infection, multiple sclerosis or other inflammatory and vascular disease.

Q. What are the **causes** of TM?

A. As follows:

1. **Traumatic**
2. **Infection:**
   - Viral—coxsackie, polio, EBV, herpes virus, HIV
   - Bacterial—pyogenic, tuberculous, syphilitic (rare)
   - Others—parasitic, fungal, schistosomiasis
3. **Vascular**—arteritis, anterior spinal artery occlusion
4. **Nutritional myelopathy**
5. **Miscellaneous**—postinfectious or postvaccinal inflammation, ADEM, multiple sclerosis, sarcoidosis, neuromyelitis optica
6. **Collagen vascular disease** (SLE, Sjogren syndrome, MCTD)
7. **Idiopathic.**

Q. What is the common **site** of transverse myelitis?

A. Mid thoracic region.

Q. What are the **features** of transverse myelitis?

A. Occurs in any age, follows viral illness or vaccination:

- Onset within hours to days, usually bilateral
- Fever may be present and acute or subacute onset of paralysis or paraparesis associated with back pain
- At the level of lesion, girdle constriction with hyperesthesia just above the lesion may be present
- Usually there is no root pain, spinal tenderness or spinal deformity
- The patient complains of urinary problem like retention, incontinence as bladder involvement is early
- There is partial or complete sensory loss, with a definite upper level
- MRI should be done to exclude compressive lesion
- Lumbar puncture and CSF study shows high protein and lymphocyte. Often there is high polymorph at the onset
- Outcome is variable. In some cases, near complete recovery occurs, despite severe initial deficit. Some patients go to develop multiple sclerosis in later years.

Q. How to **treat** TM?

A. As follows:

1. **General measures:**
   - Reassurance and psychological support
   - Care of bowel (manual evacuation may be necessary)
   - Care of bladder (catheterization)
   - Care of skin (to prevent bedsore)
   - Passive physiotherapy
   - Spasticity may be helped by baclofen, diazepam, tinazidine or botulinum toxin
   - Rehabilitation.
2. Treatment of specific cause, if any.
3. In patient with severe and rapidly progressive disease, initial empirical treatment usually includes administration of high dose glucocorticoid and IV acyclovir, while definite diagnostic tests are pending.
4. **Plasmapheresis**—those who do not respond to medicine.

MYOPATHY

CHIEF COMPLAINTS

- Weakness for … months
- Wasting of muscles for … months.

HISTORY

History of present illness: According to the statement of the patient, he was reasonably well … months back. Since then, he has been suffering from generalized weakness. Initially, he was feeling weakness of the upper limbs for which he was unable to raise his arms above head and feels difficulty in combing. For the last … months, he also experiences weakness of both lower limbs for which he feels difficulty in standing from sitting position and climbing stairs. It is not related to any physical exercise or activity, no diurnal variation and no muscular pain. He also complains of gradual wasting of muscles, initially of the upper limbs and then lower limbs. There is no history of fever, skin rash, tingling and numbness, sensory loss or involuntary movements, breathlessness, palpitaion, bowel or bladder abnormality. Other systemic enquiry revealed no abnormality.

History of past illness

Drug and treatment history

Personal history

Socioeconomic history: Mention according to the patient's statement

Family history: There is no history of consanguinous marriage among the parents.

GENERAL EXAMINATION

- Ill looking and emaciated
- Mildly anemic
- No jaundice, cyanosis, clubbing, koilonychia, leukonychia or edema
- No lymphadenopathy or thyromegaly
- Pulse: 72/min
- BP: 120/70 mm Hg
- Temperature: Normal
- Respiration: Normal.

SYSTEMIC EXAMINATION

Nervous System

1. **Higher psychic functions:** Intact
2. **Cranial nerves:** Intact
3. **Motor system:**
   - Muscle tone—diminished in both upper and lower limbs
   - Muscle power—reduced (grade 3/5) in proximal muscles of all four limbs, and 5/5 in other group of muscles
   - Gower's sign is positive

- Wasting of shoulder and upper arm muscles
- Reflexes:

Jerks	Biceps	Triceps	Supinator	Knee	Ankle	Plantar
Right	Normal	Normal	Normal	Normal	Normal	Flexor
Left	Normal	Normal	Normal	Normal	Normal	Flexor

- Coordination—could not be performed due to weakness
- Rombergism—absent
- Gait—wadling gait
- Involuntary movement—absent

4. **Cerebellar functions:** Intact
5. **Sensory system:** Intact.

Examination of the other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 19 years old, student, normotensive, nondiabetic, nonsmoker, hailing from …, presented with generalized weakness for … months. Initially, he was feeling weakness of the upper limbs for which he is unable to raise his arms above head and feels difficulty in combing. For the last … months, he also experiences weakness of both lower limbs for which he feels difficulty in standing from sitting position and climbing stairs. It is not related to any physical exercise or activity, no diurnal variation and no muscular pain. He also complains of gradual wasting of muscles, initially of the upper limbs and then lower limbs. There is no history of fever, skin rash, tingling and numbness, sensory loss or involuntary movements, breathlessness, palpitation, bowel or bladder abnormality. Other systemic enquiry revealed no abnormality. There is no history of similar illness in his family. He was treated with multiple vitamins and calcium tablets by local physicians.

On examination
General examination (mention as above)
Systemic examination (mention as above).

My diagnosis is myopathy, more likely limb girdle muscular dystrophy.

Q. Why it is myopathy?

A. Because:
- Gradual onset of symmetrical proximal muscle weakness such as difficulty in standing, difficulty in raising arms above head and difficulty in combing hair
- Tendon reflexes are normal
- No sensory loss.

All indicate muscular, not neurological problem.

Q. Why not neuropathy?

A. Because:
- In neuropathy, usually there is peripheral involvement
- The patient will complain of paresthesia, tingling and numbness
- In sensory neuropathy, there will be loss of sensation and reflexes
- In motor neuropathy, there is loss of reflex
- Onset is acute or subacute.

Q. What are your **differential diagnoses?**

A. As follows:

- Malnutrition (vitamin D deficiency)
- Tuberculosis
- Diabetes mellitus
- Thyrotoxicosis
- Hypoparathyroidism
- Other myopathy like facio-scapulo-humeral dystrophy, Duchenne muscular dystrophy, Becker's muscular dystrophy, etc.
- Drugs (zidovudine, statin, alcohol).

Q. What are the **causes** of emaciation or cachexia?

A. As follows:

- Tuberculosis
- Diabetes mellitus
- Thyrotoxicosis
- Malabsorption or malnutrition
- Malignancy
- Anorexia nervosa in young female
- Any chronic debilitating disease
- HIV infection.

Q. What **investigations** should be done in myopathy?

A. As follows:

- Creatine phosphokinase (CPK) is very high, up to 40-fold in Duchenne type (in other types, slightly raised)
- EMG shows short duration, low amplitude spiky polyphasic action potential (spontaneous fibrillation is also seen occasionally), reduction in motor unit amplitude and duration with normal number of units activated during effort
- ECG (cardiomyopathy and dysrhythmia), echocardiography, blood sugar
- Muscle biopsy (shows variation of muscle fiber size, degenerative changes, regeneration and replacement by fat. On immunological staining, there is absence of dystrophin. This is commonly found in Duchenne muscular dystrophy)
- Lactic acid (to exclude mitochondrial myopathy)
- Molecular genetic testing.

Q. What are the **differences** between neuropathy and myopathy?

A. As follows:

- Myopathy usually involves proximal muscles (except myotonia dystrophica, which involves distal muscles)
- Neuropathy usually involves distal muscles (except diabetic amyotrophy), GBS, amyloidosis, Lyme disease.

RELATED QUESTIONS AND ANSWERS

Q. What is **myopathy?**

A. It means disease of the skeletal muscle (voluntary) muscle.

Q. What is **muscular dystrophy**? What are the **types** of muscular dystrophy?

A. It is a group of hereditary muscular disorder characterized by progressive degeneration of groups of muscles without the involvement of nervous system with absence or reduced dystrophin. The types are:

1. **Hereditary muscular dystrophy:**
   - Duchenne type (pseudohypertrophic)
   - Becker muscular dystrophy
   - Limb girdle myopathy
   - Fascio-scapulo-humeral dystrophy
   - Myotonia dystrophica
   - Myotonia congenita
   - Others are oculopharyngeal or ocular myopathy, and congenital muscular dystrophy.
2. **Congenital myopathy (rare):**
   - Central core
   - Nemaline myopathy
   - Myotubular myopathy.
3. **Secondary myopathy** (such as endocrine disease and drugs).

Q. What is **Duchenne muscular dystrophy?** What are the **features**?

A. It is inherited as X-linked recessive disorder (30% spontaneous mutation). Duchenne gene is on the short arm of X-chromosome, Xp21 and its product called dystrophin is absent (diagnosed by western blot analysis of muscle biopsy).

- Affects only male, age of onset 3 to 4 years
- The child presents with difficulty in walking or getting up from sitting or lying position. There is history of frequent fall and delayed motor activity (e.g. walking)
- Gower's sign is positive (while the child gets up from lying position, he uses the hands to climb up)
- There is pseudohypertrophy in early stage involving calf and deltoid muscles. Later, there is weakness, first involves the proximal muscles
- Gait-waddling (duck like)
- Other features include dilated cardiomyopathy, kyphoscoliosis and mental retardation. There is early respiratory involvement
- Prognosis is poor, chair bound by the age of 10 years and few survive up to 20 years
- Causes of death are dilated cardiomyopathy and respiratory failure or inanition.

Q. What is **Becker muscular dystrophy**?

A. It is inherited as X-linked disorder, only males are affected and features are same as Duchenne type with the exception of:

- Onset is late (5 to 25 years)
- Less severe, less rapid progression and less incidence of cardiomyopathy. Mental retardation and kyphoscoliosis are uncommon. Respiratory involvement is a late feature
- Chair bound at about 25 years after the onset
- Survival—fourth to fifth decade.

Causes of pseudohypertrophy of calf muscles:

- Duchenne muscular dystrophy
- Becker muscular dystrophy.

Q. What is **limb girdle myopathy**?

A. It is a type of muscular dystrophy, inherited as an autosomal dominant (type 1)—10% and autosomal recessive (type 2)—90%, characterized by the involvement of shoulder and pelvic girdle muscles

- Age of onset is 10 to 30 years, male and female are equally affected
- May involve cardiac muscle (may cause conduction abnormality or heart failure)
- Intelligence is normal, face is normal, muscle enzymes are normal or slightly elevated
- Prognosis is poor, chair-bound at 20 to 25 years of age (10 to 20 years after the onset of disease).

Q. What is **fascio-scapulo-humeral dystrophy**? What are the **features**?

A. It is a type of muscular dystrophy, inherited as an autosomal dominant, characterized by the involvement of muscles of the face and shoulder girdle.

- Onset is 10 to 40 years of age
- Course is variable, but usually relatively benign
- There is wasting of muscles of face, neck and shoulder girdle (lower trapezzi, pectoralis, biceps, triceps). Hypertrophy of the deltoid
- Winging of scapula (due to the involvement of serratus anterior muscle)
- Pain in shoulder girdle is common
- Face looks dull, expressionless, lips open and slack, inability to whistle and puff the cheek
- Eyes—bilateral partial ptosis
- There may be distal lower limb weakness
- Intelligence is normal
- Prognosis—normal life span, and slowly progressive
- Muscle enzymes are usually normal or slightly elevated
- Inflammatory and perivascular inflammation may be seen in muscle biopsy. Also, retinal microvascular abnormality may be found.

Q. What is **myotonia?** What are the **causes?**

A. It is the continued contraction of the muscles with slow relaxation after cessation of voluntary contraction. Causes are:

- Myotonia dystrophica
- Myotonia congenita (Thomsen's disease)
- Others—hyperkalemic periodic paralysis, myxedema (Hoffman's syndrome), hereditary paramyotonia (autosomal dominant), cold-induced myotonia and drug (clofibrate).

Note Remember the following:

Patients with myotonia tolerate anesthesia poorly

Q. How to **elicit** myotonia?

A. As follows:

- The patient is asked to close the hands tightly. If asked to open, it relaxes slowly. Same thing happens if asked to close the eyes, which opens slowly
- Inability to relax hands after handshake (grip myotonia)
- Percussion over the thenar eminence with fingers produces dimples or depressions, which fill up slowly (percussion myotonia). Similar percussion over the tongue produces same finding.

Q. What is **myotonia congenita?**

A. It is an inherited disorder (autosomal dominant), characterized by failure to relax the muscle after forceful contraction. Present at birth with feeding difficulty, inability to open the eyes and a peculiar

cry. It is a mild disease, improves with age. Other features of myotonia dystrophica are absent. There may be diffuse muscular hypertrophy due to continuous involuntary isometric contraction.

Treatment of myotonia—procainamide, quinidine, mexiletine may be helpful
Prognosis—normal life expectancy.

Q. What are the features of **myotonia dystrophica?**

A. As follows:

1. **In face:**
   - Frontal baldness (patient may be wearing wig)
   - Long, lean, triangular, sad and expressionless face (hatchet facies)
   - Wasting of temporalis and masseter.
2. **Eyes:**
   - Partial ptosis (usually bilateral, may be unilateral) with smooth forehead
   - Cataract (stellate cataract). May be subcapsular fine deposit
   - Difficulty in opening the eyes after firm closure.
3. **Neck**—wasting of sternomastoid and shoulder girdle muscles. There is weakness of flexion and normal extension.
4. **Hands:**
   - The patient is asked to close the hands tightly, which relaxes slowly if asked to open
   - Inability to relax hands after handshake
   - Percuss on thenar eminence with fingers. There are dimples or depressions, which fill up slowly.
5. **Others:**
   - Percussion may be done on the tongue (dimples or depressions are seen)
   - Wasting of distal muscles of arms (forearm wasting first) and legs
   - Testes (atrophy)
   - Gynecomastia
   - Heart (cardiomyopathy and conduction defect).

Other features of myotonia dystrophica:

- Inherited as autosomal dominant
- Males are affected more than females
- Age of onset may be any (usually 20 to 50 years)
- Diabetes mellitus and impaired glucose tolerance (IGT) may occur
- Intellect and personality may have mild deterioration
- Small pituitary fossa and hypogonadism may occur
- Low serum IgG levels
- Tolerate anesthesia poorly.

Q. What are the **EMG findings of myotonia?**

A. High-frequency activity that varies repeatedly (waxing and waning of potentials), to cause a characteristic sound on loud speaker (called **Dive-Bomber effect).**

Q. What are the **EMG findings in myopathy?**

A. Short duration, spiky, polyphasic muscle action potential are seen. Spontaneous fibrillation is occasionally recorded.

Q. How to **treat** myotonia dystrophica?

A. Only symptomatic. No specific treatment.

- Myotonia may be treated by phenytoin (procainamide or quinidine may be used, but may worsen cardiac conduction)
- Genetic counselling

Q. What are the **causes** of proximal myopathy?

A. As follows:

- Dermatomyositis or polymyositis
- Myasthenia gravis
- Myasthenic myopathic syndrome (Eaton–Lambert syndrome)
- Myopathy (limb girdle, fascio-scapulo humeral and mitochondrial), except myotonic dystrophy
- Cushing's syndrome
- Diabetic amyotrophy
- Thyrotoxicosis (also hypothyroidism)
- Polymyalgia rheumatica
- Osteomalacia
- Hyperparathyroidism
- Periodic paralysis
- Alcohol and drugs (steroid, chloroquine, amiodarone, lithium and zidovudine)
- McArdle's syndrome (myophosphorylase deficiency, there is stiffness and cramps of muscle after exercise, which is hard and painful on movement).

Q. What are the causes of **distal** muscle weakness?

A. As follows:

- Myotonic dystrophy
- Charcot-Marie-Tooth disease
- Peripheral neuropathy (except diabetic amyotrophy)
- Distal myopathy.

Q. What are the **causes of painful muscle**?

A. As follows:

- Physiological (after exercise)
- Polymyositis or dermatomyositis
- Polymyalgia rheumatica
- Fibromyalgia syndrome
- Viral infection
- Chronic alcoholism
- Hypoparathyroidism
- Vitamin D deficiency
- Following convulsion
- Associated with rheumatological disease
- Functional.

Q. What are the **causes of acute** or **sudden muscular weakness**?

A. As follows:

- Guillain-Barré syndrome
- Hypokalemia and hyperkalemia
- Familial periodic paralysis
- Thyrotoxic periodic paralysis
- Functional (hysterical conversion reaction, HCR).

Q. What are the **drugs** causing myopathy?

A. Steroid, penicillamine, hydroxychloroquine or chloroquine, statins (lovastatin), zidovudine and clofibrate (also alcohol and cocaine cause myopathy).

Q. What are the causes of **high CPK?**

A. As follows

- Exercise
- Intramuscular injection
- Muscle trauma or road traffic accident
- Convulsion
- Alcoholism
- Dermatomyositis or polymyositis
- Acute myocardial infarction (CPK-MB)
- Myopathy (Duchenne type of muscular dystrophy)
- Rhabdomyolysis
- Chronic liver disease (CLD)
- Drugs include statins, busulphan, narcotics, colchicine and chloroquine
- Neuroleptic malignant syndrome
- Malignant hyperthermia.

Note Remember the following:

CPK is normal in myasthenia gravis, Eaton-Lambert syndrome and usually normal in myotonia (myotonic dystrophy)

Q. What are the CPK normal myopathies?

A. As follows:

- Facioscapulohumeral myopathy
- Scapulo-peroneal myopathy
- Distal myopathy (mostly)
- Zidovudine induced myopathy.

Iso-enzymes of CPK:

- MM (mainly in skeletal muscle)
- MB (mainly in cardiac muscle)
- BB (in brain).

WILSON'S DISEASE

CHIEF COMPLAINTS

- Tremor of hands and difficulty in writing for … months
- Difficulty in speech for … days
- Involuntary movements of hands and other parts of the body for … days.

HISTORY

History of present illness: The patient says that he was reasonably well … months ago. Since then he is complaining of tremor of both hands and difficulty in writing. It is aggravated on attempted movement and relieved by rest. It is gradually progressive and hampering his daily activities. He also complains of difficulty in speech for last … days. His mother stated that she noticed involuntary movements of hands and feet which are repetitive, semi purposive and is absent during sleep. His intellect is average and there had been no deterioration of his academic performance. There is no history of fever, weight loss, convulsion, head trauma or unconsciousness. His bowel and bladder habits are normal.

History of past illness: He suffered from three episodes of jaundice in his early childhood, with spontaneous recovery from each episode.

Family history: There is history of consanguineous marriage among his parents. There is no history of such illness in his family.

Drug history: He was treated by local physicians by multiple drugs, the name of which he cannot mention.

Personal history: He is a student of class 10, he is from a middle class family.

GENERAL EXAMINATION

- Appearance: Anxious
- Anemia, jaundice, cyanosis, clubbing, koilonychia, leuconychia, edema, dehydration—absent
- No thyromegaly or lymphadenopathy
- Pulse: 72/min
- BP: 100/60 mm Hg
- Temperature: Normal.

SYSTEMIC EXAMINATION

Neurological Examination

1. **Higher cerebral function:** Normal
2. **Speech:** Scanning
3. **Cranial nerves including fundoscopy:** Normal except presence of horizontal nystagmus
4. **Examination of the eyes:** KF ring present in both eyes, on the left eye at 11 o'clock position and in right eye on 10 o'clock position
5. **Motor function:** Intact except hypotonia in all four limbs and fine tremor of outstretched hand. Gait is ataxic

6. **Sensory function:** Intact.
7. **Cerebellar function:**
   - Horizontal nystagmus
   - Scanning speech
   - Intention tremor with past pointing
   - Hypotonia.

Examination of other systems reveals normal findings.

SALIENT FEATURE

Mr …, 14 years of age, student, right handed boy, hailing from …, presented with tremor of both hands and difficulty in writing for … months. It is aggravated on attempted movement and relieved by rest. It is gradually progressive and hampering his daily activities. He also complains of difficulty in speech for last … days. His mother stated that she noticed involuntary movements of hands and feet which are repetitive, semi-purposive and is absent during sleep. His intellect is average and there had been no deterioration of his academic performance. There is no history of fever, weight loss, convulsion, head trauma or unconsciousness. His bowel and bladder habits are normal. He suffered from three episodes of jaundice in his early childhood, with spontaneous recovery from each episode. There is history of consanguineous marriage among his parents. There is no history of such illness in his family. He was treated by local physicians by multiple drugs, the name of which he cannot mention.

On examination
General examination (mention as above)
Systemic examination (mention as above).

My diagnosis is wilson's disease

Q. Why Wilson's disease?

A. Because, there is history of previous hepatitis, involuntary movement, cerebellar sign and presence of KF ring. All are suggestive of Wilson's disease.

Q. What are your **differential diagnoses?**

A. As follows:
- Cerebellitis
- Drug induced cerebellar syndrome
- Post-encephalitic syndrome.

Q. What is **KF ring?**

A. It is greenish brown pigmentation at the sclerodermal junction due to deposition of copper in the Decimet's membrane of the cornea, occasionally seen by slit lamp examination. May be absent or less in young children but always present in neurological Wilson's disease.

Q. What are the causes of **KF ring?**

A. As follows:
- Wilson's disease
- Primary billiary cirrhosis
- Chronic active hepatitis with cirrhosis
- Cryptogenic cirrhosis
- Long-standing intrahepatic cirrhosis of childhood.

Q. What investigations should be done in Wilson's disease?

A. As follows:

- Serum ceruloplasmin—low
- Serum-free copper—high
- 24 hours urinary copper—high (normal <40 mg, in Wilson's disease—100 to 1000 mg or 0.6 mmol/24 h)
- 24 hours urinary copper following penicillamine therapy >25 mmol is a confirmatory test
- Liver biopsy with quantitative measurement of copper (high hepatic copper, usually not done).

RELATED QUESTIONS AND ANSWERS

Q. What is Wilson's disease? What is the **primary defect**?

A. Wilson's disease is an inborn error of copper metabolism, inherited as autosomal recessive trait, characterized by failure of biliary excretion of copper and its deposition in and damage of different organs such as liver, brain, eye, kidney, bone, etc. There is more absorption of copper from the small intestine but less excretion by liver. Ceruloplasmin production is less due to unknown mechanism.

Q. What are the **manifestations** of Wilson's disease?

A. Usually commonly in patients 5 to 30 years. In early age, usually hepatitis and in adult usually neurological features are common. Features are as follows:

1. **Hepatic:**
   - Acute or chronic hepatitis, often recurrent manifested by attacks of jaundice
   - Eventually, multilobular cirrhosis
   - Rarely, cirrhosis alone
   - Hepatic abnormality may be asymptomatic with only elevated transaminases
   - Unexplained hepatosplenomegaly
   - Hypersplenism with thrombocytopenia and bleeding
   - In severe hepatic failure, hemolytic anemia.
2. **Renal:**
   - Acute tubulopathy with renal tubular acidosis
   - Nephrolithiasis
   - Microscopic hematuria
   - Fanconi syndrome—excretion of phosphates, amino acids, glucose or urates.
3. **Neurologic:**
   - Three main movement disorder: Dystonia, Incordination, Tremor (DIT)
   - Extrapyramidal manifestation: Parkinsonian syndrome (tremor, slowness of movement, rigidity, flexed limb postures), oropharyngeal abnormality (dysphagia, dysarthria, hoarseness), chorea, athetosis, dystonia
   - Cerebellar syndrome (ataxia and intention tremor)
   - Seizure (6%), dementia
   - Autonomic disturbance: Orthostatic hypotension, sweating abnormality, bowel, bladder and sexual dysfunction
   - No sensory abnormality.
4. **Eye:**
   - Kayser-Fleischer rings (commonly 10 to 12 o'clock position, in upper periphery)
   - Sun-flower cataracts (rare, due to deposition of copper in the lens).

5. **Psychiatric:**
   - Behavioral disturbances with onset 5 years before diagnosis occurs in half of the patient. They includes—loss of emotional control- temper tantrums, crying bouts, depression, hyperactivity, loss of sexual inhibition, gradual development of intellectual faculties.
6. **Others:**
   - Hemolytic anemia
   - Aminoaciduria or Fanconi syndrome
   - Osteoporosis
   - Cholelithiasis
   - Spontaneous abortion
   - Amenorrhea.

Q. How to **treat** Wilson's disease?

A. As follows:

1. **Penicillamine** (drug of choice, 1 to 3 g/day in divided dose with pyridoxine 25 mg/day to prevent anemia) or trientine. Treatment should be continued lifelong
2. **Zinc-acetate** (inhibits absorption of copper from GIT—ineffective alone)—100 to150 mg/day
3. **Liver transplantation** in fulminating hepatic failure or in advanced cirrhosis
4. **Symptomatic treatment:**
   - Dystonia—trihexyphenidyl/clonazepam/diazepam
   - Seizure—anti-epileptics
   - Psychosis—antipsychotic
5. **General measures**—reduction of dietary copper intake (< 1 mg/day)
   - Avoidance of copper rich foods—liver, mushrooms, beans, cocoa, chocolates, nuts, shelfish, colored leafy vegetables, red meat, organ meat—kidney, liver, brain, bone marrow.
   - Aviodance of copper containing drugs
   - Aviodance of copper containing vergetables.
6. **Premarital screening**. Avoid consanguineous marriage.
7. **Follow up**—clinical improvement of S/S with measurement of urinary copper.

Q. How to **treat** in pregnancy?

A. Same treatment should be given.

Q: What is the **prognosis** of Wilson's disease?

A: Prognosis is excellent, provided the treatment is started before irreversible damage. Sibling and children must be investigated and treatment should be given, even they are asymptomatic.

INTRACRANIAL SPACE OCCUPYING LESION (ICSOL)

CHIEF COMPLAINTS

- Buzzing in the left ear for … months
- Progressive deafness of left ear for … months
- Headache and facial pain on the left side for … months.

HISTORY

History of present illness: Miss …, 23 years, was apparently well … months back. Since then, she has been suffering from buzzing sounds in the left ear, which is gradually becoming worse day by day. It is associated with deafness in the same side for last … months. Initially it was mild, but gradually it became worse and now she cannot hear anything with her left ear. The patient also complains of left sided headache and pain in the left side of the face. The pain is dull in nature, intermittent, more marked in the morning after waking from sleep, not associated with nausea or vomiting. There is no history of fever, pain or any discharge form left ear, weight loss, convulsion, difficulty in walking or unconsciousness. Her bowel and bladder habits are normal.

History of past illness: Nothing contributory.

Drug History: Nothing contributory.

Family history: Nothing contributory.

Personal history: Nothing contributory.

Menstrual history: Regular flow at 28–30 days interval.

GENERAL EXAMINATION

- Appearance: Depressed, some flickering movement of face in left side
- Anemia, jaundice, cyanosis, clubbing, leuconychia, koilonychias, edema—absent.
- No thyromegaly or lymphadenopathy
- Pulse: 76/ min
- BP: 110/65 mm Hg
- Temperature: Normal.

SYSTEMIC EXAMINATION

Neurological Examination

1. **Higher cerebral function:** Normal.
2. **Speech:** Scanning.
3. **Cranial nerves including fundoscopy:**
   - 5th nerve—all modalities of sensation are diminished over the face on left side. Corneal reflex is absent, on left side
   - 6th nerve—impaired abduction of left eye and diplopia on movement of the left eye (image of finger is parallel)
   - 7th nerve—normal
   - 8th nerve—sensory neural deafness in left ear

- Palatal movement – slightly restricted on left side.
- Other cranial nerves are normal.
- Fundoscopy—bilateral early papilledema.

4. **Motor function:** Intact except hypotonia in all four limbs. Gait is normal.
5. **Sensory function:** Intact.
6. **Cerebellar function:**
   - Horizontal nystagmus
   - Scanning speech
   - Hypotonia.

Examination of other systems reveals normal findings.

SALIENT FEATURE

Miss …, 23 years, right handed, normotensive and non-diabetic, hailing from …, presented with buzzing sounds in the left ear for … months, which is gradually becoming worse day by day. It is associated with deafness in the same side for last … months. Initially it was mild, but gradually it became worse and now she cannot hear anything with her left ear. The patient also complains of left sided headache and pain in the left side of the face. The pain is dull in nature, intermittent, more marked in the morning after waking from sleep, not associated with nausea or vomiting. There is no history of fever, pain or any discharge form left ear, weight loss, convulsion, difficulty in walking or unconsciousness. Her bowel and bladder habits are normal. There is no family history of such illness. She was treated by local physicians with prochlorperazin, cinnarizine, paracetamol and vitamins but there was no response.

On examination
General examination (mention as above)
Systemic examination (mention as above).

With this history and physical findings, my clinical diagnosis is intracranial space occupying lesion, more likely acoustic neuroma.

Q. Why **acoustic nerumoa?**

A. Because, there is history of tinnitus and progressive deafness on left side. On examination, there are lesions involving 5th, 6th and 8th nerve and also cerebellar sign. All indicates lesion in cerebellopontine angle, acoustic neuroma is the most common cause.

Q. What is the other **CP angle tumor?**

A. Meningioma. (Cholesteatoma may give similar picture).

Q. Mention one **investigation** to confirm your diagnosis.

A. MRI of brain.

Q. What other investigations would you suggest in a suspected case of brain tumor?

A. As follows:

- CT scan with contrast
- Chest X-ray (to see any primary lesion, there may be secondaries in the brain)
- In suspected cases—CT scan of chest, abdomen and pelvis
- Bone scan
- CSF cytology for lymphoma, meningeal metastasis and ependymoma
- Biopsy (for confirmation).

RELEVANT QUESTIONS AND ANSWERS

Q. What are the **features** of raised intracranial pressure?

A. As follows:

1. **Symptoms:**
   - Headache (deep seated, dull aching, worse by exertion, coughing, bending forward, more marked in the morning after waking from sleep)
   - Impairment of consciousness, drowsiness, even coma
   - Vomiting (may be projectile, usually without nausea)
   - Convulsion (may be generalized or focal).
2. **Signs:**
   - Bradycardia
   - Arterial hypertension
   - Respiration—deep and slow
   - Fundoscopy shows papilledema
   - Bulged anterior fontanelle in infant.
3. **X-ray skull shows**—silver bitten appearance, sutural diastasis (in infants).

Q. What is **cerebello-pontine angle** (CP angle)?

A. CP angle is the area of lateral cistern containing CSF, arachnoid tissue, cranial nerves and their associated vessels. The borders of CP angle are:

- Medial border—lateral surface of the brainstem
- Lateral border—petrous bone
- Superior border—middle cerebellar peduncle and cerebellum
- Inferior border—arachnoid tissue of lower cranial nerves
- Posterior border—cerebellar pedunclue.

Q. What are the common tumors of the posterior fossa or cerebellopontine angle?

A. As follows:

- Acoustic neuroma (or vestibular schwannoma > 80%)
- Others—meningioma, epidermoid or dermoid cyst, 7th or 5th nerve neuromas, giant basilar aneurysm, cerebellar glioma, pontine glioma, nasopharyngeal tumor extension, metastatic tumors (very rare), etc.

CP angle tumors are the most common posterior fossa tumors. Majority are benign.

Q. What are the clinical features of CP angle tumor?

A. As follows:

- Combination of 8th, 7th, ophthalmic branch of 5th, with or without ipsilateral cerebellar signs, is the hallmark of CP angle lesion
- Common presenting features are ipsilateral hearing loss, tinnitus, vertigo, unsteadiness and sensory abnormality in face
- Features of raised intracranial pressure may be present
- There may be signs of brainstem compression, particularly contralateral hemiparesis
- May result in 9th and 10th nerve palsies when tumor is very large.

Q. What is acoustic neuroma?

A. Acoustic neuroma (or vestibular schwannoma) is a benign tumor of Schwann cells of the 8th cranial nerve. It may occur in isolation or as a part of neurofibromatosis type II where it is often bilateral and associated with other central neoplasms like meningioma, cerebral and optic nerve glioma, spinal neurofibroma, etc. and few or no cutaneous lesion. MRI is the investigation of choice to diagnose acoustic neuroma.

Treatment:

- Surgical excision
- Stereotactic radiosurgery is used to slow down or stop the tumor growth, not to cure or remove the tumor. Often performed in elderly or sick patients who are unable to tolerate brain surgery.

Q. Why headache in intracranial tumor?

A. Headache is due to raised intracranial pressure or due to the traction on the pain sensitive intracranial structures.

Q. What is the classification of intracranial tumors?

A. As follows:

1. **Malignant:**
   - Glioma (astrocytoma)
   - Oligodendroglioma
   - Medulloblastoma
   - Ependymoma
   - Cerebral lymphoma.
2. **Benign:**
   - Meningioma
   - Neurofibroma
   - Craniopharyngioma
   - Pituitary adenoma
   - Colloid cyst
   - Pineal tumors.

Q. What are the tumors of the pituitary region?

A. As follows:

- Pituitary adenoma—microadenoma (<1 cm) and macroadenoma
- Craniopharyngioma
- Optic nerve glioma
- Suprasellar meningioma.

Q. What are the common clinical features of intracranial mass lesions?

A. As follows:

- Local effects on adjacent brain tissue—seizures, focal signs (depends upon the localization of the tumors)
- Features due to raised ICP—headache, vomiting, papilledema, depressed level of consciousness
- False localizing signs—unilateral or bilateral sixth nerve palsy, ipsilateral hemiparesis, bilateral extensor plantar responses
- Others—mental changes, depression, fatigability.

Q. What are the common focal signs of intracranial tumors?

A. As follows:

1. **Frontal lobe:**
   - Contralateral face, arm or leg weakness
   - Expressive dysphasia (dominant hemisphere)
   - Personality change—antisocial behavior, loss of initiatives
   - Profound dementia.
2. **Parietal lobe:**
   - Disturbed sensation

- Visual field defect
- Right left confusion
- Finger agnosia
- Acalculia
- Agraphia
- Sensory or motor neglect.

3. **Temporal lobe:**
   - Receptive dysphasia
   - Visual field defect.
4. **Cerebellopontine angle tumors:**
   - Eighth nerve damage causing gradually progressive sensorineuronal deafness, vertigo, tinnitus
   - Fifth nerve damage causing facial pain, numbness and paresthesia, depression of corneal reflex is an important early sign
   - Ninth, 10th and 11th nerve damage occasionally causes swallowing difficulty, voice change and palatal weakness
   - Cerebellar and pontine damage causing ataxia, ipsilateral incoordination and nystagmus. Pontine damage may produce contralateral hemiparesis.
5. **Pituitary tumors:**
   - Hyper or hyposecretion of hormones
   - Stunted growth
   - Visual field defect
   - Headache.

Q. How to **treat** brain tumors?

A. As follows:

- Surgery
- Chemotherapy
- Radiotherapy.

CHAPTER 9

Endocrinology

- Hypothyroidism 565
- Graves' Disease (with Thyrotoxicosis) 573
- Cushing's Syndrome 583
- Addison's Disease 591
- Hypopituitarism (due to Sheehan's Syndrome) 597
- Acromegaly 601
- Diabetes Mellitus 608
- Obesity 619
- Short Stature 623
- Multiple Endocrine Neoplasia (MEN) 627

HYPOTHYROIDISM

CHIEF COMPLAINTS

- Weight gain and swelling of the whole body for … months
- Cold intolerance for … months
- Increased sleepiness, lethargy, anorexia and weakness for … months
- Constipation for … months
- Lack of concentration and poor memory for … months.

HISTORY

History of present illness: According to the statement of the patient, she was alright … months back. Since then, she is suffering from weight gain and generalized swelling of the whole body, which is progressively increasing in spite of her less appetite. The patient also complains of intolerance to cold and prefers warm environment. For the last … months, she feels very lethargic, extremely weak, generalized body ache and constipation. She also feels sleepiness during most of the time even during working hours, lack of concentration and disturbance of memory since the beginning of her illness. Recently, her voice has changed and become hoarse. She also noticed that her skin is rough and dry. There is no history of chest pain, palpitation, breathlessness, tingling, numbness of hands or feet or loss of consciousness.

History of past illness: There is no history of thyroid disease, thyroid surgery, radiation to the neck or drugs. She denies childbirth or difficult delivery (within the last 6 months).

Menstrual history: She complains of excessive menstrual bleeding for the last 3 months, though it was normal previously.

Family history: No such illness in her family. All the family members are alright.

Socioeconomic history: She is a housewife in a middle-class family.

Drug and treatment history: Prior to her present illness, she did not take any drugs. There is no history of taking any oral contraceptive pill. After the illness, she has only taken multivitamin tablets and iron tables prescribed by a local physician.

GENERAL EXAMINATION

- The patient looks pale and apathetic
- The whole body is swollen
- The face is coarse and puffy with periorbital swelling, baggy eye lids and loss of outer one-third of the eyebrows
- She is mildly anemic, but there is no jaundice, cyanosis, clubbing, koilonychia or leukonychia
- There is nonpitting edema
- Skin is dry, rough, cold and thick (There may be yellow skin due to carotenemia, vitiligo and erythema ab igne, mention if present)
- Thyroid gland—not enlarged (mention, if enlarged)
- Pulse—50/min, high volume
- BP—120/90 mm Hg

SYSTEMIC EXAMINATION

Cardiovascular System

- Pulse—50/min, regular, high volume, normal in character
- BP—120/90 mm Hg
- Neck veins—not engorged
- Precordium—no abnormality detected.

Central Nervous System (CNS)

- Higher psychic functions:
  - Speech—voice is coarse and husky (or croaky)
  - Memory—slightly impaired (may be normal).
- Motor functions:
  - Slow relaxation of the ankle jerks
  - (Evidence of carpal tunnel syndrome may be present, mention if any.)
- Sensory functions—intact.

Musculoskeletal System

- Muscle and joints—tender (may be normal).

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mrs. …, 35 years old, housewife, normotensive, nondiabetic, hailing from …, presented with the weight gain and generalized swelling of the whole body for … months, which is progressively increasing inspite of her less appetite. The patient also complains of intolerance to cold and prefers warm environment. For the last … months, she feels very lethargic, extremely weak, generalized body ache and constipation. She also feels sleepiness during most of the time even during working hours, lack of concentration and disturbance of memory since the beginning of her illness. Recently, her voice has changed and become hoarse. She also noticed that her skin is rough and dry. There is no history of chest pain, palpitation, breathlessness, tingling, numbness of hands or feet or loss of consciousness. She also complains of excessive menstrual bleeding for the last 3 months, although it was normal previously. There is no history thyroid disease, thyroid surgery, radiation to the neck or drugs. She denies childbirth or difficult delivery (within the last 6 months). She gives no history of taking drugs including oral contraceptive pills prior to her present illness. There is no family history of similar illness. She was treated with calcium tablet and vitamins.

On Examination

General examination—mention as above
Systemic examination—mention as above.

My diagnosis is hypothyroidism (myxedema).

Q. What is the **difference** between myxedema and hypothyroidism?

A. Myxoedema is always associated with hypothyroidism, due to deposition of mucopolysaccharide substances, but all hypothyroidism may not be associated with deposition of mucopolysaccharide

substances, so may not be associated with myxedema. (In secondary hypothyroidism, there is no myxedematous change).

Q. What are your **differential diagnoses?**

A. As follows:

- Nephrotic syndrome
- Cushing's syndrome.

Q. Why not this is **nephrotic syndrome**?

A. In nephrotic syndrome, swelling usually starts at the face, later becomes generalized. Edema is pitting in nature. There is history of scanty micturition. All these are absent in this patient. On the other hand, the patient has cold intolerance, sleepiness, lack of concentration, non pitting edema and slow relaxation of ankle jerk and change of voice. These are not found in nephrotic syndrome.

Q. Why not **Cushing's syndrome**?

A. In Cushing's syndrome, there is central obesity along with relatively thin limbs. Other signs include plethoric moon face, buffalo hump, purple striae, etc. All these are absent in this patient (there may be history of prolong intake of steroid.)

Q. What do you think the **cause** in this case?

A. Spontaneous atrophic or autoimmune (because there is no goiter).

Q. If there is goiter with hypothyroidism, what is the **likely cause**?

A. Hashimoto's thyroiditis (Others – Graves' disease. In such case, there is exophthalmos).

Q. What **investigations** do you suggest in hypothyroidism?

A. As follows:

1. Serum FT_3, FT_4 and TSH (low FT_3, low FT_4 and high TSH).
2. Autoantibody (for Hashimoto's thyroiditis – antiperoxidase and antithyroglobulin antibody. However, if hypothyroid is associated with Graves' disease – TSH receptor antibody may be done).
3. Other routine tests:
   - CBC, ESR and PBF (there may be anemia, which is usually normocytic and normochromic, may be macrocytic anemia)
   - Ultrasonogram of the neck
   - ECG (low voltage tracing, sinus bradycardia)
   - X-ray chest (cardiomegaly due to pericardial effusion, heart failure)
   - Serum total cholesterol, LDL and triglyceride (high)
   - CPK, LDH, SGOT (all may be high—not done routinely).

Q. Tell one **single** investigation to diagnose hypothyroidism.

A. Serum TSH level.

Q. What are the **biochemical abnormalities** (other than thyroid hormones) in hypothyroidism?

A. As follows:

- Hypercholesterolemia and hypertriglyceridemia
- Hyponatremia (due to SIADH)
- High CPK and LDH
- Hyperprolactinemia.

Q. What is the **treatment of hypothyroidism**?

A. Thyroxine—it should be started with low dose. The dose should be increased gradually after three weeks. Single dose is preferable, should be taken before breakfast. TSH should be repeated after 6

to 8 weeks. Once TSH is normal, maintenance dose should be continued as a single daily therapy. For follow up—annual thyroid function test should be done.

Note. Remember the following -

If the patient has deficiency of cortisol (as in hypopituitarism or Addison's disease), corticosteroid should be given first and then thyroxine. Otherwise, if thyroxine is given first without correcting cortisol deficiency, there will be severe Addisonian crisis.

Q. Why thyroxine should be started in low dose?

A. Because if high dose is given, it may precipitate anginal attack.

Q. How long will you continue the treatment?

A. Life long.

Q. In hypothyroidism, if there is no response after thyroxine therapy, what are the possibilities?

A. As follows:

- Noncompliance or insufficient dose
- Associated hypopituitarism or Addison's disease
- Pernicious anemia.

RELATED QUESTIONS AND ANSWERS

Q. What are the causes of hypothyroidism?

A. As follows:

1. Autoimmune:
- Spontaneous atrophic hypothyroidism
- Hashimoto's thyroiditis
- Graves' disease (associated with TSH receptor blocking antibody).

2. Iatrogenic:
- Radioiodine therapy for thyrotoxicosis
- After surgery (thyroidectomy)
- Post-radiotherapy in neck
- Drugs—such as lithium, amiodarone and antithyroid drug therapy.

3. Others:
- Endemic iodine deficiency
- Postpartum thyroiditis
- Rarely, dyshormonogenesis
- Secondary to hypopituitarism and hypothalamic disorders (rare).

Q. What are the causes of goitrous hypothyroidism?

A. As follows:

- Hashimoto's thyroiditis
- Graves' disease (in such case, there is also exophthalmos and diffuse goiter with dermopathy)
- Endemic iodine deficiency (less common)
- Drugs—lithium, amiodarone, iodide
- Rarely, dyshormonogenesis.

Q. What are the causes of nongoitrous hypothyroidism?

A. As follows:

- Autoimmune or idiopathic (spontaneous atrophic)—commonest cause
- Following radio-iodine therapy for thyrotoxicosis
- Post radiotherapy in the neck
- After surgery (thyroidectomy)
- Secondary to hypopituitarism, hypothalamic disorders.

Q. What are the thyroid functions in secondary hypothyroidism?

A. Low FT_3, FT_4 and TSH (Usually all thyroid hormones are low).

Q. How to investigate in such case?

A. Causes may be in the pituitary or hypothalamus. TRH stimulation test should be done. After giving TRH, if TSH is high, the cause is in the hypothalamus. If there is no or little rise of TSH, the cause is in the pituitary.

Q. If the patient has ischemic heart disease with hypothyroidism, how to treat?

A. As follows:

- Thyroxine should be given in low dose (25μg). Dose should be increased slowly up to the optimum dose
- β-blocker (propranolol) should be added
- Coronary dilator, calcium antagonist may be added
- Coronary angiography followed by angioplasty or coronary artery bypass surgery may be needed.

Q. How to treat an elderly patient with hypothyroidism?

A. Treatment is same. But one should take care whether the patient is suffering from any ischemic heart disease. Following thyroxine, it may precipitate angina and myocardial infarction. Treatment is same as above.

Q. Why hypothyroidism in Graves' disease?

A. Natural history of Graves' disease is hyperthyroidism, followed by euthyroidism and hypothyroidism (however, hypothyroidism may occur after radioiodine therapy or surgical treatment).

Q. What bedside physical sign will you see in myxedema?

A. Ankle jerk, which shows slow relaxation, also called "hung-up reflex" (other jerks may also show slow relaxation).

Q. How slow relaxation is best elicited in the ankle? Why slow relaxation?

A. It is best elicited in kneel down position on a chair or bedside. Slow relaxation is due to decreased rate of muscle contraction and relaxation.

Q. Why nonpitting edema in myxedema?

A. Due to deposition of mucopolysaccharide substances.

Q. What are the types of anemia in hypothyroidism?

A. Anemia may be:

- Usually normocytic normochromic
- Iron deficiency, if menorrhagia (in female)
- May be macrocytic due to associated pernicious anemia (due to deficiency of vitamin B_{12}).

Q. What are the causes of anemia in hypothyroidism?

A. Causes of anemia:

- Anemia of chronic disorder
- Iron deficiency
- Vitamin B_{12} deficiency

- Folate deficiency
- Other factors responsible—menorrhagia in female, anorexia.

Note

Macrocytosis in peripheral blood, but normoblastic bone marrow occurs in hypothyroidism

Q. What are the **cardiovascular** problems in myxedema?

A. As follows:
- Sinus bradycardia
- Pericardial effusion and pericarditis
- Congestive cardiac failure
- Atherosclerosis (because of hyperlipidemia)
- Ischemic heart disease
- Hypertension.

Q. What are the **neurological** features in hypothyroidism?

A. As follows:
1. Carpal tunnel syndrome (or tarsal tunnel syndrome).
2. Psychosis (myxedema madness).
3. Myxedema coma.
4. Cerebellar syndrome.
5. Deafness (Trotter's syndrome).
6. Others:
   - Epileptic fit (due to SIADH)
   - Peripheral neuropathy
   - Myotonia (Hoffman's syndrome)
   - Proximal myopathy
   - Pseudodementia
   - Drop attack.

Q. What is **Hoffman's syndrome**?

A. In a patient with myxedema, there may be myotonia with pain and swelling in the muscles after exercise, called Hoffman's syndrome.

Q. What is **Pendred's syndrome**?

A. It is an autosomal recessive disorder in which there is sensori-neural deafness with goiter. It is due to inborn error of thyroid hormone synthesis.

Q. What is **subclinical hypothyroidism** (borderline hypothyroidism or compensated euthyroidism)?

A. In this condition, T_3 and T_4 are in the lower limit of normal and TSH is slightly high. The patient may be clinically euthyroid. This may persist for many years, though overt hypothyroidism may occur. Conversion to overt hypothyroidism is more common in men or when thyroid peroxidase (TPO) antibody is present or TSH level is more than 10 mU/L.

Treatment—thyroxine therapy may be given if TSH is persistently raised above 10 mU/L or when there are symptoms or high titre of thyroid antibodies or lipid abnormalities. If only TSH is marginally high with vague symptoms, thyroxine may be given sometimes. However, in female TSH should be normalized during pregnancy to avoid any adverse effect in fetus.

If TSH is marginally raised, the test should be repeated after 3 to 6 months.

Q. What is the **difference** between primary and secondary hypothyroidism?

A. As follows:

- Primary hypothyroidism means cause in the thyroid gland. It is usually associated with myxedema.
- Secondary hypothyroidism means cause in the pituitary (or rarely hypothalamus). In such case, myxedema is rare. There are other features of hypopituitarism also.

Q. What is **myxedema coma?** What are the **mechanisms**? How to **treat**?

A. Myxedema coma is characterized by depressed level of consciousness or even coma. Convulsion may occur. It is rare, may occur in severe hypothyroidism, usually in elderly. CSF studies shows high pressure and protein is also high. There is 50% mortality.

Causes of myxedema coma:

- Syndrome of inappropriate ADH secretion (SIADH. Coma is due to hyponatremia)
- Hypoxemia
- Hypercapnia
- Hypothermia
- Hypoglycemia
- Other factors—cardiac failure, infection, use of sedative.

Treatment of myxedema coma: It is better to be treated in ICU. Before starting treatment, blood is taken for FT_3, FT_4, TSH and cortisol.

1. T_3 (rapidly acting) 20 µg, 8 hourly usually IV given (parenteral T_4 is not available, also slow to start action). If parenteral T_3 is not available, oral thyroxine through Ryle's tube should be given.
2. IV hydrocortisone—100 mg 8 hourly (especially if suspicion of hypopituitarism).
3. Other treatment:
   - Slow rewarming
   - High flow O_2 therapy
   - IV fluid and glucose
   - Antibiotic, if infection is suspected
   - Assisted ventilation may be necessary (as in any unconscious patient).

Q. What is **myxedema madness?**

A. It may occur in severe hypothyroidism in the elderly. There is dementia or psychosis or delusion. Sometimes, these features may occur shortly after starting thyroxine replacement. Depression is common in hypothyroidism.

Q. What is **sick euthyroid syndrome?**

A. In any severe acute nonthyroidal illness or after surgery, there may be abnormal thyroid function tests although the patient is euthyroid, it is called sick euthyroid syndrome. It may occur after myocardial infarction, pneumonia, cerebrovascular disease (CVD) and drugs (dopamine and steroid). Usually, there is normal TSH, normal or low T_4 and low T_3. Levels are usually mildly below normal and thought to be mediated by interleukins (IL-1 and IL-6). Test should be repeated after recovery of systemic illness.

Biochemical thyroid function should not be done in patient with acute nonthyroidal illness, unless there is good evidence of thyroid disease (such as goiter and exophthalmos).

Mechanisms of sick euthyroid syndrome:

- Reduced production or affinity of TBG to T_4 and T_3.
- Reduced peripheral conversion of T_4 to T_3, occasionally, more rT_3 (inactive reverse T_3).
- Reduced hypothalamic pituitary TSH production, hence low T_3 and T_4.

Q. How to investigate and treat **hypothyroidism in pregnancy**?

A. Hypothyroidism is difficult to diagnose in pregnancy, as normal pregnancy may be associated with many features of hypothyroidism such as cold skin, cold intolerance, weight gain, constipation. High degree of suspicion is essential.

- Most sensitive investigation is TSH, which is high. Also, FT_3 and FT_4 should be done (Total T_3 and T_4 may be high in normal pregnancy due to increase TBG).
- Treatment—thyroxine should be given (100 to 150 µg once daily). Requirement of thyroxine is relatively high (40 to 50%) in pregnancy, because of increased metabolism of thyroxine by the placenta and also increased serum TBG in pregnancy which binds thyroxine, resulting in less FT_3 and FT_4.
- Dose of thyroxine should be adjusted to maintain normal TSH (serum TSH and FT4 should be measured during each trimester).

Q. What is **Hashimoto's thyroiditis**?

A. It is an autoimmune thyroiditis characterized by destructive lymphoid infiltration of thyroid leading to atrophic change with regeneration and goiter formation. It is more common in middle aged woman.

- The goiter is usually diffuse, moderately enlarged and firm or rubbery. Sometimes, it may be soft to hard.
- Antithyroid antibody (very high, >1000 IU/L)—antimicrosomal (antiperoxidase) in 90% and antithyroglobulin antibodies (no rise of TSH-receptor antibody).
- About 25% patients are hypothyroid at presentation. In the remaining patients, serum T4 is normal and TSH is normal or raised. There is risk of developing overt hypothyroidism in future. Initially, the patient may present with features of toxicosis, called Hashi-toxicosis.
- In young patients (<20 years), ANF may be positive.
- Since this is an autoimmune disease, it may be associated with other autoimmune diseases like – Addison's disease, diabetes mellitus, premature ovarian failure, rheumatoid arthritis, Sjogren's syndrome, ulcerative colitis, autoimmune hemolytic anemia.
- Treatment – thyroxine (it reduces the size of goiter also).

Q. What is the **radio-iodine uptake** in Hashimoto's thyroiditis?

A. It shows the following:

- Initially—increased (toxic phase)
- After few days or weeks—normal uptake
- Later on—less uptake (hypothyroid phase).

Q. What are the **histological** findings in Hashimoto's thyroiditis?

A. As follows:

- Lymphocyte infiltration, also monocyte and plasma cell
- Hyperplasia and fibrosis
- Hurthle cell.

GRAVES' DISEASE (WITH THYROTOXICOSIS)

CHIEF COMPLAINTS

- Excessive sweating and heat intolerance for … months
- Weight loss for … months
- Palpitation for … months
- Insomnia, irritability and restlessness for … months
- Occasional loose motion for … months.

HISTORY

History of present illness: According to the statement of the patient, she was reasonably well … months back. Since then, she has been suffering from excessive sweating and heat intolerance. She prefers and feels comfortable in cold environment. She also noticed significant loss of weight inspite of her good appetite. She feels very hungry and takes more food, also experiences palpitation, even at rest which is more marked on exertion. She also complains of insomnia, irritability and restlessness for the last … months. The patient also complains of occasional loose stool, 3 to 4 times per day, which is not associated with mucus or blood and not related to intake of any food or milk. There is no history of fever, excessive thirst, polyuria or abdominal or chest pain.

History of past illness: Nothing significant

Family history: There is no such illness in her family. All the members of the family are in good health

Menstrual history: Her menstruation was regular. But for the last few months, she is amenorrhoic

Socioeconomic history: Mention according to the patient's statement

Drug and treatment history: There is no history of taking drugs that may cause these symptoms

GENERAL EXAMINATION

- The patient is emaciated and there is excessive sweating.
- The face appears anxious and frightened. There is bilateral exophthalmos with periorbital edema.
- Signs of thyrotoxicosis are present (tachycardia, warm sweaty palm, and fine tremor of outstretched hands).
- There is pretibial myxoedema (mention, if any).
- Pulse – 110/min, regular.
- BP – 160/85 mm Hg.

SYSTEMIC EXAMINATION

Thyroid Gland

- **Inspection**: The thyroid gland is diffusely enlarged, measuring 10 × 10 cm, right lobe is slightly larger than the left.
- **Palpation**: The gland is soft, nontender, mobile, surface is smooth, not fixed with underlying structure or overlying skin. Not associated with lymphadenopathy.
- **Percussion**: There is no retrosternal extension.
- **Auscultation**: There is bruit over the right lobe.

Eyes

- Exophthalmos—present in both eyes.
- Lid retraction and lid lag—present.
- Joffroy's sign—present.
- Mobius' sign and Stellwag's sign are absent.
- Movement of the eyeball—normal in all directions.

Note

Mention according to your findings

Cardiovascular System

- Pulse—110/min, regular, high volume.
- BP—160/85 mm Hg.
- Precordium—both first and second heart sounds are loud, no other abnormality detected.

Nervous System

- Higher psychic functions: She is irritable with a poor memory and concentration.
- Motor system:
  - Fine tremor of the outstretched hands
  - All the jerks—slightly brisk
  - Planter—flexor on both sides.
- Sensory system—intact.

SALIENT FEATURES

Mrs. …, 32 years old, housewife, normotensive, nondiabetic, hailing from …, presented with the complaints of excessive sweating and heat intolerance for … months. She prefers and feels comfortable in cold environment. She also noticed significant loss of weight inspite of her good appetite. She feels very hungry and takes more food, also experiences palpitation, even at rest which is more marked on exertion. She also complains of insomnia, irritability and restlessness for the last … months. The patient also complains of occasional loose stool, 3 to 4 times per day, which is not associated with mucus or blood and not related to intake of any food or milk. There is no history of fever, excessive thirst, polyuria or abdominal or chest pain. There is no such illness in her family. Her menstruation was regular. But for the last few months she is amenorrhoic. There is no history of taking drugs that may cause these symptoms. There is no family history of similar illness.

On Examination

General examination – mention as above.

Systemic examination – mention as above.

My diagnosis is thyrotoxicosis due to Graves' disease.

Q. Why it is Graves' disease?

A. Because, she has bilateral exophthalmos, diffuse goiter and dermopathy (pretibial myxedema).

Note. Remember the following -

If there is no exophthalmos, then tell the diagnosis as **thyrotoxicosis**. Then question may be asked, "What is the likely cause of thyrotoxicosis in this case?" Your answer will be "still it may be due to Graves' disease, as this is the commonest cause of thyrotoxicosis." Then mention other common causes of thyrotoxicosis.

Q. Why do you think this is a case of thyrotoxicosis?

A. Because:

- In the history, there is excessive sweating, weight loss inspite of good appetite, intolerance to heat, palpitation, and occasional loose motion.
- On examination, she is emaciated and signs of thyrotoxicosis, such as—tachycardia, warm sweaty palm and fine tremor of the out-stretched hands are present.

Note. Remember the following -

If a patient having loss of weight despite good appetite, think of thyrotoxicosis. (Other cause is diabetes mellitus). However, loss of appetite in thyrotoxicosis may occur in the elderly.

Q. What is your differential diagnosis?

A. Toxic nodular goiter, toxic multinodular goiter (sometimes, there may be small nodules which may not be palpable**.** Ultrasonogram of thyroid will show single or multiple nodular goiter).

Q. What are the differences between Graves' disease and toxic multinodular goiter?

A. As follows:

Features	Graves' disease	Toxic multinodular goiter
1. Age	20 to 40 years	Middle aged or elderly
2. Past history	Not specific	Nodular goiter for long time
3. Thyroid gland	Diffusely enlarged	Multinodular goiter
4. Cause	Autoimmune disease	Usually iodine deficiency
5. Ophthalmopathy	Common	Rare
6. Dermopathy	Common	Absent
7. Heart complications	Less common	More common
8. Thyroid acropachy	May occur	Absent
9. Hypothyroidism	May occur later	Usually does not occur

Q. What investigations do you suggest in thyrotoxicosis?

A. As follows:

1. To confirm thyrotoxicosis -

- FT_3, FT_4 and TSH (low TSH, high T_3 and T_4. But in T3 toxicosis, TSH is low and T_4 is normal, but T_3 is high).
- Radioiodine uptake test (RAIU) and thyroid scanning. RAIU shows rapid uptake and rapid turnover. There is high uptake in 2 or 4 and 24 hours, but rapid fall after 48 hours. Technetium scintigraphy is better than RAIU test because, it is quicker to perform and requires lower dose of radioactivity.

2. To find out causes:
   - Ultrasonography (USG) of the neck (to see single, multinodular and diffuse goiter).
   - Thyroid autoantibody (in Graves' disease) – TRAb (thyroid receptor antibody). TSH receptor stimulating antibody (TSI) is responsible for toxicosis.
   - Anti-peroxidase and anti-thyroglobulin antibody (very high in Hashimoto's thyroiditis, but slight to moderately high in Graves' disease).
3. Other tests:
   - Fine needle aspiration cytology, (FNAC, if goiter is present)
   - Electrocardiography (ECG)
   - Chest X-ray (to see retrosternal extension of goiter and cardiomegaly)
   - Blood sugar (may be high as secondary DM may occur)
   - Serum cholesterol (low in thyrotoxicosis)
   - For ophthalmopathy – ocular ultrasonography, CT scan of the orbit.

Q. What are the **findings** of radio iodine uptake test in thyrotoxicosis?

A. It shows—rapid uptake and rapid turnover (After 2 or 4 and 24 hours, uptake is high. After 48 hours, uptake falls).

Q. What are the causes of **thyrotoxicosis with low radioiodine uptake?**

A. As follows:
- Subacute thyroiditis (De Quervain's thyroiditis).
- Postpartum thyroiditis.
- Factitious thyrotoxicosis.
- Iodine induced (if the patient is on iodine or amiodarone, which contains iodine).
- Ectopic thyroid tissue producing thyrotoxicosis (struma ovarii, choriocarcinoma and hydatidiform mole).

QUESTIONS AND ANSWERS RELATED TO GRAVES' DISEASE

Q. What is **Graves' disease?**

A. It is an autoimmune thyroid disease due to stimulating antibody against TSH receptors (thyroid stimulating immunoglubulin- TSI), characterized by **triad** of:
- Exophthalmos
- Diffuse goiter
- Dermopathy (pretibial myxedema).

Q. What is the **cause** of Graves' disease?

A. Autoimmune disease due to IgG antibody against TSH receptor, producing excess thyroid hormones. TRAb antibody acts similar to TSH. Common in female, M:F = 1:5. TRAb is of two types: (1) TSI, 80% to 95%, causing thyrotoxicosis and (2) TSH receptor blocking antibody, causing hypothyroidism.

Q. What is the significance of **thyroid bruit**?

A. It is pathognomonic of Graves' disease, and it rarely occurs in other thyroid diseases. It indicates increased vascularity, probably due to autoimmune mechanism.

Q. What is the **natural history** of Graves' disease?

A. It may be hyperthyroid, euthyroid followed by hypothyroidism.

Q. What is **euthyroid** Graves' disease?

A. The patient is clinically and biochemically euthyroid, but there is ophthalmopathy (also there is diffuse goiter, dermopathy). Thyroid releasing hormone (TRH) stimulation test show flat response curve.

Q. What is **hypothyroid Graves' disease**?

A. In this condition, the patient has features of Graves' disease (see above) with the following features of hypothyroidism:

- Coarse puffy face, periorbital puffiness (baggy eye lids)
- Dry, cold and scaly skin
- Nonpitting edema, slow relaxation of the ankle jerk
- Coarse and croaky voice.

Q. What is the **mechanism** of thyroid ophthalmopathy? What are the **changes** and how to **treat?**

A. It is immunologically mediated. Within the orbit, there is cytokine-mediated proliferation of fibroblast, which secretes hydrophilic glycosaminoglycans.

The following changes occur in ophthalmopathy:

- Excessive interstitial fluid and infiltration of chronic inflammatory cells in the orbit (lymphocytes, plasma cells and mast cells)
- Swelling and edema of extraocular muscles
- Increased retrobulbar pressure and eyeball is pushed forward (proptosis). In severe cases, optic nerve compression may occur.

Clinical features: Increased lacrimation, gritty sensation in the eye, pain due to conjunctivitis or corneal ulcer, reduced visual acuity and diplopia. It increases with poor control of thyroid function and also following radioiodine therapy. Ophthalmopathy is common in cigarette smoker. However, cigarette smoking is weakly associated with Graves' disease.

Treatment:

- Reassurance and general treatment of the eye. Methylcellulose eyedrops (relieves grittiness). To prevent exposure keratitis, use tinted glass and lateral tarsorrhaphy (if corneal ulcer).
- If visual field defect, loss of visual acuity and papilledema or progressive exophthalmos, steroid in high dose (prednisolone 60 to 120 mg/day) may be helpful.
- Pulse methylprednisolone and cytotoxic drug (cyclophosphamide) may be helpful.
- In severe cases—irradiation of the orbit.
- If no response in 7 to 10 days or loss of visual acuity, orbital decompression may be necessary.
- For diplopia—correction of eye muscle by surgery (but should be delayed for 6 months, until degree of diplopia is stable).

Note. Remember, ophthalmopathy in Graves' disease -

- Eye problems occur in 5% to 10% of the cases.
- Ophthalmopathy occurs in 50% in the first presentation, may develop after treatment of hyperthyroidism and precedes many years before hyperthyroidism.
- Not related to toxicosis. It may be present in euthyroid or hypothyroid.
- If hypothyroidism develops, exophthalmos may be aggravated, especially if treated with radioiodine therapy.
- Lid retraction resolves when the patient is euthyroid, but exophthalmos resolves slowly and may take up to 2 to 3 years.

Eponyms of eye signs in thyroid disease:

- Lid lag—von Graefe's sign
- Absence of wrinkling of forehead on upward gaze—Joffroy's sign
- Impaired convergence of eye—Möebius' sign
- Infrequent blinking—Stellwag's sign

- Paralysis of extraocular muscles—Jendrassik sign.
- Weakness of at least one extraocular muscle—Ballet sign.

Q. What is **malignant exophthalmos?**

A. It is the severe, progressive exophthalmos which may lead to blindness due to optic nerve compression. Treated with high dose of prednisolone up to 120 mg/day. Decompression may be needed, sometimes orbital irradiation may be given.

Q. What is **pretibial myxedema** (dermopathy)?

A. In this condition, there is firm, nodular, thickened or plaque-like lesion, pink or brown, giving a peau d'orange appearance. It is due to the deposition of mucopolysaccharide in the dermis. Usually, present in the shin of legs up to the dorsum of foot (but may occur in any part of the body, especially at pressure point). It may be pruritic and hyperpigmented. It is present only in Graves' disease in 10% cases, almost always associated with ophthalmopathy and is not a manifestation of hypothyroidism (pretibial myxedema is a misnomer). Occasionally, pretibial myxedema develops after treatment of hyperthyroidism, especially with radioiodine therapy.

Treatment is rarely necessary. Local injection of triamcinolone or ointment betamethasone may be helpful.

Q. Is there any **evidence of cancer** in Graves' disease?

A. Unusual, but highly suspicious if there is associated cold nodule.

Q. How to **treat** Graves' disease?

A. Graves' disease is an autoimmune disease which may present with hyper, hypo or euthyroid state.

- If there is thyrotoxicosis or hypothyroidism treat accordingly
- In euthyroid cases, treatment is only symptomatic and supportive.

QUESTIONS AND ANSWERS RELATED TO THYROTOXICOSIS

Q. What are the **causes** of thyrotoxicosis?

A. As follows:

1. Graves' disease—commonest cause (76%).
2. Toxic multinodular goiter (14%).
3. Toxic nodular goiter (5%, toxic adenoma or hot nodule called Plummer's disease).
4. Thyroiditis (subacute thyroiditis, also called De Quervain's thyroiditis, and postpartum thyroiditis. All are transient).
5. Hashimoto's thyroiditis, also called Hashitoxicosis (ultimately hypothyroidism develops).
6. Factitious thyrotoxicosis (self-intake of thyroxine).
7. Iodine induced (Jod-Basedow's phenomenon) and drug (amiodarone).
8. Others (rare):
   - Carcinoma of thyroid (follicular)
   - Struma ovarii (secretes thyroid hormone)
   - Hydatidiform mole and choriocarcinoma (both secrete thyroid-stimulating hormone, TSH).

Q. What is **factitious thyrotoxicosis?**

A. Features of thyrotoxicosis that occur following deliberate intake of thyroxine to reduce weight, usually in emotionally disturbed person. Clues for diagnosis are high thyroid hormones and low radioiodine uptake. Thyroglobulin level is zero or low. There is high ratio of T_4:T_3 = 70:1 (in conventional thyrotoxicosis, the ratio is 30:1). Combination of negligible radioiodine uptake, high T_4:T_3 ratio and low thyroglobulin is diagnostic.

Note. Remember the following points:

- In elderly patient, there may not be obvious features of thyrotoxicosis. Sometimes, the patient may present only with atrial fibrillation, tachycardia or heart failure, which masks the features of thyrotoxicosis.
- Children may present with excess growth, behavior problem like hyper-reactivity and increase in weight rather than loss.
- Apathetic thyrotoxicosis may be present in elderly patient. There are features of thyrotoxicosis associated with features of hypothyroidism also. High degree of suspicion is essential for the diagnosis of such case.

Q. What is **thyrotoxic periodic paralysis** (TPP)?

A. If a thyrotoxic patient develops sudden or periodic weakness, it is called TPP. It is due to hypokalemia (caused by entry of potassium into the cell), common in Asians. It may occur following excess intake of carbohydrate or glucose or after heavy exercise and may persists for 7 to 72 hours. Treatment of thyrotoxicosis improves the condition.

Q. How to **treat** thyrotoxicosis?

A. Three modes of treatment: drugs (carbimazole and propylthiouracil), radioiodine therapy and surgery.

1. Drugs:

- Carbimazole or propylthiouracil: These drugs reduce the synthesis of thyroid hormones by inhibiting the iodination of tyrosine.
  - Carbimazole 45 to 60 mg daily. When the patient is euthyroid, reduce the dose, then 5 to 20 mg daily for 18 to 24 months. Periodic complete blood count (CBC) is necessary, as there may be agranulocytosis. Also, FT_4 and TSH should be measured.
  - Propylthiouracil 400 to 600 mg daily. Dose is reduced when the patient becomes euthyroid.
- β-blocker: Propranolol (up to 160 mg/day). It reduces sympathetic symptoms (such as tremor, tachycardia and sweating).

Indications of drug:

- Usually given in first episode in patient < 40 years of age.
- Small goiter.
- Mild features of thyrotoxicosis.

Disadvantages of drugs:

- Relapse in 50% of the cases within 2 years of stopping the drug (surgery or radioiodine or long-term drug therapy may be needed in such case).
- Complication such as hypersensitive skin rash and agranulocytosis.
- Compliance may be poor.
- Costly.

Note. Remember the following -

Advise the patient with carbimazole therapy—if sore throat or fever develops, which may be due to agranulocytosis, stop the drug and inform the doctor.

2. Radioiodine therapy: It acts by destroying the functioning thyroid cells and by inhibiting their ability to replicate. About 5 to 10 mCi is given orally, depending on the size of goiter. It is effective

in 75% cases in 4 to 12 weeks. In this period, propranolol is given. In severe cases, carbimazole may be given, which should be started 48 hours after radioiodine therapy. If the drug is started before 48 hours, it reduces the efficacy of radioiodine.

Indications of radioiodine therapy:

- Usually, above 40 years of age (however, some advocate to use in young)
- Recurrence after surgery or drugs, irrespective of age
- Toxic multinodular goiter or toxic adenoma or hot nodule
- In early age, with major serious other illness
- Some cases of carcinoma thyroid (follicular, papillary after surgery)
- Ablative therapy with severe atrial fibrillation, also in heart failure
- Psychosis
- Poor drug compliance
- Hypersensitivity to the drug.

Contraindications of radioiodine therapy:

- Pregnancy or planned pregnancy within 6 months of treatment.
- During lactation.
- Active or malignant Graves' ophthalmopathy.

Disadvantages of radioiodine therapy:

- Hypothyroidism: It occurs in 40% in first year and 80% in 15 years.
- Early discomfort and exaggeration of hyperthyroidism may occur (due to radiation thyroiditis). Hence, the patient should be rendered euthyroid using drug, which should be stopped 2 to 5 days before radioiodine therapy.
- Exacerbation of ophthalmopathy.

Note. Remember the following -

In severe thyrotoxicosis, initially carbimazole is given for 4 to 8 weeks. Then radioiodine therapy is given. Carbimazole is stopped 48 hours before radioiodine therapy. If no response after 12 to 24 weeks, a second dose of radioiodine is given.

3. Surgery (subtotal thyroidectomy): The patient should be made euthyroid by antithyroid drug before operation. Two weeks before operation, potassium iodide should be added 60 mg 8 hourly. It inhibits thyroid hormone release, reduces the size and vascularity of gland, making surgery technically easier.

Indications of surgery:

- Large goiter or multinodular goiter
- Relapse or no response to drug
- Drug hypersensitivity
- Noncompliance with drug
- Suspicion of malignancy
- Pressure effect
- Cosmetic purpose.

Complications of surgery:

- Hypothyroidism in 25%

- Transient hypoclcemia (10%)
- Permanent hypoparathyroidism (1%)
- Recurrent laryngeal nerve palsy, causing hoarseness of voice due to vocal cord palsy (1%).

Note. Remember the following -

In toxic nodular or multinodular goiter, treatment of choice is radioiodine therapy or surgery. Drug treatment is not helpful.

Q. How to **treat** thyrotoxicosis **with atrial fibrillation**?

A. Atrial fibrillation occurs in 10% cases, common in the elderly > 60 years, more in toxic multinodular goiter, and may occur in subclinical hyperthyroidism. It is treated by:

- β-blocker: Propranolol (digoxin has little role). Verapamil and amiodarone may be used, if β-blocker is contraindicated.
- Antithyroid drug, followed by radioiodine therapy.
- Anticoagulant: Aspirin in elderly and warfarin in younger.
- 50% AF reverts spontaneously to sinus rhythm. If persistent AF is present, cardioversion may be done, provided FT_4 and TSH are normal.

Q. How to **treat** thyrotoxicosis in **pregnancy**?

A. The patient with thyrotoxicosis is unlikely to get pregnant as anovulatory cycles are common. Autoimmune thyroid disease is also less common as maternal immune response is suppressed in pregnancy. Diagnosis may be difficult, because of the overlap symptoms of normal pregnancy (e.g. palpitation) and also misleading thyroid function test, although TSH is usually reliable.

Because of high thyroxine binding globulin (TBG), total T_4 and T_3 are high, and TSH is low. Hence, high FT_4 and FT_3, and low TSH level is suggestive of thyrotoxicosis. In pregnancy, thyrotoxicosis is usually due to Graves' disease. TRAb (TSI) can cross placenta and develop thyrotoxicosis in fetus also.

Treatment of thyrotoxicosis in pregnancy:

- Propylthiouracil is preferred (carbimazole can cross placenta, causing fetal goiter and scalp skin defect in child called aplasia cutis). Propylthiouracil is given in lowest dose, less than 150 mg daily to prevent fetal hypothyroidism and goiter. TRAb is measured in last trimester. If it is not high, the drug can be stopped 4 weeks before delivery (to prevent neonatal hypothyroidism).
- If needed, propylthiouracil can be given after delivery and breastfeeding should be continued, as little drug is excreted in breast milk.
- If surgery is necessary, it should be done in middle trimester.

Note. Remember the following -

Radioiodine therapy is absolutely contraindicated in pregnancy.

Q. What is **thyrotoxic crisis**? How to **treat**?

A. Thyrotoxic crisis is characterized by life threatening increase of signs and symptoms of thyrotoxicosis (also called thyroid storm).

Features of thyrotoxic crisis are:

- High fever
- Restlessness, agitation and irritability

- Nausea, vomiting, diarrhea and abdominal pain
- Tachycardia, AF and in elderly, cardiac failure
- Confusion, delirium and coma.

Precipitating factors for thyroid crisis:

- Infection
- Stress
- Surgery in unprepared patient
- Following radioiodine therapy (due to radiation thyroiditis).

Diagnosis—mostly clinical and high degree of suspicion is vital. FT_3, FT_4 and TSH should be done immediately.

Treatment (blood sample is taken for T_3, T_4 and TSH):

- The patient should be treated in intensive care unit (ICU).
- Propranolol 80 mg 6 hourly (or 1 to 5 mg IV 6 hourly).
- IV fluid (normal saline and glucose).
- Carbimazole 40 to 60 mg daily. Or propylthiouracil 150 mg 6 hourly (if needed, through Ryle's tube). Carbimazole can be given per rectally also.
- Other therapy—sodium ipodate, a radiographical contrast media, 500 mg daily is rapidly effective. Or potassium iodide or Lugol's iodine may be given. Dexamethasone 2 mg 6 hourly and amiodarone are also effective.
- Broad spectrum antibiotic.
- General measures—control of temperature and O_2 therapy.
- After 10 to 14 days, the patient can usually be maintained on carbimazole alone.

Mortality rate in thyrotoxic crisis is 10%.

CUSHING'S SYNDROME

CHIEF COMPLAINTS

- Excessive weight gain for … months
- Weakness for … months
- Backache and generalized bodyache for … months
- Bleeding spots on the skin for … days.

HISTORY

History of present illness: According to the statement of the patient, she was reasonably well … months back. Since then, she is gaining weight which is progressively increasing inspite of normal food intake. She also feels extremely weak and lethargic. The patient also complains of backache and generalized bodyache for the last … months. The pain is more marked with activity and the patient feels comfortable by taking rest. Sometimes, she feels difficulty in standing from sitting position. For the last … months, she noticed multiple bleeding spots on the skin, involving mostly the forearms and legs. There is no history of headache, visual problem, cough or chest pain. Her bowel and bladder habits are normal. There is no history of intolerance to cold, or increased sleepiness.

History of past illness: Nothing significant.

Menstrual history: She gives history of oligomenorrhea (or amenorrhea) for … months, previously it was regular.

Family history: Nothing significant.

Socioeconomic history: Nothing significant.

Drug and treatment history: There is no history of intake of steroid and alcohol.

GENERAL EXAMINATION

- The patient is obese. There is more truncal obesity with relatively lean and thin limbs (lemon on a match stick appearance)
- Face is moonlike, puffy and plethoric with acne, hirsutism and frontal baldness
- There is buffalo hump at the root of the neck and increased fat above both the supraclavicular fossa
- There are multiple pink striae on abdomen, back and axilla
- Skin is thin, with multiple purpura and bruise
- Pulse—90/min, regular
- BP—155/90 mm Hg
- Temperature—98.6ºF
- Respiration—16/min.

SYSTEMIC EXAMINATION

Abdomen

- The abdomen looks distended and flanks are full
- There are multiple pink striae of variable size and shape
- No organomegaly
- Ascites—absent (as evidenced by absent fluid thrill and shifting dullness)

Cardiovascular System

- Pulse—90/min
- BP—155/90 mm Hg
- Precordium—normal.

Nervous System

- Higher psychic functions—normal
- Cranial nerves—intact
- Motor system—proximal muscular weakness of both upper and lower limbs. Reflexes are normal
- Sensory system– normal.

Musculoskeletal System

- Proximal myopathy is present more marked in the lower limb than upper limb
- There is slight kyphosis
- Spine is tender at lumbar region (due to osteoporosis).

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mrs. …, 40 years old, housewife, normotensive, nondiabetic, hailing from …, presented with weight gain for … months, which is progressively increasing inspite of normal food intake. She also feels extremely weak and lethargic. The patient also complains of backache and generalized bodyache for the last … months. The pain is more marked with activity and the patient feels comfortable by taking rest. Sometimes, she feels difficulty in standing from sitting position. For the last … months, she noticed multiple bleeding spots on the skin, involving mostly the forearms and legs. There is no history of headache, visual problem, cough or chest pain. Her bowel and bladder habits are normal. There is no history of intolerance to cold, or increased sleepiness. She gives history of oligomenorrhea (or amenorrhea) for … months, previously it was regular. There is no history of intake of steroid and alcohol.

On Examination—

General examination – mention as above.

Systemic examination – mention as above.

My diagnosis is cushing's syndrome.

Q. What are your **differential diagnoses?**

A. As follows:

- Simple obesity
- Hypothyroidism
- Metabolic syndrome
- PCOS (in early age).

Q. How to **investigate** Cushing's syndrome?

A. Initial tests are done to confirm the diagnosis and further tests are done to find out the cause.

1. Tests to confirm Cushing's syndrome:
   - First line screening test:

- 24 hours urinary free cortisol measurement
- Overnight dexamethasone suppression test—1 mg dexamethasone is given orally at 11 p.m. Blood sample is taken at 9 a.m. in the next morning to measure serum cortisol. Normally, almost total suppression of cortisol (< 100 nmol/L). Failure of suppression indicates Cushing's syndrome due to any cause (This test is simple, can be done as an outpatient screening test, but gives some false positive results).

♦ Second line screening test (if above are abnormal)
- Serum cortisol level (8 a.m. and 12 midnight)—shows loss of circadian rhythm. Normally, serum cortisol is high in morning and low in midnight (called circadian rhythm).
- Low dose dexamethasone suppression test—0.5 mg 6 hourly for 2 days. Measure serum cortisol at 9 a.m. on days 0 and 2. Failure of suppression of cortisol (< 60 nmol/L on second sample) indicates Cushing's syndrome due to any cause. Or, 24 hour urine free cortisol < 100 nmol/day also excludes Cushing syndrome.

2. Tests to find out the cause (to localize the site of lesion):
   ♦ Serum ACTH:
   - If ACTH is low or undetectable, adrenal cause is likely. Then USG, CT or MRI of abdomen is done to find adrenal tumor. If no mass is seen, then adrenal vein sampling or adrenal scintigraphy should be done.
   - If ACTH is high—likely cause is pituitary lesion (Cushing's disease) or ectopic ACTH syndrome. Then, high dose dexamethasone suppression test or corticotrophin releasing hormone test is done to differentiate between these two.
     a. High dose dexamethasone suppression test—2 mg 6 hourly for 2 days. Plasma cortisol is measured at 9 am on days 0 and 2. Plasma cortisol on day 2 less than 50% of that in day 0 suggests Cushing's disease (in 90% cases). Failure of suppression occurs in ectopic ACTH and adrenal tumor. Urine cortisol < 50% of basal suggests Cushing's disease and > 50% of basal suggests ectopic ACTH syndrome.
     b. Corticotropin releasing hormone (CRH) test—100 µg bovine CRH IV is given. Measure serum ACTH and cortisol for 2 hours. It increases in Cushing's disease, but no response in ectopic ACTH (Peak plasma cortisol >120% and/or ACTH > 150% of basal values suggest pituitary disease).

   ♦ If Cushing's disease is present—CT or MRI of skull. MRI will show pituitary microadenoma in 70% cases. If no mass is seen, selective catheterisation of inferior petrosal sinus to measure ACTH for pituitary lesion.
   ♦ If ectopic ACTH syndrome is the cause—chest X-ray, CT scan of chest (to see carcinoma of bronchus or bronchial carcinoid).
3. Other tests (to see the effect):
   ♦ Electrolytes (hypokalemia).
   ♦ Blood sugar
   ♦ Bone mass density to see osteoporosis.

Note. Remember the following points:

- Plasma cortisol levels are highly variable. So, random measurement of daytime plasma cortisol level is of no value.
- In pituitary tumor, there is high ACTH and high cortisol.
- In ectopic ACTH syndrome, there is high ACTH and high cortisol.
- In adrenal tumor, there is low or undetectable ACTH and high cortisol.
- Cushing's disease and cortisol secreting adrenal tumor are 4 times common in women than men. But ectopic ACTH syndrome is more in men.

Systematic investigation in cushing syndrome

Q. Why dexamethasone is used in suppression test? **Why** not other steroids like prednisolone?

A. Because, dexamethasone does not cross react in radioimmunoassay for cortisol. But other steroids can cross react.

Q. Why the patient may complain of **backache**?

A. Osteoporosis (may cause vertebral collapse and kyphosis).

Q. How to **treat** Cushing's syndrome?

A. It depends on the cause.

1. Cushing's disease:
   - Transphenoidal removal of microadenoma
   - If surgery is not possible or unsuccessful, bilateral adrenalectomy should be done. Later, the patient may develop Nelson's syndrome (see below)
   - If surgery is not possible, sometimes only pituitary irradiation may be given. External irradiation is given. It is slowly effective in 50% to 60% cases, response in children is better than adults, 80% may be cured

- To reduce ACTH production—bromocriptine or cyproheptadine is rarely effective
- Drugs such as metyrapone and ketoconazole may be given.

2. Adrenal tumor:
   - In adrenal adenoma or carcinoma, surgical resection is done (adrenalectomy)
   - In carcinoma, there is chance of recurrence. Then, radiotherapy or chemotherapy or adrenolytic drugs like mitotane may be given
   - Other drugs—metyrapone or ketoconazole may be used (which inhibits biosynthesis of cortisol).
3. Ectopic ACTH:
   - If possible, the primary lesion should be surgically removed (like bronchial carcinoma or carcinoid). Other treatment of the primary cause like radiotherapy or chemotherapy should be considered
   - If surgery is not possible, medical therapy as above or bilateral adrenalectomy may be considered.

RELATED QUESTIONS AND ANSWERS

Q. What is **Cushing's syndrome**? What are the common **features**?

A. It is defined as symptoms and sign due to chronic glucocorticoid excess whatever its cause. High glucocorticoid leads to constellation of symptoms and signs, commonly:

- Weight gain but weakness
- Proximal muscular weakness (characterized by difficulty in combing, raising the hands above the head, standing from squatting)
- Hirsutism in female
- Amenorrhea or oligomenorrhea
- Loss of libido
- Backache, pathological fracture (due to osteoporosis), collapse of the vertebra with reduction of height
- Easy bruising, purple abdominal striae
- Hypertension, diabetes mellitus (30%) or IGT
- Frequent infection, especially fungal infection, slow wound healing
- Mood disturbance like depression, insomnia, irritability, lethargy
- On examination—moon face, buffalo hump, truncal obesity, hirsutism, acne on face, pink striae, growth retardation in children.

Q. What are the causes of **moon face** or puffy face?

A. As follows:

- Cushing's syndrome (plethoric moon face, with hirsutism, acne)
- Myxedema (puffy with baggy eyelids, fall of lateral eyebrows, malar flush)
- Nephrotic syndrome and acute glomerulonephritis (puffy with periorbital oedema)
- Superior vena caval obstruction (engorged and non pulsatile veins, plethoric face with subconjunctival effusion)
- Angioedema (localized, swollen lip or face)
- Chronic alcoholism (plethoric, puffy face)
- Simple obesity
- Surgical emphysema (history of trauma, also swelling is extended upto the neck and chest. There are multiple crepitations on palpation).

Q. What are the causes of **periorbital edema?**

A. As follows:
- Nephrotic syndrome
- Acute glomerulonephritis
- Myxedema
- Angioedema
- Dermatomyositis
- Orbital cellulitis
- Malignant exophthalmos.

Q. What is the **commonest cause** of Cushing's syndrome?

A. Iatrogenic steroid therapy or ACTH (for long time). Non-iatrogenic Cushing's syndrome is very rare.

Q. What are the **causes** of Cushing's syndrome?

A. Commonest cause is steroid therapy. Other causes:

1. ACTH dependent
   - Pituitary microadenoma < 10 mm, called Cushing's disease (in 80% cases). Common in women
   - Ectopic ACTH syndrome (due to oat cell carcinoma of bronchus, bronchial adenoma, bronchial carcinoid and carcinoma of pancreas)
   - ACTH therapy.
2. Non-ACTH dependent
   - Prolong steroid therapy—the commonest cause (even topical or inhaled steroid for long time in susceptible cases may be responsible)
   - Adrenal adenoma and adrenal carcinoma (common in women).
3. Others—Pseudo-Cushing's syndrome (due to alcohol, depression and obesity).

According to source, causes may be:

1. Exogenous: Prolong steroid therapy (ACTH independent).
2. Endogenous:
   - Pituitary cause (85%, ACTH dependent)
   - Adrenal tumor (ACTH independent)
   - Ectopic production of ACTH (ACTH dependent).

Q. What is the **difference** between Cushing's disease and Cushing's syndrome?

A. As follows:
- Cushing's disease—there is increased production of ACTH from pituitary that stimulates adrenals
- Cushing's syndrome is caused by excess glucocorticoid due to any cause.

Q. What is **Pseudo-Cushing's** syndrome?

A. Cortisol excess due to other illness without involvement of the pituitary adrenal axis is called Pseudo-Cushing's syndrome. There is increased urinary excretion of steroid, absent diurnal variation of cortisol and failure of suppression by dexamethasone.
- It may occur in chronic alcoholism, severe depression and in simple obesity. All the features of Cushing's syndrome revert to normal after removal of the cause (features in favor of Cushing's syndrome are bruise, myopathy and hypertension, all of which are usually absent in Pseudo-Cushing's syndrome).
- To differentiate from Cushing's syndrome—insulin induced hypoglycemia is helpful. In Cushing's syndrome, almost no response. But in Pseudo-Cushing's syndrome, there is excess cortisol secretion.

Note. Remember the following -

Remember, if there is history of alcohol intake, advice the patient to stop taking alcohol. Repeat the cortisol or dexamethasone suppression test. It may be normal. Then further test is not recommended.

Q. What are the indications of **long-term steroid therapy**?

A. Steroid is used for long time in:

- Replacement therapy in Addison's disease and also in hypopituitarism (lifelong)
- Systemic lupus erythematosus (SLE).
- Idiopathic fibrosing alveolitis
- Dermatomyositis
- Pemphigus vulgaris
- Chronic active hepatitis (CAH)
- Giant cell arteritis.

Q. Tell one **absolute indication** of steroid therapy?

A. Pemphigus vulgaris (also, Addison's disease, bilateral adrenalectomy, giant cell arteritis, severe SLE, etc.)

Q. What are the **striae** in Cushing's syndrome?

A. Striae are pink or purple coloured lesions in the skin of abdomen and other parts of body.

Q. What is **striae**? What are the **causes**?

A. These are wrinkled, linear, white or pink-colored marks over the skin. Striae is due to stretching of skin, causing rupture of elastic fibres. Causes of striae are:

- Striae gravidarum (white or pink, narrow lines, in abdominal wall due to pregnancy and usually below the umbilicus).
- Obesity (whitish narrow lines, usually longitudinal, < 2 mm).
- Cushing's syndrome (wide lines, pink or purple or red, mostly horizontal or oblique. Pink or red color is due to increased vascularity).

Q. How to **differentiate clinically** different types of Cushing's syndrome?

A. By history, physical examination and investigation:

1. In Cushing's syndrome due to adrenal cause:
   - In adrenal adenoma—clinical features of glucocorticoid excess are present but androgenic effect like hirsutism and virilisation are absent and no pigmentation.
   - In adrenal carcinoma—clinical features of glucocorticoid excess are present and androgenic effect like hirsutism and virilisation are rapidly progressive.
2. In ectopic ACTH syndrome—usually there is short history, excess pigmentation due to high ACTH level, weight loss (rather than obesity) and severe hypokalemic alkalosis. Hypertension and edema are more common. Classical features of Cushing's syndrome are usually absent. Features of the primary lesion are present.
3. In Cushing's disease—classic features of Cushing's syndrome are present. If there is pituitary macroadenoma, visual disturbance and features of hypopituitarism may be present. There may be features of raised intracranial pressure like headache.
4. Marked hypoklemia suggests ectopic ACTH syndrome.
5. History of alcoholism and depression or simple obesity suggests pseudo-Cushing's syndrome.

Q. What are the **causes of death** in Cushing's syndrome?

A. Death may be due to:

- Hypertension and its complications
- Myocardial infarction
- Heart failure
- Infections.

Q. What is **Nelson's syndrome**?

A. After bilateral adrenalectomy in Cushing's disease, there may be increased pigmentation due to excess ACTH, it is called Nelson's syndrome. It is due to enlarging pituitary tumor in the absence of negative feedback suppression, due to absence of cortisol after adrenalectomy.

It occurs in around 20% cases. The tumor is locally invasive. It can be prevented by pituitary radiotherapy soon after adrenalectomy.

Treatment: Surgical removal of the tumor. Occasionally, radiotherapy (if not given previously).

ADDISON'S DISEASE

CHIEF COMPLAINTS

- Weakness and weight loss for … months.
- Loss of appetite, nausea, dizziness and vertigo for … months.
- Pigmentation in different parts of the body for … months.

HISTORY

History of present illness: According to the statement of the patient, she was reasonably well … months back. Since then, she has been suffering from severe weakness with gradual loss of about 10 kg of bodyweight. The patient also complains of loss of appetite, nausea, dizziness and vertigo for the last … months. Her dizziness and vertigo are more marked when sitting from lying position and on standing. There is no history of fever, cough, bowel or bladder abnormality, excessive sweating, palpitation or heat intolerance. For the last … months, she also noticed some pigmentation involving different parts of the body. There is no history of injury or recent scar.

History of past illness: She gives no history of tuberculosis, abdominal trauma or surgery.

Family history: Nothing significant. There is no history of such illness in the family.

Socioeconomic history: Mention according to the statement of the patient.

Menstrual history: Amenorrhea for the last 4 months, but it was regular previously.

Drug and treatment history: There is no history of intake of steroid or any other drugs.

GENERAL EXAMINATION

- The patient is ill looking and emaciated
- There is generalized pigmentation, more marked on the face, neck, mucous membrane of the mouth, palmar crease, knuckles, knees and elbows
- One vitiligo is present over the right thigh
- Sparse (or less) axillary and pubic hair
- No anemia, jaundice, cyanosis, clubbing, koilonychia, leukonychia, edema
- Pulse—96/min
- BP—lying 100/60 mm Hg and standing 70/40 mm Hg.

Examination of other systems reveals normal findings.

SALIENT FEATURES

Mrs. …, 35 years old, housewife, hailing from …, presented with the complaints of severe weakness with gradual loss of about 10 kg of bodyweight for … months. She also complains of loss of appetite, nausea, dizziness and vertigo for the last … months. Her dizziness and vertigo are more marked when sitting from lying position and on standing. There is no history of fever, cough, bowel or bladder abnormality, excessive sweating, palpitation, heat or cold intolerance. For the last … months, she also noticed some pigmentation involving different parts of the body. There is no history of injury or recent scar. She never suffered from tuberculosis in the past. She has been amenorrheic for the last 4 months. She did not take steroids or any other drugs. There is no family history of similar illness.

On Examination

General examination – mention as above.

Systemic examination – mention as above.

My diagnosis is Addison's disease.

Q. Why **your diagnosis** is Addison's disease?

A. There is weakness and weight loss, hypotension with postural drop and pigmentation. All these are suggestive of Addison's disease.

Q. What are your **differential diagnoses?**

A. As follows:

- Tuberculosis
- Hemochromatosis
- Diabetes mellitus
- Malabsorption syndrome.

Q. What **investigations** should be done to diagnose Addison's disease?

A. As follows:

1. Routine tests:
- CBC (shows high eosinophil, lymphocyte and ESR). Anemia may be present, specially associated with pernicious anemia
- Blood glucose (low or lower limit, especially during Addisonian crisis)
- Electrolytes (hyponatremia and hyperkalemia. Hyponatremia is more important than hyperkalemia. Mild acidosis may be present)
- Other tests—serum renin (increases), aldosterone (low) and serum calcium (may be high).

2. Test to confirm:
- Plasma ACTH and cortisol measurement is confirmatory (there is high ACTH, >80 ng/L, and low or lower normal cortisol)
- Short synacthen test should be done. If cortisol level does not rise, it indicates primary or secondary adrenocortical deficiency. Then plasma ACTH should be done. ACTH is high in Addison's disease and low or undetectable in ACTH deficiency. If ACTH test is unavailable, then long synacthen test can be done to differentiate between primary and secondary adrenocortical deficiency. (See below).

3. Tests to find out causes:
- Chest X-ray (to diagnose tuberculosis)
- Plain X-ray abdomen (to see adrenal calcification in TB)
- Adrenal auto-antibody
- USG or CT scan of adrenals (to look for calcification in TB or malignancy).

4. Other tests:
- Screening for pernicious anemia and other autoimmune disorders
- Thyroid screening
- Other tests according to suspicion of cause (e.g. sarcoidosis, amyloidosis, hemochromatosis, HIV, histoplasmosis, metastatic carcinoma, etc).

Q. How to perform **synacthen** test?

A. Short synacthen test may be done anytime of the day, but better at 9 a.m., non-fasting. It is usually done for:

1. Diagnosing Addison's disease.
2. Screening test for ACTH deficiency.

Procedure:

- Short synacthen test—250 µg ACTH (synacthen or tetracosactrin) IM or IV is given. Serum cortisol is measured at 0 and 30 minutes. If cortisol raises > 460 nmol/L, it rules out Addison's disease. Failure to rise may indicate primary or secondary adrenocortical insufficiency.
- Long synacthen test—1 mg ACTH IM daily for 3 days. Serum cortisol is measured at 0, 4, 8 and 24 hours on each day. Progressive rise of cortisol indicates secondary adrenocortical insufficiency. Failure to rise indicates Addison's disease (cortisol remains < 700 nmol/L 8 hours after last injection).

Note. Remember the following -

- If the patient is on dexamethasone or betamethasone, it will not interfere with cortisol assay (as these do not cross react).
- Random cortisol is usually low in Addison's disease, but in some cases, it may be within normal or inappropriately low in seriously ill patient. So, random cortisol measurement is of no importance. However, if random cortisol is <100 nmol/L, it is highly suggestive of Addison's disease. Also, if the serum cortisol is > 460 nmol/L, it rules out Addison's disease.
- Single test for diagnosis of Addison's disease is simultaneous measurement of ACTH and serum cortisol level (ACTH is high, cortisol is low).

Q. How to **treat** Addison's disease?

A. As follows:

1. Replacement of hormones:

- Glucocorticoid:
  - Hydrocortisone—15 mg in morning (after waking) and 5 mg in afternoon (6 pm). According to some authority, 10 mg after waking, 5 mg at 12 noon and 5 mg at 6 pm.
  - Or, if hydrocortisone is not available, prednisolone 5 mg on waking in morning and 2.5 mg at 6 pm in afternoon.
- Mineralocorticoid—Fludrocortisone 0.05 to 0.1 mg (50 to 300 µg) daily.
- Androgen—Dehydroepiandrosterone (DHEA) 50 mg/day may be given in female. It increases libido and sense of well-being, but complications like acne and hirsutism may occur.

2. Treatment of the cause, as for example, antitubercular therapy in tuberculosis.

General advice to the patient:

1. The patient should always carry a bracelet and steroid card, which should contain informations regarding the diagnosis, dose of steroid and doctor's contact address.
2. Good nutrition, regular meal, high carbohydrate and sufficient salt.
3. The patient should keep ampules of hydrocortisone at home. If oral therapy is impossible, the patient should take injection by himself, family members or GP.
4. The patient should know how to increase steroid replacement dose for intercurrent illness. During intercurrent stress (fever, cold and trauma), the dose should be doubled.

Monitoring of the patient:

- Proper history regarding overall well-being
- Measurement of BP and weight
- Serum electrolyte.

Note. Remember the following points during stress -

- Intercurrent stress (fever, cold and trauma)—double dose of steroid.
- During surgery:
  - Minor surgery—hydrocortisone 100 mg IM or IV premedication.
  - Major surgery—hydrocortisone 100 mg IM or IV 6 hourly for 24 hours, then 50 mg 6 hourly. It should be continued until the patient is capable of taking by mouth.
- If gastroenteritis—IV or IM hydrocortisone should replace oral therapy.

RELATED QUESTIONS AND ANSWERS

Q. What is Addison's disease?

A. It is the primary adrenocortical insufficiency, resulting in glucocorticoid and mineralocorticoid insufficiency. There is destruction of the adrenal cortex.

Q. What are the causes of Addison's disease?

A. As follows:

1. Common causes:
- Autoimmune mechanism—80% of the cases (more in female)
- Tuberculosis of adrenal gland (in 10% cases)
- Secondary deposit in adrenals
- HIV infection
- Bilateral adrenalectomy.

2. Other causes (less common or rare):
- Amyloidosis
- Sarcoidosis
- Hemochromatosis
- Bilateral adrenal hemorrhage—following meningococcal septicemia (Waterhouse-Friedrichsen syndrome) and trauma
- Lymphoma.

Q. What are the sites of pigmentation in Addison's disease?

A. As follows:
- May be generalized
- Exposed parts (face, neck)
- Skin crease (palmar crease) and knuckles
- Pressure points (elbow, knee)
- Recent scar.

Q. What are the diagnostic criteria in Addison's disease?

A. Triad of:
- Weakness or emaciation (100% cases)
- Pigmentation (90% cases)
- Hypotension (88%)

(Other features—gastroenteritis in 56%, postural symptoms 12%, salt craving 19%).

Q. Why postural hypotension occurs in Addison's disease?

A. It is due to hypovolemia and sodium loss. Mineralocorticoid deficiency is responsible for hypotension.

Q. What is the size of the **heart** in Addison's disease?

A. Small heart.

Q. What **diseases are associated** with Addison's disease?

A. It is an autoimmune disease, so may be associated with other autoimmune diseases, such as—Graves' disease, Hashimoto's thyroiditis, pernicious anemia, primary ovarian failure, myasthenia gravis, type I DM etc.

Q. What are the **presentations** of Addison's disease?

A. As follows:

- Chronic adrenocortical insufficiency (weakness, pigmentation, hypotension)
- Addisonian crisis.

Q. Why **vitiligo** occurs in Addison's disease?

A. It is due to autoimmunity. Vitiligo is present in 10 to 20% cases.

Q. Why **pigmentation** occurs in Addison's disease?

A. It is due to excess ACTH that stimulates excess melanin production.

Q. How to **differentiate** between primary and secondary adrenocortical insufficiency?

A. As follows:

Primary	Secondary
1. Primary involvement of adrenal gland	Cause in pituitary or prolonged use of steroid
2. Pigmentation is present	Usually pallor
3. BP—low	BP—normal, because aldosterone secretion is not dependent on ACTH
4. Secondary sex characters are normal	Early loss of secondary sex characters. Also there are features of deficiency of other pituitary hormones
5. ACTH—high	ACTH—Low
6. Electrolytes—low Na+, high K+	Usually normal electrolytes
7. Autoimmune diseases are associated	Unlikely

Q. What is **Addisonian crisis?**

A. It is an acute severe adrenocortical insufficiency, characterized by circulatory shock with severe hypotension. It is often precipitated by intercurrent disease, surgery or infection. The patient presents with muscle cramps, nausea, vomiting, diarrhea, acute abdomen, collapse and unconsciousness. There may be unexplained fever. Laboratory findings include hyponatremia, hyperkalemia and in some cases, hypoglycemia and hypercalcemia.

Causes:

- Sudden withdrawal of steroid (common cause, if the patient on steroid for long time)
- Stress (severe infection and operation)
- Bilateral adrenal hemorrhage (meningococcal septicemia, injury and anticoagulant)
- Thyroxine therapy in a patient with hypopituitarism without steroid therapy.

Treatment:

- Blood is taken to measure cortisol, glucose and electrolytes
- Three problems are present—shortage of salt, sugar and steroid (**3S**)
- IV fluid, normal saline rapidly (1 L in 30 to 60 minutes). Subsequently, several liters of normal saline may be required in 24 hours
- IV 10% glucose
- IV hydrocortisone 100 mg stat. Then hydrocortisone 100 mg IV or IM 6 hourly, which is continued until the patient is stable and can take by mouth. Then oral steroid is started. Initially, hydrocortisone 20 mg 8 hourly, reducing to 20 to 30 mg in divided doses over a few days (then original replacement therapy should be given)
- Treatment of underlying cause (e.g. infection, adrenal or pituitary pathology, etc).

Note. Remember the following -

- In severe hyponatremia (<125 mmol/L), hypertonic saline is unnecessary, plasma Na should not be increased >10 mmol/L/day. This may cause central pontine myelinolysis (osmotic demyelination syndrome).
- During crisis or acute illness, mineralocorticoid such as fludrocortisone is unnecessary, as high dose of steroid provides sufficient mineralocorticoid activity. It can be started later on.
- For hyperkalemia, volume replacement is sufficient. No extra treatment is usually necessary, but occasionally requires specific therapy.

Q. What **drug is avoided** in acute abdominal pain in Addison's disease?

A. Morphine, as the patient is more sensitive to this drug.

HYPOPITUITARISM (DUE TO SHEEHAN'S SYNDROME)

CHIEF COMPLAINTS

- Weakness, dizziness and giddiness for … months
- Failure to breast feed for … months
- Amenorrhea for … months
- Weight loss for the same duration
- Cold intolerance and constipation for the same duration.

HISTORY

History of present illness: According to the statement of the patient, she was reasonably well … months back. Following delivery of her last baby, which was complicated by prolonged profuse vaginal bleeding, she has been suffering from severe weakness, dizziness and giddiness. She also complains of failure to breastfeed and amenorrhea since the birth of her baby. The patient also complains of significant weight loss, though her appetite is quite good. For the last --- month, she also experiences intolerance to cold and occasional constipation. She noticed hair loss and also decreased libido for the same duration. There is no history of headache, visual disturbance, convulsion, or head injury. She denies excessive thirst or polyuria.

History of past illness: Mention according to the statement of the patient.

Family history: Mention according to the statement of the patient.

Socioeconomic history: Mention according to the statement of the patient.

Menstrual history: Her menstrual period was regular prior to this incident.

Drug and treatment history: She received 5 units of blood transfusion during the bleeding episode.

GENERAL EXAMINATION

- The patient is ill looking, pale and emaciated
- Mildly anemic
- No jaundice, cyanosis, clubbing, koilonychia, leukonychia, edema
- No lymphadenopathy or thyromegaly
- Skin is fine and wrinkled
- There is loss of axillary and pubic hair
- Pulse: 96/min
- BP: Lying 105/70 mm Hg, standing 90/60 mm Hg
- Respiration: 14/min
- Temperature: Normal.

Examination of other systems revealed no abnormalities.

SALIENT FEATURES

Mrs. …, 33 years old, housewife, normotensive, nondiabetic, hailing from …, gave birth to her last baby … months back during which there was prolonged profuse vaginal bleeding. Since then, she has been suffering from severe weakness, dizziness and giddiness. She also complains of failure to

breastfeed and amenorrhea since the birth of her baby. The patient also complains of significant weight loss, though her appetite is quite good. For the last--month also experiences intolerance to cold and occasional constipation. She noticed hair loss and also decreased libido for the same duration. There is no history of headache, visual disturbance, convulsion, or head injury. She denies excessive thirst or polyuria. Her menstrual period was regular prior to this incident. She received 5 units of blood transfusion during the bleeding episode. She was treated with vitamins and calcium tablets. There is no history of similar illness in her family.

On Examination

General examination (mention as above).

Systemic examination (mention as above).

My diagnosis is hypopituitarism (due to Sheehan's syndrome).

Q. Why is it Sheehan's syndrome?

A. There is history of persistent prolonged severe bleeding following delivery. After that, there is failure of lactation, persistent amenorrhea and reduction of secondary sex characteristics (breast atrophy, loss of axillary and pubic hair).

Q. What are your **differential diagnoses?**

A. As follows:

- Addison's disease
- Diabetes mellitus.

Q. What **investigations** do you suggest in hypopituitarism due to Sheehan's syndrome?

A. As follows:

1. Routine: CBC with ESR, serum electrolytes, RBS.
2. Serum hormone measurement:
   - For adrenocortical insufficiency—Serum cortisol and ACTH level (if needed, synacthen test)
   - For thyroid—FT_4 (low) and TSH (usually low, may be normal or in lower limit)
   - For gonadotrophins—FSH and LH
   - GH is not routinely done. Only considered, if growth hormone replacement is possible.
3. MRI of the head to see the pituitary gland.

Note. Remember the following points:

- If hypopituitarism is due to other cause, investigate accordingly.
- Hypopituitarism in male – serum testosterone level is measured. If it is low, then FSH and LH levels are also done to differentiate between primary and secondary hypogonadism.
- Because of deficiency of ADH, the patient may develop cranial diabetes insipidus. However, the symptoms are masked due to deficiency of ACTH and glucocorticoid. Features of diabetes insipidus may appear after steroid therapy.

RELATED QUESTIONS AND ANSWERS

Q. What is **Sheehan's syndrome?**

A. It is a syndrome of hypopituitarism due to infarction of the pituitary gland following prolonged postpartum hemorrhage. Postpartum pituitary infarction occurs, because the enlarged pituitary gland in pregnancy is more vulnerable to ischemia after prolonged and massive postpartum hemorrhage and hypotension. Failure of lactation is the earliest symptom. Other symptoms appear over months or years.

Q. How to **treat Sheehan's syndrome?**

A. As follows:

- Hydrocortisone 15 mg in morning (after waking) and 5 mg in afternoon (6 pm). According to some authority, 10 mg after waking, 5 mg at 12 pm and 5 mg at 6 pm (If hydrocortisone is not available, prednisolone 5 mg on waking in morning and 2.5 mg at 6 pm in afternoon).
- Thyroxine 50 to 150 μg in the morning before meal.
- Sex hormone replacement (to restore sexual function and also, to prevent osteoporosis). Usually, oestrogen and androgen (DHEA) are given. Or combination of contraceptive pill may be given.
- If the patient wishes for fertility—hCG plus FSH or pulsatile GnRH may be given.
- Steroid card should be maintained.

Note. Remember the following:

- In any patient with hypopituitarism, always start first with cortisol, then thyroxine. It is dangerous to start thyroxine without first giving glucocorticoid. If thyroxine is started first without giving cortisol in adrenal deficiency, there may be adrenal crisis.
- In premenopausal women, estrogen from 1 to 21 days plus progesterone from 14 to 21 days.
- In postmenopausal women, treatment is same as premenopausal woman (in patient with hysterectomy, progesterone is not necessary).
- In male patient with hypopituitarism, testosterone (oral, IM, intradermal or implant) is given.
- In child with hypopituitarism, growth hormone replacement should be given. In adult, sometimes growth hormone replacement may be considered, if there is GH deficiency, which has effect on muscle mass and well being.

Q. What is **panhypopituitarism**? What is the **sequence** of loss of pituitary hormones in panhypopituitarism?

A. Panhypopituitarism is a syndrome produced by complete or near complete destruction of the pituitary, causing deficiency of all the pituitary hormones. It is characterized by asthenia, loss of sexual function and loss of target organ functions like thyroid, adrenal gland and gonads. In panhypopituitarism, first there is loss of growth hormone and gonadotrophin (LH and FSH), followed by ACTH, TSH.

Q. What is the common **presentation** of a patient with hypopituitarism?

A. As follows:

- Weakness, lassitude, malaise
- Loss of libido
- Absence of secondary sex characters.

Q. How to **differentiate** between Addison's disease and hypopituitarism?

A. As follows:

Addison's disease	Hypopituitarism
1. Primary involvement of adrenal gland	Cause in pituitary
2. Pigmentation present	Usually pallor
3. BP—low	BP—normal, because aldosterone secretion is not dependent on ACTH
4. Secondary sex characters are normal	Early loss of secondary sex characters. Also associated with other pituitary hormone deficiency.

5. ACTH—high	ACTH—low
6. Electrolytes—low Na+, high K+	Usually normal electrolytes.
7. Ocular sign absent.	May be present, if it is due to pituitary tumor
8. Autoimmune diseases—associated	Unlikely

Q. What are the **causes** of hypopituitarism?

A. As follows:

1. Pituitary cause:
   - Pituitary masses:
     - Pituitary adenoma, carcinoma (rare), secondaries including leukemia and lymphoma
     - Pituitary cyst
     - Pituitary granuloma (tuberculosis, syphilitic gumma)
   - Pituitary surgery (resection or removal of tumor)
   - Pituitary irradiation
   - Pituitary trauma
   - Pituitary apoplexy
   - Sheehan's syndrome
   - Infiltrative disorder—hemochromatosis, lymphocytic hypophysitis, sarcoidosis, amyloidosis
   - Others—autoimmune hypophysitis, idiopathic, congenital, Langerhans cell histiocytosis, MEN-I.
2. Extrapituitary causes:
   - Craniopharyngioma
   - Other: meningioma, germinoma, glioma, pinealoma.
3. Secondary to hypothalamic disorder.

Q. What are the **commonest cause** of hypopituitarism?

A. Pituitary tumor, surgery, radiotherapy, head injury, craniopharyngioma, meningioma.

Q. What are the causes of **coma** in hypopituitarism?

A. As follows:

- Hypoglycemia
- Hyponatremia
- Water intoxication
- Hypothyroidism
- Hypothermia.

Q. How to **treat coma** in hypopituitarism?

A. As follows:

- IV fluid (normal saline)
- IV glucose
- IV hydrocortisone 100 mg 6 hourly
- Control infection
- Thyroxine may be needed (IV triiodothyronine is preferred).

ACROMEGALY

CHIEF COMPLAINTS

- Progressive enlargement of the body for … months
- Weakness and weight gain for … months
- Change in voice for … months
- Headache for … months
- Joint pain for … months
- Excessive sweating for … months.

HISTORY

History of present illness: According to the statement of the patient, he was reasonably well … years back. Since then, he has been experiencing progressive enlargement of body, mainly his head, hands and feet. His face is also enlarged, including the jaw, leading to difficulty in chewing. He also complains of severe weakness despite significant weight gain. His voice has recently changed and become hoarse.

The patient also complains of frequent headache involving the whole head, more marked in the morning, which is not associated with nausea or vomiting. For the last … months, he is also complaining of joint pain involving both the knees, ankles and elbows. The pain is aggravated by activity and relieved by taking rest. It is not associated with morning stiffness. Recently he noticed excessive sweating even at rest. There is no history of any visual disturbance, cold intolerance, sleepiness. His bowel and bladder habits are normal.

History of past illness

Family history

Socioeconomic history

Drug and treatment history: Mention accordingly.

GENERAL EXAMINATION

- The patient looks obese with large coarse face, large jaw with widely apart teeth prominent supra-orbital ridge, increased wrinkling of the forehead and baggy eyelids. Nose, lips and ears are large
- Scalp is large (bulldog scalp)
- Hands are large, warm and sweaty with doughy feeling, fingers are spade like
- Feet are large
- Skin is thick, greasy, and sweaty (hyperhydrosis)
- Coarse body hair
- Voice is husky, cavernous
- Gynecomastia: Present
- Clubbing: Present (involving all fingers and toes)
- Thyromegaly (diffusely enlarged)
- There is no anemia, jaundice, cyanosis, koilonychia, leukonychia, edema
- Pulse: 96/min
- BP: 150/90 mm Hg
- Temperature: 99°F
- Respiratory rate: 14/min.

(There may be kyphosis, scoliosis, axillary skin tag, acanthosis nigricans).

SYSTEMIC EXAMINATION

Gastrointestinal System

- Tongue, lips and jaw are enlarged. Lower jaw is protruded with malocclusion of teeth (prognathism).
- Abdomen—hepatomegaly (may be).

Nervous System

- Voice is hoarse, husky and cavernous.
- Visual field defect—bitemporal hemianopia.

Cardiovascular System

- Cardiomegaly (evidenced by shifting of the apex beat, which is heaving).

Musculoskeletal System

- Both the knee and ankle joints, elbow joints, also joints of hands are tender, but no restricted movement.

Examination of other systems reveals normal findings.

SALIENT FEATURES

Mr. …, 46 years old, businessman, normotensive, nondiabetic, hailing from …, presented with progressive enlargement of body, mainly his head, hands and feet, for … months. His face is also enlarged, including the jaw, leading to difficulty in chewing. He also complains of severe weakness despite significant weight gain. His voice has recently changed and become hoarse. The patient also complains of frequent headache involving the whole head, more marked in the morning, which is not associated with nausea or vomiting. For the last … months, he is also complaining of joint pain involving both the knees, ankles and elbows. The pain is aggravated by activity and relieved by taking rest. It is not associated with morning stiffness. Recently he noticed excessive sweating even at rest. There is no history of any visual disturbance, cold intolerance, sleepiness. His bowel and bladder habits are normal. There is no family history of such illness. He was treated with different medicine the name of which he cannot mention.

On Examination

General examination (mention as above).

Systemic examination (mention as above).

My diagnosis is acromegaly.

Q. What are your **differential diagnoses**?

A. Hypothyroidism

Q. What **investigations** should be done in acromegaly?

A. As follows:

1. Radiology:
   - X-ray of skull (there is enlarged sella-turcica, erosion of the clinoid process, enlarged skull, mandible and sinuses, double floor sella, prognathism)

- X-ray of hands (there is large soft tissue, bones, widening of joint spaces, tufting of the terminal phalanges)
- X-ray of feet—to see heel-pad (normally, female—up to 18 mm and male—21.5 mm. If it is >25 mm—highly suggestive). Other changes like hand.
- X-ray of chest (shows enlarged heart).
- Other radiological tests like X-ray of the knee joints or other joints, if needed.

2. GH assay (radio-immunoassay)—normally, < 1 mU in adult (except in stress).
3. GTT with simultaneous measurement of GH (more diagnostic)—normally during GTT, there is suppression of GH < 2 mU. But in acromegaly, there is failure of suppression of GH, occasionally paradoxical rise of GH.
4. Measurement of IGF-1 (also called somatomedin-C)—usually increased.
5. CT scan or MRI of skull (MRI is more preferable) with gadolinium enhancement.
6. Others:
   - Assessment of other anterior pituitary hormones
   - Comparison with old photographs
   - Perimetry (to see bitemporal hemianopia)
   - Blood sugar (there is DM in 10% cases, IGT in 25% cases)
   - ECG
   - Serum calcium (increased in MEN-I).

Q. How to **treat** acromegaly?

A. As follows

1. Surgery:
   - Trans-sphenoidal removal of microadenoma is the treatment of choice (there is high success rate, rapid reduction of growth hormone and low incidence of hypopituitarism). Cure rate is 80% in microadenoma, 40% in macroadenoma.
   - After 3 months postoperative, measure growth hormone and pituitary function tests. If growth hormone remains high, adjuvant medical or radiotherapy may be needed
   - Occasionally, transfrontal surgery is done in large macroadenoma with suprasellar extension. Total removal of tumor may not be possible due to more complications. Postoperative radiotherapy should be given.
2. Radiotherapy:
   - It is used as a second line therapy. External irradiation by linear accelerator is given in acromegaly which persists after surgery, to stop the tumor growth and to lower growth hormone levels. However, growth hormone level falls very slowly over many years (previously, implantation of Yttrium was used).
   - Radiotherapy can be used in combination with somatostatin analogue or dopamine agonist, because of slow biochemical response to radiotherapy.
3. Drugs: Given if surgery is not possible or persistent acromegaly after surgery.
   - Somatostatin analogue (octreotide or lanreotide) may be used as a slow release injection, every 2 to 4 weeks.
   - Bromocriptine: It is a dopamine agonist, given in high dose, reduces GH level and the size of tumor. But it is less potent in lowering growth hormone and recurs after withdrawal of the drug. Its main side effects are nausea, vomiting and postural hypotension. Alternatively, cabergoline 0.5 mg/day may be given, or quinagolide may be used.
   - A peptide GH receptor antagonist (pegvisomant) may be used.
4. Other treatment:
   - Control of hypertension and diabetes mellitus (both improve with the treatment of acromegaly).
   - Cardiac problems—whether improves with the treatment of acromegaly is not clear.

Note. Remember the following -

Aims of treatment is to reduce the growth hormone level below 5 mU/L which shows reduced mortality. A normal IGF-1 level is also a goal of therapy. So, the progress can be assessed by monitoring growth hormone and IGF-1 level.

RELATED QUESTIONS AND ANSWERS

Q. What is acromegaly?

A. Acromegaly is characterized by generalized enlargement of the whole body, due to excess growth hormone secretion from pituitary macroadenoma (> 10 mm) after union of epiphysis. If occurs before the union of epiphysis, it is called gigantism.

Q. Why it is called acromegaly?

A. Because of the enlargement of peripheral (acral) parts of body (acral means periphery and megaly means big).

Q. Can acromegaly and gigantism exist together?

A. Yes, if excess growth hormone starts in adolescence and persists in adult life, the two conditions may be present together.

Q. What is the cause of acromegaly?

A. Eosinophilic adenoma of pituitary (macroadenoma) causing excessive GH secretion, after the fusion of the epiphysis (so there is enlargement of the soft tissue and flat bones). Very rarely, ectopic production of GHRH may cause acromegaly (in pancreatic islet cell tumor, oat cell carcinoma of bronchus, medullary carcinoma of thyroid).

Q. What are the changes in the eyes in acromegaly?

A. In the eyes:

- Visual field defect, usually bitemporal hemianopia (due to pressure on optic chiasma).
- Others—optic atrophy, papilledema, angioid streaks in retina.

Q. What are the causes of prominent supraorbital ridge?

A. As follows:

- Ricket
- Paget's disease
- Achrondroplasia
- Hydrocephalus
- Hereditary hemolytic anemia.

Q. What are the causes of macroglossia?

A. As follows:

- Acromegaly
- Hypothyroidism
- Amyloidosis
- Down's syndrome.

Q. What are the causes of baggy eyelids?

A. As follows:

- Old age
- Myxedema.

- Acromegaly
- Alcoholism
- Nephrotic syndrome or acute glomerulonephritis.

Q. What are the **presentations** of acromegaly?

A. As follows:

- Progressive increase of the size of the body (there may be history of change in size of rings, shoes, hats)
- Weight gain but weakness
- Visual field defect (the patient gives history of collision with doors, persons, because of the defective temporal field of vision)
- Headache (common)
- Excessive sweating
- Features of hypertension, diabetes mellitus
- The patient may give history of frequent visit to the dentist
- Sleep apnea syndrome.

Q. What are the signs of **active acromegaly**?

A. Signs of activity:

- Progressive increase in the size of the body
- Excessive sweating
- Increasing visual field defect
- Large skin tags (Molluscum fibrosum)
- Presence of glycosuria (diabetes mellitus)
- Hypertension
- Progressive headache
- Enlarging thyroid.

Q. What are **causes of death** in acromegaly?

A. As follows:

- Heart failure
- Complications of hypertension
- Complications of DM
- Coronary artery disease
- Tumor expansion (mass effect)
- There is an increased death due to neoplasia, especially large bowel tumor
- Pituitary apoplexy—rapid expansion of a pituitary tumor due to infarction or hemorrhage within the tumor. The patient may complain of sudden severe headache followed by loss of consciousness. Immediate neurosurgical intervention should be done.

Q. How to **assess the response** of therapy in acromegaly?

A. As follows:

- Clinical improvement (decreased facial puffiness, body size, less sweating, improvement of hypertension, DM).
- Progress can be assessed by GH and IGF-1 measurement.

Q. What are the **long term complications** of acromegaly?

A. As follows:

- Increase incidence of large bowel carcinoma
- Increase atherosclerosis.

Q. What are the causes of **hyperprolactinemia?**

A. As follows:

1. Physiological—severe stress, pregnancy, lactation, exercise, coitus, sleep.
2. Drugs:
   - Dopamine antagonist group of drugs—
     - Antipsychotic (phenothiazine, butyrophenons)
     - Antiemetic (metoclopramide, domperidone)
     - Antidepressant.
   - Dopamine depleting drugs (methyldopa).
   - Estrogen therapy (e.g. oral contraceptive pill).
3. Pathological:
   - Prolactinoma (usually microadenoma <10 mm)
   - Pituitary macroadenoma
   - Macroprolactinemia (there is high prolactin without clinical features of hyperprolactinemia)
   - Primary hypothyroidism
   - Polycystic ovarian syndrome
   - Rarely—renal failure, liver failure, hypothalamic tumor, ectopic tumor, post-ictal state, chest wall injury or reflex (e.g. postherpes zoster)
   - Idiopathic.

Clinical features of hyperprolactinemia:

- Galactorrhea, hypogonadism (commonest symptoms)
- In male—decrease libido, impotence, lethargy
- In female—amenorrhea, oligomenorrhea, menorrhagia, infertility.

Investigations:

- Serum prolactin (very high)
- CT scan or MRI of brain
- Other investigations according to the suspicion of cause, as for example, thyroid function, renal function.

Note. Remember the following points –

- If serum prolactin is high, repeat measurement is indicated to reconfirm
- If serum prolactin is 500 to 1000 mU/L, it is more likely due to stress or drugs
- If serum prolactin is 1000 to 5000 mU/L, may be due to stress or drugs or microadenoma
- Serum prolactin >5000 mU/L is highly suggestive of macroprolactinoma.

Treatment:

- Treatment of primary cause and stop the responsible drugs, if any
- Dopamine agonist drugs (such as bromocriptine, cabergoline and quinagolide) are usually given as a first line therapy
- Trans-sphenoidal surgery—may be done in microadenoma. It is also done in macroadenoma though complete removal may not be possible
- Radiotherapy—if macroadenoma fails to shrink following dopamine agonist drugs or total surgical removal is not possible
- In pregnancy, tumor size may be enlarged and may cause headache and visual field defect. In such case, dopamine agonist therapy should be started, if there are symptoms.

Indications of surgery:

- Intolerance to drugs
- Resistance to drugs
- Rapid expansion causing mass effect like visual field defect
- Large cystic macroadenoma.

DIABETES MELLITUS

CHIEF COMPLAINTS

- Weight loss and weakness for … months.
- Excessive thirst and frequent passage of urine for … months.
- Burning sensation of the hands and feet for … weeks.
- Dimness of vision for … months.

HISTORY

History of present illness: According to the statement of the patient, he was alright … months back. Since then, he has been suffering from gradual loss of weight, about 12 kg, despite good appetite. It is associated with extreme weakness and excessive thirst for which he used to take plenty of water every day. He also complains of frequency of micturition, passage of large volume of urine and waking up from sleep to void. For the last … weeks, he has been experiencing burning sensation, heaviness, tingling and numbness of both hands and feet. His vision is progressively deteriorating over the last … months. There is no history of loss of consciousness (diabetic ketoacidosis, hypoglycemia), generalized swelling of body or legs (nephropathy), chest pain (IHD), dizziness or giddiness (postural hypotension) or any skin abnormality (dermopathy, infection). He denies any history of heat intolerance, tremor (thyrotoxicosis), bowel abnormality (malabsorption), cough, hemoptysis or evening rise of temperature (TB).

History of past illness: There is no history of previous significant illness.

Family history: His father is diabetic for the last 25 years and his mother is hypertensive. He has two brothers and one sister. All of them are in good health.

Socioeconomic history: Mention accordingly.

Drug and treatment history: He is now taking tablets. Glibenclamide, 2 tablets daily.

GENERAL EXAMINATION

- Ill looking and emaciated. (look for height, weight and BMI)
- There is no anemia, jaundice, clubbing, koilonychia, leukonychia or edema
- No thyromegaly or lymphadenopathy
- There is no ulceration or skin abnormality
- Pulse—96/min (look for peripheral pulses, may be feeble)
- BP—130/80 mm Hg lying and 125/80 mm Hg standing
- Temperature—98ºF
- Respiratory rate—14/min.

SYSTEMIC EXAMINATION

Nervous System

1. Higher psychic functions: Intact.
2. Cranial nerves: Intact.
3. Motor system:

- Muscle tone diminished in the lower limbs
- Muscle power is diminished, grade 3/ 5 in the lower limbs
- There is wasting of all the groups of muscle in the feet, legs and thighs.
- Reflexes—

Jerks	Biceps	Triceps	Supinator	Knee	Ankle	Plantar
Right	Diminished	Diminished	Diminished	Diminished	Absent	Equivocal
Left	Diminished	Diminished	Diminished	Diminished	Absent	Equivocal

- Superficial reflexes (abdominal reflex)—absent
- Co-ordination—impaired in the lower limbs
- Romberg's sign—positive
- Gait—normal
- Involuntary movement—absent.

4. Sensory system:
   - Superficial sensation (pain, touch, temperature)—diminished in the foot up to mid leg and hands (glove and stocking distribution)
   - Deep sensation (vibration, position sense)—absent in both the lower limbs.
5. Cerebellar test: Normal.
6. Autonomic function: Normal, as evidenced by normal pulse, no postural hypotension.
7. Fundoscopy: Few dot and blot hemorrhages in the 6 o'clock position, 2 disc diameter away from the optic disc in the right eye. Few dot hemorrhages in 10 o'clock position, 1 disc diameter away from the optic disc.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 55 years old, businessman, diabetic, nonhypertensive, nonsmoker, hailing from …, presented with gradual loss of about 12 kg body weight, despite good appetite. It is associated with extreme weakness and excessive thirst for which he used to take plenty of water every day. He also complains of frequency of micturition, passage of large volume of urine and waking up from sleep to void. For the last … weeks, he has been experiencing burning sensation, heaviness, tingling and numbness of both hands and feet. His vision is progressively deteriorating over the last … months. There is no history of loss of consciousness, generalized swelling of body or legs, chest pain, dizziness or giddiness or any skin abnormality. He denies any history of heat intolerance, tremor, bowel abnormality, cough, hemoptysis or evening rise of temperature. There is no history of previous significant illness. His father was diabetic for 25 years, mother is hypertensive. He has two brothers and one sister; all of them are in good health. He is now taking tablet Glibenclamide, 2 tab daily.

On Examination

General examination (mention as above).

Systemic examination (mention as above).

My diagnosis is diabetes mellitus with peripheral neuropathy with diabetic retinopathy.

Q. What **investigations** do you suggest in this case?

A. As follows:

- Urine R/M/E
- Blood sugar (fasting and 2 hours after breakfast)

- HbA_{1C}
- CBC with ESR
- Blood urea and serum creatinine
- Serum lipid profile
- USG of whole abdomen
- CXR P/A view
- Plain X-ray abdomen to see pancreatic calcification
- ECG.

RELATED QUESTIONS AND ANSWERS

Q. What are the **criteria** for the diagnosis of DM?

A. Criteria for diagnosis of DM are:

- Fasting plasma venous blood sugar level > 7.0 mmol/L (or 2 hour postprandial blood sugar level > 11.1 mmol/L).
- Random blood sugar > 11.1 mmol/L.
- During OGTT, > 11.1 mmol/L 2 hour after 75 g glucose.

Note. Remember the following points:

- Random means without regard to time since the last meal
- Fasting means no calorie intake for 8 hours at least (not more than 16 hours)
- FBS (fasting blood glucose) < 5.6 mmol/L is normal
- In symptomatic patient, one abnormal finding is diagnostic of diabetes mellitus
- In asymptomatic patients, 2 values are required
- For OGTT, only fasting glucose and 2 hours after 75 glucose is sufficient for diagnosis
- OGTT should be done only in borderline cases (fasting glucose 6.1 to 7.0 mmol/L or random glucose 7.8 to 11.0 mmol/L) and also for the diagnosis of gestational diabetes mellitus.

Q. What is **impaired glucose tolerance (IGT)?**

A. When fasting glucose is less than 7 mmol, but during OGTT, 2 hours after the glucose load is 7.8 to 11.0 mmol, it is called IGT. The patient who has IGT are at increased risk of developing frank DM type 2 with time and also macrovascular complications are more (mainly cardiovascular).

Lifestyle modification for type 2 DM and annual check-up for glucose are recommended for this patient. Cardiovascular risk factors should be treated aggressively.

Q. What is **impaired fasting glucose (IFG)**?

A. IFG is defined as the fasting glucose level between 6.1 to 6.9 mmol/L (110 to 125 mg/dL) according to WHO. However, ADA defines it as fasting glucose level between 5.6 to 6.9 mmol/L (100 to 125 mg/dL). These patients are prone to develop frank diabetes mellitus and cardiovascular disease. The patient is advised for weight reduction about 5 to 10% of their body weight, regular exercise and follow up. Usually no drug therapy is recommended.

Note. Remember the following -

Patients with IGT and/or IFG are now regarded as **prediabetes**.

Q. What is **latent diabetes?**

A. It means blood glucose is usually normal, but may be high under certain stressful conditions. Examples are - pregnancy, infection, obesity, stress or drugs like steroid, thiazide diuretics, etc.

Q. What is **potential** diabetes?

A. It means blood sugar usually is normal, but the patient has increased risk of developing diabetes mellitus in future due to genetic reasons like:

- Both parents are diabetic
- One parent is diabetic and the other has family history of diabetes
- Has a diabetic sibling
- In a twin, if one is diabetic.

Q. What is **brittle diabetes?**

A. Brittle diabetes (or unstable diabetes or labile diabetes) refers to uncontrolled insulin dependent diabetes mellitus with recurrent, dramatic, large swings in blood glucose levels, often without any apparent reason. This leads to irregular and unpredictable hyperglycemia, frequently with ketosis, and sometimes serious hypoglycemia.

Brittle diabetes occurs in 1 to 2% of diabetics, usually in young (age 15 to 30 years) patient with type 1 diabetes mellitus, but may also be found in elderly patient with type 1 or type 2 diabetes mellitus. It often develops after total pancreatectomy. It may be caused by gastrointestinal absorption problems including delayed stomach emptying (gastroparesis), drug interactions, problem with insulin absorption or hormonal malfunction.

Q. What is the **Aetiological classification** of DM?

A. As follows:

1. Type 1 DM:
   - Idiopathic
   - Immune mediated
2. Type 2 DM
3. Gestational DM
4. Other specific types:
   - Genetic defects of β cell function
   - Genetic defects of insulin action
   - Genetic syndromes such as Down's syndrome, Klinefelters' syndrome, Turner's syndrome and DIDMOAD syndrome
   - Pancreatic diseases such as chronic pancreatitis and hemochromatosis
   - Endocrine diseases such as acromegaly, Cushing's syndrome, glucagonoma and thyrotoxicosis
   - Drug induced (e.g. corticosteroid)
   - Viral infections (e.g. congenital rubella, mumps and Coxsackie virus B)
   - Uncommon form of immune-mediated DM.

Q. What is **gestational diabetes mellitus (GDM)?** How is it **diagnosed**?

A. It is defined as any degree of glucose intolerance with the onset or first recognition during pregnancy. It constitutes 90% of women with pregnancy complicated by diabetes. More than 50% women ultimately develop diabetes in the next 20 years and this is linked with obesity. Mostly they develop type 2 DM.

OGTT with 75 g glucose is used as screening test for GDM for women between 24 and 28 weeks of gestation. Blood glucose is measured at fasting, 1 hour and 2 hours after glucose load. GDM is diagnosed if blood glucose is:

- Fasting > 5.1 mmol/L
- After 1 hour 10 mmol/L
- After 2 hour 8.5 mmol/L.

Q. What are the complications of fetus in DM during pregnancy?

A. As follows:

- Teratogenicity (if DM is present in early pregnancy, in the first 6 weeks), there may be cardiac, renal and skeletal malformations, characteristically caudal regression syndrome, neural tube defect
- Fetal macrosomia (if DM is present in later pregnancy)
- Neonatal hypoglycemia (as maternal glucose crosses the placenta, but insulin cannot. As a result, fetal islet cells secrete excess insulin, which may cause neonatal hypoglycemia)
- Increased risk of polycythemia, hyperbilirubinemia and hypocalcemia
- Hyaline membrane disease.

Q. What is the cause of macrosomia in DM?

A. Macrosomia means large or big baby (birth weight > 90 percentile for gestational age). It is due to persistent maternal hyperglycemia leading to fetal hyperglycemia and prolonged fetal hyperinsulinism. This stimulates excessive somatic growth mediated by insulin like growth factors (IGFs). Macrosomia affects all organs except the brain.

Q. What are the complications of DM?

A. As follows:

I. Acute complications:
- Hypoglycemia
- Diabetic ketoacidosis
- Hyperosmolar nonketotic diabetic coma
- Lactic acidosis
- Infections—boils, carbuncle, abscess, cellulitis, tuberculosis.

II. Long-term complications:
- Microvascular—
  - Neuropathy—peripheral neuropathy (sensory, motor or mixed), mononeuritis multiplex, mononeuropathy, autonomic neuropathy
  - Nephropathy (CKD)
  - Eye complications (retinopathy, cataract)
  - Foot complications (ulcers, gangrene, arthropathy).
- Macrovascular—
  - Coronary circulation—myocardial ischemia, infarction
  - Cerebral circulation—TIA, CVD
  - Peripheral circulation—ischemia, claudication
  - Foot complications (ulcers, gangrene, arthropathy).

Note. Remember the following -

Diabetes mellitus can cause painless or silent myocardial infarction. Foot complications are due to both macro and micro vascular lesions.

Q. What are the causes of painless myocardial infarction?

A. As follows:

- Diabetes mellitus with autonomic neuropathy
- Elderly patient with dementia
- CVD.

Q. What are the causes of **sudden death** in diabetes mellitus?

A. It is more likely due to autonomic neuropathy. The patient usually die from sudden cardiorespiratory arrest.

Q. What are **dawn phenomenon** and **Somogyi phenomenon?**

A. As follows:

- Dawn phenomenon or effect is defined as an abnormal early morning (between 3 am to 7 am) increase in the blood sugar level in a patient with diabetes mellitus (mainly type 1). During sleep, there is a surge of secretion of counter regulatory hormones like cortisol, glucagon, growth hormone and catecholamines, which cause release of glucose from liver and increase insulin resistance leading to hyperglycemia. It is often related to insufficient insulin dosage at night and may require increasing the night dose of insulin. The patient should be advised to avoid taking carbohydrate at bedtime.
- Somogyi phenomenon or effect is defined as pre-breakfast hyperglycemia, which follows nocturnal hypoglycemia (which often goes unrecognized) that leads to increased release of counter regulatory hormones that produce high blood glucose. In this case, the previous night insulin dose is often higher than required. It is commonly seen in children. Treatment is by decreasing the overnight insulin dose.

To differentiate between dawn and Somogyi phenomenon, an early morning (3 am) and morning (fasting) blood sugar level is measured. In dawn phenomenon, both samples show hyperglycemia. In Somogyi phenomenon (3 am) blood sample shows hypoglycemia and the morning fasting blood level shows hyperglycemia.

Q. What are the **features** of **autonomic neuropathy** in DM?

A. In both type 1 and 2 DM, there may be autonomic neuropathy, which involves multiple systems of the body. Features are:

- CVS—postural hypotension, fixed heart rate, resting tachycardia and sometimes, sudden death.
- GIT—gastroparesis and nocturnal diarrhea, constipation.
- Genitourinary—urinary incontinence, difficulty in micturition, erectile dysfunction and retrograde ejaculation.
- Sudomotor—gustatory sweating, nocturnal sweating without hypoglycemia, hyperhydrosis of upper extremity and anhydrosis of lower extremity, and anhydrosis of foot can cause cracked skin and ulcer.
- Vasomotor—cold feet due to loss of vasomotor response, dependent edema due to loss of vasomotor tone and increased vascular permeability.
- Autonomic neuropathy can reduce counter-regulatory hormone release, leading to an inability to sense hypoglycemia appropriately.
- Pupillary—decreased pupil size, resistance to mydriatic and delayed or no reflex to light (called pseudo-Argyll Robertson pupil).

Q. What is **insulin resistance syndrome** or **metabolic syndrome** or **syndrome X**?

A. Presence of type 2 DM, central obesity, hypertension and dyslipidemia (elevated LDL and triglyceride, low HDL) is called metabolic syndrome. Other features are hyperinsulinemia, microalbuminuria, elevated fibrinogen and plasminogen activator inhibitor 1, plasma uric acid and increased sympathetic activity. The primary defect is insulin resistance. This predisposes to an increased risk of cardiovascular disease.

Q. What are the **types of neuropathy** in DM?

A. As follows:
- Sensory neuropathy (common)
- Mixed motor and sensory neuropathy
- Asymmetrical motor neuropathy (diabetic amyotrophy)
- Autonomic neuropathy
- Mononeuropathy
- Mononeuritis multiplex.

Mechanism of neuropathy in DM:
- Axonal degeneration
- Patchy or segmental demyelination
- Involvement of intraneural capillaries.

Q. What is **diabetic amyotrophy**?

A. A type of motor neuropathy in diabetic patient, characterized by asymmetrical wasting of muscles, usually involving the quadriceps (also in upper limb). Affected area may be tender, commonly accompanied by severe pain in anterior aspect of thigh. It may be the first presentation of DM. The patient is occasionally cachexic (neuropathic cachexia) and extremely ill, unable to get out of bed. Hyperesthesia or paresthesia is common. There is reduction of muscle power, tone, loss of knee jerk with occasional extensor plantar response on the affected side. CSF protein is increased.

Q. Where is the **site of lesion** or **cause** of diabetic amyotrophy?

A. It is probably due to acute infarction of lower motor neuron of lumbosacral plexus.

Q. How to **treat** diabetic amyotrophy?

A. As follows:
- Good control of DM
- Intensive insulin therapy
- For pain—amitriptyline, imipramine or carbamazepine. Aldose reductase inhibitor may help.

Q. What is the **prognosis**?

A. Prognosis is good, usually recovers, but may take a long time (over months to 2 years).

Q. What are the causes of **loss of vision** in DM?

A. As follows:
- Diabetic retinopathy
- Cataract
- Age-related macular degeneration
- Retinal vein occlusion
- Retinal artery occlusion
- Nonarteritic ischemic optic neuropathy
- Glaucoma.

Q. What are the **causes of unilateral wasting** of leg?

A. As follows:
- Diabetic amyotrophy
- Old poliomyelitis
- Arthritis or trauma
- Cerebral palsy
- Disc prolapse.

Q. What are the **causes** of ulcer in DM?

A. As follows:
- Ischemia
- Neuropathy
- Combined ischemia and neuropathy
- Secondary infection.

Q. What is the **pathology** of ischemic ulcer?

A. As follows:
- Usually microangiopathy
- Associated atherosclerosis of large and medium vessels.

Note. Remember the following -

If the ulcer is painful, the cause is vasculitis and if it is painless, the cause is neuropathy.

Q. How to **treat** a case of diabetic ulcer?

A. As follows:
- Good control of diabetes mellitus
- Local dressing. Avoid weight bearing
- Antibiotic to control secondary infection
- Avoid bare foot, tight shoes and smoking
- Consult with chiropodist
- Surgery may be required (amputation or angioplasty).

Causes of neuropathic ulcer:
- Leprosy
- Diabetes mellitus
- Polyneuropathy (due to any cause)
- Tabes dorsalis
- Syringomyelia
- Amyloidosis
- Porphyria
- Progressive sensory neuropathy.

Q. What are the **differences** between ischemic ulcer and neuropathic ulcer?

A. As follows:

Features	Neuropathic ulcer	Ischemic ulcer (arterial)
1. Area	Warm, dry and pink	Cold, shiny, atrophy and loss of hair
2. Pulse	Bounding	Absent or reduced
3. Sensation	Reduced or absent	Normal
4. Ulcer	Painless and mostly plantar	Painful, over heels and toes
5. Edema	Localised (may be present)	Absent (dry)
6. Reflex	Reduced or absent, equivocal plantar response	Normal

Q. What are the differences between **diabetic ketoacidosis (DKA) and hyperosmolar nonketotic diabetic coma (HNDC)?**

A. As follows:

Points	DKA	HNDC
1. Age	Young, may be any age	Elderly, >40 yrs
2. Precipitating factors	Insulin deficiency (common in type 1)	Partial insulin deficiency (common in type 2)
3. Breath	Acetone present	Absent
4. Kussmaul's breathing	Present	Absent
5. Sodium	Low	High
6. Bicarbonate	Low	Normal
7. pH	6.8 to 7.3	> 7.3
8. Ketonuria	Present	Absent
9. Osmolality	Normal	High
10. Blood glucose	High	Very high
11. Mortality	5 to 10%	30 to 40%

Q. What are the differences between **diabetic ketoacidosis and lactic acidosis?**

A. As follows:

Points	DKA	Lactic acidosis
1. Precipitating factors	Insulin deficiency, infection (not biguanide)	Biguanide
2. Dehydration	Present	Absent
3. Breath	Acetone present	Absent
4. Ketonuria	Present	Absent or mild
5. Serum lactate	Normal	High >5 mmol/L
6. Mortality	5 to 10%	>50%

Q. What is **hyperosmolar nonketotic diabetic coma (HNDC)**? Why **no ketoacidosis** in such case?

A. It is characterized by very high blood glucose (>50 mmol/L) and high plasma osmolality without ketosis. Here insulin deficiency is partial and low level of endogenous insulin is present, which is sufficient to inhibit hepatic ketogenesis, but insufficient to control hyperglycemia. It may be the first presentation of diabetes mellitus. It is common in elderly with NIDDM.

Common precipitating factors are:

- Consumption of glucose rich diet or fruits
- Concurrent medication like thiazide or steroid
- Myocardial infarction
- Intercurrent illness.

Serum osmolarity is extremely high. The resultant high osmolarity can cause cerebral damage. The patient is extremely sensitive to insulin. Hyperchloremic mild acidosis may be present due to

starvation, increased lactic acid and retention of inorganic acid. Plasma sodium is usually high (may be false low due to pseudohyponatremia). There may be high BUN, urea, creatinine and serum osmolality may be very high. Mortality rate may be up to 40%.

Treatment:

- IV 1/2 strength saline (0.45%) should be given. When osmolality is normal, 0.9% normal saline should be given. However, if hypovolemia is present as evidenced by hypotension and oliguria, 0.9% saline may be given. Usually 4 to 6 liters fluid may be required in first 8 to 10 hours.
- When glucose is 250 mg/dL, fluid replacement should include 5% dextrose in either aqua or 0.45% saline or 0.9% saline. Rate of glucose infusion should be adjusted to maintain glucose level between 250 to 300 mg/dL in order to reduce the risk of cerebral edema. When the urinary output is 50 ml/hr or more, IV fluid may be stopped.
- Low dose soluble insulin (preferably with insulin pump, 2 to 6 units hourly). Insulin dose is adjusted to reduce the glucose level by 50 to 70 mg/dL/h.
- Other treatment: NG tube feeding, catheter if needed, antibiotic if infection, correction of electrolytes, low dose heparin (as thrombosis is common).

Read the following in relation to metabolic acidosis:

Causes of metabolic acidosis with normal anion gap are:

- Renal tubular acidosis
- Diarrhea
- Ureterosigmoidostomy
- Acetazolamide therapy
- Ammonium chloride ingestion.

Causes of metabolic acidosis with high anion gap:

- Diabetic ketoacidosis
- Renal failure
- Lactic acidosis
- Salicylate poisoning.

Anion gap is calculated by (Na + K) – (Cl + HCO_3) in mmol/L. Normal value is 8 to 14 mmol/L.

Osmolality is calculated by 2 × Na + 2 × K + plasma glucose + plasma urea (all in mmol/L). Normal osmolarity is 285 to 300 mosm/kg. If it is > 340 mosm, consciousness is depressed.

Q. What are the **differences** between hypoglycemic coma and diabetic coma (coma with ketoacidosis)?

A. As follows:

Points	Hypoglycemic coma	Diabetic coma (DKA)
1. History	Excess insulin, but no or insufficient food intake, following heavy exercise	Too little or no insulin, concurrent infection or digestive disturbance
2. Onset	Rapid onset, usually after taking insulin. Patient is in good health prior to this	Slow onset, the patient has ill health for several days
3. Symptoms	Weakness, tremor, sweating, palpitation, hunger, occasional vomiting from depot insulin	Intense thirst, polyuria, dehydration, vomiting, air hunger and abdominal pain

4. Signs		
» Skin and tongue	» Moist	» Dry
» Eyes	» Normal	» Sunken
» Pulse	» High volume, tachycardia	» Weak
» BP	» Normal or raised	» Low
» Breathing	» Shallow or normal	» Kussmaul's breathing
» Acetone smell	» Absent	» Present
» Reflexes	» Brisk	» Diminished
» Plantar response	» Often extensor	» Usually flexor
» Intraocular pressure	» Normal	» Decreased
5. Urine		
» Ketonuria	» Absent	» Present
» Glycosuria	» Absent	» Present
6. Blood	»	
» Glucose	» Hypoglycemia (< 60 mg/dL)	» Hyperglycemia (> 300 mg/dL)
» Bicarbonate	» Normal	» Reduced
» pH	» Normal	» Low
» Acetone	» Normal	» High
7. Treatment	Oral or IV glucose	Insulin and others
8. Prognosis	Good	Bad

Q. How to diagnose clinically a case of **hypoglycemic coma** and **hyperglycemic coma**?

A. Typical features of hypoglycemic coma are:
- Excessive sweating
- Tachycardia
- Tremor
- Other—Jerks may be brisk, planter—bilaterally extensor.

Typical features of hyperglycemic coma are:
- Severe dehydration
- Pulse—weak, BP—low
- Air-hunger is present—Kussmaul's breathing and acetone in the breath are present
- Others—Reflexes are reduced, planter will be flexor.

OBESITY

CHIEF COMPLAINTS

- Weight gain for … years.

HISTORY

History of present illness: According to the statement of the patient, though he is apparently well, but complaining of gaining weight for the last … years. His food intake is normal, not taking any excessive food or sweet. There is no history of intolerance to cold, weakness, constipation or excessive sleep. On query, there is no history of taking any drug.

History of past illness: Nothing significant

Family history: His father is normal but mother is slightly obese. He has two brothers and one sister. All are normal.

Personal history: He is a service holder, working mostly in his office which does not involve physical exertion. He is a nonsmoker and non-alcoholic.

Socioeconomic history: He is from a middle class family.

Drug and treatment history: He does not take any drug.

GENERAL EXAMINATION

- The patient looks obese involving central as well as peripheral parts of the body. Face is rounded, moon shaped but not plethoric.
- Height is 170 cm, weight is 120 kg, BMI is 41.52 kg/m^2.
- There is no anemia, jaundice, clubbing, koilonychia, leukonychia or edema.
- No thyromegaly or lymphadenopathy.
- There are multiple linear striae involving abdomen, thighs and shoulders. No bruise.
- No proximal myopathy.
- Both breasts are enlarged (bilateral lipomastia).
- Pulse– 84/min.
- BP–130/80 mm Hg lying and 125/80 mm Hg standing.
- Temperature – 99ºF.
- Respiratory rate –14/min.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 42 years, service holder, normotensive, nondiabetic, nonsmoker, hailing from …, presented with the complaints of gaining of weight for the last … years. His food intake is normal, not taking any excessive food or sweet. There is no history of intolerance to cold, weakness, constipation or excessive sleep. On query, there is no history of taking any drug. There is no family history of similar illness.

On Examination

General examination (mention as above).

Systemic examination (mention as above).

My diagnosis is primary obesity.

Q. What are the **differential diagnoses** of simple obesity?

A. As follows:
- Hypothyroidism
- Cushing's syndrome
- Metabolic syndrome.

Q. Why **not** this is hypothyroidism?

A. In the history, there is no cold intolerance, sleepiness, lethargy, etc. There is no nonpitting edema, no coarse puffy face, no slow relaxation of the ankle jerk.

Q. Why **not** this is Cushing's syndrome?

A. In Cushing's syndrome, there is usually central obesity with relatively thin limbs, plethoric moon face, multiple purple striae, proximal muscular weakness, etc. All are absent in this case.

RELATED QUESTIONS AND ANSWERS

Q. What is **obesity**?

A. It is defined as excessive accumulation of fat, classically when the BMI is > 30 kg/m^2. It is diagnosed by the following:
- Measuring weight
- BMI
- Skin fold thickness over the middle of the triceps. Normal values are 20 mm in men and 30 mm in women
- Waist or hip circumference ratio of > 1.0 in men and > 0.9 in women (central distribution of body fat), indicates obesity.

It is associated with a higher risk of morbidity and mortality.

Q. What are the **causes** of obesity?

A. There are multiple factors:
1. Physical inactivity
2. Genetic
3. Excessive food intake
4. Psychological factors
5. Drugs—steroid, oral contraceptive pill, sodium valproate, TCA
6. Secondary disease:
   - Endocrine causes – hypothyroidism, Cushing's syndrome, insulinoma.
   - PCOS in female.
   - Hypothalamic disorder (tumors, injury). This causes polyphagia and obesity.
   - Metabolic syndrome.
   - Genetic syndrome – Laurence-Moon-Biedle syndrome, Prader-Willi syndrome.
   - Others—Pickwickian syndrome, Alstrom syndrome.

Q. What are the **reversible conditions** in obesity?

A. Hypothyroidism, Cushing's syndrome, insulinoma, hypothalamic disorder.

Q. What are the syndrome in which obesity is a **predominant feature?**

A. Cushing syndrome, Laurence-Moon-Biedle syndrome, Prader-Willi syndrome, Pickwickian syndrome, Alstrom's syndrome, PCOS.

Q. What is the **link** between obesity and diabetes mellitus?

A. Fat cells release free fatty acids and also TNF-α which are responsible for insulin resistance. A new protein called resistin secreted by the fat cells, also causes insulin resistance.

Q. What are the **mechanism** of obesity?

A. As follows:

- Insensitivity to leptin presumably in hypothalamus.
- Neuropeptide Y induced hyperphagia.
- Deficiency of production or action of anorexigenic hypothalamic neuropeptides.
- Increased secretion of insulin and glucocorticoids.
- Mutation in the gene of PPAR-γ accelerates differentiation of adipocyte and may cause obesity.

Q. What are the **complications** of obesity?

A. As follows:

- Psychological – Low self esteem, depression.
- Mechanical – Osteoarthritis of knee and hips, back strain, varicose veins, urinary incontinence, hiatus hernia, abdominal hernia, flat foot.
- Hepatobiliary – Non-alcoholic steatohepatitis, cirrhosis, gallstones.
- Respiratory – Exertional dyspnea, obstructive sleep apnea, Pickwickian syndrome.
- Cardiovascular – Hypertension, atherosclerosis, ischemic heart disease, heart failure, thrombo-embolism.
- Stroke
- Metabolic – Diabetes mellitus (type 2), hyperlipidemia, atherosclerosis, hyperuricemia and gout.
- Increased cancer risk – breast, uterus, colorectal, prostate, ovary.
- Skin infection – groin and submammary candidiasis.
- Menstrual abnormalities.
- Increased morbidity and mortality.
- Postoperative problems.
- Accident proneness.

Q. What is the **classification (or grading)** of obesity?

A. It is done according to BMI (kg/m^2):

1. Normal – 18.5 to 24.9
2. Overweight – 25 to 29.9 (mildly increased risk of co-morbidities).
3. Obese – >30, this is again divided in 3 classes according to BMI –
   a. Class I – 30 to 35 (moderate risk of co-morbidities).
   b. Class II – 35 to 40 (severe risk of co-morbidities).
   c. Class III – > 40 (very severe risk of co-morbidities).

Q. What is **BMI**?

A. Body mass index is a measure to determine the excessive adipose tissue. It is calculated as weight in kg divided by height in meter^2. Normal BMI is 18.5 to 24.9 kg/m^2.

Q. What is **morbid obesity**?

A. If the relative weight is > 200% (BMI > 40 kg/m^2), it is called morbid obesity. It is associated with 10 fold increase in mortality.

Q. How to **investigate** a case of obesity?

A. In any case of obesity, detail history of the patient, specially dietary history, physical activity or sedentary work, any drug, alcohol should be taken. Whether the weight gain is recent or rapid (to

exclude secondary disease like Cushing's syndrome or hypothyroidism). Then following routine investigations should be done:

- Fasting blood sugar
- Lipid profile
- Thyroid function test (FT_3, FT_4, TSH)
- Investigate for Cushing's syndrome
- Liver function test (transaminase, USG of hepatobiliary system to see fatty liver)
- X-ray chest, ECG, echocardiography – to see cardiac status
- Lung function test for sleep apnea
- X-ray of the individual joints in osteoarthrosis
- In female, if PCOS is suspected, investigate accordingly (such as USG of ovary, serum FSH and LH).

Q. How to **treat** a patient with simple obesity?

A. Multidisciplinary approach including:

- Hypocaloric diets
- Exercise
- Social support
- Avoidance of drugs, smoking, alcohol
- Treatment of secondary cause
- Drug treatment:
  - Sibutramine (it blocks serotonergic pathways)
  - Orlistat (pancreatic and gastric lipase inhibitor). It inhibits dietary fat absorption
  - Incretins (Glucagon like peptide 1)
  - Biguanide like metformin

  (Other drugs like phenfluramine, amphetamine, phentarmine, etc. are not recommended).
- Surgical management:
  - Bariatric surgery—to reduce the size of stomach.
  - Cosmetic surgery (liposuction).

Q. What are the **indication of surgery?**

A. In some cases of morbid obesity (BMI >40 kg/m^2) or BMI > 35 kg/m^2 and obesity related complications, after conventional treatment have failed.

SHORT STATURE

CHIEF COMPLAINTS

- Failure to increase in height.

HISTORY

History of present illness: According to the statement of the patient's mother, though the patient is of 20 years old, he has failed to attain adequate growth as much as his classmates and other children. There is no record regarding pregnancy of his mother. There is no history of weight gain, drug intake, long standing diarrhea, feeding problem, cold intolerance, constipation or any systemic disease. His eating habit is normal. There is no abnormality regarding bowel and bladder habits.

History of past illness: No history of any significant past illness.

Family history: His parents have normal height. He has one brother and one sister who have normal height for their age.

Socioeconomic history: He is a college student. His academic performance is good.

Drug and treatment history: He did not take any drugs.

GENERAL EXAMINATION

- The patient looks short. His height is … feet. The limbs are proportionately short.
- There is no anemia, jaundice, clubbing, koilonychia, leukonychia or edema.
- No thyromegaly or lymphadenopathy.
- Skin is normal.
- Pulse– 80/min.
- BP–120/75 mm Hg lying and 115/75 mm Hg standing.
- Temperature – 98ºF.
- Respiratory rate –14/min.
- Any features of hypogonadism (axillary or pubic hair, testicular volume, stretched penile length, Tanner stage).

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr. …, 20 years old, a student, normotensive, nondiabetic presented with failure of attaining adequate growth. There is no record regarding pregnancy of his mother. There is no history of weight gain, drug intake, long standing diarrhea, feeding problem, cold intolerance, constipation or any systemic disease. His eating habit is normal. There is no abnormality regarding bowel and bladder habits. There is no history of any significant past illness. His parents have normal height. He has one brother and one sister who have normal height for their age. He is a college student. His academic performance is good. He did not take any drugs.

On Examination

General examination (mention as above)

Systemic examination (mention as above).

My diagnosis is short stature (with or without delayed puberty).

Q. What are the **differential diagnoses** of short stature?

A. As follows:
- Familial
- Turner's syndrome
- Cretinism
- Hypopituitarism
- Isolated growth hormone deficiency.

Q. What do you think **the cause** in your case?

A. Constitutional or hypopituitarism.

Q. **Why not** hypopituitarism?

A. Because, secondary sexual characters are normal.

Q. **Why not** hypothyroidism?

A. There is no history of weight gain, cold intolerance, increased sleepiness, constipation.

RELATED QUESTIONS AND ANSWERS

Q. What are the **causes** of short stature?

A. As follows:
1. Constitutional (the commonest cause)
2. Familial or genetic
3. Physiological growth delay
4. Emotional deprivation and psychological factors
5. Chronic systemic disease:
   - Cardiac – congenital cyanotic heart disease like Fallot's tetralogy
   - Renal – Renal failure, renal tubular acidosis
   - Respiratory – Brochiectasis, brochial asthma
   - GIT – Small bowel disease like celiac disease, Hirschsprung's disease
   - Cystic fibrosis.
6. Endocrine diseases:
   - Hypopituitarism (pituitary dwarfism)
   - Isolated GH deficiency
   - Cretinism (hypothyroidism)
   - Cushing's syndrome
   - Pseudohypoparathyroidism (characterized by short stature, round face, mental retardation, epileptic attack, basal ganglia and subcutaneous calcification, short metacarpal. Hypoparathyroidism is due to defect in end organ resistance to parathormone)
   - Pseudopseudohypoparathyroidism
   - Uncontrolled Juvenile diabetes mellitus.
7. Nutritional:
   - Protein energy malnutrition like marasmus and Kwashiorkor
   - Ricket.
8. Chromosomal or genetic abnormalities:
   - Down's syndrome
   - Turner's syndrome

- Noonan's syndrome (male Turner)
- Prader-Willi syndrome
- Laurence-Moon-Biedl syndrome.

9. Skeletal dysplasia:
   - If there is short limb and normal trunk, may be due to achondroplasia
   - If there is short limb and short spine, may be due to mucopolysaccharidoses (Hurler's syndrome or Gargoylism).
10. Gross kyphoscoliosis
11. Drugs like steroid.

Q. How to **investigate** short stature?

A. A detailed history should be taken and the patient should be examined to exclude systemic diseases. It should be done as follows:

1. History to be taken:
   - Family history (parents and relatives)
   - Pregnancy record (growth retardation and weight at birth, and any congenital disease)
   - Rate of growth
   - Comparison with peers at school and siblings
   - Systemic disease (respiratory, cardiac, GIT and renal)
   - Nutrition (less intake and malabsorption)
   - Age of appearance of secondary sexual characters (pubic hair, breast, menarche)
   - Use of steroid during childhood
   - Psychosocial deprivation.
2. Physical examination:
   - Height and weight chart (if height is below third percentile, it is considered as short stature)
   - Arm span and height (achondroplasia)
   - Short limbs compared to trunk (achondroplasia)
   - Reduction of weight and height (malnutrition and systemic disease)
   - More weight but short height indicates endocrine disease (hypothyroidism, Cushing's syndrome), and genetic syndrome (Prader-Willi syndrome, Laurence-Moon-Biedl syndrome)
   - Grading of secondary sexual characteristics
   - Look for evidence of systemic disease (heart, kidney and respiratory)
   - Others (Turner's syndrome, Noonan's syndrome and pseudohypoparathyroidism).

After exclusion of systemic disease, proceed as follows:

1. Thyroid function test—serum TSH and FT_4 to exclude hypothyroidism.
2. GH status:
   - GH response to insulin is the gold standard.
   - Blood level of insulin like growth factor 1 (IGF-1) and insulin like growth factor binding protein 3 (IGF-BP3) may provide evidence of GH under secretion.
   - Basal growth hormone level is of little value. Urinary growth hormone level may be used as a screening.
3. Bone age—non-dominant hand and wrist X-rays for the assessment of bone age by comparison with standard charts.
4. Lateral skull X-ray (may show calcification—in craniopharyngioma).
5. Karyotyping in females—to exclude Turner's syndrome.
6. Other tests according to suspicion of causes.

Q. What is **dwarfism**?

A. Dwarfism may be defined as condition where the height of a person is much below the normal according to the chronological age.

Body ratio in dwarfism:

1. If upper and lower segments are equal, the causes are –
   - Hereditary
   - Constitutional
   - Pituitary dwarfism.
2. If upper segment is bigger than lower segment, the causes are –
   - Achondroplasia
   - Cretinism
   - Juvenile myxedema.
3. If upper segment is smaller than lower segment, the causes are –
   - Spinal deformity.

Q. How to **treat?**

A. As follows:

- Any systemic disease should be treated accordingly
- Nutritional supplementation
- Psychological support
- In growth hormone deficiency—recombinant growth hormone (somatropin) is given.

MULTIPLE ENDOCRINE NEOPLASIA (MEN)

CASE 1

Chief Complaints

- Excessive thirst and urination for … months
- Lethargy, depression, and nausea for … months
- Abdominal pain, heart burn and diarrhea for … months
- Swelling of right mid arm for … months
- Recurrent dizzy spells for … month.

HISTORY

History of present illness: The patient state that she was well about … months back. Since then, she has been suffering from excessive thirst and urine output, which are present throughout day and night. She also complains of abdominal pain, nausea and occasional vomiting. The pain is mostly in upper abdomen, burning in nature, improves after taking food, antacid but there is no radiation. She also complains of watery diarrhea but no mucus or blood. About 2 months back, she had fracture of her right arm following fall from standing height. For the last 1 month, she is complaining of repeated dizzy spells after prolonged fast, during exercise or on awakening from sleep. It improves after taking food in every time. There is no history of weight loss, fever, chest pain.

History of past illness: No history of any significant past illness.

Family history: Her mother had neck surgery. Other family members are in good health.

Socioeconomic history: She is a house wife.

Drug and treatment history: The patient consulted with orthopedic surgeon for fracture and was managed by conservative treatment. Currently she is taking omeprazole and antacids.

Menstrual History: The patient is amenorrheic for 2 months. Previously cycle was regular.

GENERAL EXAMINATION

- Appearance: Ill looking
- Built: Average
- BMI: 25kg/m^2
- Mildly anemic, there is no jaundice, clubbing, koilonychia, leukonychia or edema
- No thyromegaly or lymphadenopathy
- Skin is normal
- Dehydration is mild
- There is plaster cast over right arm
- Pulse: 84 min regular
- BP:145/95 mm Hg.

SYSTEMIC EXAMINATION

- Mental status—mood is depressed.
- Abdomen—epigastric tenderness is present, otherwise normal.
- All other systemic examinations reveal no abnormalities.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mrs. …, a 40-year-old, hypertensive, house wife presented with the complaints of excessive thirst and urine output, which are present throughout day and night. She also complains of abdominal pain, nausea and occasional vomiting. The pain is mostly in upper abdomen, burning in nature, improves after taking food, antacid but there is no radiation. She also complains of watery diarrhea but no mucus or blood. About 2 months back, she had fracture of her right arm following fall from standing height. For the last 1 month, she is complaining of repeated dizzy spells after prolonged fast, during exercise or on awakening from sleep. It improves after taking food in every time. There is no history of weight loss, fever, chest pain. She was treated with omeprazole, antacid and vitamins. There is no history of such illness in her family.

My diagnosis is MEN-1 (components are primary hyperparathyroidism, Gastrinoma, Insulinoma).

Q. What are your **differential diagnoses?**

A. As follows:
- Diabetes Mellitus with PUD
- Sporadic primary hyperparathyroidism
- Multiple myeloma.

Q. What **investigations** would you do?

A. As follows:
- Serum calcium, phosphate
- Serum albumin
- Serum PTH, gastrin, prolactin, GH, ACTH
- Ultrasonogram of neck
- Sestamibi scan of parathyroid gland
- Plain X-ray abdomen
- Endoscopic ultrasound, CT abdomen, octreotide scanning
- Fasting Insulin and Glucose, endoscopic ultrasound, CT/MRI abdomen
- X-ray skull, MRI of pituitary gland.

Q. What is the **treatment** of MEN-I?

A. As follows:
1. Therapy for MEN-1 includes surgical resection of hyperplastic parathyroid tissue and pituitary adenomas; surgical cure for the associated pancreatic tumor is usually not possible.
2. For gastrinoma proton pump inhibitor is the mainstay of treatment.
3. Surgery is the treatment of choice in case of insulinoma and non surgical candidate can be managed with diazoxide or verapamil.

CASE 2

Chief Complaints

- Pain in the epigastrium for … months.
- Anorexia, nausea and constipation for … months.
- Recurrent attack of headache, sweating, insomnia and palpitation for … months.

History of present illness: The patient states that she was well about … months back. Since then, she has been suffering from pain in the epigastrium, which is burning in nature, sometimes relieved

by taking food, but no radiation. She also complains of anorexia, nausea and occasional vomiting for … months. The patient is experiencing recurrent attack of headache, sweating, insomnia and palpitation for the last … months. There is no history of weight loss, fever, chest pain.

Other history: Mention accordingly.

Examination: BP 185/120 mm Hg, pulse 110/min. A small goiter, irregular, nodular, non-tender and hard in consistency, no bruit.

Salient feature: Mention as above.
My diagnosis is MEN-IIa.

Q. Why MEN-IIa?

A. In this patients there is goiter (may be medullary carcinoma of thyroid), features of pheochromocytoma (hypertension, recurrent headache, sweating) and hypercalcemia (anorexia, nausea, constipation – may be hyperparathyroidism).

Q. What **investigation** should be done in MEN-2a?

A. As follows:
- For hyperparathyroidism – serum calcium (high), phosphate (low), alkaline phosphatase (high).
- For pheochromocytoma – serum catecholamine (high), 24 hours urinary VMA (high).
- For MTC – serum calcitonin (high).
- Other investigations – accordingly.

RELATED QUESTIONS AND ANSWERS

Q. What is **MEN**?

A. MEN is a group of genetic syndromes, transmitted as autosomal dominant manner characterized by neoplasm of two or more different hormonal tissue of the body. It is a common and mostly in **4th and 5th** decades.

Q. What **other features** you would search for in this case?

A. Presence of galactorrhea as pituitary adenoma, mostly prolactin secreting, is an important component of MEN-1

Q. What are the types of MEN?

A. Two types:
MEN-1 (Wermer's syndrome): It comprises primary hyperparathyroidism, pituitary adenoma and pancreatic tumor.
- Primary hyperparathyroidism—most common feature and earliest manifestation of MEN-1. There are four gland hyperplasia.
- Pancreatic neuriendocrine tumor—gastrinoma (40% to 60%), insulinoma (20%).
- Pituitary adenomas—the majority secrete prolactin.

MEN-2a (Sipple's syndrome): It comprises:
- Medullary carcinoma of thyroid
- Primary hyperparathyroidism (usually hyperpalasia)
- Pheochromocytoma.

MEN-2b: MEN-2a when associated with:
- Marfanoid body habitus
- Abnormal dental enamel

- Multiple mucosal neuromas
- Skeletal abnormalities.

Q. Is hyperparathyroidism in **MEN-1** is similar to sporadic hyperparathyroidism?

A. No. Hyperparathyroidism associated with MEN-1 results from hyperplasia of all four glands, whereas sporadic primary hyperparathyroidism is usually characterized by adenoma in a single gland.

Q. What **other pancreatic tumors** may be seen in MEN-1?

A. Glucagonoma, somatostatinoma, VIPomas.

Q. At what age screening for **MEN-1** should begin?

A. Screening should not begin before the age of 15 and may be unnecessary for people after the age of 50, who are disease free.

Q. What are the **treatments** of MEN-2?

A. Treatment for MEN-2 includes surgery for medullary carcinoma of thyroid and pheochromocytoma.

CHAPTER 10

Hematology

- Chronic myeloid Leukemia 633
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- Henoch-Schonlein Purpura 668
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CHRONIC MYELOID LEUKEMIA

CHIEF COMPLAINTS

- Weakness and dizziness for … months
- Feeling of a lump in the left upper abdomen for … months
- Anorexia, weight loss, palpitation for … months
- Occasional gum bleeding for … months.

HISTORY

History present illness: The patient states that he was alright … months back. Since then, he has been suffering from severe weakness with occasional dizziness. He finds it difficult to perform regular daily activities. The patient also feels a lump in the left upper abdomen which is associated with heaviness and occasional dull pain for … months. He also complains of loss of appetite, loss of about 20 kg of body weight, palpitation and occasional gum bleeding for … months. There is no history of fever, bowel or bladder abnormality or other bleeding manifestations.

History of past illness

Family history

Personal history

Socioeconomic history

Drug history: Mention according to the patient's statement

GENERAL EXAMINATION

- The patient looks pale and emaciated
- Moderately anemic
- No jaundice, clubbing, cyanosis, koilonychia, leukonychia or edema
- No lymphadenopathy or thyromegaly
- There is sternal tenderness
- Pulse: 80/min
- BP: 130/85 mm Hg
- Temperature: 97ºF.

SYSTEMIC EXAMINATION

Gastrointestinal System

- Lips, gums, teeth and tonsils—normal
- Tongue and oral cavity—pale.

Abdomen

Inspection:

- Distension in upper abdomen, more marked in left upper quadrant.

Palpation:

- Liver—just palpable, 2 cm from the right costal margin in the midclavicular line, margin is sharp, surface is smooth, nontender and firm in consistency, no bruit or rub.
- Spleen—hugely enlarged, 15 cm from the left costal margin in the anterior axillary line towards the right iliac fossa.
- Kidneys—not ballotable.

Percussion:

- No evidence of ascites (no fluid thrill, no shifting dullness).

Auscultation:

- No abnormality detected.

Cardiovascular System

- There is a systolic murmur in the apical area (likely to be flow murmur).

Examination of other systems reveals no abnormalities.

SALIENT FEATURE

Mr …, 42 years old, government service holder, normotensive, nondiabetic, nonsmoker, hailing from …, presented with severe weakness with occasional dizziness for … months. He finds it difficult to perform regular daily activities. The patient also feels a lump in the left upper abdomen which is associated with heaviness and occasional dull pain for … months. He also complains of loss of appetite, loss of about 20 kg of body weight, palpitation and occasional gum bleeding for … months. There is no history of fever, bowel or bladder abnormality or other bleeding manifestations. He was treated with ranitidin, iron tablets and vitamins. There is no such illness in his family.

On examination—general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is hepatosplenomegaly with severe anemia for which I have some differential diagnoses:

- Chronic myeloid leukemia
- Chronic liver disease with portal hypertension
- Myelofibrosis
- Tropical splenomegaly syndrome.

Q. What are the causes of **massive splenomegaly?**

A. As follows:

- Chronic myeloid leukemia
- Kala-azar
- Malaria
- β thalassemia major
- Myelofibrosis
- Gaucher's disease
- Hairy cell leukemia.

Q. Mention **one single investigation** which will help in diagnosis or exclude other diagnosis.

A. Full blood count with PBF. It will help:
- To diagnose CML.
- Myelofibrosis (it will show leukoerythroblastic blood picture with tear or pear drop poikilocytes).
- Pancytopenia (due to hypersplenism).

Q. What **investigations** do you suggest in CML?

A. As follows:

1. FBC. It shows:
- Leukocytosis (may be very high)
- Differential count (DC) shows increase in myelocyte, promyelocyte. Metamyelocyte, myeloblast < 10%, increase in neutrophil, also basophil and eosinophil
- Platelets are increased
- Nucleated red cells are common.

2. Bone marrow study (hypercellular marrow with increase myeloid precursors). Cytogenetic analysis for Philadelphia chromosome, also RNA analysis to see the presence of BCR-ABL gene product.

3. Other tests:
- Philadelphia chromosome (positive in 95% cases)
- LAP score (decreases)
- Serum uric acid (increases)
- Serum vitamin B12 (increases)
- Serum LDH (increases).

RELATED QUESTIONS AND ANSWERS

Q. What is the **CML**?

A. It is a myeloproliferative disorder, characterized by overproduction of myeloid cells and presence of Philadelphia chromosome. It is common in 40 to 60 years, and peak age is 55 years.

Q. What are the **myeloproliferative disorder**?

A. Group of disease consisting of:
- Chronic myelocytic leukemia
- Myelofibrosis
- Polycythemia rubra vera
- Essential thrombocythemia.

These disorders are grouped together, because any of the disease may evolve from one form to another. All myeloproliferative disorders may progress to acute myeloid leukemia.

Q. How does the patient usually **present**?

A. As follows:
- May be asymptomatic (25%)
- Splenomegaly (90%). In 10% cases, there may be huge splenomegaly. The Patient may complain of mass or discomfort or heaviness or pain in left hypochondrium. A friction rub may indicate splenic infarction
- Unexplained aneia
- General features—weakness, tiredness, lethargy, anorexia, loss of weight and night sweating
- Repeated infection

- Breathlessness
- Bleeding, bruising (due to thrombocytopenia)
- Hepatomegaly (in 50% cases).

Q. What are the **clinical phases or types** of CML?

A. Three phases:
- Chronic phase
- Accelerated phase
- Blastic crisis.

Q. What is **blastic** crisis? How can you **suspect** blastic crisis clinically in CML?

A. It means the disease is transformed to acute leukemia. It may be myeloid (70%) or lymphatic type (30%), and it occurs at a rate of 10% per year, relatively refractory to treatment and is the cause of death in majority of cases. Prognosis is poor in myeloid type of blastic crisis.

Blastic crisis in CML can be suspected, if:
- Rapid deterioration of the patient
- Increasing splenomegaly
- Blood picture shows increase in number of blast cells and increasing basophil.

Q. What are the **causes of death** in CML?

A. As follows:
- Blastic crisis
- Secondary infection
- Myelofibrosis.

Q. How to **treat** CML?

A. Treatment depends on the phase of the disease such as chronic phase and accelerated or blastic crisis:

1. Treatment of chronic phase:
- Imatinib is the first line therapy. It shows 76% (95% in some cases) response with disappearance of Ph chromosome after 18 months. It is a tyrosine kinase inhibitor, acts by blocking the enzymatic action of BCR-ABL fusion protein. It reduces uncontrolled proliferation of WBC. Dose is 400 mg daily. In some cases, 600 to 800 mg may be given to overcome the resistance. It can be continued indefinitely.
- If failure to respond to imatinib, second generation tyrosine kinase inhibitor such as desatinib or nilotinib or allogenic bone marrow transplantation should be considered.
- Alternately, hydroxyurea or α-interferon that were previously used for initial control, are still useful. However, hydroxyurea does not diminish Ph-chromosome or affect blastic crisis. α-interferon was given alone or with the chemotherapeutic agent Ara-C. It controls CML in chronic phase in about 70% of patients and causes disappearance of Philadelphia chromosome in 20% cases. It was a first line drug before imatinib.
- Busulphan was used previously. Not used now a days.
- Bone marrow transplantation (BMT) from allogenic matched sibling donor (usually below the age of 40 years and in early chronic phase), 70% cure.

2. Treatment of accelerated phase and blastic crisis:
- Treatment is difficult, imatinib is indicated if the patient has not received it.
- Hydroxyurea (hydroxycarbamide) can be effective.
- Low-dose cytarabine can be given.

Note Remember the following points regarding the previous chemotherapeutic drugs:

- Both busulphan and hydroxyurea—less or no use now
- Busulphan controls leukocyte quickly, but greater risk of marrow depression and rarely interstitial fibrosis of lung (**Busulphan lung**). Also increased pigmentation.
- Hydroxyurea is preferred than busulphan, but controls leukocyte count less quickly than busulphan and bone marrow depression is also less.
- None of these drugs affect the onset of blast transformation or diminishes Philadelphia chromosome and little effect on survival.
- Bone marrow transplantation is indicated in whom the disease is not well controlled, in whom the disease progress after initial control or for those who have accelerated phase disease.

Q. What are the therapies that may **cure** CML?

A. Bone marrow transplantation (BMT), imatinib and α-interferon.

Q. What is the **prognosis** of CML?

A. As follows:

- With imatinib therapy, complete hematological remission in up to 95% cases, and 70 to 80% of these have no detectable BCR-ABL transcript. Event free and overall survival appear to be better
- Following stem cell transplantation, there is 70% cure in chronic phase in young patients
- Without treatment median survival is 3 to 4 years, some may survive up to 10 years
- If there is blastic crisis, prognosis is poor. Median survival is 6 months
- CML may transform to myelofibrosis.

CHRONIC LYMPHATIC LEUKEMIA

CHIEF COMPLAINTS

- Weakness for … months
- Occasional fever with cough for … months
- Lumps in the neck and inguinal region for … days.

HISTORY

History of present illness: The patient states that he was alright … months back. Since then, he has been suffering from severe generalized weakness, which interferes with his day to day activities. He also complains of occasional fever and cough for … months. Fever is usually low grade, not associated with chills and rigor, no evening rise of temperature, does not subside with sweating. Cough is usually dry, not associated with difficulty in breathing or hemoptysis. For the last few days, the patient noticed painless lumps involving both sides of the neck and inguinal region, which are gradually increasing in size. There is no history of weight loss, bleeding from any site, polyarthritis, skin rash, contact with TB patients or history of exposure.

History of past illness

Family history

Personal history

Socioeconomic history

Drug history: Write according to the statement of the patient.

GENERAL EXAMINATION

- The patient is ill-looking and mildly anemic
- No jaundice, clubbing, cyanosis, koilonychia, leukonychia or edema
- No thyromegaly
- There are generalized lymphadenopathy involving cervical, axillary and inguinal lymph nodes of both sides. The lymph nodes are of variable size and shape, largest one being 2 × 2 cm, nontender, firm in consistency, discrete, not adherent to the underlying structure or to the overlying skin. There is no discharging sinus
- Pulse: 80/min
- BP: 130/85 mm Hg
- Temperature: 98ºF
- Respiratory rate: 18/min.

SYSTEMIC EXAMINATION

Gastrointestinal System

- Lips, gums, teeth, tongue, oral cavity and tonsils—normal.

Abdomen

Inspection:

- No abnormality detected.

Palpation:

- Liver—just palpable, 1 cm from the right costal margin in the midclavicular line, margin is sharp, surface is smooth, nontender and firm in consistency, no hepatic bruit or rub.
- Spleen—just palpable, 2 cm from the left costal margin in the anterior axillary line towards the right iliac fossa.
- Kidneys—not ballotable.

Percussion:

- No evidence of ascites (no fluid thrill, no shifting dullness).

Auscultation:

- No abnormality detected.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr. …, 28 years old, businessman, normotensive, nondiabetic, nonsmoker, hailing from …, presented with severe generalized weakness for … months, which interferes with his day to day activities. He also complains of occasional fever and cough for … months. Fever is usually low grade, not associated with chills and rigor. Cough is usually dry, not associated with difficulty in breathing or hemoptysis. For the last few days, the patient noticed painless lumps involving both sides of the neck and inguinal region, which are gradually increasing in size. There is no history of weight loss, bleeding from any site, polyarthritis, skin rash, contact with TB patients or history of exposure. He was treated with paracetamol and several antibiotics, the name of which he cannot mention. There is no family history of such illness.

On examination—general examination (mention as above, describe specially the lymph nodes).

Systemic examination—hepatosplenomegaly (mention as above).

Examination of other systems reveals no abnormalities.

Provisional diagnosis—With this history and clinical findings of lymphadenopathy and hepatosplenomegaly, I have some differential diagnoses:

- Chronic lymphatic leukemia
- Lymphoma
- Acute lymphoblastic leukemia
- Disseminated tuberculosis.

Q. What **investigations** do you suggest in CLL?

A. As follows:

1. CBC, showsL
   - Hb% (low)
   - Leukocytosis (50 to 200 × 10^9/L)
   - Differential count (DC) shows increased lymphocytes (95%), mostly small lymphocytes
   - Platelet is normal, low or slightly increased.

2. Bone marrow (increased lymphocytes).

3. Others:
   - Reticulocyte (high in autoimmune hemolytic anemia)
   - Coombs' test (positive in autoimmune hemolytic anemia)
   - Paraproteins (may be increased)
   - Uric acid (high)
   - Immunophenotyping of B-cell antigen (CD19 and CD23) and T-cell antigen (CD5).

RELATED QUESTIONS AND ANSWERS

Q. What is chronic lymphatic leukemia?

A. It is a neoplastic disorder of lymphocyte, usually involving the B lymphocytes (95%) and rarely T lymphocytes (5%). It is more in males than females (2:1), usually after 45 years.

Q. How does the patient of CLL usually present?

A. CLL is common in the elderly, 65 to 70 years. M:F = 2:1.

- Asymptomatic (25%), diagnosed incidentally in routine examination.
- General features like malaise, weakness, fatigue, weight loss and night sweating.
- Features of anemia (usually slowly developing anemia).
- Recurrent infections.
- Generalized lymphadenopathy (detected on routine examination).
- Hepatosplenomegaly (huge splenomegaly, if autoimmune hemolytic anemia).
- Bleeding manifestations—uncommon.

Q. Why there is anemia in CLL?

A. Anemia is due to bone marrow infiltration or autoimmune hemolytic anemia.

Q. What are the stages of CLL?

A. Three stages (**Binet staging**):

- Stage A (60%)—survival > 10 years.
  - No anemia
  - No thrombocytopenia
  - Less than 3 areas of lymph nodes involvement.
- Stage B (30%)—survival 7 years.
  - No anemia
  - No thrombocytopenia
  - 3 or more areas of lymph nodes involvement.
- Stage C (10%)—survival 2 years.
  - Anemia
  - With or without thrombocytopenia
  - Regardless of area of lymph nodes involvement.

Note Remember the following:

Lymphoid enlargements include cervical, axillary, inguinal and liver and spleen enlargement.

Another staging (**Rai staging**):

- **Stage 0:** Lymphocytosis (in blood and bone marrow) >15000/cmm, without lymphadenopathy, hepatosplenomegaly, anemia or thrombocytopenia
- **Stage I:** Lymphocytosis with lymphadenopathy (without hepatosplenomegaly, anemia or thrombocytopenia)

- **Stage II:** Lymphocytosis with hepatomegaly or splenomegaly (with or without lymphadenopathy)
- **Stage III:** Lymphocytosis with anemia (Hb% <11g/dL) with or without hepatomegaly or splenomegaly
- **Stage IV:** Lymphocytosis with thrombocytopenia (<100000/cmm) with or without lymphadenopathy, hepatomegaly, splenomegaly or anemia.

Q. How to **treat** CLL?

A. Many early indolent cases of CLL require no treatment, even in 30% case will never require any intervention. Otherwise, treatment depends on stage of disease:

- Stage A—No treatment, unless progression occurs. The patient survives for long time (reassurance and follow up). Life expectancy is normal in older patients
- Stage B—No treatment, if the patient is asymptomatic
- Stage C—Usually treatment is necessary.

Indications of treatment in CLL:

- Evidence of marrow failure indicated by worsening of anemia or thrombocytopenia
- Massive or progressive lymphadenopathy or splenomegaly
- Doubling of lymphocyte count in 6 months
- Symptoms (fever, night sweating and weight loss)
- Presence of hemolysis or other immune mediated cytopenias
- Recurrent infection.

Mode of treatment:

1. Symptomatic:
   - For anemia and thrombocytopenia—prednisolone, blood transfusion should be given. If it is refractory or recurrent, then splenectomy may be done, which is also indicated for hypersplenism
   - Infection—antibiotic, immunoglobulin (gamma globulin 0.4 g/kg/month)
   - Local radiotherapy for LN causing discomfort or local obstruction and symptomatic splenomegaly.
2. Specific:
   - Chlorambucil 5 mg daily, adjust the dose according to blood count.
   - Fludarabine alone or with cyclophosphamide or mitoxantrone (with or without steroid) is very helpful. Fludarabine should be avoided in autoimmune hemolytic anemia as it aggravates anemia.
   - Combination therapy with rituximab plus fludarabine with or without cyclophosphamide is the treatment of choice. Rituximab alone is ineffective.
   - Alemtuzumab may be used in patient that progress after fludarabine.
   - Allogenic stem cell transplantation may be curative, but only used in those patient whose disease cannot be controlled by standard therapies.

Q. What is the **prognosis** of CLL?

A. As follows:

- Median survival is about 6 years
- Stage A may be normal life expectancy
- In stage C, median survival is 2 to 3 years
- About 50% dies from infection and 30% from causes unrelated to CLL
- Rarely, acute blastic crisis may occur.

Q. What is **Richter's syndrome?**

A. When CLL is transformed to aggressive high-grade lymphoma, it is called Richter's syndrome. Its prognosis is poor with median survival less than 1 year.

LYMPHOMA

CHIEF COMPLAINTS

- Fever with cough for … months
- Weakness, loss of weight, loss of appetite for … months
- Lumps in the neck and inguinal region for … days.

HISTORY

History of present illness: The patient states that he was alright … months back. Since then, he has been suffering from occasional fever which is low grade, continued, not associated with chill and rigor. There is occasional evening rise of temperature and night sweating. He also complains of cough which is dry, worse at night, associated with difficulty in breathing and more marked on moderate to severe exertion. There is no history of orthopnea or paroxysmal nocturnal dyspnea. The patient also complains of severe weakness, marked loss of weight and appetite for … months. For the last … days, he noticed painless lumps initially on the right side of his neck, and then on the axilla and groins. These lumps are gradually increasing in size. There is no history of bleeding from any site, polyarthritis, skin rash, contact with TB patients or history of exposure. His bowel and bladder habits are normal.

History of past illness

Family history

Personal history

Socioeconomic history

Drug history: Mention according to the statement of the patient.

GENERAL EXAMINATION

- The patient is cachexic and moderately anemic
- No jaundice, clubbing, cyanosis, koilonychia, leukonychia or edema
- Thyromegaly absent
- There is generalized lymphadenopathy involving right cervical, both axillary and inguinal region. The lymph nodes are of variable size and shape, largest one being 2 × 2 cm, nontender, firm in consistency, discrete, not adherent to the underlying structure or to the overlying skin. There is no discharging sinus
- There is no sternal tenderness
- Pulse: 100/min
- BP**:** 100/85 mm Hg.

SYSTEMIC EXAMINATION

Gastrointestinal System

- Lips, gums, teeth, oral cavity and tonsils—normal
- Tongue—pale and smooth.

Abdomen

Inspection:

- No abnormality detected.

Palpation:

- Liver—palpable, 4 cm from the right costal margin in the midclavicular line, margin is sharp, surface is smooth, nontender and firm in consistency, no hepatic bruit or rub.
- Spleen—palpable, 10 cm, from the left costal margin in the anterior axillary line towards the right iliac fossa.

Percussion:

- No evidence of ascites (no fluid thrill, no shifting dullness).

Auscultation:

- No abnormality detected.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 38 years old, fisherman, normotensive, nondiabetic, nonsmoker, hailing from …, presented with occasional fever for … months that is low grade, not associated with chill and rigor. There is occasional evening rise of temperature and night sweating. He also complains of cough which is dry, worse at night, associated with difficulty in breathing and more marked on moderate to severe exertion. There is no history of orthopnea or paroxysmal nocturnal dyspnea. The patient also complains of severe weakness, marked loss of weight and appetite for … months. For the last … days, he noticed painless lumps initially on the right side of his neck, and then on the axilla and groins. These lumps are gradually increasing in size. There is no history of bleeding from any site, polyarthritis, skin rash, contact with TB patients or history of exposure. His bowel and bladder habits are normal. There is no family history of such illness. He has been treated with paracetamol, cough syrup, salbutamol and various antibiotics the name of which he could not mention.

On examination—general examination (mention as above).

Systemic examination (mention as above).

Provisional diagnosis: With this history of fever, lymphadenopathy and hepatosplenomegaly, I have some differential diagnoses:

- Lymphoma
- Disseminated tuberculosis
- Sarcoidosis
- Chronic lymphatic leukemia
- SLE.

Q. What are the causes of **generalized lymphadenopathy?**

A. As follows:

1. Hematological malignancy—lymphoma, ALL, CLL
2. Viral fever—infectious mononucleosis, CMV infection, HIV
3. Disseminated tuberculosis, brucellosis, toxoplasmosis
4. Sarcoidosis

5. SLE
6. Drugs—phenytoin or diphenylhydantoin (called pseudolymphoma).

Q. Could it be kala-azar?

A. It could be kala-azar, because of long term fever and hepatosplenomegaly. But lymphadenopathy is not common in kala-azar (However it is common in African and Chinese kala-azar).

Q. What investigations do you suggest for this patient?

A. As follows:

1. Full blood count with PBF examination
2. X-ray chest
3. USG of whole abdomen
4. Urine R/E
5. Others according to the suspicion of cause:
   - If lymphoma is suspected—FNAC or biopsy (biopsy is preferable) of lymph nodes
   - If leukemia is suspected—bone marrow study
   - If disseminated tuberculosis—MT, lymph node FNAC or biopsy
   - If SLE—ANA, anti-ds-DNA, etc.

RELATED QUESTIONS AND ANSWERS (LYMPHOMA)

Q. What is lymphoma?

A. Lymphoma is a group of disorders due to neoplastic proliferation of lymphoid tissue. Majority are B cell origin. There are 2 types:

- Hodgkin's disease (HD).
- Non-Hodgkin's lymphoma (NHL).

Q. What is Hodgkin's disease?

A. It is a type of lymphoma characterized by painless, progressive enlargement of lymph nodes associated with **Reed Sternberg giant cell** (hallmark of the disease). It usually occurs in adolescence and young adults (20 to 35 years of age), also after 45 years of age (50 to 70 years, two peaks of incidence). Median age is 31 year. More in males than females (1.5:1). It is three times more with past history of infectious mononucleosis.

Q. What is Reed–Sternberg cell?

A. It is a malignant cell of B-cell origin, characterized by:

- Large cell with paired mirror image nuclei that resembles "Owl's eye" appearance.
- Prominent nucleoli.

Reed-Sternberg cell is the hallmark of Hodgkin's disease. Rarely, found in infectious mononucleosis, recurrent Burkitt's lymphoma and CLL.

Q. What are the types of Hodgkin's disease?

A. There are two types of Hodgkin's disease:

1. Nodular lymphocyte predominant Hodgkin's lymphoma (HL)—5%, slowly growing, localized and rarely fatal.

2. Classical HL, which is of 4 types:
   - Nodular sclerosing (70%, common in young, female. Mainly involves cervical, supraclavicular and mediastinal lymph node.)
   - Mixed cellularity (20%, common in elderly, men, associated with B symptoms)

- Lymphocyte rich (5%, common in men, characterized by an infiltrate of many small lymphocytes and Reed-Sternberg cells. It often involves the peripheral lymph nodes. It is usually an indolent disease, which presents at a higher median age)
- Lymphocyte depleted (rare, probably represents large cell or anaplastic NHL. There is lack of cellular infiltrate with numerous Reed-Sternberg cells. It typically presents with advanced stage and B symptoms. It is seen in Hodgkin's disease associated with HIV).

Q. How does the patient **present** in Hodgkin's disease?

A. As follows:

- May be asymptomatic
- The patient may present with generalized lymphadenopathy starting in cervical glands, then axillary and inguinal. These are painless, discrete and rubbery. Pattern of spread is contiguous
- Dry cough, shortness of breath (due to mediastinal lymphadenopathy)
- Systemic features—fever, drenching night sweat, loss of weight, malaise, weakness and pruritus (10%)
- Hepatosplenomegaly
- After alcohol intake, pain at the site of LN involvement.

Q. What is **Pel–Ebstein fever**?

A. Recurrent bouts of pyrexia followed by apyrexial period. May occur in 10% cases of HD.

Q. What are the **stages** of HD?

A. According to Ann-Arbor staging classification, there are is stages:

- Stage I—Involvement of a single LN region (I) or extralymphatic site (I_E).
- Stage II—Involvement of two or more LN regions (II) or an extralymphatic site and LN regions on the same side of diaphragm (II_E).
- Stage III—Involvement of LN regions on both sides of diaphragm with (III_E) or without (III) localized extralymphatic involvement or involvement of spleen (III_S) or both (III_{SE}).
- Stage IV—Diffuse involvement of one or more extralymphatic tissue with or without LN involvement (bone marrow, liver and lung).

(Lymphatic structures include LN, spleen, thymus, Waldeyer's ring, appendix and Peyer's patch.)

Depending on systemic features, each stage is divided into 2 phase:

- No systemic features.
- With systemic features (B symptoms)—such as fever (temperature > 38ºC), drenching sweats, unexplained loss of > 10% of body weight within the previous 6 months.

Q. What **investigations** are done in HD?

A. As follows:

1. CBC—may be normal. There may be normocytic normochromic anemia, lymphopenia, high eosinophil and high ESR.
2. Chest X-ray (shows bilateral hilar lymphadenopathy and widening of mediastinal shadow).
3. FNAC or biopsy—biopsy is preferable (to see the architecture of lymph node which may not be detected by FNAC, also biopsy is necessary for staging).
4. USG of whole abdomen.
5. CT scan of chest and abdomen including pelvis (necessary for staging).
6. Others:
   - PET (Positron emission tomography)—used for staging, assessment of response and direction of therapy.
   - Bone marrow study (involved in advanced stage).

- Renal function tests—mainly creatinine (necessary prior to treatment).
- Liver function tests—mainly SGPT (necessary prior to treatment)
- Serum uric acid (necessary prior to treatment).
- Serum lactate dehydrogenase (LDH).

Note Remember the following points:

- Lymphopenia, high LDH and lymph node > 10 cm are poor prognostic factors
- High ESR is an indicator of disease activity
- High alkaline phosphatase (biliary obstruction) indicates involvement of lymph nodes in porta hepatis.

Q. How is **staging** done and why?

A. For staging, following tests are done:

- Chest X-ray
- Bone marrow
- USG of whole abdomen
- CT scan (whole abdomen and chest).

Staging is done for selection of therapy (radiotherapy or chemotherapy) and prognosis.

Q. How to **treat** HD?

A. As follows:

1. Majority of HD patients are now treated with chemotherapy and adjunctive radiotherapy. ABVD (Adriamycin or doxorubicin, Bleomycin, Vinblastine and Dacarbazine) regimen is widely used. ABVD chemotherapy can cause cardiac and pulmonary toxicity, due to doxorubicin and bleomycin respectively. Infertility and secondary myelodysplasia or AML is low with this regime.
2. Patient with early stage HD (IA, IIA, no bulk) is treated with 2 to 4 cycles of ABVD followed by radiotherapy (20 to 30 Gy) to the involved lymph nodes. Treatment response is monitored by CT scan or PET scan.
3. Patient with advanced disease is usually treated with chemotherapy alone. Usually 6 to 8 cycles of ABVD is given. Radiotherapy at the bulk site used previously is now avoided. Achieving PET negative remission predicts a better long term remission rate. Overall, the long term disease control or cure rates are lower with advanced disease.
4. New regimens are being tested for those who fail with above therapy (about 25%). This includes BEACOPP (Bleomycin, Etoposide, Adriamycin or doxorubicin, Cyclophosphamide, Oncovin or vincristine, Procarbazine, Prednisolone).
5. Patient who is resistant to chemotherapy may be considered for autologous bone marrow transplantation.

Other chemotherapeutic regimen that were previously used are as follows:

- MOPP—Mechlorethamine, Oncovin (vincristine), Procarbazine and Prednisolone.
- COPP—Cyclophosphamide, Oncovin (vincristine), Procarbazine and Prednisolone.

Q. What is the **prognosis** of HD?

A. Prognosis depends on the stage:

- Early stage HD—complete remission in > 90%, when treated with chemotherapy followed by radiotherapy. The majority are cured.
- Advanced stage HD—50 to 70% can be cured.
- Patients who fail to respond to initial chemotherapy have a poor prognosis, but some may achieve long term survival after autologous bone marrow transplantation.

- Patients relapsing within a year of initial chemotherapy have a good salvage rate with autologous BMT.
- Patients relapsing after 1 year may obtain long term survival with further chemotherapy alone.
- Presence of B symptoms indicate adverse prognosis.

Note Remember the following points:

- Fertility is usually preserved after radiotherapy.
- In young women with mediastinal disease, radiotherapy to the breast may cause breast cancer (hence, needs follow up).
- Patients who continue to smoke after chest radiotherapy, lung cancer may occur.
- Cardiac disease may occur after supradiaphragmatic mantle field radiation.

Q. What is **disease free** or **cure** in HD?

A. If no relapse after 5 years of withdrawal of treatment, it is called cure or disease-free.

BRIEF DISCUSSION ABOUT NON-HODGKIN'S LYMPHOMA

Q. What is **non-Hodgkin's lymphoma (NHL)**? What are the **types (grading)**?

A. The NHL is characterized by malignant proliferation of lymphoid cells, and majority are B-cells (70%) and few T-cells (30%).

Types or grading (depending on the rate at which the cells are dividing):

1. **Low grade (indolent)** shows the following characteristics:
   - Low cell proliferation rate
   - Asymptomatic for many years
   - Slow indolent course
   - Remitting and relapsing course
   - Good response to minimal therapy
   - Incurable, but the patient survives for long time
   - Most nodular lymphoma are of low grade
   - Small cell disease (mature lymphocyte) is associated with low-grade lymphoma
   - No treatment is required, if the disease is not advanced and asymptomatic
   - Median survival up to 10 years
   - Transformation to high grade is associated with poor prognosis.
2. **High grade (aggressive)** shows the following characteristics:
   - Cell divisions occur quickly
   - Early symptoms are common
   - Fatal, if untreated
   - Responds better to treatment and patient may achieve a long-term remission, if treated properly (potentially a curable disease)
   - 80% respond to initial therapy, and 35% are disease free for 5 years
   - Large cell disease (immature lymphoid cells) is of high grade
   - Most diffuse lymphomas are of high grade.

Note Remember the following:

Stages of NHL are similar to Hodgkin's lymphoma (HL).

Q. What are the **causes** of NHL?

A. Actual cause is unknown. Probable causes are:

- Specific lymphoma types are associated with EBV, human herpes virus 8 (HHV8) and human T-cell lymphotropic virus (HTLV) infection.
- *Helicobacter pylori* is an etiological factor in gastric MALT lymphoma.
- A late manifestation of HIV infection. Primary brain lymphoma, immunoblastic diffuse large B-cell lymphoma and Burkitt's lymphoma may occur in AIDS.
- Lymphoma occurs in congenital and acquired immunodeficiency states. Acquired immunodeficiency, as a result of organ transplantation, is strongly associated with NHL. These are commonly extranodal and most frequently occur in the first year after transplantation.
- Gastric lymphomas are associated with specific chromosome lesions. The t(14:18) translocation in follicular lymphoma results in the dysregulated expression of the BCL-2 gene product, which inhibits apoptotic cell death.
- A number of familial cancer syndromes are also associated with NHL.
- In autoimmune disorders, high risk of NHL is reported, e.g. Sjogren's syndrome, and extranodal marginal zone lymphoma.
- There may be an association with exposure to pesticide, hair dyes, organic solvents, etc.

Q. What are the **clinical features of NHL**?

A. As follows:

- NHL can occur at any age, but peak incidence is 65 to 70 years.
- It is multicentric in origin and spreads rapidly to noncontiguous areas. The disease is usually widespread at the time of diagnosis.
- Discrete, painless, firm, lymph nodal enlargement is the most common presentation. Waldeyer's ring and epitrochlear lymph nodes are frequently involved.
- B symptoms of fever, night sweats and weight loss are less prominent.
- Extranodal presentations are more common than Hodgkin's disease. May involve gastrointestinal tract (stomach), lung, thyroid, skin, testes and CNS. Skin involvement (T-cell lymphoma) presents as mycosis fungoides and Sezary syndrome. Oropharyngeal involvement occurs rarely. Compression syndrome may occur, such as paraplegia due to compression of spinal cord by an extradural lymphoma, dysphagia, breathlessness, vomiting, intestinal obstruction, ascites and limb edema, SVC obstruction.
- Bone marrow involvement is more common in low grade (60%) and less in high grade (10%).
- Involvement of liver and spleen results in hepatosplenomegaly.
- Bone involvement may manifest as pathological fractures with pain.

Q. What **investigations** are done in NHL?

A. Similar to HL, plus the following:

- Routine bone marrow aspiration and trephine.
- Immunotyping of surface antigen to distinguish T-cell and B-cell tumors (done on blood, marrow or nodal material). CD 20 should be done.
- Immunoglobulin determination (IgG or IgM paraprotein, which serve as markers for treatment response).
- Uric acid.

Q. What are the **treatment** of NHL?

A. As follows:

1. **Low-grade NHL**—Not cured by any therapy. No therapy, if the patient is asymptomatic. Indications of treatment are:
   - Marked systemic symptoms.
   - Bone marrow failure.
   - Features of compression (superior vena caval obstruction, spinal cord, gut obstruction and ascites).
   - Large lymphadenopathy causing discomfort or disfigurement.

   Treatment options include:
   - Radiotherapy, for stage I.
   - Chemotherapy is needed in most cases. Majority responds well to oral chlorambucil, which is well tolerated but not curative. More aggressive intravenous chemotherapy may be tried in younger age to provide better quality of life, but no survival benefit.
   - Monoclonal antibody—rituximab (anti-CD 20 antibody) is effective in 60% cases. Synergistic effects are seen with standard chemotherapy. Rituximab in combination with cyclophosphamide, vincristine and prednisolone (R-CVP) is recommended as first line therapy.
   - High dose chemotherapy and bone marrow transplantation can be tried in patient with relapse.
2. **High-grade NHL**—always needs treatment. Options are:
   - Majority (>90%) are treated with combination chemotherapy—CHOP (Cyclophosphamide, Hydroxydaunorubicin, Oncovin (vincristine) and Prednisolone).
   - Radiotherapy may be given in stage I. It is also indicated for the residual localized site of bulk disease after chemotherapy, for spinal cord and other compression syndrome.
   - Rituximab may be combined with CHOP therapy (R-CHOP). This helps in complete response rates and improves overall survival. It is the current first line therapy for those with stage II or greater diffuse large cell lymphoma.
   - Autologous bone marrow transplantation for relapse chemosensitive disease.

Q. What is the **prognosis?**

A. As follows:

1. Low grade lymphoma has a slow indolent course. Median survival up to 10 years. Transformation to high grade is associated with poor prognosis.
2. In high grade lymphoma, 80% respond to initial therapy, and 35% are disease free for 5 years.
3. Adverse prognostic factors in NHL includes:
   - Age > 60 years
   - Stage III or IV (advanced disease)
   - High serum LDH level
   - Performance status ECOG 2 or more
   - More than 1 extranodal site of involvement.
4. In case of high grade NHL, 5 year survival of patient with adverse prognostic factors (high risk score) is 25%, while that of patients without adverse prognostic factors (low risk score) is 75%.
5. Relapse is associated with a poor response to further chemotherapy (<10% 5-year survival), but in patients under 65 years, bone marrow transplantation improves survival.

Q. What is **Waldeyer's ring**?

A. It is a circle of lymphatic tissue in posterior part of oropharynx and nasopharynx, which includes tonsils and adenoids. It is involved in NHL, and rarely in HL.

Q. What are the **differences** between HL and NHL?

A. As follows:

Features	Hodgkin's lymphoma	Non-Hodgkin's lymphoma
1. Age	Bimodal. First peak at 20 to 30 years, and second peak at 50 to 70 years	Median age 65 to 70 years
2. LN involvement	Unifocal, usually localized to a single axial group (cervical and mediastinal)	Multicentric, more frequent involvement of peripheral LN
3. Mesenteric LN and Waldeyer's ring	Rarely involved	Commonly involved
4. Epitrochlear lymph node	Rarely involved	Commonly involved
5. LN spread	Orderly spread by contiguity	Noncontiguous spread (via blood)
6. Extranodal involvement	Less common, occurs late	More common, occurs early
7. Systemic features or B symptoms	Common	Less common
8. Alcohol induced discomfort at lymph node site	Present	Absent
9. Pel-Ebstein fever	May occur	Does not occur
10. Pruritus	Common	Less common
11. Histology	Reed-Sternberg cells (hallmark)	Absent
12. Bone marrow involvement	Early	Late
13. Prognosis	High cure rate	Low cure rate (low grade tumors are incurable)

APLASTIC ANEMIA

CHIEF COMPLAINTS

- Severe weakness, palpitation, dizziness for … months
- Occasional gum bleeding and nasal bleeding for … months
- Multiple bleeding spots in different parts of the body for … months
- Occasional fever and sore throat for … months.

HISTORY

History present illness: The patient states that he was alright … months back. Since then, he has been suffering from severe weakness, palpitation and dizziness, which is more marked even on mild activity. He also complains of occasional spontaneous bleeding from gum and nose for the same duration. For the last … months, he also noticed multiple bleeding spots in skin of different parts of body including hands, legs, abdomen, etc. There is also history of occasional fever, which is of low grade and associated with sore throat. He does not give any history of taking drugs, or exposure to radiation or chemicals. His bowel and bladder habits are normal.

History of past illness—Nothing significant.

Family history—There is no family history of bleeding disorder (like hemophilia).

Personal history—He is a day labor working in village (note that occupations like worker in radiotherapy, radiology, dye industry, naphthalene, etc. is very important, mention if any).

Socioeconomic history—mention according to the statement of the patient.

Drug & Treatment history— He took some antibiotics for his recurrent sore throat. He received 4 units of blood transfusions in the last 2 months.

GENERAL EXAMINATION

- The patient is ill looking and pale, severely anemic
- No jaundice, clubbing, cyanosis, koilonychia, leukonychia or edema
- No lymphadenopathy or thyromegaly
- No sternal tenderness
- There are multiple purpuric spots, bruises and ecchymoses on the arms, legs and trunks. These are of variable size and shape, painless and does not blanch on pressure
- Pulse: 110/min
- BP: 100/65 mm Hg.

SYSTEMIC EXAMINATION

Gastrointestinal System

- Lips, mouth, oral cavity—marked pallor
- Tongue—pale, smooth, shiny in appearance.

Abdomen

Inspection:

- Multiple purpuric spots and bruises are present. No organomegaly.

Palpation:

- Liver—not enlarged
- Spleen—not enlarged
- Kidneys—not ballotable.

Percussion:

- No evidence of ascites (no fluid thrill, no shifting dullness).

Auscultation:

- No abnormality detected.

Cardiovascular System

- There is a systolic murmur in the apical area (likely to be flow murmur).

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 31 years old, a day laborer, normotensive, nondiabetic, nonsmoker, hailing from …, presented with severe weakness, palpitation and dizziness for … months, which is more marked even on mild activity. He also complains of occasional spontaneous bleeding from gum and nose for the same duration. For the last … months, he also noticed multiple bleeding spots in skin of different parts of body including hands, legs, abdomen, etc. There is also history of occasional fever, which is of low grade and associated with sore throat. He does not give any history of taking drugs, or exposure to radiation or chemicals. His bowel and bladder habits are normal. There is no family history of bleeding disorder like hemophilia. He took some antibiotics for his recurrent sore throat. He received 4 units of blood transfusions in the last 2 months. There is no family history of similar illness.

On examination—general examination (mention as above).

Systemic examination (mention as above).

With this history and findings like severe anemia, multiple purpuric spots and ecchymoses, I have some **differential diagnoses**:

- Aplastic anemia
- Acute leukemia
- Idiopathic thrombocytopenic purpura.

Q. What **single investigation** do you suggest in this patient?

A. Full blood count with platelet and PBF. It shows the following:

- In aplasia—there will be pancytopenia.
- In acute leukemia—there may be leukocytosis with immature WBC (blast cells).
- In ITP—there will be thrombocytopenia.

Q. What **next** investigation do you suggest?

A. Bone marrow investigation. It shows following:

- In aplasia—either dry tap or markedly acellular or hypocellular marrow
- In acute leukemia—hypercellular with increased immature cells of WBC series
- ITP—increased megakaryocytes.

Q. What **investigations** do you suggest for aplastic anemia?

A. As follows:

- Full blood count—Pancytopenia (anemia, leukopenia and thrombocytopenia). Anemia is usually normocytic normochromic.
- Bone marrow study (aspiration and trephine biopsy)—either dry tap or markedly acellular or hypocellular marrow.

Q. What is **severe** aplastic anemia?

A. It is defined as:

- Neutrophil count < 500/cmm.
- Platelet < 20,000 / cmm.
- Reticulocyte < 1%.
- Bone marrow cellularity < 20%.

Q. What are the **causes** of aplastic anemia?

A. It may be primary or acquired.

1. Primary—may be congenital (Fanconi's anemia, Diamond-Blackfan anemia), may be idiopathic acquired (probably autoimmune).
2. Acquired or secondary. Causes are:
   - Drugs—cytotoxic drugs, antibiotics (chloramphenicol, sulfonamide), antithyroid drugs (carbimazole), carbamazepine, penicillamine.
   - Radiotherapy.
   - Chemicals—benzene, lindane, DDT.
   - Infection—viral hepatitis, EBV infection, HIV, parvoviral infection.
   - Miscellaneous—paroxysmal nocturnal hemoglubinurea, secondary deposits in bone marrow, lymphoma, multiple myeloma.

Q. What are the **presentations** of aplastic anemia?

A. As follows:

- Features of anemia—weakness, palpitation, dizziness or vertigo
- Bleeding manifestations
- Occasionally infection.

Note Remember the following:

On examination—Only physical findings are anemia and bleeding spots. No lymphadenopathy, hepatomegaly, splenomegaly or bony tenderness (which may be present in secondary deposit or secondary causes of aplastic anemia).

Q. What is the **treatment** of aplastic anemia?

A. As follows:

1. Removal of causative agent, if any.
2. Supportive therapy—blood transfusion, control of infection.
3. Allogenic bone marrow transplantation (with HLA matched siblings)—if the patient is below 30 years with severe idiopathic aplastic anemia. 75 to 90% long-term cure.

4. In older patient or if HLA matched donor is not available—immunosuppressive therapy with cyclosporine and anti thymocyte globulin (ATG) should be given. 5 years survival is about 75%. Tacrolimus may be used instead of cyclosporine. Steroids are used for serum sickness, due to ATG.
5. Other treatment—indicated if bone marrow transplantation is not possible:
   - Androgens (e.g. oxymetholone) are sometimes useful in patients not responding to immunosuppression and in patients with moderately severe aplastic anemia.
   - Prednisolone helpful in some cases specially congenital pure red cell aplasia (Diamond-Blackfan disease), also in adult with pure red cell aplasia. If associated with thymoma in adult pure red cell aplasia (30%), thymectomy may be done.

Q. What are the causes of **pancytopenia**?

A. As follows:
- Aplastic anemia
- Hypersplenism
- Megaloblastic anemia
- Banti's disease
- Aleukemic leukemia
- Some myelodysplastic syndrome
- Paroxysmal nocturnal hemoglobinuria
- Others—SLE, myelofibrosis, hairy cell leukemia, disseminated tuberculosis, leishmaniasis, brucellosis, HIV, multiple myeloma, lymphoma.

HEREDITARY HEMOLYTIC ANEMIA

CHIEF COMPLAINTS

- Severe weakness, palpitation, dizziness for … months
- Yellow discoloration of the eyes and high colored urine for … months
- Feeling of a mass in the left upper abdomen for … months
- Darkening of the skin color for … months.

HISTORY

History present illness: The patient states that he was alright … months back. Since then, he has been suffering from weakness, which is increasing day by day and now feels extremely tired even after mild activity. The patient also complains of palpitation with mild activity and dizziness on standing for … months. The patient also noticed yellow coloration of the eyes and high colored urine, which is not associated with pruritus or pale colored stool. There is no history of contact with a jaundice patient or any injection or infusion, but there is history of several units of blood transfusion every 4 to 6 months. The patient also states that he feels a mass in the left upper abdomen, which is progressively increasing in size and is not associated with pain but heaviness only. His skin is becoming dark, which is not associated joint pain, leg ulcer, hematemesis or melena.

History of past illness

Family history: One of his sisters is suffering from similar illness.

Personal history

Socioeconomic history: Mention according to the patient's statement

Drug and treatment history: He was hospitalized two times and received several units of blood transfusion during the last few years.

GENERAL EXAMINATION

- The patient is short for his age, pale and ill looking
- Face is mongoloid with prominent malar bones and supra orbital ridges, also frontal and parietal bossing
- Severely anemic, mildly icteric
- There is generalized pigmentation of skin
- No clubbing, cyanosis, koilonychia, leukonychia or edema
- No lymphadenopathy or thyromegaly
- No sternal tenderness
- Pulse: 120/min
- BP: 95/65 mm Hg.

SYSTEMIC EXAMINATION

Gastrointestinal System

- Lips, mouth, oral cavity—marked pallor, also looks yellow.
- Tongue—pale, smooth, shiny in appearance, also yellowish.

Abdomen

Inspection:

- Left upper abdomen is distended.

Palpation:

- Liver—enlarged, 10 cm from the right costal margin in the midclavicular line, surface is smooth, margin is sharp, nontender and firm in consistency, no hepatic bruit or rub.
- Spleen—hugely enlarged, 15 cm from the left costal margin in the anterior axillary line towards the right iliac fossa.
- Kidneys—not ballotable.

Percussion:

- No evidence of ascites (no fluid thrill, no shifting dullness).

Auscultation:

- No abnormality detected.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 18 years old, student, normotensive, nondiabetic, nonsmoker, hailing from …, presented with weakness for … months, which is increasing day by day and now he feels extremely tired even after mild activity. The patient also complains of palpitation with mild activity and dizziness on standing for … months. The patient also noticed yellow coloration of the eyes and high colored urine, which is not associated with pruritus or pale colored stool. There is no history of contact with a jaundice patient or any injection or infusion, but there is history of several units of blood transfusion every 4 to 6 months. The patient also states that he feels a mass in the left upper abdomen, which is progressively increasing in size and is not associated with pain but heaviness only. For his skin is becoming dark, which is not associated joint pain, leg ulcer, hematemesis or melena. One of his sisters is suffering from similar illness. He was hospitalized two times and received several units of blood transfusion during the last few years.

On examination—general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is hereditary hemolytic anemia, which may be:

- β-thalassemia major
- Hb E disease
- β-thalassemia Hb E disease (double heterozygous)
- Hereditary spherocytosis.

Q. What are your **differential diagnoses?**

A. As follows:

- Chronic liver disease with portal hypertension
- Lymphoma
- Kala-azar.

Q. Mention one **single investigation** which is helpful for your diagnosis.

A. Full blood count with PBF (which shows microcytic hypochromic blood picture).

Q. What **another hematological investigation** is helpful for your diagnosis?

A. Reticulocyte count (by supravital stain)—increased.

Q. How will you **confirm** your diagnosis?

A. Hemoglobin electrophoresis.

Q. What are the **findings** in Hb-electrophoresis in β-thalassemia?

A. As follows:

- β-Thalassemia major—Hb-F is high and Hb-A is less or absent.
- β-Thalassemia minor—Hb-A_2 is high.

Q. What are the causes of the **microcytic hypochromic blood picture**?

A. Causes are:

- Iron deficiency anemia—(commonest cause)
- β-thalassemia (major and minor)
- Sideroblastic anemia
- Anemia of chronic disease.

Q. What are the **diagnostic criteria** of hemolytic anemia?

A. **Triad** of:

- Anemia
- Jaundice
- Splenomagaly.

Q. What **investigations** should be done for hereditary hemolytic anemia?

A. As follows:

1. Hb%, TC, DC, ESR, PBF (microcytic hypochromic blood picture).
2. Reticulocyte count (by supravital stain)—increased.
3. Hemoglobin electrophoresis.
4. Others:
   - Serum bilirubin (also urinary urobilinogen will be high)
   - X-ray skull (also other skeletal survey)
   - X-ray chest
   - Serum iron profile (iron, TIBC, ferritin, % saturation).

RELATED QUESTIONS AND ANSWERS

Q. What is **thalassemia?**

A. It is an inherited disorder in which there is impairment of hemoglobin production due to partial or complete failure to synthesize the specific type of globin chain. It is of 2 types:

1. β-Thalassemia: In this case, there is an inadequate production of β-chain, causing less production of HbA. It is of 2 types.
   - β-Thalassemia major—HbA is less, HbF is more
   - β-Thalassemia minor—HbA_2 is increased.
2. α-Thalassemia: In this case, there is an inadequate production of α-chain, therefore less HbA, HbF and HbA_2, as all of them contain α-chain.

3. Thalassemia intermedia, characterized by the combination of homozygous mild β-thalassemia plus α-thalassemia. It is usually less severe and does not require blood transfusion, as anemia is mild to moderate.

Q. What are the **radiological findings** in skull in β-thalassemia major?

A. As follows:
- Widening of diploic space
- Thinning of outer table
- Thickening and coarsening of trabeculae giving rise to hair-on-end appearance.
- Sometimes, skull is enlarged with widening of suture.

Q. How to **treat** β-thalassemia major?

A. As follows:
1. Correction of anemia—Blood transfusion to keep Hb% above 10 g%, every 4 months (lifespan of RBC is 4 months).
2. Folic acid 5 mg daily, to be continued.
3. Iron containing drugs and diet are avoided (iron can only be given, if there is deficiency).
4. Repeated blood transfusion may cause hemosiderosis, which can be prevented by chelating agent, desferrioxamine subcutaneously with infusion pump overnight. Ascorbic acid 200 mg daily may be added (it causes urinary excretion of iron). Oral iron chelating agents such as deferiprone or deferasirox may be used.
5. Other treatment—
   - Injection erythropoietin. It stimulates the bone marrow, increases normal hemoglobin to some extent.
   - Hydroxyurea 1 to 2 g daily may be helpful (it prevents ineffective erythropoiesis).
6. Specific therapy—Allogenic bone marrow transplantation from HLA compatible sibling. Also, gene therapy.
7. Splenectomy.
8. Genetic counseling should be offered. It is necessary for prenatal diagnosis which is available.

Indication of splenectomy

- Huge splenomegaly with pressure symptoms
- Hypersplenism—as suggested by repeated transfusion in a short interval. Full blood count shows pancytopenia.

Note Remember the following:

In patient with mild thalassemia (β-thalassemia minor or α-thalassemia trait) requires no treatment. Only avoid iron therapy.

Q. What are the **complications** of repeated blood transfusion?

A. As follows:
- Repeated transfusion may cause hemosiderosis (usually when more than 30 to 50 L of blood is transfused).
- Infections such as hepatitis B, C, D and HIV.

Q. How hemosiderosis can be **prevented**?

A. Hemosiderosis can be prevented by using chelating agent desferrioxamine (1.5 to 2 g with each unit of blood). It is usually given subcutaneously in the anterior abdominal wall with infusion pump for 12 hours. It may also be given with infusion drip (normal saline or aqua). Oral chelating agent

such as deferiprone, 75 mg/kg in 2 to 4 divided doses, is also available. Other oral chelating agent include deferasirox. Vitamin C 200 mg daily orally also helps in iron excretion.

Q. If the patient develops severe **abdominal pain**, what is the likely cause?

A. Cholelithiasis (usually pigment stone, due to hemolysis). There may also be splenic infarction. Acute pancreatitis may also occur.

Q. When **anemia** develops in a patient with thalassemia major?

A. Anemia develops at the age of 4 to 6 months. In a normal person, HbF disappears 4 to 6 months after birth. In adults, HbF is < 1%. But in thalassemia major, HbF is increased.

Q. How can it be **diagnosed before birth**?

A. Prenatal diagnosis is possible by obtaining chorionic villus material for DNA. It should be done if both parents suffer from β-thalassemia minor. If β-thalassemia is found in the fetus, then termination of pregnancy is indicated.

Q. What are the presentations of **thalassemia minor**? What is the **differential diagnosis**?

A. As follows:

- May be asymptomatic.
- There may be features of anemia (microcytic hypochromic).
- Incidentally during blood count (microcytic hypochromic blood picture).
- Hemoglobin electrophoresis shows high A_2.

Thalassemia minor confuses with iron deficiency anemia. However, anemia is more marked in iron deficiency and relatively less in thalassemia minor. Also, in iron deficiency, there is low iron, low ferritin and high total iron-binding capacity.

Brief discussion on α-thalassemia

This is characterized by reduced or absent α-globin chain synthesis. It is common in southeast Asia and China. Normally, adults have 4 α-globin chain genes.

- When one α-gene is absent the patient is hematologically normal (silent carrier).
- When two α-genes are absent it is said to have α-thalassemia trait. The patient is clinically normal, life expectancy is normal but there is mild microcytic hypochromic anemia.
- When three alpha genes are absent the patient has hemoglobin H (β-chain tetramer) disease. There is chronic hemolytic anemia with variable severity. Physical examination shows severe anemia with splenomegaly.
- If all four α-globin chains are absent affected fetus is stillborn due to hydrops fetalis.

IDIOPATHIC THROMBOCYTOPENIC PURPURA

CHIEF COMPLAINTS

- Multiple spots on the skin all over the body for … days
- Anorexia, malaise and weakness for … days.

HISTORY

History present illness: The patient states that she was alright … days back. Since then, she noticed multiple red spots which first appeared in the arms and legs, subsequently involving the other parts of the body. These were initially red, which became bluish and black after few days. There are also some larger bleeding areas in different parts of the body. She also complains of loss of appetite, malaise and weakness for the same duration. There is no history of fever, sore throat, polyarthritis, skin rash, abdominal pain or mouth ulcer. She did not take any drug prior to the illness. Her bowel and bladder habits are normal.

History of past illness: There is no history of bleeding disorder.

Family history: There is no history of any bleeding disorder in the family.

Personal history: Mention as per statement of the patient.

Socioeconomic history: Mention as per statement of the patient.

Drug and Treatment history: There is no history of intake of any drug related to his symptoms.

GENERAL EXAMINATION

- The patient is mildly anemic
- There are multiple purpuric spots on different parts of the body of varying sizes, which are painless, do not blanch on pressure
- No jaundice, cyanosis, clubbing, koilonychia, leukonychia or edema
- No lymphadenopathy or thyromegaly
- No sternal tenderness
- Pulse: 120/min
- BP: 100/55 mm Hg.

SYSTEMIC EXAMINATION

Gastrointestinal System

- Lips and oral cavity—There are some bleeding spots over the palate
- Tongue—Normal.

Abdomen

Inspection:

- No abnormality.

Palpation:

- Liver—not palpable
- Spleen—not enlarged
- Kidneys—not ballotable.

Percussion:

- No evidence of ascites (no fluid thrill, no shifting dullness).

Auscultation:

- No abnormality detected.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Ms …, 19 years old, student, normotensive, nondiabetic, nonsmoker, hailing from …, presented with multiple red spots for … days. These first appeared in the arms and legs, subsequently involving the other parts of the body. These were initially red, which became bluish and black after few days. There are also some larger bleeding areas in different parts of the body. She also complains of loss of appetite, malaise and weakness for the same duration. There is no history of fever, sore throat, polyarthritis, skin rash, abdominal pain or mouth ulcer. She did not take any drug prior to the illness. Her bowel and bladder habits are normal. There is no history of bleeding disorder. There is no history of any bleeding disorder in the family.

On general examination (mention as above).

On systemic examination (mention as above).

With this history and physical findings, I have some differential diagnoses:

- Idiopathic thrombocytopenic purpura
- Acute leukemia
- Aplastic anemia.

Q. What is the **more likely** diagnosis? **Why**?

A. Idiopathic thrombocytopenic purpura. Because, there are multiple purpuric spots, no history of taking any drugs or secondary causes.

Q. Why not acute leukemia?

A. It may be acute leukemia, but less likely because there is no fever, lymphadenopathy, hepatosplenomegaly and bony tenderness.

Q. Why not aplastic anemia?

A. There is no history of any secondary cause like drugs, radiation, etc. Usually there is severe anemia, bleeding is usually in the form of ecchymoses or bruises. But it should be excluded.

Q. What **investigations** do you suggest in ITP?

A. As follows:

- Full blood count—there is thrombocytopenia
- Bone marrow—increased immature megakaryocytes (may be normal sometimes)
- Bleeding time is prolonged, but clotting time is normal
- Antiplatelet antibody is present in 60 to 70% cases
- Anticardiolipin antibody is positive in 30% cases.

Q. What are the causes of **thrombocytopenia?**

A. As follows:

1. Less production:
   - Aplastic anemia (primary or idiopathic)

- Bone marrow infiltration—secondary deposit, multiple myeloma, leukemia, lymphoma
- Marrow suppression by radiotherapy or cytotoxic drugs
- Megaloblastic anemia
- Myelofibrosis
- HIV infection.

2. Excessive destruction or consumption:
   - Immune—ITP, drug induced (heparin, thiazide, penicillin, quinine), SLE, CLL, virus, post-transfusional.
   - Nonimmune—DIC, thrombotic thrombocytopenic purpura, hemolytic uremic syndrome, hypersplenism, massive blood transfusion (dilutional).

RELATED QUESTIONS AND ANSWERS

Q. What is **idiopathic thrombocytopenic purpura?**

A. It is a type of thrombocytopenic purpura due to auto-antibody against platelet (IgG type). The auto-antibody forms against platelet membrane glycoprotein IIb and IIIa, which causes premature removal of platelet by monocytemacrophage system.

Q. What are the **presentations** of ITP?

A. As follows:

- In child—Usually acute presentation, previous history of viral infection followed by bleeding or purpura, easy bruising, etc. Chronic ITP is rare in children.
- In adult—common in female, usually insidious onset without preceding viral infection. Presents with purpura, easy bruising, epistaxis or menorrhagia. Features of SLE may be present at presentation or may develop after long time. It may be associated with other autoimmune diseases like thyroid disorder and autoimmune hemolytic anemia, chronic lymphocytic leukemia, solid tumor, HIV infection.

On physical examination—apart from bleeding points, no other physical findings. Splenomegaly is very rare (in 10%).

Note Remember the following points:

- Spontaneous bleeding occurs when the platelet is < 20,000/cmm
- At higher count, there may be bruising, epistaxis and menorrhagia
- If platelet count is > 50,000/cmm, there may not be any features, diagnosed on routine test.

Q. What are the **diseases to be excluded**, if ITP is suspected?

A. As follows:

1. Commonly SLE is to be excluded. In 10% cases, thrombocytopenia may be the initial manifestation of SLE for many years.
2. Primary antiphospholipid syndrome may present with thrombocytopenia.
3. Other primary hemorrhagic disorders should be excluded.
4. For this purpose, following investigations should be done—
   - ANA, anti ds-DNA, antiphospholipid antibody and anticardiolipin antibody
   - Bone marrow

Note Remember these points:

- In 10% case, ITP may be associated with autoimmune hemolytic anemia called **Evan's syndrome**.
- Patient > 65 years old should have bone marrow examination to look for accompanying B-cell malignancy.
- HIV testing should be considered, if there is strong suspicion.

Q. How to **treat** ITP?

A. Treatment is as follows:

i. In child: Usually self limiting, does not require treatment in most cases. If there is no improvement—

- Prednisolone (2mg/kg) should be given if moderate to severe thrombocytopenia (<10,000) and bruising, epistaxis or other bleeding.
- If still persistent bleeding, IV immunoglobulin (IgG) should be given.
- In some case, platelet transfusion may be required, when there is persistent bleeding (epistaxis, GIT bleeding, retinal hemorrhage, intracranial bleeding).

ii. In adult: Persistent thrombocytopenia is common. Most patients with platelet count > 30×10^9/L are stable and do not require treatment unless they are about to undergo a surgery.

1. First line therapy:
   - If spontaneous bleeding, prednisolone 1mg/kg, to be given for 4 to 6 weeks, then tapered. 66% will respond, but relapse is common when the steroid dose is reduced or stopped. 10 to 20% usually have long term remission. If relapse, steroid should be started again.
   - IV immunoglobulin may be given, mainly if there is severe hemostatic failure or slow response to steroid alone or surgery is required. Dose of immunoglobulin is 1gm/kg for 3 to 5 days. Its effect is temporary, persists for 3 to 4 weeks and it is quite expensive. Steroid may be added with immunoglobulin.
2. Second line therapy:
   - If there is frequent relapse (usually 2 relapses), in primary refractory disease or require high dose of steroid to maintain safe platelet level, splenectomy should be done. There is complete remission in 70% cases and improvement in 20 to 25% cases. 5 to 10% require further medical therapy.
3. Third line therapy:
   - If there is failure after splenectomy, other therapy should be considered—corticosteroid, IV immunoglobulin, anti-D infusion, danazol, immunosuppressive therapy (azathioprine, cyclophosphamide, dapsone, vincristine, vinblastine, ciclosporin), mycophenolate mofetil. Also monoclonal antibody like rituximab as well as recombinant thrombopoietin may be given.
4. Platelet transfusion is not usually used. However, it is used only if persistent or potentially life threatening bleeding or where emergency splenectomy is done.

Note Remember the following points

- In nonresponder after splenectomy, think of presence of accessory spleen (confirm by radionuclide scan).
- After splenectomy, there is more chance of infection by *Pneumococcus*, *Meningococcus* and *H. influnzae* (vaccination against these is essential).

Q. What are the **differences** between ITP in children and adults (or acute and chronic ITP)?

A. As follows:

Features	Child (acute)	Adult (chronic)
1. Age	Usually 2 to 6 years	20 to 30 years
2. Sex	Any	Common in female
3. Onset	Acute	Chronic
4. Previous infection	Common	Unusual
5. Platelet count	<20,000/cmm	>20,000/cmm
6. Spontaneous remission	Common	Less <20%
7. Duration	2 to 4 weeks	Chronic, months to years

BRIEF DISCUSSION ON PURPURA

Q. What is **purpura**? What are the **types**?

A. It is the spontaneous bleeding or extravasation of blood from the capillary in the skin and mucous membrane that does not blanch on pressure, and there is progressive color change.

There are **two types** of purpura:

- Small and discrete of pin head size, called petechiae.
- Large and ill defined, called ecchymosis.

Q. What are the **causes of purpura?**

A. As follows:

- Thrombocytopenic
- Vascular
- Coagulation defect.

Thrombocytopenic purpura:

1. Primary or ITP.
2. Secondary:
   - Aplastic anemia (due to any cause)
   - Leukemia
   - Secondary deposit in bone marrow
   - SLE
   - Others—DIC, CLD and TTP (thrombotic thrombocytopenic purpura), massive blood transfusion.

Vascular purpura:

1. Congenital (hereditary hemorrhagic telangiectasia, Ehlers–Danlos syndrome).
2. Acquired:
   - Senility (in elderly)
   - Henoch-Schönlein purpura (in children, and rarely in elderly)
   - Drug-induced (NSAIDs, thiazide, steroid, sulfonamide, penicillin and thiouracil)
   - Infections—SBE, typhoid, meningococcal infection, septicemia and viral infections (infectious mononucleosis, measles, chicken pox, dengue hemorrhagic fever)

- Scurvy
- Metabolic disorder (CRF and Cushing's syndrome)
- Collagen disease (RA and SLE)
- Paraproteinemia (purpura is due to vasculitis or thrombocytopenia or platelet functional abnormality)
- Amyloidosis (periorbital).

Coagulation abnormality:

1. Hemophilia.
2. Christmas disease.
3. Anticoagulant therapy.

Q. What are the common **causes of** purpura according to the age?

A. As follows:

1. In the **elderly**, the causes are:
   - Senile purpura (usually on extensor surface of forearm and leg).
   - Drug induced purpura (distribution is like senile purpura), and the usual drugs are steroids, NSAIDs and anticoagulant.
   - Leukemia.
   - Aplastic anemia.
   - Scurvy.
   - Paraproteinemia.
2. In **young** or **child**, the causes are:
   - ITP
   - Henoch-Schönlein purpura (involving buttock and legs)
   - Drug induced
   - Acute leukemia
   - Infections—viral (dengue) or meningococcal septicemia.

Note In any age, mention the causes as follows (if present):

- If Cushingoid facies, due to steroid
- If patient looks toxic, due to septicemia
- If evidence of RA, SLE, due to disease itself or due to NSAIDs or steroids.

Q. In a child, there is purpura in the leg. What **else** do you want to see?

A. Purpura in buttock, history of arthritis, abdominal pain, bloody diarrhea, hematuria (all features are suggestive of Henoch-Schönlein purpura).

Q. What should you **examine** in a patient with purpura?

A. As follows:

1. Whether they blanch on pressure or not (purpura does not blanch).
2. Whether they are palpable and painful or not (palpable painful purpura is of vascular origin and nonpalpable purpura indicates thrombocytopenia).
3. Color change (progressive color change in purpura from red to dark pigmented).
4. Distribution of purpura:
   - Buttock, ankle (Henoch-Schönlein purpura).
   - Extensor surface of fore arm, dorsum of hand, leg (senile purpura and drugs).
   - Generalized purpura.

Q. What are the **differential diagnoses** of purpura?

A. As follows:

- Drug rash
- Spider angioma or telangiectasia (blanch on pressure, but purpura does not)
- Erythema nodosum (painful and nodular)
- Mosquito bite (usually blanch on pressure, but sometimes may not blanch, if there is extravasation of blood)
- Campbell de Morgan spots (common in elderly)—these are small, nodular, reddish lesions that do not blanch on pressure, occur on trunk and upper abdomen and resolve spontaneously. These are benign angioma, common in middle aged and elderly. Malignant change occurs rarely (suggested by itching, rapid increase in size and increased pigmentation).

Q. What **investigations** should be done in purpura?

A. As follows:

1. Hb%, TC, DC, ESR, platelet and PBF.
2. If pancytopenia or thrombocytopenia, perform bone marrow study (dry tap in aplastic anemia, increased megakaryocyte in ITP).
3. Other investigations (according to suspicion of causes):
   - Coagulation screen (BT, CT, PT, APTT and FDP) for hemophilia and Christmas disease and other coagulation factors, screening for DIC.
   - Blood culture (if septicemia).
   - ANA, anti-double-strand DNA (for SLE).
   - Anti-phospholipid antibody.
   - Liver function tests (in CLD).
   - Renal function tests (in CRF).

Q. What is **Hess's test**?

A. It is a bedside test, also called tourniquet test. In this test, a sphygmomanometer cuff over the upper arm is inflated in between systolic and diastolic pressure, wait for 5 minutes. Then deflate the cuff, wait for another 5 minutes. Look for petechiae in cubital fossa and near the wrist. Normally, there may be <5. If >10, it is an indication of thrombocytopenia. If >20, then abnormal. If platelet is <60,000, it is usually positive.

Causes: Thrombocytopenia or platelet functional abnormality or increase in capillary fragility (This test is frequently done to diagnose dengue hemorrhagic fever).

Q. What are the **causes** of platelet functional abnormality?

A. Platelet functional abnormality (thrombasthenia) occur in:

- Chronic renal failure
- Chronic liver disease
- Paraproteinemia
- Myeloproliferative diseases
- Drugs—NSAIDs (aspirin, indomethacin and ibuprofen).

Q. How to **differentiate** in bleeding or purpura whether due to bleeding abnormality or coagulation abnormality?

A. As follows:

Coagulation abnormality	Bleeding abnormality
1. Family history usually present	Family history may or may not be present
2. There is history of prolonged bleeding	No history of prolonged bleeding
3. Usually there is bleeding into the joint or muscle, purpura is less common or rare	Bleeding into the skin and mucous membrane, purpura is more common
4. Clotting time is prolonged, but bleeding time and platelet count are normal	Clotting time is normal, but bleeding time is prolonged and platelet count is low
5. Particular coagulation factor is low or absent, e.g. in hemophilia, factor VIII is absent or low	Coagulation factor is normal, and it is due to either low or defect in platelet function or vascular defect

HENOCH-SCHONLEIN PURPURA

CHIEF COMPLAINTS

- Multiple skin rashes over lower limbs for … days
- Pain in abdomen for … days
- Joint pain for … days
- Low grade fever, anorexia, weakness for … days.

HISTORY

History present illness: The patient states that he was alright … days back. Since then, he noticed multiple red spots involving both lower limbs. These were initially red, which became bluish and black after few days. The lesions are painful but not itching. He also complains of occasional colicky abdominal pain for … days, which is not related to any food and there is no radiation. It is associated with loose motion, mixed with fresh blood. For the last … days, he has been suffering from pain and swelling of both knee joints, which is very severe and aggravates on movement. The patient also complains of low grade continued fever, lost his appetite and become very weak for the same duration. There is no history of mouth ulcer, sore throat, photosensitivity, etc. His bladder habit is normal.

History of past illness

Family history

Personal history

Socioeconomic history

Drug and treatment history: Mention according to the patient's statement.

GENERAL EXAMINATION

- The patient looks ill, mildly anemic.
- There are multiple purpuric spots on both lower limbs, including buttocks. These are of variable size and shape, palpable, painful and don't blanch on pressure.
- No jaundice, cyanosis, clubbing, koilonychia, leukonychia or edema.
- No lymphadenopathy or thyromegaly.
- No sternal tenderness.
- Pulse: 120/min.
- BP: 100/55 mm Hg.

SYSTEMIC EXAMINATION

Gastrointestinal System

- Lips and oral cavity—There are some bleeding spots in palate
- Tongue—Normal.

Abdomen

Inspection:

- No abnormality.

Palpation:

- Diffusely tender.
- Liver—not palpable.
- Spleen—not enlarged.
- Kidneys—not ballotable.

Percussion:

- No evidence of ascites (no fluid thrill, no shifting dullness).

Auscultation:

- No abnormality detected.

Locomotor System

- Both knees and ankle joints are swollen and painful
- Movement is restricted.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 14 years old, student, normotensive, nondiabetic, hailing from …, presented with multiple red spots involving both lower limbs for … days. These were initially red, which became bluish and black after few days. The lesions are painful but not itching. He also complains of occasional colicky abdominal pain for … days, which is not related to any food and there is no radiation. It is associated with loose motion, mixed with fresh blood. For the last … days, he has been suffering from pain and swelling of both knee joints, which is very severe and aggravates on movement. The patient also complains of low grade continued fever, lost his appetite and become very weak for the same duration. There is no history of mouth ulcer, sore throat, photosensitivity, etc. His bladder habit is normal. There is no family history of similar illness. He was treated with ranitidin, antispasmodics and vitamins.

On general examination (mention as above).

On systemic examination (mention as above).

My diagnosis is Henoch-Schonlein purpura.

Q. Why this is Henoch-Schönlein purpura?

A. There is history of arthritis, abdominal pain and bloody diarrhea. On examination, there are multiple purpuric skin rash involving lower limbs and buttocks. All are suggestive of Henoch-Schonlein purpura.

Q. What are your differential diagnoses?

A. As follows:

- Drug rash
- ITP
- SLE
- Septicemia
- Thrombotic thrombocytopenic purpura (TTP).

Q. Why not this is a case of ITP?

A. In ITP, there may be previous history of viral infection followed by purpura only. There is no arthritis or abdominal pain in ITP.

Q. What **investigations** should be done in HSP?

A. As follows:

- Full blood count and platelet (nonthrombocytopenic purpura).
- Urine (proteinuria and hematuria).
- Serum IgA is high in 50% cases (IgA-containing immune complex is also high).
- Skin biopsy from normal and involved skin (it will show leukocytoclastic vasculitis with deposition of IgA and complement C_3 in blood vessels).
- Kidney biopsy.

Q. Suggest one **investigation** that is helpful for prognosis.

A. Renal biopsy—it shows focal and segmental proliferative glomerulonephritis, sometimes with mesangial hypercellularity. In more severe cases, epithelial crescents may be present, developing rapidly progressing glomerulonephritis and renal failure. This is less in children. There is IgA deposition within and around blood vessels, glomerular mesangium (it may be confused with IgA nephropathy).

Prognosis of HSP: It is related to the severity of renal involvement.

RELATED QUESTIONS AND ANSWERS

Q. What is **Henoch–Schönlein purpura** (anaphylactoid purpura)?

A. It is a small vessel vasculitis characterized by purpura or skin rash, joint pain (in big joints), abdominal pain and glomerulonephritis. It is a type III reaction precipitated by an upper respiratory tract infection (usually viral) that occurrs 1 to 3 weeks ago.

It is due to circulating IgA - containing immune complex. Occurs 1 to 3 weeks after upper respiratory infection (usually viral). Other factors responsible include food, drugs or vaccination.

Q. What are the **clinical features** of HSP?

A. HSP is more common in boy, 5 to 15 years of age, but may occur in any age. The common features are:

- Skin lesion—Purpura is common in legs and buttock, face and trunk are spared. May resolves in 2 to 4 weeks and fresh crops may appear. Angioedema occurs in 50% cases.
- Polyarthritis occurs in 70%, commonly involves knee and ankle, may be fleeting type.
- Abdominal pain, colicky in nature, associated with nausea, vomiting, bloody diarrhea, intussusception and perforation. There is vasculitis, bowel is edematous and inflamed, causing bleeding and obstruction. This may be confused with acute surgical condition.
- Renal disease occurs in 30 to 70% cases, present with hematuria and proteinuria. It is usually mild. There may be nephrotic syndrome and rarely renal failure.

Q. How will you **treat** a patient with HSP?

A. As follows:

- It is usually self-limiting, spontaneous cure in majority of cases.
- Steroid is indicated, if there is GIT and joint symptoms. However, steroid does not affect the course and progression of disease. Abdominal pain may be improved in 24 hours following the use of steroid.
- In renal involvement, pulse IV steroid and cytotoxic drugs should be given.
- Recurrence may occur. If so, dapsone may help, specially in cutaneous recurrence.

Q. What is the **prognosis**?

A. Good in children, relatively bad in adults. Adverse factors in adults include hypertension, abnormal renal function and proteinuria > 1.5 g/day. But only 1% of patients develop end stage renal failure.

Features of Henoch-Schönlein purpura in adults:

- Skin involvement is common (70%), more than children
- Renal involvement is more common than children
- Gut and joint involvement occur in 20% cases, less than children
- Myocardial involvement may occur rarely
- Prognosis is worse in adults than children.

Note Remember the following:

In children, gastrointestinal vasculitis is more common, renal and skin involvement are less common. Prognosis is better.

HEMOPHILIA

CHIEF COMPLAINTS

- Persistent bleeding after injury since childhood
- Occasional swelling of right knee since childhood.

HISTORY

History present illness: According to the mother of the patient, she noticed that her son has been suffering from persistent and prolong bleeding from any injury since his childhood. There is also history of prolonged and profuse bleeding after circumcision and one tooth extraction. The patient's mother also states that following trauma or fall, there are multiple bruises in different parts of the body. Occasionally, his right knee is swollen after trauma or physical exertion and become painful. There is no history of bleeding from nose, gum or passage of black stool.

History of past illness: Mention according to the statement of the patient.

Family history: One of his maternal uncle also has similar history of prolong bleeding after any injury.

Personal history: Mention according to the statement of the patient.

Socioeconomic history: Mention according to the statement of the patient.

Drug and treatment history: For this illness, the patient received multiple blood transfusions over last few years.

GENERAL EXAMINATION

- The patient is mildly anemic
- There are multiple bruises over the trunk and legs
- The right knee is swollen and tender
- No jaundice, cyanosis, clubbing, koilonychia, leukonychia or edema
- No lymphadenopathy or thyromegaly
- No sternal tenderness
- Pulse: 100/min.
- BP: 100/60 mm Hg.

SYSTEMIC EXAMINATION

Gastrointestinal System

- Lips, tongue and oral cavity—normal.

Abdomen

Inspection:

- No abnormality.

Palpation:

- Liver—not palpable
- Spleen—not enlarged
- Kidneys—not ballotable.

Percussion:

- No evidence of ascites (no fluid thrill, no shifting dullness).

Auscultation:

- No abnormality detected.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr. …, 14 years old boy, student, hailing from …, presented with persistent and prolong bleeding from any injury since his childhood. There is also history of prolonged and profuse bleeding after circumcision and one tooth extraction. The patient's mother also states that following trauma or fall, there are multiple bruises in different parts of the body. Occasionally, his right knee is swollen after trauma or physical exertion and become painful. There is no history of bleeding from nose, gum or passage of black stool. One of his maternal uncles also has similar history of prolong bleeding after any injury. For this illness, the patient received multiple blood transfusions over last few years.

On examination, general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is hemophilia.

Q. What are your differential diagnoses?

A. As follows:

- Christmas disease
- ITP.

Q. Why not this is ITP?

A. In ITP, there should be no persistent bleeding, only purpura. No joint pain also.

Q. What investigations are done in hemophilia?

A. As follows:

- FBC—usually normal
- Bleeding time, prothrombin time, platelet count, von Willebrand factor (vWF) and fibrinogen level—all normal
- Clotting time and activated partial thromboplastin time (APTT) are prolonged
- Factor VIII: C assay—deficient or absent
- X-ray of the involved joints, if needed.

Note Remember the following:

APTT is prolonged, which is corrected by addition of normal plasma. If not corrected after the addition of normal plasma, more likely there is antibody formation or the presence of antiphospholipid antibody.

Q. Is antenatal diagnosis possible?

A. Yes. Antenatal diagnosis may be done by molecular analysis of fetal tissue obtained by chorionic villous biopsy at 11 to 12 weeks of pregnancy.

RELATED QUESTIONS AND ANSWERS

Q. What is **hemophilia**?

A. It is an X-linked inherited disorder due to deficiency of factor VIII or antihemophilic factor, characterized by prolonged bleeding. Male is the sufferer, female is the carrier.

Q. What are the **types** of hemophilia?

A. Normal factor VIII level is 50 to 150 IU/dL. According to severity, it is of 3 types—

1. Mild—factor VIII is 10 to 50% (> 5 but < 40 IU/dL). Bleeding occurs following injury or surgery.
2. Moderate—factor VIII is 2 to 10% (1 to 5 IU/dL). There is severe bleeding following injury or surgery, also spontaneous bleeding sometimes.
3. Severe—factor VIII is <2% (<1 IU/dL). There is frequent spontaneous bleeding, also bleeding into the joints and muscles.

Q. What is the **pedigree** of hemophilia?

A. As follows:

1. If father is affected:
- All daughters are carriers
- All sons are normal.

2. If mother is carrier:
- 50% daughters are carriers
- 50% sons are sufferers.

Note Remember the following points:
- In a female carrier, factor VIII is < 50% of normal, because of randomised inactivation of one X chromosome.
- Usually female is the carrier and male is the sufferer.

Q. Can a **female be** the **sufferer** in hemophilia?

A. Yes, rarely a female can be a sufferer, because of the following reasons:
- If a carrier female is married to an affected male, the female baby may be a sufferer.
- According to lyonisation theory, there is randomized inactivation of one X chromosome in the developing fetus. Then the number of affected X chromosome may be predominant. Female may be affected, if normal X chromosome is disproportionately inactivated.
- Turner's syndrome (because there is XO, if the only X is affected).

Q. How the patient usually **presents**?

A. Depends on whether factor VIII deficiency is mild, moderate or severe
- Prolonged and persistent bleeding after trauma or injury, tooth extraction
- Sometimes, spontaneous bleeding may occur in severe cases
- Bleeding into the large joints and muscles (psoas and calf muscle) is also common.

Q. What happens if the patient has **bleeding into the psoas muscle**?

A. As follows:
- Severe pain in lower abdomen
- Paresthesia in thigh and weakness of quadriceps due to compression of femoral nerve.

Q. What are the **complications** of hemophilia?

A. As follows:

1. Due to repeated hemorrhage:
   - Arthropathy due to repeated bleeding in joint (e.g. knee, elbow)
   - Atrophy or wasting of muscles secondary to hematoma in muscle
   - Mononeuropathy due to pressure by hematoma
   - Death may occur due to intracerebral hemorrhage.
2. Due to therapy:
   - Infections—hepatitis A, B, C, D. Also, HIV
   - Factor VIII antibody (20 to 30%).

Q. How will you **manage** hemophilia?

A. As follows:

1. Bleeding episodes are treated with intravenous infusion of factor VIII concentrate, usually two to three times daily (its half life is 12 hours).
   - For minor bleeding—factor VIII level should be raised to 20 to 30 IU/dL.
   - Severe bleeding—factor VIII should be raised to at least 50 IU/dL.
   - Major surgery—factor VIII should be raised to 100 IU/dL preoperatively and maintained above 50 IU/dL until healing has occurred.
2. If factor VIII is not available, cryoprecipitate, fresh frozen plasma or fresh blood can be given.
3. Synthetic vasopressin (desmopressin—an analog of vasopressin)—intravenous, subcutaneous or intranasal, produces a rise in factor VIII:C. It avoids the complications associated with blood products and is useful for treating bleeding episodes in mild hemophilia and as prophylaxis before minor surgery. It is ineffective in severe hemophilia. Repeated use of desmopressin may cause water retention leading to hyponatremia.
4. Genetic counceling.

Note Remember the following points:

- Factor VIII was initially prepared from plasma. It is now prepared from recombinant DNA technology (there is less risk of transfusion transmitted infection but more expensive).
- Advice to the patient—avoid trauma, NSAIDs and IM injection. Precaution should be taken before tooth extraction and surgery.

Q. If factor VIII **antibody** develops, how can it be suspected and treated?

A. Upto 30% cases with severe hemophilia may develop antibodies to factor VIII that inhibits its action. It is suspected if there is no response to factor VIII therapy. This antibody rarely develops in mild and moderate hemophilia, often disappears spontaneously or with continued treatment.

It is very difficult to treat when antibody develops. Following options are available:

- Increasing the dose and frequency of factor VIII therapy. It may or may not be helpful.
- Factor IX may be used. It helps bypassing the inhibitors.
- Recombinant factor VIIa—helps bypassing the inhibitors.
- Factor VIII inhibitor bypassing activity (FEIBA—an activated concentrate of factors II, IX and X).
- Sometimes, immunosuppressive therapy such as steroid, azathioprine or cytotoxic drugs may be given.

Brief notes on Hemophilic Arthritis

Q. What are the **presentations** of hemophilic arthritis?

A. Hemarthrosis occurs when plasma level of factor VIII: C is < 1%. Arthritis may be spontaneous without trauma or may follow even minor trauma.

- Initially, tingling, abnormal sensation, stiffness and instability of the joint.
- Later on, the joint is red, hot, swollen and painful.

Progression of arthritis depends on repeated hemarthrosis which leads to:
- Synovium hypertrophy
- Fibrotic change in synovium
- Destruction of cartilage
- Reduction of joint space
- Subchondral cyst formation
- Bone shows erosion, marginal sclerosis, osteophyte formation and ankylosis of joint.

Q. Which **joints are commonly involved** in hemophilic arthritis?

A. Commonly knee, elbow, ankle and hip joints are involved.
- In infants—hip joint is commonly involved.
- In older children—knee joint is commonly involved.

Q. What are the **radiological signs** in hemophilic arthritis?

A. As follows:
- Initially, joint space is increased and widening of intercondylar notch occurs (in knee joint, indicates long-standing hemorrhage).
- Later on—there is reduction of joint space, periarticular osteopenia, marginal sclerosis, subchondral cyst formation, secondary osteoarthrosis (with osteophyte) and ankylosis of joint.

Q. What are the causes of **widening** of intercondylar notch?

A. As follows:
- Hemophilia
- Christmas disease
- Long-standing effusion in knee joint.

Q. What are the causes of **hemarthrosis**?

A. As follows:
- Trauma
- Hemophilia
- Christmas disease
- Von Willebrand's disease
- Others—sickle cell disease, excess anticoagulant, rarely malignancy.

Q. How to **treat** hemophilic arthritis?

A. As follows:
- Complete rest, if needed splinting of joint.
- Factor VIII transfusion—20 to 30 IU/kg. It is repeated after 12 hours, also after 24 and 36 hours (higher dose is required, if treatment is delayed).
- For pain—COX 2 inhibitors like celecoxib may be used. Orally opioid may be given.
- Physiotherapy—once bleeding is settled, mobilization and physiotherapy should be started. Usually, after 48 hours (isometric exercise, followed by active movement, and hydrotherapy or short wave diathermy).
- Arthrocentesis is rarely necessary, but in some cases with massive bleeding, aspiration of blood from joint followed by factor VIII therapy may be needed.
- To prevent recurrent bleeding into the joint—the patient with severe hemophilia are given factor VIII infusions regularly 3 times per week.

ANEMIA

CHIEF COMPLAINTS

- Weakness for … months
- Occasional dizziness for … months
- Tingling and numbness in lower limbs for … months
- Anorexia, weight loss and palpitation for … months.

HISTORY

History present illness: The patient states that she was alright … months back. Since then, she has been suffering from severe weakness which is gradually worsening and now she finds it difficult to perform regular daily activities. For the last … months, she also experiences occasional dizziness, light-headedness, tingling and numbness in both feet and occasional cramps in calf muscles. The patient also complains of palpitation, loss of appetite and weight loss for … months. There is no history of fever, difficulty in swallowing, bleeding from any sites or menorrhagia and bowel or bladder abnormality.

History of past illness

Family history

Personal history

Menstrual history

Socioeconomic history

Drug history: Mention according to the patient's statement.

GENERAL EXAMINATION

- The patient looks pale
- Moderately anemic
- No jaundice, clubbing, cyanosis, koilonychia, leukonychia or edema
- No lymphadenopathy or thyromegaly
- Sternal tenderness: Absent
- Pulse: 120/min.
- BP: 95/65 mm Hg.

SYSTEMIC EXAMINATION

Gastrointestinal System

- Tongue is smooth, shiny with atrophy of papillae
- Lips, gums, teeth, oral cavity and tonsils—normal.

Abdomen

Inspection:

- No abnormality.

Palpation:

- Diffusely tender
- Liver—not palpable
- Spleen—not enlarged
- Kidneys—not ballotable.

Percussion:

- No evidence of ascites (no fluid thrill, no shifting dullness).

Auscultation:

- No abnormality detected.

Cardiovascular System

- There is a systolic murmur in the apical area (likely to be flow murmur).

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mrs. …, 40 years old, housewife, normotensive, nondiabetic, nonsmoker, hailing from …, presented with severe weakness for … months, which is gradually worsening and now she finds it difficult to perform regular daily activities. For the last … months, she also experiences occasional dizziness, light-headedness, tingling and numbness in both feet and occasional cramps in calf muscles. The patient also complains of palpitation, loss of appetite and weight loss for … months. There is no history of fever, difficulty in swallowing, bleeding from any sites or menorrhagia and bowel or bladder abnormality. The patient was treated by local physicians with iron tablets, multivitamin and ranitidin. There is no family history of similar illness.

On examination—general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is moderate anemia for which I have some differential diagnoses:

- Iron deficiency anemia
- Megaloblastic anemia
- Acute leukemia.

Q. What is **anemia**?

A. Anemia is a clinical condition characterized by reduced hemoglobin concentration, which is usually but not invariably associated with reduced RBC.

RELATED QUESTIONS AND ANSWERS

Q. **Classify** anemia.

A. Anemia may be classified in two ways—etiological (based on cause) and morphological (based on morphology of RBC).

Etiological:

1. Hemorrhagic anemia (due to blood loss):

- Acute—Trauma, postpartum bleeding, hematemesis, melena, epistaxis.
- Chronic—Hook worms, hemorrhoids, excessive menstrual loss, bleeding peptic ulcer, etc.

2. Dyshemopoietic anemia (due to inadequate production of RBC):
   - Deficiency anemia—Iron, vitamin B_{12}, folate deficiency.
   - Aplastic anemia (bone marrow failure which may be primary or secondary to some other diseases or drugs).
   - Anemia of chronic disorder (ACD)—SLE, rheumatoid arthritis, CRF.
   - Others—Hypothyroidism, sideroblastic anemia, malignancy.
3. Hemolytic anemia:
   - Genetic—Red cell membrane defect (e.g. hereditary spherocytosis, eliptocytosis, stomatocytosis), hemoglobin abnormality (thalassemia, sickle cell anemia) or enzyme defects (glucose-6-phosphate dehydrogenase deficiency, pyruvate-kinase deficiency).
   - Acquired—Autoimmune, toxic, mechanical and infectious causes.

Morphological (depending on MCV and MCHC):
1. Normocytic normochromic anemia (normal MCV and MCHC).
2. Microcytic hypochromic anemia (low MCV < 76 fl, low MCHC < 30 g/dL).
3. Macrocytic anemia (high MCV > 96 fl).
4. Diamorphic anemia (two cell lines—macrocytes and microcytes).

Q. What are the causes of **normocytic normochromic anemia**?

A. As follows:
- Anemia of chronic disorder
- Chronic infection (e.g. tuberculosis)
- Collagen disease (e.g. SLE, rheumatoid arthritis)
- Malignancy
- Endocrine disease
- Sideroblasitic anemia.

Q. What are the causes of **microcytic hypochromic** anemia?

A. As follows:
- Iron deficiency anemia
- β-thalassemia major
- Sideroblastic anemia
- Anemia of chronic disorder (ACD).

Q. What are the causes of **macrocytic anemia**?

A. As follows:
1. Macrocytosis with megaloblastic marrow are found in:
   - Vitamin B_{12} deficiency
   - Folic acid deficiency.
2. Macrocytosis with normoblastic marrow are found in:
   - Chronic liver disease
   - Chronic alcoholism
   - Hypothyroidism
   - Hemorrhage
   - Hemolysis
   - Others—sideroblastic anemia, pure red cell aplasia, azathioprine therapy.

Q. What is **dimorphic anemia**? What are the **causes**?

A. When both microcytes and macocytes are found, this is called dimorphic anemia. Causes are:
- Combined iron, B_{12} and folate deficiency

- Sideroblastic anemia
- Treatment of anemia.

Q. What are the causes or mechanisms of **anemia of chronic disorder**?

A. Actual mechanism is unknown. It is due to abnormality of iron metabolism and erythropoiesis. There is less erythropoietin. Also red cell survival is short.

Q. What are the **signs** that may point to a specific cause of anemia?

A. As follows:

Sign	Cause of anemia
1. Triad of anemia, jaundice and splenomegaly	Hemolytic anemia
2. Angular cheilitis, glossitis, koilonychia	Iron deficiency anemia
3. Glossitis	Iron deficiency anemia, vitamin B_{12} deficiency, folate deficiency
4. Splenomegaly	Malaria, chronic hemolytic anemia, acute infection, leukemia, lymphoma, portal hypertension
5. Neurological changes (dementia, optic atrophy and features of subacute combined degeneration of spinal cord) and lemon yellow tint	Vitamin B_{12} deficiency (megaloblastic anemia)
6. Bony change (frontal and parietal bossing)	Hereditary hemolytic anemia
7. Leg ulcer	Sickle cell anemia, PNH
8. Bony tenderness	Acute leukemia, multiple myeloma, lymphoma, myelofibrosis

Q. What is **spurious anemia**?

A. When plasma volume is increased, hemoglobin is relatively low, it is called spurious anemia. It is found in pregnancy.

Q. What is **spurious polycythemia**?

A. Here hemoglobin is relatively increased due to low plasma volume. This is found in dehydration.

Q. How to **investigate** a patient with anemia?

A. Detailed history, physical examination and finally relevant laboratory investigations are done to investigate a patient with anemia.

History of the patient:

- Dietary history (to diagnose deficiency anemia like iron, vitamin B_{12} and folic acid deficiency).
- Malabsorption.
- Any history of bleeding (hemorrhoid, epistaxis, hematemesis, melena, menorrhagia in female, etc.).
- In female—multiple pregnancies, repeated abortion.
- Drug history—NSAIDs, steroid, drugs causing bone marrow suppression (e.g. cytotoxic drugs), drugs causing hemolysis (e.g. sulfasalazine, methyldopa, etc.).

- History of surgery—gastrectomy or partial gastrectomy, ileal surgery (responsible for vitamin B_{12} absorption).
- Family history (in case hereditary hemolytic anemia).
- History of any chronic disease (e.g. SLE, CRF, etc.).

Clinical examination—See the box above.

Laboratory investigations:

1. Full blood count (Hb%, TC, DC, ESR, platelet count):
   - Pancytopenia—which may be due to aplastic anemia, hypersplenism, megaloblastic anemia, aleukemic leukemia.
2. PBF examination: Following findings may be found which indicates particular causes of anemia (see below in the table).
3. Reticulocyte count: High in hemolytic anemia.
4. MCV and MCHC.
5. Bone marrow examination: Megaloblastic anemia, aplastic anemia, bone marrow infiltration (secondary deposit), ring sideroblasts (in sideroblastic anemia).
6. Other investigations in relation to suspicion and primary cause of diseases.

Further investigation of microcytic hypochromic anemia (low MCV and low MCHC):

- For iron deficiency anemia—Serum iron, TIBC, serum ferritin.
- For hereditary hemolytic anemia—Hemoglobin electrophoresis, skeletal survey.
- For sideroblastic anemia—According to history, bone marrow examination (ring sideroblasts)
- For anemia of chronic disease—Test should be done according to history of the patient.

Further investigations for macrocytic anemia (high MCV):

- Bone marrow is done. If megaloblast seen, serum B_{12} and folic acid assay should be done. If normoblast, further investigation should be according to history (see above).

Q. What diseases may be **diagnosed from PBF**?

A. As follows:

Finding	Description	Common diagnoses
1. Anisocytosis	Variation in size of RBC	Iron deficiency anemia, megaloblastic anemia, sideroblastic anemia
2. Poikilocytosis	Variation in shape of RBC	Iron deficiency anemia, thalassemia, sideroblastic anemia
3. Microcytosis	MCV < 76 fl	Iron deficiency anemia, thalassemia, sideroblastic anemia, anemia of chronic disorder
4. Macrocytosis	MCV > 100 fl	Vitamin B_{12} and folic acid deficiency, chronic liver disease, alcohol, hypothyroidism, zidovudine
5. Hypochromia	Central pallor of RBC is increased in size (lower hemoglobin content)	Iron deficiency anemia, thalassemia, sideroblastic anemia, anemia of chronic disorder

Contd...

Contd...

6. Basophilic stippling or punctate basophilia	Deep blue dots scattered in cytoplasm of RBC (seen with Romanowsky staining)	Chronic lead poisoning, dyshemopoiesis
7. Target cells	Flat red cells with a central mass of hemoglobin (dense area), surrounded by a ring of pallor (pale area) and an outer ring of hemoglobin (dense area)	Iron deficiency anemia, thalassemia, hemoglobic C disease, CLD, splenectomy
8. Howell-Jolly bodies	Small round remnants of nuclear material in RBC. These are normally removed by spleen	Hyposplenism, post splenectomy, dyshemopoiesis
9. Heinz's bodies (Ehrlich's bodies)	Formed from denatured aggregated hemoglobin in red cells (seen with supravital staining with brilliant cresyl blue)	Thalassemia, hemolysis in glucose 6 phosphate dehydrogenase deficiency, asplenia and CLD, drug like sulfasalazine, dapsone
10. Acanthocytes (spur cells)	RBC with irregular spicules	Abetalipoproteinemia
11. Burr cells	RBC with regularly placed spicules	CRF
12. Schistocytes	Fragmented RBC. These are found in microangiopathic hemolytic anemia	Causes—DIC, HUS, TTP, disseminated carcinomatosis, malignant or pregnancy induced hypertension (eclampsia)
13. Spherocytes	Small, densely packed RBC with loss of central pallor	Hereditary spherocytosis, autoimmune hemolytic anemia, post-splenectomy
14. Sickle cell	Sickle shaped	Sickle cell anemia
15. Blister cells		Glucose-6-phosphate dehydrogenase deficiency
16. Nucleated RBC	Normoblasts	Bone marrow infiltration, severe hemolysis, myelofibrosis, acute hemorrhage
17. Polychromatia	Young red cells, reticulocytes (bluish tinge)	Hemolysis, acute hemorrhage, increased red cell turnover

Q. What is **sideroblastic anemia**?

A. Sideroblastic anemias are inherited or acquired disorders characterized by refractory anemia, a variable number of hypochromic cells in the peripheral blood, and excess iron and ring siderblasts. Blood film usually shows microcytic anemia, may be dimorphic.

Classification:

1. Herediatry:
   a. X-linked disease, transmitted by females.

2. Acqurried:
   a. Primary (one of the myelodysplastic syndromes).
   b. Secondary:
      - Inflammatory—rheumatoid arthritis
      - Neoplastic—lymphoma, leukemia, carcinoma, myeloproliferative disorders, multiple myeloma, carcinoma
      - Drugs—INH, pyrazinamide, cyclosporine
      - Alcohol abuse
      - Lead poisoning
      - Other disorders, e.g. megaloblastic and hemolytic anemias, malabsorption, severe malnutrition, erythroleukemia.

Treatment:
- Treatment of the primary cause, if present. For example, withdrawal of drug, stop alcohol intake, etc.
- Some case may respond to pyridoxine, folic acid.
- Correction of anemia by blood transfusion.

Q. What is **ring sideroblast**?

A. It is characterized by accumulation of iron in mitochondria of erythroblast around the nucleus, giving a ring shaped appearance in the bone marrow.

CHAPTER 11

Dermatology

- Exfoliative Dermatitis or Erythroderma 687
- Psoriasis 695
- Darier's Disease or Keratosis Follicularis 707
- Post Kala-azar Dermal Leishmaniasis (PKDL) 715
- Lepromatous Leprosy 721
- Pityriasis Rubra Pilaris 733
- Pemphigus Vulgaris 740
- Bullous Pemphigoid 748
- Lichen Planus 753
- Arsenicosis 759
- Leg Ulcer (Venous Ulcer) 763
- Leukocytoclastic Vasculitis (Small Vessel Vasculitis) 767
- Erythema Nodosum 771

EXFOLIATIVE DERMATITIS OR ERYTHRODERMA

CHIEF COMPLAINTS

- Generalized scaling and redness for … months
- Pruritus all over the body for … months
- Chill and shivering for … days.

HISTORY

History of present illness: The patient states that he was reasonably well … months back. Since then, he has been suffering from recurrent pruritic lesions on the back of elbows, front of knees, extensor surfaces of extremities and lower back. Later on, the scalp and nails were involved. The lesions were elevated, circular, reddish and scaly. The scales were silvery white in color. He noticed bleeding after scratching of the lesions. The patient also noticed appearance of new lesions on scratch marks. These lesions are not associated with exposure to any allergen or food or exposure to sun. This type of attack occurred several times over the last … months.

For the last … months, the patient noticed generalized scaling and redness almost all over the body that is associated with extreme weakness, itching and loss of appetite. This is associated with chill and also occasional shivering for … days. He mentioned that following use of some topical medicine prescribed by a physician, there was some improvement. But there is recurrence of the same lesions after few days. His bowel and bladder habits are normal. There is no history of fever, arthralgia or arthritis, mouth ulcer, etc.

History of past illness: The patient did not suffer from any serious illness in the past.

Family history: There is no history of similar illness in the family. All the members of the family are in good health.

Personal history: He is married and has a son. He smokes 3 to 4 sticks/day for the last 10 years, but nonalcoholic. There is extramarital sexual exposure 3 years back.

Drug and treatment history: He was treated by local physicians with several antibiotics, systemic and topical steroid, antifungal agents, etc.

Socioeconomic condition: He is a businessman and comes from a middle class family. He lives in a semi pakka house with good sanitation and water supply.

GENERAL EXAMINATION

- The patient looks ill and emaciated with poor nutrition
- Mildly anemic
- No jaundice, cyanosis, clubbing, koilonychia, leukonychia, edema
- Few lymph nodes are palpable in cervical region that are discrete, soft in consistency and nontender
- No thyromegaly
- Pulse: 110/min
- Blood pressure: 110/70 mm of Hg
- Respiratory rate: 16/min
- Temperature: 98ºF.

SYSTEMIC EXAMINATION

Integumentary System

- Skin: Generalized exfoliation and erythema covering all over the body. Scales are white in color. Desquamation occurs in sheets from palms and soles. Skin is warm and dry. There is no tenderness.
- Hair: Color and texture of scalp hair is normal. Body hair is sparse.
- Nail: Brittle, yellow, dystrophic with subungual hyperkeratosis and distal onycholysis, nail folds are separated. Beau's line is present in some of the nails.
- Oral mucosa: Normal.
- Conjunctiva: Normal.
- Genitalia: Normal.

Examination of the other systems reveals no abnormalities.

SALIENT FEATURE

Mr …, 35 years old, businessman, normotensive, nondiabetic, hailing from … presented with recurrent pruritic lesions on the back of elbows, front of knees, extensor surfaces of extremities and lower back for … months. Later on, the scalp and nails were involved. The lesions were elevated, circular, reddish and scaly. The scales were silvery white in color. He noticed bleeding after scratching of the lesions. The patient also noticed appearance of new lesions on scratch marks. These lesions are not associated with exposure to any allergen or food or exposure to sun. This type of attack occurred several times over the last … years.

For the last … months, the patient noticed generalized scaling and redness almost all over the body that is associated with extreme weakness, itching and loss of appetite. This is associated with chill and also occasional shivering for … days. He mentioned that following use of some topical medicine prescribed by a physician, there was some improvement. But there is recurrence of the same lesions after few days. His bowel and bladder habits are normal. There is no history of fever, arthralgia or arthritis, mouth ulcer, etc. There is no significant family history. He is nonalcoholic but smokes 3 to 4 sticks/day for the last 10 years.

On general examination – mention as above

On examination of integumentary system, there was generalized exfoliation and erythema covering almost all over the body. Skin is dry and warm. Koebner's phenomenon was observed. Nails are brittle, yellowish with subungual hyperkeratosis, onycholysis and dystrophy.

Examination of the other systems reveals no abnormalities.

My diagnosis is exfoliative dermatitis due to psoriasis.

Q. Why your diagnosis is exfoliative dermatitis due to psoriasis?

A. Because, there is history of scaly plaque type lesions on the elbow, knee, sacrum, scalp and extensor surface of the extremities. Scales are silvery white in color. Koebner's phenomenon is positive. All are suggestive of psoriasis.

Q. What are your **differential diagnoses?**

A. As follows:

- Exfoliative dermatitis because of drugs
- Exfoliative dermatitis because of Pityriasis rubra pilaris
- Exfoliative dermatitis because of Pemphigus foliaceous.

Q. What are the **points in favor and against** your differential diagnoses?

A. As follows:

Differential diagnoses	Points in favor	Points against
1. Exfoliative dermatitis because of drugs	Generalized exfoliation	No history of taking drugs that usually causes erythroderma Long history with recurrence and remission
2. Exfoliative dermatitis because of pityriasis rubra pilaris	Generalized exfoliation Involvement of palms and soles	Age is not suggestive No follicular papules, islands of normal skin or appearance of exaggerated goose flesh
3. Exfoliative dermatitis because of pemphigus foliaceus	Generalized exfoliation	No history of bullae Sites and nature of the previous skin lesions are not suggestive

Q. What **investigations** do you suggest in your case?

A. As follows:

1. Routine investigations:
   - Complete blood count and PBF (there may be normochromic normocytic anemia, leukocytosis, eosinophilia, high ESR, immature cells in leukemia).
   - Chest X-ray P/A view (to see complication like pneumonia, in suspected cases of lymphoma, sarcoidosis, etc.).
   - Urine R/M/E (to see proteinuria).
   - Total protein, albumin and globulin ratio (hypoproteinemia, altered A:G ratio).
   - Serum electrolytes (hypokalemia, hyponatremia, hypochloremia).
   - Blood urea and serum creatinine.
   - Serum uric acid level.
   - Serum IgE (elevated in some cases, especially in cases of atopic dermatitis).
2. Definitive diagnosis by skin biopsy for histopathology:
   - Histopathological findings help to identify the cause of erythroderma in up to 50% cases, particularly if multiple skin biopsies are examined. In psoriasis, papillomatosis and clubbing of the papillary zones may be seen. In pemphigus, superficial acantholysis will be present. In ichthyosiform erythroderma and pityriasis rubra pilaris, repeated biopsy from carefully selected sites may reveal their characteristic features.
   - Direct immunofluorescence test should be done to see immunoglobulin deposits in pemphigus foliaceus or lichen planus, etc.
3. Others to exclude primary cause:
   - Skin scraping for fungus and fungal culture in suspected cases of dermatophytosis
   - HIV cases (Anti HIV I and II, Western blot)
   - Ultrasonogram of the whole abdomen (to exclude malignancy or to see hepatomegaly and splenomegaly)
   - Bone marrow examination (to exclude leukemia)
   - CT and MRI (in some cases).

Q. How to **treat** the case?

A. As follows:

1. **General measures:**
   - Maintenance of fluid balance (intake and output monitoring)
   - Maintenance of electrolyte balance

- Good nutrition and protein balance by high protein diet
- Maintenance of environmental temperature
- Frequent bathing.

2. **Topical treatment:**
   - Lubricant and emollient (e.g. liquid paraffin)—apply two times daily
   - Mild topical steroid ointment (hydrocortisone)—apply once daily.
3. **Symptomatic treatment:**
   - Antihistamine (e.g. cetirizine, loratidine)
   - Antibiotic, if secondary infection is suspected
   - Iron, vitamin, folic acid supplement.
4. **Specific systemic treatment:**
   - Psoriatic erythroderma—Methotrexate (7.5 to 10 mg in single or 2 divided doses weekly). Other drugs—cyclosporine, acitretin, etc. may be given.
   - Isotretinoin may be used in pityriasis rubra pilaris.
   - PUVA therapy can be used in mycosis fungoides or psoriasis.
   - Immunosuppressives, such as azathioprine, cyclophosphamide may be required occasionally.
5. **Treatment of primary causes,** such as specific therapy for lymphoma and leukemias.

Q. What are the different **emollients and lubricants** that can be used in erythroderma?

A. Liquid paraffin, Vaseline, olive oil or lac hydrin (12% ammonium lactate) can be used as emollients.

Q. What are the **new drugs** that are used in psoriasis?

A. New drugs that are being used in psoriasis are tacrolimus, mycophenolate mofetil, hydroxyurea, 6 thioguanine and biologic agents, such as infliximab, etanercept, alefacept.

Q. What is the role of **systemic steroid in erythroderma?**

A. Systemic steroid should be avoided if possible, because of the dangers of fluid retention, secondary infection, diabetes and other complications. Steroid is also avoided in psoriatic erythroderma, because it may provoke the development of pustular psoriasis.

However, it may be used cautiously in atopic and seborrheic dermatitis. Only in severe persistent cases, systemic steroid is given. In that case, triamcinolone acetonide 80 mg is injected intramuscularly as initial dose. It can be repeated in 4th, 7th and 10th day, according to the condition of the patient.

RELATED QUESTIONS AND ANSWERS

Q. What are the **causes** of exfoliative dermatitis?

A. As follows:

1. Primary or Idiopathic.
2. Secondary to:
   - Cutaneous disease—psoriasis, atopic dermatitis, contact dermatitis, dermatophytosis, dermatomyositis, Hailey-Hailey disease, ichthyosiform erythroderma, Leiner's disease, lichen planus, SLE, mastocytosis, mycosis fungoides, Norwegian scabies, pemphigoid, pemphigus foliaceus, pityriasis rubra pilaris, Reiter's syndrome, sarcoidosis, seborrheic dermatitis, stasis dermatitis.
   - Systemic disease or malignancy—acute and chronic leukemia, lymphoma, carcinoma of the lung, rectum, fallopian tubes, multiple myeloma, mycosis fungoides, HIV infection, graft versus host disease.
   - Drugs—allopurinol, carbamazepine, sulfonamide, aminoglycosides, arsenic, aspirin, barbiturates, calcium channel blocker, captopril, cephalosporin, chlorpromazine, dapsone,

diltiazem, isoniazid, lithium, minocycline, neomycin, nalidixic acid, penicillin, phenothiazines, ranitidine, rifampicin, streptomycin, sulfonylurea, thiazides, trimethoprim, vancomycin.

Q. What are the causes of **Koebner's phenemenon?**

A. The following diseases show Koebner's phenomenon:
- Psoriasis
- Lichen planus
- Viral wart (verruca plana)
- Pityriasis rubra pilaris
- Nummular eczema
- Infectious eczematoid dermatitis
- Molluscum contagiosum
- Darier's disease
- Vitiligo
- Keratoacanthoma
- Reactive perforating collagenosis
- Erythema multiformi.

Q. What are the causes of **psoriasiform lesions?**

A. Causes of psoriasiform lesions are:
- Psoriasis
- Seborrheic dermatitis
- Pityriasis rubra pilaris
- Pityriasis rosea
- Parapsoriasis
- Subacute cutaneous lupus erythematosus
- Secondary syphilis
- Premycotic stage of mycosis fungoides.

Q. What are the causes of **erythroderma in adults?**

A. As follows:
- Idiopathic
- Psoriasis
- Atopic dermatitis
- Neurodermatitis
- Drug allergy
- Lymphoma
- Leukemia
- Contact dermatitis
- Seborrheic dermatitis
- Stasis dermatitis
- Pityriasis rubra pilaris
- Pemphigus foliaceus.

Q. What are the causes of **erythroderma in childhood?**

A. As follows:
- Atopic dermatitis
- Drugs
- Leukemia
- Childhood dermatomyositis
- Bullous ichthyosiform erythroderma

- Non-bullous ichthyosiform erythroderma
- Lamellar ichthyosis
- Pityriasis rubra pilaris
- Idiopathic
- Generalized dermatophytosis
- Leiner's disease.

Q. How a patient **presents** with exfoliative dermatitis?

A. The patient presents with:
- Generalized scaling
- Widespread erythema
- Dehydration or edema.

> **Note Remember the following:**
>
> Males are affected 2 to 3 times more frequently than females.

Q. What are the **clinical features** of exfoliative dermatitis?

A. Clinical features are is similar in most patients and characterized by:

1. Cutaneous manifestations:
   - Universal or extensive scaling covering more than 90% of the body surface
   - Pruritus and widespread erythema
   - Skin thickening
   - Loss of hair (often)
   - Nails may be dystrophic
   - Palms and soles are involved
   - Mucous membranes are usually spared although mucous membrane of the upper respiratory tract and conjunctiva (ectropion) may be involved.
2. Systemic manifestations:
   - Diarrhea
   - Anemia
   - Edema
   - Tachycardia
   - Lymphadenopathy (due to reactive hyperplasia)
   - Hepatomegaly (in 7% to 37% of the cases)
   - Splenomegaly (in 3% to 23% of the cases)
   - Occasionally, gynecomastia.

Q. What is the **pathogenesis** of psoriasis?

A. There is increase in the rate of epidermal turnover. The number of germinative cells and their absolute mitotic rate is increased. Transit time of the cells through the epidermis is shortened. Consequently, more material is lost from the epidermis. The desquamated cells show increased amount of nucleic acids and their degenerative products, decreased amount of free amino acids and increased amount of soluble protein.

Q. What **skin dysfunctions** occur in exfoliative dermatitis?

A. As follows:
- Loss of permeability barrier
- Marked scaling

- Marked vasopermeability
- Marked vasodilatation.

Q. What are the **complications** of exfoliative dermatitis?

A. There are multiple metabolic and systemic complications, such as:
- Secondary bacterial infection (cutaneous, subcutaneous and respiratory)
- Fluid loss, dehydration and electrolyte imbalance
- Protein loss (hypoalbuminema), leading to edema
- Xerosis
- Hypothermia
- High output cardiac failure
- Dermatogenic enteropathy
- Thrombophlebitis.

Q. What are the other causes of **dermatogenic enteropathy (diarrhea)?**

A. As follows:
- Dermatitis herpetiformis
- Pellagra
- Acrodermatitis enteropathica
- Candidiasis
- HIV.

Q. What are the causes of **ectropion?**

A. Causes of ectropion are:
- Exfoliative dermatitis
- Lamellar ichthyosis
- Non-bullous ichthyosiform erythroderma
- Sezary syndrome
- Lepromatous leprosy
- Lupus vulgaris
- Congenital eryhropoietic porphyria.

Q. What are the causes of **exfoliative dermatitis with nail changes?**

A. As follows:
- Psoriasis
- Pityriasis rubra pilaris
- Lichen planus
- Dermatophytosis
- Atopic dermatitis.

Q. What are the **bullous diseases causing exfoliative dermatitis?**

A. As follows:
- Congenital bullous ichthyosiform erythroderma
- Bullous pemphigoid
- Pemphigus foliaceus
- Hailey Hailey disease.

Q. Why **hypoproteinemia** occurs in exfoliative dermatitis?

A. As follows:
- Increased protein loss through scaling or leaking through the skin
- Protein loosing enteropathy

- Decreased synthesis and increased catabolism of protein
- Dilution by increased plasma volume.

Q. What are the **histopathological findings of psoriasis?**

A. Histopathology in psoriasis shows:

- Hyperkeratosis and parakeratosis (parakeratosis is more prominent, characterized by immature cells in stratum corneum).
- Presence of neutrophilic microabcess (Munro's) in the stratum corneum.
- Granular layer is thin or absent over the tips of dilated dermal papilla.
- Acanthosis (hyperplasia of the stratum malpighii) with test tube like elongation of rete ridges.
- Spongiform pustule in the spinous layer.
- Dilated and tortuous blood vessels in dermal papillae.
- Perivascular mononuclear cell infiltrate.

Q. What are the **prognoses** of exfoliative dermatitis?

A. As follows:

- Prognosis is good in drug induced cases after the offending drug is withdrawn
- Prognosis is poor in cases of idiopathic erythroderma
- Frequent recurrences or chronic symptoms require long-term steroid therapy and its sequelae
- In patient with the underlying disease or malignancy, prognosis depends on the primary cause
- The mean duration of the disease is 5 years with a median of 10 months
- Mortality rate is 20 to 40%
- Cause of death is unrelated to erythroderma in 20%.

PSORIASIS

CHIEF COMPLAINTS

- Multiple erythematous lesions with silvery white scales on different sites of the body for … years
- Occasional itching for … months.

HISTORY

History of present illness: The patient states that he was reasonably well … years back. Since then, he has been suffering from multiple reddish, scaly lesions of different shapes and sizes on scalp, front of knees, back of elbows, over the sacrum and extensor surfaces of the extremities. The scales are dry, white, thick and in some places large sheet-like. There is no oozing or discharge, but there is occasional itching. He noticed bleeding upon scratching of the lesions and appearance of new lesions on the scratch marks. In the scalp, the lesions does not causes fall of hair. He was treated with some topical emollients and antihistamine as prescribed by local doctors with some benefits. But the lesions recurred after some days and he had several attacks over the last … years. The lesions are gradually increasing,

These lesions are not associated with exposure to any allergen or food or exposure to sunlight. He did not take any drugs prior to this illness. There is no history of joint pain, photosensitivity, atopy, cough, chest pain, shortness of breath, jaundice, diarrhea, urethral discharge, eye changes, mouth ulcer, proximal muscular pain or weakness. He denies any extramarital exposure. His bowel and bladder habits are normal.

History of past illness

Family history: His father suffered from similar scaly skin disease.

Personal history

Drug and treatment history

Socioeconomic condition: Mention according to the patient's statement.

GENERAL EXAMINATION

- Mildly anemic
- No jaundice, cyanosis, clubbing, koilonychia, leukonychia, edema
- No lymphadenopathy or thyromegaly
- Pulse: 100/min
- Blood pressure: 110/70 mm of Hg
- Respiratory rate: 16/min
- Temperature: 98ºF.

SYSTEMIC EXAMINATION

Integumentary System

- Skin: There are multiple, well defined, erythematous, scaly plaques with silvery white scales involving scalp, elbows, knees, sacrum and extensor surfaces of the body. Auspitz sign is positive. Koebner phenomenon is positive.

- Hair: Normal.
- Nail: Subungual hyperkeratosis, nail pitting, oil drop sign positive.
- Mucous membrane:
  - Mouth—normal
  - Conjunctiva—normal
  - Genitalia—normal.

Examination of the other systems reveals no abnormalities.

SALIENT FEATURE

Mr …, 35 years old, businessman, normotensive, nondiabetic, hailing from …, presented with multiple elevated, circular, reddish, scaly lesions of different shapes and sizes on scalp, front of knees, back of elbows, over the sacrum and extensor surfaces of the extremities for … years. The scales are dry, silvery white, thick and in some places large sheet-like. There is no oozing or discharge, but there is occasional itching. He noticed bleeding upon scratching of the lesions and appearance of new lesions on the scratch marks. In the scalp, the lesions do not cause fall of hair. He was treated with some topical emollients and antihistamine as prescribed by local doctors with some benefits. But the lesions recurred after some days and he had several attacks over the last … years. The lesions are gradually increasing, not associated with exposure to any allergen or food or exposure to sunlight. He did not take any drugs prior to this illness. There is no history of joint pain, photosensitivity, atopy, cough, chest pain, shortness of breath, jaundice, diarrhea, urethral discharge, eye changes, mouth ulcer, proximal muscular pain or weakness. He denies any extramarital exposure. His bowel and bladder habits are normal. His father suffered from similar scaly skin disease. There is no family history of similar illness. He was treated with several creams and ointments and antihistamine tablets by local physicians.

General examination (as above).

Examination of integumentary system (as above).

Examination of the other systems reveals no abnormalities.

My diagnosis is psoriasis (plaque type).

Q. Why do you think this is a case of psoriasis?

A. Because the patient gives a long history of skin lesions, mostly on extensor surface, with relapse and remission and occasional itching. On examination, there are well-defined erythematous scaly plaques with silvery white scale involving scalp, elbows, knees, sacrum and extensor surfaces of the body with positive Auspitz sign and Koebner phenomenon. There is also subungual hyperkeratosis, nail pitting and oil drop sign on the nails. So my diagnosis is psoriasis.

Q. What are your differential diagnoses?

A. As follows (for details, see below):

- Pityriasis rubra pilaris
- Seborrheic dermatitis
- Lichen planus
- Pityriasis rosea
- Subacute cutaneous lupus erythematosus (SCLE)
- Parapsoriasis—large and small plaque
- Psoriasiform sarcoid
- Psoriasiform secondary syphilis

- Plaque stage of mycosis fungoides
- Dermatophytosis
- Dermatomyositis.

Q. What **investigations** should be done in psoriasis?

A. As follows:

1. Routine:
   - Complete blood count (CBC)
   - Liver function test (LFT)
   - Serum creatinine
   - Lipid profile
   - X-ray chest
   - Urine R/M/E (to see proteinuria)
   - Serum electrolytes (hypokalemia, hyponatremia, hypochloremia)
   - Serum uric acid level
   - Serum IgE (to differentiate from atopic dermatitis).
2. To establish the diagnosis, the following procedures may be performed:
   - Skin biopsy for histopathology (definitive)
   - Antistreptolysin O (ASO) titer (high in guttate psoriasis)
   - Throat swab culture and sensitivity (in guttate psoriasis)
   - X-ray of the affected joints (to see psoriatic arthritis).
3. To exclude other causes, the following tests may be performed:
   - VDRL, TPHA, anti-nuclear antibody (ANA), anti SS-A, anti SS-B, direct immunofluorescence (DIF) and skin scraping for fungus.

Q. What are the **histological findings?**

A. As follows:

- Hyperkeratosis, parakeratosis, orthokeratosis
- Neutrophilic microabscess of Munro in the stratum corneum
- Granular layer is absent or thin over the dermal papilla
- Spongiform pustule of Kogoj in stratum spinosum
- Regular elongation of rete ridges that are club shaped
- Dermal capillary dilatation and tortuosity surrounded by a mixed neutrophilic and lymphohistiocytic perivascular infiltrate.

QUESTIONS RELATED TO PSORIASIS

Q. What are the **sites** of psoriatic skin lesion?

A. Extensor surfaces of knee, elbow, wrist, back of ear, scalp, hairline, extensor of limbs, sacrum, around the umbilicus, intergluteal cleft and flexures (natal cleft, axillary fold) and submammary fold.

Q. What **areas** have you examined other than skin to diagnose psoriasis?

A. As follows:

- Nails—pitting, oil spot, cracking of free edges, onycholysis (separation of nail plate from its bed), thickening and subungual hyperkeratosis
- Joints—arthropathy
- Eye—iritis (may be blepharitis, keratitis and conjunctivitis)
- (Tongue—geographical tongue may be associated).

Q. What are your **differential diagnoses**?

A. As follows:

- Pityriasis rubra pilaris (sandle-like palmo-plantar keratoderma, islands of normal skin, follicular papules).
- Seborrheic dermatitis (greasy, yellowish scale on eyebrows, nasolabial crease, gluteal crease, ears, sternal region, axilla, submammary folds, umbilicus and groin).
- Lichen planus (usually on flexor surface, Wickham striae, violaceous flat-topped papules and adherent scale, white violaceous lacy patch on buccal mucosa).
- Pityriasis rosea (short duration, herald patch and collarette scaling on trunk, upper arms and thighs).
- Subacute cutaneous lupus erythematosus (SCLE) (female sex, photosensitivity, photodistributed area and over back).
- Parapsoriasis (large and small plaque, long duration, asymptomatic, fine scale, truncal involvement, patches of variable size).
- Psoriasiform sarcoid (truncal involvement, no nail change, systemic symptoms of sarcoidosis, such as fever, cough, breathlessness on exertion, joint pain).
- Psoriasiform secondary syphilis (history of extramarital exposure, duration is less than 3 months, history of chancre on genitalia, generalized lymphadenopathy, condyloma lata, mucous patches on oral cavity).
- Plaque stage of mycosis fungoides (middle aged patient, severely pruritic).
- Dermatophytosis (tinea corporis, cruris and pedis. There is itching, scaly patch active papulo-vesicular border and central clearing).
- Dermatomyositis (heliotrope sign, atrophy and poikiloderma, muscular weakness).

Q. What is **mycosis fungoides**?

A. Mycosis fungoides (cutaneous T cell lymphoma) is a rare skin tumor that develops slowly over many years (sometimes 20 to 30 years). It is characterized by reddish-brown, scaly and itchy plaques that, in early stages, resemble erythematous lesions of psoriasis or eczema. There may be enlargement of lymph nodes. Occasionally, it can progress to a cutaneous nodular or tumor stage. In elderly male, the disease may progress rarely to an erythrodermic variant accompanied by lymphadenopathy and peripheral blood involvement (Sezary syndrome).

Skin biopsy confirms the diagnosis.

Early cutaneous disease can be left untreated or treated with topical steroid or PUVA. In advanced cases, radiotherapy, chemotherapy (e.g. methotrexate), immunotherapy or electron beam therapy may be used.

Q. What is **Sezary's syndrome**?

A. Sezary's syndrome is erythrodermic variant of mycosis fungoides (cutaneous T cell lymphoma), characterized by erythroderma, lymphadenopathy and large mononuclear cells (Sezary cells) in the skin and blood. It is often resistant to treatment and carries poor prognosis.

Q. What is **Auspitz's sign** and **Koebner's phenomenon** in psoriasis?

A. As follows:

- Auspitz's sign: When the silvery scales are plucked, capillary bleeding occurs.
- Koebner's phenomenon: New psoriatic lesion is produced when the normal skin of a psoriatic patient is scratched or injured (may occur in surgical scar).

Note Remember the following:

There is moist red surface on removal of the scales called Bulkeley's sign.

Q. What is **Koebner's phenomenon**? What are the **causes** of Koebner's phenomenon?

A. Koebner's phenomenon is the appearance of isomorphic skin lesions at the site of trauma, burn or scratch mark in normal skin. Causes are:

- Psoriasis
- Lichen planus
- Warts (verruca plana)
- Others—vitiligo, pityriasis rubra pilaris, molluscum contagiosum, nummular eczema and Darier's disease.

Q. What are the factors that **aggravate** psoriasis?

A. The aggravating factors are:

1. Trauma
2. Infections—β-hemolytic streptococci (aggravates guttate psoriasis) and HIV infection
3. Psychological factors—emotion and anxiety
4. Drugs:
   - β-Blockers
   - Antimalarial (chloroquine and hydroxychloroquine)
   - Lithium
   - Alcohol
   - Angiotensin-converting enzyme (ACE) inhibitors
   - NSAIDs (e.g. indomethacin)
   - Systemic steroid—the disease is aggravated after withdrawal of steroid (rebound phenomenon) and also after stopping following prolonged use of local steroid
   - Terbinafine
   - Gemfibrozil
   - Glyburide
   - Granulocyte colony stimulating factor
   - Interleukins
   - Interferons
5. Rarely, sunlight (UVR may worsen)
6. Metabolic (hypocalcemia and dialysis).

Q. What is **psoriasis**? What are the various **types** of psoriasis?

A. It is a chronic inflammatory disease of skin characterized by well-defined erythematous plaque with silvery white scales, involving commonly the extensor surface, elbows, knees and sacral regions associated with recurrence and remission. It affects 1 to 2% of the population.

There are four types:

- Chronic plaque psoriasis (Common. Well demarcated, red with a dry silvery white scale. It commonly involves elbow, knee and lower back, but may also involve scalp, nails, flexures, palms).
- Guttate psoriasis (Raindrop-like psoriasis is a variant, common in children and young adults. An explosive eruption of very small circular or oval plaques appears over the trunk about 2 weeks after a streptococcal sore throat. Majority of the patients develop plaque psoriasis in later life).
- Pustular psoriasis (It may be localized involving palm and sole or rarely generalized that may be serious).
- Erythrodermic psoriasis (> 90% of body surface area becomes red and scaly).

Q. What are the **clinical patterns** of psoriasis?

A. According to some authorities, psoriasis is of the following types:

1. Psoriasis vulgaris, chronic stationary psoriasis, plaque type psoriasis

2. Guttate (eruptive) psoriasis
3. Small plaque psoriasis
4. Inverse psoriasis
5. Erythrodermic psoriasis
6. Pustular psoriasis:
   - Generalized pustular psoriasis of von Zumbusch
   - Exanthematic pustular psoriasis
   - Annular pustular psoriasis
   - Localized pustular psoriasis
7. Atypical forms:
   - Linear and zonal lesions
   - Sebopsoriasis
   - Mucosal lesions (rare but has been associated with cutaneous)
   - Ocular lesions—blepharitis, conjunctivitis, keratitis.

Q. What is the **pathology** of psoriasis?

A. Rapid proliferation and abnormal differentiation of epidermis (because of hyperproliferation of keratinocyte) and infiltration of inflammatory cells (polymorph, T-lymphocyte and other inflammatory cells). Accelerated epidermopoiesis is considered to be the fundamental pathological event in psoriasis.

Q. What are the **types of arthritis** in psoriasis?

A. There are 5 clinical patterns of arthritis in psoriasis:
- Asymmetrical DIP joint involvement with nail damage
- Symmetrical polyarthritis, such as rheumatoid arthritis with claw hands
- Asymmetrical oligoarthritis with swelling and tenosynovitis of one or a few hand joints
- Ankylosing spondylitis alone or with peripheral arthritis
- Arthritis mutilans with osteolysis of phalanges and metacarpals.

Q. What are the **complications** of psoriasis?

A. As follows:
- Psoriatic arthropathy
- Exfoliative dermatitis
- Secondary infection
- Hyperuricemia and gout
- Others—amyloidosis, renal failure, hepatic failure and high output cardiac failure because of erythroderma.

Q. How to assess the **severity** of psoriasis?

A. As follows:
- Patient's own perception of disability
- Objective assessment of disability—usually estimated by using the Psoriasis Area and Severity Index (PASI). The areas of involvement, erythema, induration, desquamation (EID) are considered. Maximal score on this index is 72 with mild, moderate and severe having scores of <10, 10 to 50 and > 50 respectively.

Q. Name the drugs that will help to cure **both psoriasis and arthritis**.

A. Methotrexate, azathioprine and acitretin.

Q. How to **treat** psoriasis?

A. As follows:

1. General measures:
   - Explanation and reassurance
   - Avoid trauma, precipitating drugs and anxiety.
2. Specific treatment:
   - Local therapy
   - Systemic therapy
   - Combination therapy.

Local therapy (topical therapy on the lesion):

- Emollient—Lubricate and soothe dry, scaly and inflamed skin. It is helpful in reducing dryness, scaling, cracking, soreness and itching. Common emollients are petrolatum, paraffin, urea (up to 10%), olive oil, etc.
- Salicylic acid (≥ 5%)—It is keratolytic, used to soften and remove scale from psoriatic plaques. It is often combined with other topical medications to enhance their effectiveness (betamethasone dipropionate and salicylic acid). Widespread application may lead to salicylic toxicity, such as tinnitus, acute confusion and refractory hypoglycemia especially in patient with diabetes and compromised renal function.
- Crude tar (3 to 5%)—It inhibits DNA synthesis. Exact action is unknown but has antiproliferative and anti-inflammatory effect. Allergic reactions, folliculitis, carcinoma, offensive odor, staining of clothing are side effects.
- Dithranol (inhibits DNA synthesis).
- Calcipotriol—It is a vitamin D3 analog. It inhibits epidermal proliferation and restores normal horny layer. It is applied locally twice daily, very effective in the treatment of plaque type and scalp psoriasis. It may cause hypercalcemia and hypercalciuria. Combination therapy with calcipotriene and high potency steroids may provide greater response rates, fewer side effects and steroid sparing. Calcipotriene is unstable in the presence of many other topical agents and degrades in the presence of UV light.
- Tazarotene—3rd generation topical retinoid. It acts by modulating keratinocyte differentiation and hyperproliferation, also by suppressing inflammation. Combining its use with a topical corticosteroid and weekend pulse therapy can decrease irritation.
- Topical steroid (mildly potent to super potent according to severity of disease).
- UVR therapy—Narrow band UVB (peak emission around 311 nm) has been proved more effective than broadband UVB. However, it may cause burning. Patients are treated 3 to 5 times per week. On clearing, either treatment is discontinued or patients are subjected to maintenance therapy for 1 to 2 months. During this period, the frequency of UVB therapy is reduced while maintaining the last dose given at the time of clearing.
- Tacrolimus and pimecrolimus—Helpful for thin lesions in areas prone to atrophy or steroid acne. Burning sensation occurs with these agents, but may be avoided by prior treatment with corticosteroid, and by application to dry skin, rather than after bathing.
- Excimer laser—The monochromatic 308 nm excimer laser can deliver supra-erythemogenic doses of light focally to the lesional skin, given twice weekly. The role of this treatment seems to be indicated for patients with stable recalcitrant plaques particularly in the elbow and knee region.

Systemic therapy:

- PUVA (psoralen and UVA)—Long-term use may cause squamous cell carcinoma, basal cell carcinoma and melanoma.
- Retinoid (acitretin)—May help for arthritis and psoriasis (especially pustular and also plaque). Avoid in young female patients (it is teratogenic).
- Methotrexate.

- Azathioprine.
- Cyclosporine is given in patient with widespread, severe inflammatory or erythrodermic psoriasis, mainly if there is failure of other treatment and if the patient cannot tolerate other drugs. It is used as a rotational therapeutic option or as a first line treatment in generalized plaque type psoriasis.
  It acts by down modulation of proinflammatory epidermal cytokines (IL-2, IFN-γ). The dose is 2 to 5 mg/kg/day in adults and 5 to 7 mg/kg/day in children. It can be started with 2.5 mg/kg/day, increased every 2 to 4 weeks up to 5 mg/kg/day. Tapering is recommended on discontinuation. It is effective in up to 90% cases. Nephrotoxicity, hypertension, neurotoxicity and nonmelanoma skin cancers are the side effects. It is not teratogenic. It reduces the effectiveness of progestin based contraceptives.
- Biologic agents—Monoclonal antibody can produce dramatic response in some patients. These agents suppress the normal immune response. Commonly used drug is anti-tumor necrosis factor alpha (anti-TNF-α, such as infliximab, etanercept, adalimumab and efulizumab), and it may be given, when all other drugs fail. Other biologic agents are—alefacept, human interleukin-12/23 monoclonal antibody, etc.
- Other drugs—Tacrolimus, mycophenolate mofetil, hydroxyurea and thioguanine.

Combination therapy:
- MTX plus topical agent
- MTX plus retinoid
- Retinoid plus PUVA
- MTX plus infliximab.

Alternative therapies for psoriasis:
- Mycophenolate mofetil
- Sulfasalazine
- Paclitaxel
- Azathioprine
- Fumeric acid esters
- Climatotherapy
- Grenz ray therapy.

For nail disease:
- Systemic agents
- Topical retinoids
- Local triamcinolone injections
- Topical fluorouracil.

BRIEF DESCRIPTION ABOUT THE DRUGS IN PSORIASIS

Psoralen ultraviolet A (PUVA) therapy:

All types of psoriasis respond to PUVA, though the management of erythrodermic or generalized pustular psoriasis is more difficult.

Mechanism of action:
- Photoconjugation of Psoralens to DNA with subsequent suppression of mitosis, DNA synthesis and cell proliferation, expected to revert increased cell rates in psoriasis to normal.
- May act by affecting immune function through a direct phototoxic effect on lymphocytes in skin infiltrates.

8-Methoxypsoralen (8 MOP) (Oxsoralen) in a dosage of 0.6 mg/kg is administered orally 2 hours before UVA irradiation.

Some patients treated with PUVA are able to achieve long-term remission even without maintenance therapies.

Treatments are administered 2 to 3 times per week and after 20 to 30 treatments, nearly 90% of patients achieved marked improvement or clearing.

Side effects of PUVA:
- Nausea (develops shortly after methoxsalen is ingested)
- Burns
- Lentigines
- Nonmelanoma skin cancer (SCC, BCC)
- Malignant melanoma.

Bath PUVA consists of 15 to 20 minutes of whole body emersion in solution of 0.5 to 5.0 mg 8 MOP per liter of bath water.

This treatment is highly effective for psoriasis of palm and soles that is usually recalcitrant to treatment.

Methotrexate:

Indications:
- Psoriatic erythroderma
- Psoriatic arthritis
- Acute pustular psoriasis (von Zumbusch type)
- Widespread body surface involvement
- Localized pustular psoriasis, palmo-plantar psoriasis that impairs normal function and employment.

Mechanism of action:
- MTX was thought to act directly to inhibit epidermal hyperproliferation via inhibition of dihydrofolate reductase (DHFR).
- It is now thought that the inhibition of DHFR is not the main mechanism of anti-inflammatory action of MTX but rather the inhibition of an enzyme involved in purine metabolism [5 aminoimidazole-4-carboxamide ribonucleotide (AICAR) transformylase].
- This leads to accumulation of extracellular adenosine that has potent anti-inflammatory activity particularly for neutrophils.
- Consistent with a DHFR independent mechanism of action, concomitant administration of folic acid (1 to 5 mg/kg) reduces certain side effects, such as nausea and megaloblastic anemia without diminishing the efficacy of anti-psoriatic treatment.

Dosage:
- Single weekly dose (or 3 divided doses over a 24-hour period)
- A test dose of 5 to 10 mg is given. CBC and liver function test are done 6 to 7 days later
- Dose is gradually increased (2.5 to 5 mg/week), to see the response
- Most patients respond at 10 to 15 mg/week, rarely up to 30 mg/week
- When there is maximum response, MTX is tapered by 2.5 mg/week to see the lowest possible dose that controls the disease
- If single dose exceeds 25 mg, oral absorption is unpredictable and subcutaneous injection is recommended
- Pediatric dose—0.2 to 0.4 mg/kg/wk or 10 mg/m^2/wk.

Adverse effects:
- Nausea, anorexia, vomiting, diarrhea
- Oral and cutaneous ulceration
- Alopecia
- Headache
- Fatigue
- Bone marrow suppression
- Miscarriage and birth defect
- Temporarily effect fertility in males
- Acute pneumonitis
- Hepatotoxicity.

Monitoring guideline:
1. Baseline monitoring:
   - History and physical examination
   - Identification of patients at increased risk for toxicity
   - Recording concomitant medications that may interact with MTX
   - CBC and platelet count
   - Liver function tests
   - Serologic test for hepatitis A, B, C antibodies
   - Renal function tests (BUN, creatinine)
   - HIV testing, if any risk.
2. Follow-up monitoring:
   - CBC, platelet count and LFTs—Every 1 to 2 weeks for 2 to 4 weeks, then 1 to 2 weeks after dose escalation and finally gradually decrease frequency of tests to every 3 to 4 months long-term.
   - Renal function tests (once or twice yearly).

Liver biopsy:
- After every 1.5 to 2.0 g total dose for low-risk patients
- After every 1.0 g total dose for higher-risk patients
- Every 6 months for patients with grade IIIA liver biopsy changes
- Some groups have recommended the use of aminoterminal type III procollagen peptide assay for screening of liver biopsy. But, this is not yet approved by FDA.

Acitretin:

Indications:
- Generalized pustular psoriasis
- Erythrodermic psoriasis
- Severe recalcitrant psoriasis
- Severe plaque type psoriasis.

Mechanism of action:
- Antiproliferative effect
- Anti-inflammatory effect.

Dose:
- 25 mg/day with a maintenance dose of 20 to 50 mg/day
- Pediaric dose is 0.25 mg/kg/day

- Acitretin induces clearance of psoriasis in a dose dependent fashion (higher starting doses appeared to clear psoriasis faster).

Adverse effects:
- Cheilitis
- Dry skin
- Hair loss
- Failure to develop normal nail plate
- Periungual pyogenic granuloma
- Hyperlipidemia (particularly triglyceridemia)
- Pseudotumor cerebri (headache)
- Osteoporosis
- Calcification of ligaments
- Skeletal hyperostosis.

Fertile women with severe psoriasis who take acitretin must follow two methods of contraception or abstinence and have monthly pregnancy test during therapy and for an additional 3 years after withdrawal of drug.

Monitoring guideline:
1. Baseline monitoring:
   - History and physical examination
   - Pregnancy test
   - CBC and platelet count
   - Liver function test
   - Lipid profile
   - Renal function test (creatinine, BUN)
   - Urine analysis (if patients have renal diseases, proteinuria, diabetes or hypertension)
   - Consider baseline X-rays of wrist, ankles, or thoracic spine, for long-term retinoid therapy.
2. Follow-up monitoring—Monthly for the first 3 to 6 months, then every 3 months:
   - History and physical examination
   - CBC with platelet counts
   - Liver function test (AST, ALT)
   - Lipid profile (TG, cholesterol)
   - Renal function test
   - Urine analysis
   - Pregnancy test.

Most patients relapse within 2 months after discontinuing acitretin.

Acitretin should be discontinued if liver dysfunction, hyperlipidemia or diffuse idiopathic hyperostosis occurs.

Topical corticosteroid:

Topical application of corticosteroids in creams, ointments, lotions, foams and sprays is the most frequently prescribed therapy for psoriasis. Therapy can be continued with pulse applications on weekends to reduce the incidence of local adverse effects. Low to mid-strength steroids are preferred in the intertriginous areas and on the face. Areas with thick keratotic scales should be hydrated and covered with occlusive dressing after giving potent or super potent steroid.

Mechanism of action:

- Potent anti-inflammatory effects by inhibiting the release of phospholipase A_2
- They reduce T-cell proliferation and induce T-cell apoptosis
- Several cytokines are directly affected by corticosteroids including IL-1, TNF-α, GM-CSF and IL-8.
- The antiproliferative effect is mediated by inhibition of DNA synthesis and mitosis.

Side effects:

- Epidermal atrophy, thinning
- Striae
- Steroid acne
- Miliaria
- Pyoderma
- Hypopigmentation, persistent erythema, telangiectasia, hypertrichosis
- Tachyphylaxis.

No more than 45 g/week of potent or 100 g/week of weak or moderately potent topical corticosteroid should be applied, if systemic absorption is to be avoided.

DARIER'S DISEASE OR KERATOSIS FOLLICULARIS

CHIEF COMPLAINTS

- Multiple hyperpigmented pruritic elevated lesions over the different parts of the body for … months.
- Pain over some of the lesions for … months.

HISTORY

History of present illness: The patient states that he was quite well … months back. Since then, he noticed multiple hyperpigmented, rough, elevated lesions with mild pruritus over the scalp and nose. Gradually there is involvement of the forehead, face, ears, retro-auricular region, front of the chest, dorsum of both hands, back, lower legs and feet. Initially the lesions were relatively small, but gradually increased in size and extent, larger lesions involved the legs. Most of the lesions are covered with greasy crusts. The lesions are painful for the last … months. The pain is dull in nature that increases in intensity by touch or movement. He noticed occasional bleeding from the lesions on the lower part of the legs. There is no history of weight loss, anorexia, fever and joint pain. His bowel and bladder habits are normal.

History of past illness: The patient suffered from eczema on hands … years back. No other serious illness.

Drug history: He was treated by local physicians with azithromycin, doxycycline, aspirin, prednisolone, triamcinolone injection, etc. but there was no significant improvement.

Family history: His parents and siblings are all in good health and there is no such illness in his family.

Personal history: He is a shop-keeper,, smoker, used to take 3 to 5 sticks per day for 10 years. There is no history of sexual exposure.

Socioeconomic condition: He comes from a poor family with a monthly income of about 2000 Rs. He lives in a small house with poor sanitation and water supply.

GENERAL EXAMINATION

- The patient is ill looking and emaciated
- He is mildly anemic
- No jaundice, cyanosis, clubbing, koilonychia, leukonychia, edema
- There is no thyromegaly or lymphadenopathy
- Pulse: 72/min
- Blood pressure: 130/80 mm of Hg
- Temperature: 98ºF
- Respiratory rate: 18/min.

Integumentary System

1. **Skin:**
   - **Inspection**—There are multiple dirty, warty, greasy, crusted, bilaterally symmetrical papules are present over face, scalp, ear, front of the chest, back of the hands, lower part of both legs and dorsum of both feet. Some of the lesions of lower legs fused to form vegetating growths that are malodorous, fissured and eroded. Purulent exudate is present in between some of the lesions.
   - **Palpation**—The lesions are rough and firm in consistency, mostly non-tender but few on the legs are tender. After removal of the crust, there is eroded surface with bleeding points. Palms and soles are uniformly thickened.
2. **Hair:** Scalp is covered by greasy crust and hair is sparse.
3. **Nails:** Fragile with subungual hyperkeratosis, splintering, triangular nicking and alternate white and red streaks.
4. **Mucous membrane:**
   - Conjunctiva—normal
   - Oral mucosa—small white papules (cobble stone papules) on the palate
   - Genitalia—normal.

Examination of other systems reveals no abnormalities.

SALIENT FEATURE

Mr …, 25 years, shopkeeper, normotensive, nondiabetic, smoker, hailing from …, presented with the complaints of multiple hyperpigmented, dirty, warty, greasy, crusted papules and pruritus for … months. The lesions appeared first on forehead and nose and then gradually involved other parts, such as scalp, ear, front of the chest and limbs. These gradually increased in size and extent. He also complains of pain in some of the lesions for … months. The lesions on the lower part of the legs are larger, painful, malodourous and bleed occasionally. For this illness, he took azithromycin, aspirin, doxycycline, prednisolone, triamcinolone, etc. as advised by local physicians but there was no significant improvement. He had suffered from eczema … years back. There is no such illness in the family. He smokes 3 sticks of cigarette a day for the last 10 years.

On general examination – describe as above.

Examination of integumentary system – describe as above.

Examination of other systems reveals no abnormalities.

My diagnosis is Darier's disease.

Q. What are your **differential diagnoses?**

A. As follows:
- Arsenicosis
- Seborrheic folliculitis
- Pityriasis rubra pilaris
- Kyrle's disease.

Q. What are the **points in favor** and **against**?

A. As follows:

Differential diagnoses	Points in favor	Points against
1. Arsenicosis	» Drinks tubewell water » Keratotic papules present	» Punctate keratosis absent in palms and soles » No rain drop pigmentation » Face is affected severely
2. Seborrheic folliculitis	» Greasy papules present in seborrheic areas » Pruritus present	» Papules are dirty and warty » These are present in areas other than seborrheic areas, such as lower legs, palms, soles, nails and palate
3. Kyrle's disease	» Keratotic papules » Limbs, head, neck affected	» Dirty, warty, greasy crusted papule » Seborrheic area affected » Young age » Nondiabetic
4. Pityriasis rubra pilaris	» Follicular papules present » Plantar hyperkeratosis present	» Papules over the back of the fingers absent. » No nutmeg grater and islands of normal skin » Lesions are not papillosquamous

Q. What **investigations** should be done in this case?

A. As follows:

1. Routine:
   - Complete blood count
   - Blood sugar
   - Stool R/M/E
   - Urine R/M/E
   - Chest X-ray P/A view
   - Bleeding time, clotting time
   - Hair arsenic level (to exclude arsenicosis)
   - Others—Lipid profile (before starting retinoids), ECG, USG of whole abdomen
2. To confirm diagnosis—skin biopsy for histopathology.

RELATED QUESTIONS AND ANSWERS

Q. How to **treat?**

A. As follows:

A. Local treatment:
   - Dressing of the ulcerated lesions
   - Mupirocin ointment
   - Isotretinoin cream.

B. Systemic treatment:
   - Acitretin 10 mg daily
   - If infection, antibiotic should be given
   - Iron, vitamin and mineral may be used.

Q. What is **Darier's** disease?

A. Darier's disease is a genodermatosis, inherited as autosomal dominant with high penetrance (95%). New mutations are common. It does not manifest at birth, but majority is seen before 30 years. Males and females are affected equally. Prevalence is from 1 in 50,000 to 1 in 100,000.

Q. What are the diseases that show **disorders of keratinization?**

A. Diseases due to disorders of keratinization are:
- Darier's disease
- Congenital and acquired ichthyosis
- Pityriasis rotunda
- Porokeratosis
- Acrokeratosis verruciformis
- Palmoplantar keratoderma
- Knuckle pads.

Q. What are the **sites of involvement** of Darier's disease? How does it **manifest?**

A. As follows:
1. Seborrheic area: Face, scalp, forehead, nasolabial furrows, retroauricular region, lip, front of the chest, back, axilla, anogenital region, natal cleft. In these areas, the disease is manifested by dirty, warty, greasy, crusted papules that are usually symmetrical and widespread. As the lesions grow older, they fuse to form malodorous papillomatous and vegetating growths. These are eroded, fissured and covered by purulent exudate. There may be pain, pruritus and bleeding from the lesions and photokoebner.
2. Sites without sebaceous glands: Palms and soles. In these sites, features may be:
   - Uniform horny thickening
   - Punctate or filiform keratosis
   - Minutes pits (pathognomonic)
   - Dermatoglyphics will be normal.
3. Mucous membrane: White cobblestone papules may be seen on the palate, tongue, buccal mucosa, epiglottis. Pharyngeal wall, esophagus, rectum, larynx and vulva may also be involved. Confluence of the papules may simulate leukoplakia.
4. Nails: Show subungual hyperkeratosis, fragility, splintering with longitudinal alternating white and red streaks. Triangular nicking of the free edges will also be present.
5. There can be blockage of external auditory meatus and salivary glands also. Cornea may be affected rarely.

Q. What are the **types** of Darier's disease?

A. Four types:
1. Classical or seborrheic
2. Unilateral or zosteriform
3. Hypertrophic-in flexure like axilla, groin
4. Vesico bullous form.

Q. What are the diseases with **seborrheic presentation?**

A. As follows:
- Seborrheic dermatitis
- Darier's disease
- Seborrheic keratosis
- Letterer Siwe disease
- Pellagra
- Brazilian pemphigus.

Q. What are the diseases with **seasonal variations?**

A. As follows:

- Darier's disease—worse in summer
- Pellagra—worse in spring
- Eruptive keratoacanthoma—worse in summer
- Pityriasis rotunda—summer remission
- Hailey-Hailey disease—more protracted during summer.

Q. What are the **complications** of Darier's disease?

A. As follows:

- Herpes simplex infection
- Chronic pyogenic infection
- Kaposis varicelliform eruption
- Pox virus infection
- Defect in cell mediated immunity (complete anergy to skin test of delayed hypersensitivity). No abnormality to humoral immunity.

Q. What are the **differential diagnoses** of Darier's disease?

A. According to site of involvement, it may be confused with:

- Scalp—simulate seborrheic dermatitis
- Face—acne, seborrheic dermatitis
- Dorsum of hand, foot and shin—acrokeratosis verruciformis of Hopf, angiokeratoma, arsenicosis, follicular—pityriasis rubra pilaris, phrynoderma, keratosis pilaris, Kyrle's disease
- Trunk—arsenicosis, epidermodysplasia verruciformis
- Linear lesion—linear epidermal nevus
- Flexural—acanthosis nigricans, reticular papillomatosis, pemphigus vegetans.

Q. What are the **histopathological findings** of Darier's disease?

A. As follows:

- Hyperkeratosis, parakeratosis, acanthosis.
- Formation of suprabasal cleft lacuna via acantholysis with villi in the lacuna. In the lacuna, acantholytic dyskeratotic keratinocytes termed corps ronds and grains are present.
- Dermis shows chronic inflammatory infiltrate. Basal keratinocytes herniate into the dermis through the defect in the basal lamina.
- Vesicobullous lesion—lacuna are smaller in size. It contains numerous shrunken cells with appearance of grains.
- Mucosal lesion—similar but definite corps ronds and grains are usually absent.

Note Remember the following:

- Lacuna is formed by the changes in tonofilaments that become separated from desmosomes. Villi are the irregular upward proliferation into the lacuna of papilla lined by single layer of basal cells.
- Corps ronds are present mainly in the spinous layer. These are keratinocytes with a basophilic nucleus surrounded by a halo. Peripheral to the halo, basophilic dyskeratotic material lie as a shell. Due to the halo, they are conspicuous. These cells show premature partial keratinization.
- Grains are small dark cells with shrunken cytoplasm and pyknotic nucleus. They lie mostly in stratum corneum and as acantholytic cells in the lacuna.

Q. What are the types of dyskeratosis?

A. Two types:

1. Acantholytic dyskeratosis—occurs as corps ronds that are seen in:
   - Darier's disease
   - Warty dyskeratoma
   - Focal acantholytic dyskeratoma
   - Benign familial pemphigus.
2. Neoplastic dyskeratosis—also referred to as individual cell keratinization, manifests itself as homogeneous, eosinophilic bodies about 10 micron in diameter that occasionally show remnants of their nucleus. These may be seen in Bowen's disease, solar keratosis, squamous cell carcinoma, keratoacanthoma. It is not necessarily an indication of malignancy.

Q. What are the diseases associated with Darier's disease?

A. As follows:

- Retinitis pigmentosa
- Asymptomatic bone cyst
- Renal and testicular agenesis
- Autoimmune thyroid disease
- Epilepsy and encephalopathy.

Q. What are the modalities of treatment of Darier's disease?

A. As follows:

1. General measures:
   - Mild disease requires no treatment other than a simple emollient
   - The patient should be advised about the effects of sunshine.
2. Topical treatment:
   - Retinoids, such as tretinoin, 13-cis-retinoic acid, adalpene, tazarotene can be used.
3. Systemic treatment:
   - Isotretinoin, acitretin, cyclosporine can be used to control severe flares
   - Secondary infection with *Staphylococcus aureus* is responsible for some flares. In such case, antibiotic, such as cloxacillin, fluocloxacillin or cephalosporin should be given.
4. For hypertrophic lesions:
   - Dermabrasion
   - Laser excision
   - Excision and grafting

Q. What are the characteristics of autosomal dominant diseases? Name some autosomal diseases with dermatological manifestations.

A. Characteristics of autosomal dominant disease:

- It affects both male and female
- Affected individuals are heterozygous for the abnormal allele
- Every patient will have an affected parent apart from new mutations
- Half of the children of the affected parents will be affected
- Age of onset of the disease is variable. Affected person may remain symptom free up to adult life
- Severity of the disease will vary among the affected members of the family
- A few of the patients show lack of penetrance. These patients inherit the gene but do not show the disorder.

Autosomal dominant diseases with dermatological manifestations are:

- Neurofibromatosis

- Tuberous sclerosis
- Benign familial pemphigus
- Epidermolysis bullosa simplex
- Pseudoxanthoma elasticum
- Cutis laxa
- Darier's disease
- Acrokeratosis verruciformis of Hopf
- Pachyonychia congenita
- Monilethrix
- Peutz-Jeghers syndrome.

Q. What are the characteristics of **autosomal recessive** (AR) diseases? Name some AR disease with dermatological manifestation.

A. Characteristics of AR diseases are:
- It affects both male and female
- Affected individuals are homozygous for the abnormal allele
- Autosomal disorder occurs in a person whose healthy parents carry the same recessive gene
- Average 1 in 4 of children of heterozygous parents will be affected
- There is no family history although the defective gene may pass generation to generation
- It occurs within the group of brother and sister
- Consanguinity increases the risk of autosomal recessive disorders
- The offspring of the affected patient will be normal provided the other parent is normal
- The diseases are severe. Many of the autosomal recessive disorders are inborn error of metabolism.

Autosomal recessive diseases with dermatological manifestations are:
- Junctional epidermolysis bullosa
- Dystrophic epidermolysis bullosa, recessive form
- Werner's syndrome
- Harlequin fetus
- Lamellar ichthyosis
- Nonbullous ichthyosiform erythroderma
- Albinism
- Xeroderma pigmentosa
- Bloom syndrome
- Ataxia telangiectasia.

Q. What are the characteristics of **X-linked recessive** (XR) disorders? Name some XR diseases.

A. The characteristics of XR diseases are:
- Only males are affected
- The disorder is transmitted through healthy female carrier
- A female carrier will transmit the disease to half of her sons and half of her daughters will be the carrier
- When a male is affected, all his daughters will be the carrier
- This trait cannot be transmitted from father to son
- Frequently mother's brother will be affected
- X-linked disorders should be considered when family history indicates affected male in different generations
- Family history may not be always positive, as new mutations are common.

Some of the X-linked diseases are the following:

1. **Dermatological:**
   - Anhidrotic ectodermal dysplasia
   - X-linked ichthyosis
   - Ehler Danlos syndrome-type V
   - Ocular albinism
   - Menkes syndrome
   - Chronic granulomatous disease.
2. **Musculoskeletal:**
   - Duchenne muscular dystrophy.
3. **Blood:**
   - Hemophilia A and B
   - Glucose-6-phosphatase dehydrogenase deficiency.
4. **Immune:**
   - Agammaglobulinemia
   - Wiskott Aldrich syndrome.
5. **Metabolic:**
   - Diabetes insipidus.
6. **Nervous:**
   - Fragile X syndrome.

POST KALA-AZAR DERMAL LEISHMANIASIS (PKDL)

CHIEF COMPLAINTS

- Several hypopigmented lesions all over the body for … years
- Few nodules on the face and ulcer on the lower part of the right leg for … years
- Reddish skin lesions over face and upper arms for … months.

HISTORY

History of present illness: The patient states that he noticed several round hypopigmented skin lesions all over the body for the last … years. Initially, there were few non-itchy and painless lesions on the trunk. These slowly spread all over the body. He also noticed few painless nodular lesions of variable size and shape over the face, ear lobule and chin, some of which are gradually increasing in size. He also complains of two leg ulcers on the medial aspect of lower part of right leg that started as a small papule, became nodular and then ulcerated. These are slightly painful, itchy, and did not heal with local and systemic antibiotic therapy. For the last … months, the patient has also noticed few reddish skin lesions over the face and upper arms. There is no history of loss of appetite or weight loss. His bladder and bowel habits are normal.

History of past illness: He suffered from kala-azar (leishmaniasis) … years back and was treated with 20 injections of sodium stibogluconate.

Family history: Mention according to the patient's statement.

Personal history: He is a nonsmoker, nonalcoholic. There is no history of exposure.

Socioeconomic condition: Mention according to the patient's statement.

Treatment history: For the present problem, he has taken many antibiotics as prescribed by various doctors, but his condition did not improve.

GENERAL EXAMINATION

- The patient is anxious
- Mildly anemic
- No jaundice, cyanosis, clubbing, koilonychia, leukonychia, edema
- There is no thyromegaly or lymphadenopathy
- Pulse: 80/min
- Blood pressure: 120/80 mm of Hg
- Temperature: 98ºF
- Respiratory rate: 20/min.

Integumentary System

1. **Skin:**
   - Inspection:
     - There are multiple nodules of various size and shape on the nose, cheeks and ear lobules. These are pale, pink and wart-like.
     - Reddish lesions of various sizes and shapes are present on the face and flexor aspect of both forearms.

- There are bilateral, symmetrical, multiple hypopigmented macules and patches of various shape and size, seen on both the extremities and trunk. There is no scaling.
- There are two ulcers measuring 3 cm × 2.5 cm and 1.25 cm × 1.5 cm, situated on the anterolateral aspect of right leg near ankle. These are round in shape with irregular margin. Base is covered with crust. There is some oozing. Surrounding skin is hyperpigmented and erythematous.

♦ Palpation: Nodules are firm in consistency, nontender, mobile. Hypopigmented and erythematous macules and patches are also nontender with intact sensation. Edges of the ulcers are firm and slightly tender.

♦ Peripheral nerves are neither enlarged, nor tender. Peripheral pulses are normal.

2. **Mucous membrane:** Conjunctiva, oral mucosa and genital mucosa are normal.
3. **Hair:** Normal.
4. **Nails:** Discoloration of all fingernails.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, a 65 year old farmer, nonsmoker, nondiabetic, hailing from …, presented with several hypopigmented, non-itchy, painless skin macules and patches on the trunk for the last … years that slowly spread all over the body. He also noticed few painless nodular lesions of variable size and shape over the face, ear lobule and chin, some of that are gradually increasing in size. The patient also complains of two leg ulcers on the medial aspect of lower part of right leg that started as a small papule, became nodular and then ulcerated. These are slightly painful, itchy, and did not heal with local and systemic antibiotic therapy. For the last … months, the patient also noticed few reddish skin macules and patches over the face and upper arms.

The patient had suffered from kala-azar about … years back and was treated with 20 injections of sodium stibogluconate. For the current problem, he was treated with many antibiotics and local ointments from various local doctors, but his condition did not improve. There is no family history of similar illness.

On general examination – mention as above.

Examination of the integumentary system – as above.

Examination of other systems reveals no abnormalities.

My diagnosis is post kala-azar dermal leishmaniasis.

Q. How to **confirm** PKDL?

A. To confirm PKDL the following investigations may be done:

❖ Demonstration of amastigote form of LD bodies in smear prepared from biopsy material from nodular lesions (No LD bodies are found in depigmented lesion).

❖ PCR and monoclonal antibodies may detect parasites in more than 80% of cases.

Note Remember the following:

Serological tests and the leishmanin skin test are of limited value.

Q. What are your **differential diagnoses**?

A. As follows:

❖ Lepromatous leprosy

- Pityriasis versicolor
- Dermatomyositis
- SLE
- MCTD
- Others (rare)—Acne rosacea, syphilis (secondary), rhinophyma (irregular thickening of skin of nose with enlarged follicular orifice).

Q. What are the **points in favor** and **against** your differential diagnoses?

A. As follows:

Differential diagnoses	Points in favor	Points against
1. Lepromatous leprosy	» Bilateral, symmetrical hypopigmented macules and erythematous patches » Nodules over face and ear lobules	» Past history of kala-azar » Absence of madarosis » No nerve enlargement » Skin sensation—intact
2. Pityriasis versicolor	» Hypopigmented macules	» Long history, also history of kala-azar » Absence of pruritus, scaling » Presence of erythematous plaques
3. Dermatomyositis	» Only multiple skin lesions	» No muscular complaints, polyarthritis, proximal myopathy, heliotrope rash » No history of malignancy
4. SLE	» Only skin lesion	» History of kala-azar » No other systemic features or vital organ involvement » Does not fulfill the diagnostic criteria of SLE

RELATED QUESTIONS AND ANSWERS

Q. What is **post kala-azar dermal leishmaniasis**?

A. It is a non-ulcerative cutaneous lesion that occurs after treatment and apparent recovery from visceral disease. Initially, the lesions start as macules, become erythematous, followed by wart-like nodular lesions. It mainly involves the face, especially around the chin, also ear lobules. There may be butterfly like distribution of the lesion. Hypopigmented macules can occur in all parts of the body. No systemic symptoms and no spontaneous healing. Amastigotes are scanty in the lesion.

Note Remember the following:

In a small proportion of patients with PKDL, there is no preceding history of visceral disease suggesting a subclinical infection.

Q. How many **forms** are found in PKDL?

A. It is found in two forms:

1. African form (Sudanese form):
   - About 50% patients with visceral leishmaniasis develop PKDL. In Sudan, children are more affected than Indian subcontinent.
   - This may develop concurrently with visceral leishmaniasis or within 6 months afterwards.
   - The lesions are composed of discrete papules on the cheeks, chin, ears, extensor surfaces of forearms, buttocks and lower legs.
   - In addition to dermatological features described above, measles like maculopapular rash may develop all over the body.
   - It improves spontaneously in 3/4th cases within 1 year.
   - Leishmanin test is positive.
   - Histology reveals tuberculoid type with scanty parasites.
2. Indian form:
   - In Indian type, PKDL occurs in a small minority of patients 6 months to > 3 years after initial infection.
   - Lesions appear on the face, trunk, extremities (confused with lepromatous leprosy).
   - These are progressive and seldom heal spontaneously.
   - Tongue, palate and genitalia may be involved.
   - There may be lymphadenopathy but viscera are spared and there is no evidence of relapse of previous systemic infection.
   - Leishmanin test is negative.
   - Histopathology reveals differentiated infiltrate of chronic inflammatory cells with variable number of parasites in dermal macrophage.

Q. What are the **mechanisms** of PKDL?

A. After treatment, visceral infection disappears, but there is persistence of skin infection. After variable period, skin resistance is lost with resurgence of old infection that causes PKDL. It is considered as an important parasitic reservoir and source of transmission of kala-azar.

Q. How to **treat** PKDL?

A. As follows:

- Injection sodium stibogluconate (given in cycle), 20 mg/kg daily for 20 days. After 10 days interval, the injection is repeated. Totally 6 cycles are needed with an interval of 10 days.
- If a second course is required, it should be given after an interval of 2 months.
- In Sudan, sodium stibogluconate is given for 2 months.
- Several courses of amphotericin B infusion may also be given.
- Miltefosine may also be effective in PKDL.

Note Remember the following:

Treatment is always needed in Indian PKDL. In Sudan, most cases cure spontaneously, but severe and chronic cases should be treated.

Q. What are **other drugs** that can be given in PKDL?

A. Systemic drugs that are reported to be effective are ketoconazole, itraconazole, rifampicin and dapsone.

Note Remember the following:

Pentamidine is ineffective in PKDL.

Q. What are the **types** of lesions in PKDL?

A. These are mainly of 3 types:

1. **Macular:** May be hypopigmented, depigmented, hyperpigmented or erythematous (butterfly like rash, which is aggravated by sunlight).
2. **Elevated lesion:** Papular, nodular, plaque, hypertrophic, verrucous (around nose), xanthomatous around chin, fibroid around calf muscle.
3. **Ulcerative:** Rarely in nodular lesions.

Q. What are the **differential diagnoses** of PKDL?

A. The differential diagnoses vary according to the type of lesion:

1. **Macular:**
   - Lepromatous leprosy
   - Pityriasis versicolor
   - Pityriasis alba
   - Vitiligo
   - Nutritional dyschromia.
2. **Plaque:**
   - Lepromatous leprosy
   - Sarcoidosis
   - Deep mycosis
   - Tertiary syphilis
   - Leukemia cutis
   - Mycosis fungoides.
3. **Nodular:**
   - Lepromatous leprosy
   - Neurofibromatosis
   - Eruptive xanthoma
   - Familial lipomatosis
   - Sarcoidosis
   - Deep mycosis
   - Tertiary syphilis
   - Leukemia cutis
   - Mycosis fungoides.

Q. What are the **complications** of PKDL? **Why treatment** is given?

A. The PKDL itself has no complication other than disfigurement. PKDL patients serve as an important source of infection. Treatment should be given for the benefit of the community.

Q. What are the **differences** between PKDL and lepromatous leprosy?

A. As follows:

Points	PKDL	Lepromatous leprosy
1. Induration	Usually absent	Usually present
2. Loss of eyebrows	Absent	Present
3. Nerve enlargement	Absent	Present
4. Sensation	Intact	Impaired
5. Lymphadenopathy	May be present	Absent

Contd...

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6. Visceral involvement	Spared	Involved
7. Slit skin smear	LD bodies	AFB
8. Complication	No complication except reservoir	Many complications, such as nerve damage, claw hand, foot drop, iritis, iridocyclitis, involvement of liver, spleen, testicles, etc.

Q. Which form of PKDL contains **amastigote** form of parasite?

A. Amastigotes can be found in warty papular eruptions.

Q. Which type of patients usually develops **Indian form** of PKDL?

A. There is evidence that patients who will develop this condition have marker interleukin-10 in their keratinocytes and sweat glands.

LEPROMATOUS LEPROSY

CHIEF COMPLAINTS

- Multiple nodular lesions on ear lobe, face, forearm and legs for … months
- Hypopigmented lesions on both side of nose for … months
- Generalized weakness for … months.

HISTORY

History of present illness: The patient states that he was alright … months back. Since then, he noticed some nodules on different parts of the body, first on the front of the legs and dorsum of feet and later on the face, ears and forearms. These nodules are painless, non-itchy and without any discomfort. There are also few painless, non-itchy hypopigmented lesions on both sides of nose for … months. He does not feel any abnormal sensation over these lesions.

The patient also complains of generalized weakness for … months for which he is unable to perform his daily duties. There is no history of fever, arthralgia, mouth ulcer, etc. His bowel and bladder habits are normal.

History of past illness

Family history

Personal history

Socioeconomic condition

Drug history: Mention according to the statement of the patient.

GENERAL EXAMINATION

- Appearance normal
- Mildly anemic
- No jaundice, cyanosis, clubbing, koilonychia, leukonychia, edema
- No thyromegaly or lymphadenopathy
- Pulse: 88/min
- Blood pressure: 110/70 mm of Hg
- Temperature: 98ºF
- Respiratory rate: 18/min.

Integumentary System

1. **Skin:**
   - Inspection:
     - Multiple nodules of variable size and shape are present on ears, face, forearms, legs and feet that are bilateral and symmetrical.
     - There are also hypopigmented macules on both sides of nose that are ill defined and blend into the surrounding skin.
   - Palpation:
     - The nodules are nontender, firm in consistency and without any loss of sensation.
     - The hypopigmented macules are nontender. There is no loss of sensation.

2. **Hair:** Hair is lost on the outer-third of the eyebrows.
3. **Mucous membrane:**
   - Conjunctiva—normal
   - Oral mucosa—normal
   - Mucosa—normal.

Nervous System

- Supraorbital, great auricular, median, ulnar, radial, lateral popliteal and posterior tibial nerves are thickened bilaterally, but nontender
- There is no loss of sensation
- Reflexes are normal.

Examination of other systems reveals no abnormalities.

SALIENT FEATURE

Mr …, 50 years old, shopkeeper, normotensive, nondiabetic, hailing from …, was admitted into the hospital with the complaints of multiple nodular lesions on ear lobe, face, forearm and legs for … months and hypopigmented lesions on both side of nose for … months. The nodules first started on the front of the legs and dorsum of feet. Later, these lesions involved the face, ears and forearms. These are not associated with pain, itching or any discomfort. There are also few painless, non-itchy hypopigmented lesions on both side of nose for … months. He does not feel any abnormal sensation over these lesions. The patient also complains of generalized weakness for … months for which he is unable to perform his daily duties. There is no history of fever, arthralgia, mouth ulcer, etc. His bowel and bladder habits are normal. The patient was treated with vitamins and different types of creams and ointments by local physicians. There is no family history of similar illness.

On general examination – (mention as above).

On examination of the integumentary system – (mention as above).

Examination of other systems reveals no abnormalities.

My diagnosis is lepromatous leprosy.

Q. Why your diagnosis is lepromatous leprosy?

A. Because:
- The patient is from endemic zone
- Typical nodular lesion (leonine facies), hypopigmented macules and thickening of multiple nerves are highly suggestive.

Q. What are your differential diagnoses?

A. As follows:
- PKDL
- Neurofibromatosis
- Others: Sarcoidosis, drug rash, acne rosacea, dermatomyositis, SLE.

Q. What are the points in favor and against your differential diagnoses?

A. As follows:

Differentials	Points in favor	Points against
1. PKDL	Bilaterally symmetrical nodules and macules on face, ears, forearms and legs	No history of kala-azar in the past All peripheral nerves are thickened
2. Neuro-fibromatosis	Multiple nodules all over the body	No family history Nodules are firm in consistency Buttonholing sign absent Café au lait macule absent

Q. What specific **investigations** are done to diagnose (confirmatory) leprosy?

A. As follows:

- Demonstration of acid fast bacilli from slit skin smear, nasal scraping or biopsy material from skin or thickened nerve (Slit skin smear is prepared by Ziehl-Neelson method using 5% sulfuric acid. In developed countries, Fite-faraco stain is used).
- Skin biopsy for histopathology.

Q. What are the **histological findings** in leprosy?

A. As follows:

- In tuberculoid type, epithelioid granuloma may be found.
- In lepromatous leprosy, *M. leprae* may be found in skin macrophage (also Schwann cells and perineurium).

Q. What are the other **investigations** done to diagnose leprosy?

A. As follows:

- Histamine test: A drop of 1:1000 solution of histamine is put into the test area and outside area. A pin prick is made with each drop. A wheal forms, but red flare is absent in the affected area.
- Methacholine test: Skin is painted with 2% iodine. 1 mL of methacholine is injected intradermally in the affected area. Powder starch is dusted over the part. Powder turns blue by the interaction of sweat and iodine in the unaffected area that is absent in the affected area.
- Lepromin test to assess immune status.
- Newer diagnostic test:
  - Fluorescent lepromin antibody absorption test—low specificity.
  - Antibody against PGL-1, lipoarabinomannan and the protein antigens of *M. leprae*. PGL-1 antibody is positive in 90% of multibacillary, 40 to 50% of paucibacillary and 5 to 10% of healthy controls.
  - PCR.

Q. What are the **supportive investigations** of leprosy?

A. As follows:

- Full blood count (may be anemia, lymphopenia, high ESR because of hyperglobulinemia).
- Urine RME (may be proteinuria due to focal glomerulonephritis).
- Increased serum lysozyme and angiotensin converting enzyme due to accumulation of macrophages that synthesize these proteases.
- Increased FSH and LH and decreased testosterone (due to involvement of testicles).
- Organ specific antibodies against thyroid, nerve, testis and gastric mucosa.
- Nonorgan specific—RA, ANA, biological false positive test for syphilis.

Q. How can you **diagnose** leprosy?

A. As follows:

- Clinically leprosy can be diagnosed on the basis of two out of 3 findings:
  - Anesthesia of a skin lesion or in the distribution of a peripheral nerve or over dorsal surfaces of hand and feet.
  - Thickened nerve at the site of predilection.
  - Typical skin lesion.
- By demonstration of AFB in slit skin lesions.
- Histology: Typical of leprosy.

RELATED QUESTIONS AND ANSWERS

Q. What is **leprosy?**

A. Leprosy is a chronic granulomatous disabling disease caused by *Mycobacterium leprae* affecting the peripheral nerves, skin, mucous membrane, anterior segment of eye, bone and viscera. It is mildly communicable with good prognosis, if treated early and adequately.

M. leprae is a Gram-positive, acid fast and alcohol fast bacillus, also called Hansen's bacillus. Man is the only reservoir of infection. Route of transmission—nasal, oral, sometimes skin contact (if ulcerated).

Q. What are the types (or **classification)** of leprosy?

A. There are five types (according to Ridley and Jopling):

- Tuberculoid leprosy (TT)
- Borderline tuberculoid (BT)
- Borderline-borderline leprosy (BB)
- Borderline lepromatous leprosy (BL)
- Lepromatous leprosy (LL).

Depending on the cell mediated immunity (CMI), leprosy is divided into 2 polar forms and a borderline form.

Also, classified into **two types:**

- Paucibacillary: Few organisms in tissue. Skin smear for *M. leprae* bacilli is negative or few (found in TT and BT).
- Multibacillary: Large number of organisms in tissue. Skin smear for *M. leprae* bacilli is positive (found in BT, all BB, BL and LL).

Q. What are the **findings** in different types of leprosy?

A. As follows:

Points	Tuberculoid (TT)	Borderline tuberculoid (BT)	Borderline (BB)	Borderline lepromatous (BL)	Lepromatous leprosy (LL)
1. Host resistance	High resistance	Unstable resistance			No resistance
2. Lesions	One to three	Few	Few or many Asymmetrical	Many	Numerous and symmetrical
3. Smear for bacilli	0	1+	2+	3+	4+
4. Lepromin test	3+	2+	+	±	0
5. Histology	Epitheloid cells, nerve destruction, sarcoid like granuloma	Decreasing	Decreasing	Increasing foam cells, xanthoma	Histocytes granuloma

Q. What are the **differences** between tuberculoid and lepromatous leprosy?

A. As follows:

Points	Tuberculoid	Lepromatous
1. Number	1 to 5	Numerous
2. Distribution	Asymmetric, anywhere especially face, limb and trunk (sparing scalp, axilla, perineum)	Symmetrical except spared areas
3. Margin	Well-defined	Ill-defined
4. Lesion	Plaque or macule	Macule, plaque, nodule and infiltration
5. Size	Usually large	Usually small
6. Anesthesia, autonomic loss and nerve enlargement	Early and marked, localized to the lesional skin or major peripheral nerve	Late and extensive
7. Skin texture	Dry, hard, pebbled	Smooth, shiny, normal texture
8. Hair growth	Absent in lesion	Normal
9. Mucosal involvement	Absent	Common
10. Bacillary index	Absent	Present in large number
11. Lepromin test	Strongly positive	Negative
12. Other organ involvement	Nil	Eye, bone, testis, kidney, reticuloendothelial system is involved

Q. What are the **differential diagnoses** of leprosy?

A. As follows:

1. Macular lesion:
- Vitiligo
- Pityriasis versicolor
- Pityriasis alba
- PKDL
- Healed herpes zoster
- Nevus anemicus
- Nutritional dyschromia.

2. Plaque type lesion:
- Lupus vulgaris
- Lupus erythematosus
- Tinea circinata
- Psoriasis
- Seborrheic dermatitis
- Annular syphilides
- Sarcoidosis
- PKDL.

3. Nodular:
- PKDL
- Neurofibromatosis
- Cutaneous leishmaniasis
- Mycosis fungoides
- Leukemia cutis
- Sarcoidosis
- Tertiary syphilis.

Q. What are the causes of **sensory impairment** with or without muscle atrophy?

A. As follows:
- Peripheral neuropathy due to any cause
- Cord compression due to any cause (loss of sensation below the level of lesion)
- Primary amyloidosis of peripheral nerve
- Congenital sensory neuropathy
- Peroneal muscular atrophy
- Trauma
- Cervical rib
- Syringomyelia
- Herpes zoster
- Thalamic lesion
- Functional.

Q. What are the **differences** between leprosy and syringomyelia?

A. As follows:

Points	Syringomyelia	Leprosy
1. Cause	Elongation of central canal with compression of lateral tract	Infectious disease caused by *M. leprae*

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2. Site	Mainly upper limb, thumb, index and middle finger	Anywhere but sparing the axilla, perineum and scalp
3. Pattern of anesthesia	Dissociate anesthesia (loss of pain and temperature and intact tactile sensation)	Sequential loss of temperature, light touch, pain and deep touch sensations
4. Histamine and methacholine test	Positive	Negative

Q. What are the causes of **claw hand**?

A. As follows:
- Motor neuron disease
- Syringomyelia
- Charcot Marie Tooth disease
- Poliomyelitis
- Rheumatoid arthritis (in advanced stage)
- Trauma
- Dupuytren's contracture
- Congenital flexion of fingers.

Q. What are the causes of **neuropathic ulcer**?

A. As follows:
- Diabetes mellitus
- Leprosy
- Peripheral neuropathy due to any cause
- Syringomyelia
- Amyloidosis
- Porphyria
- Tabes dorsalis
- Planter corn.

Q. What are the causes of **nerve enlargement**?

A. Causes are:
- Leprosy
- Hereditary hypertrophic neuropathy
- Amyloidosis
- Acromegaly
- Sarcoidosis
- Chronic inflammatory demyelinating polyneuropathy (CIDP)
- Repeated friction or trauma
- Neurofibromatosis.

Q. What is **leonine face**? What are the **causes** of it?

A. Leonine face is characterized by facial skin thickening associated with papules, nodules or diffuse infiltration in the skin that is called leonine face. It resembles the face of a lion. There may be depressed bridge of the nose, broad nose with nasal collapse (saddle nose). Lateral 1/3rd of eyebrows may be lost (called madarosis). Causes are:
- Lepromatous leprosy
- PKDL

- Mycosis fungoides
- Sezary syndrome
- Leukemia cutis
- Mucinosis
- Paget's disease of bone
- Mastocytosis
- Lichen myxedematosus.

Q. What are the causes of **saddle nose?**

A. As follows:
- Lepromatous leprosy
- Wegener's granulomatosis
- Lupus vulgaris
- Congenital syphilis
- Idiopathic midline granuloma.

Q. Which **nerves** are commonly involved in leprosy? Where are they **palpated?**

A. As follows:
- Facial nerve: Crossing the zygomatic arch
- Great auricular nerve: Posterior triangle of the neck
- Radial nerve: In the radial groove of humerus at the insertion of deltoid muscle
- Radial cutaneous nerve: In the wrist
- Ulnar nerve: In elbow, in between the medial epicondyle and olecranon process
- Median nerve: Middle of the front of wrist
- Lateral popliteal or common peroneal nerve: Around the neck of fibula
- Posterior tibial nerve: Ankle, a little below and posterior to medial malleoli.

Q. What is **madarosis**? What are the **causes**?

A. It is the loss of hair from the outer third of eyebrow. Causes are:
- May be a normal finding (common cause)
- Lepromatous leprosy
- Hypothyroidism
- Secondary syphilis
- Local fungal infection
- Follicular mucinosis
- As a part of alopecia.

Q. What are the causes of **anesthesia in skin**?

A. As follows:
- Leprosy
- Syringomyelia
- Trauma
- Tabes dorsalis
- Follicular mucinosis
- Diabetes mellitus
- Congenital sensory neuropathy.

Q. What are the lesions that show **central clearing**?

A. As follows:
- Tinea circinata

- Tuberculoid leprosy
- Granuloma annulare
- Parakeratosis
- Secondary syphilis
- Psoriasis
- Lichen planus
- Lupus vulgaris
- Sarcoidosis.

Q. How to **treat** leprosy?

A. WHO recommended protocol is as follows:

- **Paucibacillary** (three to five skin lesions, skin smear negative or few, tuberculoid and BT)—Rifampicin 600 mg monthly (supervised) **plus** dapsone 100 mg daily (self-administered) for 6 months.
- **Paucibacillary single lesion—**Rifampicin 600 mg **plus** ofloxacin 400 mg **plus** minocycline 100 mg, in single dose (ROM therapy).
- **Multibacillary** (more than five skin lesions, skin smear positive, BT, all BB, BL and LL)—Rifampicin 600 mg and clofazimine 300 mg monthly (supervised) **plus** dapsone 100 mg and clofazimine 50 mg daily (self-administered) for 12 months or until the findings on smear are negative (may be up to 24 months), whichever is longer.

Common **side effects** of anti-leprosy drugs are:

- Dapsone: Hemolytic anemia, agranulocytosis, exfoliative dermatitis, hepatitis, hypoproteinemia, psychosis.
- Clofazimine: Red coloration of skin, urine and body secretions, pruritus, anorexia, nausea, vomiting, abdominal pain.

Q. What are the **antigens** of leprosy?

A. As follows:

- **Phenolic glycolipid (PGL-1):** Present in the waxy exterior of bacteria and is a target of antibody response.
- **Lipoarabinomannan:** A lipoglycan is inserted into the cell membrane of *M. leprae* and courses the outer membrane. It is a target of both antibody and T-cell response.
- Highly immunologic proteins are located in the cytoplasm and are associated with the cell wall. These include highly conserved immunologic proteins of molecular mass 10 KD, 65 KD, and 70 KD each bearing *M. leprae* specific and mycobacterial cross reactive epitope.

Q. What are the **atypical presentations** of leprosy?

A. As follows:

1. In tuberculoid leprosy:
   - Pure neural leprosy
   - Tenosynovitis—painful swelling over the hands of one or both hands, rarely dorsum of foot. It may be a complication of type I reaction, but commonly associated with other evidence of BT
   - Spontaneous ulceration of skin because of exaggerated hypersensitivity of type I reaction.
2. In lepromatous leprosy:
   - Single nodule
   - Histoid leprosy—so called because microscopic appearance shows spindle shaped cells resembling dermatofibroma. They are well-defined hemisphere up to 3 cm in diameter.

They do not extend deeply into the skin, but feel like a button in the superficial dermis. Well-defined edge, shiny coppery red in color
- Spontaneous ulceration
- Lucio leprosy.

Q. What are the **complications** of leprosy?

A. Complications can be divided into:

I. Complications due to massive invasion of tissues by *Mycobacterium leprae*:

1. Ocular:
   - Miliary lepromat
   - Nodular lepromat
   - Chronic granulomatous iritis
   - Acute diffuse iridocyclitis
   - Corneal opacity
   - Avascular keratitis
   - Interstitial keratitis
   - Pannus formation.
2. Mucous membrane involvement:
   - Nose—chronic nasal congestion, perforation of nasal septum with collapse of nasal bridge, saddle nose deformity
   - Nodules in vocal cords, produces hoarseness of voice
   - Loss of upper incisor teeth deformity.
3. Visceral involvement: Mainly involves lymph nodes, bone marrow, liver, spleen. Testicular atrophy with resultant gynecomastia and premature osteoporosis.

II. Complications due to nerve damage:
- Sensory—anesthesia
- Motor—wasting of muscles, paralysis, claw hand, wrist drop, foot drop, lagophthalmos, mask face
- Autonomic—dry skin, crack, fissure, ulcer
- Secondary complication following nerve damage includes tissue necrosis, plantar ulceration, secondary bacterial cellulitis, osteomyelitis, progressive loss of digits of hands and feet, malum perforans pedis.

III. Complications due to reaction:

1. Type I –
   - Rapid swelling of one or more nerves with pain and tenderness at the site of nerve swelling and nerve abscess
   - Edema of hands, feet and face
   - Claw hand, foot drop, facial palsy.
2. Type II –
   - Iritis, iridocyclitis, keratitis, conjunctivitis
   - Epistaxis, muscle pain, bone pain, joint pain, lymphadenitis, epididymo-orchitis
   - Hepatomegaly, pleuritis, nephritis, orchitis
   - Paralysis occurs but does not threaten so quickly.

IV. Complication due to drug resistance: Most dapsone resistance is secondary and occurring up to 15% of cases of multibacillary patients. It may start as typical lepromatous like or new discrete lesions appear against a background of healed lesions.

Q. What is **lepra reaction**?

A. Lepra reactions are immunologically mediated acute reactions that occur in patients with the borderline or lepromatous leprosy, usually during treatment. It may be the first manifestation of the disease.

It may be insidious or rapid, destroying the affected tissue within hours. It is of two types: type I and type II.

Type I lepra reaction (reversal): It is a delayed hypersensitivity reaction (type IV) that occurs in 30% borderline patients (BT, BB and BL). It occurs spontaneously or may be precipitated by treatment. There is rapid swelling of one or more nerves with pain and tenderness at the site of nerve swelling. Nerve function is lost rapidly, foot drop may occur overnight. Also, there may be claw hand, facial palsy, etc. Skin lesions become erythematous and swollen and new skin lesion may appear. There may be edema of hands, feet and face. Reversal of reactions may occur spontaneously, after starting treatment and after completion of multidrug therapy.

Treatment:

- In mild case, aspirin 600 mg 6 hourly.
- In severe case, prednisolone 40 to 60 mg daily. The dose should be reduced by 5 mg/day each month, should be tapered over 3 to 6 months.
- Clofazimine can be added upto 300 mg daily. If fails, cyclosporine 5 to 10 mg/kg may be given.
- Treatment of leprosy should be continued.

Type II lepra reaction (erythema nodosum leprosum, ENL): Type II lepra reaction, which is due to immune complex deposition (type III hypersensitivity reaction). It occurs in BL and in LL patient who produce antibodies and have a high antigen load. It is characterized by fever, arthralgia and crops of small pink painful nodules on the face and limbs. Iritis, iridocyclitis, keratitis, conjunctivitis and episcleritis are common. Other signs are neuritis, orchitis, myositis, nephritis, epistaxis, pleurisy, bone pain, arthritis, lymphadenitis and hepatomegaly. ENL may be the first manifestation of leprosy in 50% lepromatous and 25% borderline lepromatous leprosy, either during the course of the disease or more commonly in the second year of treatment. ENL may continue intermittently for several years.

Treatment:

- In mild cases, analgesic (aspirin 600 mg 6 hourly).
- In severe cases, thalidomide (100 mg 6 hourly). When symptoms improve, reduce the dose slowly over weeks or months, maintenance dose is 50 to 100 mg daily. It is a potent teratogenic drug (contraindicated in pregnancy).
- If thalidomide is not available, prednisolone (40 to 60 mg) should be given, and reduce the dose over 1 to 6 months. Chloroquine can also be used.
- The dose of clofazimine (300 mg daily) should be increased for few weeks. It will reduce the reaction and help to reduce the dose of prednisolone.
- Anti-leprosy therapy must be continued.

Q. How would you **differentiate** between two types of lepra reactions?

A. As follows:

Points	Type I reversal or downgrading	Type II
1. Type	» Mostly in BT, BB, BL	» Mostly in LL
2. Onset	» Upgrading—during first 6 months of therapy in BT and BB but longer duration in BL » Downgrading—in untreated or in interrupted treatment	» After 1 or 2 years of therapy or untreated case of long duration

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3. Cause	» Upgrading or reversal—increase in CMI » Downgrading—decrease in CMI (type 1V)	» Immune complex syndrome due to precipitation of antigen antibody complex in tissue spaces, blood and lymphatic vessels (type III)
4. Clinical features	» Some or all of the existing lesions show signs of inflammation	» Existing lesions do not show clinical aggravation » Sudden appearance of crops of evanescent tender nodules or plaques » May become vesicular, pustular, bullous or gangrenous
5. Associated features	» Rapid swelling of one or more nerves. Nerve abscess may occur	» Nerve damage does not threaten so quickly » Commonly associated features are iritis, iridocyclitis, epistaxis, muscle pain, bone pain, nerve pain, joint pain, lymphadenitis, epididymo-orchitis, proteinuria
6. Histology	» Upgrading—increase in lymphocytes, epithelioid cells and giant cells. The number of bacilli decreases » Downgrading—macrophages and increase no of bacilli	» Large number of polymorphs » Bacilli numerous, fragmented and granular
7. Lepromin test	» Upgrading—positive » Downgrading—negative	» Negative
8. Hematological finding	» Nil	» IgG, IgM, C2, C3
9. Course	» Seldom persists more than a few months	» Mild ENL disappears rapidly but severe ENL may persist for years and may result in death

Q. What is bacterial or **bacteriological index** (BI)?

A. It indicates the density of leprosy bacilli in smears and includes both living (solid staining) and dead (fragmented or granular) bacilli. Bacteriological index in LL is 5 to 6 and in TT is 0.

Q. What is **morphological index** (MI)?

A. It is the percentage of presumably living bacilli in relation to the total number of bacilli in the smear.

PITYRIASIS RUBRA PILARIS

CHIEF COMPLAINTS

- Widespread papular eruption for … years
- Scaling patches for … years
- Thickening of palms and soles for … years.

HISTORY

History of present illness: The patient states that he was alright … years back. Since then, he noticed multiple papules on different parts of the body that initially started on the dorsum of phalanges and later gradually spread to the neck, trunk and extensor surface of the extremities. He also noticed yellowish scaling patches on the scalp for … years. There are also widespread areas of sharply marginated patches of various sizes on both sides of the body. The lesions are slightly itchy. The patient also noticed gradual thickening of palms and soles that is painless and non-itchy. His nails are rough and thickened. The patient observed development of papules at the sites of scratches and also at the site of injury. There is no history of fever or joint pain or mouth ulcer. The lesions are not aggravated by sun exposure. His bowel and bladder habits are normal.

History of past illness

Treatment history

Family history

Personal history

Socioeconomic condition: Mention according to the statement of the patient.

GENERAL EXAMINATION

- Appearance normal
- Mildly anemic
- No jaundice, cyanosis, clubbing, edema, dehydration, koilonychia, leukonychia
- Lymph nodes and thyroid gland are not enlarged
- Pulse: 92/min
- BP: 90/60 mm Hg
- Temparature: 98ºF.
- Respiratory rate: 20/min.

Integumentary System

1. **Skin:**
   - Inspection:
     - Small, pinhead, reddish brown, follicular papules that are topped by central horny plug and disseminated yellowish scaling patches are present almost all over the body, especially on backs of the first and second phalanges, the sides of the neck, trunk and extensor surface of the extremities. Patches look like exaggerated goose flesh.
     - There are islands of normal skin within the affected areas.

- Koebner phenomenon is found on the back in a scratch mark.
- Scalp shows erythema and scaling.

♦ Palpation:
- Patches feel like nutmeg
- Palms and soles are uniformly thickened. Hyperkeratosis extends up to the sides forming sandal appearance.

2. **Nails** are rough, thickened, brittle, striated.
3. **Mucous membrane:** Not involved.

Examination of other systems reveals no abnormalities.

SALIENT FEATURE

Mr …, … years old, student, normotensive, nondiabetic, nonsmoker, hailing from …, presented with multiple papules on different parts of the body that initially started on the dorsum of phalanges and later gradually spread to the neck, trunk and extensor surface of the extremities. He also noticed yellowish scaling patches on the scalp for … years. There are also widespread areas of sharply marginated patches of various sizes on both sides of the body. The lesions are slightly itchy. The patient also noticed gradual thickening of palms and soles that is painless and non-itchy. His nails are rough and thickened. The patient observed development of papules at the sites of scratches and at the site of injury. There is no history of fever or joint pain or mouth ulcer. The lesions are not aggravated by sun exposure. His bowel and bladder habits are normal. He was treated with antihistamine tablets, vitamins and several ointments. There is no history of such illness in his family.

On general examination – (mention as above).

On examination of the integumentary system – (mention as above).

Examination of other systems reveals no abnormalities.

My diagnosis is pityriasis rubra pilaris.

Q. What are your **differential diagnoses?**

A. As follows:
- Psoriasis
- Lichen planus.

Q. What are the **points in favor** and **against** your differential diagnoses?

A. As follows:

Differential diagnoses	Points in favor	Points against
1. Psoriasis	» Papules and scaling patches » Koebner's phenomenon present	» Scales are not silvery white in color » Islands of normal skin within the affected areas » Plantar hyperkeratosis extends up to the sides
2. Lichen planus	» Papular eruption » Koebner's phenomenon present	» Absence of shiny, flat-topped violaceous papules » Oral mucosa is not involved

Q. What **investigations** do you suggest?

A. As follows:

1. Routine:
   - TC, DC, Hb%, ESR
   - Blood sugar
   - Urine R/M/E
   - Lipid profile (retinoids cannot be given in hyperlipidemia)
   - Liver function tests.
2. Skin biopsy for histopathology and DIF.

RELATED QUESTIONS AND ANSWERS

Q. What is **pityriasis rubra pilaris (PRP)**?

A. PRP is a chronic skin disease characterized by small follicular papules, disseminated, yellowish pink scaling patches and often solid palmoplantar hyperkeratosis.

Q. What are the **types** of PRP?

A. As follows:

- Type I – Adult onset classical
- Type II – Adult onset atypical
- Type III – Juvenile onset classical
- Type IV – Juvenile onset circumscribed
- Type V – Juvenile onset atypical
- Type VI – HIV associated.

Q. What is the **etiology** of PRP?

A. The exact etiology is unknown. The disease is usually transmitted as autosomal dominant trait in juvenile onset PRP. Histological and clinical features suggest that it is a vitamin deficiency disorder, particularly of vitamin A. Some patients have low serum levels of retinol binding protein. Both sexes are affected with equal frequency.

Q. What are the **histopathological and DIF findings** in PRP?

A. As follows:

- Skin biopsy for histopathology shows the following features (specimens should be obtained from skin sites where hair follicles are numerous):
  - Hyperkeratosis
  - Parakeratosis
  - Follicular plugging at the follicular orifice
  - Alternating vertical and horizontal parakeratosis in the interfollicular stratum corneum is said to be characteristic
  - Inflammatory infiltrate in the dermis is composed of mononuclear cells and mild.
- DIF is negative. It is done to differentiate from Lichen planus.

Q. What are the different **treatment** modalities in PRP?

A. As follows:

- Systemic retinoids are effective
- Isotretinoin in doses of 0.5 to 2 mg /kg /day for several months
- Vitamin A in doses of 300,000 to 500,000 units daily with vitamin E 400 units two or three times daily

- Systemic steroid can be given for acute short-term management
- Methotrexate 2.5 mg orally alternating one day with 5 mg the next
- Combination of isotretinoin or acitretin with low dose methotrexate
- Azathioprine is also effective
- In severe cases, extracorporeal photochemotherapy with systemic retinoids and cyclosporine.
- Treatment of secondary infection, if present.

Q. How would you **differentiate** between PRP and psoriasis?

A. As follows:

Points	PRP	Psoriasis
1. Age of onset	Bimodal, highest incidence is during first 5 years or between ages 51 and 55	2nd to 4th decade
2. Scales	Yellowish pink over the body Furfuraceus over scalp	Silvery white Adherent scale over scalp
3. Islands of normal skin	Present	Not common
4. Auspitz sign	Absent	Present
5. Keratoderma	Constant	Less common
6. Nail change	Striated, brittle, rough	Pitting, oil spots, subungual hyperkeratosis
7. Nail growth rate	Moderate increase	Marked increase
8. Histopathology – Munro's microabscess – Follicular plugging	 Absent Present	 Common Absent
9. Seronegative arthropathy	Very rare	Common
10. Response to UVB	Poor	Good
11. Response to corticosteroid	Poor	Positive
12. Response to methotrexate	Variable	Good

Q. What are the **differential diagnoses** of PRP?

A. Diseases that simulate PRP are:

- Psoriasis
- Lichen planus
- Phrynoderma
- Subacute cutaneous lupus erythematosus
- Dermatomyositis.

Q. What are the **complications** of PRP?

A. As follows:

- Exfoliative dermatitis
- Prolonged erythema
- Ectropion
- Peripheral edema

- High output cardiac failure
- Eruptive seborrheic keratosis.

Q. What are the diseases that **involve hair follicles**?

A. Follicular involvement can be classified into:

1. Infective folliculitis:
   - Bacterial—*Staphylococcus*, *Streptococcus*, *Pseudomonus*, *Proteus*, *Klebsiella*, follicular syphilides, follicular chancroid, lichen scrofulosorum (by *Mycobacterium tuberculosis*)
   - Viral—Herpes simplex
   - Parasitic—*Demodex folliculorum*
   - Fungal—Tinea capitis, Tinea barbae, pityrosporum folliculitis.
2. Noninfective:
   - Eosinophilic folliculitis
   - Perforating folliculitis
   - Pseudofolliculitis barbae
   - Keloidal folliculitis
   - Folliculitis decalvans
   - Acne vulgaris
   - Fox Fordyce's disease
   - Pityriasis rubra pilaris
   - Lichen plano pilaris
   - Phrynoderma
   - Kyrle's disease
   - Keratosis pilaris
   - Darier's disease
   - Lichen spinolosus.

Q. What are the diseases that show **disorders of keratinization**?

A. The following diseases show disorder of keratinization:

- Psoriasis
- PRP
- Exfoliative dermatitis
- Parapsoriasis
- Ichthyosiform disorder
- Darier's disease
- Parakeratosis
- Acrokeratosis verruciformis of Hopf.

Q. What are the causes of **palmoplantar keratoderma**?

A. Causes of palmoplantar keratoderma can be classified into the following:

1. Acquired type:
   - Psoriasis
   - PRP
   - Lichen planus
   - Contact dermatitis
   - Tinea pedis
   - Arsenical keratoses
   - Corn
   - Callus

- Wart
- Cancer associated paraneoplastic disorder
- Syphilis.

2. Hereditary:

- Hereditary palmoplantar keratoderma
- Punctate palmoplantar keratoderma
- Mal de Meleda
- Darier's disease
- Ichthyosis
- Pachyonychia congenita
- Dyskeratosis congenita.

Q. What are the types of **systemic retinoids**?

A. Widely used retinoids are:

First generation (nonaromatic):

- Isotretinoin
- Tretinoin.

Second generation (monoaromatic):

- Etretinate
- Acitretin.

Third generation (polyaromatic):

- Adapalene
- Tazarotene.

Q. What are the **indications** of systemic retinoids?

A. As follows:

- PRP
- Recalcitrant and nodulocystic acne
- Hidradenitis suppurativa
- Pustular and erythrodermic psoriasis
- Darier's disease
- Ichthyosis
- Gram-negative folliculitis
- Mycosis fungoidis
- Melanoma
- Multiple basal cell carcinoma.

Q. What **precautions** are to be taken before giving systemic retinoids?

A. As follows:

- Consent from the patient
- Contraception
- Documentation of absence of pregnancy
- Avoidance of smoking and alcohol
- Low fat diet to keep the lipid level normal.

Q. What are the **side effects** of retinoids?

A. Side effects of retinoids are:

1. **Cutaneous:**
   - Cheilitis
   - Conjunctivitis
   - Facial dermatitis
   - Dry eyes
   - Dry mouth
   - Xerosis with pruritus
   - Hair thinning and hair loss.
2. **Systemic:**
   - Teratogenicity
   - Pseudotumor cerebri (headache, papilledema)
   - Arthralgia
   - Osteoporosis
   - Premature epiphyseal closure and vertebral abnormalities.
3. **Laboratory:**
   - Hyperlipidemia.
   - Abnormal liver function test.

Q. What are the causes of **papulosquamous diseases**?

A. The following diseases are considered to be papulosquamous:

- Psoriasis
- PRP
- Parapsoriasis
- Pityriasis rosea
- Seborrheic dermatitis
- Lichen planus
- Secondary syphilides
- Subacute cutaneous lupus erythematosus
- Mycosis fungoides
- Sarcoidosis.

PEMPHIGUS VULGARIS

CHIEF COMPLAINTS

- Multiple blisters in different parts of the body for … months
- Painful ulcerations inside the mouth for … months
- Generalized weakness and loss of weight for … months.

HISTORY

History of present illness: The patient states that she was reasonably well … months back. Since then, she noticed multiple blisters in skin of different parts of the body. Initially blisters were few, starting over the groin, but gradually appeared in the scalp, face, neck, axilla and genitals. Some of the blisters ruptured spontaneously forming ulceration with oozing and bleeding. Later on, some lesions became covered with crusts. For the last … months, she also noticed few blisters inside the mouth that ruptured to form painful ulceration. The lesions increased in size, involved the lips and formed crusts. The patient also complains of generalized weakness, gradual weight loss, difficulty in swallowing and offensive odor in the mouth. There is no history of fever, joint pain, and bowel or bladder abnormality.

History of past illness

Treatment history

Family history

Personal

Socioeconomic condition

Drug history: Mention according to the patient's statement.

GENERAL EXAMINATION

- The patient is ill looking and emaciated
- Moderately anemic
- No jaundice, cyanosis, clubbing, edema, dehydration, koilonychias, leukonychia
- Lymph nodes and thyroid gland are not enlarged
- Pulse: 108/min
- Blood pressure: 90/60 mm of Hg
- Temperature: 100 °F
- Respiratory rate: 24/min.

Integumentary System

1. **Skin:**
   - Multiple thin walled, flaccid bullae are present over scalp, face, neck, axilla, groin and genitals. Some are on normal skin and some are on erythematous bases.
   - Some of the bullae are ruptured forming denuded areas that enlarge by confluence.
   - In some bullae, there is clear fluid and in some, the fluid is hemorrhagic.
   - Denuded areas are partially covered with crusts.
   - Few areas of hyperpigmentation are present on the trunk that are indicative of healed lesions without scarring.
   - Nikolsky and Asboe-Hansen signs are positive (mention if any).

2. **Mucous membrane:**
   - Conjunctiva—normal
   - Oral cavity—multiple irregular ulcerations are seen in the oral mucous membrane and palate, few lesions on the lips and form heavy crusts. Partially detached membranous sheets cover the tongue
   - Vulva—multiple erosions within the mucosa of vulva.
3. **Nails:** Nails of index and little fingers of left side show paronychia around them.
4. **Hair:** Normal.

Note

Genital parts should be examined and mentioned, if there is any finding, e.g. erosions.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mrs …, 50 years, housewife, normotensive, nondiabetic, nonsmoker, hailing from …, presented with the complaints of multiple blisters in skin of different parts of the body for … months. Initially, the blisters were few, starting over the groin, but gradually appeared in the scalp, face, neck, axilla and genitals. Some of the blisters ruptured spontaneously forming ulceration with oozing and bleeding. Later on, some lesions became covered with crusts. For the last … months, she also noticed few blisters inside the mouth that ruptured to form painful ulceration. The lesions increased in size, involved the lips and formed crusts. The patient also complains of generalized weakness, gradual weight loss, difficulty in swallowing and offensive odor in the mouth. There is no history of fever, joint pain, and bowel or bladder abnormality. There is no history of taking any drugs responsible for this lesion.

On general examination – (mention as above).

On examination of the integumentary system – (mention as above).

Examination of other systems reveals no abnormalities.

My diagnosis is pemphigus vulgaris.

Q. What are your **differential diagnoses?**

A. As follows:
- Bullous pemphigoid
- Stevens-Johnson syndrome.

Q. What are the **points in favor** and **against** your differential diagnoses?

A. As follows:

Differential diagnoses	Points in favor	Points against
1. Bullous pemphigoid	» Blisters over the groin and axilla » Oral mucosa is involved	» Flaccid, thin walled, easily ruptured bullae » Denuded areas enlarging by confluence » More than one mucous membranes are involved » Nikolsky and Asboe-Hansen signs are positive

Contd...

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2. Stevens-Johnson syndrome	» Blisters on the trunk » Two mucous membranes are involved	» Absence of febrile prodrome, no history of drug, absence of target lesions

Q. What are the **investigations** done in pemphigus vulgaris?

A. As follows:

1. Routine:
   - FBC
   - Blood sugar
   - Urine RME
   - Liver function tests
   - Renal function tests.
2. Diagnostic:
   - **Skin biopsy** for histopathology and immunofluorescence test (early intact bullae < 12 hours duration should be taken with perilesional area).
   - Cytological (**Tzanck method)**—Smears are taken from the base of a bulla and (using Giemsa stain) is used for rapid demonstration of acantholytic cell (that shows no intercellular bridge, darkly staining cytoplasm and large nuclei surrounded by lightly staining halo).
   - **Direct immunofluorescence** shows intercellular deposition of IgG throughout epidermis (both involved and normal skin) or oral mucosa and C3 deposition in acantholytic area (net-like, honeycomb or mosaic pattern).

Histological findings:

- Acantholysis (separation of individual keratinocyte from one another)
- Superficial intraepidermal split
- Intraepidermal blister above basal layer (in pemphigus vulgaris) or subcorneal epidermal split (in pemphigus foliaceus)
- Acantholytic cells are found lining the bulla as well as lying free in the bulla cavity
- Eosinophilic spongiosis and occasionally neutrophilic spongiosis may be seen in the spongiotic epidermis in pemphigus vulgaris.

Q. How **biopsy and DIF materials** are collected?

A. A small early intact bulla should be taken. Site of biopsy is frozen with aerosol refrigerant spray so that the punch may include firm tissue. Tissue for biopsy is taken in test tube containing formalin. Normal appearing perilesional skin is taken for DIF in saline soaked gauze.

Q. How would you **treat** the patient?

A. As follows:

1. General measures:
- Bed rest
- Daily bath to remove thick crusts and foul odor
- Maintenance of fluid and electrolyte balance and nutrition
- Antibiotic and blood transfusion (if necessary).

2. Topical:
- 1% silver sulfadiazine is applied topically
- Antiseptic mouth wash and viscous xylocaine are to be applied in the mouth
- Care of the eye.

3. **Systemic:**
   - High dose prednisolone—100 to 200 mg/day. The dose should be tapered when remission occurs with no new blister. Maintenance dose is required for long time (may require lifelong treatment). If new blister occurs during treatment, the dose of prednisolone should be increased.
   - **Other treatment:**
     a. IV methylprednisolone 1 g/day for 5 days (pulse therapy)
     b. Mycophenolate mofetil 1 to 1.5 g is given twice a day (commonly used as steroid sparing drug)
     c. Other drugs—azathioprine, cyclophosphamide, methotrexate, cyclosporine and dapsone
     d. In resistant case, IV immunoglobulin may be tried
     e. Biologic agents (infliximab, rituximab and etanercept)
     f. Extracorporeal photochemotherapy.

Prognosis: Prognosis is bad and recurrence is common with high mortality.

RELATED QUESTIONS AND ANSWERS

Q. What is **pemphigus vulgaris**?

A. It is an autoimmune blistering disease characterized by thin walled, flaccid, easily ruptured bullae that appear on both apparently normal skin and mucous membrane or on erythematous bases. On direct immunofluorescence test, it shows the presence of intercellular antibodies throughout the epidermis and oral epithelium.

Q. What are the **types** of pemphigus?

A. Pemphigus can be classified into:

1. Pemphigus vulgaris:
   - Pemphigus vegetans (localized)
   - Drug induced.
2. Pemphigus foliaceus:
   - Pemphigus erythematosus (localized)
   - Fogo selvagem (endemic)
   - Drug induced.
3. Paraneoplastic pemphigus.
4. IgA pemphigus.

Q. What are the **causes** of pemphigus vulgaris?

A. Exact etiology is unknown. Probable factors are:

- Autoimmunity, as suggested by the intercellular deposition of IgG and C3 complement in epidermis
- Genetic predisposition (associated with HLA DR4 and DR6)
- Drugs (penicillin, penicillamine, captopril, rifampicin, cephalosporin, pyrazolone, etc.)
- UV light, PUVA and ionizing radiation
- Increased incidence in myasthenia gravis and thymoma.

Q. What is the **pathogenesis** of pemphigus vulgaris?

A. Circulating antibody binds to cell surface glycoprotein that result in activation of plasmin, which causes enzymatic destruction of intercellular cement and desmosomes with formation of intraepidermal blister.

Q. What are the **presentations** of pemphigus vulgaris?

A. It is common in middle age, 50 to 60 years, and it is equally present in both sexes. The patient presents with:

- Thin-walled flaccid bullae that easily rupture, causing erosion, ulcer and crust formation with oozing and bleeding.
- Mouth ulcer is common (in 60%), also conjunctival and genital ulcer are noted.
- Ulcer heals slowly with hyperpigmented patch without scarring.

Q. What is **acantholysis**?

A. Acantholysis is loss of coherence between epidermal or epithelial cells.

1. Primary acantholysis occurs among unaltered cells as a result of dissolution of intercellular cement substance. It is seen in:
   - Pemphigus vulgaris
   - Pemphigus foliaceus
   - Benign familial pemphigus
   - Darier's disease.
2. Secondary acantholysis occurs among altered or damaged cells. It is seen in:
   - Viral vesicles
   - Impetigo
   - Subcorneal pustular dermatosis
   - Solar keratosis.

Q. What is the **bedside test** in pemphigus vulgaris?

A. As follows:

1. Nikolsky sign—Rubbing of unaffected skin results in separation of epidermis leaving a moist surface. This can be seen in:
   - Pemphigus vulgaris (common cause)
   - Staphylococcal scalded skin syndrome (SSSS)
   - Toxic epidermal necrolysis
   - Epidermolysis bullosa dystrophic
2. Bullae spread phenomenon or Asboe-Hansen sign. Pressure on the intact bullae gently forces the fluid to wander under the skin away from pressure site. It demonstrates the lack of cohesion.

Q. What are the **complications** of pemphigus vulgaris?

A. Secondary bacterial infection (pneumonia, septicemia), hypoproteinemia, side effects of systemic prednisolone.

Q. How do you **differentiate** between pemphigus vulgaris and pemphigus foliaceus?

A. As follows:

Points	Pemphigus vulgaris	Pemphigus foliaceus
1. Type of bullae	Flaccid or ruptured bulla on normal or erythematous skin	Flaccid bullae with exfoliation on erythematous skin only
2. Oral involvement	60% oral lesion	Oral lesion absent
3. Denuded area	Present	No denuded area, there will be crust, below that moist area is present that bleeds
4. General health	Affected	Not affected
5. Age	5th and 6th decade	4th and 5th decade
6. Histopathology	Suprabasal cleft and blister	Subcorneal cleft and blister
7. Antigen	Desmoglein 3 and 1	Desmoglein 1 and Plakoglobin

Q. What are the malignant diseases associated with **paraneoplastic pemphigus**?

A. As follows:
- Non-Hodgkin lymphoma
- Chronic lymphocytic leukemia
- Castleman's tumor
- Sarcoma
- Thymoma.

Q. What type of pemphigus is initiated by **infectious agents** carried by mosquito or black flies?

A. Brazilian pemphigus or Fogo Selvagem.

Q. What are the causes of **blisters** of the skin?

A. The causes of blisters are the following:

1. Infective:
   - Bacterial—bullous impetigo, SSSS, impetigo contagiosa, congenital syphilis
   - Viral—herpes simplex, herpes zoster, chicken pox
   - Fungal—bullous tinea pedis
   - Parasitic—bullous scabies.
2. Noninfective:
   - Autoimmune blistering—pemphigus vulgaris, bullous pemphigoid, dermatitis herpetiformis
   - Autoimmune connective tissue—bullous SLE
   - Metabolic—DM, primary systemic amyloidosis, porphyria cutanea tarda
   - Drugs—sulfonamide, tetracycline, penicillin, captopril, frusemide
   - Physical agents—burn, pressure, radiation, friction
   - Chemical agents—acid, alkali
   - Miscellaneous—bullous lichen planus, erythema multiforme, Stevens Johnson syndrome, lichen sclerosus atrophicus, irritant contact dermatitis.

Q. What are the causes of **hemorrhagic bullae**?

A. As follows:
- Pemphigus vulgaris
- Bullous pemphigoid
- Herpes zoster
- Toxic epidermal necrolysis
- Leukocytoclastic vasculitis
- Lichen sclerosus atrophicus
- Epidermolysis bullosa acquisita
- Primary systemic amyloidosis
- Epidermolysis bullosa simplex (ogna)
- Allergic granulomatosis
- Cutaneous manifestation of systemic candidiasis.

Q. What are the **autoimmune blistering diseases**?

A. As follows:
- Pemphigus with its variants
- Bullous pemphigoid
- Linear IgA dermatosis
- Dermatitis herpetiformis
- Herpes gestationis

- Cicatricial pemphigoid
- Epidermolysis bullosa acquisita
- Chronic bullous disease of childhood.

Q. What are the **causes** of bullous lesion in skin with mouth ulcer?

A. As follows:
- Pemphigus vulgaris
- Bullous pemphigoid
- Stevens Johnson syndrome
- Toxic epidermal necrolysis
- Behçet's syndrome
- Bullous SLE.

Q. What are the diseases that can be diagnosed by **DIF**?

A. DIF helps in the diagnosis of the following diseases:
- All autoimmune blistering diseases mentioned above
- SLE
- DLE
- Lichen planus
- Leukocytoclastic vasculitis.

Q. What are the **DIF findings in different diseases**?

A. As follows:

Diseases	Preferred biopsy site	Precipitated immunoreactants	Site	Pattern
1. Pemphigus vulgaris and foliaceus	Perilesional	IgG	Intraepidermal site (IES)	Net-like/ honeycomb/ lacelike/ mosaic
2. Pemphigus erythamatosus	Perilesional	IgG and C3	Intercellular and basement membrane zone (BMZ)	Net like or lace-like
3. IgA pemphigus	Perilesional	IgA	IES	Lace-like
4. Paraneoplastic	Perilesional	IgG and C3	IES and BMZ	Lace-like Linear or granular
5. Bullous pemphigoid	Perilesional	C3 (100%) and IgG (80%)	BMZ	Linear
6. Cicatricial pemphigoid	Perilesional	IgG and C3	BMZ	Linear
7. Dermatitis herpetiformis	Perilesional or normal	IgA with or without C3	BMZ at the tips of dermal papilla	Granular
8. Herpes gestationis	Perilesional	C3	BMZ	Linear

Contd...

Contd...

9. Epidermolysis bullosa acquisita	Perilesional	C3, IgG	BMZ	Linear
10. Bullous SLE	Perilesional	C3, IgG	BMZ	Linear
11. Lupus erythematosus	Lesional or normal	IgM, IgG, C3	BMZ	Granular
12. Linear IgA dermatosis	Perilesional	IgA	BMZ	Linear
13. Leukocytoclastic vasculitis	Lesional (early lesion)	IgM, IgG, C3	In vessel wall	Granular
14. Lichen planus	Lesional	IgM, less commonly IgA, IgG, C3	Subepidermally	Linear

BULLOUS PEMPHIGOID

CHIEF COMPLAINTS

- Multiple blisters over different parts of the body for … months
- Red patches over the trunk for … months
- Itching for … months.

HISTORY

History of present illness: The patient states that he was alright … months back. Since then, he has been suffering from multiple blisters over different parts of the body. The blisters at first appeared over forearms and gradually involved axilla, groin and front and back of trunk. Most of the blisters are large and tense, few are small. Some blisters have ruptured leaving denuded areas that have healed spontaneously. He also noticed erythematous patches over the front and back of the trunk, some of which healed spontaneously. There is no involvement of the mouth or genitalia.

The patient also complains of mild generalized itching for the same duration. He did not complain of difficulty in swallowing. There is no history of fever, joint pain, muscle pain or intake of any drugs prior to the appearance of these blisters. His bowel and bladder habits are normal.

History of past illness: He had similar attack 3 years back, but the lesions were sparse and recovered completely.

Family history

Personal history

Socioeconomic condition

Treatment history: Mention according to the statement of the patient.

GENERAL EXAMINATION

- The patient looks very ill and apathetic
- Mildly anemic
- No jaundice, cyanosis, edema, dehydration, clubbing, koilonychias, leukonychia
- No lymphadenopathy and no thyromegaly
- Pulse—98/min
- Blood pressure—110/70 mm of Hg
- Temperature—98 °F
- Respiratory rate—20/min.

Integumentary System

1. **Skin:**
   - Multiple large tense bulla are present over flexor aspect of forearms, groin, axilla, front and back of the trunk, some are on normal skin and some are on erythematous skin. Intact blisters contain clear fluid. Some bullae are ruptured. There are multiple denuded areas that do not increase by confluence. Most of the ruptured bullae are in healing stage and some are healed with mild hyperpigmentation.

- Erythematous patches are mostly observed over the trunk. Most of the lesions show central clearing.
- Nikolsky and Asboe-Hansen signs are negative.

2. **Hair:** Normal.
3. **Nail:** Normal.
4. **Mucous membrane:**
   - Conjunctival—normal.
   - Oral—normal.
   - Genital—normal.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 65 years old, retired police officer, normotensive, nondiabetic, nonsmoker, hailing from … presented with multiple blisters over different parts of the body for … months. The blisters at first appeared over forearms and gradually involved axilla, groin and front and back of trunk. Most of the blisters are large and tense, few are small. Some blisters have ruptured leaving denuded areas that have healed spontaneously. He also noticed erythematous patches over the front and back of the trunk, some of which healed spontaneously. There is no involvement of the mouth or genitalia.

The patient also complains of mild generalized itching for the same duration. He had similar attack 3 years back, but the lesions were sparse and recovered completely. He did not complain of difficulty in swallowing. There is no history of fever, joint pain, muscle pain or intake of any drugs prior to the appearance of these blisters. His bowel and bladder habits are normal.

On general examination – (mention as above).

On examination of the integumentary system – (mention as above).

Examination of other systems reveals no abnormalities.

My diagnosis is bullous pemphigoid.

Q. What are your **differential diagnoses?**

A. As follows:

- Pemphigus vulgaris
- Dermatitis herpetiformis
- Stevens Johnson syndrome
- Toxic epidermal necrolysis (TEN).

Q. What **investigations** do you suggest?

A. As follows:

1. Routine:
   - Complete blood count
   - Random blood sugar
   - Urine R/M/E.
2. Confirmatory:
   - Tzanck test
   - Skin biopsy for histopathology and DIF.

Q. How to **confirm** the diagnosis of bullous pemphigoid?

A. Skin biopsy for histopathology and direct immunofluorescence shows deposition of IgG and complement C3 at the basement membrane (in a linear pattern).

Histopathological findings are:

- Subepidermal bullae
- Absence of acantholysis
- Superficial dermal infiltration of many eosinophils.

Q. What are the **points in favor** and **against** your differential diagnoses?

A. As follows:

Differential diagnoses	Points if favor	Points against
1. Pemphigus vulgaris	» Bullae over the groin, axilla, trunk	» Bullae are large, tense » Ruptured bulla heals spontaneously » No mucous membrane involvement » Nikolsky and Asboe-Hansen signs are negative
2. Dermatitis herpetiformis	» Tense blisters over the forearms » Pruritus present » Mucous membranes are not involved	» Old age » Bullae and erythematous patches present, but lesions are not polymorphous

Q. How to **treat** bullous pemphigoid?

A. As follows:

1. General treatment: Bed rest, maintenance of electrolyte, adequate nutrition, etc.
2. Steroid:
   - Prednisolone 0.5 to 0.75 mg/kg/day, should be tapered slowly over few weeks after clinical improvement (may be required to continue for 2 to 3 years).
   - Potent topical steroid can be given alone.
   - In severe cases, methylprednisolone 15 mg/kg IV daily for 3 doses.
3. Tetracycline 500 mg 6 hourly with nicotinamide 500 mg 8 hourly.
4. Other drugs include dapsone, azathioprine, methotrexate, cyclophosphamide, cyclosporine and mycophenolate mofetil.
5. IV immunoglobulin.
6. Antihistamine, if needed.

Note

Bullous pemphigoid responds to lower dose of prednisolone.

RELATED QUESTIONS AND ANSWERS

Q. How do you **differentiate** pemphigus vulgaris from bullous pemphigoid?

A. As follows:

Points	Pemphigus vulgaris	Bullous pemphigoid
1. Age	Middle age (50 to 60 years)	Elderly (> 60 years), few in infants and children
2. Distribution	Scalp, face, flexures, may be generalized	Trunk, limb, flexures
3. Mucosa of mouth conjunctiva and genitalia	Commonly involved (60%)	Rarely involved (20%), oral mucosa is involved usually
4. Lesion	Intraepidermal flaccid bullae that rupture easily and has a less tendency to heal	Subepidermal, large, tense blisters that do not rupture easily and has a more tendency to heal Urticarial plaques, erythematous patches, papules and nodules may be found
5. Asboe-Hansen and Nikolsky signs	Positive	Negative
6. Target antigen	Desmoglein 3, sometimes desmoglein 1	BP 230 and BP 180
7. Antigens (κDa)	130 κDa and 160 κDa	230 κDa and 180 κDa
8. Direct immuno-fluorescence	Intercellular deposition of IgG and C3 in mosaic pattern (C3 only lesional)	Basement membrane deposition of IgG and C3 in linear pattern (C3 both lesional and non-lesional)
9. Treatment	Steroid with higher dose	Steroid with lower dose
10. Prognosis	Variable prognosis. May be fatal because of treatment complications and sepsis. Recurrence is common	Better prognosis. Does not affect general health. Usually self-limited over 5 to 6-year-period, may be fatal in very elderly person

Q. What is the **pathogenesis** of bullous pemphigoid?

A. IgG autoantibody binds to BP antigen in the lamina lucida. Complement is activated that produces factors with anaphylatoxic and chemotactic activity. Mast cells are activated and degranulated with the release of eosinophil chemotactic factors. Eosinophils accumulate in the dermis and adhere to the basement membrane. They release tissue destructive enzymes and reactive oxygen intermediates. Resultant injury to the zone causes dermoepidermal separation and blister formation.

Q. What are the **presentations** of pemphigoid?

A. It is common in the elderly, > 60 years. The patient presents with:

- Tense bullae, red urticarial patch, less rupture, with a tendency to heal, may be urticarial, mostly in trunk, limbs and flexures.
- Mouth involvement (rare, and in < 20%).

Note

Pemphigoid may be associated with lymphoma.

Q. What is the **site of lesion** in pemphigoid?

A. The lesion is in the basement membrane between epidermis and dermis **(subepidermal),** hence fewer tendencies to rupture.

Q. What are the diseases that cause **subepidermal bullae**?

A. The following diseases show subepidermal blister histopathologically:

- Bullous pemphigoid
- Dermatitis herpetiformis
- Herpes gestationis
- Linear IgA dermatosis
- Porphyria cutanea tarda
- Lichen planus
- Bullous SLE
- Lichen sclerosus atrophicus.

Q. What is **herpes gestationalis (pemphigoid gestationis)?**

A. It is the pregnancy-related skin lesions characterized by an itchy blistering urticated eruption that starts on the abdomen, often involving the umbilicus, and may become widespread. Large bullae may be present. It usually appears in the fifth or sixth month of pregnancy but may occur earlier, even in first trimester. It is a self-limited disease, but may recur in subsequent pregnancy. Diagnosis is confirmed by histology and immunofluorescence study. The blisters are eosinophil rich and subepidermal, with C3 in the basement membrane and serum complement-fixing immunoglobulin antibody. In mild case, topical corticosteroid is used but in severe case systemic steroid is needed. The dose may need to be increased after delivery as there is often a postpartum flare up of the disease. Oral contraceptive pills should be avoided, since they also flare up the disease. A transient bullous eruption occurs in 5% of infants, but there is no increase in fetal mortality.

Q. What are the diseases **associated** with bullous pemphigoid?

A. The following diseases are found to be associated with bullous pemphigoid:

- Diabetes mellitus
- Rheumatoid arthritis
- Dermatomyositis
- Ulcerative colitis
- Myasthenia gravis
- Thymoma.

Q. What are the **mechanisms** of blister formation?

A. Blisters are formed by the following mechanisms:

- Autoimmune mediated (dissolution of intracellular cement substance via acantholysis, e.g. pemphigus).
- Detachment of horny layer (subcorneal pustular dermatosis).
- Due to intracellular degeneration causing separation of cells from one another (e.g. friction blisters).
- Spongiotic blister due to intercellular edema (irritant contact dermatitis).
- Acantholysis due to ballooning degeneration (herpes simplex).
- Degeneration of basal cells causing loose contact with dermis (lichen planus).
- Degenerative changes in the basal membrane zone (bullous pemphigoid).

LICHEN PLANUS

CHIEF COMPLAINTS

- Multiple itchy papules in all extremities and over trunk for … months.

HISTORY

History of present illness: According to the statement of the patient, he was reasonably well … months back. Since then, he has been suffering from multiple violaceous papules that first involved the flexor aspect of forearms. The papules are extremely itchy. Gradually, there are also multiple papules that have involved the legs, thigh, arms and trunk. Some of the papules enlarged in size and turned into large plaques. After some days, the patient experienced the involvement of the nails and mouth cavity. There is no history of fever, joint pain, muscle pain or bleeding from any site. He did not take any drug prior to the lesions. His bowel and bladder habits are normal.

Past history

Family history

Personal history

Drug history: Mention according to the statement of the patient.

GENERAL EXAMINATION

- The patient is emaciated
- Mildly anemic
- No jaundice, cyanosis, clubbing, koilonychia, leukonychia, edema
- No lymphadenopathy or thyromegaly
- Pulse: 110/min
- Blood pressure: 110/70 mm of Hg
- Respiratory rate: 16/min
- Temperature: 98°F.

Integumentary System

1. **Skin:**
   - Inspection: There are bilateral symmetrical multiple flat-topped violaceous papules and plaques in both upper and lower extremities, more numerous in flexor aspect of forearms and shins. Koebner's phenomenon is seen in the extremities. Wickham's striae is present (mention if any).
   - Palpation: The papules are firm in consistency, nontender and not fixed to the underlying structure.
2. **Oral mucosa:** Violaceous, reticulate lesions on the inner aspect of cheeks, consisting of pinhead size silvery white papules.
3. **Nails** of ring and middle fingers of right hand show longitudinal ridging and grooving, also onycholysis involving ring and small fingers of the left hand.
4. **Hair** shows no abnormality.

   Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 26 years old, businessman, nonsmoker, nondiabetic, hailing from …, presented with multiple violaceous papules that first involved the flexor aspect of forearms for … months. The papules are extremely itchy. Gradually, there are also multiple papules that have involved the legs, thigh, arms and trunk. Some of the papules enlarged in size and turned into large plaques. After some days, the patient experienced involvement of the nails and mouth cavity. There is no history of fever, joint pain, muscle pain or bleeding from any site. He did not take any drug prior to the lesions. His bowel and bladder habits are normal. There is no history of previous skin disease. For his present complaints, he was treated with some drugs by local doctors, but he could not remember the name.

On examination, general examination – mention as above.

Integumentary system – mention as above.

Examination of other systems shows no abnormalities.

My diagnosis is lichen planus.

Q. What investigations should be done in lichen planus?

A. As follows:

1. Routine:
   - Complete blood count
   - Viral marker for hepatitis B and C
   - Liver function tests and renal function tests for therapeutic purpose.
2. Specific: Skin biopsy for histopathology and DIF.

RELATED QUESTIONS AND ANSWERS

Q. Describe a **typical lesion** of lichen planus.

A. It is characterized by flat-topped, pruritic, polygonal violaceous papules on the flexors of wrist, trunk, medial aspect of thighs and shins. Wickham striae and Koebner phenomenon are present. Oral mucosa shows reticulated whitish (or violaceous) plaques consisting of pin head papules on the inner aspect of cheeks. Nail shows longitudinal grooving, proximal and distal onycholysis, ridging and splitting.

Q. What are the other **causes** of flat topped papules?

A. As follows:

- Lichen amyloidosis
- Lichen nitidus
- Lichen myxedematosus.

Q. What is the cause of **Wickham striae**?

A. It is because of focal increase in the thickness of granular layer and total epidermis. It is better seen with a hand lens (and by aniline dye).

Q. What are the **different types** of mucosal lesions?

A. As follows:

- Ulcerative—50%
- Reticulate—30%
- Atrophic—20%.

Q. What are the **drugs** that may cause lichenoid drug reactions?

A. Beta blockers, thiazides, spironolactone, frusemide, ACE inhibitors, calcium channel blockers, antimalarials, heavy metals, arsenic, lithium, iodides.

Q. What are the **types of lichen planus?**

A. As follows:

1. According to configuration:
   - Linear
   - Annular.
2. According to morphology of lesions:
   - Hypertrophic
   - Atrophic
   - Vesicobullous
   - Ulcerative and erosive
   - Actinic
   - Follicular
   - Lichen planus pigmentosus
   - Guttate and perforating.
3. According to site of involvement:
   - Lichen planus of the scalp
   - Mucosal lichen planus
   - Lichen planus of nails
   - Palmoplantar lichen planus
   - Inverse lichen planus in axilla, inframammary, groin, popliteal and antecubital areas.
4. Special variants:
   - Drug induced LP
   - Lichen planus and LE overlap
   - Lichen planus pemphigoides
   - Keratosis lichenoides chronica
   - Lichenoid reaction of graft versus host disease
   - Lichenoid keratosis
   - Lichenoid dermatitis.

Q. What are the **differences** between lichen planus and lichen nitidus?

A. As follows:

Points	Lichen planus	Lichen nitidus
1. Size	Variable, usually large	1 to 2 mm
2. Shape	Polygonal	Round
3. Color	Erythematous to violaceous	Shiny, discrete
4. Wickham striae	Present	Absent
5. Pruritus	Marked	Uncommon
6. Mucosal change	Frequently present	Rare

Q. What are the **differences** between lichenoid drug reaction and lichen planus?

A. As follows:

Points	Lichenoid drug reaction	Lichen planus
1. Site	Sun exposed areas	Flexor areas
2. Lesions	Larger and scaly	Smaller
3. Wickham striae	Absent	Present
4. Alopecia	More	Less
5. Mucosal involvement	Less	More

Q. What are the **differential diagnoses** of lichen planus?

A. Differential diagnosis of lichen planus depends on type:

1. Hypertrophic:
   - Lichen simplex chronicus
   - Psoriasis
   - Lichen amyloidosis.
2. Annular:
   - Granuloma annulare
   - Annular syphilis
   - Annular psoriasis.
3. Linear:
   - Lichen striatus
   - Linear morphea.
4. Atrophic:
   - Lichen sclerosus atrophicus
   - DLE.
5. Guttate:
   - Guttate psoriasis
   - Pityriasis rosea.
6. Oral:
   - Candidiasis
   - Secondary syphilis.
7. Follicular:
   - Lichen spinulosus
   - Lupus erythematosus.

Q. What are the histopathological and DIF findings in lichen planus?

A. As follows:

- Histopathology shows—hyperkeratosis, beaded hypergranulosis and saw tooth pattern of epidermal hyperplasi**.** There is destruction of basal layer that is squamatized. In superficial dermis, there is dense band like infiltrate of lymphocytes and melanophages. Civatte bodies represent necrotic keratinocytes.
- DIF shows—clumps of IgM and less frequently IgA, IgG and C_3 subepidermally corresponding to civatte bodies.

Q. How to treat lichen planus?

A. Treatment depends according to the type and extent of the disease:

1. General measures:
   - Avoid drugs, such as diuretics, beta blockers, antimalarials
   - Protection from trauma.

2. Cutaneous lesions:
   - First line:
     - Topical –
       - Topical steroids
       - Intralesional
       - Tacrolimus
       - Pimecrolimus.
     - Physical – Psoralen and ultraviolet light
     - Systemic –
       - Systemic steroid – Prednisolone 30 to 80 mg/day
       - Etretinate 10 to 75 mg/day
       - Acitretin 30 mg/day
       - Isotretinoin 20 to 40 mg/day.
   - Second line:
     - Cyclosporine 3 to 10 mg/kg/day
     - Dapsone 200 mg/day
     - Hydroxychloroquine 200 to 400 mg/day
     - Azathioprine 50 mg bid
     - Mycophenolate mofetil 1500 mg bid.
3. Oral lesions:
   - Topical steroid in orabase, nystatin with clobetasol, topical tretinoin with steroid, 1% topical tacrolimus.
   - PUVA and 308 nm excimer laser.
   - Systemic—hydroxychloroquine 200 mg to 400 mg daily for 6 months. Thalidomide 150 mg/day.
   - Other agents used in cutaneous lesions also improve oral lesions.
4. Special forms:
   - Doxycycline, tetracycline and nicotinamide—LP pemphigoides
   - Interferon α and β generalized
   - Metronidazole generalized
   - Cyclophosphamide—refractory LP
   - Methotrexate—refractory LP.

Q. What is the course or prognosis of lichen planus?

A. Two-third of patients will have lichen planus of less than 1 year. Many patients cure spontaneously within 1 year. Recurrence occurs in half of the patients.

Q. What are the medical causes of itching?

A. As follows:

1. Liver disease—primary biliary cirrhosis, obstructive jaundice
2. Chronic renal failure
3. Hematological—polycythemia rubra vera (after warm bath), lymphoma (especially Hodgkin's disease), leukemia, multiple myeloma, iron deficiency anemia
4. Endocrine cause—hypothyroidism, thyrotoxicosis, diabetes mellitus (especially associated with candidiasis).
5. Any internal malignancy
6. HIV
7. Psychogenic.

Q. What are the **dermatological manifestations of internal malignancy**?

A. As follows:

- Dermatomyositis—bronchial carcinoma, malignancy of GIT, genitourinary.
- Acanthosis nigricans—may be found in malignancies of GIT, lung, liver.
- Paget's disease of nipple—ductal carcinoma of breast.
- Erythroderma—lymphoma, leukemia.
- Tylosis—esophageal carcinoma.
- Ichthyosis—lymphoma.
- Erythema gyratum repens (concentric rings of erythema)—malignancies of lung, breast.
- Necrolytic migratory erythema (burning, geographic and spreading annular areas of erythema) —glucagonoma.

ARSENICOSIS

CHIEF COMPLAINTS

- Multiple hyper and hypopigmented lesions in different parts of the body for … months
- Thickening and pigmentation of the palms and soles for … months
- Nausea, vomiting and weight loss for … months.

HISTORY

History of present illness: According to the statement of the patient, he was reasonably well … months back. Since then, he has observed numerous hyper and hypopigmented lesions in different parts of the body that first appeared on the trunk and then gradually involved the rest of the body. These are painless, non-itchy and not associated with any loss of sensation. For the last … months, he has noticed gradual thickening and pigmentation of the palms and soles that are painless and non-itchy. The patient also complains of nausea and occasional vomiting for … days that is not related to intake of food. There is no difficulty in deglutition. He also complains of loss of appetite, substantial weight loss, constipation and progressive weakness. His bladder habit is normal. There is no history of fever, cough, muscular pain or joint pain.

Past history

Family history

Personal history

Socioeconomic history: The patient used to drink water from tubewell for long time. Recently, it has been marked red due to high arsenic level. Now, he drinks water from arsenic free tubewell.

Drug history: Mention according to the statement of the patient.

GENERAL EXAMINATION

- The patient looks emaciated
- Mildly anemic
- No jaundice, cyanosis, clubbing, koilonychia, leukonychia, edema
- No lymphadenopathy or thyromegaly
- Pulse: 105/min
- Blood pressure: 110/65 mm of Hg
- Respiratory rate: 16/min
- Temperature: 98°F.

Integumentary System

1. **Skin:**
   - There are multiple hyperpigmented lesions involving both upper and lower limbs and trunk with scattered hypopigmented area giving rise to rain drop appearance.
   - Multiple hard papular and plaque like lesions with hyperpigmentation are seen over the front of the chest.
   - There is hyperkeratosis of palms and soles.

2. **Oral mucosa:** Normal.
3. **Nails** are brittle. Some has transverse white striae (Mee's line).
4. **Hair** is dry and spars.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 56 years old, farmer, nonsmoker, nondiabetic, hailing from …, presented with numerous hyper and hypopigmented lesions on different parts of the body for … months. These first appeared on the trunk and then gradually involved the rest of the body. These are painless, non-itchy and not associated with any loss of sensation. For the last … months, he has noticed gradual thickening and pigmentation of the palms and soles that are painless and non-itchy. The patient also complains of nausea and occasional vomiting for … days that is not related to intake of food. There is no difficulty in deglutition. He also complains of loss of appetite, substantial weight loss, constipation and progressive weakness. His bladder habit is normal. There is no history of fever, cough, muscular pain or joint pain. The patient used to drink water from a tubewell for a long time that was recently marked in red due to high arsenic concentration.

On examination, general examination – mention as above.

Integumentary system – mention as above.

Examination of other systems shows no abnormalities.

My diagnosis is arsenicosis (or chronic arsenic toxicity).

Q. What are your **differential diagnoses**?

A. As follows:
- Hemochoromatosis
- Lepromatous leprosy
- Tinea versicolor
- Addison's disease.

Q. What **investigations** are done in chronic arsenic toxicity?

A. As follows:

1. Routine:
   - FBC
   - Urine for routine examination
   - Chest X-ray
   - Liver function tests
   - Renal function tests
   - ECG
   - EEG
   - Nerve conduction test
2. Confirmatory—Measurement of arsenic concentration in hair, nail, urine and serum.

Q. How to **confirm** chronic arsenic poisoning?

A. By measuring the arsenic concentration in hair, nail, urine and serum.

Normal value of arsenic:
- Blood < 3 mg/L (or 5 to 50 ppb/mg/L)
- Urine 0.005 to 0.04 mg/L

- Hair 0.08 to 0.25 mg/kg (pubic hair is preferred due to lack of contamination)
- Nail 0.43 to 1.08 mg/kg
- Daily urinary excretion < 0.1 mg/L.

Note Remember the following points

- Skin manifestations require 1 year to develop
- Systemic manifestations require 10 years to develop
- Early signs of arsenic toxicity—conjunctivitis, transient icterus and hyperhidrosis.

RELATED QUESTIONS AND ANSWERS

Q. What is the **mechanism** of arsenic toxicity?

A. After absorption, arsenic is widely distributed to all the tissues of body. It combines with sulfhydryl-containing substances and inhibits the activity of many enzymes. It interferes with cell enzymes, cell respiration and mitosis.

Q. What are the **clinical presentations** of arsenicosis?

A. As follows:

- Melanosis—hyperpigmentation (generalized or localized) with few scattered hypopigmented areas giving raise to **raindrop** appearance.
- Hyperkeratosis of mainly palm and sole. May be multiple, punctate, hard, discrete, papule and verrucous plaque.
- Nails—brittle, may show transverse white striae of finger nails **(Mees' line).**
- Hair—dry, may fall off.
- Eye—conjunctivitis.
- Nose—rhinitis, epistaxis, nasal obstruction and septal perforation.
- It may involve any system of the body (liver, kidney, lung and heart).

Q. What are the **diagnostic signs** of arsenicosis?

A. As follows:

- Hyperkeratosis of palms and soles
- Hyperpigmentation and hypopigmentation (on trunk and extremities) are the hallmarks.

Q. What are the **systemic effects** of chronic arsenic toxicity?

A. As follows:

1. GIT: Anorexia, nausea and vomiting.
2. Hepatic: Hepatomegaly, cirrhosis of liver and noncirrhotic portal hypertension.
3. Central nervous system (CNS): Peripheral neuropathy, seizure, confusion and encephalopathy.
4. Hematological: Anemia, leukopenia and thrombocytopenia.
5. Musculoskeletal: Myalgia, arthralgia and atrophy of extensor muscles causing wrist drop or foot drop.
6. Renal: Dysuria, anuria and renal tubular necrosis.
7. Heart: Cardiomyopathy, arrhythmia and heart failure.
8. Vascular: Peripheral vascular insufficiency causing black foot disease.
9. Endocrine: Diabetes mellitus may be precipitated.
10. Malignancy:
    - Skin—squamous cell carcinoma, basal cell carcinoma and Bowen's disease.
    - Carcinoma of lung, kidney, urinary bladder, liver (angiosarcoma), prostate and colon.

Q. How to **treat** chronic arsenic toxicity?

A. As follows:

1. Drinking of arsenic contaminated water must be stopped.
2. High protein diet.
3. Antioxidant (vitamin A 50,000 IU, vitamin C 500 mg and vitamin E 200 mg daily for 3 months).
4. Vitamins and minerals supplement.
5. Vegetables and fresh fruits.
6. *Spirulina* (an algae), which is rich in high protein, may help to clear arsenic.
7. For skin lesion: Keratolytic emollients (salicylic acid, urea and retinoic acid), cryotherapy, electrocautery and laser therapy.
8. Drugs (chelating agent may be used):
   - D-penicillamine (250 mg TDS) for 3 months, or
   - Dimercaprol (BAL), dimercaptosuccinic acid (DMSA) and dimercaptopropane sulfonate (DMPS). BAL has a tendency to redistribute arsenic to brain and testes. DMSA and DMPS are more preferable, because of their low toxicity.

Dose:

- DMSA—10 mg/kg/day for 7 days followed by 10 mg/kg/day three times for 14 days.
- DMPS—100 mg TDS to QDS for every alternate week for three courses.

Preventive therapy: Drinking water should be safe.

Q. What are the **differential diagnoses** of arsenicosis?

A. As follows:

1. For pigmentation:
- Lepromatous leprosy
- Hemochromatosis
- Addison's disease
- Xeroderma pigmentosum
- Guttate psoriasis
- Tinea versicolor
- Idiopathic guttate hypomelanosis
- Postinflammatory hypopigmentation and hyperpigmentation
- Drug melanosis.

2. For keratosis:
- Epidermodysplasia verruciformis
- Multiple corn or callosities
- Verruca vulgaris
- Hereditary palmoplantar keratoderma
- Acrokeratosis verruciformis.

LEG ULCER (VENOUS ULCER)

CHIEF COMPLAINTS

- Swelling of both legs for … years
- Gradual darkening of skin on both legs for … months
- Appearance of an ulcer on the inner aspect of right lower leg for … days.

HISTORY

History of present illness: The patient states that he was reasonably well … years back. Since then, he has been suffering from swelling of both legs. This is more marked during the evening, disappears in the morning and also occasionally after prolonged lying. For the last … months, the patient also complains of gradual darkening of his feet and lower legs, followed by an itchy, oozing lesion that became ulcerated on the inner aspect of his right lower leg. The ulcer is slightly painful with oozing, but no bleeding and there is no sign of healing. He did not give any history of blister before ulceration (to differentiate from pyoderma gangrenosum) or any rash. The patient agreed that he has to stay standing for a long time due to his occupation as a policeman.

He did not give any history of trauma, tingling or numbness of his toes, loss of sensation, muscular weakness, joint pain, pain on back of legs while walking, fatigue or weakness, loss of hair or reduced temperature. The swelling of the legs are not associated with breathlessness, cough, chest pain, palpitation, jaundice or any urinary complaint. His bowel and bladder habits are normal.

History of past illness: He is not diabetic or hypertensive. He is suffering from varicose vein for the last … years.

Family history: Nothing significant.

Personal history: He is a nonsmoker.

Drug and treatment history: He was treated with local and oral antibiotics, antihistamines and furosemide.

Socioeconomic condition: He drinks arsenic free water from a tubewell.

GENERAL EXAMINATION

- The patient looks normal
- No anemia, jaundice, cyanosis, clubbing, koilonychia, leukonychia
- Bilateral pitting edema present
- No lymphadenopathy or thyromegaly
- Pulse: 110/min. All the peripheral pulses are present
- Blood pressure: 120/70 mm of Hg
- Respiratory rate: 16/min
- Temperature: 98ºF.

Examination of lower limbs:

- **Skin:** There are pin-pointed hyperpigmented macules and patches involving both lower legs and feet with crusted, oozing plaque on medial aspect of left leg. There is a solitary ulcer over the right medial malleoli, 4 cm × 2 cm in diameter, margin is irregular, floor is clear, base is tender but no oozing. Surrounding skin is pigmented and warm.

- There are bilateral varicose veins, of variable size and shape.
- All the peripheral pulses are present. There is no pallor on elevation or redness of the foot on lowering the leg (dependent rubor).
- **Hair:** Normal.
- **Nail:** Normal.

Mucous membrane: Normal.

Conjunctiva: Normal.

Genitalia: Normal.

Nervous system: No sensory or motor impairment in both lower limbs.

Examination of the other systems reveals no abnormalities.

SALIENT FEATURE

Mr …, 45 years old, a policeman, normotensive, nondiabetic, nonsmoker, hailing from …, presented with swelling of both legs for … months. This is more marked during the evening, disappears in the morning and also occasionally after prolonged lying. For the last … months, the patient also complains of gradual darkening of his feet and lower legs, followed by an itchy, oozing lesion that became ulcerated on the inner aspect of his right lower leg. The ulcer is slightly painful with oozing, but no bleeding and there is no sign of healing. He did not give any history of blister before ulceration (to differentiate from pyoderma gangrenosum) or any rash. The patient agreed that he has to stay standing for a long time due to his occupation as a policeman.

He did not give any history of trauma, tingling or numbness of his toes, loss of sensation, muscular weakness, joint pain, pain on back of legs while walking, fatigue or weakness, loss of hair or reduced temperature. The swelling of the legs are not associated with breathlessness, cough, chest pain, palpitation, jaundice or any urinary complaint. His bowel and bladder habits are normal. He is suffering from varicose vein for the last … years. He was treated with local and oral antibiotics, antihistamines and frusemide.

General examination (as above).

Examination of integumentary system (as above).

Examination of the other systems reveals no abnormalityies.

My diagnosis is venous ulcer.

Q. Why not this is arterial ulcer?

A. Usually arterial ulcer is more on the lateral surface of the ankle or on the distal digits. It is usually tender, punched-out with cold skin, loss of hair, and absent or reduced pulse. There may be dry gangrene.

Q. What are the other causes of leg ulcer?

A. As follows:

1. If the patient is elderly, probable causes are:
   - Trauma
   - Atherosclerosis
   - Diabetes mellitus
   - Tuberculosis

- Leprosy
- Leishmaniasis.

2. If the patient is younger, probable causes are:
   - Trauma
   - Diabetes mellitus
   - Hematological disease (thalassemia, hereditary spherocytosis)
   - Collagen disease (SLE, rheumatoid arthritis).

Q. What **investigations** should be done in leg ulcer?

A. As follows:

- Hb%, TC, DC and ESR
- Blood sugar
- Lipid profile (in atherosclerosis)
- Pus (if any), for C/S, AFB, LD bodies
- Doppler USG of lower limb vessels
- X-ray of leg (calcification in artery may be seen)
- Arteriography
- Biopsy
- Others—according to suspicion of causes, e.g. ANF, cold agglutinin and RA test.

Q. What are the **causes** of leg ulcer?

A. As follows:

1. Traumatic.
2. Infection (pyogenic, lupus vulgaris, leprosy, cutaneous leishmaniasis, sporotrichosis, blastomycosis, coccidioidomycosis, cryptococcosis, histoplasmosis, schistosomiasis, late gummatous syphilis).
3. Arterial causes are atherosclerosis, peripheral vascular disease (including Buerger's disease, Raynaud's disease, etc.) and arterial occlusion. Arterial ulcer (or ischemic ulcer) occurs more on the lateral surface of the ankle or the distal digits. It is usually tender, punched-out with cold skin, loss of hair, and absent or reduced pulse. There is pallor on elevation and redness of foot on lowering the leg (dependent rubor). There may be dry gangrene.
4. Venous ulcer occurs usually due to varicose vein. It is common around malleoli or in medial side. The leg is edematous. There may be wet gangrene, pigmentation, eczema, lipodermatosclerosis (combination of induration, reddish brown pigmentation and inflammation—a fibrosing panniculitis of the subcutaneous tissue) and scarring white atrophy with telangiectasia (atrophie blanche).
5. Neuropathic ulcer occurs in diabetes mellitus, tabes dorsalis, syringomyelia, leprosy, polyneuropathy due to any cause. This type of ulcer is usually painless and more on the plantar surface of foot, callosities and pressure points. There is impaired sensation on the affected part.
6. Collagen diseases, such as SLE, rheumatoid arthritis, Felty's syndrome, cryoglobulinemia, polyarteritis nodosa, etc.
7. Hematological diseases, such as sickle cell anemia, thalassemia, hereditary spherocytosis, paroxysmal nocturnal hemoglobinuria, thrombotic thrombocytopenic purpura and macroglobulinemia.
8. Neoplastic disorders, such as squamous cell carcinoma, basal cell carcinoma, lymphoma and Kaposi's sarcoma.
9. Miscellaneous: Pyoderma gangrenosum, dermatitis artefacta, drugs.

Q. How to **treat** leg ulcer?

A. As follows:

1. General measures:

- Smoking should be stopped
- Control of DM, hypertension, obesity (if any)
- Treatment of primary cause
- Local care (cleaning and dressings).

2. Specific measures:
   - Antibiotic, if any infection
   - Low dose aspirin
   - In some cases, surgery (balloon dilatation) and if necessary, amputation
   - Consult with chiropodist.

LEUKOCYTOCLASTIC VASCULITIS (SMALL VESSEL VASCULITIS)

CHIEF COMPLAINTS

- Multiple painful pigmented elevated lesions on upper and lower extremities for 3 weeks.
- Joint pain and leg edema for 3 weeks.
- Fever for 1 week.

HISTORY

History of present illness: According to the patient, she was reasonably well 3 weeks ago. Since then, she has noticed multiple painful pigmented elevated lesions on her upper and lower limbs including buttocks. The lesions first appeared on the legs and then gradually spread to other sites including palm and soles. The lesions showed progressive color change from red to dark pigmented and smaller pigmented lesions coalesces to form larger lesions. There is no itching, burning, discharge or exfoliation from the lesions. She also complains of pain in large and small joints of upper and lower limbs without any swelling. She also noticed swelling of both feet and ankles for 3 weeks. There is no variation in swelling throughout the day. She did not give any history of medication, throat pain, abdominal pain, bloody diarrhea, gum bleeding, oral ulcer, photosensitivity, hair loss, high color urine, cough, chest pain, hemoptysis, shortness of breath, jaundice. She also complains of low grade continued fever without any chill, rigor or sweating.

History of past illness:

Family history

Personal history

Drug and treatment history: She was treated by some local doctors by some painkillers, the name of which she cannot mention.

Socioeconomic condition

GENERAL EXAMINATION

- The patient looks normal
- No anemia, jaundice, cyanosis, clubbing, koilonychia, leukonychia
- Bilateral pitting edema present
- No lymphadenopathy or thyromegaly
- Pulse: 110/min. All the peripheral pulses are present
- Blood pressure: 120/70 mm of Hg
- Respiratory rate: 16/min
- Temperature: 98ºF.

Integumentary System

- **Skin:** There are multiple purpura that are painful, palpable, some are erythematous and some are hyperpigmented, involving both upper and lower extremities including palm and soles. There is no ulceration, ecchymosis, nodules, plaques, urticaria or scarring.
- **Hair:** Normal.
- **Nail:** Normal.

- **Mucous membrane:** Normal.
- **Conjunctiva:** Normal.
- **Genitalia:** Normal.

Joints

- Grade 1 tenderness involving the ankles, knees, wrists, elbows and small joints of the hands. There is no swelling.

Examination of the other systems reveals no abnormalities.

SALIENT FEATURE

Ms …, 20 year old, student, normotensive, nondiabetic, nonsmoker, hailing from …, presented with multiple painful pigmented elevated lesions on her upper and lower limbs including buttocks for 3 weeks. The lesions first appeared on the legs and then gradually spread to other sites including palm and soles. The lesions showed progressive color change from red to dark pigmented and smaller pigmented lesions coalesces to form larger lesions. There is no itching, burning, discharge or exfoliation from the lesions. She also complains of pain in large and small joints of upper and lower limbs without any swelling. She also noticed swelling of both feet and ankles for 3 weeks. There is no variation in swelling throughout the day. She did not give any history of medication, throat pain, abdominal pain, bloody diarrhea, gum bleeding, oral ulcer, photosensitivity, hair loss, high color urine, cough, chest pain, hemoptysis, shortness of breath, jaundice. She also complains of low grade continued fever without any chill, rigor or sweating. She was treated by some local doctors by some painkillers, the name of which she cannot mention.

General examination (as above).

Examination of integumentary system (as above).

Examination of the other systems reveals no abnormalities.

My diagnosis is idiopathic cutaneous small vessel vasculitis (leukocytoclastic vasculitis).

Q. What are your **differential diagnoses?**

A. As follows:

- Henoch Schonlein purpura
- Urticarial vasculitis
- Connective tissue disease (such as SLE, rheumatoid arthritis)
- Microscopic polyangiitis
- Churg Strauss syndrome
- Wegener's granulomatosis
- Cryoglobulinemic vasculitis
- Polyarteritis nodosa
- Lymphoma (HD).

Q. What **investigations** do you suggest in this patient?

A. As follows:

1. Routine:
   - CBC, platelet count, PBF
   - Urine R/M/E
   - X-ray chest.

2. To exclude other cause:
   - Throat culture and ASO titer
   - Hepatitis B and C serology
   - ANA, anti-ds-DNA
   - RA test, RW test, Anti-CCP antibody
   - pANCA, cANCA
   - Serum complement.
3. Specific: Skin biopsy with DIF (perilesional in case of Henoch Schonlein purpura).

Q. What are the **biopsy** findings?

A. As follows:

- There is angiocentric segmental inflammation of the postcapillary venule with expansion of the vessel wall, fibrin deposition, and infiltration by neutrophils that show fragmentation of their nuclei (karyorrhexis or leukocytoclasia).
- Endothelial cell swelling is common, may be endothelial necrosis in serious illness (including septic vasculitis, ANCA associated vasculitis).

Q. What are the **DIF** findings?

A. As follows:

- Immunoglobulins, complement components and fibrin deposits within postcapillary venule walls if the biopsy is taken within the first 24 hours.
- Later, fibrin is prominent but immunoglobulin deposits may be absent. But, in Henoch Schonlein purpura, there is prominent IgA deposit even in more advanced lesions.

Q. What is **leukocytoclastic vasculitis** (LCV)?

A. It is the most common cutaneous small vessel vasculitis. Usually there is symmetrical palpable purpura involving the lower legs. Systemic involvement is rare. It may be caused by drugs, infection, inflammatory disease or malignant disease, but often no cause is found (55 to 60%). Investigations are only necessary with persistent lesions or associated signs and symptoms. It often resolves spontaneously, but treatment with analgesia, support stockings, dapsone or prednisolone may be needed to control the pain and to heal up any ulceration.

Q. What is the pathogenesis of **cutaneous small vessel vasculitis**?

A. Cutaneous small vessel vasculitis is due to circulating immune complexes, which involves the vessel walls and activate complement. Various inflammatory mediators are produced, contributing to endothelial injury.

Q. What are the **treatments** of cutaneous small vessel vasculitis?

A. Most of the cases are acute, self-limiting and do not involve the internal organ. In such cases, the following measures should be taken:

1. General measures:
   - Rest and elevation of the legs
   - Avoidance of trauma and cold
   - Analgesics, for pain
   - Treatment of the primary cause, if any.
2. If the disease is limited to the skin, colchicines 0.6 mg 2 to 3 times daily or dapsone 50 to 200 mg/day for 2 to 3 weeks.
3. In severe, intractable or recurrent case or if there is internal organ involvement:
   - Systemic corticosteroid (prednisolone 60 to 80 mg/day).
   - In refractory case, immunosuppressive agents, such as mycophenolate mofetil 2 to 3 g/day, methotrexate 5 to 25 mg/week, azathioprine 50 to 200 mg/day may be given.

- In more difficult cases, cyclophosphamide, monthly intravenous pulse corticosteroid or cyclophosphamide, cyclosporine 3 to 5 mg/kg/day may be given.
- TNF-α blockers like infliximab may be used.

Q. What is **vasculitis**?

A. Inflammation of the vessel walls is called vasculitis.

Q. What is the **classification** of vasculitis?

A. As follows:

1. Cutaneous small vessel (postcapillary venule):
   a. Idiopathic cutaneous small vessel vasculitis:
   b. Henoch Schonlein purpura
   c. Acute hemorrhagic edema of infancy
   d. Urticarial vasculitis
   e. Cryoglobulinemic vasculitis
   f. Erythema elevatum diutinum
   g. Granuloma faciale
   h. Other disease with leukocytoclastic vasculitis: Drug induced vasculitis, malignancy (lymphoreticular more common than solid tumor), connective tissue diseases, hyperglobulinemic purpura, inflammatory bowel disease, bowel associated dermatitis arthritis syndrome (bowel bypass), HIV infection and neutrophilic dermatoses (Behcet's syndrome, Sweet syndrome, erythema nodosum leprosum, septic vasculitis, autoinflammatory disease—familial Mediterranean fever, serum sickness).
2. Medium vessel:
   a. Polyarteritis nodosa:
      - Benign cutaneous forms
      - Systemic form.
   b. Kawasaki's disease.
3. Mixed size (medium and small) vessel disease:
   a. Connective tissue disease associated (usually rheumatoid vasculitis)
   b. Septic vasculitis
   c. ANCA associated:
      - Microscopic polyangiitis
      - Wegener's granulomatosis
      - Allergic granulomatosis (Churg-Strauss syndrome)
      - Drug induced (most are post capillary venule only).
4. Large vessel vasculitis:
   a. Giant cell arteritis.
   b. Takayasu's arteritis.

ERYTHEMA NODOSUM

CHIEF COMPLAINTS

- Multiple reddish painful lesions over front of both legs for … days
- Pain in multiple joints for … week
- Dry cough for … weeks.

HISTORY

History of present illness: According to the patient he was reasonably well … days ago. Since then, he noticed multiple nodules of variable size and shape, present over the front of both lower legs. The nodules are painful, some are red and some are purple in color. He also complains of pain in knees, right ankle, right elbow and right wrist joints for … weeks, but there is no swelling. The patient has dry cough for … weeks, which is not associated with breathlessness or chest pain. There is no diurnal variation. It is not associated with exertion or exposure to allergens. He did not complain of any fever, sore throat. His bowel and bladder habits are normal.

History of past illness

Family history

Personal history

Drug and treatment history: He did not take any drugs prior to this illness. For the present complains, he took some cough syrup and analgesics but could not mention the names.

Socioeconomic condition: Mention according to the patient's statement.

GENERAL EXAMINATION

- The patient looks ill
- No anemia, jaundice, cyanosis, clubbing, koilonychia, leukonychia
- Bilateral pitting edema present
- No lymphadenopathy or thyromegaly
- Pulse: 92/min. All the peripheral pulses are present
- Blood pressure: 130/70 mm of Hg
- Respiratory rate: 18/min
- Temperature: 98ºF.

Integumentary System

- **Skin:** There are multiple nodular, tender lesions of variable size and shape, some are red and some are pigmented in the right or left or both shin.
- **Hair:** Normal.
- **Nail:** Normal.
- **Mucous membrane:** Normal.
- **Conjunctiva:** Normal.
- **Genitalia:** Normal.

Gastrointestinal Tract

- **Throat:** Normal
- **Liver:** Not palpable
- **Spleen:** Not palpable.

Examination of the other systems reveals no abnormalities.

SALIENT FEATURE

Mr …, 23 years old, student, normotensive, nondiabetic, nonsmoker, hailing from …, presented with multiple nodules of variable size and shape, present over the front of both lower legs for … days. The nodules are painful, some are red and some are purple in color. He also complains of pain in knees, right ankle, right elbow and right wrist joints for … weeks, but there is no swelling. The patient has dry cough for … weeks, which is not associated with breathlessness or chest pain. There is no diurnal variation. It is not associated with exertion or exposure to allergens. He did not complain of any fever, sore throat. His bowel and bladder habits are normal. He did not take any drugs prior to this illness. For the present complaints, he took some cough syrup and analgesics but could not mention the names.

General examination (as above).

Examination of integumentary system (as above).

Examination of the other systems reveals no abnormalities.

My diagnosis is erythema nodosum.

Q. What are your **differential diagnoses**?

A. As follows:
- Drug rash
- Erythema multiforme
- Purpura
- Cellulitis
- Erythema induratum
- Others: Nodular panniculitis, meningococcal septicemia, vasculitis (SLE and PAN).

Q. What **investigations** are done in erythema nodosum?

A. As follows:
- CBC, ESR, PBF (leukocytosis in streptococcal infection, high ESR in TB).
- Anti-streptolysin O (ASO) titer, throat swab for C/S, blood for C/S (in streptococcal infection).
- Chest X-ray (TB and sarcoidosis).
- Mantoux test (MT) and sputum for AFB (in case of TB).
- Lymph node FNAC and/or biopsy (sarcoidosis, lymphoma and TB).
- Inflammatory bowel disease (double contrast barium enema, sigmoidoscopy or colonoscopy, barium follow through).
- Other investigations: According to suspicion of cause.

RELATED QUESTIONS AND ANSWERS

Q. What is **erythema nodosum**? What are the **histological findings**?

A. It is an inflammatory disorder characterized by non-suppurative, painful, palpable, tender, erythematous nodular lesion in the skin, common in shin below the knee.

Usually, associated with fever, malaise and arthralgia. Nodules may be 2 to 6 cm in diameter, occur in crops, over 2 weeks, then resolves slowly over months leaving a bruise staining in the skin. It never ulcerates, may be recurrent and common in adult female.

Microscopy: Panniculitis (inflammatory reaction in fat), infiltration of lymphocytes, histiocytes, multinucleated giant cells and eosinophils, immune-complex deposition in dermal vessels.

Q. What are the **causes** of erythema nodosum?

A. As follows:

- Acute sarcoidosis
- Streptococcal β-hemolyticus infection (in throat)
- Primary pulmonary tuberculosis
- Drugs (sulfonamide, penicillin, estrogen-containing oral contraceptive pill, salicylates, barbiturates, sulfonylureas, bromides and iodides)
- Inflammatory bowel disease (Crohn's disease, ulcerative colitis)
- Fungal infections (histoplasmosis, coccidioidomycosis and blastomycosis, and is common in the USA)
- Protozoal (toxoplasmosis)
- Leprosy (erythema nodosum leprosum (ENL))
- Idiopathic (up to 50% cases)
- Physiological: Pregnancy (often unilateral).
- Others: *Salmonella*, *Shigella*, *Yersinia*, brucellosis, *Chlamydia*, rickettsial and mycoplasma infection, viral infection, lymphoma, cat-scratch disease, Behçet's syndrome and SLE.

Q. How to **treat** erythema nodosum?

A. As follows:

- Rest
- NSAIDs (indomethacin)
- Treatment of primary cause (e.g. penicillin, if streptococcal infection)
- In severe cases, corticosteroid should be given. In some cases dapsone 100 mg daily, colcichine 500 mg twice daily may be helpful
- Potassium iodide 400 to 900 mg daily may be helpful.

Q. What is **Erythema induratum (Bazin's disease)**?

A. Erythema induratum of Bazin type is a nodular vasculitis (which is a multifactorial syndrome of lobular panniculitis), related to tuberculous origin. It is one of the sequelae of immunologic reactions against antigenic components of *Mycobacterium tuberculosis* that spreads through blood. It represents a delayed type hypersensitivity reaction to tubercle bacillus. Recently, hepatitis C virus has been suspected as a cause. It is more common in women, aged 20 to 30 years, mostly occurring in lower extremities, usually in calves, may also be in shins. Differential diagnoses are chilblain, erythema nodosum, erythema nodosum leprosum, pancreatic panniculitis, lupus panniculitis, etc. Diagnosis is based on routine blood count, ESR, PCR and biopsy of the involved tissue. Treated with antituberculous therapy. Steroid may be indicated. Potassium iodide is sometimes needed for local application. Complication of untreated or inadequately treated erythema induratum involves persistent ulceration. If treated properly, the prognosis is good.

Q. What are the **differences** between erythema nodosum and erythema induratum?

A. As follows:

Points	Erythema nodosum	Erythema induratum
1. Duration	Short	Long
2. Site	Shin	Calf
3. Occurrence	Lesions occur simultaneously	Lesions occur serially in crops
4. Ulceration	Absent	Present
5. Pain	More	Less
6. Scarring	Absent	Present
7. Cause	Multiple causes	Usually TB
8. Histology	Septal panniculitis	Lobular panniculitis

CHAPTER 12

Miscellaneous

- Kala-azar 777
- Pyrexia of Unknown Origin (PUO) 785
- Takayasu's Disease 790
- PUO (HIV/AIDS) 793

KALA-AZAR

CHIEF COMPLAINTS

- Fever for ... months
- Loss of weight for … months
- Heaviness in left upper abdomen for … months
- Blackening of skin for ... months.

HISTORY

History of present illness: According to the statement of the patient, he was alright … months back. Since then, he has been suffering from fever, which is intermittent in nature, persists for 2 to 3 hours, subsides spontaneously, again reappears, 2 to 3 times daily. There is no history of chill or rigor, or any sweating. The patient also complaints of substantial loss of weight over last … months despite good appetite. There is no history of diarrhea, vomiting or urinary abnormality. He also complains of heaviness in left upper abdomen and fullness after taking food. For the last ... months, he also noticed blackening of skin involving the whole body. There is no history of cough, hemoptysis, hematemesis, melena or any other bleeding manifestation.

History of past illness: Mention according to the patient's statement.

Family history: Mention according to the patient's statement.

Personal history: Mention according to the patient's statement.

Drug history: The patient took paracetamol and some antibiotic prescribed by local physician the name of which he cannot mention.

GENERAL EXAMINATION

- The patient is emaciated.
- There is generalized pigmentation.
- Moderately anemic.
- No cyanosis, jaundice, edema, clubbing, koilonychias or leukonychia.
- No lymphadenopathy or thyromegaly.
- Pulse: 120/min.
- BP: 90/70 mm Hg.
- Temperature: 99ºF.

SYSTEMIC EXAMINATION

Gastrointestinal System

1. Lips, gum, teeth, tongue, oral cavity and tonsils - normal or pigmented.
2. **Abdomen:**
   - **Inspection:** Abdomen is distended, more marked in left upper quadrant.
   - **Palpation:**
     - Liver is enlarged, 5 cm in the midclavicular line from the right costal margin, surface is smooth, margin is sharp, non-tender and firm in consistency.

- Spleen is hugely enlarged, 15 cm from the left costal margin in the anterior axillary line towards the right iliac fossa.
- Kidneys are not ballotable.

- **Percussion:** Ascites is absent as evidenced by absence of fluid thrill and shifting dullness.
- **Auscultation:** No abnormality detected.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr. …, 40-years-old, farmer, normotensive, nondiabetic, nonsmoker, hailing from …, presented with fever for … months. The fever is intermittent in nature, which persists for 2 to 3 hours, subsides spontaneously, again reappears 2 to 3 times daily. There is no history of chill or rigor, or any sweating. The patient also complaints of substantial loss of weight over last … months despite good appetite. There is no history of diarrhea, vomiting or urinary abnormality. He also complains of heaviness in left upper abdomen and fullness after taking food. For the last ... months, he also noticed blackening of skin involving the whole body. There is no history of cough, hemoptysis, hematemesis, melena or any other bleeding manifestation. For this the patient took paracetamol and some antibiotic prescribed by local physician the name of which he cannot mention.

On examination—general examination (mention as above).

Systemic examination (mention as above).

With this history and physical findings, I have some differential diagnoses:

- Malaria.
- Kala-azar.
- Chronic myeloid leukemia.
- Lymphoma.
- Others—disseminated tuberculosis, brucellosis, histoplasmosis, schistosomiasis, tropical splenomegaly syndrome.

Q. Why is it spleen and **not kidney**?

A. Differences between spleen and kidney:

Spleen	Kidney
1. It is in the left hypochondrium	1. It is in the lumbar region/loin
2. Moves with respiration towards right iliac fossa	2. Moves downward and forward
3. Well defined medial border	3. Round in shape
4. Notch-present	4. Absent
5. Finger cannot be insinuated between the mass and left costal margin	5. Finger can be insinuated between the mass and left costal margin
6. On percussion—dullness over the mass which is continuous with left lower chest	6. Colonic resonance over the mass
7. Palpable	7. Ballotable

Note

If kidney is hugely enlarged, colonic resonance may be absent and get above the swelling may not be possible.

RELATED QUESTIONS AND ANSWERS

Q. What are the **presentations** of kala-azar?

A. Incubation period is 1 to 2 months (may be months to years, even 10 years).

- Fever—usually intermittent, either double or triple rise daily. Sometimes, fever may be irregular, low-grade continuous, occasionally undulant fever (pyrexia followed by apyrexial period). There may be associated chill and rigor.
- Usually no anorexia, no malaise, no coated tongue.
- Bleeding (due to thrombocytopenia).

Physical findings are:

- Emaciation.
- Anemia (always present, may be severe).
- Splenomegaly which may be huge (firm to hard).
- Hepatomegaly.
- Lymphadenopathy—common in African and Chinese kala-azar, rare in Indian Kala-azar.
- Skin—pigmented, dry thin, scaly. Sometimes there may be diffuse, warty, non-ulcerative skin lesion containing parasite.

Q. What is the **appetite** in Kala-azar?

A. Usually good.

Q. What are the causes of **good appetite but loss of weight**?

A. As follows:

- Diabetes mellitus.
- Thyrotoxicosis.
- Kala-azar.
- Sometimes in malabsorption syndrome.

Organism—Leishmania Donovani complex.

- L. donovani (India and South East Asia).
- L. infantum (Middle East, Mediterranean area).
- L. chagasi (South, Central America).

Source/reservoir—Human (Indian kala-azar).

Mode of transmission:

- Bite by infected female sandfly (common).
- Congenital—transplacental.
- Blood transfusion.

Note Remember the following points:

- Human is the only reservoir in Indian subcontinent.
- Other reservoirs are dog, jackal, fox and wild rodents in other countries.
- Leishmania has two forms - amastigote and promastigote.
- Amastigote form (oval) is found in human, LD body is found in monocyte/macrophage system.
- Promastigote form (flagellate) is found in sandfly, and in culture media.

Q. What **investigations** are done to diagnose kala-azar?

A. As follows:

1. CBC—leukopenia, high lymphocyte and monocyte, neutropenia, absence of eosinophil, thrombocytopenia and high ESR. If CBC is repeated after some days, there is **progressive leukopenia**.
2. Immunological tests, based on antibody:
   - Direct agglutination test (DAT)—it is called DAT because promastigote is used as antigen. May be positive after 2 weeks (usually within month). It remains positive years after cure (so it does not indicate active infection). Disadvantage of DAT—cannot differentiate past, subclinical and active infection. False positive DAT may occur in leprosy, African trypanosomiasis, TB and hepatitis B.
   - Immunochromatographical test (ICT)—also called rapid dipstick rk-39 test.
   - Indirect hemagglutination assay (IHA)
   - Indirect fluorescent antibody test (IFAT)
   - ELISA.
   - Complement fixation test (CFT)—it is nonspecific, positive after 3 weeks. False positive occurs in TB, leprosy, cirrhosis of liver and multiple myeloma. This test is performed by using Kedrowski's bacillus.
   - Aldehyde test—still helpful where there is no facility. This test is non-specific and positive when there is associated hypergammaglobulinemia. It may be false positive in TB, leprosy, cirrhosis of liver, multiple myeloma, SLE, leukemia and thalassemia. This test is positive in kala-azar in 2 to 3 months (negative after 6 months).
3. Detection of antigen—done by latex agglutination test (Katex) for detecting leishmanial antigen in urine. This test is very simple, more specific than antibody-based test, highly sensitive (96%) and also specific (100%). This test indicates active disease. The antigen is detected in urine within a week, disappears from urine within 3 weeks following successful treatment. Hence, this test is helpful for early diagnosis and also to see the response to therapy.
4. Definitive diagnosis by isolation of Leishman-Donovan (LD) body from bone marrow and spleen puncture, also from liver, lymph node and skin lesion. Smears are stained by Leishman, Giemsa or Wright's stain. Culture is done in NNN media (Nicolle-Nove-McNeal). LD body is positive as follows:
   - Spleen—90 to 95% (splenic puncture is avoided in case of soft spleen, prolong prothrombin time (PT) and platelet count is 40,000/mm^3).
   - Bone marrow and liver—85%.
   - Lymph node—65%.
   - LD body is rarely found in peripheral blood in buffy coat preparation. It may also be found in thick film (present in monocyte).
5. PCR (from lymph node or bone marrow aspiration), positive up to 100% case.
6. Blood for total protein and A/G ratio (high total protein, low albumin and high globulin).

Note

Culture is done for identification of species and if the number of organisms are less, it may grow in culture media. Organism may grow after 1 week, may take 4 weeks.

Q. What are the mechanisms of **anemia** in kala-azar?

A. Due to:
- Hypersplenism (which causes sequestration and splenic pooling, destruction of RBC in spleen).
- Short lifespan of RBC
- Hemolysis
- Ineffective erythropoiesis, infiltration of marrow by parasite
- Bleeding, hemodilution.

Q. Why **bleeding** occurs in kala-azar?

A. As follows:
- Bleeding may occur before treatment due to thrombocytopenia
- Bleeding may occur during treatment with sodium stibogluconate.

Q. Why **bleeding** during treatment with sodium stibogluconate?

A. Actual mechanism is unknown. It may be due to:
- Abnormality in preparation of drug
- Decomposed or expired date of drug
- Functional abnormality of platelet by the drug (pentavalent antimony is transformed to trivalent, which may cause thrombasthenia)
- Bleeding due to other causes (CLD and blood dyscrasias).

Q. How to **treat** if there is bleeding?

A. As follows:
- Drug should be stopped
- Platelet count, PT, APTT and liver function tests should be done
- Other causes of bleeding should be looked for
- Symptomatic treatment should be given, may require blood transfusion
- After improvement, drug should be started with low dose, then increase the dose (batch of the drug may be changed). If again bleeding, alternative drug may be given.

Q. What are the **complications** of kala-azar?

A. As follows:
- Secondary infection (pneumonia, tuberculosis)
- Anemia
- Bleeding
- Gastroenteritis, bacillary dysentery
- Liver disease (cirrhosis of liver)
- PKDL
- Rarely, cancrum oris.

Causes of death in Kala-azar—If no treatment is given, patient may die within 1 to 2 year due to:
- Secondary infection
- Bleeding.

Q. How to **treat** kala-azar?

A. As follows:

- Sodium stibogluconate—20 mg/kg for 28 days IV or IM. Can be given in infusion with normal saline. IM injection is very painful, may be given, if any ECG abnormality (arrhythmia or long QT interval).
- Meglumine antimoniate—50 mg/kg is an alternative drug.
- Liposomal amphotericin B—drug of choice, 3 to 4 mg/kg daily, given on days 1 to 5, 14 and 21. May be repeated. Dose for immunoincompetent is 4 mg/kg on day 1 to 5, 10, 17, 24, 31 and 38. It is expensive and not widely available. Preferable to conventional amphotericin B, as it is more effective, less toxic, less protein bound, concentrated and retained in macrophage-rich organs (RE system) other than kidney (not nephrotoxic). Safe in pregnancy.
- Conventional amphotericin B—1 mg/kg for 20 days, given in slow infusion for 4 to 6 hours. It is more protein bound and nephrotoxic.
- New oral drug—miltefosine, a cytotoxic drug, very effective and safe for visceral leishmaniasis. Also helpful in treating resistant kala-azar. Dose is 50 to 100 mg or 2.5 mg/kg daily orally for 28 days (50 mg, if < 25 kg body weight and 100 mg, if > 25 kg body weight). Side effects are less, may cause vomiting, diarrhea, transient raise of serum glutamic pyruvic transaminase (SGPT), blood urea nitrogen (BUN) and creatinine. It has more fetal toxicity, thus not recommended during pregnancy.
- Paromomycin—11 mg/kg/day intramuscularly for 21 days.

Note Remember the following points while treating with sodium stibogluconate:

- Before starting the therapy, perform renal and hepatic function tests, ECG (to see dysrhythmia, prolonged QT and ischemia) and chest X-ray (latent TB, pneumonia).
- During IV injection, if the patient complains of chest pain or cough, stop the drug immediately.
- Monitor ECG, FBC including platelet, hepatic and renal functions.
- The drug should be stopped, if there is bleeding, ECG change (arrhythmia, prolonged corrected QT interval).
- No limitation of dose (previously it was thought that dose should not exceed 1 g /day).

Q. How to see the **response** of therapy?

A. As follows:

- Clinical improvement—improvement of fever, feeling of well-being.
- Reduction in the size of spleen (may take months).
- Weight gain.
- Laboratory findings include increased Hb%, total count of WBC and increased albumin.

Q. What do you mean by **relapse, reinfection** and **resistant** kala-azar?

A. As follows:

- Relapse means after cure, there is again occurrence of kala-azar (usually occurs within 6 months).
- Reinfection following cure, if again kala-azar occurs after 6 months.
- Resistance means no response to drug therapy. It may be primary (no response from beginning of therapy) or secondary (develops later after initial response). It is usually due to insufficient or suboptimal dose or irregular therapy.

Q. How to **treat** if there is **relapse**?

A. Same therapy with sodium stibogluconate for 60 days (double the duration).

Q. How to **treat** a resistant case of kala-azar?

A. In a resistant case of kala-azar, the following therapy should be given:

- Pentamidine isethionate. 3 to 4 mg/kg, 3 times per week for 5 to 25 weeks (at least 5 weeks and 15 injections should be given). Then, sodium stibogluconate 20 mg/kg for 30 days. Pentamidine may cause hypoglycemia, hyperglycemia and shock. It is not used as a first drug, because of more side effects and development of quick resistance.
- Amphotericin B, preferably liposomal amphotericin B.
- Plus adjuvant therapy—γ-interferon, allopurinol, ketoconazole.

Q. How to treat **kala-azar in pregnancy**?

A. Same treatment with sodium stibogluconate. Although the safety of this drug during pregnancy is not established, it should be treated since the disease is potentially dangerous.

Q. What is kala-azar treatment failure **(KATF)**?

A. When kala-azar does not respond to usual therapy with sodium stibogluconate, it is called KATF. It is usually due to inappropriate or suboptimal dose or irregular therapy. Treatment as in resistant kala-azar.

Q. What is **PKDL?**

A. It is a non-ulcerative cutaneous lesion that occurs after successful treatment of visceral leishmaniasis. Initially starts as macules, then erythematous patches, followed by wart-like nodular lesions on the face, ear lobules and limbs. Amastigotes are scanty in the lesion. After treatment, visceral infection disappears, but organisms may remain in skin. After a variable period, skin resistance is lost with resurgence of old infection. Which leads to PKDL.

In Indian subcontinent, it occurs in a small minority of patients 6 months to 3 years or more after the initial infection, creating a persistent human reservoir. They present as macules, papules, nodules (most common) and plaques on the face, mainly around the chin. The face is often erythematous. Hypopigmented macules can occur over all parts of the body and are highly variable in extent and location. There are no systemic symptoms and no spontaneous healing.

In Sudan, about 50% develop skin manifestations of PKDL concurrently with visceral leishmaniasis or within 6 months afterwards. The skin features are as above. In addition, there may be a measles-like micropapular rash all over the body. Children are more frequently affected than in India. Spontaneous healing occurs in about 3/4th cases within 1 year.

Q. What is the **presentation** of PKDL?

A. As follows:

- Multiple, pale, pink, reddish, wart-like, nodules of variable size and shape involving nose, cheek and ear lobule.
- Thick skin.

In early case, depigmented macules, erythematous, well-circumscribed lesions may be seen or all stages of lesions may be present, such as depigmented macules, erythematous lesions and nodules, or only multiple nodules of variable size and shape are seen.

Q. What are the **differential diagnoses** of PKDL?

A. As follows:

- Lepromatous leprosy
- SLE
- Dermatomyositis
- Neurofibromatosis
- Sarcoidosis
- MCTD.

- Others—lipomatosis, acne rosacea, leukemia cutis, secondary syphilis and rhinophyma (irregular thickening of skin of nose with enlarged follicular orifice).

Q. What **investigation** is done to diagnose PKDL?

A. As follows:

- Demonstration of amastigote form of LD body in lesions by slit skin smear and culture. Smear is prepared from nodular lesions (LD bodies are not found in depigmented lesion).
- Immunofluorescence and immunohistochemistry may demonstrate the parasite in skin tissue.
- In the majority of patients, serological tests (direct agglutination test or k39 strip tests) are positive. It is not helpful for diagnosis.

Q. How to **treat** PKDL?

A. As follows:

- In Indian subcontinent, injection sodium stibogluconate (given in cycles) 20 mg/kg daily for 20 days is given. After 10 days interval, the course is repeated. Total 6 cycles are needed with an interval of 10 days. Total 120 injections are needed.
- If a second course is required, it should be given after an interval of two months.
- In Sudan, same injection for 2 months is adequate.
- Alternatively, in India, several courses of amphotericin B infusions may be given.

Note

Pentamidine is ineffective in PKDL.

PYREXIA OF UNKNOWN ORIGIN (PUO)

CHIEF COMPLAINTS

- Fever for ... months
- Weight loss for … months
- Loss of appetite for the same duration.

HISTORY

History of present illness: According to the statement of the patient, he was alright … months back. Since then, he has been suffering from fever which is low grade, continuous, highest recorded temperature is 102° F. There is no history of chill and rigor or profuse sweating. The patient complains of loss of appetite and substantial loss of weight for the last … months. There is no history of diarrhea, vomiting, urinary abnormality, cough, hemoptysis, skin rash, oral ulcer, joint pain, hematemesis, melena, history of travel to malaria endemic zones, IV drug abuse, needle prick injury. He denies unprotected sexual exposure.

History of past illness

Family history

Personal history

Drug history: Mention according to the patient's statement.

GENERAL EXAMINATION

- The patient is ill and emaciated.
- He is moderately anemic.
- No cyanosis, jaundice, edema, clubbing, koilonychia or leukonychia.
- No lymphadenopathy or thyromegaly.
- Pulse: 120/min.
- BP: 90/70 mm Hg.
- Temperature: 100ºF.

CVS: No abnormality.

Respiratory system: No abnormality.

Nervous system: No neck rigidity, Kernig's sign

Gastrointestinal system: Tongue is coated with angular stomatitis. No organomegaly.

Musculoskeletal system: No spinal tenderness, no gibbus, no other abnormality.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr. …, 42-years-old, businessman, normotensive, nondiabetic, nonsmoker, hailing from …, presented with fever for ... months, which is low grade, highest recorded temperature is 102° F. There is no history of chill and rigor or profuse sweating. The patient complains of loss of appetite and substantial

loss of weight for the last … months. There is no history of diarrhea, vomiting, urinary abnormality, cough, hemoptysis, skin rash, oral ulcer, joint pain, hematemesis, melena, history of travel to malaria endemic zones, IV drug abuse, needle prick injury. He denies unprotected sexual exposure. He was treated by local doctors, but no improvement. There is no family history of any illness.

On examination—general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is pyrexia of unknown origin, which may be due to:

- Tuberculosis.
- Lymphoma.
- Collagen disease (SLE).
- Internal malignancy (in elderly patients).
- Chronic kala-azar.
- Chronic malaria.
- HIV.
- Vasculitis.
- Infective endocarditis.
- Other—hepatic amoebiasis (amoebic liver abscess), adult Still's disease, giant cell arteritis, thyrotoxicosis, myxoma of the heart.

Q. What are the **commonest** causes of PUO?

A. Tuberculosis, collagen disease (e.g. SLE), malignancy (e.g. lymphoma, renal cell carcinoma)

Q. What **investigations** do you suggest?

A. As follows:

1. CBC with ESR, PBF, MP.
2. Blood culture.
3. Blood sugar (to exclude DM).
4. Urine R/E and culture.
5. Chest X-ray P/A view.
6. MT.
7. USG of whole abdomen.
8. If a lymph node or a palpable mass is found—FNAC and/or biopsy.
9. Serum ferritin (high in adult Still's disease).
10. Echocardiography.
11. Autoimmune screen—ANA, ENA, Anti dsDNA, CRP, rheumatiod factor, cANCA, pANCA.
12. HIV screen.
13. Bone marrow examination.
14. Renal function test.
15. Liver function test.
16. Other investigation according to suspicion of cause—CT scan, MRI, PET scan, bronchoscopy, colonoscopy.

RELATED QUESTIONS AND ANSWERS

Q. What is **PUO**?

A. PUO is defined as:

- Fever higher than 38.3°C (101°F) on several occasions.

- Persisting for at least 3 weeks.
- Diagnosis is not made after more than 2 outpatient visits or 3 days in the hospital.

Presently PUO cases are classified in 4 subclasses:

- Classic.
- Nosocomial.
- Neutropenic.
- HIV related.

Types	Definition	Common causes
Classic	Temperature >38.3°C	Infection, malignancy, collagen vascular disease
	Duration of >3 weeks	
	Evaluation of at least 2 outpatient visits or 3 days in hospital	
Nosocomial	Temperature >38.3°C	Clostridium difficile enterocolitis, drug-induced, pulmonary embolism, septic thrombophlebitis, sinusitis
	Patient hospitalized ≥24 hours but no fever or incubating on admission	
	Evaluation of at least 3 days	
Immune deficient (neutropenic)	Temperature >38.3°C	Opportunistic bacterial infections, aspergillosis, candidiasis, herpes virus
	Neutrophil count ≤ 500 per mm^3	
	Evaluation of at least 3 days	
HIV-associated	Temperature >38.3°C	CMV, Mycobacterium avium-intracellulare complex, lymphoma, Pneumocystis jiroveci, Kaposi's sarcoma
	Duration of >4 weeks for outpatients, >3 days for inpatients	
	HIV infection confirmed	

Q. What are the **causes** of PUO?

A. As follows:

1. Infections (30%):

- Tuberculosis.
- Abscess (amoebic or pyogenic liver abscess, subphrenic or at any site).
- Infective endocarditis.
- Urinary tract infection, (especially prostatitis).
- Dental infection.
- Sinusitis.
- Cholecystitis or cholangitis.
- Bone and joint infections.
- Malaria, brucellosis, toxoplasmosis.
- Viral infections (CMV, HIV).
- Fungal infections.

2. Connective tissue disorders (15%):

- SLE.
- Giant cell arteritis.

- Vasculitic disorders, e.g. PAN and rheumatoid disease with vasculitis.
- Polymyalgia rheumatica.
- Adult Still's disease.
- Polymyositis.

3. **Malignancy (20%):**
   - Lymphoma and myeloma.
   - Leukemia.
   - Carcinoma of kidney, liver, colon, stomach, pancreas.
4. **Miscellaneous (20%):**
   - Drug fever.
   - Atrial myxoma.
   - Thyrotoxicosis.
   - IBD.
   - Liver disease (cirrhosis and granulomatous hepatitis).
   - Sarcoidosis.
   - Familial mediterranean fever.
   - Factitious fever.
5. **Undiagnosed (5 to 15%).** Even in 5% cases, diagnosis may not be possible after postmortem examination.

Q. What are the **drugs causing fever?**

A. As follows:

- Antibiotics, specially beta lactum antibiotics.
- Cardiovascular drugs (quinidine).
- Antineoplastic drugs.
- Drugs acting on CNS (phenytoin).
- Others—methyldopa, barbiturate.

Q. What **history** should be taken in a patient with PUO?

A. As follows:

1. For TB—low grade fever, evening rise, weight loss, night sweat, H/O of contact with tuberculous patient.
2. For other infections:
   - Cough, fever, sputum, chest pain
   - Diarrhea, abdominal pain
   - Dysuria, frequency, urgency, burning micturition
   - Place of residence and overseas travel (malaria, kala-azar, amoebiasis)
   - History of sexual exposure (HIV, Venereal disease, PID)
   - Contact with domestic or wild animals (psittacosis, brucellosis, Q-fever, leptospirosis).
3. For collagen diseases:
   - Skin rash
   - Mouth ulcer
   - Joint pain
   - Alopecia.
4. Unilateral headache, arthralgia, myalgia (giant cell arteritis, polymyalgia rheumatica).
5. Occupation (farming, veterinary surgeon, etc.).
6. Drug history to exclude drug fever.
7. History of any intervention, e.g. catheterization, A-V fistula, prosthetic valve, colonoscopy.

Q. What **physical findings** should be look for in a patient with PUO?

A. As follows:

1. Pattern of temperature.
2. Skin rash—Erythema nodosum, erythema multiforme, vasculitis rash.
3. Hand—Stigmata of infective endocarditis, rheumatoid arthritis, dermatomyositis, clubbing, puncture marks (I/V drug abuse, HIV, HBV, etc.).
4. Lymph node—Epitrochlear, axillary, cervical, inguinal.
5. Eye—Iritis, conjunctivits to exclude seronegative arthritis, collagen disease, sarcoidosis.
6. Face—Butterfly rash to exclude SLE, heliotrope rash for dermatomyositis, lupus pernio and bilateral parotid enlargement for sarcoidosis.
7. Mouth—Ulcer, gum disease, tooth, tonsil.
8. Thyroid to exclude subacute thyroiditis.
9. Chest—Bony tenderness, murmur (SBE, myxoma), prosthetic valve.
10. Abdomen—Tenderness over the liver (liver abscess, sub-diaphragmatic abscess), spleen, per rectal examination to exclude prostatic abscess, Ca- prostate.
11. Nervous system—Look for signs of meningism, focal neurological signs.
12. Fundus—Roth's spot (SBE), retinal hemorrhage or infarction (leukemia).

TAKAYASU'S DISEASE

CHIEF COMPLAINTS

- Fever for ... months
- Pain in multiple joints for … months
- Weakness of upper limbs for … months
- Loss of weight for … months.

HISTORY

History of present illness: According to the statement of the patient, she was alright … months back. Since then, she has been suffering from fever which is low grade, continued and not associated with chill, rigor or sweating. She also complains of mild to moderate pain in multiple joints including small joints of hands, wrists, elbows, knees and ankles. There is no history of swelling of the joints or morning stiffness. For last … months, she complains of weakness of both upper limbs. She noticed pain in both upper limbs which appears after 10 to 15 minutes of manual work and subsides after taking rest. The patient also complains of loss of appetite and substantial weight loss for the last ... months. There is no history of cough, chest pain, breathlessness, pain abdomen, bleeding manifestation, oral ulcer or skin rash. Her bowel and bladder habits are normal.

History of past illness: Mention according to the patient's statement.

Family history: Mention according to the patient's statement.

Personal history: Mention according to the patient's statement.

Drug history: She was treated with paracetamol, ciprofloxacin, injection ceftriaxon but no response.

GENERAL EXAMINATION

- The patient is ill looking and emaciated.
- Mildly anemic.
- No cyanosis, jaundice, edema, clubbing, koilonychias or leukonychia.
- No lymphadenopathy or thyromegaly.
- No skin rash.
- Pulse: All peripheral pulse in upper limbs are absent. In the lower limbs, pulse is present, 88/min, regular.
- BP: Not recordable in upper limbs.
- Temperature: 99ºF.
- Bruit is present over both carotids.

SYSTEMIC EXAMINATION

Cardiovascular System

1. Peripheral pulse: All peripheral pulse in upper limbs are absent. In the lower limbs, pulse is present, 88/min, regular.
2. BP: Not recordable in upper limbs. (It should be recorded in the lower limb with 18 cm cuff).
3. JVP: Not raised.
4. Precordium:
   - Inspection—There is no visible cardiac impulse

- Palpation—Apex beat is in right 5th intercostal space, 9 cm from midline, normal in character. There is no thrill.
- Auscultation—Both first and second heart sounds are normal and audible in all areas. There is a high pitched, blowing, early diastolic murmur best heard in the left lower parasternal area, with patient bending forward and breathing hold after expiration. There is no added sound.

Locomotor System

- There is no swelling of any joint.
- Small joints of hands, wrists and elbows are mildly tender.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Ms. …, 25-years-old, student, normotensive, nondiabetic, nonsmoker, hailing from …, presented with fever for … months, which is low grade, continued and not associated with chill, rigor or sweating. She also complains of mild to moderate pain in multiple joints including small joints of hands, wrists, elbows, knees and ankles. There is no history of swelling of the joints or morning stiffness. For last … months, she complains of weakness of both upper limbs. She noticed pain in both upper limbs which appears after 10 to 15 minutes of manual work and subsides after taking rest. The patient also complains of loss of appetite and substantial weight loss for the last ... months. There is no history of cough, chest pain, breathlessness, pain abdomen, bleeding manifestation, oral ulcer or skin rash. Her bowel and bladder habits are normal. There is no family history of such illness. She was treated with some drug by local doctor, the name of which she can not mention.

On examination—general examination (mention as above).

Systemic examination (mention as above).

My diagnosis is Takayasu's arteritis.

Q. Why Takayasu's disease?

A. Because all the pulses in the upper limbs are absent and there is carotid bruit.

Q. What **investigations** should be done in Takayasu's disease?

A. As follows:

- CBC (high ESR and normocytic normochromic anemia).
- Chest X-ray shows cardiomegaly and widening of aorta.
- Aortography of aortic arch and its branches, renal angiogram shows narrowing, coarctation and aneurismal dilatation.
- Serum immunoglobulin is high.

Q. What are the causes of **absent radial pulse**? Or unequal radial pulse?

A. As follows:

- Anatomical aberration (may be congenital).
- Atherosclerosis.
- Co-arctation of the aorta (before origin of the left subclavian artery).
- Takayasu's arteritis.
- Iatrogenic—blalock taussig shunt (done in TOF), AV fistula for hemodialysis.
- Occlusion by thrombosis.
- Occlusion of the subclavian artery by cervical rib or neoplasm.
- Dissecting aneurysm.

RELATED QUESTIONS AND ANSWERS

Q. What is **Takayasu's disease** (pulseless disease or aortic arch syndrome)?

A. It is a chronic inflammatory, granulomatous panarteritis of unknown cause involving the elastic arteries. It commonly involves aorta and its major branches, carotid, ulnar, brachial, radial and axillary. Occasionally, may involve pulmonary artery, rarely abdominal aorta, renal artery resulting in obstruction. Age of onset is 25 to 30 years. Common in female, F:M ratio is 8:1.

Q. What are the **pathological changes** in Takayasu's diseases?

A. Panarteritis, with inflammatory mononuclear cell infiltration with occasional giant cell. There is intimal proliferation and fibrosis, scaring and vascularization of media and disruption and degeneration of the elastic lamina. Narrowing of the lumen occurs with or without thrombosis.

Q. What are the **types** of Takayasu's disease?

A. 4 types:

- Type 1 – localized to the aorta and its branches.
- Type 2 – localized to descending thoracic and abdominal aorta.
- Type 3 – combined features of type 1 and 2.
- Type 4 – involves the pulmonary artery.

Q. What are the **clinical features**?

A. Common in adolescent girls and young women (F:M = 8:1), 25 to 30 years, more in Asians. Clinical features are:

- General symptoms are—fever, malaise, weight loss, arthralgia, myalgia, dizziness, giddiness, headache, syncope, seizure, claudication in the upper limb.
- There may be arotic regurgitation, renal artery stenosis or anginal pain. Hypertension in 32 to 93%. There may be pericarditis, myocardial infarction, congestive cardiac failure, etc.

Q. What are the **ophthalmologic** findings?

A. Ophthalmologic examination may show retinal ischemia, retinal hemorrhages, cotton-wool exudates, venous dilatation and beading, microaneurysms of peripheral retina, optic atrophy, vitreous hemorrhage and classic, wreath like peripapillary arteriovenous anastomoses.

Q. What is the **treatment**?

A. As follows:

- High dose corticosteroid—prednisolone 40 to 60 mg daily or 1 to 2 mg/kg.
- If refractory to steroid or difficult to taper steroid, methotrexate up to 25 mg weekly.
- Reconstructive vascular surgery in selected case.

Prognosis—with appropriate treatment, 5 year survival is 83%.

PUO (HIV/AIDS)

CASE NO. 1

Presenting complaints:

- Fever for … months
- Passage of loose stool for … months
- Weight loss, weakness for … months.

HISTORY

History of present illness: According to the patient's statement, he was reasonably well … months back. Since then, he has been suffering from low grade continued fever, mostly associated with evening rise. The fever is not associated with chills and rigor or sweating. He also complains of alteration of bowel habit with predominantly large volume watery diarrhea, not mixed with mucus or blood, without any tenesmus. It is associated with mild constant dull, diffuse abdominal pain without any radiation. He agreed frequent attack of sore throat and pain on swallowing for … months. The patient also complains of marked loss of weight, weakness and loss of appetite for last … year. There is no history of cough, hemoptysis, urinary abnormality, polyarthritis, and mouth ulcer or skin rash.

History of past illness: He also gives history of a severe form of flu like illness 3 years back, manifested as fever with rash, severe sore throat, neck swelling, and generalized body ache. Since then he suffered several episodes of diarrhea, which persisted for prolonged period and recurrent episodes of pneumonia, which were treated with antibiotics.

Family history: He is from middle class family and his monthly income aground 5000 taka per month.

Personal history: The patient agreed unsafe sexual practice with multiple partners. He is alcoholic and smoker. There is no history of injectable drug abuse, needle sharing or transfusion of blood or blood product.

Treatment history: He was treated with multiple antibiotics, metronidazole.

Socioeconomic history: He is from middle class family and his monthly income around 5000 take per month.

GENERAL EXAMINATION

- The patient is ill looking and emaciated.
- Mildly anemic.
- Pitting edema is present.
- No cyanosis, jaundice, clubbing, koilonychias or leukonychia.
- Generalized lymphadenopathy of variable size and shape involving anterior cervical, posterior cervical and inguinal. Some are matted some are discreet. These are non tender, firm in consistency, free from underlying structure and overlying skin.
- No thyromegaly.

- No skin rash.
- Pulse: 88/min, regular.
- BP: 100/60 mm Hg.
- Temperature: 99ºF.

SYSTEMIC EXAMINATION

Gastrointestinal System

Lips, gum, teeth—normal.

Oral cavity:

- White patches on buccal mucosa, tongue, palate and pharynx (oropharyngeal candidiasis).
- Corrugated white plaques running vertically on the side of the tongue (oral hairy leukoplakia—mention if any).

Abdomen:

1. Inspection – Normal.
2. Palpation—
   - Liver is palpable … cm from costal margin on right midclavicular line, firm in consistency, sharp lower margin, non-tender, smooth surface.
   - Spleen is enlarged, … cm from left costal margin in anterior axillary line towards right iliac fossa, firm in consistency, rounded margin, smooth surface, non-tender.
   - Kidneys are not palpable.
   - Renal angles are non-tender.
3. Percussion—No abnormality.
4. Auscultation—No abnormality.

Examination of other systems reveals no abnormalities.

SALIENT FEATURES

Mr …, 45-years-old, normotensive, nondiabetic, smoker and alcohol abuser, presented with low grade continued fever for … months. It is mostly associated with evening rise, but not with chills and rigor or sweating. He also complains of alteration of bowel habit with predominantly large volume watery diarrhea, not mixed with mucus or blood, without any tenesmus. It is associated with mild constant dull, diffuse abdominal pain without any radiation. He agreed frequent attack of sore throat and pain on swallowing for … months. The patient also complains of marked loss of weight, weakness and loss of appetite for last … year. There is no history of cough, hemoptysis, urinary abnormality, polyarthritis, and mouth ulcer or skin rash.

He also gives history of a severe form of flu like illness 3 years back, manifested as fever with rash, severe sore throat, neck swelling, and generalized body ache. Since then he suffered several episodes of diarrhea which persisted for prolonged period and recurrent episodes of pneumonia which were treated with antibiotics.

The patient agreed unsafe sexual practice with multiple partners. He is alcoholic and smoker. There is no history of injectable drug abuse, needle sharing or transfusion of blood or blood product.

He was treated with multiple antibiotics, metronidazole but without any response.

On examination—general examination (mention as above).

Systemic examination (mention as above).

This patient has fever, bowel abnormality with generalized lymphadenopathy and hepatosplenomegaly for which I have some differential diagnoses:

- Disseminated tuberculosis.
- Kala-azar.
- Malaria.
- Lymphoma.
- Collagen disease like SLE.
- Toxoplasmosis.
- Brucellosis.
- HIV infection.
- Others—fungal infection (histoplasmosis, coccidioidomycosis), chronic cryptosporidial diarrhea.

Q. Why lymphoma?

A. The patient has history of fever, night sweating and weight loss over several months, also there are lymphadenopathy and hepatosplenomegaly.

Q. Why disseminated tuberculosis?

A. The patient has history of fever, night sweating and weight loss over several months, also there are lymphadenopathy and hepatosplenomegaly. TB is endemic in patient's country of origin.

CASE NO. 2

Chief complaints:

- Fever for ... months.
- Weight loss for … months.
- Loss of appetite for … months.

History of present illness:

According to the statement of the patient, he was alright … months back. Since then, he has been suffering from fever which is continued low grade. It is not associated with chill and rigor or profuse sweating. He also complains of loss of appetite and substantial loss of weight for the last … months. There is no history of diarrhea, vomiting, urinary abnormality, cough, hemoptysis, skin rash, oral ulcer, joint pain, hematemesis, melena, history of travel to malaria endemic zones, IV drug abuse, needle prick injury. He denies unprotected sexual exposure.

He was treated by local doctors with several antibiotics, but no response. Laboratory investigations showed low hemoglobin and high ESR. Other investigations such as urine, blood C/S, chest X-ray, ultrasonogram of abdomen, MP, ICT for kala-azar—all were negative.

Two weeks later, the patient noticed a mass on the left side of the neck. Examination revealed cervical lymphadenopathy, which are firm, matted, non-tender. FNAC of the lymph node showed caseating granuloma consistent with tuberculosis. Antitubercular treatment with 4 drugs was prescribed with other supportive care. The patient was reviewed after 1 month, but his condition was deteriorating. Again all other investigations were done and all were negative. He denied any sexual abuse, travel abroad, etc. On suspicion, HIV antibody was done and it was found to be positive.

History of past illness

Family history

Personal history

Drug history: Mention according to the patient's statement.

GENERAL EXAMINATION

- The patient is ill and emaciated.
- He is moderately anemic.
- No cyanosis, jaundice, edema, clubbing, koilonychia or leukonychia.
- There are left sided cervical lymphadenopathy, which are firm, matted, non-tender, not attached to overlying skin or underlying structure, no sinus.
- Pulse: 120/min.
- BP: 120/75 mm Hg.
- Temperature: 100ºF.

CVS—No abnormality.

Respiratory system—No abnormality.

Nervous system—No neck rigidity, Kernig's sign

Gastrointestinal system—Tongue is coated with angular stomatitis. No organomegaly.

Musculoskeletal system—No spinal tenderness, no gibbus, no other abnormality.

Examination of other systems reveals no abnormalities.

My diagnosis is HIV with tubercular lymphadenitis.

RELATED QUESTIONS AND ANSWERS

Q. What is HIV?

A. Human Immunodeficiency virus (HIV) is a single stranded RNA virus, belongs to the lentivirus group of retrovirus family. Two types—HIV-1 and HIV-2.

HIV disease—It is the spectrum of disorders ranging from primary infection, with or without the acute HIV syndrome, to the asymptomatic infected state to advanced disease.

Q. What is AIDS?

A. HIV infected individual with CD4 T cell count <200 cells/mm^2 regardless of the presence of the symptoms or HIV infected individual with AIDS defining conditions (category C) regardless of CD4 count is labeled AIDS.

Q. What is the mode of transmission of HIV?

A. As follows:

1. Sexual contact with an infected person—more in homosexuals, multiple sexual partners and non-circumcised persons.
2. Transplacental, perinatal exposure and breastfeeding.
3. Parenteral exposure to infected body fluid—
   - Sharing of needles, including intravenous drug abuser.
   - Blood and blood product transfusion.
   - Occupational transmission.
   - Organ transplantation including cornea.

Routes not involved in transmission:

- Close personal contact (sleeping, shaking hands, kissing, etc).
- Social contact (e.g. at school, swimming pool, shopping mall).
- Sharing toilet.
- Staying in a common ward in hospital.
- Sharing utensils.
- Insect or animal bite.
- Respiratory droplets, sputum, etc.
- Through health-workers like doctors, nurse, etc.

Q. What is the **natural history** of HIV or AIDS?

A. Natural history is as follows:

1. **Primary infection**—It is symptomatic in 70 to 80% of cases and usually occurs 2 to 6 weeks after exposure. Features are:
   - Fever with rash
   - Pharyngitis with cervical lymphadenopathy
   - Myalgia, arthralgia
   - Headache
   - Mucosal ulceration.
2. **Asymptomatic infection**—The patient remains asymptomatic but potentially infectious to others. This stage may persist for 5 to 10 years. Laboratory investigations may show anemia, leukopenia, lymphopenia and reduced CD4 count. Also cutaneous anergy.
3. **Mildly symptomatic disease** (HIV symptomatic or indicator diseases, category B):
   - Constitutional—Low grade fever, night sweats, weight loss.
   - Oral hairy leukoplakia.
   - Recurrent oropharyngeal candidiasis, recurrent vaginal candidiasis.
   - Herpes zoster involving more than 1 dermatome.
   - Idiopathic thrombocytopenic purpura.
   - Chronic diarrhea, bacillary angiomatosis.
   - Peripheral neuropathy.
   - Cervical dysplasia, severe pelvic inflammatory disease.
4. **Acquired immunodeficiency syndrome:** AIDS-defining diseases are (category C) –
   - Esophageal candidiasis.
   - Cryptococcal meningitis.
   - Chronic cryptosporidial diarrhea.
   - Cerebral toxoplasmosis.
   - CMV retinitis or colitis.
   - Chronic mucocutaneous herpes simplex.
   - Disseminated *Mycobacterium avium intracellulare* (MAI).
   - Pulmonary or extrapulmonary tuberculosis.
   - *Pneumocystis jirovecii* (*carinii*) pneumonia.
   - Progressive multifocal leucoencephalopathy.
   - Recurrent non-typhi *Salmonella* septicemia.
   - Extrapulmonary coccidioidomycosis.
   - Invasive cervical cancer.
   - Extrapulmonary histoplasmosis.
   - Kaposi's sarcoma.
   - Non-Hodgkin's lymphoma (including Burkitt's lymphoma).
   - Primary cerebral lymphoma.

- HIV-associated wasting.
- HIV-associated dementia.

Clinical category of HIV:

CD 4 count (/ cmm)	**Category A.** Asymptomatic or persistent generalized lymphadenopathy or acute seroconversion illness	**Category B:** (see above)	**Category C:** (see above)
> 500	A1	B1	C1
200 to 499	A2	B2	C2
<200	A3	B3	C3

Note

Category C, A3, B3 (shaded area) indicates AIDS.

Q. Name some **common infections** in AIDS.

A. As follows:
- *Pneumocystis jiroveci.*
- *Candida albicans.*
- *Cryptococcus neoformans.*
- *Toxoplasma gondii.*
- *Mycobacterium* (typical and atypical).
- CMV.
- Amebiasis.
- *Cryptosporidium.*

Q. Name some **HIV related cancer.**

A. As follows:
- AIDS defining cancers—Kaposi's sarcoma and non-Hodgkin's lymphoma.
- Non-AIDS defining malignancies—Anal cancer and Hodgkin's disease.

Q. What is the correlation between **CD4 count and HIV associated diseases?**

A. As follows:
- **> 500 cells/mm^3**—acute primary infection, recurrent vaginal candidiasis, persistent generalized lymphadenopathy.
- **< 500 cells/mm^3**—pulmonary tuberculosis, herpes zoster, oropharyngeal candidiasis, oral hairy leukoplakia, Kaposi's sarcoma, HIV-associated idiopathic thrombocytopenic purpura, cervical intraepithelial neoplasia II and III.
- **< 200 cells/mm^3**—*pneumocystis jiroveci pneumonia*, mucocutaneous herpes simplex, esophageal candidiasis, miliary or extrapulmonary tuberculosis.
- **< 100 cells/mm^3**—cerebral toxoplasmosis, cryptococcal meningitis, non-Hodgkin's lymphoma, progressive multifocal leucoencephalopathy, HIV-associated dementia.
- **<50 cells/mm^3**—CMV retinitis, CMV gastrointestinal disease, primary CNS lymphoma, disseminated MAI (*Mycobacterium avium intracellulare*).

Q. What are the **cutaneous manifestations** of HIV?

A. As follows:
- Early HIV—Herpes simplex, varicella zoster, human papilloma virus.
- Late HIV—Kaposi's sarcoma, molluscum contagiosum, chronic mucocutaneous herpes simplex.

Q. What are the findings in **mouth cavity** in HIV patient?

A. Hairy leukoplakia, oropharyngeal candidiasis, aphthous ulcer, herpes simplex, periodontal disease.

Q. What are the causes of **diarrhea or enteropathy** in HIV patient?

A. Common organisms are:

- Cytomegalovirus (CMV).
- Cryptosporidium and microsporidium.
- *Mycobacterium avium intracellulare* (MAI).
- Other infections—*Isospora*, *Giardia*, *Entamoeba histolytica*, *Salmonella*, adenovirus and bacterial overgrowth, etc.

The patient presents with dysphagia, retrosternal pain, watery diarrhea often accompanied by blood, colicky abdominal pain, weight loss and fever.

Q. What are the major causes of **pulmonary disease** in HIV?

A. As follows:

- Pneumocystis jiroveci pneumonia, tuberculosis, bacterial pneumonia, fungal infection (e.g. histoplasma), cryptococcus.
- Malignancy—non-Hodgkin's lymphoma, Kaposi's sarcoma.

Note

TB in HIV usually involves the lower lobes and cavitation is uncommon.

Q. Name some **neurological manifestations** in AIDS patients.

A. As follows:

- Acute meningitis—during acute seroconversion. May be aseptic meningitis, multiple cranial nerve palsy, etc.
- Encephalitis—herpes simplex, varicella zoster virus.
- *Toxoplasma gondii* causes encephalitis characterized by headache, confusion, convulsion and focal signs. MRI shows multiple ring-enhancing lesions in cortical grey-white matter interface, basal ganglia or brain stem with edema and mass effect. Retinitis may coexist.
- Primary CNS lymphoma (5%).
- AIDS dementia complex (ADC)—may precede the diagnosis of AIDS in 25% cases.
- Progressive multifocal leucoencephalopathy (PML)—presents with hemiparesis, visual or speech defects, altered mental status, ataxia. Seizures are rare and fever is absent. MRI shows non-enhancing white mater lesions without edema.
- Retinitis—CMV, toxoplasmosis.
- Autonomic neuropathy.
- Spinal cord, root and peripheral nerve disease includes:
  - Vacuolar myelopathy—presents with spastic paraparesis and sensory ataxia. There is involvement of lateral and posterior column of spinal cord.
  - Peripheral neuropathy—by HIV or drugs.
  - Other—Guillain-Barré syndrome, transverse myelitis, brachial neuritis, polyradiculitis and peripheral neuropathy.

Q. What are the causes of **seizure** in HIV positive patient?

A. HIV encephalopathy, cerebral toxoplasmosis, cryptococcal meningitis, primary CNS lymphoma, PMLE.

Q. What are the **ocular** diseases in AIDS?

A. Commonly there is CMV retinitis. Fundoscopy shows retinal cotton wool spots, sometimes fluffy white retinal lesions with area of hemorrhage. Other cause of retinitis is—*Toxoplasma gondii*.

Q. What are the **renal, cardiac and endocrine complications of** HIV?

A. As follows:

1. **Renal**:
   - Acute renal failure due to acute infection, drug toxicity.
   - Chronic renal failure due to HIV-associated nephropathy (HIVAN).
   - HIV immune complex kidney diseases.
   - Thrombotic microangiopathy.
2. **Cardiac disease:**
   - Dilated cardiomyopathy.
   - Zidovudine induced cardiomyopathy.
   - HIV patients are at higher risk of coronary artery disease. It may be due to HIV itself and change of lipid by antiretroviral drugs.
3. **Endocrine:** Hypoadrenalism, hypogonadism, hypopituitarism.

Q. What are the **Hematological** complications in HIV?

A. It occurs in advanced HIV infection.

- Anemia—usually mild, normocytic normochromic, causes are anemia of chronic disorder, bone marrow suppression or infiltration, malabsorption, side effect of drug, etc.
- Leukopenia (neutropenia is common, also lymphopenia).
- Thrombocytopenia, may occur early and may be the only manifestation in early case.
- Lymphoma.
- Pancytopenia (may be due to underlying opportunistic infection, malignancy, *Mycobacterium avium intercellulare*, disseminated CMV, lymphoma).

Q. What are the **baseline investigations** for newly diagnosed (asymptomatic patient) HIV infected patients?

A. As follows:

1. Routine tests—CBC, PBF, LFT, renal function test, lipid profile, blood glucose, urinalysis, chest X-ray.
2. Related to HIV:
   - HIV antibody (confiramatory).
   - HIV rapid antibody test (result in 10 to 20 minutes). Should be confirmed with ELISA and Western blot.
   - CD4 count.
   - Viral load.
   - HIV genotype.
3. For other infections:
   - Hepatitis serology (A, B, C), HCV - RNA.
   - Cytomegalovirus serology, PCR.
   - Toxoplasmosis serology.
   - Syphillis serology.
   - Screening for other sexually transmitted disease.
   - Cryptococcal antigen.
4. Others:
   - Cervical cytology in women.
   - Lymphocyte subsets.

- HLA-B*5701 screen for hypersensitivity to abacavir.
- Fundoscopy.

Q. How to **diagnose** HIV or AIDS?

A. Screening by ELISA (positive 3 to 12 weeks after infection), confirmation by Western blot.

Q. What are the **pre-test and post-test counseling** for suspected HIV/AIDS patients?

A. As follows:

Pre-test counseling:

- Purpose of the test should be discussed.
- Assessment of the risk factors.
- Explanation of the natural history of HIV to the patient.
- Discussion about mode of transmission and reduction of risk.
- Coping strategy.
- Explanation of the test procedure.
- Informed consent.

Post-test counseling:

1. If the test result is negative:
   - Discussion regarding behavior modification including safer sex and needle exchange.
   - A second test should be carried out 3 months after last exposure.
2. If the test result is positive:
   - Explanation of significance and implications of result.
   - Urgent medical follow-up.
   - Strategy regarding fear of disclosure and social rejection.
   - Verbal and written information.
   - Emotional and practical support by providing phone number and name.

Q. What are the **immunizations** that should be offered to every HIV infected patients?

A. As follows:

- Hepatitis A and hepatitis B, if non-immune.
- Pneumovax (at initial diagnosis and then 3 to 5 yearly).
- Influenza (yearly).
- Tetanus booster (if injection drug-user).

Q. What are the **aims of treatment?**

A. The aims of HIV treatment are to:

- Reduce the viral load to an undetectable level for as long as possible.
- Improve the CD4 count to > 200 cells/mL, so that severe HIV related disease become unlikely.
- Improve the quantity and quality of life without unacceptable drug-related side-effects or lifestyle alteration.
- Reduce transmission.

Q. What are the **indications** of antiretroviral therapy in patients with HIV infection?

A. As follows:

1. Acute infection syndrome.
2. Chronic infection:
   - Symptomatic disease (including HIV-associated nephropathy).
   - Asymptomatic diseases:
     - CD4+ T cell count <350/μL.
     - Pregnancy.
3. Postexposure prophylaxis.

Q. What are the indications to start **HAART (highly active anti-retroviral therapy)** on the basis of CD4 count?

A. As follows:

- Seroconversion—consider treatment, if neurological presentation, CD4 count < 200 cells/mm^3 for > 3 months or AIDS diagnosis.
- CD4 count ≥350—monitor 3 to 6 monthly (consider treatment if hepatitis B or C co-infected or > 55 years of age).
- CD4 count 201 to 350—treat as soon as the patient is ready.
- CD4 count <200—treat as soon as possible.
- AIDS defining diagnosis—treat as soon as possible (except for TB, if CD4 > 350 cells/mm^3).

Q. How to **treat** AIDS?

A. As follows:

General management:

- Dietary and nutritional advice should be given.
- Advice on smoking, alcohol, drug misuse and exercise should be given.
- Proper advice on reducing the risk of HIV transmission including sexual practice must be provided.
- Psychological support is a must for the patient, family, friends and care-givers.
- Information about childbearing must be discussed.

Drug treament:

Drug treatment depends on clinical assessment, laboratory investigations including viral load and CD4 counts, also individual circumstances.

Q. Name the **drugs** used in HIV infected patients.

A. Drugs used in HIV infected patients are:

1. Reverse transcriptase inhibitors (RTI):
   - Nucleoside reverse transcriptase inhibitors (NRTIs)—zidovudine, didanosine, lamivudine, stavudine, abacavir and emtricitabine.
   - Non-nucleoside reverse transcriptase inhibitors (NNRTIs)—nevirapine, efavirenz and etravirine.
2. Protease inhibitors (PIs)—indinavir, ritonavir, lopinavir, tipranavir, atazanavir, fosamprenavir and darunavir.
3. Entry inhibitors:
   - Fusion inhibitors—enfuvirtide.
   - Co-receptor blockers—maraviroc.
4. Integrase inhibitors—raltegravir.

Q. When antiretroviral **therapy should be changed?**

A. Antiretroviral therapy should be changed in following conditions:

- Drug side-effects (early or late).
- Difficulties in adherence.
- Virological failure.
- Persistently declining CD4 plus T cell numbers.
- Clinical deterioration.

Q. When will you **stop treatment?**

A. HAART should be stopped in the following conditions:

- Drug toxicity.

- Potential drug interaction with other drugs used for other more serious illness.
- Poor compliance.
- Patient's unwillingness to take drugs.

Q. How will you **monitor** a patient taking HAART?

A. As follows:
- Clinical history and examination
- Weight
- HIV viral load
- Lymphocyte subset
- Full blood count
- Liver and renal function
- Fasting lipid profile
- Blood glucose.

Q. What is the treatment of **CMV retinitis** in a patient with HIV?

A. Ganciclovir. The usual adult dose is:
1. Induction therapy—5 mg/kg IV for 1 hour, 12 hourly for 14 to 21 days.
2. Maintenance therapy:
   - 5 mg/kg IV for 1 hour daily, 7 days/week. Or, 6 mg/kg IV daily, 5 days/week.
   - Oral—1000 mg 3 times a day. Or, 500 mg 6 times a day (every 3 hours while awake) with food.
3. If there is progression of CMV retinitis during maintenance treatment, reinduction should be given.

Q. How will you **prevent HIV infection?**

A. As follows:
- Safe sexual practice.
- Effective treatment of STI.
- Screening of blood and blood products.
- Use of clean needles and syringes for IV drug abuser.
- Anti-retroviral drugs to reduce mother to child transmission.

Q. How will you treat a person **exposed to HIV infection** (postexposure prophylaxis)**?**

A. When risk is significant, in both occupational and non-occupational settings, lopinavir, tenofovir and emtricitabine are given. The first dose given as soon as possible, preferably within 6 to 8 hours. 4 weeks of therapy is recommended. Protection is not absolute and seroconversion may occur.

Q. How will you treat a **HIV positive pregnant woman?**

A. As follows:
1. Antepartum:
   - Ritonavir-boosted PI (e.g. lopinavir) with zidovudine and lamivudine from 20 weeks given to all mothers.
   - Or, oral zidovudine monotherapy for those with viral loads < 10000 copies/mL and wild-type virus who are willing to have cesarean section.
2. During delivery:
   - ZDV IV infusion at the onset of labor given to those on ZDV alone or those on HAART but with detectable virus, undergoing normal vaginal delivery.
   - Delivery by cesarean section reduces the risk of transmission, but if the patient is on HAART is unnecessary.
3. After delivery:

- The neonate should get oral zidovudine for 6 weeks.
- Breastfeeding should be avoided.

PNEUMOCYSTIS JIROVECI PNEUMONIA (PCP)

Pneumocystis jiroveci (previously Pneumocystis carinii) is an opportunistic fungus that causes pneumonia in HIV or AIDS patients, when CD4 is <200/cmm. PCP may also occur in patients who are immunosuppressed due to cancer, corticosteroids or other immunosuppressive drugs, organ or bone marrow transplantation, etc. In a few patients, it may also infect other organs like liver, spleen and kidneys.

The organism damages alveolar epithelium, causing interstitial plasma cell pneumonia with foamy exudate in the alveoli that impedes gas exchange and reduces lung compliance.

Clinical features – develops slowly over weeks, may take months.

- Initially there is shortness of breath on exertion.
- Cough (usually dry).
- Fever, malaise, weight loss and night sweat.
- Tachypnea, tachycardia, cyanosis.
- Fine crepitations may be heard on auscultation.

Investigations:

- Chest X-ray—typically bilateral perihilar interstitial infiltrates, which can progress to confluent alveolar shadows through out the lungs. Usually sparing of apex and costphrenic angle (X-ray may be normal in early infection).
- HRCT of chest (shows ground glass appearance).
- Sputum for cytology or PCR—organism may be found in 50 to 90% cases (by silver or Giemsa staining or immunofluorescent technique. Organism cannot be cultured).
- Bronchoscopy and bronchoalveolar lavage (shows organisms in 90 to 95% cases).
- Blood gases analysis (Po_2 is low, <90% on exercise).
- PCR amplification of the fungal DNA in blood.
- Lung function tests—restrictive pattern with reduced diffusion capacity.
- Lung biopsy (shows thickened alveolar septa with fluffy eosinophilic exudate in the alveoli. Immunofluorescent or histochemical staining or molecular analysis of PCR products can confirm pneumocystis infection).
- LDH—high.

Note Remember the following points:

- PCP is confirmed by identification of the organism in sputum or bronchoalveolar lavage. Silver stain or immunofluorescence technique is used to demonstrate characteristic cysts, which resemble crushed ping-pong balls and are present in aggregates of 2 to 8.
- Pneumocystis jiroveci may be present in the lungs of normal healthy individual. So detection of the organism in sputum or BAL does not mean that the patient is suffering from PCP or AIDS.

Complications:

- Respiratory failure
- Pneumothorax

- Pleural effusion (rare)
- Bacterial superinfection.

Treatment—should be given as early as possible.

- IV co-trimoxazole (120 mg/kg daily in divided doses for 21 days) is the first line treatment.
- If sensitive to co-trimoxazole, IV pentamidine (4 mg/kg/day) or dapsone and trimethoprim are given for the same duration.
- Atovaquone or combination of clindamycin and primaquine may be given.
- Prednisolone—40 mg bid for 5 days, then 40 mg daily for 5 days and 20 mg daily for 11 days is given.
- Systemic corticosteroids may be used in severe cases (especially if PO2 < 9.5 kPa).
- CPAP or mechanical ventilation (if patient remains severely hypoxic or becomes too tired).

Prognosis:

- May cause death from respiratory failure. Short term corticosteroid may reduce death in AIDS patients with moderate to severe pneumocystis pneumonia.

Prophylaxis—secondary prophylaxis is indicated in patients who recovered from PCP and CD4 remain <200/cmm. The usual regimen is co-trimoxazole 960 mg three times a week. Patients sensitive to sulphonamide are given dapsone, pyrimethamine or nebulized pentamidine.

Primary prophylaxis therapy is recommended in:

- AIDS and CD4 counts < 200/cmm.

Note Other conditions where prophylaxis therapy is required:

- Bone marrow or organ transplant recipients.
- Patient getting long-term, high-dose corticosteroids.

It is much more important to know what sort of a patient has a disease than what sort of a disease a patient has.

Sir William Osler

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