

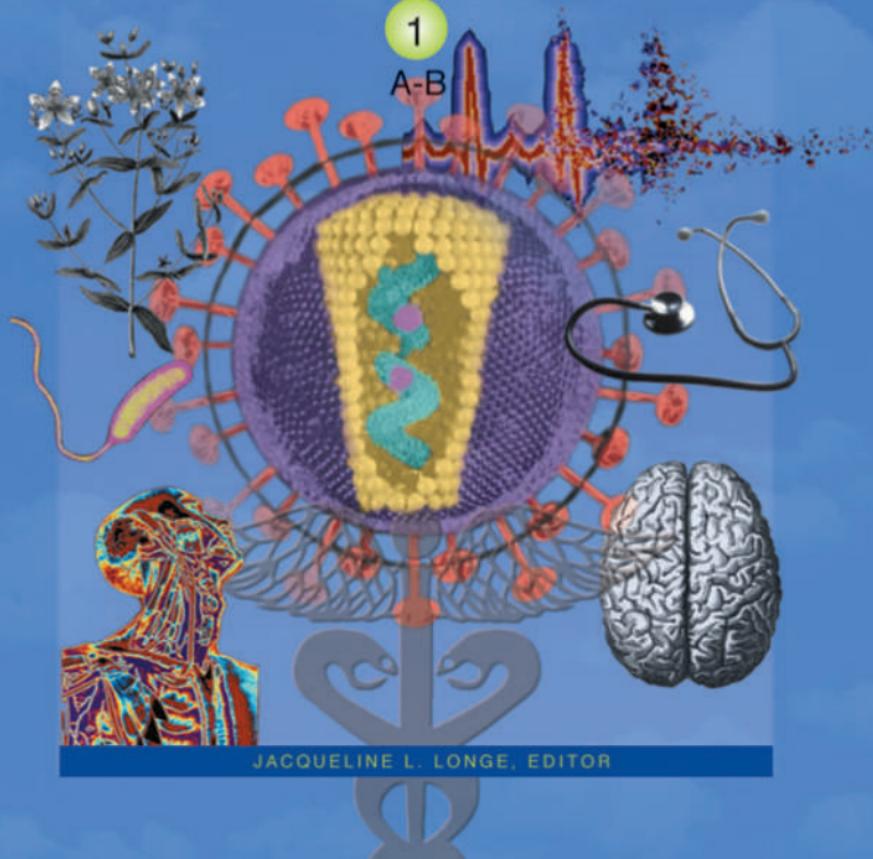
The GALE ENCYCLOPEDIA *of MEDICINE*

SECOND EDITION

VOLUME

1

A-B



JACQUELINE L. LONGE, EDITOR

The GALE
ENCYCLOPEDIA
of MEDICINE

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JACQUELINE L. LONGE, EDITOR
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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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A

Abdominal aorta ultrasound see **Abdominal ultrasound**

Abdominal aortic aneurysm see **Aortic aneurysm**

Abdominal hernia see **Hernia**

Abdominal thrust see **Heimlich maneuver**

While **pelvic ultrasound** is widely known and commonly used for fetal monitoring during **pregnancy**, ultrasound is also routinely used for general abdominal imaging. It has great advantage over x-ray imaging technologies in that it does not damage tissues with ionizing radiation. Ultrasound is also generally far better than plain x rays at distinguishing the subtle variations of soft tissue structures, and can be used in any of several modes, depending on the need at hand.

As an imaging tool, abdominal ultrasound generally is warranted for patients afflicted with: chronic or acute abdominal **pain**; abdominal trauma; an obvious or suspected abdominal mass; symptoms of liver disease, pancreatic disease, **gallstones**, spleen disease, kidney disease and urinary blockage; or symptoms of an abdominal **aortic aneurysm**. Specifically:

- **Abdominal pain.** Whether acute or chronic, pain can signal a serious problem—from organ malfunction or injury to the presence of malignant growths. Ultrasound scanning can help doctors quickly sort through potential causes when presented with general or ambiguous symptoms. All of the major abdominal organs can be studied for signs of disease that appear as changes in size, shape and internal structure.
- **Abdominal trauma.** After a serious accident, such as a car crash or a fall, internal bleeding from injured abdominal organs is often the most serious threat to survival. Neither the injuries nor the bleeding are immediately apparent. Ultrasound is very useful as an initial scan when abdominal trauma is suspected, and it can be used to pinpoint the location, cause, and severity of hemorrhaging. In the case of puncture **wounds**, from a bullet for example, ultrasound can locate the foreign object and provide a preliminary survey of the damage. The easy portability and versatility of ultrasound technology has brought it into common emergency room use, and even into limited ambulance service.
- **Abdominal mass.** Abnormal growths—tumors, cysts, abscesses, scar tissue and accessory organs—can be

Abdominal ultrasound

Definition

Ultrasound technology allows doctors to “see” inside a patient without resorting to surgery. A transmitter sends high frequency sound waves into the body, where they bounce off the different tissues and organs to produce a distinctive pattern of echoes. A receiver “hears” the returning echo pattern and forwards it to a computer, which translates the data into an image on a television screen. Because ultrasound can distinguish subtle variations between soft, fluid-filled tissues, it is particularly useful in providing diagnostic images of the abdomen. Ultrasound can also be used in treatment.

Purpose

The potential medical applications of ultrasound were first recognized in the 1940s as an outgrowth of the sonar technology developed to detect submarines during World War II. The first useful medical images were produced in the early 1950s, and, by 1965, ultrasound quality had improved to the point that it came into general medical use. Improvements in the technology, application, and interpretation of ultrasound continue. Its low cost, versatility, safety and speed have brought it into the top drawer of medical imaging techniques.

located and tentatively identified with ultrasound. In particular, potentially malignant solid tumors can be distinguished from benign fluid-filled cysts and abscesses. Masses and malformations in any organ or part of the abdomen can be found.

- Liver disease. The types and underlying causes of liver disease are numerous, though **jaundice** tends to be a general symptom. Ultrasound can differentiate between many of the types and causes of liver malfunction, and is particularly good at identifying obstruction of the bile ducts and **cirrhosis**, which is characterized by abnormal fibrous growths and reduced blood flow.
- Pancreatic disease. Inflammation and malformation of the pancreas are readily identified by ultrasound, as are pancreatic stones (calculi), which can disrupt proper functioning.
- Gallstones. Gallstones cause more hospital admissions than any other digestive malady. These calculi can cause painful inflammation of the gallbladder and also obstruct the bile ducts that carry digestive enzymes from the gallbladder and liver to the intestines. Gallstones are readily identifiable with ultrasound.
- Spleen disease. The spleen is particularly prone to injury during abdominal trauma. It may also become painfully inflamed when beset with infection or **cancer**. These conditions also lend themselves well to ultrasonic inspection and diagnosis.
- Kidney disease. The kidneys are also prone to traumatic injury and are the organs most likely to form calculi, which can block the flow of urine and cause blood **poisoning** (uremia). A variety of diseases causing distinct changes in kidney morphology can also lead to complete kidney failure. Ultrasound imaging has proven extremely useful in diagnosing kidney disorders.
- Abdominal aortic aneurysm. This is a bulging weak spot in the abdominal aorta, which supplies blood directly from the heart to the entire lower body. These aneurysms are relatively common and increase in prevalence with age. A burst aortic aneurysm is imminently life-threatening. However, they can be readily identified and monitored with ultrasound before acute complications result.

Ultrasound technology can also be used for treatment purposes, most frequently as a visual aid during surgical procedures—such as guiding needle placement to drain fluid from a cyst, or to extract tumor cells for biopsy. Increasingly, direct therapeutic applications for ultrasound are being developed.

The direct therapeutic value of ultrasonic waves lies in their mechanical nature. They are shock waves, just like audible sound, and vibrate the materials through which

they pass. These vibrations are mild, virtually unnoticeable at the frequencies and intensities used for imaging. Properly focused however, high-intensity ultrasound can be used to heat and physically agitate targeted tissues.

High-intensity ultrasound is used routinely to treat soft tissue injuries, such as strains, tears and associated scarring. The heating and agitation are believed to promote rapid healing through increased circulation. Strongly focused, high-intensity, high-frequency ultrasound can also be used to physically destroy certain types of tumors, as well as gallstones and other types of calculi. Developing new treatment applications for ultrasound is an active area of medical research.

Precautions

Properly performed, ultrasound imaging is virtually without risk or side effects. Some patients report feeling a slight tingling and/or warmth while being scanned, but most feel nothing at all. Ultrasound waves of appropriate frequency and intensity are not known to cause or aggravate any medical condition, though any woman who thinks she might be pregnant should raise the issue with her doctor before undergoing an abdominal ultrasound.

The value of ultrasound imaging as a medical tool, however, depends greatly on the quality of the equipment used and the skill of the medical personnel operating it. Improperly performed and/or interpreted, ultrasound can be worse than useless if it indicates that a problem exists where there is none, or fails to detect a significant condition. Basic ultrasound equipment is relatively inexpensive to obtain, and any doctor with the equipment can perform the procedure whether qualified or not. Patients should not hesitate to verify the credentials of technicians and doctors performing ultrasounds, as well as the quality of the equipment used and the benefits of the proposed procedure.

In cases where ultrasound is used as a treatment tool, patients should educate themselves about the proposed procedure with the help of their doctors—as is appropriate before any surgical procedure. Also, any abdominal ultrasound procedure, diagnostic or therapeutic, may be hampered by a patient's body type or other factors, such as the presence of excessive bowel gas (which is opaque to ultrasound). In particular, very obese people are often not good candidates for abdominal ultrasound.

Description

Ultrasound includes all sound waves above the frequency of human hearing—about 20 thousand hertz, or cycles per second. Medical ultrasound generally uses frequencies between one and 10 million hertz (1-10 MHz).

KEY TERMS

Accessory organ—A lump of tissue adjacent to an organ that is similar to it, but which serves no important purpose, if functional at all. While not necessarily harmful, such organs can cause problems if they grow too large or become cancerous. In any case, their presence points to an underlying abnormality in the parent organ.

Benign—In medical usage, benign is the opposite of malignant. It describes an abnormal growth that is stable, treatable and generally not life-threatening.

Biopsy—The surgical removal and analysis of a tissue sample for diagnostic purposes. Usually, the term refers to the collection and analysis of tissue from a suspected tumor to establish malignancy.

Calculus—Any type of hard concretion (stone) in the body, but usually found in the gallbladder, pancreas and kidneys. They are formed by the accumulation of excess mineral salts and other organic material such as blood or mucus. Calculi (pl.) can cause problems by lodging in and obstructing the proper flow of fluids, such as bile to the intestines or urine to the bladder.

Cirrhosis—A chronic liver disease characterized by the invasion of connective tissue and the degeneration of proper functioning—jaundice is often an accompanying symptom. Causes of cirrhosis include alcoholism, metabolic diseases, syphilis and congestive heart disease.

Common bile duct—The branching passage through which bile—a necessary digestive enzyme—travels from the liver and gallbladder into the small intestine. Digestive enzymes from the pancreas also enter the intestines through the common bile duct.

Computed tomography scan (CT scan)—A specialized type of x-ray imaging that uses highly focused and relatively low energy radiation to produce detailed two-dimensional images of soft tissue structures, particularly the brain. CT scans are the chief competitor to ultrasound and can yield higher quality images not disrupted by bone or gas. They are, however, more cumbersome, time consuming

and expensive to perform, and they use ionizing electromagnetic radiation.

Doppler—The Doppler effect refers to the apparent change in frequency of sound wave echoes returning to a stationary source from a moving target. If the object is moving toward the source, the frequency increases; if the object is moving away, the frequency decreases. The size of this frequency shift can be used to compute the object's speed—be it a car on the road or blood in an artery. The Doppler effect holds true for all types of radiation, not just sound.

Frequency—Sound, whether traveling through air or the human body, produces vibrations—molecules bouncing into each other—as the shock wave travels along. The frequency of a sound is the number of vibrations per second. Within the audible range, frequency means pitch—the higher the frequency, the higher a sound's pitch.

Ionizing radiation—Radiation that can damage living tissue by disrupting and destroying individual cells at the molecular level. All types of nuclear radiation—x rays, gamma rays and beta rays—are potentially ionizing. Sound waves physically vibrate the material through which they pass, but do not ionize it.

Jaundice—A condition that results in a yellow tint to the skin, eyes and body fluids. Bile retention in the liver, gallbladder and pancreas is the immediate cause, but the underlying cause could be as simple as obstruction of the common bile duct by a gallstone or as serious as pancreatic cancer. Ultrasound can distinguish between these conditions.

Malignant—The term literally means growing worse and resisting treatment. It is used as a synonym for cancerous and connotes a harmful condition that generally is life-threatening.

Morphology—Literally, the study of form. In medicine, morphology refers to the size, shape and structure rather than the function of a given organ. As a diagnostic imaging technique, ultrasound facilitates the recognition of abnormal morphologies as symptoms of underlying conditions.

Higher frequency ultrasound waves produce more detailed images, but are also more readily absorbed and so cannot penetrate as deeply into the body. Abdominal ultrasound imaging is generally performed at frequencies between 2-5 MHz.

An ultrasound machine consists of two parts: the transducer and the analyzer. The transducer both produces the sound waves that penetrate the body and receives the reflected echoes. Transducers are built around piezoelectric ceramic chips. (Piezoelectric refers to electricity that is produced when you put pressure on certain crystals such as quartz). These ceramic chips react to electric pulses by producing sound waves (they are transmitting waves) and react to sound waves by producing electric pulses (receiving). Bursts of high frequency electric pulses supplied to the transducer causes it to produce the scanning sound waves. The transducer then receives the returning echoes, translates them back into electric pulses and sends them to the analyzer—a computer that organizes the data into an image on a television screen.

Because sound waves travel through all the body's tissues at nearly the same speed—about 3,400 miles per hour—the microseconds it takes for each echo to be received can be plotted on the screen as a distance into the body. The relative strength of each echo, a function of the specific tissue or organ boundary that produced it, can be plotted as a point of varying brightness. In this way, the echoes are translated into a picture. Tissues surrounded by bone or filled with gas (the stomach, intestines and bowel) cannot be imaged using ultrasound, because the waves are blocked or become randomly scattered.

Four different modes of ultrasound are used in medical imaging:

- A-mode. This is the simplest type of ultrasound in which a single transducer scans a line through the body with the echoes plotted on screen as a function of depth. This method is used to measure distances within the body and the size of internal organs. Therapeutic ultrasound aimed at a specific tumor or calculus is also A-mode, to allow for pinpoint accurate focus of the destructive wave energy.
- B-mode. In B-mode ultrasound, a linear array of transducers simultaneously scans a plane through the body that can be viewed as a two-dimensional image on screen. Ultrasound probes containing more than 100 transducers in sequence form the basis for these most commonly used scanners, which cost about \$50,000.
- M-Mode. The M stands for motion. A rapid sequence of B-mode scans whose images follow each other in sequence on screen enables doctors to see and measure range of motion, as the organ boundaries that produce reflections move relative to the probe. M-

mode ultrasound has been put to particular use in studying heart motion.

- Doppler mode. **Doppler ultrasonography** includes the capability of accurately measuring velocities of moving material, such as blood in arteries and veins. The principle is the same as that used in radar guns that measure the speed of a car on the highway. Doppler capability is most often combined with B-mode scanning to produce images of blood vessels from which blood flow can be directly measured. This technique is used extensively to investigate valve defects, arteriosclerosis and **hypertension**, particularly in the heart, but also in the abdominal aorta and the portal vein of the liver. These machines cost about \$250,000.

The actual procedure for a patient undergoing an abdominal ultrasound is relatively simple, regardless of the type of scan or its purpose. **Fasting** for at least eight hours prior to the procedure ensures that the stomach is empty and as small as possible, and that the intestines and bowels are relatively inactive. Fasting also allows the gall bladder to be seen, as it contracts after eating and may not be seen if the stomach is full. In some cases, a full bladder helps to push intestinal folds out of the way so that the gas they contain does not disrupt the image. The patient's abdomen is then greased with a special gel that allows the ultrasound probe to glide easily across the skin while transmitting and receiving ultrasonic pulses.

This procedure is conducted by a doctor with the assistance of a technologist skilled in operating the equipment. The probe is moved around the abdomen to obtain different views of the target areas. The patient will likely be asked to change positions from side to side and to hold their breath as necessary to obtain the desired views. Discomfort during the procedure is minimal.

The many types and uses of ultrasound technology makes it difficult to generalize about the time and costs involved. Relatively simple imaging—scanning a suspicious abdominal mass or a suspected abdominal aortic aneurysm—will take about half an hour to perform and will cost a few hundred dollars or more, depending on the quality of the equipment, the operator and other factors. More involved techniques such as multiple M-mode and Doppler-enhanced scans, or cases where the targets not well defined in advance, generally take more time and are more expensive.

Regardless of the type of scan used and the potential difficulties encountered, ultrasound remains faster and less expensive than **computed tomography scans** (CT), its primary rival in abdominal imaging. Furthermore, as abdominal ultrasounds are generally undertaken as "medically necessary" procedures designed to detect the presence of suspected abnormalities, they are covered

under most types of major medical insurance. As always, though, the patient would be wise to confirm that their coverage extends to the specific procedure proposed. For nonemergency situations, most underwriters stipulate prior approval as a condition of coverage.

Specific conditions for which ultrasound may be selected as a treatment option—certain types of tumors, lesions, **kidney stones** and other calculi, muscle and ligament injuries, etc.—are described in detail under the appropriate entries in this encyclopedia.

Preparation

A patient undergoing abdominal ultrasound will be advised by their physician about what to expect and how to prepare. As mentioned above, preparations generally include fasting and arriving for the procedure with a full bladder, if necessary. This preparation is particularly useful if the gallbladder, ovaries or veins are to be examined.

Aftercare

In general, no aftercare related to the abdominal ultrasound procedure itself is required.

Risks

Abdominal ultrasound carries with it no recognized risks or side effects, if properly performed using appropriate frequency and intensity ranges. Sensitive tissues, particularly those of the reproductive organs, could possibly sustain damage if violently vibrated by overly intense ultrasound waves. In general though, such damage would only result from improper use of the equipment.

Any woman who thinks she might be pregnant should raise this issue with her doctor before undergoing an abdominal ultrasound, as a fetus in the early stages of development could be injured by ultrasound meant to probe deeply recessed abdominal organs.

Normal results

As a diagnostic imaging technique, a normal abdominal ultrasound is one that indicates the absence of the suspected condition that prompted the scan. For example, symptoms such as a persistent **cough**, labored breathing, and upper abdominal pain suggest the possibility of, among other things, an abdominal aortic aneurysm. An ultrasound scan that indicates the absence of an aneurysm would rule out this life-threatening condition and point to other, less serious causes.

Abnormal results

Because abdominal ultrasound imaging is generally undertaken to confirm a suspected condition, the results

of a scan often will prove abnormal—that is they will confirm the diagnosis, be it kidney stones, cirrhosis of the liver or an aortic aneurysm. At that point, appropriate medical treatment as prescribed by a patient's doctor is in order. See the relevant disease and disorder entries in this encyclopedia for more information.

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ORGANIZATIONS

- American College of Gastroenterology. 4900 B South 31st St., Arlington, VA 22206-1656. (703) 820-7400. <<http://www.acg.gi.org>>.
 American Institute of Ultrasound in Medicine. 14750 Sweitzer Lane, Suite 100, Laurel, MD 20707-5906. (800) 638-5352. <<http://www.aium.org>>.
 American Society of Radiologic Technologists. 15000 Central Ave., SE, Albuquerque, NM 87123-3917. (505) 298-4500. <<http://www.asrt.org>>.

Kurt Richard Sternlof

Abdominal wall defects

Definition

Abdominal wall defects are birth (congenital) defects that allow the stomach or intestines to protrude.

KEY TERMS

Hernia—Movement of a structure into a place it does not belong.

Umbilical—Referring to the opening in the abdominal wall where the blood vessels from the placenta enter.

Viscera—Any of the body's organs located in the chest or abdomen.

Description

Many unexpected and fascinating events occur during the development of a fetus inside the womb. The stomach and intestines begin development outside the baby's abdomen and only later does the abdominal wall enclose them. Occasionally, either the umbilical opening is too large, or it develops improperly, allowing the bowels or stomach to remain outside or squeeze through the abdominal wall.

Causes and symptoms

There are many causes for **birth defects** that still remain unclear. Presently, the cause(s) of abdominal wall defects is unknown, and any symptoms the mother may have to indicate that the defects are present in the fetus are nondescript.

Diagnosis

At birth, the problem is obvious, because the base of the umbilical cord at the navel will bulge or, in worse cases, contain viscera (internal organs). Before birth, an ultrasound examination may detect the problem. It is always necessary in children with one birth defect to look for others, because birth defects are usually multiple.

Treatment

Abdominal wall defects are effectively treated with surgical repair. Unless there are accompanying anomalies, the surgical procedure is not overly complicated. The organs are normal, just misplaced. However, if the defect is large, it may be difficult to fit all the viscera into the small abdominal cavity.

Prognosis

If there are no other defects, the prognosis after surgical repair of this condition is relatively good. However,

10% of those with more severe or additional abnormalities die from it. The organs themselves are fully functional; the difficulty lies in fitting them inside the abdomen. The condition is, in fact, a **hernia** requiring only replacement and strengthening of the passageway through which it occurred. After surgery, increased pressure in the stretched abdomen can compromise the function of the organs inside.

Prevention

Some, but by no means all, birth defects are preventable by early and attentive prenatal care, good **nutrition**, supplemental **vitamins**, diligent avoidance of all unnecessary drugs and chemicals—especially tobacco—and other elements of a healthy lifestyle.

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J. Ricker Polsdorfer, MD

Abnormal heart rhythms see **Arrhythmias**

ABO blood typing see **Blood typing and crossmatching**

ABO incompatibility see **Erythroblastosis fetalis**

Abortion, habitual see **Recurrent miscarriage**

Abortion, partial birth

Definition

Partial birth abortion is a method of late-term abortion that terminates a **pregnancy** and results in the **death** and intact removal of a fetus. This procedure is most commonly referred to as intact dilatation and extraction (D & X).

Purpose

Partial birth abortion, or D&X, is performed to end a pregnancy and results in the death of a fetus, typically in

the late second or third trimester. Although D&X is highly controversial, some physicians argue that it has advantages that make it a preferable procedure in some circumstances. One perceived advantage is that the fetus is removed largely intact, allowing for better evaluation and **autopsy** of the fetus in cases of known fetal anomalies. Intact removal of the fetus may also confer a lower risk of puncturing the uterus or damaging the cervix. Another perceived advantage is that D&X ends the pregnancy without requiring the woman to go through labor, which may be less emotionally traumatic than other methods of late-term abortion. In addition, D&X may offer a lower cost and shorter procedure time.

Precautions

Women considering D&X should be aware of the highly controversial nature of this procedure. A controversy common to all late-term abortions is whether the fetus is viable, or able to survive outside of the woman's body. A specific area of controversy with D&X is that fetal death does not occur until after most of the fetal body has exited the uterus. Several states have taken legal action to limit or ban D&X and many physicians who perform abortions do not perform D&X. This may restrict the availability of this procedure to women seeking late-term abortion.

Description

Intact D&X, or partial birth abortion first involves administration of medications to cause the cervix to dilate, usually over the course of several days. Next, the physician rotates the fetus to a footling breech position. The body of the fetus is then drawn out of the uterus feet first, until only the head remains inside the uterus. Then, the physician uses an instrument to puncture the base of the skull, which collapses the fetal head. Typically, the contents of the fetal head are then partially suctioned out, which results in the death of the fetus, and reduces the sizes of the fetal head enough to allow it to pass through the cervix. The dead and otherwise intact fetus is then removed from the woman's body.

Preparation

Medical preparation for D&X involves an outpatient visit to administer medications, such as *laminaria*, to cause the cervix to begin dilating.

In addition, preparation may involve fulfilling local legal requirements, such as a mandatory waiting period, counseling, or an informed consent procedure reviewing stages of fetal development, **childbirth**, alternative abortion methods, and adoption.

KEY TERMS

Cervix—The narrow outer end of the uterus that separates the uterus from the vaginal canal.

Footling breech—A position of the fetus while in the uterus where the feet of the fetus are nearest the cervix would be the first part of the fetus to exit the uterus, with the head of the fetus being the last part to exit the uterus.

Laminaria—A medical product made from a certain type of seaweed that is physically placed near the cervix to cause it to dilate.

Aftercare

D&X typically does not require an overnight hospital stay, so a follow up appointment may be scheduled to monitor the woman for any complications.

Risks

With all abortion, the later in pregnancy an abortion is performed, the more complicated the procedure and the greater the risk of injury to the woman. In addition to associated emotion reactions, D&X carries the risk of injury to the woman, including heavy bleeding, blood clots, damage to the cervix or uterus, pelvic infection, and anesthesia-related complications. There is also a risk of incomplete abortion, meaning that the fetus is not dead when removed from the woman's body. Possible long-term risks include difficulty becoming pregnant or carrying a future pregnancy to term.

Normal results

The expected outcome of D&X is the termination of a pregnancy with removal of a dead fetus from the woman's body.

Resources

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ORGANIZATIONS

Planned Parenthood Federation of America. 810 Seventh Ave., New York, NY 10019. (212) 541-7800. FAX: (212) 245-1845.

OTHER

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Stefanie B. N. Dugan, M.S.

■ Abortion, selective

Definition

Selective abortion, also known as selective reduction, refers to choosing to abort a fetus, typically in a multi-fetal **pregnancy**, to decrease the health risks to the mother in carrying and giving birth to more than one or two babies, and also to decrease the risk of complications to the remaining fetus(es). The term selective abortion also refers to choosing to abort a fetus for reasons such as the woman is carrying a fetus which likely will be born with some birth defect or impairment, or because the sex of the fetus is not preferred by the individual.

Purpose

A woman may decide to abort for health reasons, for example, she is at higher risk for complications during pregnancy because of a disorder or disease such as diabetes.

However, selective reduction is recommended often in cases of multi-fetal pregnancy, or the presence of more than one fetus, typically, at least three or more fetuses. In the general population, multi-fetal pregnancy happens in only about 1-2% of pregnant women. But multi-fetal pregnancies occur far more often in women using fertility drugs.

Precautions

Because women or couples who use fertility drugs have made an extra effort to become pregnant, it is possible that the individuals may be unwilling or uncomfortable with the decision to abort a fetus in cases of multi-fetal pregnancy. Individuals engaging in fertility treatment should be made aware of the risk of multi-fetal pregnancy and consider the prospect of recommended reduction before undergoing fertility treatment.

Description

Selective reduction is usually performed between nine and 12 weeks of pregnancy and is most successful

when performed in early pregnancy. It is a simple procedure and can be performed on an outpatient basis. A needle is inserted into the woman's stomach or vagina and potassium chloride is injected into the fetus.

Preparation

Individuals who have chosen selective reduction to safeguard the remaining fetuses should be counseled prior to the procedure. Individuals should receive information regarding the risks of a multi-fetal pregnancy to both the fetuses and the mother compared with the risks after the reduction.

Individuals seeking an abortion for any reason should consider the ethical implications whether it be because the fetus is not the preferred sex or because the fetus would be born with a severe birth defect.

Aftercare

Counseling should continue after the abortion because it is a traumatic event. Individuals may feel guilty about choosing one fetus over another. Mental health professionals should be consulted throughout the process.

Risks

About 75% of women who undergo selective reduction will go into **premature labor**. About 4-5% of women undergoing selective reduction also miscarry one or more of the remaining fetuses. The risks associated with multi-fetal pregnancy is considered higher.

Normal results

In cases where a multi-fetal pregnancy, three or more fetuses, is reduced to two, the twin fetuses typically develop as they would as if they were conceived as twins.

Resources**BOOKS**

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KEY TERMS

Multi-fetal pregnancy—A pregnancy of two or more fetuses.

Selective reduction—Typically referred to in cases of multifetal pregnancy, when one or more fetuses are aborted to preserve the viability of the remaining fetuses and decrease health risks to the mother.

ORGANIZATIONS

The American Society for Reproductive Medicine. 1209 Montgomery Highway, Birmingham, AL 35216-2809. (205) 978-5000. <<http://www.asrm.org>>.

The Alan Guttmacher Institute. 120 Wall Street, New York, NY 10005. (212) 248-1111. <<http://www.agi-usa.org>>.

Meghan M. Gourley

Abortion, spontaneous see **Miscarriage**

■ Abortion, therapeutic

Definition

Therapeutic abortion is the intentional termination of a **pregnancy** before the fetus can live independently. Abortion has been a legal procedure in the United States since 1973.

Purpose

An abortion may be performed whenever there is some compelling reason to end a pregnancy. Women have abortions because continuing the pregnancy would cause them hardship, endanger their life or health, or because prenatal testing has shown that the fetus will be born with severe abnormalities.

Abortions are safest when performed within the first six to 10 weeks after the last menstrual period. The calculation of this date is referred to as the gestational age and is used in determining the stage of pregnancy. For example, a woman who is two weeks late having her period is said to be six weeks pregnant, because it is six weeks since she last menstruated.

About 90% of women who have abortions do so before 13 weeks and experience few complications. Abortions performed between 13-24 weeks have a higher

rate of complications. Abortions after 24 weeks are extremely rare and are usually limited to situations where the life of the mother is in danger.

Precautions

Most women are able to have abortions at clinics or outpatient facilities if the procedure is performed early in pregnancy. Women who have stable diabetes, controlled epilepsy, mild to moderate high blood pressure, or who are HIV positive can often have abortions as outpatients if precautions are taken. Women with heart disease, previous **endocarditis**, **asthma**, lupus erythematosus, uterine fibroid tumors, blood clotting disorders, poorly controlled epilepsy, or some psychological disorders usually need to be hospitalized in order to receive special monitoring and medications during the procedure.

Description

Very early abortions

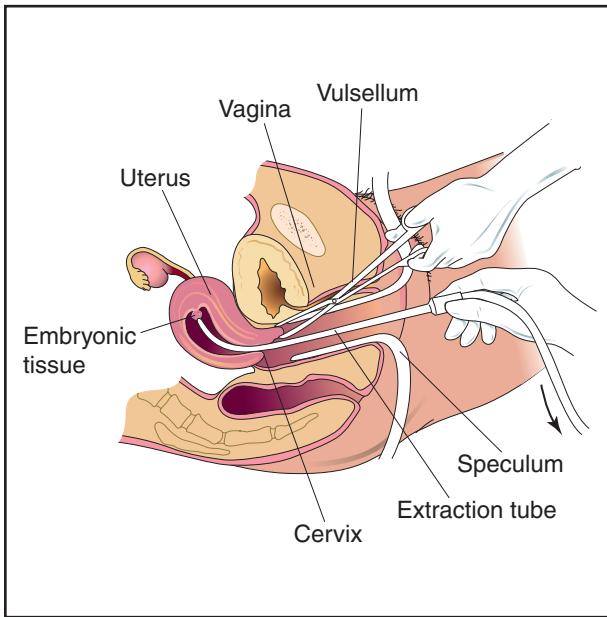
Between five and seven weeks, a pregnancy can be ended by a procedure called menstrual extraction. This procedure is also sometimes called menstrual regulation, mini-suction, or preemptive abortion. The contents of the uterus are suctioned out through a thin (3-4 mm) plastic tube that is inserted through the undilated cervix. Suction is applied either by a bulb syringe or a small pump.

Another method is called the “morning after” pill, or emergency **contraception**. Basically, it involves taking high doses of birth control pills within 24 to 48 hours of having unprotected sex. The high doses of hormones causes the uterine lining to change so that it will not support a pregnancy. Thus, if the egg has been fertilized, it is simply expelled from the body.

There are two types of emergency contraception. One type is identical to ordinary birth control pills, and uses the hormones estrogen and progestin. This type is available with a prescription under the brand name Preven. But women can even use their regular birth control pills for emergency contraception, after they check with their doctor about the proper dose. About half of women who use birth control pills for emergency contraception get nauseated and 20 percent vomit. This method cuts the risk of pregnancy 75 percent.

The other type of morning-after pill contains only one hormone: progestin, and is available under the brand name Plan B. It is more effective than the first type with a lower risk of **nausea and vomiting**. It reduces the risk of pregnancy 89 percent.

Women should check with their physicians regarding the proper dose of pills to take, as it depends on the



Between 5 and 7 weeks, a pregnancy can be ended by a procedure called menstrual extraction. The contents of the uterus are suctioned out through a thin extraction tube that is inserted through the undilated cervix. (*Illustration by Electronic Illustrators Group.*)

brand of birth control pill. Not all birth control pills will work for emergency contraception.

Menstrual extractions are safe, but because the amount of fetal material is so small at this stage of development, it is easy to miss. This results in an incomplete abortion that means the pregnancy continues.

First trimester abortions

The first trimester of pregnancy includes the first 13 weeks after the last menstrual period. In the United States, about 90% of abortions are performed during this period. It is the safest time in which to have an abortion, and the time in which women have the most choice of how the procedure is performed.

MEDICAL ABORTIONS. Medical abortions are brought about by taking medications that end the pregnancy. The advantages of a first trimester medical abortion are:

- The procedure is non-invasive; no surgical instruments are used.
- Anesthesia is not required.
- Drugs are administered either orally or by injection.
- The procedure resembles a natural **miscarriage**.

Disadvantages of a medical abortion are:

- The effectiveness decreases after the seventh week.

- The procedure may require multiple visits to the doctor.
- Bleeding after the abortion lasts longer than after a surgical abortion.
- The woman may see the contents of her womb as it is expelled.

Two different medications can be used to bring about an abortion. Methotrexate (Rheumatrex) works by stopping fetal cells from dividing which causes the fetus to die.

On the first visit to the doctor, the woman receives an injection of methotrexate. On the second visit, about a week later, she is given misoprostol (Cytotec), an oxygenated unsaturated cyclic fatty acid responsible for various hormonal reactions such as muscle contraction (prostaglandin), that stimulates contractions of the uterus. Within two weeks, the woman will expel the contents of her uterus, ending the pregnancy. A follow-up visit to the doctor is necessary to assure that the abortion is complete.

With this procedure, a woman will feel cramping and may feel nauseated from the misoprostol. This combination of drugs is 90-96% effective in ending pregnancy.

Mifepristone (RU-486), which goes by the brand name Mifeprex, works by blocking the action of progesterone, a hormone needed for pregnancy to continue, then stimulates uterine contractions thus ending the pregnancy. It can be taken as early as 49 days after the first day of a woman's last period. On the first visit to the doctor, a woman takes a mifepristone pill. Two days later she returns and, if the miscarriage has not occurred, takes two misoprostol pills, which causes the uterus to contract. Five percent of women won't need to take misoprostol. After an observation period, she returns home.

Within four days, 90% of women have expelled the contents of their uterus and completed the abortion. Within 14 days, 95-97% of women have completed the abortion. A third follow-up visit to the doctor is necessary to confirm through observation or ultrasound that the procedure is complete. In the event that it is not, a surgical abortion is performed. Studies show that 4.5 to 8 percent of women need surgery or a blood **transfusion** after taking mifepristone, and the pregnancy persists in about 1 percent of women. In this case, surgical abortion is recommended because the fetus may be damaged. Side effects include nausea, vaginal bleeding and heavy cramping. The bleeding is typically heavier than a normal period and may last up to 16 days.

Mifepristone is not recommended for women with **ectopic pregnancy**, an **IUD**, who have been taking long-

term steroid therapy, have bleeding abnormalities or on blood-thinners such as Coumadin.

Surgical abortions

First trimester surgical abortions are performed using vacuum aspiration. The procedure is also called dilation and evacuation (D & E), suction dilation, vacuum curettage, or suction curettage.

Advantages of a vacuum aspiration abortion are:

- It is usually done as a one-day outpatient procedure.
- The procedure takes only 10-15 minutes.
- Bleeding after the abortion lasts five days or less.
- The woman does not see the products of her womb being removed.

Disadvantages include:

- The procedure is invasive; surgical instruments are used.
- Infection may occur.

During a vacuum aspiration, the woman's cervix is gradually dilated by expanding rods inserted into the cervical opening. Once dilated, a tube attached to a suction pump is inserted through the cervix and the contents of the uterus are suctioned out. The procedure is 97-99% effective. The amount of discomfort a woman feels varies considerably. Local anesthesia is often given to numb the cervix, but it does not mask uterine cramping. After a few hours of rest, the woman may return home.

Second trimester abortions

Although it is better to have an abortion during the first trimester, some second trimester abortions may be inevitable. The results of **genetic testing** are often not available until 16 weeks. In addition, women, especially teens, may not have recognized the pregnancy or come to terms with it emotionally soon enough to have a first trimester abortion. Teens make up the largest group having second trimester abortions.

Some second trimester abortions are performed as a D & E. The procedures are similar to those used in the first trimester, but a larger suction tube must be used because more material must be removed. This increases the amount of cervical dilation necessary and increases the risk of the procedure. Many physicians are reluctant to perform a D & E this late in pregnancy, and for some women is it not a medically safe option.

The alternative to a D & E in the second trimester is an abortion by induced labor. Induced labor may require an overnight stay in a hospital. The day before the procedure, the woman visits the doctor for tests, and to either

KEY TERMS

Endocarditis—An infection of the inner membrane lining of the heart.

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.

Lupus erythematosus—A chronic inflammatory disease in which inappropriate immune system reactions cause abnormalities in the blood vessels and connective tissue.

Prostaglandin—Oxygenated unsaturated cyclic fatty acids responsible for various hormonal reactions such as muscle contraction.

Rh negative—Lacking the Rh factor, genetically determined antigens in red blood cells that produce immune responses. If an Rh negative woman is pregnant with an Rh positive fetus, her body will produce antibodies against the fetus's blood, causing a disease known as Rh disease. Sensitization to the disease occurs when the woman's blood is exposed to the fetus's blood. Rh immune globulin (RhoGAM) is a vaccine that must be given to a woman after an abortion, miscarriage, or prenatal tests in order to prevent sensitization to Rh disease.

have rods inserted in her cervix to help dilate it or to receive medication that will soften the cervix and speed up labor.

On the day of the abortion, drugs, usually prostaglandins to induce contractions, and a salt water solution, are injected into the uterus. Contractions begin, and within eight to 72 hours the woman delivers the fetus.

Side effects of this procedure include nausea, vomiting, and **diarrhea** from the prostaglandins, and **pain** from uterine cramps. Anesthesia of the sort used in **childbirth** can be given to mask the pain. Many women are able to go home a few hours after the procedure.

Very early abortions cost between \$200-\$400. Later abortions cost more. The cost increases about \$100 per week between the thirteenth and sixteenth week. Second trimester abortions are much more costly because they often involve more risk, more services, anesthesia, and sometimes a hospital stay. Insurance carriers and HMOs may or may not cover the procedure. Federal law pro-

hibits federal funds including Medicaid funds, from being used to pay for an elective abortion.

Preparation

The doctor must know accurately the stage of a woman's pregnancy before an abortion is performed. The doctor will ask the woman questions about her menstrual cycle and also do a **physical examination** to confirm the stage of pregnancy. This may be done at an office visit before the abortion or on the day of the abortion. Some states require a waiting period before an abortion can be performed. Others require parental or court consent for a child under age 18 to receive an abortion.

Despite the fact that almost half of all women in the United States have had at least one abortion by the time they reach age 45, abortion is surrounded by controversy. Women often find themselves in emotional turmoil when deciding if an abortion is a procedure they wish to undergo. Pre-abortion counseling is important in helping a woman resolve any questions she may have about having the procedure.

Aftercare

Regardless of the method used to perform the abortion, a woman will be observed for a period of time to make sure her blood pressure is stable and that bleeding is controlled. The doctor may prescribe **antibiotics** to reduce the chance of infection. Women who are Rh negative (lacking genetically determined antigens in their red blood cells that produce immune responses) should be given a human Rh immune globulin (RhoGAM) after the procedure unless the father of the fetus is also Rh negative. This prevents blood incompatibility complications in future pregnancies.

Bleeding will continue for about five days in a surgical abortion and longer in a medical abortion. To decrease the risk of infection, a woman should avoid intercourse and not use tampons and douches for two weeks after the abortion.

A follow-up visit is a necessary part of the woman's aftercare. Contraception will be offered to women who wish to avoid future pregnancies, because menstrual periods normally resume within a few weeks.

Risks

Serious complications resulting from abortions performed before 13 weeks are rare. Of the 90% of women who have abortions in this time period, 2.5% have minor complications that can be handled without hospitalization. Less than 0.5% have complications that require a hospital stay. The rate of complications increases as the pregnancy progresses.

Complications from abortions can include:

- uncontrolled bleeding
- infection
- blood clots accumulating in the uterus
- a tear in the cervix or uterus
- missed abortion where the pregnancy continues
- incomplete abortion where some material from the pregnancy remains in the uterus

Women who experience any of the following symptoms of post-abortion complications should call the clinic or doctor who performed the abortion immediately.

- severe pain
- fever over 100.4°F (38.2°C)
- heavy bleeding that soaks through more than one sanitary pad per hour
- foul-smelling discharge from the vagina
- continuing symptoms of pregnancy

Normal results

Usually the pregnancy is ended without complication and without altering future fertility.

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ORGANIZATION

National Abortion Federation. (800) 772-9100. <<http://www.prochoice.org>>.

Debra Gordon

Abrasions see **Wounds**

Abruptio placentae see **Placental abruption**

Abscess

Definition

An abscess is an enclosed collection of liquefied tissue, known as pus, somewhere in the body. It is the result of the body's defensive reaction to foreign material.

Description

There are two types of abscesses, septic and sterile. Most abscesses are septic, which means that they are the result of an infection. Septic abscesses can occur anywhere in the body. Only a germ and the body's immune response are required. In response to the invading germ, white blood cells gather at the infected site and begin producing chemicals called enzymes that attack the germ by digesting it. These enzymes act like acid, killing the germs and breaking them down into small pieces that can be picked up by the circulation and eliminated from the body. Unfortunately, these chemicals also digest body tissues. In most cases, the germ produces similar chemicals. The result is a thick, yellow liquid—pus—containing digested germs, digested tissue, white blood cells, and enzymes.

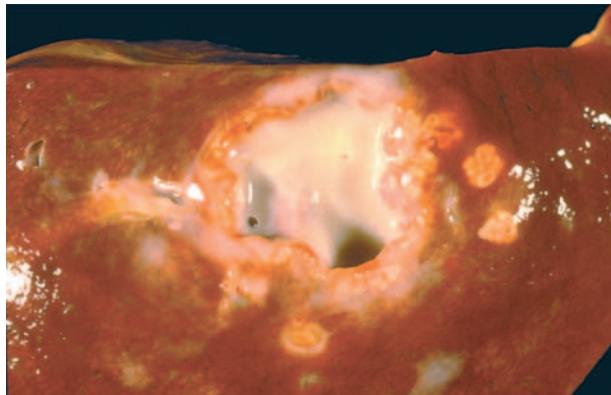
An abscess is the last stage of a tissue infection that begins with a process called inflammation. Initially, as the invading germ activates the body's immune system, several events occur:

- Blood flow to the area increases.
- The temperature of the area increases due to the increased blood supply.
- The area swells due to the accumulation of water, blood, and other liquids.
- It turns red.
- It hurts, because of the irritation from the swelling and the chemical activity.

These four signs—heat, swelling, redness, and pain—characterize inflammation.

As the process progresses, the tissue begins to turn to liquid, and an abscess forms. It is the nature of an abscess to spread as the chemical digestion liquefies more and more tissue. Furthermore, the spreading follows the path of least resistance—the tissues most easily digested. A good example is an abscess just beneath the skin. It most easily continues along beneath the skin rather than working its way through the skin where it could drain its toxic contents. The contents of the abscess also leak into the general circulation and produce symptoms just like any other infection. These include chills, fever, aching, and general discomfort.

Sterile abscesses are sometimes a milder form of the same process caused not by germs but by non-living irritants such as drugs. If an injected drug like penicillin is not absorbed, it stays where it was injected and may cause enough irritation to generate a sterile abscess—sterile because there is no infection involved. Sterile abscesses are quite likely to turn into hard, solid lumps as they scar, rather than remaining pockets of pus.



An amoebic abscess caused by *Entameoba histolytica*.
(Phototake NYC. Reproduced by permission.)

Causes and symptoms

Many different agents cause abscesses. The most common are the pus-forming (pyogenic) bacteria like *Staphylococcus aureus*, which is nearly always the cause of abscesses under the skin. Abscesses near the large bowel, particularly around the anus, may be caused by any of the numerous bacteria found within the large bowel. Brain abscesses and liver abscesses can be caused by any organism that can travel there through the circulation. Bacteria, amoeba, and certain fungi can travel in this fashion. Abscesses in other parts of the body are caused by organisms that normally inhabit nearby structures or that infect them. Some common causes of specific abscesses are:

- skin abscesses by normal skin flora
- dental and throat abscesses by mouth flora
- lung abscesses by normal airway flora, **pneumonia** germs, or **tuberculosis**
- abdominal and anal abscesses by normal bowel flora

Specific types of abscesses

Listed below are some of the more common and important abscesses.

- Carbuncles and other **boils**. Skin oil glands (sebaceous glands) on the back or the back of the neck are the ones usually infected. The most common germ involved is *Staphylococcus aureus*. **Acne** is a similar condition of sebaceous glands on the face and back.
- Pilonidal abscess. Many people have as a birth defect a tiny opening in the skin just above the anus. Fecal bacteria can enter this opening, causing an infection and subsequent abscess.

KEY TERMS

- Cellulitis**—Inflammation of tissue due to infection.
- Enzyme**—Any of a number of protein chemicals that can change other chemicals.
- Fallopian tubes**—Part of the internal female anatomy that carries eggs from the ovaries to the uterus.
- Flora**—Living inhabitants of a region or area.
- Pyogenic**—Capable of generating pus. *Streptococcus*, *Staphylococcus*, and bowel bacteria are the primary pyogenic organisms.
- Sebaceous glands**—Tiny structures in the skin that produce oil (sebum). If they become plugged, sebum collects inside and forms a nurturing place for germs to grow.
- Septicemia**—The spread of an infectious agent throughout the body by means of the blood stream.
- Sinus**—A tubular channel connecting one body part with another or with the outside.

- Retropharyngeal, parapharyngeal, peritonsillar abscess. As a result of throat infections like **strep throat** and **tonsillitis**, bacteria can invade the deeper tissues of the throat and cause an abscess. These abscesses can compromise swallowing and even breathing.
- Lung abscess. During or after pneumonia, whether it's due to bacteria [common pneumonia], tuberculosis, fungi, parasites, or other germs, abscesses can develop as a complication.
- Liver abscess. Bacteria or amoeba from the intestines can spread through the blood to the liver and cause abscesses.
- Psoas abscess. Deep in the back of the abdomen on either side of the lumbar spine lie the psoas muscles. They flex the hips. An abscess can develop in one of these muscles, usually when it spreads from the appendix, the large bowel, or the fallopian tubes.

Diagnosis

The common findings of inflammation—heat, redness, swelling, and pain—easily identify superficial abscesses. Abscesses in other places may produce only generalized symptoms such as fever and discomfort. If the patient's symptoms and **physical examination** do not help, a physician may have to resort to a battery of tests to

locate the site of an abscess, but usually something in the initial evaluation directs the search. Recent or chronic disease in an organ suggests it may be the site of an abscess. Dysfunction of an organ or system—for instance, seizures or altered bowel function—may provide the clue. **Pain** and tenderness on physical examination are common findings. Sometimes a deep abscess will eat a small channel (sinus) to the surface and begin leaking pus. A sterile abscess may cause only a painful lump deep in the buttock where a shot was given.

Treatment

Since skin is very resistant to the spread of infection, it acts as a barrier, often keeping the toxic chemicals of an abscess from escaping the body on their own. Thus, the pus must be drained from the abscess by a physician. The surgeon determines when the abscess is ready for drainage and opens a path to the outside, allowing the pus to escape. Ordinarily, the body handles the remaining infection, sometimes with the help of **antibiotics** or other drugs. The surgeon may leave a drain (a piece of cloth or rubber) in the abscess cavity to prevent it from closing before all the pus has drained out.

Alternative treatment

If an abscess is directly beneath the skin, it will be slowly working its way through the skin as it is more rapidly working its way elsewhere. Since chemicals work faster at higher temperatures, applications of hot compresses to the skin over the abscess will hasten the digestion of the skin and eventually result in its breaking down, releasing the pus spontaneously. This treatment is best reserved for smaller abscesses in relatively less dangerous areas of the body—limbs, trunk, back of the neck. It is also useful for all superficial abscesses in their very early stages. It will “ripen” them.

Contrast **hydrotherapy**, alternating hot and cold compresses, can also help assist the body in resorption of the abscess. There are two homeopathic remedies that work to rebalance the body in relation to abscess formation, *Silica* and *Hepar sulphuris*. In cases of septic abscesses, bentonite clay packs (bentonite clay and a small amount of *Hydrastis* powder) can be used to draw the infection from the area.

Prognosis

Once the abscess is properly drained, the prognosis is excellent for the condition itself. The reason for the abscess (other diseases the patient has) will determine the overall outcome. If, on the other hand, the abscess ruptures into neighboring areas or permits the infectious

agent to spill into the bloodstream, serious or fatal consequences are likely. Abscesses in and around the nasal sinuses, face, ears, and scalp may work their way into the brain. Abscesses within an abdominal organ such as the liver may rupture into the abdominal cavity. In either case, the result is life threatening. Blood **poisoning** is a term commonly used to describe an infection that has spilled into the blood stream and spread throughout the body from a localized origin. Blood poisoning, known to physicians as septicemia, is also life threatening.

Of special note, abscesses in the hand are more serious than they might appear. Due to the intricate structure and the overriding importance of the hand, any hand infection must be treated promptly and competently.

Prevention

Infections that are treated early with heat (if superficial) or antibiotics will often resolve without the formation of an abscess. It is even better to avoid infections altogether by taking prompt care of open injuries, particularly puncture **wounds**. Bites are the most dangerous of all, even more so because they often occur on the hand.

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J. Ricker Polsdorfer, MD

Abscess drainage see **Abscess incision and drainage**

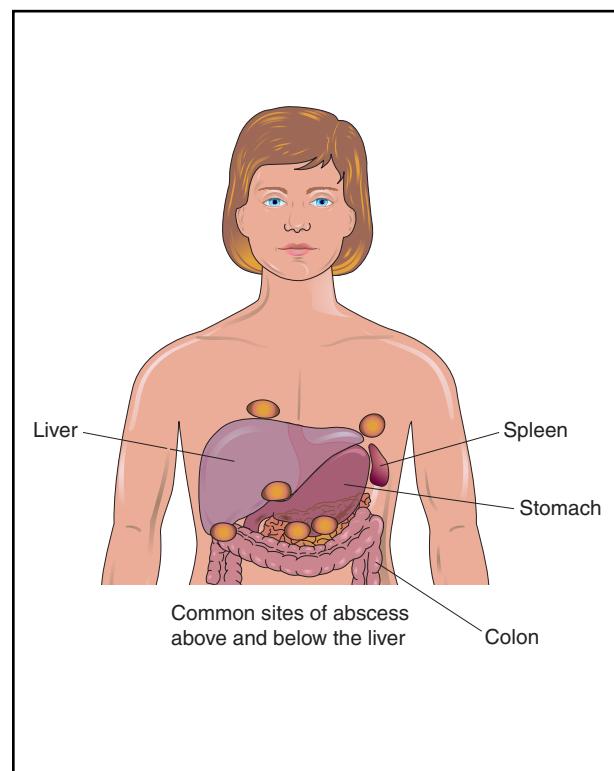
Abscess incision & drainage

Definition

An infected skin nodule that contains pus may need to be drained via a cut if it does not respond to **antibiotics**. This allows the pus to escape, and the infection to heal.

Purpose

An **abscess** is a pus-filled sore, usually caused by a bacterial infection. The pus is made up of both live and dead organisms and destroyed tissue from the white



Although abscesses are often found in the soft tissue under the skin, such as the armpit or the groin, they may develop in any organ, such as the liver. (Illustration by Electronic Illustrators Group.)

blood cells that were carried to the area to fight the infection. Abscesses are often found in the soft tissue under the skin, such as the armpit or the groin. However, they may develop in any organ, and are commonly found in the breast and gums. Abscesses are far more serious and call for more specific treatment if they are located in deep organs such as the lung, liver or brain.

Because the lining of the abscess cavity tends to interfere with the amount of the drug that can penetrate the source of infection from the blood, the cavity itself may require draining. Once an abscess has fully formed, it often does not respond to antibiotics. Even if the antibiotic does penetrate into the abscess, it doesn't function as well in that environment.

Precautions

An abscess can usually be diagnosed visually, although an imaging technique such as a computed tomography scan may be used to confirm the extent of the abscess before drainage. Such procedures may also be needed to localize internal abscesses, such as those in the abdominal cavity or brain.

KEY TERMS

White blood cells—Cells that protect the body against infection.

Description

A doctor will cut into the lining of the abscess, allowing the pus to escape either through a drainage tube or by leaving the cavity open to the skin. How big the incision is depends on how quickly the pus is encountered.

Once the abscess is opened, the doctor will clean and irrigate the wound thoroughly with saline. If it is not too large or deep, the doctor may simply pack the abscess wound with gauze for 24–48 hours to absorb the pus and discharge.

If it is a deeper abscess, the doctor may insert a drainage tube after cleaning out the wound. Once the tube is in place, the surgeon closes the incision with simple stitches, and applies a sterile dressing. Drainage is maintained for several days to help prevent the abscess from reforming.

Preparation

The skin over the abscess will be cleansed by swabbing gently with an antiseptic solution.

Aftercare

Much of the **pain** around the abscess will be gone after the surgery. Healing is usually very fast. After the tube is taken out, antibiotics may be continued for several days. Applying heat and keeping the affected area elevated may help relieve inflammation.

Risks

If there is any scarring, it is likely to become much less noticeable as time goes on, and eventually almost invisible. Occasionally, an abscess within a vital organ (such as the brain) damages enough surrounding tissue that there is some permanent loss of normal function.

Normal results

Most abscesses heal after drainage alone; others require drainage and antibiotic drug treatment.

Resources

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ORGANIZATIONS

National Institute of Arthritis and Musculoskeletal and Skin Diseases. 9000 Rockville Pike, Bldg. 31, Rm 9A04, Bethesda, MD 20892.

Carol A. Turkington

Abuse

Definition

Abuse is defined as any thing that is harmful, injurious, or offensive. Abuse also includes excessive and wrongful misuse of anything. There are several major types of abuse: physical and sexual abuse of a child or an adult, substance abuse, elderly abuse, and emotional abuse.

Description

Physical abuse of a child is the infliction of injury by an other person. The injuries can include punching, kicking, biting, burning, beating, or pulling the victim's hair. The physical abuse inflicted on a child can result in **bruises, burns, poisoning, broken bones, and internal hemorrhages**. Physical assault against an adult primarily occurs with women, usually in the form of domestic violence. It is estimated that approximately three million children witness domestic violence every year.

Sexual abuse of a child refers to sexual behavior between an adult and child or between two children, one of whom is dominant or significantly older. The sexual behaviors can include touching breasts, genitals, and buttocks; either dressed or undressed. The behavior can also include exhibitionism, cunnilingus, fellatio, or penetration of the vagina or anus with sexual organs or objects.

Pornographic photography is also used in sexual abuse with children. Reported sex offenders are 97% male. Females are more often perpetrators in child-care settings, since children may confuse sexual abuse by a female with normal hygiene care. Sexual abuse by stepfathers is five times more common than with biological fathers. Sexual abuse of daughters by stepfathers or fathers is the most common form of incest.

Sexual abuse can also take the form of rape. The legal definition of rape includes only slight penile penetration in the victim's outer vulva area. Complete erection and ejaculation are not necessary. Rape is the perpetration of an act of sexual intercourse whether:

- will is overcome by force or fear (from threats or by use of drugs).

- mental impairment renders the victim incapable of rational judgment.
- if the victim is below the legal age established for consent.

Substance abuse is an abnormal pattern of substance usage leading to significant distress or impairment. The criteria include one or more of the following occurring within a 12-month period:

- recurrent substance use resulting in failure to fulfill obligations at home, work, or school.
- using substance in situations that are physically dangerous (i.e., while driving).
- recurrent substance-related legal problems.
- continued usage despite recurrent social and interpersonal problems (i.e., arguments and fights with significant other).

Abuse in the elderly is common and occurs mostly as a result of caretaker burnout, due to the high level of dependency frail, elderly patients usually require. Abuse can be manifested by physical signs, fear, and delaying or not reporting the need for advanced medical care. Elderly patients may also exhibit financial abuse (money or possessions taken away) and abandonment.

Emotional abuse generally continues even after physical assaults have stopped. In most cases it is a personally tailored form of verbal or gesture abuse expressed to illicit a provoked response.

Causes and symptoms

Children who have been abused usually have a variety of symptoms that encompass behavioral, emotional, and psychosomatic problems. Children who have been physically abused tend to be more aggressive, angry, hostile, depressed, and have low self-esteem. Additionally, they exhibit fear, **anxiety**, and nightmares. Severe psychological problems may result in suicidal behavior or posttraumatic stress disorder. Physically abused children may complain of physical illness even in the absence of a cause. They may also suffer from eating disorders and encopresis. Children who are sexually abused may exhibit abnormal sexual behavior in the form of aggressiveness and hyperarousal. Adolescents may display promiscuity, sexual acting out, and—in some situations—homosexual contact.

Physical abuse directed towards adults can ultimately lead to **death**. Approximately 50% of women murdered in the United States were killed by a former or current male partner. Approximately one-third of emergency room consultations by women were prompted due to domestic violence. Female victims who are married also have a higher rate of internal injuries and unconscious-

KEY TERMS

Encopresis—Abnormalities relating to bowel movements that can occur as a result of stress or fear.

ness than victims of stranger assault (mugging, robbery). Physical abuse or rape can also occur between married persons and persons of the same gender. Perpetrators usually sexually assault their victims to dominate, hurt, and debase them. It is common for physical and sexual violence to occur at the same time. A large percentage of sexually assaulted persons were also physically abused in the form of punching, beating, or threatening the victim with a weapon such as a gun or knife. Usually males who are hurt and humiliated tend to physical assault persons whom they are intimately involved with, such as spouses and/or children. Males who assault a female tend to have experienced or witnessed violence during childhood. They also tend to abuse alcohol, to be sexually assaultive, and are at increased risk for assaultive behavior directed against children. Jealous males tend to monitor the women's movements and whereabouts and to isolate other sources of protection and support. They interpret their behavior as betrayal of trust and this causes resentment and explosive anger outbursts during periods of losing control. Males may also use aggression against females in an effort to control and intimidate partners.

Abuse in the elderly usually occurs in the frail, elderly community. The caretaker is usually the perpetrator. Caretaker abuse can be suspected if there is evidence suggesting behavioral changes in the elderly person when the caretaker is present. Additionally, elderly abuse can be possible if there are delays between injuries and treatment, inconsistencies between injury and explanations, lack of hygiene or clothing, and prescriptions no being filled.

Diagnosis

Children who are victims of domestic violence are frequently injured attempting to protect their mother from an abusive partner. Injuries are visible by inspection or self-report. Physical abuse of an adult may be also be evident by inspection with visible cuts and/or bruises or self report.

Sexual abuse of both a child and an adult can be diagnosed with a history from the victim. Victims can be assessed for ejaculatory evidence from the perpetrator. Ejaculatory specimens can be retrieved from the mouth, rectum, and clothing. Tests for **sexually transmitted diseases** may be performed.

Elderly abuse can be suspected if the elderly patient demonstrates a fear from the caretaker. Additionally, elderly abuse can be suspected if there are signs indicating intentional delay of required medical care or a change in medical status.

Substance abuse can be suspected in a person who continues to indulge in their drug of choice despite recurrent negative consequences. The diagnosis can be made after administration of a comprehensive bio-psychosocial exam and standardized chemical abuse assessments by a therapist.

Treatment

Children who are victims of physical or sexual abuse typically require psychological support and medical attention. A complaint may be filed with the local family social services that will initiate investigations. The authorities will usually follow up the allegation or offense. Children may also be referred for psychological evaluation and/or treatment. The victim may be placed in foster care pending the investigation outcome. The police may also investigate physical and sexual abuse of an adult. The victim may require immediate medical care and long-term psychological treatment. It is common for children to be adversely affected by domestic violence situations and the local family services agency may be involved.

Substance abusers should elect treatment, either inpatient or outpatient, depending on severity of **addiction**. Long term treatment and/or medications may be utilized to assist in abstinence. The patient should be encouraged to participate in community centered support groups.

Prognosis

The prognosis depends on the diagnosis. Usually victims of physical and sexual abuse require therapy to deal with emotional distress associated with the incident. Perpetrators require further psychological evaluation and treatment. Victims of abuse may have a variety of emotional problems including depression, acts of suicide, or anxiety. Children of sexual abuse may as adults enter abusive relationships or have problems with intimacy. The substance abuser may experience relapses, since the cardinal feature of all addictive disorders is a tendency to return to symptoms. Elderly patients may suffer from further medical problems and/or anxiety, and in some cases neglect may precipitate death.

Prevention

Prevention programs are geared to education and awareness. Detection of initial symptoms or characteris-

tic behaviors may assist in some situations. In some cases treatment may be sought before incident. The professional treating the abused persons must develop a clear sense of the relationship dynamics and the chances for continued harm.

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ORGANIZATIONS

- National Clearinghouse on Child Abuse and Neglect Information. 330 C Street SW, Washington, DC 20447. (800) 392-3366.

OTHER

- Elder Abuse Prevention. <<http://www.oaktrees.org/elder>>.
- National Institute on Drug Abuse. <<http://www.nida.nih.gov>>.

Laith Farid Gulli, M.D.
Bilal Nasser, M.Sc.

Acceleration-deceleration cervical injury
see **Whiplash**

ACE inhibitors see **Angiotensin-converting enzyme inhibitors**

Acetaminophen

Definition

Acetaminophen is a medicine used to relieve **pain** and reduce **fever**.

Purpose

Acetaminophen is used to relieve many kinds of minor aches and pains—headaches, muscle aches, backaches, toothaches, menstrual cramps, arthritis, and the aches and pains that often accompany colds.

Description

This drug is available without a prescription. Acetaminophen—or APAP—is sold under various brand names, including Tylenol, Panadol, **Aspirin** Free Anacin, and Bayer Select Maximum Strength **Headache** Pain Relief Formula. Many multi-symptom cold, flu, and sinus medicines also contain acetaminophen. Check the ingredients listed on the container to see if acetaminophen is included in the product.

Studies have shown that acetaminophen relieves pain and reduces fever about as well as aspirin. But differences between these two common drugs exist. Acetaminophen is less likely than aspirin to irritate the stomach. However, unlike aspirin, acetaminophen does not reduce the redness, stiffness, or swelling that accompany arthritis.

Recommended dosage

The usual dosage for adults and children age 12 and over is 325–650 mg every 4–6 hours as needed. No more than 4 grams (4000 mg) should be taken in 24 hours. Because the drug can potentially harm the liver, people who drink alcohol in large quantities should take considerably less acetaminophen and possibly should avoid the drug completely.

For children ages 6–11 years, the usual dose is 150–300 mg, three to four times a day. Check with a physician for dosages for children under age 6 years.

Precautions

Never take more than the recommended dosage of acetaminophen unless told to do so by a physician or dentist.

Patients should not use acetaminophen for more than 10 days to relieve pain (5 days for children) or for more than 3 days to reduce fever, unless directed to do so by a physician. If symptoms do not go away—or if they get worse—contact a physician. Anyone who drinks three or more alcoholic beverages a day should check with a physician before using this drug and should never take more than the recommended dosage. A risk of liver damage exists from combining large amounts of alcohol and acetaminophen. People who already have kidney or liver disease or liver infections should also consult with a physician before using the drug. So should women who are pregnant or breastfeeding.

Smoking cigarettes may interfere with the effectiveness of acetaminophen. Smokers may need to take higher doses of the medicine, but should not take more than the recommended daily dosage unless told by a physician to do so.

KEY TERMS

Arthritis—Inflammation of the joints. The condition causes pain and swelling.

Fatigue—Physical or mental weariness.

Inflammation—A response to irritation, infection, or injury, resulting in pain, redness, and swelling.

Many drugs can interact with one another. Consult a physician or pharmacist before combining acetaminophen with any other medicine. Do not use two different acetaminophen-containing products at the same time.

Acetaminophen interferes with the results of some medical tests. Before having medical tests done, check to see whether taking acetaminophen will affect the results. Avoiding the drug for a few days before the tests may be necessary.

Side effects

Acetaminophen causes few side effects. The most common one is lightheadedness. Some people may experience trembling and pain in the side or the lower back. Allergic reactions do occur in some people, but they are rare. Anyone who develops symptoms such as a rash, swelling, or difficulty breathing after taking acetaminophen should stop taking the drug and get immediate medical attention. Other rare side effects include yellow skin or eyes, unusual bleeding or bruising, weakness, **fatigue**, bloody or black stools, bloody or cloudy urine, and a sudden decrease in the amount of urine.

Overdoses of acetaminophen may cause nausea, vomiting, sweating, and exhaustion. Very large overdoses can cause liver damage. In case of an overdose, get immediate medical attention.

Interactions

Acetaminophen 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. Among the drugs that may interact with acetaminophen are alcohol, **nonsteroidal anti-inflammatory drugs** (NSAIDs) such as Motrin, **oral contraceptives**, the antiseizure drug phenytoin (Dilantin), the blood-thinning drug warfarin (Coumadin), the cholesterol-lowering drug cholestyramine (Questran), the antibiotic Isoniazid, and zidovudine (Retrovir, AZT).

Check with a physician or pharmacist before combining acetaminophen with any other prescription or nonprescription (over-the-counter) medicine.

Nancy Ross-Flanigan

Acetylsalicylic acid see **Aspirin**

Achalasia

Definition

Achalasia is a disorder of the esophagus that prevents normal swallowing.

Description

Achalasia affects the esophagus, the tube that carries swallowed food from the back of the throat down into the stomach. A ring of muscle called the lower esophageal sphincter encircles the esophagus just above the entrance to the stomach. This sphincter muscle is normally contracted to close the esophagus. When the sphincter is closed, the contents of the stomach cannot flow back into the esophagus. Backward flow of stomach contents (reflux) can irritate and inflame the esophagus, causing symptoms such as **heartburn**. The act of swallowing causes a wave of esophageal contraction called peristalsis. Peristalsis pushes food along the esophagus. Normally, peristalsis causes the esophageal sphincter to relax and allow food into the stomach. In achalasia, which means “failure to relax,” the esophageal sphincter remains contracted. Normal peristalsis is interrupted and food cannot enter the stomach.

Causes and symptoms

Causes

Achalasia is caused by degeneration of the nerve cells that normally signal the brain to relax the esophageal sphincter. The ultimate cause of this degeneration is unknown. Autoimmune disease or hidden infection is suspected.

Symptoms

Dysphagia, or difficulty swallowing, is the most common symptom of achalasia. The person with achalasia usually has trouble swallowing both liquid and solid foods, often feeling that food “gets stuck” on the way down. The person has chest **pain** that is often mistaken for **angina pectoris** (cardiac pain). Heartburn and difficulty belching

are common. Symptoms usually get steadily worse. Other symptoms may include nighttime **cough** or recurrent **pneumonia** caused by food passing into the lower airways.

Diagnosis

Diagnosis of achalasia begins with a careful medical history. The history should focus on the timing of symptoms and on eliminating other medical conditions that may cause similar symptoms. Tests used to diagnose achalasia include:

- **Esophageal manometry.** In this test, a thin tube is passed into the esophagus to measure the pressure exerted by the esophageal sphincter.
- **X ray of the esophagus.** Barium may be swallowed to act as a contrast agent. Barium reveals the outlines of the esophagus in greater detail and makes it easier to see its constriction at the sphincter.
- **Endoscopy.** In this test, a tube containing a lens and a light source is passed into the esophagus. Endoscopy is used to look directly at the surface of the esophagus. This test can also detect tumors that cause symptoms like those of achalasia. **Cancer** of the esophagus occurs as a complication of achalasia in 2–7% of patients.

Treatment

The first-line treatment for achalasia is balloon dilation. In this procedure, an inflatable membrane or balloon is passed down the esophagus to the sphincter and inflated to force the sphincter open. Dilation is effective in about 70% of patients.

Three other treatments are used for achalasia when balloon dilation is inappropriate or unacceptable.

- **Botulinum toxin injection.** Injected into the sphincter, botulinum toxin paralyzes the muscle and allows it to relax. Symptoms usually return within one to two years.
- **Esophagomyotomy.** This surgical procedure cuts the sphincter muscle to allow the esophagus to open. Esophagomyotomy is becoming more popular with the development of techniques allowing very small abdominal incisions.
- **Drug therapy.** Nifedipine, a calcium-channel blocker, reduces muscle contraction. Taken daily, this drug provides relief for about two-thirds of patients for as long as two years.

Prognosis

Most patients with achalasia can be treated effectively. Achalasia does not reduce life expectancy unless esophageal carcinoma develops.

KEY TERMS

Botulinum toxin—Any of a group of potent bacterial toxins or poisons produced by different strains of the bacterium *Clostridium botulinum*. The toxins cause muscle paralysis.

Dysphagia—Difficulty in swallowing.

Endoscopy—A test in which a viewing device and a light source are introduced into the esophagus by means of a flexible tube. Endoscopy permits visual inspection of the esophagus for abnormalities.

Esophageal manometry—A test in which a thin tube is passed into the esophagus to measure the degree of pressure exerted by the muscles of the esophageal wall.

Esophageal sphincter—A circular band of muscle that closes the last few centimeters of the esophagus and prevents the backward flow of stomach contents.

Esophagomyotomy—A surgical incision through the muscular tissue of the esophagus.

Esophagus—The muscular tube that leads from the back of the throat to the entrance of the stomach.

Peristalsis—The coordinated, rhythmic wave of smooth muscle contraction that forces food through the digestive tract.

Reflux—An abnormal backward or return flow of a fluid.



An x-ray image of an achondroplastic person's head and chest. (Custom Medical Stock Photo. Reproduced by permission.)

Description

Achondroplasia is one of a number of chondodystrophies, in which the development of cartilage, and therefore, bone is disturbed. The disorder appears in approximately one in every 10,000 births. Achondroplasia is usually diagnosed at birth, owing to the characteristic appearance of the newborn.

Normal bone growth depends on the production of cartilage (a fibrous connective tissue). Over time, calcium is deposited within the cartilage, causing it to harden and become bone. In achondroplasia, abnormalities of this process prevent the bones (especially those in the limbs) from growing as long as they normally should, at the same time allowing the bones to become abnormally thickened. The bones in the trunk of the body and the skull are mostly not affected, although the opening from the skull through which the spinal cord passes (foramen magnum) is often narrower than normal, and the opening (spinal canal) through which the spinal cord runs in the back bones (vertebrae) becomes increasingly and abnormally small down the length of the spine.

Prevention

There is no known way to prevent achalasia.

Resources

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Richard Robinson

Achondroplasia

Definition

Achondroplasia is the most common cause of dwarfism, or significantly abnormal short stature.

Causes and symptoms

Achondroplasia is caused by a genetic defect. It is a dominant trait, meaning that anybody with the genetic defect will display all the symptoms of the disorder. A parent with the disorder has a 50% chance of passing it

KEY TERMS

Cartilage—A flexible, fibrous type of connective tissue which serves as a base on which bone is built.

Foramen magnum—The opening at the base of the skull, through which the spinal cord and the brainstem pass.

Hydrocephalus—An abnormal accumulation of fluid within the brain. This accumulation can be destructive by pressing on brain structures, and damaging them.

Mutation—A new, permanent change in the structure of a gene, which can result in abnormal structure or function somewhere in the body.

Spinal canal—The opening that runs through the center of the column of spinal bones (vertebrae), and through which the spinal cord passes.

Vertebrae—The individual bones of the spinal column which are stacked on top of each other. There is a hole in the center of each bone, through which the spinal cord passes.

on to the offspring. Although achondroplasia can be passed on to subsequent offspring, the majority of cases occur due to a new mutation (change) in a gene. Interestingly enough, the defect seen in achondroplasia is one of only a few defects known to increase in frequency with increasing age of the father (many genetic defects are linked to increased age of the mother).

People with achondroplasia have abnormally short arms and legs. Their trunk is usually of normal size, as is their head. The appearance of short limbs and normal head size actually makes the head appear to be oversized. The bridge of the nose often has a scooped out appearance termed “saddle nose.” The lower back has an abnormal curvature, or sway back. The face often displays an overly prominent forehead, and a relative lack of development of the face in the area of the upper jaw. Because the foramen magnum and spinal canal are abnormally narrowed, nerve damage may occur if the spinal cord or nerves become compressed. The narrowed foramen magnum may disrupt the normal flow of fluid between the brain and the spinal cord, resulting in the accumulation of too much fluid in the brain (**hydrocephalus**). Children with achondroplasia have a very high risk of serious and repeated middle ear infections, which can result in **hearing loss**. The disease does not affect either mental capacity, or reproductive ability.

Diagnosis

Diagnosis is often made at birth due to the characteristically short limbs, and the appearance of a large head. X-ray examination will reveal a characteristic appearance to the bones, with the bones of the limbs appearing short in length, yet broad in width. A number of measurements of the bones in x-ray images will reveal abnormal proportions.

Treatment

No treatment will reverse the defect present in achondroplasia. All patients with the disease will be short, with abnormally proportioned limbs, trunk, and head. Treatment of achondroplasia primarily addresses some of the complications of the disorder, including problems due to nerve compression, hydrocephalus, bowed legs, and abnormal curves in the spine. Children with achondroplasia who develop middle ear infections (acute **otitis media**) will require quick treatment with **antibiotics** and careful monitoring in order to avoid hearing loss.

Prognosis

Achondroplasia is a disease which causes considerable deformity. However, with careful attention paid to the development of dangerous complications (nerve compression, hydrocephalus), most people are in good health, and can live a normal lifespan.

Prevention

The only form of prevention is through **genetic counseling**, which could help parents assess their risk of having a child with achondroplasia.

Resources

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ORGANIZATIONS

- Little People of America, c/o Mary Carten. 7238 Piedmont Drive, Dallas, TX 75227-9324. (800) 243-9273.

Rosalyn Carson-DeWitt, MD

Achromatopsia see **Color blindness**

Acid indigestion see **Heartburn**

Acid phosphatase test

Definition

Acid phosphatase is an enzyme found throughout the body, but primarily in the prostate gland. Like all enzymes, it is needed to trigger specific chemical reactions. Acid phosphatase testing is done to diagnose whether **prostate cancer** has spread to other parts of the body (metastasized), and to check the effectiveness of treatment. The test has been largely supplanted by the prostate specific antigen test (PSA).

Purpose

The male prostate gland has 100 times more acid phosphatase than any other body tissue. When prostate **cancer** spreads to other parts of the body, acid phosphatase levels rise, particularly if the cancer spreads to the bone. One-half to three-fourths of persons who have metastasized prostate cancer have high acid phosphatase levels. Levels fall after the tumor is removed or reduced through treatment.

Tissues other than prostate have small amounts of acid phosphatase, including bone, liver, spleen, kidney, and red blood cells and platelets. Damage to these tissues causes a moderate increase in acid phosphatase levels.

Acid phosphatase is very concentrated in semen. Rape investigations will often include testing for the presence of acid phosphatase in vaginal fluid.

Precautions

This is not a screening test for prostate cancer. Acid phosphatase levels rise only after prostate cancer has metastasized.

Description

Laboratory testing measures the amount of acid phosphatase in a person's blood, and can determine from what tissue the enzyme is coming. For example, it is important to know if the increased acid phosphatase is from the prostate or red blood cells. Acid phosphatase from the prostate, called prostatic acid phosphatase (PAP), is the most medically significant type of acid phosphatase.

KEY TERMS

Enzyme—A substance needed to trigger specific chemical reactions.

Metastasize—Spread to other parts of the body; usually refers to cancer.

Prostate gland—A gland of the male reproductive system.

Subtle differences between prostatic acid phosphatase and acid phosphatases from other tissues cause them to react differently in the laboratory when mixed with certain chemicals. For example, adding the chemical tartrate to the test mixture inhibits the activity of prostatic acid phosphatase but not red blood cell acid phosphatase. Laboratory test methods based on these differences reveal how much of a person's total acid phosphatase is derived from the prostate. Results are usually available the next day.

Preparation

This test requires drawing about 5-10 mL of blood. The patient should not have a rectal exam or prostate massage for two to three days prior to the test.

Aftercare

Discomfort or bruising may occur at the puncture site, and the person may feel dizzy or faint. Applying pressure to the puncture site until the bleeding stops will reduce bruising. Warm packs to the puncture site will relieve discomfort.

Normal results

Normal results vary based on the laboratory and the method used.

Abnormal results

The highest levels of acid phosphatase are found in metastasized prostate cancer. Diseases of the bone, such as Paget's disease or **hyperparathyroidism**; diseases of blood cells, such as **sickle cell disease** or **multiple myeloma**; or lysosomal disorders, such as Gaucher's disease, will show moderately increased levels.

Certain medications can cause temporary increases or decreases in acid phosphatase levels. Manipulation of the prostate gland through massage, biopsy, or rectal exam before a test can increase the level.

Resources

BOOKS

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Nancy J. Nordenson

Acid reflux see **Heartburn**

Acidosis see **Respiratory acidosis; Renal tubular acidosis; Metabolic acidosis**

Acne

Definition

Acne is a common skin disease characterized by pimples on the face, chest, and back. It occurs when the pores of the skin become clogged with oil, dead skin cells, and bacteria.

Description

Acne vulgaris, the medical term for common acne, is the most common skin disease. It affects nearly 17 million people in the United States. While acne can arise at any age, it usually begins at **puberty** and worsens during adolescence. Nearly 85% of people develop acne at some time between the ages of 12-25 years. Up to 20% of women develop mild acne. It is also found in some newborns.

The sebaceous glands lie just beneath the skin's surface. They produce an oil called sebum, the skin's natural moisturizer. These glands and the hair follicles within which they are found are called sebaceous follicles. These follicles open onto the skin through pores. At puberty, increased levels of androgens (male hormones) cause the glands to produce too much sebum. When excess sebum combines with dead, sticky skin cells, a hard plug, or comedo, forms that blocks the pore. Mild noninflammatory acne consists of the two types of comedones, whiteheads and blackheads.

Moderate and severe inflammatory types of acne result after the plugged follicle is invaded by *Propionibacterium acnes*, a bacteria that normally lives on the

skin. A pimple forms when the damaged follicle weakens and bursts open, releasing sebum, bacteria, and skin and white blood cells into the surrounding tissues. Inflamed pimples near the skin's surface are called papules; when deeper, they are called pustules. The most severe type of acne consists of cysts (closed sacs) and nodules (hard swellings). Scarring occurs when new skin cells are laid down to replace damaged cells.

The most common sites of acne are the face, chest, shoulders, and back since these are the parts of the body where the most sebaceous follicles are found.

Causes and symptoms

The exact cause of acne is unknown. Several risk factors have been identified:

- Age. Due to the hormonal changes they experience, teenagers are more likely to develop acne.
- Gender. Boys have more severe acne and develop it more often than girls.
- Disease. Hormonal disorders can complicate acne in girls.
- Heredity. Individuals with a family history of acne have greater susceptibility to the disease.
- Hormonal changes. Acne can flare up before menstruation, during **pregnancy**, and **menopause**.
- Diet. No foods cause acne, but certain foods may cause flare-ups.
- Drugs. Acne can be a side effect of drugs including tranquilizers, antidepressants, **antibiotics**, **oral contraceptives**, and anabolic steroids.
- Personal hygiene. Abrasive soaps, hard scrubbing, or picking at pimples will make them worse.
- Cosmetics. Oil-based makeup and hair sprays worsen acne.
- Environment. Exposure to oils and greases, polluted air, and sweating in hot weather aggravate acne.
- Stress. Emotional stress may contribute to acne.

Acne is usually not conspicuous, although inflamed lesions may cause **pain**, tenderness, **itching**, or swelling. The most troubling aspects of these lesions are the negative cosmetic effects and potential for scarring. Some people, especially teenagers, become emotionally upset about their condition, and have problems forming relationships or keeping jobs.

Diagnosis

Acne patients are often treated by family doctors. Complicated cases are referred to a dermatologist, a skin

disease specialist, or an endocrinologist, a specialist who treats diseases of the body's endocrine (hormones and glands) system.

Acne has a characteristic appearance and is not difficult to diagnose. The doctor takes a complete medical history, including questions about skin care, diet, factors causing flare-ups, medication use, and prior treatment. **Physical examination** includes the face, upper neck, chest, shoulders, back, and other affected areas. Under good lighting, the doctor determines what types and how many blemishes are present, whether they are inflamed, whether they are deep or superficial, and whether there is scarring or skin discoloration.

In teenagers, acne is often found on the forehead, nose, and chin. As people get older, acne tends to appear towards the outer part of the face. Adult women may have acne on their chins and around their mouths. The elderly may develop whiteheads and blackheads on the upper cheeks and skin around the eyes.

Laboratory tests are not done unless the patient appears to have a hormonal disorder or other medical problem. In this case, blood analyses or other tests may be ordered. Most insurance plans cover the costs of diagnosing and treating acne.

Treatment

Acne treatment consists of reducing sebum production, removing dead skin cells, and killing bacteria with topical drugs and oral medications. Treatment choice depends upon whether the acne is mild, moderate, or severe.

Drugs

TOPICAL DRUGS. Treatment for mild noninflammatory acne consists of reducing the formation of new comedones with topical tretinoin, benzoyl peroxide, adapalene, or salicylic acid. Tretinoin is especially effective because it increases turnover (**death** and replacement) of skin cells. When complicated by inflammation, topical antibiotics may be added to the treatment regimen. Improvement is usually seen in two to four weeks.

Topical medications are available as cream, gel, lotion, or pad preparations of varying strengths. They include antibiotics (agents that kill bacteria), such as erythromycin, clindamycin (Cleocin-T), and mecloxycline (Meclan); comedolytics (agents that loosen hard plugs and open pores) such as the vitamin A acid tretinoin (Retin-A), salicylic acid, adapalene (Differin), resorcinol, and sulfur. Drugs that act as both comedolytics and antibiotics, such as benzoyl peroxide, azelaic acid (Azelex), or benzoyl peroxide plus erythromycin (Benza-



Acne vulgaris affecting a woman's face. Acne is the general name given to a skin disorder in which the sebaceous glands become inflamed. (Photograph by Biophoto Associates, Photo Researchers, Inc. Reproduced by permission.)

mycin), are also used. These drugs may be used for months to years to achieve disease control.

After washing with mild soap, the drugs are applied alone or in combination, once or twice a day over the entire affected area of skin. Possible side effects include mild redness, peeling, irritation, dryness, and an increased sensitivity to sunlight that requires use of a sunscreen.

ORAL DRUGS. Oral antibiotics are taken daily for two to four months. The drugs used include tetracycline, erythromycin, minocycline (Minocin), doxycycline, clindamycin (Cleocin), and trimethoprim-sulfamethoxazole (Bactrim, Septra). Possible side effects include allergic reactions, stomach upset, vaginal yeast infections, **dizziness**, and tooth discoloration.

The goal of treating moderate acne is to decrease inflammation and prevent new comedone formation. One effective treatment is topical tretinoin along with a topical

KEY TERMS

Androgens—Male sex hormones that are linked with the development of acne.

Antiandrogens—Drugs that inhibit the production of androgens.

Antibiotics—Medicines that kill bacteria.

Comedo—A hard plug composed of sebum and dead skin cells. The mildest type of acne.

Comedolytic—Drugs that break up comedones and open clogged pores.

Corticosteroids—A group of hormones produced by the adrenal glands with different functions, including regulation of fluid balance, androgen activity, and reaction to inflammation.

Estrogens—Hormones produced by the ovaries, the female sex glands.

Isotretinoin—A drug that decreases sebum production and dries up acne pimples.

Sebaceous follicles—A structure found within the skin that houses the oil-producing glands and hair follicles, where pimples form.

Sebum—An oily skin moisturizer produced by sebaceous glands.

Tretinoin—A drug that works by increasing the turnover (death and replacement) of skin cells.

or oral antibiotic. A combination of topical benzoyl peroxide and erythromycin is also very effective. Improvement is normally seen within four to six weeks, but treatment is maintained for at least two to four months.

A drug reserved for the treatment of severe acne, oral isotretinoin (Accutane), reduces sebum production and cell stickiness. It is the treatment of choice for severe acne with cysts and nodules, and is used with or without topical or oral antibiotics. Taken for four to five months, it provides long-term disease control in up to 60% of patients. If the acne reappears, another course of isotretinoin may be needed by about 20% of patients, while another 20% may do well with topical drugs or oral antibiotics. Side effects include temporary worsening of the acne, dry skin, nosebleeds, vision disorders, and elevated liver enzymes, blood fats and cholesterol. This drug must not be taken during pregnancy since it causes **birth defects**.

Anti-androgens, drugs that inhibit androgen production, are used to treat women who are unresponsive to other therapies. Certain types of oral contraceptives (for

example, Ortho-Tri-Cyclen) and female sex hormones (estrogens) reduce hormone activity in the ovaries. Other drugs, for example, spironolactone and **corticosteroids**, reduce hormone activity in the adrenal glands. Improvement may take up to four months.

Oral corticosteroids, or anti-inflammatory drugs, are the treatment of choice for an extremely severe, but rare type of destructive inflammatory acne called acne fulminans, found mostly in adolescent males. Acne conglobata, a more common form of severe inflammation, is characterized by numerous, deep, inflammatory nodules that heal with scarring. It is treated with oral isotretinoin and corticosteroids.

Other treatments

Several surgical or medical treatments are available to alleviate acne or the resulting scars:

- Comedone extraction. The comedo is removed from the pore with a special tool.
- Chemical peels. Glycolic acid is applied to peel off the top layer of skin to reduce scarring.
- Dermabrasion. The affected skin is frozen with a chemical spray, and removed by brushing or planing.
- Punch grafting. Deep scars are excised and the area repaired with small skin grafts.
- Intralesional injection. Corticosteroids are injected directly into inflamed pimples.
- Collagen injection. Shallow scars are elevated by collagen (protein) injections.

Alternative treatment

Alternative treatments for acne focus on proper cleansing to keep the skin oil-free; eating a well-balanced diet high in fiber, zinc, and raw foods; and avoiding alcohol, dairy products, **smoking**, **caffeine**, sugar, processed foods, and foods high in iodine, such as salt. Supplementation with herbs such as burdock root (*Arctium lappa*), red clover (*Trifolium pratense*), and milk thistle (*Silybum marianum*), and with nutrients such as essential fatty acids, vitamin B complex, zinc, vitamin A, and chromium is also recommended. Chinese herbal remedies used for acne include cnidium seed (*Cnidium monnieri*) and honeysuckle flower (*Lonicera japonica*). Wholistic physicians or nutritionists can recommend the proper amounts of these herbs.

Prognosis

Acne is not curable, although long-term control is achieved in up to 60% of patients treated with

isotretinoin. It can be controlled by proper treatment, with improvement taking two or more months. Acne tends to reappear when treatment stops, but spontaneously improves over time. Inflammatory acne may leave scars that require further treatment.

Prevention

There are no sure ways to prevent acne, but the following steps may be taken to minimize flare-ups:

- gentle washing of affected areas once or twice every day
- avoid abrasive cleansers
- use noncomedogenic makeup and moisturizers
- shampoo often and wear hair off face
- eat a well-balanced diet, avoiding foods that trigger flare-ups
- unless told otherwise, give dry pimples a limited amount of sun exposure
- do not pick or squeeze blemishes
- reduce stress

Resources

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American Academy of Dermatology. 930 N. Meacham Road, P.O. Box 4014, Schaumburg, IL 60168-4014. (847) 330-0230. <<http://www.aad.org>>.

Mercedes McLaughlin

Acne rosacea see **Rosacea**

Acoustic neurinoma see **Acoustic neuroma**

Acoustic neuroma

Definition

An acoustic neuroma is a benign tumor involving cells of the myelin sheath that surrounds the vestibulocochlear nerve (eighth cranial nerve).

Description

The vestibulocochlear nerve extends from the inner ear to the brain and is made up of a vestibular branch, often called the vestibular nerve, and a cochlear branch, called the cochlear nerve. The vestibular and cochlear nerves lie next to one another. They also run along side other cranial nerves. People possess two of each type of vestibulocochlear nerve, one that extends from the left ear and one that extends from the right ear.

The vestibular nerve transmits information concerning balance from the inner ear to the brain and the cochlear nerve transmits information about hearing. The vestibular nerve, like many nerves, is surrounded by a cover called a myelin sheath. A tumor, called a schwannoma, can sometimes develop from the cells of the myelin sheath. A tumor is an abnormal growth of tissue that results from the uncontrolled growth of cells. Acoustic neuromas are often called vestibular schwannomas because they are tumors that arise from the myelin sheath that surrounds the vestibular nerve. Acoustic neuromas are considered benign (non-cancerous) tumors since they do not spread to other parts of the body. They can occur anywhere along the vestibular nerve but are most likely to occur where the vestibulocochlear nerve passes through the tiny bony canal that connects the brain and the inner ear.

An acoustic neuroma can arise from the left vestibular nerve or the right vestibular nerve. A unilateral tumor is a tumor arising from one nerve and a bilateral tumor arises from both vestibular nerves. Unilateral acoustic neuromas usually occur spontaneously (by chance). Bilateral acoustic neuromas occur as part of a hereditary con-

dition called **Neurofibromatosis Type 2 (NF2)**. A person with NF2 has inherited a predisposition for developing acoustic neuromas and other tumors of the nerve cells.

Acoustic neuromas usually grow slowly and can take years to develop. Some acoustic neuromas remain so small that they do not cause any symptoms. As the acoustic neuroma grows it can interfere with the functioning of the vestibular nerve and can cause vertigo and balance difficulties. If the acoustic nerve grows large enough to press against the cochlear nerve, then **hearing loss** and a ringing (**tinnitus**) in the affected ear will usually occur. If untreated and the acoustic neuroma continues to grow it can press against other nerves in the region and cause other symptoms. This tumor can be life threatening if it becomes large enough to press against and interfere with the functioning of the brain.

Causes and symptoms

Causes

An acoustic neuroma is caused by a change or absence of both of the NF2 tumor suppressor genes in a nerve cell. Every person possesses a pair of NF2 genes in every cell of their body including their nerve cells. One NF2 gene is inherited from the egg cell of the mother and one NF2 gene is inherited from the sperm cell of the father. The NF2 gene is responsible for helping to prevent the formation of tumors in the nerve cells. In particular the NF2 gene helps to prevent acoustic neuromas.

Only one unchanged and functioning NF2 gene is necessary to prevent the formation of an acoustic neuroma. If both NF2 genes become changed or missing in one of the myelin sheath cells of the vestibular nerve then an acoustic neuroma will usually develop. Most unilateral acoustic neuromas result when the NF2 genes become spontaneously changed or missing. Someone with a unilateral acoustic neuroma that has developed spontaneously is not at increased risk for having children with an acoustic neuroma. Some unilateral acoustic neuromas result from the hereditary condition NF2. It is also possible that some unilateral acoustic neuromas may be caused by changes in other genes responsible for preventing the formation of tumors.

Bilateral acoustic neuromas result when someone is affected with the hereditary condition NF2. A person with NF2 is typically born with one unchanged and one changed or missing NF2 gene in every cell of their body. Sometimes they inherit this change from their mother or father. Sometimes the change occurs spontaneously when the egg and sperm come together to form the first cell of the baby. The children of a person with NF2 have a 50% chance of inheriting the changed or missing NF2 gene.

A person with NF2 will develop an acoustic neuroma if the remaining unchanged NF2 gene becomes spontaneously changed or missing in one of the myelin sheath cells of their vestibular nerve. People with NF2 often develop acoustic neuromas at a younger age. The mean age of onset of acoustic neuroma in NF2 is 31 years of age versus 50 years of age for sporadic acoustic neuromas. Not all people with NF2, however, develop acoustic neuromas. People with NF2 are at increased risk for developing **cataracts** and tumors in other nerve cells.

Most people with a unilateral acoustic neuroma are not affected with NF2. Some people with NF2, however, only develop a tumor in one of the vestibulocochlear nerves. Others may initially be diagnosed with a unilateral tumor but may develop a tumor in the other nerve a number of years later. NF2 should be considered in someone under the age of 40 who has a unilateral acoustic neuroma. Someone with a unilateral acoustic neuroma and other family members diagnosed with NF2 probably is affected with NF2. Someone with a unilateral acoustic neuroma and other symptoms of NF2 such as cataracts and other tumors may also be affected with NF2. On the other hand, someone over the age of 50 with a unilateral acoustic neuroma, no other tumors and no family history of NF2 is very unlikely to be affected with NF2.

Symptoms

Small acoustic neuromas usually only interfere with the functioning of the vestibulocochlear nerve. The most common first symptom of an acoustic neuroma is hearing loss, which is often accompanied by a ringing sound (tinnitus). People with acoustic neuromas sometimes report difficulties in using the phone and difficulties in perceiving the tone of a musical instrument or sound even when their hearing appears to be otherwise normal. In most cases the hearing loss is initially subtle and worsens gradually over time until deafness occurs in the affected ear. In approximately 10% of cases the hearing loss is sudden and severe.

Acoustic neuromas can also affect the functioning of the vestibular branch of the vestibulocochlear nerve and can cause vertigo and dysequilibrium. Twenty percent of small tumors are associated with periodic vertigo, which is characterized by **dizziness** or a whirling sensation. Larger acoustic neuromas are less likely to cause vertigo but more likely to cause dysequilibrium. Dysequilibrium, which is characterized by minor clumsiness and a general feeling of instability, occurs in nearly 50% of people with an acoustic neuroma.

As the tumor grows larger it can press on the surrounding cranial nerves. Compression of the fifth cranial nerve can result in facial **pain** and/or numbness. Compression of the seventh cranial nerve can cause spasms, weakness or

KEY TERMS

Benign tumor—A localized overgrowth of cells that does not spread to other parts of the body.

Chromosome—A microscopic structure, made of a complex of proteins and DNA, that is found within each cell of the body.

Computed tomography (CT)—An examination that uses a computer to compile and analyze the images produced by x rays projected at a particular part of the body.

Cranial nerves—The set of twelve nerves found on each side of the head and neck that control the sensory and muscle functions of a number of organs such as the eyes, nose, tongue face and throat.

DNA testing—Testing for a change or changes in a gene or genes.

Gene—A building block of inheritance, made up of a compound called DNA (deoxyribonucleic acid) and containing the instructions for the production of a particular protein. Each gene is found on a specific location on a chromosome.

Magnetic resonance imaging (MRI)—A test which

uses an external magnetic field instead of x rays to visualize different tissues of the body.

Myelin sheath—The cover that surrounds many nerve cells and helps to increase the speed by which information travels along the nerve.

Neurofibromatosis type 2 (NF2)—A hereditary condition associated with an increased risk of bilateral acoustic neuromas, other nerve cell tumors and cataracts.

Protein—A substance produced by a gene that is involved in creating the traits of the human body such as hair and eye color or is involved in controlling the basic functions of the human body.

Schwannoma—A tumor derived from the cells of the myelin sheath that surrounds many nerve cells.

Tinnitus—A ringing sound or other noise in the ear.

Vertigo—A feeling of spinning or whirling.

Vestibulocochlear nerve (Eighth cranial nerve)—Nerve that transmits information, about hearing and balance from the ear to the brain.

paralysis of the facial muscles. Double vision is a rare symptom but can result when the 6th cranial nerve is affected. Swallowing and/or speaking difficulties can occur if the tumor presses against the 9th, 10th, or 12th cranial nerves.

If left untreated, the tumor can become large enough to press against and affect the functioning of the brain stem. The brain stem is the stalk like portion of the brain that joins the spinal cord to the cerebrum, the thinking and reasoning part of the brain. Different parts of the brain stem have different functions such as the control of breathing and muscle coordination. Large tumors that impact the brain stem can result in headaches, walking difficulties (gait ataxia) and involuntary shaking movements of the muscles (**tremors**). In rare cases when an acoustic neuroma remains undiagnosed and untreated it can cause nausea, vomiting, lethargy and eventually **coma**, respiratory difficulties and **death**. In the vast majority of cases, however, the tumor is discovered and treated long before it is large enough to cause such serious manifestations.

Diagnosis

Anyone with symptoms of hearing loss should undergo hearing evaluations. Pure tone and speech **audiometry**

are two screening tests that are often used to evaluate hearing. Pure tone audiometry tests to see how well someone can hear tones of different volume and pitch and speech audiometry tests to see how well someone can hear and recognize speech. An acoustic neuroma is suspected in someone with unilateral hearing loss or hearing loss that is less severe in one ear than the other ear(asymmetrical).

Sometimes an auditory brainstem response (ABR, BAER) test is performed to help establish whether someone is likely to have an acoustic neuroma. During the ABR examination, a harmless electrical impulse is passed from the inner ear to the brainstem. An acoustic neuroma can interfere with the passage of this electrical impulse and this interference can, sometimes be identified through the ABR evaluation. A normal ABR examination does not rule out the possibility of an acoustic neuroma. An abnormal ABR examination increases the likelihood that an acoustic neuroma is present but other tests are necessary to confirm the presence of a tumor.

If an acoustic neuroma is strongly suspected then **magnetic resonance imaging (MRI)** is usually performed. The MRI is a very accurate evaluation that is

able to detect nearly 100% of acoustic neuromas. Computerized tomography (CT scan, CAT scan) is unable to identify smaller tumors; but it can be used when an acoustic neuroma is suspected and an MRI evaluation cannot be performed.

Once an acoustic neuroma is diagnosed, an evaluation by genetic specialists such as a geneticist and genetic counselor may be recommended. The purpose of this evaluation is to obtain a detailed family history and check for signs of NF2. If NF2 is strongly suspected then DNA testing may be recommended. DNA testing involves checking the blood cells obtained from a routine blood draw for the common gene changes associated with NF2.

Treatment

The three treatment options for acoustic neuroma are surgery, radiation, and observation. The physician and patient should discuss the pros and cons of the different options prior to making a decision about treatment. The patient's, physical health, age, symptoms, tumor size, and tumor location should be considered.

Microsurgery

The surgical removal of the tumor or tumors is the most common treatment for acoustic neuroma. In most cases the entire tumor is removed during the surgery. If the tumor is large and causing significant symptoms, yet there is a need to preserve hearing in that ear, then only part of the tumor may be removed. During the procedure the tumor is removed under microscopic guidance and general anesthetic. Monitoring of the neighboring cranial nerves is done during the procedure so that damage to these nerves can be prevented. If preservation of hearing is a possibility, then monitoring of hearing will also take place during the surgery.

Most people stay in the hospital four to seven days following the surgery. Total recovery usually takes four to six weeks. Most people experience **fatigue** and head discomfort following the surgery. Problems with balance and head and neck stiffness are also common. The mortality rate of this type of surgery is less than 2% at most major centers. Approximately 20% of patients experience some degree of post-surgical complications. In most cases these complications can be managed successfully and do not result in long term medical problems. Surgery brings with it a risk of **stroke**, damage to the brain stem, infection, leakage of spinal fluid and damage to the cranial nerves. Hearing loss and/or tinnitus often result from the surgery. A follow-up MRI is recommended one to five years following the surgery because of possible regrowth of the tumor.

Stereotactic Radiation therapy

During stereotactic **radiation therapy**, also called radiosurgery or radiotherapy, many small beams of radiation are aimed directly at the acoustic neuroma. The radiation is administered in a single large dose, under local anesthetic and is performed on an outpatient basis. This results in a high dose of radiation to the tumor but little radiation exposure to the surrounding area. This treatment approach is limited to small or medium tumors. The goal of the surgery is to cause tumor shrinkage or at least limit the growth of the tumor. The long term efficacy and risks of this treatment approach are not known. Periodic MRI monitoring throughout the life of the patient is therefore recommended.

Radiation therapy can cause hearing loss which can sometimes occur even years later. Radiation therapy can also cause damage to neighboring cranial nerves, which can result in symptoms such as numbness, pain or paralysis of the facial muscles. In many cases these symptoms are temporary. Radiation treatment can also induce the formation of other benign or malignant schwannomas. This type of treatment may therefore be contraindicated in the treatment of acoustic neuromas in those with NF2 who are predisposed to developing schwannomas and other tumors.

Observation

Acoustic neuromas are usually slow growing and in some cases they will stop growing and even become smaller or disappear entirely. It may therefore be appropriate in some cases to hold off on treatment and to periodically monitor the tumor through MRI evaluations. Long-term observation may be appropriate for example in an elderly person with a small acoustic neuroma and few symptoms. Periodic observation may also be indicated for someone with a small and asymptomatic acoustic neuroma that was detected through an evaluation for another medical problem. Observation may also be suggested for someone with an acoustic neuroma in the only hearing ear or in the ear that has better hearing. The danger of an observational approach is that as the tumor grows larger it can become more difficult to treat.

Prognosis

The prognosis for someone with a unilateral acoustic neuroma is usually quite good provided the tumor is diagnosed early and appropriate treatment is instituted. Long term hearing loss and tinnitus in the affected ear are common, even if appropriate treatment is provided. Regrowth of the tumor is also a possibility following surgery or radiation therapy and repeat treatment may be necessary. The prognosis can be poorer for those with NF2 who have an increased risk of bilateral acoustic neuromas and other tumors.

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- Acoustic Neuroma Association of Canada Box 369, Edmonton, AB T5J 2J6. 1-800-561-ANAC(2622). (780)428-3384. anac@compusmart.ab.ca. <<http://www.anac.ca>>. 28 June 2001.
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Lisa Andres, M.S., CGC

Acquired hypogammaglobulinemia see
Common variable immunodeficiency

Acquired immunodeficiency syndrome see
AIDS

Acrocyanosis

Definition

Acrocyanosis is a decrease in the amount of oxygen delivered to the extremities. The hands and feet turn blue because of the lack of oxygen. Decreased blood supply to the affected areas is caused by constriction or spasm of small blood vessels.

Description

Acrocyanosis is a painless disorder caused by constriction or narrowing of small blood vessels in the skin of affected patients. The spasm of the blood vessels decreases the amount of blood that passes through them, resulting in less blood being delivered to the hands and feet. The hands may be the main area affected. The affected areas turn blue and become cold and sweaty. Localized swelling may also occur. Emotion and cold temperatures can worsen the symptoms, while warmth can decrease symptoms. The disease is seen mainly in women and the effect of the disorder is mainly cosmetic. People with the disease tend to be uncomfortable, with sweaty, cold, bluish colored hands and feet.

Causes and symptoms

The sympathetic nerves cause constriction or spasms in the peripheral blood vessels that supply blood to the extremities. The spasms are a contraction of the muscles in the walls of the blood vessels. The contraction decreases the internal diameter of the blood vessels, thereby decreasing the amount of blood flow through the affected area. The spasms occur on a persistent basis, resulting in long term reduction of blood supply to the hands and feet. Sufficient blood still passes through the blood vessels so that the tissue in the affected areas does not starve for oxygen or die. Mainly, blood vessels near the surface of the skin are affected.

Diagnosis

Diagnosis is made by observation of the main clinical symptoms, including persistently blue and sweaty hands and/or feet and a lack of pain. Cooling the hands increases the blueness, while warming the hands decreases it.

KEY TERMS

Sympathetic nerve—A nerve of the autonomic nervous system that regulates involuntary and automatic reactions, especially to stress.

es the blue color. The acrocyanosis patient's pulse is normal, which rules out obstructive diseases. **Raynaud's disease** differs from acrocyanosis in that it causes white and red skin coloration phases, not just bluish discoloration.

Treatment

Acrocyanosis usually isn't treated. Drugs that block the uptake of calcium (**calcium channel blockers**) and alpha-one antagonists reduce the symptoms in most cases. Drugs that dilate blood vessels are only effective some of the time. Sweating from the affected areas can be profuse and require treatment. Surgery to cut the sympathetic nerves is performed rarely.

Prognosis

Acrocyanosis is a benign and persistent disease. The main concern of patients is cosmetic. Left untreated, the disease does not worsen.

Resources

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John T. Lohr, PhD

Acromegaly and gigantism

Definition

Acromegaly is a disorder in which the abnormal release of a particular chemical from the pituitary gland in the brain causes increased growth in bone and soft tissue, as well as a variety of other disturbances throughout the body. This chemical released from the pituitary gland is called growth hormone (GH). The body's ability to

process and use nutrients like fats and sugars is also altered. In children whose bony growth plates have not closed, the chemical changes of acromegaly result in exceptional growth of long bones. This variant is called gigantism, with the additional bone growth causing unusual height. When the abnormality occurs after bone growth stops, the disorder is called acromegaly.

Description

Acromegaly is a relatively rare disorder, occurring in approximately 50 out of every one million people (50/1,000,000). Both men and women are affected. Because the symptoms of acromegaly occur so gradually, diagnosis is often delayed. The majority of patients are not identified until they are middle aged.

Causes and symptoms

The pituitary is a small gland located at the base of the brain. A gland is a collection of cells that releases certain chemicals, or hormones, which are important to the functioning of other organs or body systems. The pituitary hormones travel throughout the body and are involved in a large number of activities, including the regulation of growth and reproductive functions. The cause of acromegaly can be traced to the pituitary's production of GH.

Under normal conditions, the pituitary receives input from another brain structure, the hypothalamus, located at the base of the brain. This input from the hypothalamus regulates the pituitary's release of hormones. For example, the hypothalamus produces growth hormone-releasing hormone (GHRH), which directs the pituitary to release GH. Input from the hypothalamus should also direct the pituitary to stop releasing hormones.

In acromegaly, the pituitary continues to release GH and ignores signals from the hypothalamus. In the liver, GH causes production of a hormone called insulin-like growth factor 1 (IGF-1), which is responsible for growth throughout the body. When the pituitary refuses to stop producing GH, the levels of IGF-1 also reach abnormal peaks. Bones, soft tissue, and organs throughout the body begin to enlarge, and the body changes its ability to process and use nutrients like sugars and fats.

In acromegaly, an individual's hands and feet begin to grow, becoming thick and doughy. The jaw line, nose, and forehead also grow, and facial features are described as "coarsening". The tongue grows larger, and because the jaw is larger, the teeth become more widely spaced. Due to swelling within the structures of the throat and sinuses, the voice becomes deeper and sounds more hollow, and patients may develop loud **snoring**. Various hormonal changes cause symptoms such as:

- heavy sweating
- oily skin
- increased coarse body hair
- improper processing of sugars in the diet (and sometimes actual diabetes)
- high blood pressure
- increased calcium in the urine (sometimes leading to kidney stones)
- increased risk of **gallstones**; and
- swelling of the thyroid gland

People with acromegaly have more skin tags, or outgrowths of tissue, than normal. This increase in skin tags is also associated with the development of growths, called polyps, within the large intestine that may eventually become cancerous. Patients with acromegaly often suffer from headaches and arthritis. The various swellings and enlargements throughout the body may press on nerves, causing sensations of local tingling or burning, and sometimes result in muscle weakness.

The most common cause of this disorder (in 90% of patients) is the development of a noncancerous tumor within the pituitary, called a pituitary adenoma. These tumors are the source of the abnormal release of GH. As these tumors grow, they may press on nearby structures within the brain, causing headaches and changes in vision. As the adenoma grows, it may disrupt other pituitary tissue, interfering with the release of other hormones. These disruptions may be responsible for changes in the menstrual cycle of women, decreases in the sexual drive in men and women, and the abnormal production of breast milk in women. In rare cases, acromegaly is caused by the abnormal production of GHRH, which leads to the increased production of GH. Certain tumors in the pancreas, lungs, adrenal glands, thyroid, and intestine produce GHRH, which in turn triggers production of an abnormal quantity of GH.

Diagnosis

Because acromegaly produces slow changes over time, diagnosis is often significantly delayed. In fact, the characteristic coarsening of the facial features is often not recognized by family members, friends, or long-time family physicians. Often, the diagnosis is suspected by a new physician who sees the patient for the first time and is struck by the patient's characteristic facial appearance. Comparing old photographs from a number of different time periods will often increase suspicion of the disease.

Because the quantity of GH produced varies widely under normal conditions, demonstrating high levels of GH in the blood is not sufficient to merit a diagnosis of acromegaly. Instead, laboratory tests measuring an



Enlarged feet is one deformity caused by acromegaly. (*Custom Medical Stock Photo. Reproduced by permission.*)

increase of IGF-1 (3-10 times above the normal level) are useful. These results, however, must be carefully interpreted because normal laboratory values for IGF-1 vary when the patient is pregnant, undergoing **puberty**, elderly, or severely malnourished. Normal patients will show a decrease in GH production when given a large dose of sugar (glucose). Patients with acromegaly will not show this decrease, and will often show an increase in GH production. **Magnetic resonance imaging** (MRI) is useful for viewing the pituitary, and for identifying and locating an adenoma. When no adenoma can be located, the search for a GHRH-producing tumor in another location begins.

Treatment

The first step in treatment of acromegaly is removal of all or part of the pituitary adenoma. Removal requires surgery, usually performed by entering the skull through the nose. While this surgery can cause rapid improvement of many acromegaly symptoms, most patients will also



A comparison of the right hand of a person afflicted with acromegaly (left) and the hand of a normal sized person. (Custom Medical Stock Photo. Reproduced by permission.)

require additional treatment with medication. Bromocriptine (Parlodel) is a medication that can be taken by mouth, while octreotide (Sandostatin) must be injected every eight hours. Both of these medications are helpful in reducing GH production, but must often be taken for life and produce their own unique side effects. Some patients who cannot undergo surgery are treated with **radiation therapy** to the pituitary in an attempt to shrink the adenoma. Radiating the pituitary may take up to 10 years, however, and may also injure/destroy other normal parts of the pituitary.

Prognosis

Without treatment, patients with acromegaly will most likely die early because of the disease's effects on the heart, lungs, brain, or due to the development of **cancer** in the large intestine. With treatment, however, a patient with acromegaly may be able to live a normal lifespan.

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KEY TERMS

Adenoma—A type of noncancerous (benign) tumor that often involves the overgrowth of certain cells found in glands.

Gland—A collection of cells that releases certain chemicals, or hormones, that are important to the functioning of other organs or body systems.

Hormone—A chemical produced in one part of the body that travels to another part of the body in order to exert an effect.

Hypothalamus—A structure within the brain responsible for a large number of normal functions throughout the body, including regulating sleep, temperature, eating, and sexual development. The hypothalamus also regulates the functions of the pituitary gland by directing the pituitary to stop or start production of its hormones.

Pituitary—A gland located at the base of the brain that produces a number of hormones, including those that regulate growth and reproductive functions. Overproduction of the pituitary hormone called growth hormone (GH) is responsible for the condition known as acromegaly.

ORGANIZATIONS

Pituitary Tumor Network Association. 16350 Ventura Blvd., #231, Encino, CA 91436. (805) 499-9973.

Rosalyn Carson-DeWitt, MD

ACT see **Alanine aminotransferase test**

ACTH test see **Adrenocorticotrophic hormone test**

Actinomyces israelii infection see
Actinomycosis

Actinomycosis

Definition

Actinomycosis is an infection primarily caused by the bacterium *Actinomyces israelii*. Infection most often occurs in the face and neck region and is characterized by the presence of a slowly enlarging, hard, red lump.

Description

Actinomycosis is a relatively rare infection occurring in one out of 300,000(1/300,000) people per year. It is characterized by the presence of a lump or mass that often forms, draining sinus tracts to the skin surface. Fifty percent of actinomycosis cases are of the head and neck region (also called “lumpy jaw” and “cervicofacial actinomycosis”), 15% are in the chest, 20% are in the abdomen, and the rest are in the pelvis, heart, and brain. Men are three times more likely to develop actinomycosis than women.

Causes and symptoms

Actinomycosis is usually caused by the bacterium *Actinomyces israelii*. This bacterium is normally present in the mouth but can cause disease if it enters tissues following an injury. *Actinomyces israelii* is an anaerobic bacterium which means it dislikes oxygen but grows very well in deep tissues where oxygen levels are low. **Tooth extraction**, tooth disease, **root canal treatment**, jaw surgery, or poor dental hygiene can allow *Actinomyces israelii* to cause an infection in the head and neck region.

The main symptom of cervicofacial actinomycosis is the presence of a hard lump on the face or neck. The lump may or may not be red. **Fever** occurs in some cases.

Diagnosis

Cervicofacial actinomycosis can be diagnosed by a family doctor or dentist and the patient may be referred to an oral surgeon or infectious disease specialist. The diagnosis of actinomycosis is based upon several things. The presence of a red lump with draining sinuses on the head or neck is strongly suggestive of cervicofacial actinomycosis. A recent history of tooth extraction or signs of **tooth decay** or poor dental hygiene aid in the diagnosis. Microscopic examination of the fluid draining from the sinuses shows the characteristic “sulfur granules” (small yellow colored material in the fluid) produced by *Actinomyces israelii*. A biopsy may be performed to remove a sample of the infected tissue. This procedure can be performed under local anesthesia in the doctor’s office. Occasionally the bacteria can be cultured from the sinus tract fluid or from samples of the infected tissue.

Actinomycosis in the lungs, abdomen, pelvis, or brain can be very hard to diagnose since the symptoms often mimic those of other diseases. Actinomycosis of the lungs or abdomen can resemble **tuberculosis** or **cancer**. x-ray results, the presence of draining sinus tracts, and microscopic analysis and culturing of infected tissue assist in the diagnosis.

Treatment

Actinomycosis is difficult to treat because of its dense tissue location. Surgery is often required to drain

KEY TERMS

Biopsy—The process which removes a sample of tissue for microscopic examination to aid in the diagnosis of a disease.

Sinus tract—A narrow, elongated channel in the body which allows the escape of fluid.

the lesion and/or to remove the site of infection. To kill the bacteria, large doses of penicillin are given through a vein daily for two to six weeks followed by six to twelve months of penicillin taken by mouth. Tetracycline, clindamycin, or erythromycin may be used instead of penicillin. The antibiotic therapy must be completed to insure that the infection does not return. Hyperbaric oxygen (oxygen under high pressure) therapy in combination with the antibiotic therapy has been successful.

Prognosis

Complete recovery is achieved following treatment. If left untreated, the infection may cause localized bone destruction.

Prevention

The best prevention is to maintain good dental hygiene.

Resources

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Belinda Rowland, PhD

Activated charcoal see **Charcoal, activated**

Activated partial thromboplastin time see
Partial thromboplastin time

Acupressure

Definition

Acupressure is a form of touch therapy that utilizes the principles of **acupuncture** and Chinese medicine. In acupressure, the same points on the body are used as in acupuncture, but are stimulated with finger pressure



Therapist working acupressure points on a woman's shoulder. (Photo Researchers, Inc. Reproduced by permission.)

instead of with the insertion of needles. Acupressure is used to relieve a variety of symptoms and **pain**.

Purpose

Acupressure massage performed by a therapist can be very effective both as prevention and as a treatment for many health conditions, including headaches, general aches and pains, colds and flu, arthritis, **allergies**, **asthma**, nervous tension, menstrual cramps, sinus problems, sprains, **tennis elbow**, and toothaches, among others. Unlike acupuncture which requires a visit to a professional, acupressure can be performed by a layperson. Acupressure techniques are fairly easy to learn, and have been used to provide quick, cost-free, and effective relief from many symptoms. Acupressure points can also be stimulated to increase energy and feelings of well-being, reduce **stress**, stimulate the immune system, and alleviate **sexual dysfunction**.

Description

Origins

One of the oldest text of Chinese medicine is the *Huang Di, The Yellow Emperor's Classic of Internal*

Medicine

, which may be at least 2,000 years old. Chinese medicine has developed acupuncture, acupressure, herbal remedies, diet, **exercise**, lifestyle changes, and other remedies as part of its healing methods. Nearly all of the forms of Oriental medicine that are used in the West today, including acupuncture, acupressure, **shiatsu**, and Chinese herbal medicine, have their roots in Chinese medicine. One legend has it that acupuncture and acupressure evolved as early Chinese healers studied the puncture **wounds** of Chinese warriors, noting that certain points on the body created interesting results when stimulated. The oldest known text specifically on acupuncture points, the *Systematic Classic of Acupuncture*, dates back to 282 A.D. Acupressure is the non-invasive form of acupuncture, as Chinese physicians determined that stimulating points on the body with massage and pressure could be effective for treating certain problems.

Outside of Asian-American communities, Chinese medicine remained virtually unknown in the United States until the 1970s, when Richard Nixon became the first U.S. president to visit China. On Nixon's trip, journalists were amazed to observe major operations being performed on patients without the use of anesthetics. Instead, wide-awake patients were being operated on,

with only acupuncture needles inserted into them to control pain. At that time, a famous columnist for the *New York Times*, James Reston, had to undergo surgery and elected to use acupuncture for anesthesia. Later, he wrote some convincing stories on its effectiveness. Despite being neglected by mainstream medicine and the American Medical Association (AMA), acupuncture and Chinese medicine became a central to alternative medicine practitioners in the United States. Today, there are millions of patients who attest to its effectiveness, and nearly 9,000 practitioners in all 50 states.

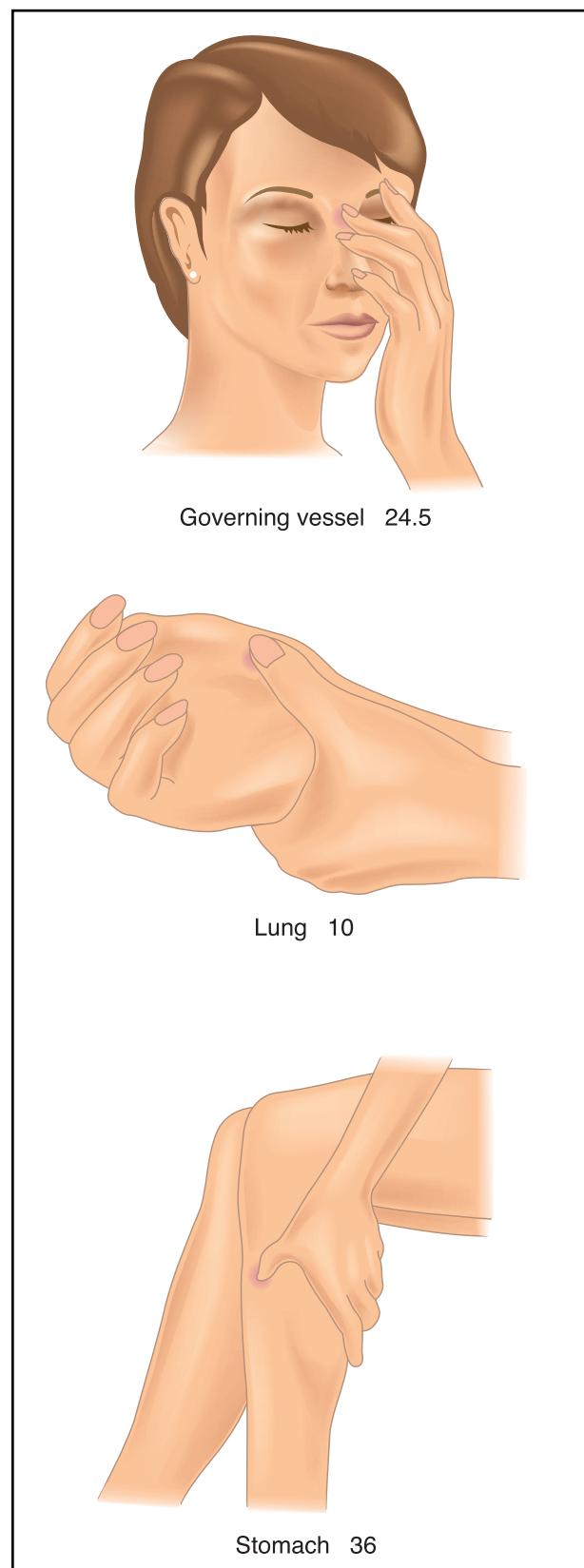
Acupressure is practiced as a treatment by Chinese medicine practitioners and acupuncturists, as well as by massage therapists. Most massage schools in America include acupressure techniques as part of their bodywork programs. Shiatsu massage is very closely related to acupressure, working with the same points on the body and the same general principles, although it was developed over centuries in Japan rather than in China. **Reflexology** is a form of bodywork based on acupressure concepts. Jin Shin Do is a bodywork technique with an increasing number of practitioners in America that combines acupressure and shiatsu principles with **qigong**, Reichian theory, and **meditation**.

Acupressure and Chinese medicine

Chinese medicine views the body as a small part of the universe, subject to laws and principles of harmony and balance. Chinese medicine does not make as sharp a distinction as Western medicine does between mind and body. The Chinese system believes that emotions and mental states are every bit as influential on disease as purely physical mechanisms, and considers factors like work, environment, and relationships as fundamental to a patient's health. Chinese medicine also uses very different symbols and ideas to discuss the body and health. While Western medicine typically describes health as mainly physical processes composed of chemical equations and reactions, the Chinese use ideas like yin and yang, chi, and the organ system to describe health and the body.

Everything in the universe has properties of yin and yang. Yin is associated with cold, female, passive, downward, inward, dark, wet. Yang can be described as hot, male, active, upward, outward, light, dry, and so on. Nothing is either completely yin or yang. These two principles always interact and affect each other, although the body and its organs can become imbalanced by having either too much or too little of either.

Chi (pronounced *chee*, also spelled *qi* or *ki* in Japanese shiatsu) is the fundamental life energy. It is found in food, air, water, and sunlight, and it travels through the body in channels called *meridians*. There are 12 major



Acupressure points to relieve hay fever, sore throat, and heartburn. (Illustration by Electronic Illustrators Group.)

KEY TERMS

Acupoint—A pressure point stimulated in acupressure.

Chi—Basic life energy.

Meridian—A channel through which chi travels in the body.

Moxibustion—An acupuncture technique that burns the herb moxa or mugwort.

Shiatsu—Japanese form of acupressure massage.

Yin/yang—Universal characteristics used to describe aspects of the natural world.

meridians in the body that transport chi, corresponding to the 12 main organs categorized by Chinese medicine.

Disease is viewed as an imbalance of the organs and chi in the body. Chinese medicine has developed intricate systems of how organs are related to physical and mental symptoms, and it has devised corresponding treatments using the meridian and pressure point networks that are classified and numbered. The goal of acupressure, and acupuncture, is to stimulate and unblock the circulation of chi, by activating very specific points, called pressure points or *acupoints*. Acupressure seeks to stimulate the points on the chi meridians that pass close to the skin, as these are easiest to unblock and manipulate with finger pressure.

Acupressure can be used as part of a Chinese physician's prescription, as a session of **massage therapy**, or as a self-treatment for common aches and illnesses. A Chinese medicine practitioner examines a patient very thoroughly, looking at physical, mental and emotional activity, taking the pulse usually at the wrists, examining the tongue and complexion, and observing the patient's demeanor and attitude, to get a complete diagnosis of which organs and meridian points are out of balance. When the imbalance is located, the physician will recommend specific pressure points for acupuncture or acupressure. If acupressure is recommended, the patient might opt for a series of treatments from a massage therapist.

In massage therapy, acupressurists will evaluate a patient's symptoms and overall health, but a massage therapist's diagnostic training isn't as extensive as a Chinese physician's. In a massage therapy treatment, a person usually lies down on a table or mat, with thin clothing on. The acupressurist will gently feel and palpate the abdomen and other parts of the body to deter-

mine energy imbalances. Then, the therapist will work with different meridians throughout the body, depending on which organs are imbalanced in the abdomen. The therapist will use different types of finger movements and pressure on different acupoints, depending on whether the chi needs to be increased or dispersed at different points. The therapist observes and guides the energy flow through the patient's body throughout the session. Sometimes, special herbs (*Artemesia vulgaris* or moxa) may be placed on a point to warm it, a process called *moxibustion*. A session of acupressure is generally a very pleasant experience, and some people experience great benefit immediately. For more chronic conditions, several sessions may be necessary to relieve and improve conditions.

Acupressure massage usually costs from \$30–70 per hour session. A visit to a Chinese medicine physician or acupuncturist can be more expensive, comparable to a visit to an allopathic physician if the practitioner is an MD. Insurance reimbursement varies widely, and consumers should be aware if their policies cover alternative treatment, acupuncture, or massage therapy.

Self-treatment

Acupressure is easy to learn, and there are many good books that illustrate the position of acupoints and meridians on the body. It is also very versatile, as it can be done anywhere, and it's a good form of treatment for spouses and partners to give to each other and for parents to perform on children for minor conditions.

While giving self-treatment or performing acupressure on another, a mental attitude of calmness and attention is important, as one person's energy can be used to help another's. Loose, thin clothing is recommended. There are three general techniques for stimulating a pressure point.

- Tonifying is meant to strengthen weak chi, and is done by pressing the thumb or finger into an acupoint with a firm, steady pressure, holding it for up to two minutes.
- Dispersing is meant to move stagnant or blocked chi, and the finger or thumb is moved in a circular motion or slightly in and out of the point for two minutes.
- Calming the chi in a pressure point utilizes the palm to cover the point and gently stroke the area for about two minutes.

There are many pressure points that are easily found and memorized to treat common ailments from headaches to colds.

- For headaches, toothaches, sinus problems, and pain in the upper body, the "LI4" point is recommended. It is located in the web between the thumb and index finger, on the back of the hand. Using the thumb and index finger of the other hand, apply a pinching pressure until

the point is felt, and hold it for two minutes. Pregnant women should never press this point.

- To calm the nerves and stimulate digestion, find the “CV12” point that is four thumb widths above the navel in the center of the abdomen. Calm the point with the palm, using gentle stroking for several minutes.
- To stimulate the immune system, find the “TH5” point on the back of the forearm two thumb widths above the wrist. Use a dispersing technique, or circular pressure with the thumb or finger, for two minutes on each arm.
- For headaches, sinus congestion, and tension, locate the “GB20” points at the base of the skull in the back of the head, just behind the bones in back of the ears. Disperse these points for two minutes with the fingers or thumbs. Also find the “yintang” point, which is in the middle of the forehead between the eyebrows. Disperse it with gentle pressure for two minutes to clear the mind and to relieve headaches.

Precautions

Acupressure is a safe technique, but it is not meant to replace professional health care. A physician should always be consulted when there are doubts about medical conditions. If a condition is chronic, a professional should be consulted; purely symptomatic treatment can exacerbate chronic conditions. Acupressure should not be applied to open wounds, or where there is swelling and inflammation. Areas of scar tissue, blisters, **boils**, **rashes**, or **varicose veins** should be avoided. Finally, certain acupressure points should not be stimulated on people with high or low blood pressure and on pregnant women.

Research and general acceptance

In general, Chinese medicine has been slow to gain acceptance in the West, mainly because it rests on ideas very foreign to the scientific model. For instance, Western scientists have trouble with the idea of chi, the invisible energy of the body, and the idea that pressing on certain points can alleviate certain conditions seems sometimes too simple for scientists to believe.

Western scientists, in trying to account for the action of acupressure, have theorized that chi is actually part of the neuroendocrine system of the body. Celebrated orthopedic surgeon Robert O. Becker, who was twice nominated for the Nobel Prize, wrote a book on the subject called *Cross Currents: The Promise of Electromedicine; The Perils of Electropollution*. By using precise electrical measuring devices, Becker and his colleagues showed that the body has a complex web of electromagnetic energy, and that traditional acupressure meridians and points contained amounts of energy that non-acupressure points did not.

The mechanisms of acupuncture and acupressure remain difficult to document in terms of the biochemical processes involved; numerous testimonials are the primary evidence backing up the effectiveness of acupressure and acupuncture. However, a body of research is growing that verifies the effectiveness in acupressure and acupuncture techniques in treating many problems and in controlling pain.

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Acupressure, foot see **Reflexology**

Acupuncture

Definition

Acupuncture is one of the main forms of treatment in **traditional Chinese medicine**. It involves the use of sharp, thin needles that are inserted in the body at very specific points. This process is believed to adjust and alter the body's energy flow into healthier patterns, and is used to treat a wide variety of illnesses and health conditions.

Purpose

The World Health Organization (WHO) recommends acupuncture as an effective treatment for over forty medical problems, including **allergies**, respiratory conditions, gastrointestinal disorders, gynecological problems, nervous conditions, and disorders of the eyes, nose and throat, and childhood illnesses, among others. Acupuncture has been used in the treatment of **alcoholism** and substance abuse. It is an effective and low-cost treatment



Woman undergoing facial acupuncture. (Photograph by Yoav Levy. Phototake NYC. Reproduced by permission.)

for headaches and chronic **pain**, associated with problems like back injuries and arthritis. It has also been used to supplement invasive Western treatments like **chemotherapy** and surgery. Acupuncture is generally most effective when used as prevention or before a health condition becomes acute, but it has been used to help patients suffering from **cancer** and **AIDS**. Acupuncture is limited in treating conditions or traumas that require surgery or emergency care (such as for broken bones).

Description

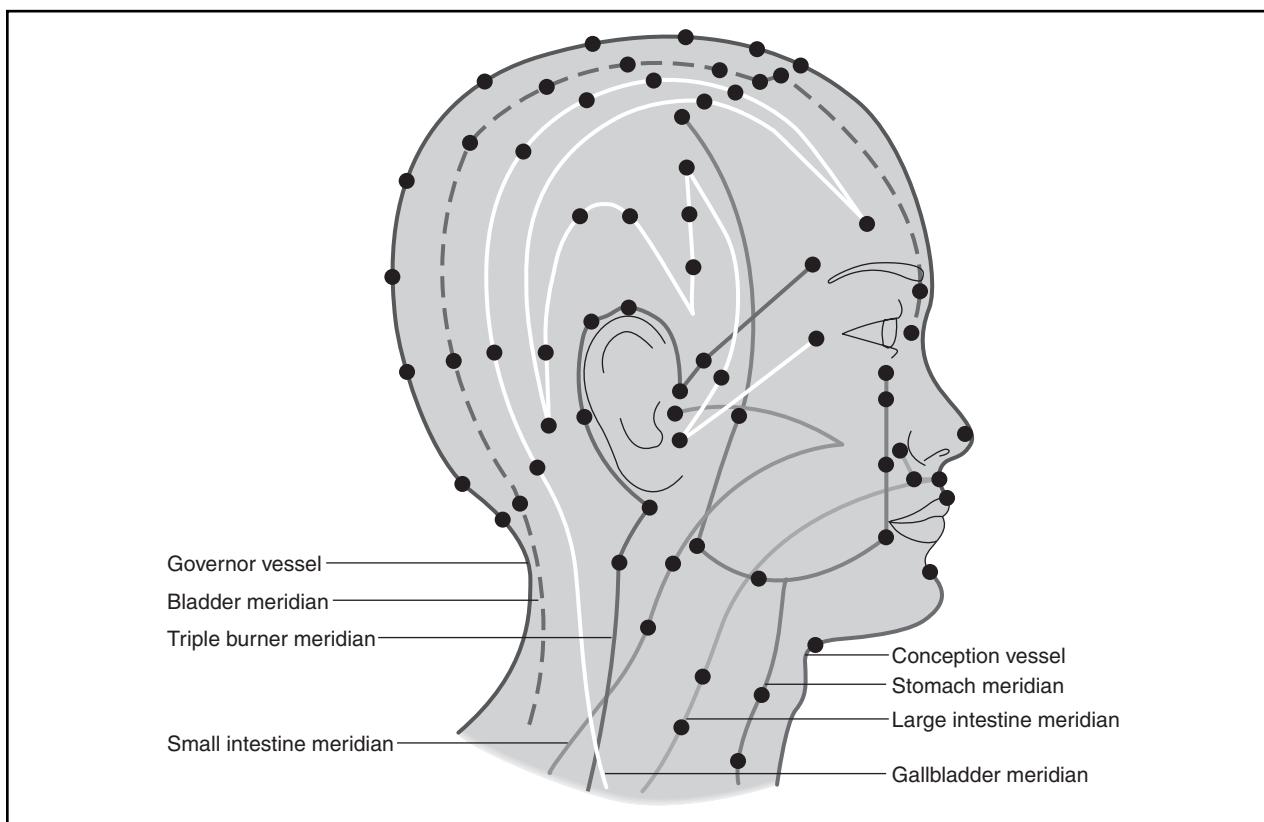
Origins

The original text of Chinese medicine is the *Nei Ching, The Yellow Emperor's Classic of Internal Medicine*, which is estimated to be at least 2,500 years old. Thousands of books since then have been written on the subject of Chinese healing, and its basic philosophies spread long ago to other Asian civilizations. Nearly all of the forms of Oriental medicine which are used in the West today, including acupuncture, **shiatsu**, **acupressure** massage, and macrobiotics, are part of or have their roots in Chinese medicine. Legend has it that acupuncture developed when early Chinese physicians observed unpredict-

ed effects of puncture **wounds** in Chinese warriors. The oldest known text on acupuncture, the *Systematic Classic of Acupuncture*, dates back to 282 A.D. Although acupuncture is its best known technique, Chinese medicine traditionally utilizes herbal remedies, dietary therapy, lifestyle changes and other means to treat patients.

In the early 1900s, only a few Western physicians who had visited China were fascinated by acupuncture, but outside of Asian-American communities it remained virtually unknown until the 1970s, when Richard Nixon became the first U.S. president to visit China. On Nixon's trip, journalists were amazed to observe major operations being performed on patients without the use of anesthetics. Instead, wide-awake patients were being operated on with only acupuncture needles inserted into them to control pain. During that time, a famous columnist for the *New York Times*, James Reston, had to undergo surgery and elected to use acupuncture instead of pain medication, and he wrote some convincing stories on its effectiveness.

Today acupuncture is being practiced in all 50 states by over 9,000 practitioners, with over 4,000 MDs including it in their practices. Acupuncture has shown notable success in treating many conditions, and over 15 million Americans have used it as a therapy. Acupuncture, how-



Acupuncture sites and meridians on the face and neck. (Illustration by Hans & Cassady.)

ever, remains largely unsupported by the medical establishment. The American Medical Association has been resistant to researching it, as it is based on concepts very different from the Western scientific model.

Several forms of acupuncture are being used today in America. Japanese acupuncture uses extremely thin needles and does not incorporate herbal medicine in its practice. Auricular acupuncture uses acupuncture points only on the ear, which are believed to stimulate and balance internal organs. In France, where acupuncture is very popular and more accepted by the medical establishment, neurologist Paul Nogier developed a system of acupuncture based on neuroendocrine theory rather than on traditional Chinese concepts, which is gaining some use in America.

Basic ideas of Chinese medicine

Chinese medicine views the body as a small part of the universe, and subject to universal laws and principles of harmony and balance. Chinese medicine does not draw a sharp line, as Western medicine does, between mind and body. The Chinese system believes that emotions and mental states are every bit as influential on disease as purely physical mechanisms, and considers fac-

tors like work, environment, lifestyle and relationships as fundamental to the overall picture of a patient's health. Chinese medicine also uses very different symbols and ideas to discuss the body and health. While Western medicine typically describes health in terms of measurable physical processes made up of chemical reactions, the Chinese use ideas like yin and yang, chi, the organ system, and the five elements to describe health and the body. To understand the ideas behind acupuncture, it is worthwhile to introduce some of these basic terms.

YIN AND YANG. According to Chinese philosophy, the universe and the body can be described by two separate but complementary principles, that of yin and yang. For example, in temperature, yin is cold and yang is hot. In gender, yin is female and yang is male. In activity, yin is passive and yang is active. In light, yin is dark and yang is bright; in direction yin is inward and downward and yang is outward and up, and so on. Nothing is ever completely yin or yang, but a combination of the two. These two principles are always interacting, opposing, and influencing each other. The goal of Chinese medicine is not to eliminate either yin or yang, but to allow the two to balance each other and exist harmoniously together. For instance, if a person suffers from symptoms

KEY TERMS

Acupressure—Form of massage using acupuncture points.

Auricular acupuncture—Acupuncture using only points found on the ears.

Chi—Basic life energy.

Meridian—Channel through which chi travels in the body.

Moxibustion—Acupuncture technique which burns the herb moxa or mugwort.

Tonification—Acupuncture technique for strengthening the body.

Yin/Yang—Universal characteristics used to describe aspects of the natural world.

of high blood pressure, the Chinese system would say that the heart organ might have too much yang, and would recommend methods either to reduce the yang or to increase the yin of the heart, depending on the other symptoms and organs in the body. Thus, acupuncture therapies seek to either increase or reduce yang, or increase or reduce yin in particular regions of the body.

CHI. Another fundamental concept of Chinese medicine is that of chi (pronounced *chee*, also spelled *qi*). Chi is the fundamental life energy of the universe. It is invisible and is found in the environment in the air, water, food and sunlight. In the body, it is the invisible vital force that creates and animates life. We are all born with inherited amounts of chi, and we also get acquired chi from the food we eat and the air we breathe. The level and quality of a person's chi also depends on the state of physical, mental and emotional balance. Chi travels through the body along channels called *meridians*.

THE ORGAN SYSTEM. In the Chinese system, there are twelve main organs: the lung, large intestine, stomach, spleen, heart, small intestine, urinary bladder, kidney, liver, gallbladder, pericardium, and the "triple warmer," which represents the entire torso region. Each organ has chi energy associated with it, and each organ interacts with particular emotions on the mental level. As there are twelve organs, there are twelve types of chi which can move through the body, and these move through twelve main channels or meridians. Chinese doctors connect symptoms to organs. That is, symptoms are caused by yin/yang imbalances in one or more organs, or by an unhealthy flow of chi to or from one

organ to another. Each organ has a different profile of symptoms it can manifest.

THE FIVE ELEMENTS. Another basis of Chinese theory is that the world and body are made up of five main elements: wood, fire, earth, metal, and water. These elements are all interconnected, and each element either generates or controls another element. For instance, water controls fire and earth generates metal. Each organ is associated with one of the five elements. The Chinese system uses elements and organs to describe and treat conditions. For instance, the kidney is associated with water and the heart is associated with fire, and the two organs are related as water and fire are related. If the kidney is weak, then there might be a corresponding fire problem in the heart, so treatment might be made by acupuncture or herbs to cool the heart system and/or increase energy in the kidney system.

The Chinese have developed an intricate system of how organs and elements are related to physical and mental symptoms, and the above example is a very simple one. Although this system sounds suspect to Western scientists, some interesting parallels have been observed. For instance, Western medicine has observed that with severe heart problems, kidney failure often follows, but it still does not know exactly why. In Chinese medicine, this connection between the two organs has long been established.

MEDICAL PROBLEMS AND ACUPUNCTURE. In Chinese medicine, disease as seen as imbalances in the organ system or chi meridians, and the goal of any remedy or treatment is to assist the body in reestablishing its innate harmony. Disease can be caused by internal factors like emotions, external factors like the environment and weather, and other factors like injuries, trauma, diet, and germs. However, infection is seen not as primarily a problem with germs and viruses, but as a weakness in the energy of the body which is allowing a sickness to occur. In Chinese medicine, no two illnesses are ever the same, as each body has its own characteristics of symptoms and balance. Acupuncture is used to open or adjust the flow of chi throughout the organ system, which will strengthen the body and prompt it to heal itself.

A VISIT TO THE ACUPUNCTURIST. The first thing an acupuncturist will do is get a thorough idea of a patient's medical history and symptoms, both physical and emotional. This is done with a long questionnaire and interview. Then the acupuncturist will examine the patient to find further symptoms, looking closely at the tongue, the pulse at various points in the body, the complexion, general behavior, and other signs like coughs or pains. From this, the practitioner will be able to determine patterns of symptoms which indicate which organs and areas are

imbalanced. Depending on the problem, the acupuncturist will insert needles to manipulate chi on one or more of the twelve organ meridians. On these twelve meridians, there are nearly 2,000 points which can be used in acupuncture, with around 200 points being most frequently used by traditional acupuncturists. During an individual treatment, one to twenty needles may be used, depending on which meridian points are chosen.

Acupuncture needles are always sterilized and acupuncture is a very safe procedure. The depth of insertion of needles varies, depending on which chi channels are being treated. Some points barely go beyond superficial layers of skin, while some acupuncture points require a depth of 1-3 in (2.5-7.5 cm) of needle. The needles generally do not cause pain. Patients sometimes report pinching sensations and often pleasant sensations, as the body experiences healing. Depending on the problem, the acupuncturist might spin or move the needles, or even pass a slight electrical current through some of them. *Moxibustion* may be sometimes used, in which an herbal mixture (moxa or mugwort) is either burned like incense on the acupuncture point or on the end of the needle, which is believed to stimulate chi in a particular way. Also, acupuncturists sometimes use *cupping*, during which small suction cups are placed on meridian points to stimulate them.

How long the needles are inserted also varies. Some patients only require a quick in and out insertion to clear problems and provide *tonification* (strengthening of health), while some other conditions might require needles inserted up to an hour or more. The average visit to an acupuncturist takes about thirty minutes. The number of visits to the acupuncturist varies as well, with some conditions improved in one or two sessions and others requiring a series of six or more visits over the course of weeks or months.

Costs for acupuncture can vary, depending on whether the practitioner is an MD. Initial visits with non-MD acupuncturists can run from \$50-\$100, with follow-up visits usually costing less. Insurance reimbursement also varies widely, depending on the company and state. Regulations have been changing often. Some states authorize Medicaid to cover acupuncture for certain conditions, and some states have mandated that general coverage pay for acupuncture. Consumers should be aware of the provisions for acupuncture in their individual policies.

Precautions

Acupuncture is generally a very safe procedure. If a patient is in doubt about a medical condition, more than one physician should be consulted. Also, a patient should always feel comfortable and confident that their acupuncturist is knowledgeable and properly trained.

Research and general acceptance

Mainstream medicine has been slow to accept acupuncture; although more MDs are using it, the American Medical Association does not recognize it as a specialty. The reason for this is that the mechanism of acupuncture is difficult to scientifically understand or measure, such as the invisible energy of chi in the body. Western medicine, admitting that acupuncture works in many cases, has theorized that the energy meridians are actually part of the nervous system and that acupuncture relieves pain by releasing endorphins, or natural pain killers, into the bloodstream. Despite the ambiguity in the biochemistry involved, acupuncture continues to show effectiveness in clinical tests, from reducing pain to alleviating the symptoms of chronic illnesses, and research in acupuncture is currently growing. The Office of Alternative Medicine of the National Institute of Health is currently funding research in the use of acupuncture for treating depression and attention-deficit disorder.

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- Acute homeopathic remedies see **Homeopathic remedies, acute prescribing**

Acute kidney failure

Definition

Acute kidney failure occurs when illness, infection, or injury damages the kidneys. Temporarily, the kidneys

cannot adequately remove fluids and wastes from the body or maintain the proper level of certain kidney-regulated chemicals in the bloodstream.

Description

The kidneys are the body's natural filtration system. They perform the critical task of processing approximately 200 quarts of fluid in the bloodstream every 24 hours. Waste products like urea and toxins, along with excess fluids, are removed from the bloodstream in the form of urine. Kidney (or renal) failure occurs when kidney functioning becomes impaired. Fluids and toxins begin to accumulate in the bloodstream. As fluids build up in the bloodstream, the patient with acute kidney failure may become puffy and swollen (edematous) in the face, hands, and feet. Their blood pressure typically begins to rise, and they may experience **fatigue** and nausea.

Unlike **chronic kidney failure**, which is long term and irreversible, acute kidney failure is a temporary condition. With proper and timely treatment, it can typically be reversed. Often there is no permanent damage to the kidneys. Acute kidney failure appears most frequently as a complication of serious illness, like **heart failure**, liver failure, **dehydration**, severe **burns**, and excessive bleeding (hemorrhage). It may also be caused by an obstruction to the urinary tract or as a direct result of kidney disease, injury, or an adverse reaction to a medicine.

Causes and symptoms

Acute kidney failure can be caused by many different illnesses, injuries, and infections. These conditions fall into three main categories: *prerenal*, *postrenal*, and *intrarenal* conditions.

Prerenal conditions do not damage the kidney, but can cause diminished kidney function. They are the most common cause of acute renal failure, and include:

- dehydration
- hemorrhage
- septicemia, or **sepsis**
- heart failure
- liver failure
- burns

Postrenal conditions cause kidney failure by obstructing the urinary tract. These conditions include:

- inflammation of the prostate gland in men (**prostatitis**)
- enlargement of the prostate gland (**benign prostatic hypertrophy**)
- bladder or pelvic tumors
- **kidney stones** (**calculi**)

Intrarenal conditions involve kidney disease or direct injury to the kidneys. These conditions include:

- lack of blood supply to the kidneys (**ischemia**)
- use of radiocontrast agents in patients with kidney problems
- drug abuse or overdose
- long-term use of nephrotoxic medications, like certain **pain** medicines
- acute inflammation of the glomeruli, or filters, of the kidney (**glomerulonephritis**)
- kidney infections (**pyelitis** or **pyelonephritis**)

Common symptoms of acute kidney failure include:

- anemia. The kidneys are responsible for producing erythropoietin (EPO), a hormone that stimulates red blood cell production. If kidney disease causes shrinking of the kidney, red blood cell production is reduced, leading to anemia.
- bad breath or bad taste in mouth. Urea in the saliva may cause an ammonia-like taste in the mouth.
- bone and joint problems. The kidneys produce vitamin D, which helps the body absorb calcium and keeps bones strong. For patients with kidney failure, bones may become brittle. In children, normal growth may be stunted. Joint pain may also occur as a result of high phosphate levels in the blood. Retention of uric acid may cause **gout**.
- edema. Puffiness or swelling in the arms, hands, feet, and around the eyes.
- 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. This makes blood pressure rise.
- increased fatigue. Toxic substances in the blood and the presence of anemia may cause the patient to feel exhausted.
- itching. Phosphorus, normally eliminated in the urine, accumulates in the blood of patients with kidney failure. An increased phosphorus level may cause the skin to itch.
- lower back pain. Patients suffering from certain kidney problems (like kidney stones and other obstructions) may have pain where the kidneys are located, in the small of the back below the ribs.
- nausea. Urea in the gastric juices may cause upset stomach.

Diagnosis

Kidney failure is diagnosed by a doctor. A nephrologist, a doctor that specializes in the kidney, may be consulted to confirm the diagnosis and recommend treatment options. The patient that is suspected of having acute kidney failure will have blood and urine tests to determine the level of kidney function. A blood test will assess the levels of creatinine, blood urea nitrogen (BUN), uric acid, phosphate, sodium, and potassium. The kidney regulates these agents in the blood. Urine samples will also be collected, usually over a 24-hour period, to assess protein loss and/or creatinine clearance.

Determining 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. X rays, **magnetic resonance imaging** (MRI), computed tomography scan (CT), ultrasound, renal biopsy, and/or arteriogram of the kidneys may be used 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 needed.

Treatment

Treatment for acute kidney failure varies. Treatment is directed to the underlying, primary medical condition that has triggered kidney failure. Prerenal conditions may be treated with replacement fluids given through a vein, **diuretics**, **blood transfusion**, or medications. Postrenal conditions and intrarenal conditions may require surgery and/or medication.

Frequently, patients in acute kidney failure require *hemodialysis*, *hemofiltration*, or *peritoneal dialysis* to filter fluids and wastes from the bloodstream until the primary medical condition can be controlled.

Hemodialysis

Hemodialysis involves circulating the patient's blood outside of the body through an extracorporeal circuit (ECC), or dialysis circuit. The ECC is made up of plastic blood tubing, a filter known as a dialyzer (or artificial kidney), and a dialysis machine that monitors and maintains blood flow and administers dialysate. Dialysate is a sterile chemical solution that is used to draw waste products out of the blood. The patient's blood leaves the body through the vein and travels through the ECC and the dialyzer, where fluid removal takes place.

During dialysis, waste products in the bloodstream are carried out of the body. At the same time, electrolytes and other chemicals are added to the blood. The purified, chemically-balanced blood is then returned to the body.

KEY TERMS

Blood urea nitrogen (BUN)—A waste product that is formed in the liver and collects in the bloodstream; patients with kidney failure have high BUN levels.

Creatinine—A protein produced by muscle that healthy kidneys filter out.

Extracorporeal—Outside of, or unrelated to, the body.

Ischemia—A lack of blood supply to an organ or tissue.

Nephrotoxic—Toxic, or damaging, to the kidney.

Radiocontrast agents—Dyes administered to a patient for the purposes of a radiologic study.

Sepsis—A bacterial infection of the bloodstream.

Vasopressors—Medications that constrict the blood vessels.

A dialysis "run" typically lasts three to four hours, depending on the type of dialyzer used and the physical condition of the patient. Dialysis is used several times a week until acute kidney failure is reversed.

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.

Hemofiltration

Hemofiltration, also called continuous renal replacement therapy (CRRT), is a slow, continuous blood filtration therapy used to control acute kidney failure in critically ill patients. These patients are typically very sick and may have heart problems or circulatory problems. They cannot handle the rapid filtration rates of hemodialysis. They also frequently need **antibiotics**, **nutrition**, vasopressors, and other fluids given through a vein to treat their primary condition. Because hemofiltration is continuous, prescription fluids can be given to patients in kidney failure without the risk of fluid overload.

Like hemodialysis, hemofiltration uses an ECC. A hollow fiber hemofilter is used instead of a dialyzer to remove fluids and toxins. Instead of a dialysis machine, a blood pump makes the blood flow through the ECC. The volume of blood circulating through the ECC in hemofiltration is less than that in hemodialysis. Filtration rates are slower and gentler on the circulatory system.

Hemofiltration treatment will generally be used until kidney failure is reversed.

Peritoneal dialysis

Peritoneal dialysis may be used if an acute kidney failure patient is stable and not in immediate crisis. In peritoneal dialysis (PD), the lining of the patient's abdomen, the peritoneum, acts as a blood filter. A flexible tube-like instrument (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 certain time period, the waste-filled dialysate is drained from the abdomen, and replaced with clean dialysate. There are three type of peritoneal dialysis, which vary according to treatment time and administration method.

Peritoneal dialysis is often the best treatment option for infants and children. Their small size can make vein access difficult to maintain. It is not recommended for patients with abdominal adhesions or other abdominal defects (like a **hernia**) that might reduce the efficiency of the treatment. It is also not recommended for patients who suffer frequent bouts of an inflammation of the small pouches in the intestinal tract (diverticulitis).

Prognosis

Because many of the illnesses and underlying conditions that often trigger acute kidney failure are critical, the prognosis for these patients many times is not good. Studies have estimated overall **death** rates for acute kidney failure at 42-88%. Many people, however, die because of the primary disease that has caused the kidney failure. These figures may also be misleading because patients who experience kidney failure as a result of less serious illnesses (like kidney stones or dehydration) have an excellent chance of complete recovery. Early recognition and prompt, appropriate treatment are key to patient recovery.

Up to 10% of patients who experience acute kidney failure will suffer irreversible kidney damage. They will eventually go on to develop chronic kidney failure or end-stage renal disease. These patients will require long-term dialysis or **kidney transplantation** to replace their lost renal functioning.

Prevention

Since acute kidney failure can be caused by many things, prevention is difficult. Medications that may impair kidney function should be given cautiously. Patients with pre-existing kidney conditions who are

hospitalized for other illnesses or injuries should be carefully monitored for kidney failure complications. Treatments and procedures that may put them at risk for kidney failure (like diagnostic tests requiring radiocontrast agents or dyes) should be used with extreme caution.

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- National Kidney Foundation. 30 East 33rd St., New York, NY 10016. (800) 622-9010. <<http://www.kidney.org>>.

Paula Anne Ford-Martin

Acute leukemias see **Leukemias, acute**

Acute lymphangitis

Definition

Acute lymphangitis is a bacterial infection in the lymphatic vessels which is characterized by painful, red streaks below the skin surface. This is a potentially serious infection which can rapidly spread to the bloodstream and be fatal.

Description

Acute lymphangitis affects a critical member of the immune system—the lymphatic system. Waste materials from nearly every organ in the body drain into the lymphatic vessels and are filtered in small organs called lymph nodes. Foreign bodies, such as bacteria or viruses, are processed in the lymph nodes to generate an immune response to fight an infection.

In acute lymphangitis, bacteria enter the body through a cut, scratch, insect bite, surgical wound, or other skin injury. Once the bacteria enter the lymphatic system, they multiply rapidly and follow the lymphatic vessel like a highway. The infected lymphatic vessel becomes inflamed, causing red streaks that are visible below the skin surface. The growth of the bacteria occurs so rapidly that the immune system does not respond fast enough to stop the infection.

If left untreated, the bacteria can cause tissue destruction in the area of the infection. A pus-filled, painful lump called an **abscess** may be formed in the infected area. **Cellulitis**, a generalized infection of the lower skin layers, may also occur. In addition, the bacteria may invade the bloodstream and cause septicemia. Lay people, for that reason, often call the red streaks seen in the skin “blood poisoning.” Septicemia is a very serious illness and may be fatal.

Causes and symptoms

Acute lymphangitis is most often caused by the bacterium *Streptococcus pyogenes*. This potentially dangerous bacterium also causes **strep throat**, infections of the heart, spinal cord, and lungs, and in the 1990s has been called the “flesh-eating bacterium.” Staphylococci bacteria may also cause lymphangitis.

Although anyone can develop lymphangitis, some people are more at risk. People who have had radical **mastectomy** (removal of a breast and nearby lymph nodes), a leg vein removed for coronary bypass surgery, or recurrent lymphangitis caused by tinea pedis (a fungal infection on the foot) are at an increased risk for lymphangitis.

The characteristic symptoms of acute lymphangitis are the wide, red streaks which travel from the site of infection to the armpit or groin. The affected areas are red, swollen, and painful. Blistering of the affected skin may occur. The bacterial infection causes a **fever** of 100–104°F (38°–40°C). In addition, a general ill feeling, muscle aches, **headache**, chills, and loss of appetite may be felt.

Diagnosis

If lymphangitis is suspected, the person should call his or her doctor immediately or go to an emergency room. Acute lymphangitis could be diagnosed by the family doctor, infectious disease specialist, or an emergency room doctor. The painful, red streaks just below the skin surface and the high fever are diagnostic of acute lymphangitis. A sample of blood would be taken for culture to determine whether the bacteria have entered the bloodstream. A biopsy (removal of a piece of infected tissue) sample may be taken for culture to identify which

KEY TERMS

Biopsy—The process which removes a sample of diseased or infected tissue for microscopic examination to aid in diagnosis.

Lymphatic system—A component of the immune system consisting of vessels and nodes. Waste materials from organs drain into the lymphatic vessels and are filtered by the lymph nodes.

Septicemia—Disease caused by the presence and growth of bacteria in the bloodstream.

type of bacteria is causing the infection. Diagnosis is immediate because it is based primarily on the symptoms. Most insurance policies should cover the expenses for the diagnosis and treatment of acute lymphangitis.

Treatment

Because of the serious nature of this infection, treatment would begin immediately even before the bacterial culture results were available. The only treatment for acute lymphangitis is to give very large doses of an antibiotic, usually penicillin, through the vein. Growing streptococcal bacteria are usually eliminated rapidly and easily by penicillin. The antibiotic clindamycin may be included in the treatment to kill any streptococci which are not growing and are in a resting state. Alternatively, a “broad spectrum” antibiotic may be used which would kill many different kinds of bacteria.

Aspirin or other medications which reduce the **pain** and the fever may also be given. Medications which reduce any inflammation of the infected region may also be provided. The patient is likely to be hospitalized to administer the antibiotic and other medications and to closely monitor his or her condition. Surgical drainage of an abscess may be necessary.

Prognosis

Complete recovery is expected if antibiotic treatment is begun at an early stage of the infection. However, if untreated, acute lymphangitis can be a very serious and even deadly disease. Acute lymphangitis that goes untreated can spread, causing tissue damage. Extensive tissue damage would need to be repaired by plastic surgery. Spread of the infection into the bloodstream could be fatal.

Prevention

Although acute lymphangitis can occur in anyone, good hygiene and general health may help to prevent infections.

Resources

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Belinda Rowland, PhD

Acute pericarditis see **Pericarditis**

KEY TERMS

Streptococcus—A gram-positive, round or oval bacteria in the genus *Streptococcus*. Group A streptococci cause a number of human diseases including strep throat, impetigo, and ASPGN.

Acute poststreptococcal glomerulonephritis

Definition

Acute poststreptococcal **glomerulonephritis** (APSGN) is an inflammation of the kidney tubules (glomeruli) that filter waste products from the blood, following a streptococcal infection such as **strep throat**. APSGN is also called postinfectious glomerulonephritis.

Description

APSGN develops after certain streptococcal bacteria (group A beta-hemolytic streptococci) have infected the skin or throat. Antigens from the dead streptococci clump together with the antibodies that killed them. These clumps are trapped in the kidney tubules, cause the tubules to become inflamed, and impair that organs' ability to filter and eliminate body wastes. The onset of APSGN usually occurs one to six weeks (average two weeks) after the streptococcal infection.

APSGN is a relatively uncommon disease affecting about one of every 10,000 people, although four or five times that many may actually be affected by it but show no symptoms. APSGN is most prevalent among boys between the ages of 3 and 7, but it can occur at any age.

Causes and symptoms

Frequent sore throats and a history of streptococcal infection increase the risk of acquiring APSGN. Symptoms of APSGN include:

- fluid accumulation and tissue swelling (**edema**) initially in the face and around the eyes, later in the legs
- low urine output (**oliguria**)
- blood in the urine (**hematuria**)
- protein in the urine (**proteinuria**)
- high blood pressure
- joint **pain** or stiffness

Diagnosis

Diagnosis of APSGN is made by taking the patient's history, assessing his/her symptoms, and performing certain laboratory tests. **Urinalysis** usually shows blood and protein in the urine. Concentrations of urea and creatinine (two waste products normally filtered out of the blood by the kidneys) in the blood are often high, indicating impaired kidney function. A reliable, inexpensive blood test called the anti-streptolysin-O test can confirm that a patient has or has had a streptococcal infection. A **throat culture** may also show the presence of group A beta-hemolytic streptococci.

Treatment

Treatment of APSGN is designed to relieve the symptoms and prevent complications. Some patients are advised to stay in bed until they feel better and to restrict fluid and salt intake. **Antibiotics** may be prescribed to kill any lingering streptococcal bacteria, if their presence is confirmed. Antihypertensives may be given to help control high blood pressure and **diuretics** may be used to reduce fluid retention and swelling. **Kidney dialysis** is rarely needed.

Prognosis

Most children (up to 95%) fully recover from APSGN in a matter of weeks or months. Most adults (up to 70%) also recover fully. In those who do not recover fully, chronic or progressive problems of kidney function may occur. Kidney failure may result in some patients.

Prevention

Receiving prompt treatment for **streptococcal infections** may prevent APSGN.

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ORGANIZATIONS

American Kidney Fund. 6110 Executive Boulevard, Rockville, MD 20852. (800) 638-8299. <<http://216.248.130.102/Default.htm>>.

National Kidney Foundation. 30 East 33rd St., New York, NY 10016. (800) 622-9010. <<http://www.kidney.org>>.

Maureen Haggerty

Acute respiratory distress syndrome see
Adult respiratory distress syndrome

KEY TERMS

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 reaction to trauma in which the mind splits off certain aspects of the trauma from conscious awareness. Dissociation can affect the patient's memory, sense of reality, and sense of identity.

Trauma—In the context of ASD, a disastrous or life-threatening event.

Acute stress disorder

Definition

Acute stress disorder (ASD) is an **anxiety** disorder characterized by a cluster of dissociative and anxiety symptoms occurring within one month of a traumatic event. (Dissociation is a psychological reaction to trauma in which the mind tries to cope by "sealing off" some features of the trauma from conscious awareness).

Description

Acute stress disorder is a new diagnostic category that was introduced in 1994 to differentiate time-limited reactions to trauma from **post-traumatic stress disorder** (PTSD).

Causes and symptoms

Acute stress disorder is caused by exposure to trauma, which is defined as a stressor that causes intense fear and, usually, involves threats to life or serious injury to oneself or others. Examples are rape, mugging, combat, natural disasters, etc.

The symptoms of stress disorder include a combining of one or more dissociative and anxiety symptoms with the avoidance of reminders of the traumatic event. Dissociative symptoms include emotional detachment, temporary loss of memory, depersonalization, and derealization.

Anxiety symptoms connected with acute stress disorder include irritability, physical restlessness, sleep problems, inability to concentrate, and being easily startled.

Diagnosis

Diagnosis of acute stress disorder is based on a combination of the patient's history and a **physical examination** to rule out diseases that can cause anxiety. The

essential feature is a traumatic event within one month of the onset of symptoms. Other diagnostic criteria include:

- The symptoms significantly interfere with normal social or vocational functioning
- The symptoms last between two days and four weeks.

Treatment

Treatment for acute stress disorder usually includes a combination of antidepressant medications and short-term psychotherapy.

Alternative treatment

Acupuncture has been recommended as a treatment for acute stress disorder. Some other alternative approaches, including **meditation**, breathing exercises, and **yoga**, may be helpful when combined with short-term psychotherapy. Homeopathic treatment and the use of herbal medicine and flower essences also can help the person with acute stress disorder rebalance on the physical, mental, and emotional levels.

Prognosis

The prognosis for recovery is influenced by the severity and duration of the trauma, the patient's closeness to it, and the patient's previous level of functioning. Favorable signs include a short time period between the trauma and onset of symptoms, immediate treatment, and appropriate social support. If the patient's symptoms are severe enough to interfere with normal life and have lasted longer than one month, the diagnosis may be changed to PTSD. If the symptoms have lasted longer than one month but are

not severe enough to meet the definition of PTSD, the diagnosis may be changed to adjustment disorder.

Patients who do not receive treatment for acute stress disorder are at increased risk for substance abuse or major **depressive disorders**.

Prevention

Traumatic events cannot usually be foreseen and, thus, cannot be prevented. However, in theory, professional intervention soon after a major trauma might reduce the likelihood or severity of ASD. In addition, some symptoms of acute stress disorder result from biochemical changes in the central nervous system, muscles, and digestive tract that are not subject to conscious control.

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Rebecca J. Frey

Acute stress gastritis see **Gastritis**

Acute transverse myelitis see **Transverse myelitis**

Acyclovir see **Antiviral drugs**

Addiction

Definition

Addiction is a dependence on a behavior or substance that a person is powerless to stop. The term has been partially replaced by the word *dependence* for substance abuse. Addiction has been extended, however, to

include mood-altering behaviors or activities. Some researchers speak of two types of addictions: substance addictions (for example, **alcoholism**, drug abuse, and **smoking**); and process addictions (for example, gambling, spending, shopping, eating, and sexual activity). There is a growing recognition that many addicts, such as polydrug abusers, are addicted to more than one substance or process.

Description

Addiction is one of the most costly public health problems in the United States. It is a progressive syndrome, which means that it increases in severity over time unless it is treated. Substance abuse is characterized by frequent relapse, or return to the abused substance. Substance abusers often make repeated attempts to quit before they are successful.

In 1995 the economic cost of substance abuse in the United States exceeded \$414 billion, with health care costs attributed to substance abuse estimated at more than \$114 billion.

By eighth grade, 52% of adolescents have consumed alcohol, 41% have smoked tobacco, and 20% have smoked marijuana. Compared to females, males are almost four times as likely to be heavy drinkers, nearly one and a half more likely to smoke a pack or more of cigarettes daily, and twice as likely to smoke marijuana weekly. However, among adolescents these gender differences are decreasing. Although frequent use of tobacco, **cocaine** and heavy drinking appears to have remained stable in the 1990s, marijuana use increased.

In 1999, an estimated four million Americans over the age of 12 used prescription **pain** relievers, sedatives, and stimulants for "nonmedical" reasons during one month.

In the United States, 25% of the population regularly uses tobacco. Tobacco use reportedly kills 2.5 times as many people each year as alcohol and drug abuse combined. According to 1998 data from the World Health Organization, there were 1.1 billion smokers worldwide and 10,000 tobacco-related deaths per day. Furthermore, in the United States, 43% of children aged 2-11 years are exposed to environmental tobacco smoke, which has been implicated in **sudden infant death syndrome**, low birth weight, **asthma**, middle ear disease, **pneumonia**, **cough**, and upper respiratory infection.

Eating disorders, such as **anorexia nervosa**, **bulimia nervosa**, and binge eating, affect over five million American women and men. Fifteen percent of young women have substantially disordered attitudes toward eating and eating behaviors. More than 1,000 women die each year from anorexia nervosa.

A 1997 Harvard study found that an estimated 15.4 million Americans suffered from a gambling addiction. Over half that number (7.9 million) were adolescents.

Causes and symptoms

Addiction to substances results from the interaction of several factors:

Drug chemistry

Some substances are more addictive than others, either because they produce a rapid and intense change in mood; or because they produce painful withdrawal symptoms when stopped suddenly.

Genetic factor

Some people appear to be more vulnerable to addiction because their body chemistry increases their sensitivity to drugs. Some forms of **substance abuse and dependence** seem to run in families; and this may be the result of a genetic predisposition, environmental influences, or a combination of both.

Brain structure and function

Using drugs repeatedly over time changes brain structure and function in fundamental and long-lasting ways. Addiction comes about through an array of changes in the brain and the strengthening of new memory connections. Evidence suggests that those long-lasting brain changes are responsible for the distortions of cognitive and emotional functioning that characterize addicts, particularly the compulsion to use drugs. Although the causes of addiction remain the subject of ongoing debate and research, many experts now consider addiction to be a brain disease: a condition caused by persistent changes in brain structure and function. However, having this brain disease does not absolve the addict of responsibility for his or her behavior, but it does explain why many addicts cannot stop using drugs by sheer force of will alone.

Social learning

Social learning is considered the most important single factor. It includes patterns of use in the addict's family or subculture, peer pressure, and advertising or media influence.

Availability

Inexpensive or readily available tobacco, alcohol, or drugs produce marked increases in rates of addiction.



Crack users. Crack, a form of cocaine, is one of the most addictive drugs. (Photograph by Roy Marsch, The Stock Market. Reproduced by permission.)

Individual development

Before the 1980s, the so-called addictive personality was used to explain the development of addiction. The addictive personality was described as escapist, impulsive, dependent, devious, manipulative, and self-centered. Many doctors now believe that these character traits develop in addicts as a result of the addiction, rather than the traits being a cause of the addiction.

Diagnosis

In addition to a preoccupation with using and acquiring the abused substance, the diagnosis of addiction is based on five criteria:

- loss of willpower
- harmful consequences
- unmanageable lifestyle
- tolerance or escalation of use
- withdrawal symptoms upon quitting

Treatment

Treatment requires both medical and social approaches. Substance addicts may need hospital treatment to manage withdrawal symptoms. Individual or group psychotherapy is often helpful, but only after substance use has stopped. Anti-addiction medications, such as **methadone** and naltrexone, are also commonly used.

The most frequently recommended social form of outpatient treatment is the twelve-step program. Such programs are also frequently combined with psychotherapy. According to a recent study reported by the American Psychological Association (APA), anyone, regardless of his or her religious beliefs or lack of religious beliefs, can benefit from participation in 12-step programs such as Alcoholics Anonymous (AA) or Narcotics Anonymous (NA). The number of visits to 12-step self-help groups exceeds the number of visits to all mental health professionals combined. There are twelve-step groups for all major substance and process addictions.

The Twelve Steps are:

- Admit powerlessness over the addiction.
- Believe that a Power greater than oneself could restore sanity.
- Make a decision to turn your will and your life over to the care of God, as you understand him.
- Make a searching and fearless moral inventory of self.
- Admit to God, yourself, and another human being the exact nature of your wrongs.
- Become willing to have God remove all these defects from your character.
- Humbly ask God to remove shortcomings.
- Make a list of all persons harmed by your wrongs and become willing to make amends to them all.
- Make direct amends to such people, whenever possible except when to do so would injure them or others.
- Continue to take personal inventory and promptly admit any future wrongdoings.
- Seek to improve contact with a God of the individual's understanding through **meditation** and prayer.
- Carry the message of spiritual awakening to others and practice these principles in all your affairs.

Alternative treatment

Acupuncture and **homeopathy** have been used to treat withdrawal symptoms. Meditation, **yoga**, and **reiki** healing have been recommended for process addictions, however, the success of these programs has not been well-documented through controlled studies.

KEY TERMS

Addiction—Dependence on a habit-forming substance or behavior that the person is powerless to stop.

Addictive personality—A concept that was formerly used to explain addiction as the result of pre-existing character defects in individuals.

Process addiction—Addiction to certain mood-altering behaviors, such as eating disorders, gambling, sexual activity, overwork, and shopping.

Tolerance—A condition in which an addict needs higher doses of a substance to achieve the same effect previously achieved with a lower dose.

Withdrawal—The unpleasant, sometimes life-threatening physiological changes that occur, due to the discontinuation of use of some drugs after prolonged, regular use.

Prognosis

The prognosis for recovery from any addiction depends on the substance or process, the individual's circumstances, and underlying personality structure. Poly-drug users have the worst prognosis for recovery.

Prevention

The most effective form of prevention appears to be a stable family that models responsible attitudes toward mood-altering substances and behaviors. Prevention education programs are also widely used to inform the public of the harmfulness of substance abuse.

Resources

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Bill Asenjo, MS, CRC

KEY TERMS

Gland—A collection of cells whose function is to release certain chemicals, or hormones, which are important to the functioning of other, sometimes distantly located, organs or body systems.

Hormone—A chemical produced in one part of the body, which travels to another part of the body in order to exert its effect.

- the functioning of muscles
- normal kidney function
- production of blood cells
- the normal processes involved in maintaining the skeletal system
- proper functioning of the brain and nerves
- the normal responses of the immune system

Aldosterone, also produced by the adrenal cortex, plays a central role in maintaining the appropriate proportions of water and salts in the body. When this balance is upset, the volume of blood circulating throughout the body will fall dangerously low, accompanied by a drop in blood pressure.

Addison's disease is also called primary adrenocortical insufficiency. In other words, some process interferes directly with the ability of the adrenal cortex to produce its hormones. Levels of both cortisol and aldosterone drop, and numerous functions throughout the body are disrupted.

Addison's disease occurs in about four in every 100,000 people. It strikes both men and women of all ages.

Addison's disease

Definition

Addison's disease is a disorder involving disrupted functioning of the part of the adrenal gland called the cortex. This results in decreased production of two important chemicals (hormones) normally released by the adrenal cortex: cortisol and aldosterone.

Description

The adrenals are two glands, each 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.

Cortisol is a very potent hormone produced by the adrenal cortex. It is involved in regulating the functioning of nearly every type of organ and tissue throughout the body, and is considered to be one of the few hormones absolutely necessary for life. Cortisol is involved in:

- the very complex processing and utilization of many nutrients, including sugars (carbohydrates), fats, and proteins
- the normal functioning of the circulatory system and the heart

Causes and symptoms

The most common cause of Addison's disease is the destruction and/or shrinking (atrophy) of the adrenal cortex. In about 70% of all cases, this atrophy is believed to occur due to an autoimmune disorder. In an autoimmune disorder, the immune system of the body, responsible for identifying foreign invaders such as viruses or bacteria and killing them, accidentally begins to identify the cells of the adrenal cortex as foreign, and destroy them. In about 20% of all cases, destruction of the adrenal cortex is caused by **tuberculosis**. The remaining cases of Addison's disease may be caused by fungal infections, such as **histoplasmosis**, coccidiomycosis, and **cryptococcosis**, which affect the adrenal gland by producing destructive, tumor-like masses

called granulomas; a disease called **amyloidosis**, in which a starchy substance called amyloid is deposited in abnormal places throughout the body, interfering with the function of whatever structure it is present within; or invasion of the adrenal glands by **cancer**.

In about 75% of all patients, Addison's disease tends to be a very gradual, slowly developing disease. Significant symptoms are not noted until about 90% of the adrenal cortex has been destroyed. The most common symptoms include **fatigue** and loss of energy, decreased appetite, nausea, vomiting, **diarrhea**, abdominal **pain**, weight loss, muscle weakness, **dizziness** when standing, **dehydration**, unusual areas of darkened (pigmented) skin, and dark freckling. As the disease progresses, the patient may appear to have very tanned, or bronzed skin, with darkening of the lining of the mouth, vagina, and rectum, and dark pigmentation of the area around the nipples (aereola). As dehydration becomes more severe, the blood pressure will continue to drop and the patient will feel increasingly weak and light-headed. Some patients have psychiatric symptoms, including depression and irritability. Women lose pubic and underarm hair, and stop having normal menstrual periods.

When a patient becomes ill with an infection, or stressed by an injury, the disease may suddenly and rapidly progress, becoming life-threatening. Symptoms of this "Addisonian crisis" include abnormal heart rhythms, severe pain in the back and abdomen, uncontrollable **nausea and vomiting**, a drastic drop in blood pressure, kidney failure, and unconsciousness. About 25% of all Addison's disease patients are identified due to the development of Addisonian crisis.

Diagnosis

Many patients do not recognize the slow progression of symptoms and the disease is ultimately identified when a physician notices the areas of increased pigmentation of the skin. Once suspected, a number of blood tests can lead to the diagnosis of Addison's disease. It is not sufficient to demonstrate low blood cortisol levels, as normal levels of cortisol vary quite widely. Instead, patients are given a testing dose of another hormone called corticotropin (ACTH). ACTH is produced in the body by the pituitary gland, and normally acts by promoting growth within the adrenal cortex and stimulating the production and release of cortisol. In Addison's disease, even a dose of synthetic ACTH does not increase cortisol levels.

To distinguish between primary adrenocortical insufficiency (Addison's disease) and secondary adrenocortical insufficiency (caused by failure of the

pituitary to produce enough ACTH), levels of ACTH in the blood are examined. Normal or high levels of ACTH indicate that the pituitary is working properly, but the adrenal cortex is not responding normally to the presence of ACTH. This confirms the diagnosis of Addison's disease.

Treatment

Treatment of Addison's disease involves replacing the missing or low levels of cortisol. In the case of Addisonian crisis, this will be achieved by injecting a potent form of steroid preparation through a needle placed in a vein (intravenous or IV). Dehydration and salt loss will also be treated by administering carefully balanced solutions through the IV. Dangerously low blood pressure may require special medications to safely elevate it until the steroids take effect.

Patients with Addison's disease will need to take a steroid preparation (hydrocortisone) and a replacement for aldosterone (fludrocortisone) by mouth for the rest of their lives. When a patient has an illness which causes nausea and vomiting (such that they cannot hold down their medications), he or she will need to enter a medical facility where IV medications can be administered. When a patient has any kind of infection or injury, the normal dose of hydrocortisone will need to be doubled.

Prognosis

Prognosis for patients appropriately treated with hydrocortisone and aldosterone is excellent. These patients can expect to enjoy a normal lifespan. Without treatment, or with substandard treatment, patients are always at risk of developing Addisonian crisis.

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ORGANIZATIONS

National Adrenal Disease Foundation. 505 Northern Boulevard, Suite 200, Great Neck, NY 11021. (516) 487-4992.

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Adenoid hyperplasia

Definition

Adenoid hyperplasia is the overenlargement of the lymph glands located above the back of the mouth.

Description

Located at the back of the mouth above and below the soft palate are two pairs of lymph glands. The tonsils below are clearly visible behind the back teeth; the adenoids lie just above them and are hidden from view by the palate. Together these four arsenals of immune defense guard the major entrance to the body from foreign invaders—the germs we breathe and eat. In contrast to the rest of the body's tissues, lymphoid tissue reaches its greatest size in mid-childhood and recedes thereafter. In this way children are best able to develop the immunities they need to survive in a world full of infectious diseases.

Beyond its normal growth pattern, lymphoid tissue grows excessively (hypertrophies) during an acute infection, as it suddenly increases its immune activity to fight off the invaders. Often it does not completely return to its former size. Each subsequent infection leaves behind a larger set of tonsils and adenoids. To make matters worse, the sponge-like structure of these hypertrophied glands can produce safe havens for germs where the body cannot reach and eliminate them. Before antibiotics and the reduction in infectious childhood diseases over the past few generations, tonsils and adenoids caused greater health problems.

Causes and symptoms

Most tonsil and adenoid hypertrophy is simply caused by the normal growth pattern for that type of tissue. Less often, the hypertrophy is due to repeated throat infections by cold viruses, **strep throat**, mononucleosis, and in times gone by, **diphtheria**. The acute infections are usually referred to as **tonsillitis**, the adenoids getting little recognition because they cannot be seen without special instruments. Symptoms include painful, bright red, often ulcerated tonsils, enlargement of lymph nodes (glands) beneath the jaw, **fever**, and general discomfort.

After the acute infection subsides, symptoms are generated simply by the size of the glands. Extremely large tonsils can impair breathing and swallowing, although that is quite rare. Large adenoids can impair nose breathing and require a child to breathe through the mouth. Because they encircle the only connection between the middle ear and the eustachian tube, hypertrophied adenoids can also obstruct it and cause middle ear infections.

KEY TERMS

Eustacian tube—A tube connecting the middle ear with the back of the nose, allowing air pressure to equalize within the ear whenever it opens, such as with yawning.

Hyperplastic—Overgrown.

Hypertrophy—Overgrowth.

Strep throat—An infection of the throat caused by bacteria of the *Streptococcus* family, which causes tonsillitis.

Ulcerated—Damaged so that the surface tissue is lost and/or necrotic (dead).

Diagnosis

A simple tongue blade depressing the tongue allows an adequate view of the tonsils. Enlarged tonsils may have deep pockets (crypts) containing dead tissue (necrotic debris). Viewing adenoids requires a small mirror or fiberoptic scope. A child with recurring middle ear infections may well have large adenoids. A **throat culture** or mononucleosis test will usually reveal the identity of the germ.

Treatment

It used to be standard practice to remove tonsils and/or adenoids after a few episodes of acute throat or ear infection. The surgery is called **tonsillectomy and adenoidectomy** (T and A). Opinion changed as it was realized that this tissue is beneficial to the development of immunity. For instance, children without tonsils and adenoids produce only half the immunity to oral **polio** vaccine. In addition, treatment of ear and throat infections with antibiotics and of recurring ear infections with surgical drainage through the ear drum (tympanostomy) has greatly reduced the incidence of surgical removal of these lymph glands.

Alternative treatment

There are many botanical/herbal remedies that can be used alone or in formulas to locally assist the tonsils and adenoids in their immune function at the opening of the oral cavity and to tone these glands. Keeping the Eustachian tubes open is an important contribution to optimal function in the tonsils and adenoids. Food **allergies** are often the culprits for recurring ear infections, as well as tonsilitis and adenoiditis. Identification and removal of the allergic food(s) can greatly assist in alle-

viating the cause of the problem. Acute tonsillitis also benefits from warm saline gargles.

Prognosis

Hypertrophied adenoids are a normal part of growing up and should be respected for their important role in the development of immunity. Only when their size causes problems by obstructing breathing or middle ear drainage do they demand intervention.

Prevention

Prevention can be directed toward prompt evaluation and appropriate treatment of sore throats to prevent overgrowth of adenoid tissue. Avoiding other children with acute respiratory illness will also reduce the spread of these common illnesses.

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J. Ricker Polsdorfer, MD

Adenoid hypertrophy see **Adenoid hyperplasia**

Adenoid removal see **Tonsillectomy and adenoidectomy**

Adenoidectomy see **Tonsillectomy and adenoidectomy**

Adenovirus infections

Definition

Adenoviruses are DNA viruses (small infectious agents) that cause upper respiratory tract infections, **conjunctivitis**, and other infections in humans.

Description

Adenoviruses were discovered in 1953. About 47 different types have been identified since then, and about half of them are believed to cause human diseases. Infants and children are most commonly affected by adenoviruses. Adenovirus infections can occur throughout the year, but seem to be most common from fall to spring.

Adenoviruses are responsible for 3-5% of acute respiratory infections in children and 2% of respiratory illnesses in civilian adults. They are more apt to cause infection among military recruits and other young people who live in institutional environments. Outbreaks among children are frequently reported at boarding schools and summer camps.

Acquired immunity

Most children have been infected by at least one adenovirus by the time they reach school age. Most adults have acquired immunity to multiple adenovirus types due to infections they had as children.

In one mode of adenovirus infection (called lytic infection because it destroys large numbers of cells), adenoviruses kill healthy cells and replicate up to one million new viruses per cell killed (of which 1-5% are infectious). People with this kind of infection feel sick. In chronic or latent infection, a much smaller number of viruses are released and healthy cells can multiply more rapidly than they are destroyed. People who have this kind of infection don't seem to be sick. This is probably why many adults have immunity to adenoviruses without realizing they have been infected.

Childhood infections

In children, adenoviruses most often cause acute upper respiratory infections with **fever** and runny nose. Adenovirus types 1, 2, 3, 5, and 6 are responsible for most of these infections. Occasionally more serious lower respiratory diseases, such as **pneumonia**, may occur.

Adenoviruses also cause acute pharyngoconjunctival fever in children. This disease is most often caused by types 3 and 7. Symptoms, which appear suddenly and usually disappear in less than a week, include:

- inflammation of the lining of the eyelid (conjunctivitis)
- fever
- **sore throat** (pharyngitis)
- runny nose
- inflammation of lymph glands in the neck (cervical adenitis)

Adenoviruses also cause acute **diarrhea** in young children, characterized by fever and watery stools. This condition is caused by adenovirus types 40 and 41 and can last as long as two weeks.

As much as 51% of all hemorrhagic **cystitis** (inflammation of the bladder and of the tubes that carry urine to the bladder from the kidneys) in American and Japanese children can be attributed to adenovirus infection. A child who has hemorrhagic cystitis has bloody urine for about three days, and invisible traces of blood can be found in the urine a few days longer. The child will feel the urge to urinate frequently—but find it difficult to do so—for about the same length of time.

Adult infections

In adults, the most frequently reported adenovirus infection is acute respiratory disease (ARD, caused by types 4 and 7) in military recruits. Influenza-like symptoms including fever, sore throat, runny nose, and **cough** are almost always present; weakness, chills, **headache**, and swollen lymph glands in the neck may also occur. The symptoms typically last three to five days.

Epidemic keratoconjunctivitis (EKC, caused by adenovirus types 8, 19, and 37) was first seen in shipyard workers whose eyes had been slightly injured by chips of rust or paint. This inflammation of tissues lining the eyelid and covering the front of the eyeball can also be caused by using contaminated contact lens solutions or by drying the hands or face with a towel used by someone who has this infection.

The inflamed, sticky eyelids characteristic of conjunctivitis develop 4–24 days after exposure and last between one and four weeks. Only 5–8% of patients with epidemic keratoconjunctivitis experience respiratory symptoms. One or both eyes may be affected. As symptoms of conjunctivitis subside, eye **pain** and watering and blurred vision develop. These symptoms of **keratitis** may last for several months, and about 10% of these infections spread to at least one other member of the patient's household.

Other illnesses associated with adenovirus include:

- encephalitis (inflammation of the brain) and other infections of the central nervous system (CNS)
- gastroenteritis (inflammation of the stomach and intestines)
- acute mesenteric **lymphadenitis** (inflammation of lymph glands in the abdomen)
- chronic interstitial fibrosis (abnormal growth of connective tissue between cells)
- intussusception (a type of intestinal obstruction)

KEY TERMS

Conjunctivitis—Inflammation of the conjunctiva, the mucous membrane lining the inner surfaces of the eyelid and the front of the eyeball.

Virus—A small infectious agent consisting of a core of genetic material (DNA or RNA) surrounded by a shell of protein.

- pneumonia that doesn't respond to antibiotic therapy
- **whooping cough** syndrome when *Bordetella pertussis* (the bacterium that causes classic whooping cough) is not found

Causes and symptoms

Specific adenovirus infections can be traced to particular sources and produce distinctive symptoms. In general, however, adenovirus infection is caused by:

- inhaling airborne viruses
- getting the virus in the eyes by swimming in contaminated water, using contaminated eye solutions or instruments, wiping the eyes with contaminated towels, or rubbing the eyes with contaminated fingers.
- not washing the hands after using the bathroom, and then touching the mouth or eyes

Symptoms common to most types of adenovirus infections include:

- cough
- fever
- runny nose
- sore throat
- watery eyes

Diagnosis

Although symptoms may suggest the presence of adenovirus, distinguishing these infections from other viruses can be difficult. A definitive diagnosis is based on culture or detection of the virus in eye secretions, sputum, urine, or stool.

The extent of infection can be estimated from the results of blood tests that measure increases in the quantity of antibodies the immune system produces to fight it. Antibody levels begin to rise about a week after infection occurs and remain elevated for about a year.

Treatment

Treatment of adenovirus infections is usually supportive and aimed at relieving symptoms of the illness. Bed rest may be recommended along with medications to reduce fever and/or pain. (**Aspirin** should not be given to children because of concerns about Reye's syndrome.) Eye infections may benefit from topical **corticosteroids** to relieve symptoms and shorten the course of the disease. Hospitalization is usually required for severe pneumonia in infants and for EKC (to prevent blindness). No effective **antiviral drugs** have been developed.

Prognosis

Adenovirus infections are rarely fatal. Most patients recover fully.

Prevention

Practicing good personal hygiene and avoiding people with infectious illnesses can reduce the risk of developing adenovirus infection. Proper handwashing can prevent the spread of the virus by oral-fecal transmission. Sterilization of instruments and solutions used in the eye can prevent the spread of EKC, as can adequate chlorination of swimming pools.

A vaccine containing live adenovirus types 4 and 7 is used to control disease in military recruits, but it is not recommended or available for civilian use. Vaccines prepared from purified subunits of adenovirus are under investigation.

Resources

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Maureen Haggerty

Adjustment disorders

Definition

An adjustment disorder is a debilitating reaction, usually lasting less than six months, to a stressful event or situation. It is not the same thing as **post-traumatic stress disorder** (PTSD), which usually occurs in reaction to a life-threatening event and can be longer lasting.

Description

An adjustment disorder usually begins within three months of a stressful event, and ends within six months after the stressor stops. There are many different subtypes of adjustment disorders, including adjustment disorder with:

- depression
- **anxiety**
- mixed anxiety and depression
- conduct disturbances
- mixed disturbance of emotions and conduct
- unspecified

Adjustment disorders are very common and can affect anyone, regardless of gender, age, race, or lifestyle. By definition, an adjustment disorder is short-lived, unless a person is faced with a chronic recurring crisis (such as a child who is repeatedly abused). In such cases, the adjustment disorder may last more than six months.

Causes and symptoms

An adjustment disorder occurs when a person can't cope with a stressful event and develops emotional or behavioral symptoms. The stressful event can be anything: it might be just one isolated incident, or a string of problems that wears the person down. The **stress** might be anything from a car accident or illness, to a divorce, or even a certain time of year (such as Christmas or summer).

People with adjustment disorder may have a wide variety of symptoms. How those symptoms combine depend on the particular subtype of adjustment disorder and on the individual's personality and psychological defenses. Symptoms normally include some (but not all) of the following:

- hopelessness
- sadness
- crying
- anxiety
- worry
- headaches or stomachaches
- withdrawal
- inhibition
- truancy
- vandalism
- reckless driving
- fighting
- other destructive acts

Diagnosis

It is extremely important that a thorough evaluation rule out other more serious mental disorders, since the treatment for adjustment disorder may be very different than for other mental problems.

In order to be diagnosed as a true adjustment disorder, the level of distress must be more severe than what would normally be expected in response to the stressor, or the symptoms must significantly interfere with a person's social, job, or school functioning. Normal expression of grief, in bereavement for instance, is not considered an adjustment disorder.

Treatment

Psychotherapy (counseling) is the treatment of choice for adjustment disorders, since the symptoms are an understandable reaction to a specific stress. The type of therapy depends on the mental health expert, but it usually is short-term treatment that focuses on resolving the immediate problem.

Therapy usually will help clients:

- develop coping skills
- understand how the stressor has affected their lives
- develop alternate social or recreational activities

Family or couples therapy may be helpful in some cases. Medications are not usually used to treat adjustment disorders, although sometimes a few days or weeks of an anti-anxiety drug can control anxiety or sleeping problems.

Self-help groups aimed at a specific problem (such as recovering from divorce or job loss) can be extremely helpful to people suffering from an adjustment disorder. Social support, which is usually an important part of self-help groups, can lead to a quicker recovery.

Prognosis

Most people recover completely from adjustment disorders, especially if they had no previous history of mental problems, and have a stable home life with strong social support. People with progressive or cyclic disorders (such as **multiple sclerosis**) may experience an adjustment disorder with each exacerbation period.

Resources

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KEY TERMS

Multiple sclerosis—A progressive disorder of the central nervous system in which scattered patches of the protective sheath covering the nerves is destroyed. The disease, which causes progressive paralysis, is marked by periods of exacerbation and remission. There is no cure.

Post-traumatic stress disorder (PTSD)—A specific form of anxiety that begins after a life-threatening event, such as rape, a natural disaster, or combat-related trauma.

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Adrenal gland cancer

Definition

Adrenal gland cancers are rare cancers occurring in the endocrine tissue of the adrenals. They are characterized by overproduction of adrenal gland hormones.

Description

Cancers of the adrenal gland are very rare. The adrenal gland is a hormone producing endocrine gland with two main parts, the cortex and the medulla. The main hormone of the adrenal cortex is cortisol and the main hormone of the adrenal medulla is epinephrine. When tumors develop in the adrenal gland, they secrete excess amounts of these hormones. A **cancer** that arises in the adrenal cortex is called an adrenocortical carcinoma and can produce high blood pressure, weight gain, excess body hair, weakening of the bones and diabetes. A cancer in the adrenal medulla is called a **pheochromocytoma** and can cause high blood pressure, **headache**, **pallitations**, and excessive perspiration. Although these cancers can happen at any age, most occur in young adults.

Causes and symptoms

It is not known what causes adrenal gland cancer, but some cases are associated with hereditary diseases.

KEY TERMS

Cortisol—A hormone produced by the adrenal cortex. It is partially responsible for regulating blood sugar levels.

Diabetes—A disease characterized by low blood sugar.

Epinephrine—A hormone produced by the adrenal medulla. It is important in the response to stress and partially regulates heart rate and metabolism. It is also called adrenaline.

Laparoscopy—The insertion of a tube through the abdominal wall. It can be used to visualize the inside of the abdomen and for surgical procedures.

Symptoms of adrenal cancer are related to the specific hormones produced by that tumor. An adrenocortical carcinoma typically secretes high amounts of cortisol, producing **Cushing's Syndrome**. This syndrome produces progressive weight gain, rounding of the face, and increased blood pressure. Women can experience menstrual cycle alterations and men can experience feminization. The symptoms for pheochromocytoma include **hypertension**, acidosis, unexplained **fever** and weight loss. Because of the hormones produced by this type of tumor, **anxiety** is often a feature also.

Diagnosis

Diagnosis for adrenal cancer usually begins with blood tests to evaluate the hormone levels. These hormones include epinephrine, cortisol, and testosterone. It also includes **magnetic resonance imaging**, and **computed tomography scans** to determine the extent of the disease. Urine and blood tests can be done to detect the high levels of hormone secreted by the tumor.

Treatment

Treatment is aimed at removing the tumor by surgery. In some cases, this can be done by **laparoscopy**. Surgery is sometimes followed by **chemotherapy** and/or **radiation therapy**. Because the surgery removes the source of many important hormones, hormones must be supplemented following surgery. If adrenocortical cancer recurs or has spread to other parts of the body (metastasized), additional surgery may be done followed by chemotherapy using the drug mitotane.

Alternative treatment

As with any form of cancer, all conventional treatment options should be considered and applied as appropriate. Nutritional support, as well as supporting the functioning of the entire person diagnosed with adrenal gland cancer through homeopathic medicine, **acupuncture**, vitamin and mineral supplementation, and herbal medicine, can benefit recovery and enhance quality of life.

Prognosis

The prognosis for adrenal gland cancer is variable. For localized pheochromocytomas the 5-year survival rate is 95%. This rate decreases with aggressive tumors that have metastasized. The prognosis for adrenal cortical cancer is not as good with a 5-year survival rate of 10-35%.

Prevention

Since so little is known about the cause of adrenal gland cancer, it is not known if it can be prevented.

Resources

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Endocrine Web. <<http://www.endocrineweb.com>>.

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Adrenal gland removal see **Adrenalectomy**

Adrenal gland scan

Definition

The adrenal gland scan is a nuclear medicine evaluation of the medulla (inner tissue) of the adrenal gland.

Purpose

The adrenal glands are a pair of small organs located just above the kidney, which contain two types of tissue. The adrenal cortex produces hormones that affect water balance and metabolism in the body. The adrenal medulla produces adrenaline and noradrenaline (also called epinephrine and norepinephrine).

An adrenal gland scan is done when too much adrenaline and noradrenaline is produced in the body and

a tumor in the adrenal gland is suspected. One such situation in which a tumor might be suspected is when high blood pressure (**hypertension**) does not respond to medication. Tumors that secrete adrenaline and noradrenaline can also be found outside the adrenal gland. An adrenal gland scan usually covers the abdomen, chest, and head.

Precautions

Adrenal gland scans are not recommended for pregnant women because of the potential harm to the developing fetus. A pregnant woman should discuss with her doctor the risks of the procedure against the benefits of the information it can provide in evaluating her individual medical situation.

People who have recently undergone tests that use barium must wait until the barium has been eliminated from their system in order to obtain accurate results from the adrenal gland scan.

Description

The adrenal gland scan takes several days. On the first day, a radiopharmaceutical is injected intravenously into the patient. On the second, third, and fourth day the patient is positioned under the camera for imaging. The scanning time each day takes approximately 30 minutes. It is essential that the patient remain still during imaging.

Occasionally, the scanning process may involve fewer than three days, or it may continue several days longer. The area scanned extends from the pelvis and lower abdomen to the lower chest. Sometimes the upper legs, thighs, and head are also included.

Preparation

For two days before and ten days after the injection of the radiopharmaceutical, patients are given either Lugol's solution or potassium iodine. This prevents the thyroid from taking up radioactive iodine and interfering with the scan.

Aftercare

The patient should not feel any adverse effects of the test and can resume normal activity immediately. Follow-up tests that might be ordered include a nuclear scan of the bones or kidney, a computed tomography scan (CT) of the adrenals, or an ultrasound of the pelvic area.

Risks

The main risk associated with this test is to the fetus of a pregnant woman.

KEY TERMS

Adrenal cortex—The outer tissue of the adrenal gland. It produces a group of chemically related hormones called corticosteroids that control mineral and water balance in the body and include aldosterone and cortisol.

Adrenal medulla—The inner tissue of the adrenal gland. It produces the hormones adrenaline and noradrenaline.

Lugol's solution—A strong iodine solution.

Normal results

Normal results will show no unusual areas of hormone secretion and no tumors.

Abnormal results

Abnormal results will show evidence of a tumor where there is excessive secretion of adrenaline or noradrenaline. Over 90% of these tumors are in the abdomen.

Resources

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A Manual of Laboratory and Diagnostic Tests. 5th ed. Ed. Francis Fishback. Philadelphia: Lippincott, 1996.

Tish Davidson

Adrenal hypofunction see **Addison's disease**

Adrenal insufficiency see **Addison's disease**

Adrenal virilism

Definition

Adrenal virilism is the development or premature development of male secondary sexual characteristics caused by male sex hormones (androgens) excessively produced by the adrenal gland. This disorder can occur before birth and can lead to sexual abnormalities in newborns. It can also occur in girls and women later in life.

Description

In the normal human body, there are two adrenal glands. They are small structures that lie on top of the

KEY TERMS

Glucocorticoid—A hormone produced by the adrenal gland; this hormone leads to an increase in blood sugar and creation of sugar molecules by the liver.

Hydrocortisone—A hormone in the group of glucocorticoid hormones.

Prednisone—A drug that functions as a glucocorticoid hormone.

kidneys. The adrenal glands produce many hormones that regulate body functions. These hormones include androgens, or male hormones. Androgens are produced in normal girls and women. Sometimes, one or both of the adrenal glands becomes enlarged or overactive, producing more than the usual amount of androgens. The excess androgens create masculine characteristics.

Causes and symptoms

In infants and children, adrenal virilism is usually the result of adrenal gland enlargement that is present at birth. This is called **congenital adrenal hyperplasia**. The cause is usually a genetic problem that leads to severe enzyme deficiencies. In rare cases, adrenal virilism is caused by an adrenal gland tumor. The tumor can be benign (adrenal adenoma) or cancerous (adrenal carcinoma). Sometimes virilism is caused by a type of tumor on a woman's ovary (arrhenoblastoma).

Newborn girls with adrenal virilism have external sex organs that seem to be a mixture of male and female organs (called female pseudohermaphroditism). Newborn boys with the disorder have enlarged external sex organs, and these organs develop at an abnormally rapid pace.

Children with congenital adrenal hyperplasia begin growing abnormally fast, but they stop growing earlier than normal. Later in childhood, they are typically shorter than normal but have well-developed trunks.

Women with adrenal virilization may develop facial hair. Typically, their menstrual cycles are infrequent or absent. They may also develop a deeper voice, a more prominent Adam's apple, and other masculine signs.

Diagnosis

Endocrinologists, doctors who specialize in the diagnosis and treatment of glandular disorders, have the most expertise to deal with adrenal virilization. Some

doctors who treat disorders of the internal organs (internists) and doctors who specialize in treating the reproductive system of women (gynecologists) may also be able to help patients with this disorder.

Diagnosis involves performing many laboratory tests on blood samples from the patient. These tests measure the concentration of different hormones. Different abnormalities of the adrenal gland produce a different pattern of hormonal abnormalities. These tests can also help determine if the problem is adrenal or ovarian. If a tumor is suspected, special x rays may be done to visualize the tumor in the body. Final diagnosis may depend on obtaining a tissue sample from the tumor (biopsy), and examining it under a microscope in order to verify its characteristics.

Treatment

Adrenal virilism caused by adrenal hyperplasia is treated with daily doses of a glucocorticoid. Usually prednisone is the drug of choice, but in infants hydrocortisone is usually given. Laboratory tests are usually needed from time to time to adjust the dosage. Girls with pseudohermaphroditism may require surgery to make their external sex organs appear more normal. If a tumor is causing the disorder, the treatment will depend on the type and location of the tumor. Information about the tumor cell type and the spread of the tumor is used to decide the best kind of treatment for a particular patient. If the tumor is cancerous, the patient will require special treatment depending on how far the **cancer** has advanced. Treatment can be a combination of surgery, medications used to kill cancer cells (**chemotherapy**), and x rays or other high energy rays used to kill cancer cells (**radiation therapy**). Sometimes the doctor must remove the adrenal gland and the surrounding tissues. If the tumor is benign, then surgically removing the tumor may be the best option.

Prognosis

Ongoing glucocorticoid treatment usually controls adrenal virilism in cases of adrenal hyperplasia, but there is no cure. If a cancerous tumor has caused the disorder, patients have a better prognosis if they have an early stage of cancer that is diagnosed quickly and has not spread.

Resources

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Richard H. Lampert

Adrenalectomy

Definition

Adrenalectomy is the surgical removal of one or both of the adrenal glands. The adrenal glands are paired endocrine glands, one located above each kidney, that produce hormones such as epinephrine, norepinephrine, androgens, estrogens, aldosterone, and cortisol. Adrenalectomy is usually performed by conventional (open) surgery, but in selected patients surgeons may use **laparoscopy**. With laparoscopy, adrenalectomy can be accomplished through four very small incisions.

Purpose

Adrenalectomy is usually advised for patients with tumors of the adrenal glands. Adrenal gland tumors may be malignant or benign, but all typically excrete excessive amounts of one or more hormones. A successful procedure will aid in correcting hormone imbalances, and may also remove cancerous tumors that can invade other parts of the body. Occasionally, adrenalectomy may be recommended when hormones produced by the adrenal glands aggravate another condition such as **breast cancer**.

Precautions

The adrenal glands are fed by numerous blood vessels, so surgeons need to be alert to extensive bleeding during surgery. In addition, the adrenal glands lie close to one of the body's major blood vessels (the vena cava), and to the spleen and the pancreas. The surgeon needs to remove the gland(s) without damaging any of these important and delicate organs.

Description

Open adrenalectomy

The surgeon may operate from any of four directions, depending on the exact problem and the patient's body type.

In the anterior approach, the surgeon cuts into the abdominal wall. Usually the incision will be horizontal, just under the rib cage. If the surgeon intends to operate

on only one of the adrenal glands, the incision will run under just the right or the left side of the rib cage. Sometimes a vertical incision in the middle of the abdomen provides a better approach, especially if both adrenal glands are involved.

In the posterior approach, the surgeon cuts into the back, just beneath the rib cage. If both glands are to be removed, an incision is made on each side of the body. This approach is the most direct route to the adrenal glands, but it does not provide quite as clear a view of the surrounding structures as the anterior approach.

In the flank approach, the surgeon cuts into the patient's side. This is particularly useful in massively obese patients. If both glands need to be removed, the surgeon must remove one gland, repair the surgical wound, turn the patient onto the other side, and repeat the entire process.

The last approach involves an incision into the chest cavity, either with or without part of the incision into the abdominal cavity. It is used when the surgeon anticipates a very large tumor, or if the surgeon needs to examine or remove nearby structures as well.

Laparoscopic adrenalectomy

This technique does not require the surgeon to open the body cavity. Instead, four small incisions (about 1/2 in diameter each) are made into a patient's flank, just under the rib cage. A laparoscope, which enables the surgeon to visualize the inside of the abdominal cavity on a television monitor, is placed through one of the incisions. The other incisions are for tubes that carry miniaturized versions of surgical tools. These tools are designed to be operated by manipulations that the surgeon makes outside the body.

Preparation

Most aspects of preparation are the same as in other major operations. In addition, hormone imbalances are often a major challenge. Whenever possible, physicians will try to correct hormone imbalances through medication in the days or weeks before surgery. Adrenal tumors may cause other problems such as **hypertension** or inadequate potassium in the blood, and these problems also should be resolved if possible before surgery is performed. Therefore, a patient may take specific medicines for days or weeks before surgery.

Most adrenal tumors can be imaged very well with a CT scan or MRI, and benign tumors tend to look different on these tests than do cancerous tumors. Surgeons may order a CT scan, MRI, or scintigraphy (viewing of the location of a tiny amount of radioactive agent) to help locate exactly where the tumor is.

KEY TERMS

Laparoscope—An instrument that enables the surgeon to see inside the abdominal cavity by means of a thin tube that carries an image to a television monitor.

Pancreas—An organ that secretes a number of digestive hormones and also secretes insulin to regulate blood sugar.

Pheochromocytoma—A tumor of specialized cells of the adrenal gland.

Spleen—An organ that traps and breaks down red blood cells at the end of their useful life and manufactures some key substances used by the immune system.

Vena cava—The large vein that drains directly into the heart after gathering incoming blood from the entire body.

The day before surgery, patients will probably have an enema to clear the bowels. In patients with lung problems or clotting problems, physicians may advise special preparations.

Aftercare

Patients stay in the hospital for various lengths of time after adrenalectomy. The longest hospital stays are required for open surgery using an anterior approach; hospital stays of about three days are indicated for open surgery using the posterior approach or for laparoscopic adrenalectomy.

The special concern after adrenalectomy is the patient's hormone balance. There may be several sets of lab tests to define hormone problems and monitor the results of drug treatment. In addition, blood pressure problems and infections are more common after removal of certain types of adrenal tumors.

As with most open surgery, surgeons are also concerned about blood clots forming in the legs and traveling to the lungs (venous thromboembolism), bowel problems, and postoperative pain. With laparoscopic adrenalectomy, these problems are somewhat less difficult, but they are still present.

Risks

The special risks of adrenalectomy involve major hormone imbalances, caused by the underlying disease,

the surgery, or both. These can include problems with wound healing itself, blood pressure fluctuations, and other metabolic problems.

Other risks are typical of many operations. These include:

- bleeding
- damage to adjacent organs (spleen, pancreas)
- loss of bowel function
- blood clots in the lungs
- lung problems
- surgical infections
- pain
- extensive scarring

Resources

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Richard H. Lampert
 Janis O. Flores

Adrenocortical insufficiency see **Addison's disease**

Adrenocorticotrophic hormone test

Definition

Adrenocorticotrophic hormone test (also known as an ACTH test or a corticotropin test) measures pituitary gland function.

Purpose

The pituitary gland produces the hormone ACTH, which stimulates the outer layer of the adrenal gland (the adrenal cortex). ACTH causes the release of the hormones hydrocortisone (cortisol), aldosterone, and androgen. The most important of these hormones released is cortisol. The ACTH test is used to determine if too much cortisol is being produced (**Cushing's syndrome**) or if not enough cortisol is being produced (**Addison's disease**).

Precautions

ACTH has diurnal variation, meaning that the levels of this hormone vary according to the time of day. The highest levels occur in the morning hours. Testing for normal secretion, as well as for Cushing's disease, may require multiple samples. For sequential follow-up, a blood sample analyzed for ACTH should always be drawn at the same time each day.

ACTH can be directly measured by an analyzing method (immunoassay) in many large laboratories. However, smaller laboratories are usually not equipped to perform this test and they may need to send the blood sample to a larger laboratory. Because of this delay, results may take several days to obtain.

Description

ACTH production is partly controlled by an area in the center of the brain (the hypothalamus) and partly controlled by the level of cortisol in the blood. When ACTH levels are too high, cortisol production increases to suppress ACTH release from the pituitary gland. If ACTH levels are too low, the hypothalamus produces corticotropin-releasing hormone (CRH) to stimulate the pituitary gland to make more ACTH. ACTH levels rise in response to **stress**, emotions, injury, infection, **burns**, surgery, and decreased blood pressure.

Cushing's syndrome

Cushing's syndrome is caused by an abnormally high level of circulating hydrocortisone. The high level may be the result of an adrenal gland tumor or enlargement of both adrenal glands due to a pituitary tumor. The high level of hydrocortisone may be the result of taking corticosteroid drugs for a long time. Corticosteroid drugs are widely used for inflammation in disorders like **rheumatoid arthritis**, inflammatory bowel disease, and **asthma**.

Addison's disease

Addison's disease is a rare disorder in which symptoms are caused by a deficiency of hydrocortisone and aldosterone. The most common cause of this disease is an autoimmune disorder. The immune system normally fights foreign invaders in the body like bacteria. In an autoimmune disorder, the immune systems attacks the body. In this case, the immune system produces antibodies that attack the adrenal glands. Addison's disease generally progresses slowly, with symptoms developing gradually over months or years. However, acute episodes, called Addisonian crises, are brought on by infection, injury, or other stresses. Diagnosis is generally made if the patient fails to respond to

KEY TERMS

Adrenal glands—A pair of endocrine glands that lie on top of the kidneys.

Pituitary gland—The most important of the endocrine glands, glands that release hormones directly into the bloodstream; sometimes called the master gland.

an injection of ACTH, which normally stimulates the secretion of hydrocortisone.

Preparation

A person's ACTH level is determined from a blood sample. The patient must fast from midnight until the test the next morning. This means that the patient cannot eat or drink anything after midnight except water. The patient must also avoid radioisotope scanning tests or recently administered radioisotopes prior to the blood test.

Risks

The risks associated with this test are minimal. They may include slight bleeding from the location where the blood was drawn. The patient may feel faint or lightheaded after the blood is drawn. Sometimes the patient may have an accumulation of blood under the puncture site (hematoma) after the test.

Normal results

Each laboratory will have its own set of normal values for this test. The normal values can range from: Morning (4-8 A.M.) 8-100 pg/mL or 10-80 ng/L (SI units) Evening (8-10 P.M.) less than 50 pg/mL or less than 50 ng/L (SI units)

Abnormal results

In Cushing's syndrome, high levels of ACTH may be caused by ACTH-producing tumors. These tumors may be either in the pituitary or in another area (like tumors from lung **cancer** or **ovarian cancer**). Low ACTH levels may be caused by adrenal enlargement due to high levels of cortisol and feedback to the pituitary.

In Addison's disease, high levels of ACTH may be caused by adrenal gland diseases. These diseases decrease adrenal hormones and the pituitary attempts to increase functioning. Low levels of ACTH may occur because of decreased pituitary function.

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Janis O. Flores

Adrenogenital syndrome see **Adrenal virilism**

Adrenoleukodystrophy

Definition

Adrenoleukodystrophy is a rare genetic disease characterized by a loss of myelin surrounding nerve cells in the brain and progressive adrenal gland dysfunction.

Description

Adrenoleukodystrophy (ALD) is a member of a group of diseases, leukodystrophies, that cause damage to the myelin sheath of nerve cells. Approximately one in 100,000 people is affected by ALD. There are three basic forms of ALD: childhood, adult-onset, and neonatal. The childhood form of the disease is the classical form and is the most severe. Childhood ALD is progressive and usually leads to total disability or **death**. It affects only boys because the genetic defect is sex-linked (carried on the X chromosome). Onset usually occurs between ages four and ten and can include many different symptoms, not all of which appear together. The most common symptoms are behavioral problems and poor memory. Other symptoms frequently seen are loss of vision, seizures, poorly articulated speech, difficulty swallowing, deafness, problems with gait and coordination, **fatigue**, increased skin pigmentation, and progressive **dementia**.

The adult-onset form of the disease, also called adrenomyeloneuropathy, is milder, progresses slowly, is usually associated with a normal life span, and usually appears between ages 21–35. Symptoms may include progressive stiffness, weakness, or **paralysis** of the lower limbs and loss of coordination. Brain function deterioration may also be seen. Women who are carriers of the disease occasionally experience the same symptoms, as well as others, including ataxia, hypertonia (excessive muscle tone), mild **peripheral neuropathy**, and urinary problems. The neonatal form affects both male and female infants and may produce **mental retardation**, facial abnormalities, seizures, retinal degeneration, poor

KEY TERMS

Amniocentesis—The collection of amniotic fluid through a needle inserted through the abdomen. Used to collect fetal cells for genetic analysis.

Ataxia—Loss of coordination of muscular movement.

Hypertonia—Having excessive muscular tone.

Myelin—A layer that encloses nerve cells and some axons and is made largely of lipids and lipoproteins.

Neuropathy—A disease or abnormality of the peripheral nerves.

muscle tone, enlarged liver, and adrenal dysfunction. Neonatal ALD usually progresses rapidly.

Causes and symptoms

The genetic defect in ALD causes a decrease in the ability to degrade very long chain fatty acids. These build up in the adrenal glands, brain, plasma, and fibroblasts. The build-up of very long chain fatty acids interferes with the ability of the adrenal gland to convert cholesterol into steroids and causes demyelination of nerves in the white matter of the brain. Demyelinated nerve cells are unable to function properly.

Diagnosis

Diagnosis is made based on observed symptoms, a biochemical test, and a family history. The biochemical test detects elevated levels of very long chain fatty acids in samples from **amniocentesis**, chorionic villi, plasma, red blood cells, or fibroblasts. A family history may indicate the likelihood of ALD because the disease is carried on the X-chromosome by the female lineage of families.

Treatment

Treatment for all forms of ALD consists of treating the symptoms and supporting the patient with physical therapy, psychological counseling, and special education in some cases. There is no cure for this disease, and there are no drugs that can reverse demyelination of nerve and brain cells. Dietary measures consist of reducing the intake of foods high in fat, which are a source of very long chain fatty acids. A mixture called Lorenzo's Oil has been shown to reduce the level of long chain fatty acids if used long term; however, the rate of myelin loss

is unaffected. Experimental **bone marrow transplantation** has not been very effective.

Prognosis

Prognosis for childhood and neonatal ALD patients is poor because of the progressive myelin degeneration. Death usually occurs between one and ten years after onset of symptoms.

Prevention

Since ALD is a genetic disease, prevention is largely limited to **genetic counseling** and fetal monitoring through amniocentesis or **chorionic villus sampling**.

Resources

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John T. Lohr, PhD

Adrenomyeloneuropathy see **Adrenoleukodystrophy**

This is the all-important site where oxygen passes from air that is inhaled to the blood, which carries it to all parts of the body. Any form of lung injury that damages this point of contact, called the alveolo-capillary junction, will allow blood and tissue fluid to leak into the alveoli, eventually filling them so that air cannot enter. The result is the type of breathing distress called ARDS. ARDS is one of the major causes of excess fluid in the lungs, the other being **heart failure**.

Along with fluid there is a marked increase in inflamed cells in the lungs. There also is debris left over from damaged lung cells, and fibrin, a semi-solid material derived from blood in the tissues. Typically these materials join together with large molecules in the blood (proteins), to form hyaline membranes. (These membranes are very prominent in premature infants who develop respiratory distress syndrome; it is often called hyaline membrane disease.) If ARDS is very severe or lasts a long time, the lungs do not heal, but rather become scarred, a process known as fibrosis. The lack of a normal amount of oxygen causes the blood vessels of the lung to become narrower, and in time they, too, may become scarred and filled with clotted blood. The lungs as a whole become very "stiff," and it becomes much harder for the patient to breathe.

Causes and symptoms

A very wide range of diseases or toxic substances, including some drugs, can cause ARDS. They include:

- Breathing in (aspiration) of the stomach contents when regurgitated, or salt water or fresh water from nearly drowning.
- Inhaling smoke, as in a fire; toxic materials in the air, such as ammonia or hydrocarbons; or too much oxygen, which itself can injure the lungs.
- Infection by a virus or bacterium, or **sepsis**, a widespread infection that gets into the blood.
- Massive trauma, with severe injury to any part of the body.
- Shock with persistently low blood pressure may not in itself cause ARDS, but it can be an important factor.
- A blood clotting disorder called disseminated intravascular coagulation, in which blood clots form in vessels throughout the body, including the lungs.
- A large amount of fat entering the circulation and traveling to the lungs, where it lodges in small blood vessels, injuring the cells lining the vessel walls.
- An overdose of a narcotic drug, a sedative, or, rarely, **aspirin**.

Adult respiratory distress syndrome

Definition

Adult respiratory distress syndrome (ARDS), also called acute respiratory distress syndrome, is a type of lung (pulmonary) failure that may result from any disease that causes large amounts of fluid to collect in the lungs. ARDS is not itself a specific disease, but a syndrome, a group of symptoms and signs that make up one of the most important forms of lung or **respiratory failure**. It can develop quite suddenly in persons whose lungs have been perfectly normal. Very often ARDS is a true medical emergency. The basic fault is a breakdown of the barrier, or membrane, that normally keeps fluid from leaking out of the small blood vessels of the lung into the breathing sacs (the alveoli).

Description

Another name for ARDS is shock lung. Its formal name is misleading, because children, as well as adults, may be affected. In the lungs the smallest blood vessels, or capillaries, make contact with the alveoli, tiny air sacs at the tips of the smallest breathing tubes (the bronchi).

KEY TERMS

Alveoli—The tiny air sacs at the ends of the breathing tubes of the lung where oxygen normally is taken up by the capillaries to enter the circulation.

Aspiration—The process in which solid food, liquids, or secretions that normally are swallowed are, instead, breathed into the lungs.

Capillaries—The smallest arteries which, in the lung, are located next to the alveoli so that they can pick up oxygen from inhaled air.

Face mask—The simplest way of delivering a high level of oxygen to patients with ARDS or other low-oxygen conditions.

Steroids—A class of drugs resembling normal body substances that often help control inflammation in the body tissues.

Ventilator—A mechanical device that can take over the work of breathing for a patient whose lungs are injured or are starting to heal.

- Inflammation of the pancreas (**pancreatitis**), when blood proteins, called enzymes, pass to the lungs and injure lung cells.
- Severe burn injury.
- Injury of the brain, or bleeding into the brain, from any cause may be a factor in ARDS for reasons that are not clear. Convulsions also may cause some cases.

Usually ARDS develops within one to two days of the original illness or injury. The person begins to take rapid but shallow breaths. The doctor who listens to the patient's chest with a stethoscope may hear "crackling" or **wheezing** sounds. The low blood oxygen content may cause the skin to appear mottled or even blue. As fluid continues to fill the breathing sacs, the patient may have great trouble breathing, take very rapid breaths, and gasp for air.

Diagnosis

A simple test using a device applied to the ear will show whether the blood is carrying too little oxygen, and this can be confirmed by analyzing blood taken from an artery. The **chest x ray** may be normal in the early stages, but, in a short time, fluid will be seen where it does not belong. The two lungs are about equally affected. A heart of normal size indicates that the problem actually is ARDS and not heart failure. Another way a physician can distinguish between these two possibilities is to place a catheter

into a vein and advance it into the main artery of the lung. In this way, the pressure within the pulmonary capillaries can be measured. Pressure within the pulmonary capillaries is elevated in heart failure, but normal in ARDS.

Treatment

The three main goals in treating patients with ARDS are:

- To treat whatever injury or disease has caused ARDS. Examples are: to treat septic infection with the proper **antibiotics**, and to reduce the level of oxygen therapy if ARDS has resulted from a toxic level of oxygen.
- To control the process in the lungs that allows fluid to leak out of the blood vessels. At present there is no certain way to achieve this. Certain steroid hormones have been tried because they can combat inflammation, but the actual results have been disappointing.
- To make sure the patient gets enough oxygen until the lung injury has had time to heal. If oxygen delivered by a face mask is not enough, the patient is placed on a ventilator, which takes over breathing, and, through a tube placed in the nose or mouth (or an incision in the windpipe), forces oxygen into the lungs. This treatment must be closely supervised, and the pressure adjusted so that too much oxygen is not delivered.

Patients with ARDS should be cared for in an intensive care unit, where experienced staff and all needed equipment are available. Enough fluid must be provided, by vein if necessary, to prevent **dehydration**. Also, the patient's nutritional state must be maintained, again by vein, if oral intake is not sufficient.

Prognosis

If the patient's lung injury does not soon begin to heal, the lack of sufficient oxygen can injure other organs, such as the kidneys. There always is a risk that bacterial **pneumonia** will develop at some point. Without prompt treatment, as many as 90% of patients with ARDS can be expected to die. With modern treatment, however, about half of all patients will survive. Those who do live usually recover completely, with little or no long-term breathing difficulty. Lung scarring is a risk after a long period on a ventilator, but it may improve in the months after the patient is taken off ventilation. Whether a particular patient will recover depends to a great extent on whether the primary disease that caused ARDS to develop in the first place can be effectively treated.

Prevention

The only way to prevent ARDS is to avoid those diseases and harmful conditions that damage the lung. For

instance, the danger of aspirating stomach contents into the lungs can be avoided by making sure a patient does not eat shortly before receiving general anesthesia. If a patient needs oxygen therapy, as low a level as possible should be given. Any form of lung infection, or infection anywhere in the body that gets into the blood, must be treated promptly to avoid the lung injury that causes ARDS.

Resources

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ORGANIZATIONS

National Heart, Lung and Blood Institute. P.O. Box 30105, Bethesda, MD 20824-0105. (301) 251-1222. <<http://www.nhlbi.nih.gov>>.

National Respiratory Distress Syndrome Foundation. P.O. Box 723, Montgomeryville, PA 18936.

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David A. Cramer, MD

AFP test see **Alpha-fetoprotein test**

African American health see **Minority health**

African sleeping sickness see **Sleeping sickness**

African trypanosomiasis see **Sleeping sickness**

Agammaglobulinemia see **Common variable immunodeficiency**

Aggression see **Conduct disorder**

the latter half of life, an individual is more prone to have problems with the various functions of the body and to develop any number of chronic or fatal diseases. The cardiovascular, digestive, excretory, nervous, reproductive and urinary systems are particularly affected. The most common diseases of aging include Alzheimer's, arthritis, cancer, diabetes, depression, and heart disease.

Description

Human beings reach a peak of growth and development around the time of their mid 20s. Aging is the normal transition time after that flurry of activity. Although there are quite a few age-related changes that tax the body, disability is not necessarily a part of aging. Health and lifestyle factors together with the genetic makeup of the individual, and determines the response to these changes. Body functions that are most often affected by age include:

- Hearing, which declines especially in relation to the highest pitched tones.
- The proportion of fat to muscle, which may increase by as much as 30%. Typically, the total padding of body fat directly under the skin thins out and accumulates around the stomach. The ability to excrete fats is impaired, and therefore the storage of fats increases, including cholesterol and fat-soluble nutrients.
- The amount of water in the body decreases, which therefore decreases the absorption of water-soluble nutrients. Also, there is less saliva and other lubricating fluids.
- The liver and the kidneys cannot function as efficiently, thus affecting the elimination of wastes.
- A decrease in the ease of digestion, with a decrease in stomach acid production.
- A loss of muscle strength and coordination, with an accompanying loss of mobility, agility, and flexibility.
- A decline in sexual hormones and sexual functioning.
- A decrease in the sensations of taste and smell.
- Changes in the cardiovascular and respiratory systems, leading to decreased oxygen and nutrients throughout the body.
- Decreased functioning of the nervous system so that nerve impulses are not transmitted as efficiently, reflexes are not as sharp, and memory and learning are diminished.
- A decrease in bone strength and density.
- Hormone levels, which gradually decline. The thyroid and sexual hormones are particularly affected.
- Declining visual abilities. Age-related changes may lead to diseases such as **macular degeneration**.

Aging

Definition

Starting at what is commonly called middle age, operations of the human body begin to be more vulnerable to daily wear and tear; there is a general decline in physical, and possibly mental, functioning. In the Western countries, the length of life is often into the 70s. The upward limit of the life span, however, can be as high as 120 years. During

- A compromised ability to produce vitamin D from sunlight.
- A reduction in protein formation leading to shrinkage in muscle mass and decreased bone formation, possibly leading to osteoporosis.

Causes and symptoms

There are several theories as to why the aging body loses functioning. It may be that several factors work together or that one particular factor is at work more than others in a given individual.

- Programmed senescence, or aging clock, theory. The aging of the cells of each individual is programmed into the genes, and there is a preset number of possible rejuvenations in the life of a given cell. When cells die at a rate faster than they are replaced, organs do not function properly, and they are soon unable to maintain the functions necessary for life.
- Genetic theory. Human cells maintain their own seed of destruction at the level of the chromosomes.
- Connective tissue, or cross-linking theory. Changes in the make-up of the connective tissue alter the stability of body structures, causing a loss of elasticity and functioning, and leading to symptoms of aging.
- Free-radical theory. The most commonly held theory of aging, it is based on the fact that ongoing chemical reactions of the cells produce free radicals. In the presence of oxygen, these free radicals cause the cells of the body to break down. As time goes on, more cells die or lose the ability to function, and the body soon ceases to function as a whole.
- Immunological theory. There are changes in the immune system as it begins to wear out, and the body is more prone to infections and tissue damage, which may finally cause **death**. Also, as the system breaks down, the body is more apt to have autoimmune reactions, in which the body's own cells are mistaken for foreign material and are destroyed or damaged by the immune system.

Diagnosis

Many problems can arise due to age-related changes in the body. Although there is no one test to be given, a thorough physical exam and a basic blood screening and blood chemistry panel can point to areas in need of further attention. When older people become ill, the first signs of disease are often nonspecific. Further exams should be conducted if any of the following occur:

- diminished or lack of desire for food
- increasing confusion

- failure to thrive
- urinary incontinence
- dizziness
- weight loss
- falling

Treatment

For the most part, doctors prescribe medications to control the symptoms and diseases of aging. In the United States, about two-thirds of people 65 and over take medications for various complaints. More women than men use these medications. The most common drugs used by the elderly are painkillers, **diuretics** or water pills, sedatives, cardiac drugs, **antibiotics**, and mental health drugs.

Estrogen replacement therapy (ERT) is commonly prescribed to postmenopausal women for symptoms of aging. It is often used in conjunction with progesterone. ERT functions to help keep bones strong, reduce risk of heart disease, restore vaginal lubrication, and to improve skin elasticity. Evidence suggests that it may also help maintain mental functions.

Expected results

Aging is unavoidable, but major physical impairment is not. People can lead a healthy, disability-free life well through their later years. A well established support system of family, friends, and health care providers, together with focus on good **nutrition** and lifestyle habits and good **stress** management, can prevent disease and lessen the impact of chronic conditions.

Alternative treatment

Nutritional supplements

Consumption of a high-quality multivitamin is recommended. Common nutritional deficiencies connected with aging include B **vitamins**, vitamins A and C, **folic acid**, calcium, magnesium, zinc, iron, chromium, and trace **minerals**. Since stomach acids may be decreased, it is suggested that the use of a powdered multivitamin formula in gelatin capsules be used, as this form is the easiest to digest. Such formulas may also contain enzymes for further help with digestion.

Antioxidants can help to neutralize damage by the free radical actions thought to contribute to problems of aging. They are also helpful in preventing and treating cancer and in treating **cataracts** and **glaucoma**. Supplements that serve as antioxidants include:

- Vitamin E, 400–1,000 IUs daily. Protects cell membranes against damage. It shows promise in prevention against heart disease, and Alzheimer's and Parkinson's diseases.
- Selenium, 50 mg taken twice daily. Research suggests that selenium may play a role in reducing the risk of cancer.
- Beta-carotene, 25,000–40,000 IUs daily. May help in treating cancer, colds and flu, arthritis, and immune support.
- Vitamin C, 1,000–2,000 mg per day. It may cause **diarrhea** in large doses. If this occurs, however, all that is needed is a decrease in the dosage.

Other supplements that are helpful in treating age-related problems including:

- B₁₂/B-complex vitamins, studies show that B₁₂ may help reduce mental symptoms, such as confusion, memory loss, and depression.
- Coenzyme Q10 may be helpful in treating heart disease, as up to three-quarters cardiac patients have been found to be lacking in this heart enzyme.

Hormones

The following hormone supplements may be taken to prevent or to treat various age-related problems. However, caution should be taken before beginning treatment, and the patient should consult his or her health care professional.

DHEA improves brain functioning and serves as a building block for many other important hormones in the body. It may be helpful in restoring declining hormone levels and in building up muscle mass, strengthening the bones, and maintaining a healthy heart.

Melatonin may be helpful for **insomnia**. It has also been used to help fight viruses and bacterial infections, reduce the risk of heart disease, improve sexual functioning, and to protect against cancer.

Human growth hormone (hGH) has been shown to regulate blood sugar levels and to stimulate bone, cartilage, and muscle growth while reducing fat.

Herbs

Garlic (*Allium sativa*) is helpful in preventing heart disease, as well as improving the tone and texture of skin. Garlic stimulates liver and digestive system functions, and also helps in dealing with heart disease and high blood pressure.

Siberian ginseng (*Eleutherococcus senticosus*) supports the adrenal glands and immune functions. It is

KEY TERMS

Antioxidants—Substances that reduce the damage of the highly reactive free radicals that are the byproducts of the cells.

Alzheimer's disease—A condition causing a decline in brain function that interferes with the ability to reason and to perform daily activities.

Senescence—Aging.

Vata—One of the three main constitutional types found under Ayurvedic principles. Keeping one's particular constitution in balance is considered important in maintaining health.

believed to be helpful in treating problems related to stress. Siberian ginseng also increases mental and physical performance, and may be useful in treating memory loss, chronic **fatigue**, and immune dysfunction.

Ginkgo biloba works particularly well on the brain and nervous system. It is effective in reducing the symptoms of conditions, such as Alzheimer's, depression, visual problems, and problems of blood circulation. It may also help treat heart disease, strokes, **dementia**, **Raynaud's disease**, head injuries, leg cramps, macular degeneration, **tinnitus**, **impotence** due to poor blood flow, and diabetes-related nerve damage.

Proanthocyanidins, or PCO, are Pycnogenol, derived from grape seeds and skin, and from pine tree bark, and may help in the prevention of cancer and poor vision.

In **Ayurvedic medicine**, aging is described as a process of increased vata, in which there is a tendency to become thinner, drier, more nervous, more restless, and more fearful, while having a loss of appetite as well as sleep. Bananas, almonds, avocados, and coconuts are some of the foods used in correcting such conditions. One of the main herbs used for such conditions is gotu kola (*Centella asiatica*), which is used to revitalize the nervous system and brain cells and to fortify the immune system. Gotu kola is also used to treat memory loss, **anxiety**, and insomnia.

In Chinese medicine, most symptoms of aging are regarded as symptoms of a yin deficiency. Moistening foods such as millet, barley soup, tofu, mung beans, wheat germ, spirulina, potatoes, black sesame seeds, walnuts, and flax seeds are recommended. Jing tonics may also be used. These include deer antler, dodder seeds, processed rehmannia, longevity soup, mussels, and chicken.

Prevention

Preventive health practices such as healthy diet, daily **exercise**, stress management, and control of lifestyle habits such as **smoking** and drinking, can lengthen the life span and improve the quality of life as people age. Exercise can improve the appetite, the health of the bones, the emotional and mental outlook, and the digestion and circulation.

Drinking plenty of fluids aids in maintaining healthy skin, good digestion, and proper elimination of wastes. Up to eight glasses of water should be consumed daily, along with plenty of herbal teas, diluted fruit and vegetable juices, and fresh fruits and vegetables with high water content.

Because of a decrease in the sense of taste, older people often increase their intake of salt, which can contribute to high blood pressure and nutrient loss. Use of sugar is also increased. Seaweeds and small amounts of honey can be used as replacements.

Alcohol, nicotine, and **caffeine** all have potential damaging effects, and should be limited or completely eliminated from consumption.

A diet high in fiber and low in fat is recommended. Processed foods should be replaced by complex carbohydrates, such as whole grains. If chewing becomes a problem, there should be an increased intake of protein drinks, freshly juiced fruits and vegetables, and creamed cereals.

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Patience Paradox

Agoraphobia

Definition

The word agoraphobia is derived from Greek words literally meaning “fear of the marketplace.” The term is used to describe an irrational and often disabling fear of being out in public.

Description

Agoraphobia is just one type of phobia, or irrational fear. People with **phobias** feel dread or panic when they face certain objects, situations, or activities. People with agoraphobia frequently also experience panic attacks, but panic attacks, or **panic disorder**, are not a requirement for a diagnosis of agoraphobia. The defining feature of agoraphobia is **anxiety** about being in places from which escape might be embarrassing or difficult, or in which help might be unavailable. The person suffering from agoraphobia usually avoids the anxiety-provoking situation and may become totally housebound.

Causes and symptoms

Agoraphobia is the most common type of phobia, and it is estimated to affect between 5-12% of Americans within their lifetime. Agoraphobia is twice as common in women as in men and usually strikes between the ages of 15-35.

The symptoms of the panic attacks which may accompany agoraphobia vary from person to person, and may include trembling, sweating, heart **palpitations** (a feeling of the heart pounding against the chest), jitters, **fatigue**, tingling in the hands and feet, nausea, a rapid pulse or breathing rate, and a sense of impending doom.

Agoraphobia and other phobias are thought to be the result of a number of physical and environmental factors. For instance, they have been associated with biochemical imbalances, especially related to certain neurotransmitters (chemical nerve messengers) in the brain. People who have a panic attack in a given situation (e.g., a shopping mall) may begin to associate the panic with that situation and learn to avoid it. According to some theories, irrational anxiety results from unresolved emotional conflicts. All of these factors may play a role to varying extents in different cases of agoraphobia.

Diagnosis

People who suffer from panic attacks should discuss the problem with a physician. The doctor can diagnose the underlying panic or anxiety disorder and make sure the symptoms aren't related to some other underlying medical condition.

The doctor makes the diagnosis of agoraphobia based primarily on the patient's description of his or her symptoms. The person with agoraphobia experiences anxiety in situations where escape is difficult or help is unavailable—or in certain situations, such as being alone. While many people are somewhat apprehensive in these situations, the hallmark of agoraphobia is that a person's active avoidance of the feared situation impairs his or her ability to work, socialize, or otherwise function.

Treatment

Treatment for agoraphobia usually consists of both medication and psychotherapy. Usually, patients can benefit from certain antidepressants, such as amitriptyline (Elavil), or **selective serotonin reuptake inhibitors**, such as paroxetine (Paxil), fluoxetine (Prozac), or sertraline (Zoloft). In addition, patients may manage panic attacks in progress with certain tranquilizers called **benzodiazepines**, such as alprazolam (Xanax) or clonazepam (Klonipin).

The mainstay of treatment for agoraphobia and other phobias is cognitive behavioral therapy. A specific technique that is often employed is called desensitization. The patient is gradually exposed to the situation that usually triggers fear and avoidance, and, with the help of breathing or relaxation techniques, learns to cope with the situation. This helps break the mental connection between the situation and the fear, anxiety, or panic. Patients may also benefit from psychodynamically oriented psychotherapy, discussing underlying emotional conflicts with a therapist or support group.

Prognosis

With proper medication and psychotherapy, 90% of patients will find significant improvement in their symptoms.

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KEY TERMS

Benzodiazepines—A group of tranquilizers often used to treat anxiety.

Desensitization—A treatment for phobias which involves exposing the phobic person to the feared situation. It is often used in conjunction with relaxation techniques.

Phobia—An intense and irrational fear of a specific object, activity, or situation.

"Panic Disorder—Panic Attacks and Agoraphobia." *American Family Physician* 52, no. 7 (15 Nov. 1995): 2067-8.

ORGANIZATIONS

American Psychiatric Association. 1400 K Street NW, Washington DC 20005. (888) 357-7924. <<http://www.psych.org>>.

Anxiety Disorders Association of America. 11900 Park Lawn Drive, Ste. 100, Rockville, MD 20852. (800) 545-7367. <<http://www.adaa.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>>.

Robert Scott Dinsmoor

Agranulocytosis see **Neutropenia**

AIDS

Definition

Acquired immune deficiency syndrome (AIDS) is an infectious disease caused by the human **immunodeficiency** virus (HIV). It was first recognized in the United States in 1981. AIDS is the advanced form of infection with the HIV virus, which may not cause recognizable disease for a long period after the initial exposure (latency). No vaccine is currently available to prevent HIV infection. At present, all forms of AIDS therapy are focused on improving the quality and length of life for AIDS patients by slowing or halting the replication of the virus and treating or preventing infections and cancers that take advantage of a person's weakened immune system.

Description

AIDS is considered one of the most devastating public health problems in recent history. In June 2000, the Centers

Risk of acquiring HIV infection by entry site

Entry site	Risk virus reaches entry site	Risk virus enters	Risk inoculated
Conjunctiva	Moderate	Moderate	Very low
Oral mucosa	Moderate	Moderate	Low
Nasal mucosa	Low	Low	Very low
Lower respiratory	Very low	Very low	Very low
Anus	Very high	Very high	Very high
Skin, intact	Very low	Very low	Very low
Skin, broken	Low	High	High
Sexual:			
Vagina	Low	High	High
Penis	Low	Low	High
Ulcers (STD)	Medium	Low	Very high
Blood:			
Products	High	High	Low
Shared needles	High	High	High
Accidental needle	High	Very High	Low
Traumatic wound	Modest	High	High
Perinatal	High	High	High

for Disease Control and Prevention (CDC) reported that 120,223 (includes only those cases in areas that have confidential HIV reporting) in the United States are HIV-positive, and 311,701 are living with AIDS (includes only those cases where vital status is known). Of these patients, 44% are gay or bisexual men, 20% are heterosexual intravenous drug users, and 17% are women. In addition, approximately 1,000-2,000 children are born each year with HIV infection. The World Health Organization (WHO) estimates that 33 million adults and 1.3 million children worldwide were living with HIV/AIDS as of 1999 with 5.4 million being newly infected that year. Most of these cases are in the developing countries of Asia and Africa.

Risk factors

AIDS can be transmitted in several ways. The risk factors for HIV transmission vary according to category:

- **Sexual contact.** Persons at greatest risk are those who do not practice safe sex, those who are not monogamous, those who participate in anal intercourse, and those who have sex with a partner with symptoms of advanced HIV infection and/or other **sexually transmitted diseases (STDs)**. In the United States and Europe, most cases of sexually transmitted HIV infection have resulted from homosexual contact, whereas in Africa, the disease is spread primarily through sexual intercourse among heterosexuals.
- **Transmission in pregnancy.** High-risk mothers include women married to bisexual men or men who have an abnormal blood condition called **hemophilia** and require blood transfusions, intravenous drug users, and women living in neighborhoods with a high rate of HIV

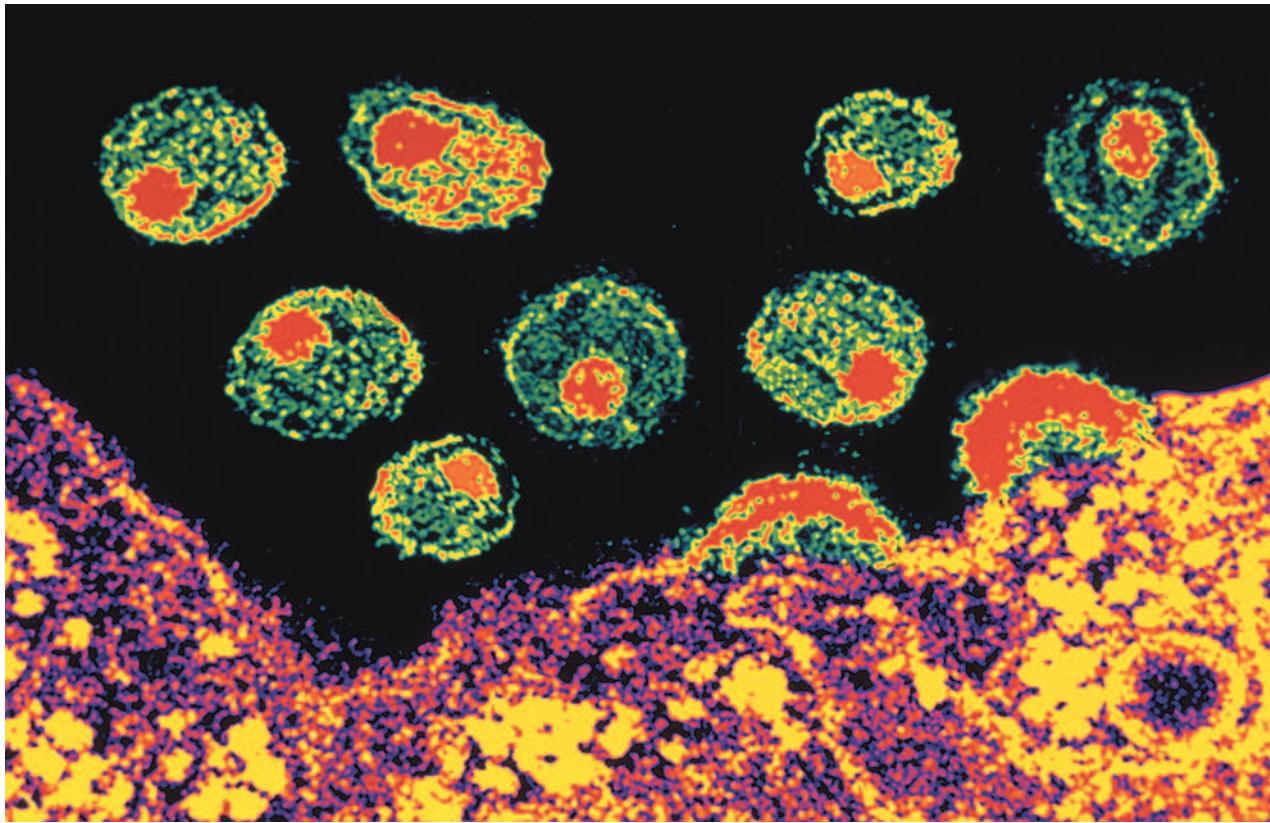
infection among heterosexuals. The chances of transmitting the disease to the child are higher in women in advanced stages of the disease. Breast feeding increases the risk of transmission by 10-20%. The use of zidovudine (AZT) during pregnancy, however, can decrease the risk of transmission to the baby.

- Exposure to contaminated blood or blood products. With the introduction of blood product screening in the mid-1980s, the incidence of HIV transmission in blood transfusions has dropped to one in every 100,000 transfused. With respect to HIV transmission among drug abusers, risk increases with the duration of using injections, the frequency of needle sharing, the number of persons who share a needle, and the number of AIDS cases in the local population.
- Needle sticks among health care professionals. Present studies indicate that the risk of HIV transmission by a needle stick is about one in 250. This rate can be decreased if the injured worker is given AZT, an anti-retroviral medication, in combination with other medication.

HIV is not transmitted by handshakes or other casual non-sexual contact, coughing or sneezing, or by blood-sucking insects such as mosquitoes.

AIDS in women

AIDS in women is a serious public health concern. Women exposed to HIV infection through heterosexual contact are the most rapidly growing risk group in the United States population. The percentage of AIDS cases diagnosed in women has risen from 7% in 1985 to 23% in 1999. Women diagnosed with AIDS may not live as long as men, although the reasons for this finding are unclear.



Mature HIV-1 viruses (above) and the lymphocyte from which they emerged (below). Two immature viruses can be seen budding on the surface of the lymphocyte (right of center). (Photograph by Scott Camazir, Photo Researchers, Inc. Reproduced by permission.)

AIDS in children

Since AIDS can be transmitted from an infected mother to the child during pregnancy, during the birth process, or through breast milk, all infants born to HIV-positive mothers are a high-risk group. As of 2000, it was estimated that 87% of HIV-positive women are of childbearing age; 41% of them are drug abusers. Between 15–30% of children born to HIV-positive women will be infected with the virus.

AIDS is one of the 10 leading causes of **death** in children between one and four years of age. The interval between exposure to HIV and the development of AIDS is shorter in children than in adults. Infants infected with HIV have a 20–30% chance of developing AIDS within a year and dying before age three. In the remainder, AIDS progresses more slowly; the average child patient survives to seven years of age. Some survive into early adolescence.

Causes and symptoms

Because HIV destroys immune system cells, AIDS is a disease that can affect any of the body's major organ systems. HIV attacks the body through three disease

processes: immunodeficiency, autoimmunity, and nervous system dysfunction.

Immunodeficiency describes the condition in which the body's immune response is damaged, weakened, or is not functioning properly. In AIDS, immunodeficiency results from the way that the virus binds to a protein called CD4, which is primarily found on the surface of certain subtypes of white blood cells called helper T cells or CD4 cells. After the virus has attached to the CD4 receptor, the virus-CD4 complex refolds to uncover another receptor called a chemokine receptor that helps to mediate entry of the virus into the cell. One chemokine receptor in particular, CCR5, has gotten recent attention after studies showed that defects in its structure (caused by genetic mutations) cause the progression of AIDS to be prevented or slowed. Scientists hope that this discovery will lead to the development of drugs that trigger an artificial mutation of the CCR5 gene or target the CCR5 receptor.

Once HIV has entered the cell, it can replicate intracellularly and kill the cell in ways that are still not completely understood. In addition to killing some lymphocytes directly, the AIDS virus disrupts the functioning of

the remaining CD4 cells. Because the immune system cells are destroyed, many different types of infections and cancers that take advantage of a person's weakened immune system (opportunistic) can develop.

Autoimmunity is a condition in which the body's immune system produces antibodies that work against its own cells. Antibodies are specific proteins produced in response to exposure to a specific, usually foreign, protein or particle called an antigen. In this case, the body produces antibodies that bind to blood platelets that are necessary for proper blood clotting and tissue repair. Once bound, the antibodies mark the platelets for removal from the body, and they are filtered out by the spleen. Some AIDS patients develop a disorder, called immune-related **thrombocytopenia** purpura (ITP), in which the number of blood platelets drops to abnormally low levels.

As of 2000, researchers do not know precisely how HIV attacks the nervous system since the virus can cause damage without infecting nerve cells directly. One theory is that, once infected with HIV, one type of immune system cell, called a macrophage, begins to release a toxin that harms the nervous system.

The course of AIDS generally progresses through three stages, although not all patients will follow this progression precisely:

Acute retroviral syndrome

Acute retroviral syndrome is a term used to describe a group of symptoms that can resemble mononucleosis and that may be the first sign of HIV infection in 50-70% of all patients and 45-90% of women. Most patients are not recognized as infected during this phase and may not seek medical attention. The symptoms may include **fever**, **fatigue**, muscle aches, loss of appetite, digestive disturbances, weight loss, skin **rashes**, **headache**, and chronically swollen lymph nodes (lymphadenopathy). Approximately 25-33% of patients will experience a form of **meningitis** during this phase in which the membranes that cover the brain and spinal cord become inflamed. Acute retroviral syndrome develops between one and six weeks after infection and lasts for two to three weeks. Blood tests during this period will indicate the presence of virus (viremia) and the appearance of the viral p24 antigen in the blood.

Latency period

After the HIV virus enters a patient's lymph nodes during the acute retroviral syndrome stage, the disease becomes latent for as many as 10 years or more before symptoms of advanced disease develop. During latency, the virus continues to replicate in the lymph nodes, where it may cause one or more of the following conditions:

PERSISTENT GENERALIZED LYMPHADENOPATHY (PGL). Persistent generalized lymphadenopathy, or PGL, is a condition in which HIV continues to produce chronic painless swellings in the lymph nodes during the latency period. The lymph nodes that are most frequently affected by PGL are those in the areas of the neck, jaw, groin, and armpits. PGL affects between 50-70% of patients during latency.

CONSTITUTIONAL SYMPTOMS. Many patients will develop low-grade fevers, chronic fatigue, and general weakness. HIV may also cause a combination of food malabsorption, loss of appetite, and increased metabolism that contribute to the so-called AIDS wasting or wasting syndrome.

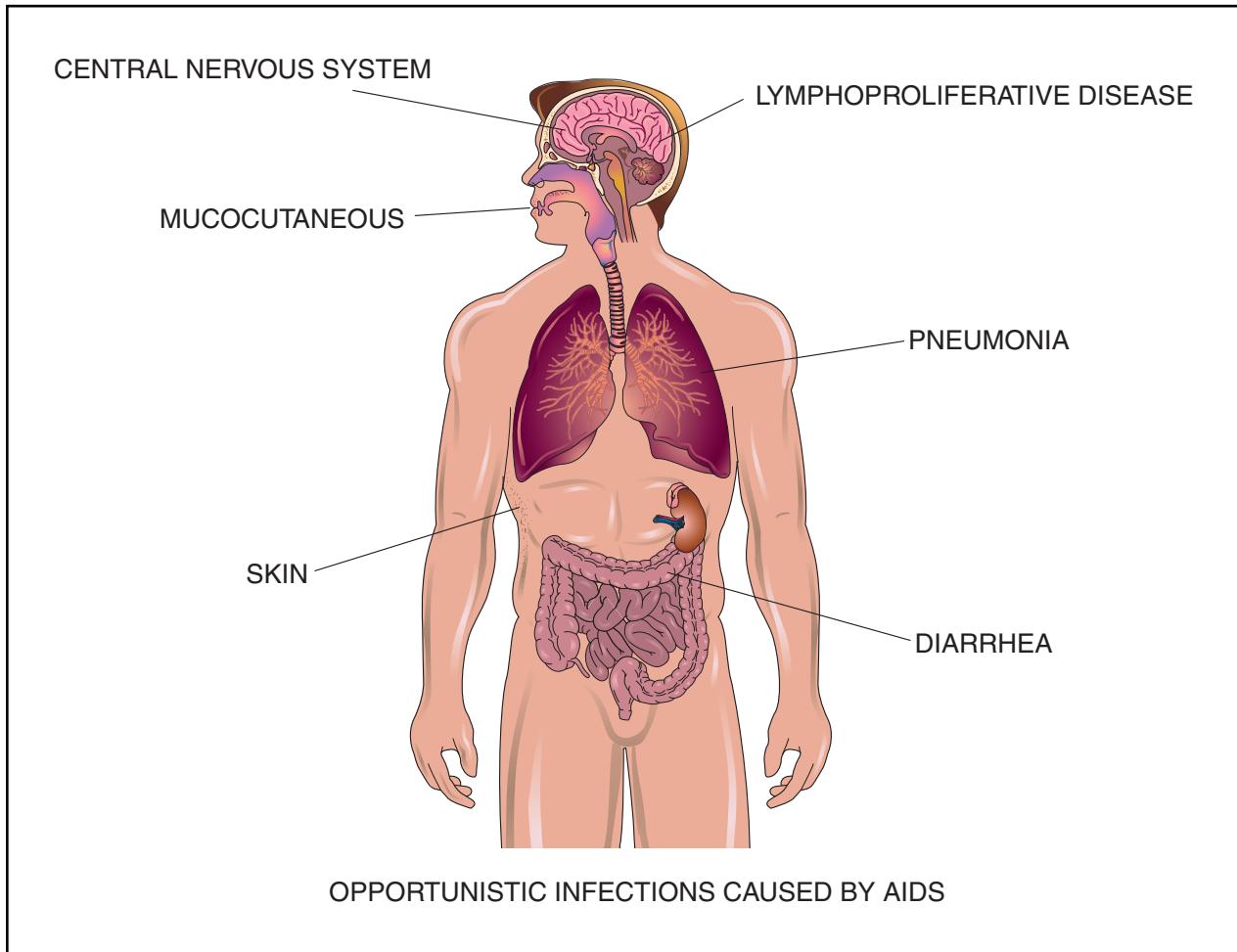
OTHER ORGAN SYSTEMS. At any time during the course of HIV infection, patients may suffer from a yeast infection in the mouth called thrush, open sores or ulcers, or other infections of the mouth; **diarrhea** and other gastrointestinal symptoms that cause **malnutrition** and weight loss; diseases of the lungs and kidneys; and degeneration of the nerve fibers in the arms and legs. HIV infection of the nervous system leads to general loss of strength, loss of reflexes, and feelings of numbness or burning sensations in the feet or lower legs.

Late-stage disease (AIDS)

AIDS is usually marked by a very low number of CD4+ lymphocytes, followed by a rise in the frequency of opportunistic infections and cancers. Doctors monitor the number and proportion of CD4+ lymphocytes in the patient's blood in order to assess the progression of the disease and the effectiveness of different medications. About 10% of infected individuals never progress to this overt stage of the disease and are referred to as nonprogressors.

OPPORTUNISTIC INFECTIONS. Once the patient's CD4+ lymphocyte count falls below 200 cells/mm³, he or she is at risk for a variety of opportunistic infections. The infectious organisms may include the following:

- **Fungi.** The most common fungal disease associated with AIDS is *Pneumocystis carinii pneumonia* (PCP). PCP is the immediate cause of death in 15-20% of AIDS patients. It is an important measure of a patient's prognosis. Other fungal infections include a yeast infection of the mouth (**candidiasis** or thrush) and cryptococcal meningitis.
- **Protozoa.** **Toxoplasmosis** is a common opportunistic infection in AIDS patients that is caused by a protozoan. Other diseases in this category include isoporiasis and cryptosporidiosis.
- **Mycobacteria.** AIDS patients may develop **tuberculosis** or MAC infections. MAC infections are caused by



Because the immune system cells are destroyed by the AIDS virus, many different types of infections and cancers can develop, taking advantage of a person's weakened immune system. (Illustration by Electronic Illustrators Group.)

Mycobacterium avium-intracellulare, and occur in about 40% of AIDS patients. It is rare until CD4+ counts falls below 50 cells/mm³.

- **Bacteria.** AIDS patients are likely to develop bacterial infections of the skin and digestive tract.
- **Viruses.** AIDS patients are highly vulnerable to cytomegalovirus (CMV), herpes simplex virus (HSV), varicella zoster virus (VZV), and Epstein-Barr virus (EBV) infections. Another virus, JC virus, causes progressive destruction of brain tissue in the brain stem, cerebrum, and cerebellum (multifocal leukoencephalopathy or PML), which is regarded as an AIDS-defining illness by the Centers for Disease Control and Prevention.

AIDS DEMENTIA COMPLEX AND NEUROLOGIC COMPLICATIONS. AIDS **dementia** complex is usually a late complication of the disease. It is unclear whether it is caused by the direct effects of the virus on the brain or by

intermediate causes. AIDS dementia complex is marked by loss of reasoning ability, loss of memory, inability to concentrate, apathy and loss of initiative, and unsteadiness or weakness in walking. Some patients also develop seizures. There are no specific treatments for AIDS dementia complex.

MUSCULOSKELETAL COMPLICATIONS. Patients in late-stage AIDS may develop inflammations of the muscles, particularly in the hip area, and may have arthritis-like pains in the joints.

ORAL SYMPTOMS. In addition to thrush and painful ulcers in the mouth, patients may develop a condition called hairy leukoplakia of the tongue. This condition is also regarded by the CDC as an indicator of AIDS. Hairy leukoplakia is a white area of diseased tissue on the tongue that may be flat or slightly raised. It is caused by the Epstein-Barr virus.

KEY TERMS

Acute retroviral syndrome—A group of symptoms resembling mononucleosis that often are the first sign of HIV infection in 50-70% of all patients and 45-90% of women.

AIDS dementia complex—A type of brain dysfunction caused by HIV infection that causes difficulty thinking, confusion, and loss of muscular coordination.

Antibody—A specific protein produced by the immune system in response to a specific foreign protein or particle called an antigen.

Antigen—Any substance that stimulates the body to produce antibody.

Autoimmunity—A condition in which the body's immune system produces antibodies in response to its own tissues or blood components instead of foreign particles or microorganisms.

CCR5—A chemokine receptor; defects in its structure caused by genetic mutation cause the progression of AIDS to be prevented or slowed.

CD4—A type of protein molecule in human blood, sometimes called the T4 antigen, that is present on the surface of 65% of immune cells. The HIV virus infects cells with CD4 surface proteins, and as a result, depletes the number of T cells, B cells, natural killer cells, and monocytes in the patient's blood. Most of the damage to an AIDS patient's immune system is done by the virus' destruction of CD4+ lymphocytes.

Chemokine receptor—A receptor on the surface of some types of immune cells that helps to mediate entry of HIV into the cell.

Hairy leukoplakia of the tongue—A white area of diseased tissue on the tongue that may be flat or slightly raised. It is caused by the Epstein-Barr virus and is an important diagnostic sign of AIDS.

Hemophilia—Any of several hereditary blood coagulation disorders occurring almost exclusively in males. Because blood does not clot properly, even minor injuries can cause significant blood loss that may require a blood transfusion, with its associated minor risk of infection.

Human immunodeficiency virus (HIV)—A transmissible retrovirus that causes AIDS in humans. Two forms of HIV are now recognized: HIV-1, which causes most cases of AIDS in Europe, North and South America, and most parts of Africa; and HIV-2, which is chiefly found in West African patients. HIV-2, discovered in 1986, appears to be less virulent than HIV-1 and may also have a longer latency period.

Immunodeficient—A condition in which the body's immune response is damaged, weakened, or is not functioning properly.

Kaposi's sarcoma—A cancer of the connective tissue that produces painless purplish red (in people with light skin) or brown (in people with dark skin) blotches on the skin. It is a major diagnostic marker of AIDS.

Latent period—Also called incubation period, the time between infection with a disease-causing agent and the development of disease.

Lymphocyte—A type of white blood cell that is important in the formation of antibodies and that can be used to monitor the health of AIDS patients.

AIDS-RELATED CANCERS. Patients with late-stage AIDS may develop **Kaposi's sarcoma** (KS), a skin tumor that primarily affects homosexual men. KS is the most common AIDS-related malignancy. It is characterized by reddish-purple blotches or patches (brownish in African-Americans) on the skin or in the mouth. About 40% of patients with KS develop symptoms in the digestive tract or lungs. KS may be caused by a herpes virus-like sexually transmitted disease agent rather than HIV.

The second most common form of **cancer** in AIDS patients is a tumor of the lymphatic system (lymphoma). AIDS-related lymphomas often affect the central nervous system and develop very aggressively.

Invasive cancer of the cervix (related to certain types of human papilloma virus [HPV]) is an important diagnostic marker of AIDS in women.

Diagnosis

Because HIV infection produces such a wide range of symptoms, the CDC has drawn up a list of 34 conditions regarded as defining AIDS. The physician will use the CDC list to decide whether the patient falls into one of these three groups:

- definitive diagnoses with or without laboratory evidence of HIV infection

KEY TERMS

Lymphoma—A cancerous tumor in the lymphatic system that is associated with a poor prognosis in AIDS patients.

Macrophage—A large white blood cell, found primarily in the bloodstream and connective tissue, that helps the body fight off infections by ingesting the disease-causing organism. HIV can infect and kill macrophages.

Monocyte—A large white blood cell that is formed in the bone marrow and spleen. About 4% of the white blood cells in normal adults are monocytes.

Mycobacterium avium (MAC) infection—A type of opportunistic infection that occurs in about 40% of AIDS patients and is regarded as an AIDS-defining disease.

Non-nucleoside reverse transcriptase inhibitors—The newest class of antiretroviral drugs that work by inhibiting the reverse transcriptase enzyme necessary for HIV replication.

Nucleoside analogues—The first group of effective anti-retroviral medications. They work by interfering with the AIDS virus' synthesis of DNA.

Opportunistic infection—An infection by organisms that usually don't cause infection in people whose immune systems are working normally.

Persistent generalized lymphadenopathy (PGL)—A condition in which HIV continues to produce chronic painless swellings in the lymph nodes during the latency period.

Pneumocystis carinii pneumonia (PCP)—An opportunistic infection caused by a fungus that is a major cause of death in patients with late-stage AIDS.

Progressive multifocal leukoencephalopathy (PML)—A disease caused by a virus that destroys white matter in localized areas of the brain. It is regarded as an AIDS-defining illness.

Protease inhibitors—The second major category of drug used to treat AIDS that works by suppressing the replication of the HIV virus.

Protozoan—A single-celled, usually microscopic organism that is eukaryotic and, therefore, different from bacteria (prokaryotic).

Retrovirus—A virus that contains a unique enzyme called reverse transcriptase that allows it to replicate within new host cells.

T cells—Lymphocytes that originate in the thymus gland. T cells regulate the immune system's response to infections, including HIV. CD4 lymphocytes are a subset of T lymphocytes.

Thrush—A yeast infection of the mouth characterized by white patches on the inside of the mouth and cheeks.

Viremia—The measurable presence of virus in the bloodstream that is a characteristic of acute retroviral syndrome.

Wasting syndrome—A progressive loss of weight and muscle tissue caused by the AIDS virus.

- definitive diagnoses with laboratory evidence of HIV infection
- presumptive diagnoses with laboratory evidence of HIV infection

Physical findings

Almost all the symptoms of AIDS can occur with other diseases. The general **physical examination** may range from normal findings to symptoms that are closely associated with AIDS. These symptoms are hairy leukoplakia of the tongue and Kaposi's sarcoma. When the

doctor examines the patient, he or she will look for the overall pattern of symptoms rather than any one finding.

Laboratory tests for HIV infection

BLOOD TESTS (SEROLOGY). The first blood test for AIDS was developed in 1985. At present, patients who are being tested for HIV infection are usually given an enzyme-linked immunosorbent assay (ELISA) test for the presence of HIV antibody in their blood. Positive ELISA results are then tested with a Western blot or immunofluorescence (IFA) assay for confirmation. The combination of the ELISA and Western blot tests is more than 99.9%

accurate in detecting HIV infection within four to eight weeks following exposure. The polymerase chain reaction (PCR) test can be used to detect the presence of viral nucleic acids in the very small number of HIV patients who have false-negative results on the ELISA and Western blot tests. These tests are also used to detect viruses and bacteria other than HIV and AIDS.

OTHER LABORATORY TESTS. In addition to diagnostic blood tests, there are other blood tests that are used to track the course of AIDS in patients that have already been diagnosed. These include blood counts, viral load tests, p24 antigen assays, and measurements of β_2 -microglobulin (β_2 M).

Doctors will use a wide variety of tests to diagnose the presence of opportunistic infections, cancers, or other disease conditions in AIDS patients. Tissue biopsies, samples of cerebrospinal fluid, and sophisticated imaging techniques, such as **magnetic resonance imaging** (MRI) and **computed tomography scans** (CT) are used to diagnose AIDS-related cancers, some opportunistic infections, damage to the central nervous system, and wasting of the muscles. Urine and stool samples are used to diagnose infections caused by parasites. AIDS patients are also given blood tests for **syphilis** and other sexually transmitted diseases.

Diagnosis in children

Diagnostic blood testing in children older than 18 months is similar to adult testing, with ELISA screening confirmed by Western blot. Younger infants can be diagnosed by direct culture of the HIV virus, PCR testing, and p24 antigen testing.

In terms of symptoms, children are less likely than adults to have an early acute syndrome. They are, however, likely to have delayed growth, a history of frequent illness, recurrent ear infections, a low blood cell count, failure to gain weight, and unexplained fevers. Children with AIDS are more likely to develop bacterial infections, inflammation of the lungs, and AIDS-related brain disorders than are HIV-positive adults.

Treatment

Treatment for AIDS covers four considerations:

TREATMENT OF OPPORTUNISTIC INFECTIONS AND MALIGNANCIES. Most AIDS patients require complex long-term treatment with medications for infectious diseases. This treatment is often complicated by the development of resistance in the disease organisms. AIDS-related malignancies in the central nervous system are usually treated with **radiation therapy**. Cancers elsewhere in the body are treated with **chemotherapy**.

PROPHYLACTIC TREATMENT FOR OPPORTUNISTIC INFECTIONS. Prophylactic treatment is treatment that is given to prevent disease. AIDS patients with a history of *Pneumocystis pneumonia*; with CD4+ counts below 200 cells/mm³ or 14% of lymphocytes; weight loss; or thrush should be given prophylactic medications. The three drugs given are trimethoprim-sulfamethoxazole, dapsone, or pentamidine in aerosol form.

ANTI-RETROVIRAL TREATMENT. In recent years researchers have developed drugs that suppress HIV replication, as distinct from treating its effects on the body. These drugs fall into three classes:

- Nucleoside analogues. These drugs work by interfering with the action of HIV reverse transcriptase inside infected cells, thus ending the virus' replication process. These drugs include zidovudine (sometimes called azidothymidine or AZT), didanosine (ddI), zalcitabine (ddC), stavudine (d4T), lamivudine (3TC), and abacavir (ABC).
- Protease inhibitors. Protease inhibitors can be effective against HIV strains that have developed resistance to nucleoside analogues, and are often used in combination with them. These compounds include saquinavir, ritonavir, indinavir, nelfinavir, amprenavir, and lopinavir.
- Non-nucleoside reverse transcriptase inhibitors. This is a new class of antiretroviral agents. Three are available, nevirapine, which was approved first, delavirdine and efavirin.

Treatment guidelines for these agents are in constant change as new medications are developed and introduced. Two principles currently guide doctors in working out drug regimens for AIDS patients: using combinations of drugs rather than one medication alone; and basing treatment decisions on the results of the patient's viral load tests.

STIMULATION OF BLOOD CELL PRODUCTION. Because many patients with AIDS suffer from abnormally low levels of both red and white blood cells, they may be given medications to stimulate blood cell production. Epoetin alfa (erythropoietin) may be given to anemic patients. Patients with low white blood cell counts may be given filgrastim or sargramostim.

Treatment in women

Treatment of pregnant women with HIV is particularly important in that anti-retroviral therapy has been shown to reduce transmission to the infant by 65%.

Alternative treatment

Alternative treatments for AIDS can be grouped into two categories: those intended to help the immune sys-

tem and those aimed at **pain** control. Treatments that may enhance the function of the immune system include Chinese herbal medicine and western herbal medicine, macrobiotic and other special **diets**, **guided imagery** and creative visualization, **homeopathy**, and vitamin therapy. Pain control therapies include **hydrotherapy**, **reiki**, **acupuncture**, **meditation**, **chiropractic** treatments, and therapeutic massage. Alternative therapies can also be used to help with side effects of the medications used in the treatment of AIDS.

Prognosis

At the present time, there is no cure for AIDS.

Treatment stresses aggressive combination drug therapy for those patients with access to the expensive medications and who tolerate them adequately. The use of these multi-drug therapies has significantly reduced the numbers of deaths, in this country, resulting from AIDS. The data is still inconclusive, but the potential exists to possibly prolong life indefinitely using these and other drug therapies to boost the immune system, keep the virus from replicating, and ward off opportunistic infections and malignancies.

Prognosis after the latency period depends on the patient's specific symptoms and the organ systems affected by the disease. Patients with AIDS-related lymphomas of the central nervous system die within two to three months of diagnosis; those with systemic lymphomas may survive for eight to ten months.

Prevention

As of 2001, there is no vaccine effective against AIDS. Several vaccines are currently being investigated, however, both to prevent initial HIV infection and as a therapeutic treatment to prevent HIV from progressing to full-blown AIDS.

In the meantime, there are many things that can be done to prevent the spread of AIDS:

- Be monogamous and practice safe sex. Individuals must be instructed in the proper use of condoms and urged to practice safe sex. Besides avoiding the risk of HIV infection, condoms are successful in preventing other sexually transmitted diseases and unwanted pregnancies. Before engaging in a sexual relationship with someone, get tested for HIV infection.
- Avoid needle sharing among intravenous drug users.
- Although blood and blood products are carefully monitored, those individuals who are planning to undergo major surgery may wish to donate blood ahead of time to prevent a risk of infection from a blood **transfusion**.

- Healthcare professionals must take all necessary precautions by wearing gloves and masks when handling body fluids and preventing needle-stick injuries.
- If you suspect that you may have become infected, get tested for HIV infection. If treated aggressively early on, the development of AIDS may be postponed indefinitely. If HIV infection is confirmed, it is also vital to let your sexual partners know so that they can be tested and, if necessary, receive medical attention.

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ORGANIZATIONS

- Gay Men's Health Crisis, Inc., 129 West 20th Street, New York, NY 10011-0022. (212) 807-6655.
- National AIDS Hot Line. (800) 342-AIDS (English). (800) 344-SIDA (Spanish). (800) AIDS-TTY (hearing-impaired).

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Rebecca J. Frey

AIDS serology see **AIDS tests**

AIDS tests

Definition

AIDS tests, short for acquired **immunodeficiency** syndrome tests, cover a number of different procedures used in the diagnosis and treatment of HIV patients. These tests are sometimes called AIDS serology tests. Serology is the branch of immunology that deals with the contents and characteristics of blood serum. Serum is the clear light yellow part of blood that remains liquid when blood cells form a clot. AIDS serology evaluates the presence of human immunodeficiency virus (HIV) infection in blood serum and its effects on each patient's immune system.

Purpose

AIDS serology serves several different purposes. Some AIDS tests are used to diagnose patients or confirm a diagnosis; others are used to measure the progression of the disease or the effectiveness of specific treatment regimens. Some AIDS tests can also be used to screen blood donations for safe use in transfusions.

In order to understand the different purposes of the blood tests used with AIDS patients, it is helpful to understand how HIV infection affects human blood and the immune system. HIV is a retrovirus that enters the blood stream of a new host in the following ways:

- by sexual contact
- by contact with infected body fluids (such as blood and urine)
- by transmission during **pregnancy**, or
- through **transfusion** of infected blood products

A retrovirus is a virus that contains a unique enzyme called reverse transcriptase that allows it to replicate within new host cells. The virus binds to a protein called CD4, which is found on the surface of certain subtypes of white blood cells, including helper T cells, macrophages, and monocytes. Once HIV enters the cell, it can replicate and kill the cell in ways that are still not completely understood. In addition to killing some lymphocytes directly, the AIDS virus disrupts the functioning of the remaining CD4 cells. CD4 cells ordinarily produce a substance called interleukin-2 (IL-2), which stimulates other cells (T cells and B cells) in the human immune system to respond to infections. Without the IL-2, T cells do not reproduce as they normally would in response to the HIV virus, and B cells are not stimulated to respond to the infection.

Precautions

In some states such as New York, a signed consent form is needed in order to administer an AIDS test. As

with all blood tests, healthcare professionals should always wear latex gloves and to avoid being pricked by the needle used in drawing blood for the tests. Also, it may be difficult to get blood from a habitual intravenous drug user due to collapsed veins.

Description

Diagnostic tests

Diagnostic blood tests for AIDS are usually given to persons in high-risk populations who may have been exposed to HIV or who have the early symptoms of AIDS. Most persons infected with HIV will develop a detectable level of antibody within three months of infection. The condition of testing positive for HIV antibody in the blood is called seroconversion, and persons who have become HIV-positive are called seroconverters.

It is possible to diagnose HIV infection by isolating the virus itself from a blood sample or by demonstrating the presence of HIV antigen in the blood. Viral culture, however, is expensive, not widely available, and slow—it takes 28 days to complete the viral culture test. More common are blood tests that work by detecting the presence of antibodies to the HIV virus. These tests are inexpensive, widely available, and accurate in detecting 99.9% of AIDS infections when used in combination to screen patients and confirm diagnoses.

ENZYME-LINKED IMMUNOSORBENT ASSAY (ELISA).

This type of blood test is used to screen blood for transfusions as well as diagnose patients. An ELISA test for HIV works by attaching HIV antigens to a plastic well or beads. A sample of the patient's blood serum is added, and excess proteins are removed. A second antibody coupled to an enzyme is added, followed by addition of a substance that will cause the enzyme to react by forming a color. An instrument called a spectrophotometer can measure the color. The name of the test is derived from the use of the enzyme that is coupled or linked to the second antibody.

The latest generation of ELISA tests are 99.5% sensitive to HIV. Occasionally, the ELISA test will be positive for a patient without symptoms of AIDS from a low-risk group. Because this result is likely to be a false-positive, the ELISA must be repeated *on the same sample of the patient's blood*. If the second ELISA is positive, the result should be confirmed by the Western blot test.

WESTERN BLOT (IMMUNOBLOTTING). The Western blot or immunoblot test is used as a reference procedure to confirm the diagnosis of AIDS. In Western blot testing, HIV antigen is purified by electrophoresis (large protein molecules are suspended in a gel and separated from one another by running an electric current through the gel).

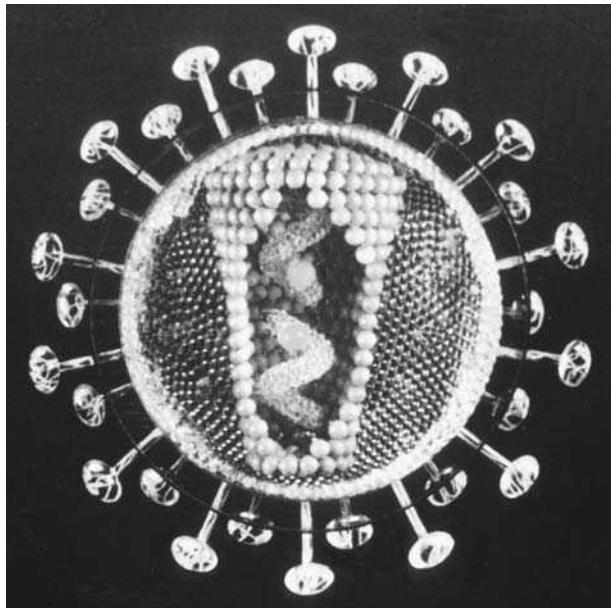
The HIV antigens are attached by blotting to a nylon or nitrocellulose filter. The patient's serum is reacted against the filter, followed by treatment with developing chemicals that allow HIV antibody to show up as a colored patch or blot. A commercially produced Western blot test for HIV-1 is now available. It consists of a prefabricated strip that is incubated with a sample of the patient's blood serum and the developing chemicals. About nine different HIV-1 proteins can be detected in the blots.

When used in combination with ELISA testing, Western blot testing is 99.9% specific. It can, however, yield false negatives in patients with very early HIV infection and in those infected by HIV-2. In some patients the Western blot yields indeterminate results.

IMMUNOFLUORESCENCE ASSAY (IFA). This method is sometimes used to confirm ELISA results instead of Western blotting. An IFA test detects the presence of HIV antibody in a sample of the patient's serum by mixing HIV antigen with a fluorescent chemical, adding the blood sample, and observing the reaction under a microscope with ultraviolet light.

POLYMERASE CHAIN REACTION (PCR). This test is used to evaluate the very small number of AIDS patients with false-negative ELISA and Western blot tests. These patients are sometimes called antibody-negative asymptomatic (without symptoms) carriers, because they do not have any symptoms of AIDS and there is no detectable quantity of antibody in the blood serum. Antibody-negative asymptomatic carriers may be responsible for the very low ongoing risk of HIV infection transmitted by blood transfusions. It is estimated that the risk is between 1 in 10,000 and 1 in 100,000 units of transfused blood.

The polymerase chain reaction (PCR) test can measure the presence of viral nucleic acids in the patient's blood even when there is no detectable antibody to HIV. This test works by amplifying the presence of HIV nucleic acids in a blood sample. Numerous copies of a gene are made by separating the two strands of DNA containing the gene segment, marking its location, using DNA polymerase to make a copy, and then continuously replicating the copies. It is questionable whether PCR will replace Western blotting as the method of confirming AIDS diagnoses. Although PCR can detect the low number of persons (1%) with HIV infections that have not yet generated an antibody response to the virus, the overwhelming majority of infected persons will be detected by ELISA screening within one to three months of infection. In addition, PCR testing is based on present knowledge of the genetic sequences in HIV. Since the virus is continually generating new variants, PCR testing could yield a false negative in patients with these new variants.



A three-dimensional model of the HIV virus. (Corbis Corporation (New York). Reproduced by permission.)

In 1999, the U.S. Food and Drug Administration (FDA) approved an HIV home testing kit. The kit contains multiple components, including material for specimen collection, a mailing envelope to send the specimen to a laboratory for analysis, and provides pre- and post-test counseling. It uses a finger prick process for blood collection. The results are obtained by the purchaser through a toll free telephone number using a personal identification number (PIN). Post test counseling is provided over the telephone by a licensed counselor. The only kit approved by the FDA as of 2001 was the Home Access test system.

Prognostic tests

Blood tests to evaluate patients already diagnosed with HIV infection are as important as the diagnostic tests. Because AIDS has a long latency period, some persons may be infected with the virus for 10 years or longer before they develop symptoms of AIDS. These patients are sometimes called antibody-positive asymptomatic carriers. Prognostic tests also help drug researchers evaluate the usefulness of new medications in treating AIDS.

BLOOD CELL COUNTS. Doctors can measure the number or proportion of certain types of cells in an AIDS patient's blood to see whether and how rapidly the disease is progressing, or whether certain treatments are helping the patient. These cell count tests include:

- Complete **blood count** (CBC). A CBC is a routine analysis performed on a sample of blood taken from the patient's vein with a needle and vacuum tube. The mea-

KEY TERMS

Antibody—A protein in the blood that identifies and helps remove disease organisms or their toxins. Antibodies are secreted by B cells. AIDS diagnostic tests work by demonstrating the presence of HIV antibody in the patient's blood.

Antigen—Any substance that stimulates the body to produce antibodies.

B cell—A type of white blood cell derived from bone marrow. B cells are sometimes called B lymphocytes. They secrete antibody and have a number of other complex functions within the human immune system.

CD4—A type of protein molecule in human blood that is present on the surface of 65% of human T cells. CD4 is a receptor for the HIV virus. When the HIV virus infects cells with CD4 surface proteins, it depletes the number of T cells, B cells, natural killer cells, and monocytes in the patient's blood. Most of the damage to an AIDS patient's immune system is done by the virus' destruction of CD4+ lymphocytes. CD4 is sometimes called the T4 antigen.

Complete blood count (CBC)—A routine analysis performed on a sample of blood taken from the patient's vein with a needle and vacuum tube. The measurements taken in a CBC include a white blood cell count, a red blood cell count, the red cell distribution width, the hematocrit (ratio of the volume of the red blood cells to the blood volume), and the amount of hemoglobin (the blood protein that carries oxygen). CBCs are a routine blood test used for many medical reasons and are not used only for

AIDS patients. They can help the doctor determine if a patient is in advanced stages of the disease.

Electrophoresis—A method of separating complex protein molecules suspended in a gel by running an electric current through the gel.

Enzyme-linked immunosorbent assay (ELISA)—A diagnostic blood test used to screen patients for AIDS or other viruses. The patient's blood is mixed with antigen attached to a plastic tube or bead surface. A sample of the patient's blood serum is added, and excess proteins are removed. A second antibody coupled to an enzyme is added, followed by a chemical that will cause a color reaction that can be measured by a special instrument.

Human immunodeficiency virus (HIV)—A transmissible retrovirus that causes AIDS in humans. Two forms of HIV are now recognized: HIV-1, which causes most cases of AIDS in Europe, North and South America, and most parts of Africa; and HIV-2, which is chiefly found in West African patients. HIV-2, discovered in 1986, appears to be less virulent than HIV-1, but may also have a longer latency period.

Immunofluorescent assay (IFA)—A blood test sometimes used to confirm ELISA results instead of using the Western blotting. In an IFA test, HIV antigen is mixed with a fluorescent compound and then with a sample of the patient's blood. If HIV antibody is present, the mixture will fluoresce when examined under ultraviolet light.

Lymphocyte—A type of white blood cell that is important in the formation of antibodies. Doctors

measurements taken in a CBC include a white blood cell count (WBC), a red blood cell count (RBC), the red cell distribution width, the **hematocrit** (ratio of the volume of the red blood cells to the blood volume), and the amount of hemoglobin (the blood protein that carries oxygen). Although CBCs are used on more than just AIDS patients, they can help the doctor determine if an AIDS patient has an advanced form of the disease. Specific AIDS-related signs in a CBC include a low hematocrit, a sharp decrease in the number of blood platelets, and a low level of a certain type of white blood cell called neutrophils.

- **Absolute CD4+ lymphocytes.** A lymphocyte is a type of white blood cell that is important in the formation

of an immune response. Because HIV targets CD4+ lymphocytes, their number in the patient's blood can be used to track the course of the infection. This blood cell count is considered the most accurate indicator for the presence of an opportunistic infection in an AIDS patient. The absolute CD4+ lymphocyte count is obtained by multiplying the patient's white blood cell count (WBC) by the percentage of lymphocytes among the white blood cells, and multiplying the result by the percentage of lymphocytes bearing the CD4+ marker. An absolute count below 200-300 CD4+ lymphocytes in 1 cubic millimeter (mm^3) of blood indicates that the patient is vulnerable to some opportunistic infections.

KEY TERMS

can monitor the health of AIDS patients by measuring the number or proportion of certain types of lymphocytes in the patient's blood.

Macrophage—A large white blood cell, found primarily in the bloodstream and connective tissue, that helps the body fight off infections by ingesting the disease organism. HIV can infect and kill macrophages.

Monocyte—A large white blood cell that is formed in the bone marrow and spleen. About 4% of the white blood cells in normal adults are monocytes.

Opportunistic infection—An infection that develops only when a person's immune system is weakened, as happens to AIDS patients.

Polymerase chain reaction (PCR)—A test performed to evaluate false-negative results to the ELISA and Western blot tests. In PCR testing, numerous copies of a gene are made by separating the two strands of DNA containing the gene segment, marking its location, using DNA polymerase to make a copy, and then continuously replicating the copies. The amplification of gene sequences that are associated with HIV allows for detection of the virus by this method.

Retrovirus—A virus that contains a unique enzyme called reverse transcriptase that allows it to replicate within new host cells.

Seroconversion—The change from HIV- negative to HIV-positive status during blood testing. Persons who are HIV-positive are called seroconverters.

Serology—The analysis of the contents and properties of blood serum.

Serum—The part of human blood that remains liquid when blood cells form a clot. Human blood serum is clear light yellow in color.

T cells—Lymphocytes that originate in the thymus gland. T cells regulate the immune system's response to infections, including HIV. CD4 lymphocytes are a subset of T lymphocytes.

Viral load test—A new blood test for monitoring the speed of HIV replication in AIDS patients. The viral load test is based on PCR techniques and supplements the CD4+ cell count tests.

Western blot—A technique developed in 1979 that is used to confirm ELISA results. HIV antigen is purified by electrophoresis and attached by blotting to a nylon or nitrocellulose filter. The patient's serum is reacted against the filter, followed by treatment with developing chemicals that allow HIV antibody to show up as a colored patch or blot. If the patient is HIV-positive, there will be stripes at specific locations for two or more viral proteins. A negative result is blank.

WBC differential—A white blood cell count in which the technician classifies the different white blood cells by type as well as calculating the number of each type. A WBC differential is necessary to calculate the absolute CD4+ lymphocyte count.

- CD4+ lymphocyte percentage. Some doctors think that this is a more accurate test than the absolute count because the percentage does not depend on a manual calculation of the number of types of different white blood cells. A white blood cell count that is broken down into categories in this way is called a WBC differential.

It is important for doctors treating AIDS patients to measure the lymphocyte count on a regular basis. Experts consulted by the United States Public Health Service recommend the following frequency of serum testing based on the patient's CD4+ level:

- CD4+ count more than 600 cells/mm³: Every six months.

- CD4+ count between 200-600 cells/mm³: Every three months.
- CD4+ count less than 200 cells/mm³: Every three months.

When the CD4+ count falls below 200 cells/mm³, the doctor will put the patient on a medication regimen to protect him or her against opportunistic infections.

HIV VIRAL LOAD TESTS. Another type of blood test for monitoring AIDS patients is the viral load test. It supplements the CD4+ count, which can tell the doctor the extent of the patient's loss of immune function, but not the speed of HIV replication in the body. The viral load test is based on PCR techniques and can measure the

number of copies of HIV nucleic acids. Successive test results for a given patient's viral load are calculated on a base 10 logarithmic scale.

BETA₂-MICROGLOBULIN (β₂M). Beta₂-microglobulin is a protein found on the surface of all human cells with a nucleus. It is released into the blood when a cell dies. Although rising blood levels of β₂M are found in patients with **cancer** and other serious diseases, a rising β₂M blood level can be used to measure the progression of AIDS.

P24 ANTIGEN CAPTURE ASSAY. Found in the viral core of HIV, p24 is a protein that can be measured by the ELISA technique. Doctors can use p24 assays to measure the antiviral activity of the patient's medications. In addition, the p24 assay is sometimes useful in detecting HIV infection before seroconversion. However, p24 is consistently present in only 25% of persons infected with HIV.

GENOTYPIC DRUG RESISTANCE TEST. Genotypic testing can help determine whether specific gene mutations, common in people with HIV, are causing drug resistance and drug failure. The test looks for specific genetic mutations of within the virus that are known to cause resistance to certain drugs used in HIV treatment. For example the drug 3TC, also known as lamivudine (Epivir), is not effective against strains of HIV that have a mutation at a particular position on the reverse transcriptase protein—amino acid 184—known as M184V (M→V, methionine to valine). So if the genotypic resistance test shows a mutation at position M184V, it is likely that person is resistant to 3TC and not likely to respond to 3TC treatment. Genotypic tests are only effective if the person is already taking antiviral medication and if the viral load is greater than 1,000 copies per milliliter (mL) of blood. The cost of the test, usually between \$300 and \$500, is usually now covered by many insurance plans.

PHENOTYPIC DRUG RESISTANCE TESTING. Phenotypic testing directly measures the sensitivity of a patient's HIV to particular drugs and drug combinations. To do this, it measures the concentration of a drug required to inhibit viral replication in the test tube. This is the same method used by researchers to determine whether a drug might be effective against HIV before using it in human clinical trials. Phenotypic testing is a more direct measurement of resistance than genotypic testing. Also, unlike genotypic testing, phenotypic testing does not require a high viral load but it is recommended that persons already be taking **antiretroviral drugs**. The cost is between \$700 and \$900 and is now covered by many insurance plans.

AIDS serology in children

Children born to HIV-infected mothers may acquire the infection through the mother's placenta or during the birth process. Public health experts recommend the testing and monitoring of all children born to mothers with HIV. Diagnostic testing in children older than 18 months is similar to adult testing, with ELISA screening confirmed by Western blot. Younger infants can be diagnosed by direct culture of the HIV virus, PCR testing, and p24 antigen testing. These techniques allow a pediatrician to identify 50% of infected children at or near birth, and 95% of cases in infants three to six months of age.

Preparation

Preparation and aftercare are important parts of AIDS diagnostic testing. Doctors are now advised to take the patient's emotional, social, economic, and other circumstances into account and to provide counseling before and after testing. Patients are generally better able to cope with the results if the doctor has spent some time with them before the blood test explaining the basic facts about HIV infection and testing. Many doctors now offer this type of informational counseling before performing the tests.

Aftercare

If the test results indicate that the patient is HIV-positive, he or she will need counseling, information, referral for treatment, and support. Doctors can either counsel the patient themselves or invite an experienced HIV counselor to discuss the results of the blood tests with the patient. They will also assess the patient's emotional and psychological status, including the possibility of violent behavior and the availability of a support network.

Risks

The risks of AIDS testing are primarily related to disclosure of the patient's HIV status rather than to any physical risks connected with blood testing. Some patients are better prepared to cope with a positive diagnosis than others, depending on their age, sex, health, resources, belief system, and similar factors.

Normal results

Normal results for ELISA, Western blot, IFA, and PCR testing are negative for HIV antibody.

Normal results for blood cell counts:

- WBC differential: Total lymphocytes 24-44% of the white blood cells.
- Hematocrit: 40-54% in men; 37-47% in women.

- T cell lymphocytes: 644-2200/mm³, 60-88% of all lymphocytes.
- B cell lymphocytes: 82-392/mm³, 3-20% of all lymphocytes.
- CD4+ lymphocytes: 500-1200/mm³, 34-67% of all lymphocytes.

Abnormal results

The following results in AIDS tests indicate progression of the disease:

- Percentage of CD4+ lymphocytes: less than 20% of all lymphocytes.
- CD4+ lymphocyte count: less than 200 cells/mm³.
- Viral load test: Levels more than 5000 copies/mL.
- β-2-microglobulin: Levels more than 3.5 mg/dL.
- P24 antigen: Measurable amounts in blood serum.

Resources

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ORGANIZATION

- National Association of People with Aids. 1413 K St.N.W., Washington, DC 20005-3442. (202) 898-0414.
- National Institute of Health. Office of Aids Research. (301) 496-0357. <<http://www.nih.gov/od/oar/index.htm>>.
- Centers for Disease Control and Prevention (CDC). 1600 Clifton Rd., Atlanta, GA 30337. (404) 639-3311. <<http://www.cdc.gov>>.

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Ken R. Wells

Air embolism see **Gas embolism**

Alanine aminotransferase test

Definition

The alanine aminotransferase test, also known as ALT, is one of a group of tests known as **liver function tests** (or LFTs) and is used to monitor damage to the liver.

Purpose

ALT levels are used to detect liver abnormalities. Since the alanine aminotransferase enzyme is also found in muscle, tests indicating elevated AST levels might also indicate muscle damage. However, other tests, such as

the levels of the MB fraction of creatine kinase should indicate whether the abnormal test levels are because of muscle or liver damage.

Description

The alanine aminotransferase test (ALT) can reveal liver damage. It is probably the most specific test for liver damage. However, the severity of the liver damage is not necessarily shown by the ALT test, since the amount of dead liver tissue does not correspond to higher ALT levels. Also, patients with normal, or declining, ALT levels may experience serious liver damage without an increase in ALT.

Nevertheless, ALT is widely used, and useful, because ALT levels are elevated in most patients with liver disease. Although ALT levels do not necessarily indicate the severity of the damage to the liver, they may indicate how much of the liver has been damaged. ALT levels, when compared to the levels of a similar enzyme, aspartate aminotransferase (AST), may provide important clues to the nature of the liver disease. For example, within a certain range of values, a ratio of 2:1 or greater for AST: ALT might indicate that a patient suffers from alcoholic liver disease. Other diagnostic data may be gleaned from ALT tests to indicate abnormal results.

Preparation

No special preparations are necessary for this test.

Aftercare

This test involves blood being drawn, probably from a vein in the patient's elbow. The patient should keep the wound from the needle puncture covered (with a bandage) until the bleeding stops. Patients should report any unusual symptoms to their physician.

Normal results

Normal values vary from laboratory to laboratory, and should be available to your physician at the time of the test. An informal survey of some laboratories indicates many laboratories find values from approximately seven to 50 IU/L to be normal.

Abnormal results

Low levels of ALT (generally below 300 IU/L) may indicate any kind of liver disease. Levels above 1,000 IU/L generally indicate extensive liver damage from toxins or drugs, viral hepatitis, or a lack of oxygen (usually resulting from very low blood pressure or a **heart attack**). A briefly elevated ALT above 1,000 IU/L that

resolves in 24-48 hours may indicate a blockage of the bile duct. More moderate levels of ALT (300-1,000IU/L) may support a diagnosis of acute or chronic hepatitis.

It is important to note that persons with normal livers may have slightly elevated levels of ALT. This is a normal finding.

Michael V. Zuck, PhD

Alanine aminotransferase test see **Liver function tests**

Albers-Schönberg disease see
Osteopetroses

Albinism

Definition

Albinism is an inherited condition present at birth, characterized by a lack of pigment that normally gives color to the skin, hair, and eyes. Many types of albinism exist, all of which involve lack of pigment in varying degrees. The condition, which is found in all races, may be accompanied by eye problems and may lead to skin cancer later in life.

Description

Albinism is a rare disorder found in fewer than five people per 100,000 in the United States and Europe. Other parts of the world have a much higher rate; for example, albinism is found in about 20 out of every 100,000 people in southern Nigeria.

There are 10 types of the most common form of the condition, known as "oculocutaneous albinism," which affects the eyes, hair, and skin. In its most severe form, hair and skin remain pure white throughout life. People with a less severe form are born with white hair and skin, which turn slightly darker as they age. Everyone with oculocutaneous albinism experiences abnormal flickering eye movements (**nystagmus**) and sensitivity to bright light. There may be other eye problems as well, including poor vision and crossed or "lazy" eyes (**strabismus**).

The second most common type of the condition is known as "ocular" albinism, in which only the eyes lack color; skin and hair are normal. There are five forms of ocular albinism; some types cause more problems—especially eye problems—than others.

KEY TERMS

Amino acids—Natural substances that are the building blocks of protein. The body breaks down the protein in food into amino acids, and then uses these amino acids to create other proteins. The body also changes amino acids into melanin pigment.

Astigmatism—An eye condition in which the lens doesn't focus light evenly on the retina, leading to problems with visual sharpness.

Carrier—A person with one normal gene and one faulty gene, who can pass on a condition to others without actually having symptoms.

DNA—The abbreviation for “deoxyribonucleic acid,” the primary carrier of genetic information found in the chromosomes of almost all organisms. The entwined double structure allows the chromosomes to be copied exactly during cell division.

DOPA—The common name for a natural chemical (3,4-dihydroxyphenylalanine) made by the body during the process of making melanin.

Enzyme—A protein that helps the body convert one chemical substance to another.

Gene—The basic unit of genetic material carried in a particular place on a chromosome. Genes are passed on from parents to child when the sperm and egg unite during conception.

Hairbulb—The root of a strand of hair from which the color develops.

Hermansky-Pudlak Syndrome (HPS)—A rare type of albinism characterized by a problem with blood clotting and a buildup of waxy material in lungs and intestines.

Melanin—Pigment made in the hair, skin and eyes.

Nystagmus—An involuntary back-and-forth movement of the eyes that is often found in albinism.

Strabismus—Crossed or “lazy” eyes, often found in albinism.

Tyrosine—A protein building block found in a wide variety of foods that is used by the body to make melanin.

Tyrosinase—An enzyme in a pigment cell which helps change tyrosine to DOPA during the process of making melanin.

Causes and symptoms

Every cell in the body contains a matched pair of genes, one inherited from each parent. These genes act as a sort of “blueprint” that guides the development of a fetus.

Albinism is an inherited problem caused by a flaw in one or more of the genes that are responsible for directing the eyes and skin to make melanin (pigment). As a result, little or no pigment is made, and the child’s skin, eyes and hair may be colorless.

In most types of albinism, a recessive trait, the child inherits flawed genes for making melanin from both parents. Because the task of making melanin is complex, there are many different types of albinism, involving a number of different genes.

It’s also possible to inherit one normal gene and one albinism gene. In this case, the one normal gene provides enough information in its cellular blueprint to make some pigment, and the child will have normal skin and eye color. They “carry” one gene for albinism. About one in 70 people are albinism carriers, with one flawed gene but no symptoms; they have a 50% chance of passing the albinism gene to their child. However, if both parents are

carriers with one flawed gene each, they have a 1 in 4 chance of passing on both copies of the flawed gene to the child, who will have albinism. (There is also a type of ocular albinism that is carried on the X chromosome and occurs almost exclusively in males because they have only one X chromosome and, therefore, no other gene for the trait to override the flawed one.)

Symptoms of albinism can involve the skin, hair, and eyes. The skin, because it contains little pigment, appears very light, as does the hair.

Although people with albinism may experience a variety of eye problems, one of the myths about albinism is that it causes people to have pink or red eyes. In fact, people with albinism can have irises varying from light gray or blue to brown. (The iris is the colored portion of the eye that controls the size of the pupil, the opening that lets light into the eye.) If people with albinism seem to have reddish eyes, it’s because light is being reflected from the back of the eye (retina) in much the same way as happens when people are photographed with an electronic flash.

People with albinism may have one or more of the following eye problems:



A man with albinism stands with his normally pigmented father. (Photograph by Norman Lightfoot, Photo Researchers, Inc. Reproduced by permission.)

- They may be very far-sighted or near-sighted, and may have other defects in the curvature of the lens of the eye (**astigmatism**) that cause images to appear unfocused.
- They may have a constant, involuntary movement of the eyeball called **nystagmus**.
- They may have problems in coordinating the eyes in fixing and tracking objects (**strabismus**), which may lead to an appearance of having “crossed eyes” at times. Strabismus may cause some problems with depth perception, especially at close distances.
- They may be very sensitive to light (**photophobia**) because their irises allow “stray” light to enter their eyes. It’s a common misconception that people with albinism shouldn’t go out on sunny days, but wearing sunglasses can make it possible to go outside quite comfortably.

In addition to the characteristically light skin and eye problems, people with a rare form of albinism called **Hermansky-Pudlak Syndrome (HPS)** also have a greater tendency to have bleeding disorders, inflammation of the large bowel (**colitis**), lung (**pulmonary**) disease, and kidney (**renal**) problems.

Diagnosis

It’s not always easy to diagnose the exact type of albinism a person has; there are two tests available that can identify only two types of the condition. Recently, a blood test has been developed that can identify carriers of the gene for some types of albinism; a similar test during **amniocentesis** can diagnose some types of albinism in an unborn child. A **chorionic villus sampling** test during the fifth week of **pregnancy** may also reveal some types of albinism.

The specific type of albinism a person has can be determined by taking a good family history and examining the patient and several close relatives.

The “hairbulb pigmentation test” is used to identify carriers by incubating a piece of the person’s hair in a solution of tyrosine, a substance in food which the body uses to make melanin. If the hair turns dark, it means the hair is making melanin (a “positive” test); light hair means there is no melanin. This test is the source of the names of two types of albinism: “ty-pos” and “ty-neg.”

The tyrosinase test is more precise than the hairbulb pigmentation test. It measures the rate at which hair con-

verts tyrosine into another chemical (DOPA), which is then made into pigment. The hair converts tyrosine with the help of a substance called "tyrosinase." In some types of albinism, tyrosinase doesn't do its job, and melanin production breaks down.

Treatment

There is no treatment that can replace the lack of melanin that causes the symptoms of albinism. Doctors can only treat, not cure, the eye problems that often accompany the lack of skin color. Glasses are usually needed and can be tinted to ease **pain** from too much sunlight. There is no cure for involuntary eye movements (nystagmus), and treatments for focusing problems (surgery or contact lenses) are not effective in all cases.

Crossed eyes (strabismus) can be treated during infancy, using eye patches, surgery or medicine injections. Treatment may improve the appearance of the eye, but it can do nothing to cure the underlying condition.

Patients with albinism should avoid excessive exposure to the sun, especially between 10 A.M. and 2 P.M. If exposure can't be avoided, they should use UVA-UVB sunblocks with an SPF of at least 20. Taking beta-carotene may help provide some skin color, although it doesn't protect against sun exposure.

Prognosis

In the United States, people with this condition can expect to have a normal lifespan. People with albinism may experience some social problems because of a lack of understanding on the part of others. When a member of a normally dark-skinned ethnic group has albinism, he or she may face some very complex social challenges.

One of the greatest health hazards for people with albinism is excessive exposure to sun without protection, which could lead to skin cancer. Wearing opaque clothes and sunscreen rated SPF 20, people with albinism can safely work and play outdoors safely even during the summer.

Prevention

Genetic counseling is very important to prevent further occurrences of the condition.

Resources

BOOKS

National Association for the Visually Handicapped. *Larry: A Book for Children with Albinism Going to School*. New York: National Association for the Visually Handicapped.

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PERIODICALS

- Campbell, Maude. "Gene Found for Albinism, Other Pigment Disorders." *Dermatology Times* (1 Apr. 1995): 1.
Siegel-Itzkovich, Judy. "Early-warning Test for Albinism." *Jerusalem Post* (4 Dec. 1994).

ORGANIZATIONS

- Albinism World Alliance. <<http://www.albinism.org/awa.html>>. American Foundation for the Blind. 15 W. 16th St., New York, NY 10011. (800) AFB-LIND.
Hermansky-Pudlak Syndrome Network, Inc. One South Road, Oyster Bay, NY 11771-1905. (800) 789-9477. <appell@theonramp.net>.
National Organization for Albinism and Hypopigmentation (NOAH). 1530 Locust St., #29, Philadelphia, PA 19102-4415. (800) 473-2310. <<http://www.albinism.org>>.

Carol A. Turkington

Albuterol see **Bronchodilators**

Alcohol-related neurologic disease

Definition

Alcohol, or ethanol, is a poison with direct toxic effects on nerve and muscle cells. Depending on which nerve and muscle pathways are involved, alcohol can have far-reaching effects on different parts of the brain, peripheral nerves, and muscles, with symptoms of memory loss, incoordination, seizures, weakness, and sensory deficits. These different effects can be grouped in three main categories: (1) intoxication due to the acute effects of ethanol, (2) withdrawal syndrome from suddenly stopping drinking, and (3) disorders related to long-term or chronic alcohol abuse. Alcohol-related neurologic disease includes Wernicke-Korsakoff disease, alcoholic cerebellar degeneration, alcoholic myopathy, alcoholic neuropathy, alcohol withdrawal syndrome with seizures and **delirium tremens**, and **fetal alcohol syndrome**.

Description

Acute excess intake of alcohol can cause drunkenness (intoxication) or even **death**, and chronic or long-term abuse leads to potentially irreversible damage to virtually any level of the nervous system. Any given

patient with long-term alcohol abuse may have no neurologic complications, a single alcohol-related disease, or multiple conditions, depending on the genes they have inherited, how well nourished they are, and other environmental factors, such as exposure to other drugs or toxins.

Neurologic complications of alcohol abuse may also result from nutritional deficiency, because alcoholics tend to eat poorly and may become depleted of thiamine or other **vitamins** important for nervous system function. Persons who are intoxicated are also at higher risk for **head injury** or for compression injuries of the peripheral nerves. Sudden changes in blood chemistry, especially sodium, related to alcohol abuse may cause central pontine myelinolysis, a condition of the brainstem in which nerves lose their myelin coating. Liver disease complicating alcoholic **cirrhosis** may cause **dementia**, delirium, and movement disorder.

Causes and symptoms

When a person drinks alcohol, it is absorbed by blood vessels in the stomach lining and flows rapidly throughout the body and brain, as ethanol freely crosses the blood-brain barrier that ordinarily keeps large molecules from escaping from the blood vessel to the brain tissue. Drunkenness, or intoxication, may occur at blood ethanol concentrations of as low as 50-150 mg per dL in people who don't drink. Sleepiness, stupor, **coma**, or even death from respiratory depression and low blood pressure occur at progressively higher concentrations.

Although alcohol is broken down by the liver, the toxic effects from a high dose of alcohol are most likely a direct result of alcohol itself rather than of its breakdown products. The fatal dose varies widely because people who drink heavily develop a tolerance to the effects of alcohol with repeated use. In addition, alcohol tolerance results in the need for higher levels of blood alcohol to achieve intoxicating effects, which increases the likelihood that habitual drinkers will be exposed to high and potentially toxic levels of ethanol. This is particularly true when binge drinkers fail to eat, because **fasting** decreases the rate of alcohol clearance and causes even higher blood alcohol levels.

When a chronic alcoholic suddenly stops drinking, withdrawal of alcohol leads to a syndrome of increased excitability of the central nervous system, called delirium tremens or "DTs." Symptoms begin six to eight hours after abstinence, and are most pronounced 24-72 hours after abstinence. They include body shaking (tremulousness), **insomnia**, agitation, confusion, hearing voices or seeing images that are not really there (such as crawling bugs), seizures, rapid heart beat, pro-

fuse sweating, high blood pressure, and **fever**. Alcohol-related seizures may also occur without withdrawal, such as during active heavy drinking or after more than a week without alcohol.

Wernicke-Korsakoff syndrome is caused by deficiency of the B-vitamin thiamine, and can also be seen in people who don't drink but have some other cause of thiamine deficiency, such as chronic vomiting that prevents the absorption of this vitamin. Patients with this condition have the sudden onset of Wernicke encephalopathy; the symptoms include marked confusion, delirium, disorientation, inattention, memory loss, and drowsiness. Examination reveals abnormalities of eye movement, including jerking of the eyes (**nystagmus**) and double vision. Problems with balance make walking difficult. People may have trouble coordinating their leg movements, but usually not their arms. If thiamine is not given promptly, Wernicke encephalopathy may progress to stupor, coma, and death.

If thiamine is given and death averted, **Korsakoff's syndrome** may develop in some patients, who suffer from memory impairment that leaves them unable to remember events for a period of a few years before the onset of illness (**retrograde amnesia**) and unable to learn new information (**anterograde amnesia**). Most patients have very limited insight into their memory dysfunction and have a tendency to make up explanations for events they have forgotten (**confabulation**).

Severe **alcoholism** can cause cerebellar degeneration, a slowly progressive condition affecting portions of the brain called the anterior and superior cerebellar vermis, causing a wide-based gait, leg incoordination, and an inability to walk heel-to-toe in tightrope fashion. The gait disturbance usually develops over several weeks, but may be relatively mild for some time, and then suddenly worsen after binge drinking or an unrelated illness.

Fetal alcohol syndrome occurs in infants born to alcoholic mothers when prenatal exposure to ethanol retards fetal growth and development. Affected infants often have a distinctive appearance with a thin upper lip, flat nose and mid-face, short stature and small head size. Almost half are mentally retarded, and most others are mildly impaired intellectually or have problems with speech, learning, and behavior.

Alcoholic myopathy, or weakness secondary to breakdown of muscle tissue, is also known as alcoholic rhabdomyolysis or alcoholic myoglobinuria. Males are affected by acute (sudden onset) alcoholic myopathy four times as often as females. Breakdown of muscle tissue (myonecrosis), can come on suddenly during binge drinking or in the first days of alcohol withdrawal. In its mildest form, this breakdown may cause no noticeable

symptoms, but may be detected by a temporary elevation in blood levels of an enzyme found predominantly in muscle, the MM fraction of creatine kinase.

The severe form of acute alcoholic myopathy is associated with the sudden onset of muscle **pain**, swelling, and weakness; a reddish tinge in the urine caused by myoglobin, a breakdown product of muscle excreted in the urine; and a rapid rise in muscle enzymes in the blood. Symptoms usually worsen over hours to a few days, and then improve over the next week to 10 days as the patient is withdrawn from alcohol. Muscle symptoms are usually generalized, but pain and swelling may selectively involve the calves or other muscle groups. The muscle breakdown of acute alcoholic myopathy may be worsened by crush injuries, which may occur when people drink so much that they compress a muscle group with their body weight for a long time without moving, or by withdrawal seizures with generalized muscle activity.

In patients who abuse alcohol over many years, chronic alcoholic myopathy may develop. Males and females are equally affected. Symptoms include painless weakness of the limb muscles closest to the trunk and the girdle muscles, including the thighs, hips, shoulders, and upper arms. This weakness develops gradually, over weeks or months, without symptoms of acute muscle injury. Muscle atrophy, or decreased bulk, may be striking. The nerves of the extremities may also begin to break down, a condition known as alcoholic **peripheral neuropathy**, which can add to the person's difficulty in moving.

The way in which alcohol destroys muscle tissue is still not well understood. Proposed mechanisms include muscle membrane changes affecting the transport of calcium, potassium, or other **minerals**; impaired muscle energy metabolism; and impaired protein synthesis. Alcohol is metabolized or broken down primarily by the liver, with a series of chemical reactions in which ethanol is converted to acetate. Acetate is metabolized by skeletal muscle, and alcohol-related changes in liver function may affect skeletal muscle metabolism, decreasing the amount of blood sugar available to muscles during prolonged activity. Because not enough sugar is available to supply needed energy, muscle protein may be broken down as an alternate energy source. However, toxic effects on muscle may be a direct result of alcohol itself rather than of its breakdown products.

Although alcoholic peripheral neuropathy may contribute to muscle weakness and atrophy by injuring the motor nerves controlling muscle movement, alcoholic neuropathy more commonly affects sensory fibers. Injury to these fibers can cause tingling or burning pain

in the feet, which may be severe enough to interfere with walking. As the condition worsens, pain decreases but numbness increases.

Diagnosis

The diagnosis of alcohol-related neurologic disease depends largely on finding characteristic symptoms and signs in patients who abuse alcohol. Other possible causes should be excluded by the appropriate tests, which may include blood chemistry, **thyroid function tests**, brain MRI (**magnetic resonance imaging**) or CT (computed tomography scan), and/or cerebrospinal fluid analysis.

Acute alcoholic myopathy can be diagnosed by finding myoglobin in the urine and increased creatine kinase and other blood enzymes released from injured muscle. The surgical removal of a small piece of muscle for microscopic analysis (muscle biopsy) shows the scattered breakdown and repair of muscle fibers. Doctors must rule out other acquired causes of muscle breakdown, which include the abuse of drugs such as heroin, **cocaine**, or amphetamines; trauma with crush injury; the depletion of phosphate or potassium; or an underlying defect in the metabolism of carbohydrates or lipids. In chronic alcoholic myopathy, serum creatine kinase often is normal, and muscle biopsy shows atrophy, or loss of muscle fibers. **Electromyography** (EMG) may show features characteristic of alcoholic myopathy or neuropathy.

Treatment

Acute management of alcohol intoxication, delirium tremens, and withdrawal is primarily supportive, to monitor and treat any cardiovascular or **respiratory failure** that may develop. In delirium tremens, fever and sweating may necessitate treatment of fluid loss and secondary low blood pressure. Agitation may be treated with **benzodiazepines** such as chlordiazepoxide, beta-adrenergic antagonists such as atenolol, or alpha 2-adrenergic agonists such as clonidine. Because Wernicke's syndrome is rapidly reversible with thiamine, and because death may intervene if thiamine is not given promptly, all patients admitted for acute complications of alcohol, as well as all patients with unexplained encephalopathy, should be given intravenous thiamine.

Withdrawal seizures typically resolve without specific anti-epileptic drug treatment, although status epilepticus (continual seizures occurring without interruption) should be treated vigorously. Acute alcoholic myopathy with myoglobinuria requires monitoring and maintenance of kidney function, and correction of imbalances

KEY TERMS

Abstinence—Refraining from the use of alcoholic beverages.

Atrophy—A wasting or decrease in size of a muscle or other tissue.

Cerebellum—The part of the brain involved in coordination of movement, walking, and balance.

Degeneration—Gradual, progressive loss of nerve cells.

Delirium—Sudden confusion with decreased or fluctuating level of consciousness.

Delirium tremens—A complication that may accompany alcohol withdrawal. The symptoms include body shaking (tremulousness), insomnia, agitation, confusion, hearing voices or seeing images that are not really there (hallucinations), seizures, rapid heart beat, profuse sweating, high blood pressure, and fever.

Dementia—Loss of memory and other higher functions, such as thinking or speech, lasting six months or more.

Myoglobinuria—Reddish urine caused by excretion of myoglobin, a breakdown product of muscle.

Myopathy—A disorder that causes weakening of muscles.

Neuropathy—A condition affecting the nerves supplying the arms and legs. Typically, the feet and hands are involved first. If sensory nerves are involved, numbness, tingling, and pain are prominent, and if motor nerves are involved, the patient experiences weakness.

Thiamine—A B vitamin essential for the body to process carbohydrates and fats. Alcoholics may suffer complications (including Wernike-Korsakoff syndrome) from a deficiency of this vitamin.

Wernicke-Korsakoff syndrome—A combination of symptoms, including eye-movement problems, tremors, and confusion, that is caused by a lack of the B vitamin thiamine and may be seen in alcoholics.

in blood chemistry including potassium, phosphate, and magnesium levels.

Chronic alcoholic myopathy and other chronic conditions are treated by correcting associated nutritional deficiencies and maintaining a diet adequate in protein and carbohydrate. The key to treating any alcohol-related disease is helping the patient overcome alcohol **addiction**. Behavioral measures and social supports may be needed in patients who develop broad problems in their thinking abilities (dementia) or remain in a state of confusion and disorientation (delirium). People with walking disturbances may benefit from physical therapy and assistive devices. Doctors may also prescribe drugs to treat the pain associated with peripheral neuropathy.

Prognosis

Complete recovery from Wernicke's syndrome may follow prompt administration of thiamine. However, repeated episodes of encephalopathy or prolonged alcohol abuse may cause persistent dementia or Korsakoff **psychosis**. Most patients recover fully from acute alcoholic myopathy within days to weeks, but severe cases may be fatal from **acute kidney failure** and disturbances in heart rhythm secondary to increased potassium levels. Recovery from chronic alcoholic myopathy may occur

over weeks to months of abstinence from alcohol and correction of **malnutrition**. Cerebellar degeneration and alcoholic neuropathy may also improve to some extent with abstinence and balanced diet, depending on the severity and duration of the condition.

Prevention

Prevention requires abstinence from alcohol. Persons who consume small or moderate amounts of alcohol might theoretically help prevent nutritional complications of alcohol use with dietary supplements including B vitamins. However, proper **nutrition** cannot protect against the direct toxic effect of alcohol or of its breakdown products. Patients with any alcohol-related symptoms or conditions, pregnant women, and patients with liver or neurologic disease should abstain completely. Persons with family history of alcoholism or alcohol-related conditions may also be at increased risk for neurologic complications of alcohol use.

Resources

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- Neiman, J., et al. "Movement Disorders in Alcoholism: A Review." *Neurology* 40 (1990): 741-6.
- Saitz, R. "Individualized Treatment for Alcohol Withdrawal. A Randomized Double-Blind Controlled Trial." *Journal of the American Medical Association* 272 (1994): 557-8.
- Victor, M. "Alcoholic Dementia." *Candian Journal of Neurological Science* 21 (1994): 88-99.

ORGANIZATIONS

National Institute on Alcohol Abuse and Alcoholism. 6000 Executive Boulevard, Willco Building, Bethesda, MD 20892-7003. <http://silk.nih.gov/silk/niaaa1>.

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Alcohol abuse see **Alcoholism**

Alcohol dependence see **Alcoholism**

Alcohol withdrawal see **Withdrawal syndromes**

Alcoholic cerebellar disease see **Alcohol-related neurologic disease**

Alcoholic hepatitis see **Hepatitis, alcoholic**

Alcoholic rose gardener's disease see **Sporotrichosis**

inflammation and irritation, acute and chronic problems with the pancreas, low blood sugar, high blood fat content, interference with reproductive fertility, and weakened bones.

On a personal level, alcoholism results in marital and other relationship difficulties, depression, unemployment, **child abuse**, and general family dysfunction.

Alcoholism causes or contributes to a variety of severe social problems including homelessness, murder, suicide, injury, and violent crime. Alcohol is a contributing factor in at least 50% of all deaths from motor vehicle accidents. In fact, about 100,000 deaths occur each year due to the effects of alcohol, of which 50% are due to injuries of some sort. According to a recent special report prepared for the U.S. Congress by the National Institute on Alcohol Abuse and Alcoholism, the impact of alcohol on society, including violence, traffic accidents, lost work productivity, and premature **death**, costs our nation an estimated \$185 billion annually. In addition, it is estimated that approximately one in four children (19 million children or 29 percent of children up to 17 years of age) is exposed at some time to familial alcohol abuse, alcohol dependence, or both. Furthermore, it has been estimated that approximately 18 percent of adults experience an episode of alcohol abuse or dependence a some time during their lives.

Causes and symptoms

There are probably a number of factors that work together to cause a person to become an alcoholic. Recent genetic studies have demonstrated that close relatives of an alcoholic are four times more likely to become alcoholics themselves. Furthermore, this risk holds true even for children who were adopted away from their biological families at birth and raised in a non-alcoholic adoptive family, with no knowledge of their biological family's difficulties with alcohol. More research is being conducted to determine if genetic factors could account for differences in alcohol metabolism that may increase the risk of an individual becoming an alcoholic.

The symptoms of alcoholism can be broken down into two major categories: symptoms of acute alcohol use and symptoms of long-term alcohol use.

Immediate (acute) effects of alcohol use

Alcohol exerts a depressive effect on the brain. The blood-brain barrier does not prevent alcohol from entering the brain, so the brain alcohol level will quickly become equivalent to the blood alcohol level. Alcohol's depressive effects result in difficulty walking, poor balance, slurring of speech, and generally poor coordination

Alcoholism

Definition

The essential feature of alcohol abuse is the maladaptive use of alcohol with recurrent and significant adverse consequences related to its repeated use. Alcoholism is the popular term for two disorders, alcohol abuse and alcohol dependence. The hallmarks of both these disorders involve repeated life problems that can be directly attributed to the use of alcohol. Both these disorders can have serious consequences, affecting an individual's health and personal life, as well as having an impact on society at large.

Description

The effects of alcoholism are quite far-reaching. Alcohol affects every body system, causing a wide range of health problems. Some such problems include poor **nutrition**, memory disorders, difficulty with balance and walking, liver disease (including **cirrhosis** and hepatitis), high blood pressure, muscle weakness (including the heart), heart rhythm disturbances, anemia, clotting disorders, decreased immunity to infections, gastrointestinal

(accounting in part for the increased likelihood of injury). The affected person may also have impairment of peripheral vision. At higher alcohol levels, a person's breathing and heart rates will be slowed, and vomiting may occur (with a high risk of the vomit being breathed into the lungs, resulting in severe problems, including the possibility of **pneumonia**). Still higher alcohol levels may result in **coma** and death.

Effects of long-term (chronic) alcoholism

Long-term use of alcohol affects virtually every organ system of the body:

- Nervous system. An estimated 30-40% of all men in their teens and twenties have experienced alcoholic blackout, which occurs when drinking a large quantity of alcohol results in the loss of memory of the time surrounding the episode of drinking. Alcohol is well-known to cause sleep disturbances, so that overall sleep quality is affected. **Numbness and tingling** may occur in the arms and legs. Two syndromes, which can occur together or separately, are known as Wernicke's and Korsakoff's syndromes. Both are due to the low thiamine (a form of vitamin B complex) levels found in alcoholics. Wernicke's syndrome results in disordered eye movements, very poor balance and difficulty walking, while **Korsakoff's syndrome** severely affects one's memory, preventing new learning from taking place.

- Gastrointestinal system. Alcohol causes loosening of the muscular ring that prevents the stomach's contents from re-entering the esophagus. Therefore, the acid from the stomach flows backwards into the esophagus, burning those tissues, and causing **pain** and bleeding. Inflammation of the stomach can also result in bleeding and pain, and decreased desire to eat. A major cause of severe, uncontrollable bleeding (hemorrhage) in an alcoholic is the development of enlarged (dilated) blood vessels within the esophagus, which are called esophageal varices. These varices are actually developed in response to liver disease, and are extremely prone to bursting and hemorrhaging. **Diarrhea** is a common symptom, due to alcohol's effect on the pancreas. In addition, inflammation of the pancreas (**pancreatitis**) is a serious and painful problem in alcoholics. Throughout the intestinal tract, alcohol interferes with the absorption of nutrients, creating a malnourished state. Because alcohol is broken down (metabolized) within the liver, that organ is severely affected by constant levels of alcohol. Alcohol interferes with a number of important chemical processes that also occur in the liver. The liver begins to enlarge and fill with fat (**fatty liver**), fibrous scar

tissue interferes with the liver's normal structure and function (cirrhosis), and the liver may become inflamed (hepatitis).

- Blood. Alcohol can cause changes to all the types of blood cells. Red blood cells become abnormally large. White blood cells (important for fighting infections) decrease in number, resulting in a weakened immune system. This places alcoholics at increased risk for infections, and is thought to account in part for the increased risk of **cancer** faced by alcoholics (ten times increased over normal). Platelets and blood clotting factors are affected, causing an increased risk of bleeding.
- Heart. Small amounts of alcohol cause a drop in blood pressure, but with increased use, alcohol begins to increase blood pressure into a dangerous range. High levels of fats circulating in the bloodstream increase the risk of heart disease. Heavy drinking results in an increase in heart size, weakening of the heart muscle, abnormal heart rhythms, a risk of blood clots forming within the chambers of the heart, and a greatly increased risk of **stroke** (due to a blood clot from the heart entering the circulatory system, going to the brain, and blocking a brain blood vessel).
- Reproductive system. Heavy drinking has a negative effect on fertility in both men and women, by decreasing testicle and ovary size, and interfering with both sperm and egg production. When **pregnancy** is achieved in an alcoholic woman, the baby has a great risk of being born with **fetal alcohol syndrome**, which causes distinctive facial defects, lowered IQ, and behavioral problems.

Diagnosis

Two different types of alcohol-related difficulties have been identified. The first is called *alcohol dependence*, which refers to a person who literally depends on the use of alcohol. Three of the following traits must be present to diagnose alcohol dependence:

- tolerance, meaning that a person becomes accustomed to a particular dose of alcohol, and must increase the dose in order to obtain the desired effect
- withdrawal, meaning that a person experiences unpleasant physical and psychological symptoms when he or she does not drink alcohol
- the tendency to drink more alcohol than one intends (once an alcoholic starts to drink, he or she finds it difficult to stop)
- being unable to avoid drinking or stop drinking once started

Symptoms Of Co-Alcohol Dependence

Psychological distress manifested in symptoms such as anxiety, aggression, anorexia nervosa, bulimia, depression, insomnia, hyperactivity, and suicidal tendency
 Psychosomatic illness (ailments that have no biological basis and clear up after the co-alcoholism clears up)
 Family violence or neglect
 Alcoholism or other drug abuse

- having large blocks of time taken up by alcohol use
- choosing to drink at the expense of other important tasks or activities
- drinking despite evidence of negative effects on one's health, relationships, education, or job

Alcohol abuse requires that one of the following four criteria is met. Because of drinking, a person repeatedly:

- fails to live up to his or her most important responsibilities
- physically endangers him or herself, or others (for example, by drinking when driving)
- gets into trouble with the law
- experiences difficulties in relationships or jobs

Diagnosis is sometimes brought about when family members call an alcoholic's difficulties to the attention of a physician. A clinician may begin to be suspicious when a patient suffers repeated injuries or begins to experience medical problems related to the use of alcohol. In fact, some estimates suggest that about 20% of a physician's patients will be alcoholics.

Diagnosis is aided by administering specific psychological assessments that try to determine what aspects of a person's life may be affected by his or her use of alcohol. Determining the exact quantity of alcohol that a person drinks is of much less importance than determining how his or her drinking affects relationships, jobs, educational goals, and family life. In fact, because the metabolism of alcohol (how the body breaks down and processes alcohol) is so individual, the quantity of alcohol consumed is not part of the criteria list for diagnosing either alcohol dependence or alcohol abuse.

One very simple tool for beginning the diagnosis of alcoholism is called the CAGE questionnaire. It consists of four questions, with the first letters of each key word spelling out the word CAGE:

- Have you ever tried to *Cut* down on your drinking?
- Have you ever been *Annoyed* by anyone's comments about your drinking?
- Have you ever felt *Guilty* about your drinking?

- Do you ever need an *Eye-opener* (a morning drink of alcohol) to start the day?

Other, longer lists of questions exist to help determine the severity and effects of a person's alcohol use. Given the recent research pointing to a genetic basis for alcoholism, it is important to ascertain whether anyone else in the person's family has ever suffered from alcoholism.

Physical examination may reveal signs suggestive of alcoholism: evidence of old injuries; a visible network of enlarged veins just under the skin around the navel (called caput medusae); fluid in the abdomen (**ascites**); yellowish-tone to the skin; decreased testicular size in men; and poor nutritional status. Lab work may reveal an increase in the size of the red blood cells; abnormalities in the white blood cells (cells responsible for fighting infection) and platelets (particles responsible for clotting); and an increase in certain liver enzymes.

Treatment

Treatment of alcoholism has two parts. The first step in the treatment of alcoholism, called **detoxification**, involves helping the person stop drinking and ridding his or her body of the harmful (toxic) effects of alcohol. Because the person's body has become accustomed to alcohol, the person will need to be supported through withdrawal. Withdrawal will be different for different patients, depending on the severity of the alcoholism, as measured by the quantity of alcohol ingested daily and the length of time the patient has been an alcoholic. Withdrawal symptoms can range from mild to life-threatening. Mild withdrawal symptoms include nausea, achiness, diarrhea, difficulty sleeping, sweatiness, **anxiety**, and trembling. This phase is usually over in about three to five days. More severe effects of withdrawal can include **hallucinations** (in which a patient sees, hears, or feels something that is not actually real), seizures, an unbearable craving for more alcohol, confusion, **fever**, fast heart rate, high blood pressure, and **delirium** (a fluctuating level of consciousness). Patients at highest risk for the most severe symptoms of withdrawal (referred to as delirium tremens) are those with other medical problems, including **malnutrition**, liver disease, or Wernicke's syndrome. Delirium

tremens usually begin about three to five days after the patient's last drink, progressing from the more mild symptoms to the more severe, and may last a number of days.

Patients going through only mild withdrawal are simply monitored carefully to make sure that more severe symptoms do not develop. No medications are necessary, however. Treatment of a patient suffering the more severe effects of withdrawal may require the use of sedative medications to relieve the discomfort of withdrawal and to avoid the potentially life-threatening complications of high blood pressure, fast heart rate, and seizures. Drugs called benzodiazapines are helpful in those patients suffering from hallucinations. Because of the patient's nausea, fluids may need to be given through a vein (intravenously), along with some necessary sugars and salts. It is crucial that thiamine be included in the fluids, because thiamine is usually quite low in alcoholic patients, and deficiency of thiamine is responsible for the Wernicke-Korsakoff syndrome.

After cessation of drinking has been accomplished, the next steps involve helping the patient avoid ever taking another drink. This phase of treatment is referred to as **rehabilitation**. The best programs incorporate the family into the therapy, because the family has undoubtedly been severely affected by the patient's drinking. Some therapists believe that family members, in an effort to deal with their loved one's drinking problem, sometimes develop patterns of behavior that accidentally support or "enable" the patient's drinking. This situation is referred to as "co-dependence," and must be addressed in order to successfully treat a person's alcoholism.

Sessions led by peers, where recovering alcoholics meet regularly and provide support for each other's recoveries, are considered some of the best methods of preventing a return to drinking (relapse). Perhaps the most well-known such group is called Alcoholics Anonymous, which uses a "12-step" model to help people avoid drinking. These steps involve recognizing the destructive power that alcohol has held over the alcoholic's life, looking to a higher power for help in overcoming the problem, and reflecting on the ways in which the use of alcohol has hurt others and, if possible, making amends to those people. According to a recent study reported by the American Psychological Association (APA), anyone, regardless of his or her religious beliefs or lack of religious beliefs, can benefit from participation in 12-step programs such as Alcoholics Anonymous (AA) or Narcotics Anonymous (NA). The number of visits to 12-step self-help groups exceeds the number of visits to all mental health professionals combined.

There are also medications that may help an alcoholic avoid returning to drinking. These have been used

with variable success. Disulfiram (Antabuse) is a drug which, when mixed with alcohol, causes unpleasant reactions including nausea, vomiting, diarrhea, and trembling. Naltrexone, along with a similar compound, Nalmefene, can be helpful in limiting the effects of a relapse. Acamprosate is helpful in preventing relapse. None of these medications would be helpful unless the patient was also willing to work very hard to change his or her behavior.

Alternative treatment

Alternative treatments can be a helpful adjunct for the alcoholic patient, once the medical danger of withdrawal has passed. Because many alcoholics have very stressful lives (whether because of or leading to the alcoholism is sometimes a matter of debate), many of the treatments for alcoholism involve dealing with and relieving **stress**. These include massage, **meditation**, and **hypnotherapy**. The malnutrition of long-term alcohol use is addressed by nutrition-oriented practitioners with careful attention to a healthy diet and the use of nutritional supplements such as **vitamins** A, B complex, and C, as well as certain fatty acids, amino acids, zinc, magnesium, and selenium. Herbal treatments include milk thistle (*Silybum marianum*), which is thought to protect the liver against damage. Other herbs are thought to be helpful for the patient suffering through withdrawal. Some of these include lavender (*Lavandula officinalis*), skullcap (*Scutellaria lateriflora*), chamomile (*Matricaria recutita*), peppermint (*Mentha piperita*), yarrow (*Achillea millefolium*), and valerian (*Valeriana officinalis*). **Acupuncture** is believed to both decrease withdrawal symptoms and to help improve a patient's chances for continued recovery from alcoholism.

Prognosis

Recovery from alcoholism is a life-long process. In fact, people who have suffered from alcoholism are encouraged to refer to themselves ever after as "a recovering alcoholic," never a recovered alcoholic. This is because most researchers in the field believe that since the potential for alcoholism is still part of the individual's biological and psychological makeup, one can never fully recover from alcoholism. The potential for relapse (returning to illness) is always there, and must be acknowledged and respected. Statistics suggest that, among middle-class alcoholics in stable financial and family situations who have undergone treatment, 60% or more can be successful at an attempt to stop drinking for at least a year, and many for a lifetime.

Prevention

Prevention must begin at a relatively young age since the first instance of intoxication (drunkenness) usu-

KEY TERMS

Blood-brain barrier—A network of blood vessels characterized by closely spaced cells that prevents many potentially toxic substances from penetrating the blood vessel walls to enter the brain. Alcohol is able to cross this barrier.

Detoxification—The phase of treatment during which a patient stops drinking and is monitored and cared for while he or she experiences withdrawal from alcohol.

Relapse—A return to a disease state, after recovery appeared to be occurring; in alcoholism, relapse refers to a patient beginning to drink alcohol again after a period of avoiding alcohol.

Tolerance—A phenomenon during which a drinker becomes physically accustomed to a particular quantity of alcohol, and requires ever-increasing quantities in order to obtain the same effects.

Withdrawal—Those signs and symptoms experienced by a person who has become physically dependent on a drug, experienced upon decreasing the drug's dosage or discontinuing its use.

ally occurs during the teenage years. It is particularly important that teenagers who are at high risk for alcoholism—those with a family history of alcoholism, an early or frequent use of alcohol, a tendency to drink to drunkenness, alcohol use that interferes with school work, a poor family environment, or a history of domestic violence—receive education about alcohol and its long-term effects. How this is best achieved, without irritating the youngsters and thus losing their attention, is the subject of continuing debate and study.

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Al-Anon, Alanon Family Group, Inc. P.O. Box 862, Midtown Station, New York, NY 10018-0862. (800)356-9996. <<http://www.recovery.org/aa>>.

Alcoholics Anonymous. Grand Central Station, Box 459, New York, NY 10163. <<http://www.alcoholics-anonymous.org/>>.

National Alliance on Alcoholism and Drug Dependence, Inc. 12 West 21st St., New York, NY 10010. (212)206-6770.

National Clearinghouse for Alcohol and Drug Information. <<http://www.health.org>>.

National Institute on Alcohol Abuse and Alcoholism (NIAAA) 6000 Executive Boulevard, Bethesda, Maryland 20892-7003. <<http://www.niaaa.nih.gov>>.

Bill Asenjo, MS, CRC

ALD see **Adrenoleukodystrophy**

Aldolase test

Definition

Aldolase is an enzyme found throughout the body, particularly in muscles. Like all enzymes, it is needed to trigger specific chemical reactions. Aldolase helps muscle turn sugar into energy. Testing for aldolase is done to diagnose and monitor skeletal muscle diseases.

Purpose

Skeletal muscle diseases increase the aldolase level found in a person's blood. Skeletal muscles are those muscles attached to bones and whose contractions make those bones move. When the muscles are diseased or damaged, such as in **muscular dystrophy**, the cells deteriorate and break open. The contents of the cells, including aldolase, spill into the bloodstream. Measuring the amount of aldolase in the blood indicates the degree of muscle damage.

As muscles continue to deteriorate, aldolase levels decrease and eventually fall below normal. Less muscle means fewer cells and less aldolase.

Muscle weakness may be caused by neurologic as well as muscular problems. The measurement of aldolase levels can help pinpoint the cause. Aldolase levels will be normal where muscle weakness is caused by neurological disease, such as poliomyelitis or **multiple sclerosis**, but aldolase levels will be elevated in cases of muscular disease, such as muscular dystrophy.

Aldolase is also found in the liver and cardiac muscle of the heart. Damage or disease to these organs, such as chronic hepatitis or a **heart attack**, will also increase aldolase levels in the blood, but to a lesser degree.

Description

Aldolase is measured by mixing a person's serum with a substance with which aldolase is known to trigger a reaction. The end product of this reaction is measured, and, from that measurement, the amount of aldolase in the person's serum is determined.

The test is covered by insurance when medically necessary. Results are usually available the next day.

Preparation

To collect the 5-10 ml of blood needed for this test, 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.

The patient should avoid strenuous **exercise** and have nothing to eat or drink, except water, for eight to ten hours before this test.

Aftercare

Discomfort or bruising may occur at the puncture site and the person may feel dizzy or faint. Pressure to the puncture site until the bleeding stops will reduce bruising. Warm packs to the puncture site will relieve discomfort.

Normal results

Newborns have the highest normal aldolase levels and adults the lowest. Normal values will vary based on the laboratory and the method used.

Abnormal results

As noted, aldolase is elevated in skeletal muscle diseases, such as muscular dystrophies. Duchenne's muscular dystrophy, the most common type of muscular dystrophy, will increase the aldolase level more than any other disease.

Nondisease conditions that affect the muscle, such as injury, **gangrene**, or an infection, can also increase the aldolase level. Also, strenuous exercise can temporarily increase a person's aldolase level.

KEY TERMS

Aldolase—An enzyme, found primarily in the muscle, that helps convert sugar into energy.

Enzyme—A substance needed to trigger specific chemical reactions.

Neurologic—Having to do with the nervous system.

Skeletal muscle—Muscle connected to, and necessary for the movement of, bones.

Certain medications can increase the aldolase level, while others can decrease it. To interpret what the results of the aldolase test mean, a physician will evaluate the result, the person's clinical symptoms, and other tests that are more specific for muscle damage and disease.

Resources

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A Manual of Laboratory and Diagnostic Tests. 5th ed. Ed.

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Nancy J. Nordenson

Aldosterone assay

Definition

This test measures the levels of aldosterone, a hormone produced by the outer part (cortex) of the two adrenal glands, organs which sit one on top of each of the kidneys. Aldosterone regulates the amounts of sodium and potassium in the blood. This helps maintain water balance and blood volume, which, in turn, affects blood pressure.

Purpose

Aldosterone measurement is useful in detecting a condition called aldosteronism, which is caused by excess secretion of the hormone from the adrenal glands.

There are two types of aldosteronism: primary and secondary. Primary aldosteronism is most commonly caused by an adrenal tumor, as in Conn's syndrome. Idiopathic (of unknown cause) **hyperaldosteronism** is another type of primary aldosteronism. Secondary aldosteronism is more common and may occur with congestive **heart failure**, **cirrhosis** with fluid in the abdominal cavity (**ascites**), certain kidney diseases, excess potassium, sodium-depleted diet, and toxemia of **pregnancy**.

To differentiate primary aldosteronism from secondary aldosteronism, a plasma renin test should be performed at the same time as the aldosterone assay. Renin, an enzyme produced in the kidneys, is high in secondary aldosteronism and low in primary aldosteronism.

Description

Aldosterone testing can be performed on a blood sample or on a 24-hour urine specimen. Several factors, including diet, posture (upright or lying down), and time of day that the sample is obtained can cause aldosterone levels to fluctuate. Blood samples are affected by short-term fluctuations. A urine specimen collected over an entire 24-hour period lessens the effects of those interfering factors and provides a more reliable aldosterone measurement.

Preparation

Fasting is not required for either the blood sample or urine collection, but the patient should maintain a normal sodium diet (approximately 0.1 oz [3 g] /day) for at least two weeks before either test. The doctor should decide if drugs that alter sodium, potassium, and fluid balance (e.g., **diuretics**, antihypertensives, steroids, **oral contraceptives**) should be withheld. The test will be more accurate if these are suspended at least two weeks before the test. Renin inhibitors (e.g., propranolol) should not be taken one week before the test, unless permitted by the physician. The patient should avoid licorice for at least two weeks before the test, because of its aldosterone-like effect. Strenuous **exercise** and **stress** can increase aldosterone levels as well. Because the test is usually performed by a method called radioimmunoassay, recently administered radioactive medications will affect test results.

Since posture and body position affect aldosterone, hospitalized patients should remain in an upright position (at least sitting) for two hours before blood is drawn. Occasionally blood will be drawn again before the patient gets out of bed. Nonhospitalized patients should arrive at the laboratory in time to maintain an upright position for at least two hours.

KEY TERMS

Aldosteronism—A condition in which the adrenal glands secrete excessive levels of the hormone aldosterone.

Renin—An enzyme produced in the kidneys that controls the activation of the hormone angiotensin, which stimulates the adrenal glands to produce aldosterone.

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 results are laboratory-specific and also vary with sodium intake, with time of day, source of specimen (e.g., peripheral vein, adrenal vein, 24-hour urine), age, sex, and posture.

Reference ranges for blood include:

- supine (lying down): 3-10 ng/dL
- upright (sitting for at least two hours): Female: 5-30ng/dL; Male: 6-22 ng/dL

Reference ranges for urine: 2-80 mg/24 hr.

Abnormal results

Increased levels of aldosterone are found in Conn's disease (aldosterone-producing adrenal tumor), and in cases of Bartter's syndrome (a condition in which the kidneys overexcrete potassium, sodium and chloride, resulting in low blood levels of potassium and high blood levels of aldosterone and renin). Among other conditions, elevated levels are also seen in secondary aldosteronism, stress, and malignant **hypertension**.

Decreased levels of aldosterone are found in aldosterone deficiency, steroid therapy, high-sodium **diets**, certain antihypertensive therapies, and **Addison's disease** (an autoimmune disorder).

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Janis O. Flores

Alemtuzumab

Definition

Alemtuzumab is sold as Campath in the United States. Alemtuzumab is a humanized monoclonal antibody that selectively binds to CD52, a protein found on the surface of normal and malignant B and T cells, that is used to reduce the numbers of circulating malignant cells of patients who have B-cell chronic lymphocytic leukemia (B-CLL).

Purpose

Alemtuzumab is a monoclonal antibody used to treat B-CLL, one of the most prevalent forms of adult chronic leukemia. It specifically binds CD52, a protein found on the surface of essentially all B and T cells of the immune system. By binding the CD52 protein on the malignant B cells, the antibody targets it for removal from the circulation. Scientists believe that alemtuzumab triggers antibody-mediated lysis of the B cells, a method that the immune system uses to eliminate foreign cells.

Alemtuzumab has been approved by the FDA for treatment of refractory B-CLL. For a patient's disease to be classified as refractory, both alkylating agents and fludarabine treatment must have been tried and failed. Thus, this drug gives patients who have tried all approved treatments for B-CLL another option. As most patients with B-CLL are in stage III or IV by the time both alkylating agents and fludarabine have been tried, the experience with alemtuzumab treatment are primarily with those stages of the disease. In clinical trials, about 30% of patients had a partial response to the drug, with 2% of these being complete responses.

This antibody has been tested with limited success in the treatment of non-Hodgkin's lymphoma (NHL) and for the preparation of patients with various immune cell malignancies for bone marrow transplantation. There is also a clinical trial ongoing to test the ability of this antibody to prevent rejection in kidney transplantation.

Description

Alemtuzumab is produced in the laboratory using genetically engineered single clones of B-cells. Like all antibodies, it is a Y-shaped molecule can bind one particular substance, the antigen for that monoclonal antibody. For alemtuzumab, the antigen is CD52, a protein found on the surface of normal and malignant B and T cells as well as other cells of the immune and male reproductive systems. Alemtuzumab is a humanized antibody, meaning that the regions that bind CD52, located on the tips of

the Y branches, are derived from rat antibodies, but the rest of the antibody is human sequence. The presence of the human sequences helps to reduce the immune response by the patient against the antibody itself, a problem seen when complete mouse antibodies are used for cancer therapies. The human sequences also help to ensure that the various cell-destroying mechanisms of the human immune system are properly triggered with binding of the antibody.

Alemtuzumab was approved in May of 2001 for the treatment of refractory B-CLL. It is approved for use alone but clinical trials have tested the ability of the antibody to be used in combination with the purine analogs pentostatin, fludarabine, and cladribine, and rituximab, a monoclonal antibody specific for the CD20 antigen, another protein found on the surface of B cells.

Recommended dosage

This antibody should be administered in a gradually escalating pattern at the start of treatment and any time administration is interrupted for seven or more days. The recommended beginning dosage for B-CLL patients is a daily dose of 3 mg of Campath administered as a two-hour IV infusion. Once this amount is tolerated, the dose is increased to 10 mg per day. After tolerating this dose, it can be increased to 30 mg, administered three days a week. Acetaminophen and diphenhydramine hydrochloride are given thirty to sixty minutes before the infusion to help reduce side effects.

Additionally, patients generally receive anti-infective medication before treatment to help minimize the serious opportunistic infections that can result from this treatment. Specifically, trimethoprim/sulfamethoxazole (to prevent bacterial infections) and famciclovir (to prevent viral infections) were used during the clinical trial to decrease infections, although they were not eliminated.

Precautions

Blood studies should be done on a weekly basis while patients are receiving the alemtuzumab treatment. Vaccination during the treatment session is not recommended, given the T cell depletion that occurs during treatment. Furthermore, given that antibodies like alemtuzumab can pass through the placenta to the developing fetus and in breast milk, use during pregnancy and breastfeeding is not recommended unless clearly needed.

Side effects

A severe side effect of alemtuzumab treatment is the possible depletion of one or more types of blood cells.

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 chemotherapeutic agent to treat B-CLL.

Antibody—A protective protein made by the immune system in response to an antigen, also called an immunoglobulin.

Autoimmune—An immune reaction of a patient against their own cells.

Humanization—Fusing the constant and variable framework region of one or more human immunoglobulins with the binding region of an animal immunoglobulin, done to reduce human reaction against the fusion antibody.

Monoclonal—Genetically engineered antibodies specific for one antigen.

Tumor lysis syndrome—A side effect of some immunotherapies, like monoclonal antibodies, that lyse the tumor cells, due to the toxicity of flooding the bloodstream with such a quantity of cellular contents.

Because CD52 is expressed on a patient's normal B and T cells, as well as on the surface of the abnormal B cells, the treatment eliminates both normal and cancerous cells. The treatment also seems to trigger autoimmune reactions against various other blood cells. This results in severe reduction of the many circulating blood cells including red blood cells (anemia), white blood cells (neutropenia), and clotting cells (thrombopenia). These conditions are treated with blood transfusions. The great majority of patients treated exhibit some type of blood cell depletion.

A second serious side effect of this drug is the prevalence of opportunistic infections that occurs during the treatment. Serious, and sometimes fatal bacterial, viral, fungal, and protozoan infections have been reported. Treatments to prevent pneumonia and herpes infections reduce, but do not eliminate these infections.

The majority of other side effects occur after or during the first infusion of the drug. Some common side effects of this drug include fever and chills, nausea and vomiting, diarrhea, shortness of breath, skin rash, and unusual fatigue. This drug can also cause low blood pressure (hypotension).

In patients with high tumor burden (a large number of circulating malignant B cells) this drug can cause a side effect called tumor lysis syndrome. Thought to be due to the release of the lysed cells' contents into the blood stream, it can cause a misbalance of urea, uric acid, phosphate, potassium, and calcium in the urine and blood. Patients at risk for this side effect must keep hydrated and can be given allopurinol before infusion.

Interactions

There have been no formal drug interaction studies done for alemtuzumab.

Michelle Johnson, M.S., J.D.

Alendronate see **Bone disorder drugs**

Alexander technique

Definition

The Alexander technique is a somatic method for improving physical and mental functioning. Excessive tension, which Frederick Alexander, the originator, recognized as both physical and mental, restricts movement and creates pressure in the joints, the spine, the breathing mechanism, and other organs. The goal of the technique is to restore freedom and expression to the body and clear thinking to the mind.

Purpose

Because the Alexander technique helps students improve overall functioning, both mental and physical, it offers a wide range of benefits. Nikolaas Tinbergen, in his 1973 Nobel lecture, hailed the "striking improvements in such diverse things as high blood pressure, breathing, depth of sleep, overall cheerfulness and mental alertness, resilience against outside pressures, and the refined skill of playing a musical instrument." He went on to quote a list of other conditions helped by the Alexander technique: "rheumatism, including various forms of arthritis, then respiratory troubles, and even potentially lethal **asthma**; following in their wake, circulation defects, which may lead to high blood pressure and also to some dangerous heart conditions; gastrointestinal disorders of many types, various gynecological conditions, sexual failures, migraines and depressive states."

Literature in the 1980s and 1990s went on to include improvements in back **pain**, chronic pain, postural prob-

lems, repetitive strain injury, benefits during **pregnancy** and **childbirth**, help in applying physical therapy and rehabilitative exercises, improvements in strain caused by computer use, improvements in the posture and performance of school children, and improvements in vocal and dramatic performance among the benefits offered by the technique.

Description

Origins

Frederick Matthias Alexander was born in 1869 in Tasmania, Australia. He became an actor and Shakespearean reciter, and early in his career he began to suffer from strain on his vocal chords. He sought medical attention for chronic hoarseness, but after treatment with a recommended prescription and extensive periods of rest, his problem persisted.

Alexander realized that his hoarseness began about an hour into a dramatic performance and reasoned that it was something he did in the process of reciting that caused him to lose his voice. Returning to his medical doctor, Alexander told him of his observation. When the doctor admitted that he didn't know what Alexander was doing to injure his vocal chords, Alexander decided to try and find out for himself.

Thus began a decade of self-observation and discovery. Using as many as three mirrors to observe himself in the act of reciting, normal speaking, and later standing, walking, and sitting, Alexander managed to improve his coordination and to overcome his vocal problems. One of his most startling discoveries was that in order to change the way he used his body he had to change the way he was thinking, redirecting his thoughts in such a way that he did not produce unnecessary tension when he attempted speech or movement. After making this discovery at the end of the nineteenth century, Alexander became a pioneer in body-mind medicine.

At first, performers and dancers sought guidance from Alexander to overcome physical complaints and to improve the expression and spontaneity of their performances. Soon a great number of people sought help from his teaching for a variety of physical and mental disorders.

The Alexander technique is primarily taught one-on-one in private lessons. Introductory workshops or workshops for special applications of the technique (e.g., workshops for musicians) are also common. Private lessons range from a half-hour to an hour in length, and are taught in a series. The number of lessons varies according to the severity of the student's difficulties with coordination or to the extent of the student's inter-

est in pursuing the improvements made possible by continued study. The cost of lessons ranges from \$40-80 per hour. Insurance coverage is not widely available, but discounts are available for participants in some complementary care insurance plans. Pre-tax Flexible Spending Accounts for health care cover Alexander technique lessons if they are prescribed by a physician.

In lessons teachers guide students through simple movements (while students are dressed in comfortable clothing) and use their hands to help students identify and stop destructive patterns of tension. Tensing arises from mental processes as well as physical, so discussions of personal reactions or behavior are likely to arise in the course of a lesson.

The technique helps students move with ease and improved coordination. At the beginning of a movement (the lessons are a series of movements), most people pull back their heads, raise their shoulders toward their ears, over-arch their lower backs, tighten their legs, and otherwise produce excessive tension in their bodies. Alexander referred to this as misuse of the body.

At any point in a movement, proper use can be established. If the neck muscles are not over-tensed, the head will carry slightly forward of the spine, simply because it is heavier in the front. When the head is out of balance in the forward direction, it sets off a series of stretch reflexes in the extensor muscles of the back. It is skillful use of these reflexes, along with reflex activity in the feet and legs, the arms and hands, the breathing mechanism, and other parts of the body, that lessons in the technique aim to develop.

Alexander found that optimal functioning of the body was very hard to maintain, even for the short period of time it took to complete a single movement. People, especially adults, have very strong tension habits associated with movement. Chronic misuse of the muscles is common. It may be caused by slouching in front of televisions or video monitors, too much sitting or driving and too little walking, or by tension associated with past traumas and injuries. Stiffening the neck after a **whiplash** injury or favoring a broken or sprained leg long after it has healed are examples of habitual tension caused by injury.

The first thing a teacher of the Alexander technique does is to increase a student's sensory awareness of this excessive habitual tension, particularly that in the neck and spine. Next the student is taught to inhibit the tension. If the student prepares to sit down, for example, he will tense his muscles in his habitual way. If he is asked to put aside the intention to sit and instead to free his neck and allow less constriction in

his muscles, he can begin to change his tense habitual response to sitting.

By leaving the head resting on the spine in its natural free balance, by keeping eyes open and focused, not held in a tense stare, by allowing the shoulders to release, the knees to unlock and the back to lengthen and widen, a student greatly reduces strain. In Alexander lessons students learn to direct themselves this way in activity and become skilled in fluid, coordinated movement.

Precautions

Side effects

The focus of the Alexander technique is educational. Teachers use their hands simply to gently guide students in movement. Therefore, both contraindications and potential physiological side effects are kept to a minimum. No forceful treatment of soft tissue or bony structure is attempted, so damage to tissues, even in the case of errors in teaching, is unlikely.

As students' sensory awareness develops in the course of Alexander lessons, they become more acutely aware of chronic tension patterns. As students learn to release excessive tension in their muscles and to sustain this release in daily activity, they may experience tightness or soreness in the connective tissue. This is caused by the connective tissue adapting to the lengthened and released muscles and the expanded range of movement in the joints.

Occasionally students may get light-headed during a lesson as contracted muscles release and effect the circulatory or respiratory functioning.

Forceful contraction of muscles and rigid postures often indicate suppression of emotion. As muscles release during or after an Alexander lesson, students may experience strong surges of emotion or sudden changes in mood. In some cases, somatic memories surface, bringing to consciousness past injury or trauma. This can cause extreme **anxiety**, and referrals may be made by the teacher for counseling.

Research and general acceptance

Alexander became well known among the intellectual, artistic, and medical communities in London, England, during the first half of the twentieth century. Among Alexander's supporters were John Dewey, Aldous Huxley, Bernard Shaw, and renowned scientists Raymond Dart, G.E. Coghill, Charles Sherrington, and Nikolaas Tinbergen.

Researchers continue to study the effects and applications of the technique in the fields of education, pre-

KEY TERMS

Direction—Bringing about the free balance of the head on the spine and the resulting release of the erector muscles of the back and legs which establish improved coordination.

Habit—Referring to the particular set of physical and mental tensions present in any individual.

Inhibition—Referring to the moment in an Alexander lesson when the student refrains from beginning a movement in order to avoid tensing of the muscles.

Sensory awareness—Bringing attention to the sensations of tension and/or release in the muscles.

ventive medicine, and **rehabilitation**. The Alexander technique has proven an effective treatment for reducing **stress**, for improving posture and performance in schoolchildren, for relieving chronic pain, and for improving psychological functioning. The technique has been found to be as effective as beta-blocker medications in controlling stress responses in professional musicians, to enhance respiratory function in normal adults, and to mediate the effects of **scoliosis** in adolescents and adults.

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ORGANIZATIONS

- American Society for the Alexander Technique, 401 East Market Street (P.O. Box 835) Charlottesville, VA 22902 USA. (800) 473-0620; or (804) 295-2840. Fax: 804-295-3947. alexandertec@earthlink.net. <<http://www.alexandertech.org>>.

Alexander Technique International, 1692 Massachusetts Ave., 3rd Floor, Cambridge, MA 02138 USA. (888) 321-0856. Fax: 617-497-2615. ati@ati-net.com. <http://www.ati-net.com>.

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Sandra Bain Cushman

Alkali-resistant hemoglobin test see Fetal hemoglobin test

Alkaline phosphatase test

Definition

Alkaline phosphatase is an enzyme found throughout the body. Like all enzymes, it is needed, in small amounts, to trigger specific chemical reactions. When it is present in large amounts, it may signify bone or liver disease or a tumor.

Purpose

Medical testing of alkaline phosphatase is concerned with the enzyme that is found in liver, bone, placenta, and intestine. In a healthy liver, fluid containing alkaline phosphate and other substances is continually drained away through the bile duct. In a diseased liver, this bile duct is often blocked, keeping fluid within the liver. Alkaline phosphatase accumulates and eventually escapes into the bloodstream.

The alkaline phosphatase of the liver is produced by the cells lining the small bile ducts (ductoles) in the liver. Its origin differs from that of other enzymes called aminotransferases. If the liver disease is primarily of an obstructive nature (cholestatic), i.e. involving the biliary drainage system, the alkaline phosphatase will be the first and foremost enzyme elevation. If, on the other hand, the disease is primarily of the liver cells (hepatocytes), the aminotransferases will rise prominently. Thus, these enzymes are very useful in distinguishing the type of liver disease—cholestatic or hepatocellular.

Growing bones need alkaline phosphatase. Any condition of bone growth will cause alkaline phosphatase

levels to rise. The condition may be normal, such as a childhood growth spurt or the healing of a broken bone; or the condition may be a disease, such as bone cancer, Paget's disease, or rickets.

During pregnancy, alkaline phosphatase is made by the placenta and leaks into the mother's bloodstream. This is normal. Some tumors, however, start production of the same kind of alkaline phosphatase produced by the placenta. These tumors are called germ cell tumors and include **testicular cancer** and certain brain tumors.

Alkaline phosphatase from the intestine is increased in a person with inflammatory bowel disease, such as **ulcerative colitis**.

Description

Alkaline phosphatase is measured by combining the person's serum with specific substances with which alkaline phosphatase is known to react. The end product of this reaction is measured; and from that measurement, the amount of alkaline phosphatase in the person's serum is determined.

Each tissue—liver, bone, placenta, and intestine—produces a slightly different alkaline phosphatase. These variations are called isoenzymes. In the laboratory, alkaline phosphatase is measured as the total amount or the amount of each of the four isoenzymes. The isoenzymes react differently to heat, certain chemicals, and other processes in the laboratory. Methods to measure them separately are based on these differences.

The test is covered by insurance when medically necessary. Results are usually available the next day.

Preparation

To collect the 5-10 ml blood needed for this test, a healthcare worker ties a tourniquet on the person'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.

A person being tested for alkaline phosphatase shouldn't have anything to eat or drink, except water, for eight to ten hours before the test. Some people release alkaline phosphatase from the intestine into the bloodstream after eating. This will temporarily increase the result of the test.

Aftercare

Discomfort or bruising may occur at the puncture site or the person may feel dizzy or faint. Pressure to the

KEY TERMS

Alkaline phosphatase—An enzyme found throughout the body, primarily in liver, bone, placenta, and intestine.

Cholestasis—Stoppage or suppression of the flow of bile.

Enzyme—A substance needed to trigger specific chemical reactions.

Hepatocellular—Of or pertaining to liver cells.

Hepatocyte—A liver cell.

Isoenzyme—A variation of an enzyme.

puncture site until the bleeding stops will reduce bruising. Warm packs to the puncture site will relieve discomfort.

Normal results

Normal results vary by age and by sex. They also vary based on the laboratory and the method used.

Abnormal results

Bone and liver disease increase alkaline phosphatase more than any other disease, up to five times the normal level. Irritable bowel disease, germ cell tumors, and infections involving the liver, such as viral hepatitis and **infectious mononucleosis**, increase the enzyme also, but to a lesser degree. Healing bones, pregnancy, and normal growth in children also increase levels.

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Nancy J. Nordenson

Alkalosis see **Metabolic alkalosis; Respiratory alkalosis**

Allergic alveolitis see **Hypersensitivity pneumonitis**

Allergic bronchopulmonary aspergillosis

Definition

Allergic bronchopulmonary **aspergillosis**, or ABPA, is one of four major types of infections in humans caused by *Aspergillus* fungi. ABPA is a hypersensitivity reaction that occurs in **asthma** patients who are allergic to this specific fungus.

Description

ABPA is an allergic reaction to a species of *Aspergillus* called *Aspergillus fumigatus*. It is sometimes grouped together with other lung disorders characterized by eosinophilia—an abnormal increase of a certain type of white blood cell in the blood—under the heading of **eosinophilic pneumonia**. These disorders are also called hypersensitivity lung diseases.

ABPA appears to be increasing in frequency in the United States, although the reasons for the increase are not clear. The disorder is most likely to occur in adult asthmatics aged 20-40. It affects males and females equally.

Causes and symptoms

ABPA develops when the patient breathes air containing *Aspergillus* spores. These spores are found worldwide, especially around riverbanks, marshes, bogs, forests, and wherever there is wet or decaying vegetation. They are also found on wet paint, construction materials, and in air conditioning systems. ABPA is a nosocomial infection, which means that a patient can get it in a hospital. When *Aspergillus* spores reach the bronchi, which are the branches of the windpipe that lead into the lungs, the bronchi react by contracting spasmodically. So the patient has difficulty breathing and usually wheezes or coughs. Many patients with ABPA also run a low-grade fever and lose their appetites.

Complications

Patients with ABPA sometimes **cough** up large amounts of blood, a condition that is called **hemoptysis**. They may also develop a serious long-term form of **bronchiectasis**, the formation of fibrous tissue in the lungs. Bronchiectasis is a chronic bronchial disorder

caused by repeated inflammation of the airway, and marked by the abnormal enlargement of, or damage to, the bronchial walls. ABPA sometimes occurs as a complication of **cystic fibrosis**.

Diagnosis

The diagnosis of ABPA is based on a combination of the patient's history and the results of blood tests, sputum tests, skin tests, and diagnostic imaging. The doctor will be concerned to distinguish between ABPA and a worsening of the patient's asthma, cystic fibrosis, or other lung disorders. There are seven major criteria for a diagnosis of allergic bronchopulmonary aspergillosis:

- a history of asthma.
- an accumulation of fluid in the lung that is visible on a **chest x ray**.
- bronchiectasis (abnormal stretching, enlarging, or destruction of the walls of the bronchial tubes).
- skin reaction to *Aspergillus* antigen.
- eosinophilia in the patient's blood and sputum.
- *Aspergillus* precipitins in the patient's blood. Precipitins are antibodies that react with the antigen to form a solid that separates from the rest of the solution in the test tube.
- a high level of IgE in the patient's blood. IgE refers to a class of antibodies in blood plasma that activate allergic reactions to foreign particles.

Other criteria that may be used to support the diagnosis include the presence of *Aspergillus* in samples of the patient's sputum, the coughing up of plugs of brown mucus, or a late skin reaction to the *Aspergillus* antigen.

Laboratory tests

The laboratory tests that are done to obtain this information include a complete **blood count** (CBC), a **sputum culture**, a blood serum test of IgE levels, and a skin test for the *Aspergillus* antigen. In the skin test, a small amount of antigen is injected into the upper layer of skin on the patient's forearm about four inches below the elbow. If the patient has a high level of IgE antibodies in the tissue, he or she will develop what is called a "wheal and flare" reaction in about 15-20 minutes. A "wheal and flare" reaction is characterized by the eruption of a reddened, **itching** spot on the skin. Some patients with ABPA will develop the so-called late reaction to the skin test, in which a red, sore, swollen area develops about six to eight hours after the initial reaction.

Aspergillus can sometimes be seen under a microscope slide made from the patient's sputum, but the diag-

nosis is considered definite only when the fungus is cultured in the laboratory. *Aspergillus* is easy to culture, and can be identified when it is stained with periodic acid-Schiff (PAS), Calcofluor, or potassium hydroxide (KOH) preparations.

Diagnostic imaging

Chest x rays and CT scans are used to check for the presence of fluid accumulation in the lungs and signs of bronchiectasis.

Treatment

ABPA is usually treated with prednisone (Meticorten) or other **corticosteroids** taken by mouth, and with **bronchodilators**.

Antifungal drugs are *not* used to treat ABPA because it is caused by an allergic reaction to *Aspergillus* rather than by direct infection of tissue.

Follow-up care

Patients with ABPA should be given periodic checkups with chest x rays and a spirometer test. A spirometer is an instrument that evaluates the patient's lung capacity.

Prognosis

Most patients with ABPA respond well to corticosteroid treatment. Others have a chronic course with gradual improvement over time. The best indicator of a good prognosis is a long-term fall in the patient's IgE level. Patients with lung complications from ABPA may develop severe airway obstruction.

Prevention

ABPA is difficult to prevent because *Aspergillus* is a common fungus; it can be found in the saliva and sputum of most healthy individuals. Patients with ABPA can protect themselves somewhat by avoiding haystacks, compost piles, bogs, marshes, and other locations with wet or rotting vegetation; by avoiding construction sites or newly painted surfaces; and by having their air conditioners cleaned regularly. Some patients may be helped by air filtration systems for their bedrooms or offices.

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KEY TERMS

Antifungal—A medicine used to treat infections caused by a fungus.

Antigen—A substance that stimulates the production of antibodies.

Bronchiectasis—A disorder of the bronchial tubes marked by abnormal stretching, enlargement, or destruction of the walls. Bronchiectasis is usually caused by recurrent inflammation of the airway and is a diagnostic criterion of ABPA.

Bronchodilator—A medicine used to open up the bronchial tubes (air passages) of the lungs.

Eosinophil—A type of white blood cell containing granules that can be stained by eosin (a chemical that produces a red stain).

Eosinophilia—An abnormal increase in the number of eosinophils in the blood.

Hemoptysis—The coughing up of large amounts of blood. Hemoptysis can occur as a complication of ABPA.

Hypersensitivity—An excessive response by the body to a foreign substance.

Immunoglobulin E (IgE)—A type of protein in blood plasma that acts as an antibody to activate allergic reactions. About 50% of patients with allergic disorders have increased IgE levels in their blood serum.

Nosocomial infection—An infection that can be acquired in a hospital. ABPA is a nosocomial infection.

Precipitin—An antibody in blood that combines with an antigen to form a solid that separates from the rest of the blood.

Spirometer—An instrument used to test a patient's lung capacity.

"Wheal and flare" reaction—A rapid response to a skin allergy test characterized by the development of a red, itching spot in the area where the allergen was injected.

Wheezing—A whistling or musical sound caused by tightening of the air passages inside the patient's chest.

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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 Organization for Rare Disorders. P.O. Box 8923, New Fairfield, CT 06812-8923. (800) 999-6673. <<http://www.rarediseases.org>>.

National Institute of Allergy and Infectious Disease. Building 31, Room 7A-50, 31 Center Drive MSC 2520, Bethesda, MD 20892-2520. (301) 496-5717. <<http://www.niaid.nih.gov/default.htm>>.

Rebecca J. Frey

Allergic purpura

Definition

Allergic purpura (AP) is an allergic reaction of unknown origin causing red patches on the skin and other symptoms. AP is also called Henoch-Schonlein purpura, named after the two doctors who first described it.

Description

"Purpura" is a bleeding disorder that occurs when capillaries rupture, allowing small amounts of blood to accumulate in the surrounding tissues. In AP, this occurs because the capillaries are blocked by protein complexes

formed during an abnormal immune reaction. The skin is the most obvious site of reaction, but the joints, gastrointestinal tract, and kidneys are also often affected.

AP affects approximately 35,000 people in the United States each year. Most cases are children between the ages of two and seven. Boys are affected more often than girls, and most cases occur from late fall to winter.

Causes and symptoms

Causes

AP is caused by a reaction involving antibodies, special proteins of the immune system. Antibodies are designed to bind with foreign proteins, called antigens. In some situations, antigen-antibody complexes can become too large to remain suspended in the bloodstream. When this occurs, they precipitate out and become lodged in the capillaries. This can cause the capillary to burst, allowing a local hemorrhage.

The source of the antigen causing AP is unknown. Antigens may be introduced by bacterial or viral infection. More than 75% of patients report having had an infection of the throat, upper respiratory tract, or gastrointestinal system several weeks before the onset of AP. Other complex molecules can act as antigens as well, including drugs such as **antibiotics** or vaccines. Otherwise harmless substances that stimulate an immune reaction are known as allergens. Drug allergens that may cause AP include penicillin, ampicillin, erythromycin, and quinine. Vaccines possibly linked to AP include those for typhoid, **measles**, **cholera**, and **yellow fever**.

Symptoms

The onset of AP may be preceded by a **headache**, **fever**, and loss of appetite. Most patients first develop an itchy skin rash. The rash is red, either flat or raised, and may be small and freckle-like. The rash may also be larger, resembling a bruise. **Rashes** become purple and then rust colored over the course of a day, and fade after several weeks. Rashes are most common on the buttocks, abdomen, and lower extremities. Rashes higher on the body may also occur, especially in younger children.

Joint **pain** and swelling is common, especially in the knees and ankles. Abdominal pain occurs in almost all patients, along with blood in the body waste (feces). About half of all patients show blood in the urine, low urine volume, or other signs of kidney involvement. Kidney failure may occur due to widespread obstruction of the capillaries in the filtering structures called glomeruli. Kidney failure develops in about 5% of all patients, and in 15% of those with elevated blood or protein in the urine.

KEY TERMS

Glomeruli—Knots of capillaries in the kidneys responsible for filtering the blood (singular, glomerulus).

Less common symptoms include prolonged headache, fever, and pain and swelling of the scrotum. Involvement of other organ systems may lead to **heart attack** (myocardial infarction), inflammation of the pancreas (**pancreatitis**), intestinal obstruction, or bowel perforation.

Diagnosis

Diagnosis of AP is based on the symptoms and their development, a careful medical history, and blood and urine tests. X rays or **computed tomography scans (CT)** may be performed to assess complications in the bowel or other internal organs.

Treatment

Most cases of AP resolve completely without treatment. Nonetheless, a hospital stay is required because of the possibility of serious complications. Non-aspirin pain relievers may be given for joint pain. **Corticosteroids** (like prednisone) are sometimes used, although not all specialists agree on their utility. Kidney involvement requires monitoring and correction of blood fluids and electrolytes.

Patients with severe kidney complications may require a **kidney biopsy** so that tissue can be analyzed. Even after all other symptoms subside, elevated levels of blood or protein in the urine may persist for months and require regular monitoring. **Hypertension** or kidney failure may develop months or even years after the acute phase of the disease. Kidney failure requires dialysis or transplantation.

Plasmapheresis, which removes antibodies from the blood, has been tried for AP with mixed results.

Prognosis

Most people who develop AP become better on their own after several weeks. About half of all patients have at least one recurrence. Cases that do not have kidney complications usually have the best prognosis.

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Richard Robinson

Allergic rhinitis

Definition

Allergic rhinitis, more commonly referred to as hay fever, is an inflammation of the nasal passages caused by allergic reaction to airborne substances.

Description

Allergic rhinitis (AR) is the most common allergic condition and one of the most common of all minor afflictions. It affects between 10-20% of all people in the United States, and is responsible for 2.5% of all doctor visits. **Antihistamines** and other drugs used to treat allergic rhinitis make up a significant fraction of both prescription and over-the-counter drug sales each year.

There are two types of allergic rhinitis: seasonal and perennial. Seasonal AR occurs in the spring, summer, and early fall, when airborne plant pollens are at their highest levels. In fact, the term hay fever is really a misnomer, since allergy to grass pollen is only one cause of symptoms for most people. Perennial AR occurs all year and is usually caused by home or workplace airborne pollutants. A person can be affected by one or both types. Symptoms of seasonal AR are worst after being outdoors, while symptoms of perennial AR are worst after spending time indoors.

Both types of **allergies** can develop at any age, although onset in childhood through early adulthood is most common. Although allergy to a particular substance is not inherited, increased allergic sensitivity may “run in the family.” While allergies can improve on their own over time, they can also become worse over time.

Causes and symptoms

Causes

Allergic rhinitis is a type of immune reaction. Normally, the immune system responds to foreign microorganisms, or particles, like pollen or dust, by producing

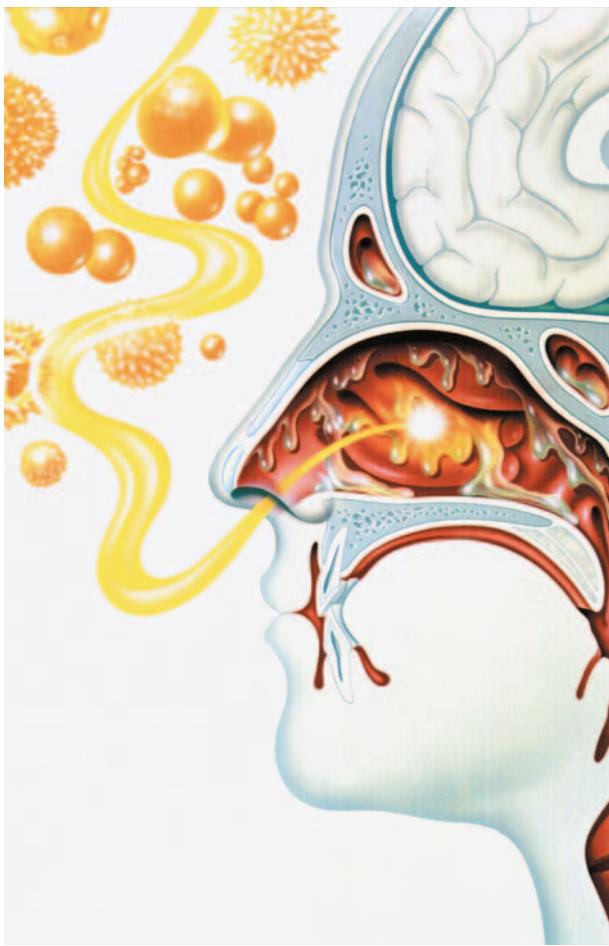
specific proteins, called antibodies, that are capable of binding to identifying molecules, or antigens, on the foreign particle. This reaction between antibody and antigen sets off a series of reactions designed to protect the body from infection. Sometimes, this same series of reactions is triggered by harmless, everyday substances. This is the condition known as allergy, and the offending substance is called an allergen.

Like all allergic reactions, AR involves a special set of cells in the immune system known as mast cells. Mast cells, found in the lining of the nasal passages and eyelids, display a special type of antibody, called immunoglobulin type E (IgE), on their surface. Inside, mast cells store reactive chemicals in small packets, called granules. When the antibodies encounter allergens, they trigger release of the granules, which spill out their chemicals onto neighboring cells, including blood vessels and nerve cells. One of these chemicals, histamine, binds to the surfaces of these other cells, through special proteins called histamine receptors. Interaction of histamine with receptors on blood vessels causes neighboring cells to become leaky, leading to the fluid collection, swelling, and increased redness characteristic of a runny nose and red, irritated eyes. Histamine also stimulates **pain** receptors, causing the itchy, scratchy nose, eyes, and throat common in allergic rhinitis.

The number of possible airborne allergens is enormous. Seasonal AR is most commonly caused by grass and tree pollens, since their pollen is produced in large amounts and is dispersed by the wind. Showy flowers, like roses or lilacs, that attract insects produce a sticky pollen which is less likely to become airborne. Different plants release their pollen at different times of the year, so seasonal AR sufferers may be most affected in spring, summer, or fall, depending on which plants provoke a response. The amount of pollen in the air is reflected in the pollen count, often broadcast on the daily news during allergy season. Pollen counts tend to be lower after a good rain that washes the pollen out of the air and higher on warm, dry, windy days.

Virtually any type of tree or grass may cause AR. A few types of weeds that tend to cause the most trouble for people include the following:

- ragweed
- sagebrush
- lamb's-quarters
- plantain
- pigweed
- dock/sorrel



This illustration depicts excessive mucus production in the nose after inhalation of airborne pollen. (Photo Researchers, Inc. Reproduced by permission.)

- tumbleweed

Perennial AR is often triggered by house dust, a complicated mixture of airborne particles, many of which are potent allergens. House dust contains some or all of the following:

- house mite body parts. All houses contain large numbers of microscopic insects called house mites. These harmless insects feed on fibers, fur, and skin shed by the house's larger occupants. Their tiny body parts easily become airborne.
- animal dander. Animals constantly shed fur, skin flakes, and dried saliva. Carried in the air, or transferred from pet to owner by direct contact, dander can cause allergy in many sensitive people.
- mold spores. Molds live in damp spots throughout the house, including basements, bathrooms, air ducts, air conditioners, refrigerator drains, damp windowsills, mattresses, and stuffed furniture. Mildew and other

molds release airborne spores which circulate throughout the house.

Other potential causes of perennial allergic rhinitis include the following:

- cigarette smoke
- perfume
- cosmetics
- cleansers
- copier chemicals
- industrial chemicals
- construction material gases

Symptoms

Inflammation of the nose, or rhinitis, is the major symptom of AR. Inflammation causes **itching**, sneezing, runny nose, redness, and tenderness. Sinus swelling can constrict the eustachian tube that connects the inner ear to the throat, causing a congested feeling and "ear popping." The drip of mucus from the sinuses down the back of the throat, combined with increased sensitivity, can also lead to throat irritation and redness. AR usually also causes redness, itching, and watery eyes. **Fatigue** and **headache** are also common.

Diagnosis

Diagnosing seasonal AR is usually easy and can often be done without a medical specialist. When symptoms appear in spring or summer and disappear with the onset of cold weather, seasonal AR is almost certainly the culprit. Other causes of rhinitis, including infection, can usually be ruled out by a **physical examination** and a nasal smear, in which a sample of mucus is taken on a swab for examination.

Allergy tests, including skin testing and provocation testing, can help identify the precise culprit, but may not be done unless a single source is suspected and subsequent avoidance is possible. Skin testing involves placing a small amount of liquid containing a specific allergen on the skin and then either poking, scratching, or injecting it into the skin surface to observe whether redness and swelling occurs. Provocation testing involves challenging an individual with either a small amount of an inhalable or ingestible allergen to see if a response is elicited.

Perennial AR can also usually be diagnosed by careful questioning about the timing of exposure and the onset of symptoms. Specific allergens can be identified through allergy skin testing.

Treatment

Avoidance of the allergens is the best treatment, but this is often not possible. When it is not possible to avoid one or more allergens, there are two major forms of medical treatment, drugs and immunotherapy.

Drugs

ANTIHISTAMINES. Antihistamines block the histamine receptors on nasal tissue, decreasing the effect of histamine release by mast cells. They may be used after symptoms appear, though they may be even more effective when used preventively, before symptoms appear. A wide variety of antihistamines are available.

Older antihistamines often produce drowsiness as a major side effect. Such antihistamines include the following:

- diphenhydramine (Benadryl and generics)
- chlorpheniramine (Chlor-trimeton and generics)
- brompheniramine (Dimetane and generics)
- clemastine (Tavist and generics).

Newer antihistamines that do not cause drowsiness are available by prescription and include the following:

- astemizole (Hismanal)
- loratadine (Claritin)
- fexofenadine (Allegra)
- azelastatin HCl (Astelin).

Hismanal has the potential to cause serious heart **arrhythmias** when taken with the antibiotic erythromycin, the antifungal drugs ketoconazole and itraconazole, or the antimalarial drug quinine. Taking more than the recommended dose of Hismanal can also cause arrhythmias. Seldane (terfenadine), the original non-drowsy antihistamine, was voluntarily withdrawn from the market by its manufacturers in early 1998 because of this potential and because of the availability of an equally effective, safer alternative drug, fexofenadine.

DECONGESTANTS. Decongestants constrict blood vessels to counteract the effects of histamine. Nasal sprays are available that can be applied directly to the nasal lining and oral systemic preparations are available. Decongestants are stimulants and may cause increased heart rate and blood pressure, headaches, and agitation. Use of topical decongestants for longer than several days can cause loss of effectiveness and rebound congestion, in which nasal passages become more severely swollen than before treatment.

TOPICAL CORTICOSTEROIDS. Topical **corticosteroids** reduce mucous membrane inflammation and are available by prescription. Allergies tend to become worse

as the season progresses because the immune system becomes sensitized to particular antigens and can produce a faster, stronger response. Topical corticosteroids are especially effective at reducing this seasonal sensitization because they work more slowly and last longer than most other medication types. As a result, they are best started before allergy season begins. Side effects are usually mild, but may include headaches, nosebleeds, and unpleasant taste sensations.

MAST CELL STABILIZERS. Cromolyn sodium prevents the release of mast cell granules, thereby preventing release of histamine and the other chemicals contained in them. It acts as a preventive treatment if it is begun several weeks before the onset of the allergy season. It can be used for perennial AR as well.

Immunotherapy

Immunotherapy, also known as desensitization or allergy shots, alters the balance of antibody types in the body, thereby reducing the ability of IgE to cause allergic reactions. Immunotherapy is preceded by allergy testing to determine the precise allergens responsible. Injections involve very small but gradually increasing amounts of allergen, over several weeks or months, with periodic boosters. Full benefits may take up to several years to achieve and are not seen at all in about one in five patients. Individuals receiving all shots will be monitored closely following each shot because of the small risk of **anaphylaxis**, a condition that can result in difficulty breathing and a sharp drop in blood pressure.

Alternative treatment

Alternative treatments for AR often focus on modulation of the body's immune response, and frequently center around diet and lifestyle adjustments. Chinese herbal medicine can help rebalance a person's system, as can both acute and constitutional homeopathic treatment. Vitamin C in substantial amounts can help stabilize the mucous membrane response. For symptom relief, western herbal remedies including eyebright (*Euphrasia officinalis*) and nettle (*Urtica dioica*) may be helpful. Bee pollen may also be effective in alleviating or eliminating AR symptoms.

Prognosis

Most people with AR can achieve adequate relief with a combination of preventive strategies and treatment. While allergies may improve over time, they may also get worse or expand to include new allergens. Early treatment can help prevent an increased sensitization to other allergens.

KEY TERMS

Allergen—A substance that provokes an allergic response.

Anaphylaxis—Increased sensitivity caused by previous exposure to an allergen that can result in blood vessel dilation (swelling) and smooth muscle contraction. Anaphylaxis can result in sharp blood pressure drops and difficulty breathing.

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.

Granules—Small packets of reactive chemicals stored within cells.

Histamine—A chemical released by mast cells that activates pain receptors and causes cells to become leaky.

Mast cells—A type of immune system cell that is found in the lining of the nasal passages and eyelids, displays a type of antibody called immunoglobulin type E (IgE) on its cell surface, and participates in the allergic response by releasing histamine from intracellular granules.

Prevention

Reducing exposure to pollen may improve symptoms of seasonal AR. Strategies include the following:

- stay indoors with windows closed during the morning hours, when pollen levels are highest
- keep car windows up while driving
- use a surgical face mask when outside
- avoid uncut fields
- learn which trees are producing pollen in which seasons, and avoid forests at the height of pollen season
- wash clothes and hair after being outside
- clean air conditioner filters in the home regularly
- use electrostatic filters for central air conditioning

Moving to a region with lower pollen levels is rarely effective, since new allergies often develop

Preventing perennial AR requires identification of the responsible allergens

Mold spores:

- keep the house dry through ventilation and use of dehumidifiers

- use a disinfectant such as dilute bleach to clean surfaces such as bathroom floors and walls

- have ducts cleaned and disinfected

- clean and disinfect air conditioners and coolers

- throw out moldy or mildewed books, shoes, pillows, or furniture

House dust:

- vacuum frequently, and change the bag regularly. Use a bag with small pores to catch extra-fine particles

- clean floors and walls with a damp mop

- install electrostatic filters in heating and cooling ducts, and change all filters regularly

Animal dander:

- avoid contact if possible

- wash hands after contact

- vacuum frequently

- keep pets out of the bedroom, and off furniture, rugs, and other dander-catching surfaces

- have your pets bathed and groomed frequently

Resources

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Richard Robinson

Allergies

Definition

Allergies are abnormal reactions of the immune system that occur in response to otherwise harmless substances.

Description

Allergies are among the most common of medical disorders. It is estimated that 60 million Americans, or more than one in every five people, suffer from some form of allergy, with similar proportions throughout much of the rest of the world. Allergy is the single largest reason for school absence and is a major source of lost productivity in the workplace.

An allergy is a type of immune reaction. Normally, the immune system responds to foreign microorganisms or particles by producing specific proteins called antibodies. These antibodies are capable of binding to identifying molecules, or antigens, on the foreign particle. This reaction between antibody and antigen sets off a series of chemical reactions designed to protect the body from infection. Sometimes, this same series of reactions is triggered by harmless, everyday substances such as pollen, dust, and animal danders. When this occurs, an allergy develops against the offending substance (an allergen.)

Mast cells, one of the major players in allergic reactions, capture and display a particular type of antibody, called immunoglobulin type E (IgE) that binds to allergens. Inside mast cells are small chemical-filled packets called granules. Granules contain a variety of potent chemicals, including histamine.

Immunologists separate allergic reactions into two main types: immediate hypersensitivity reactions, which are predominantly mast cell-mediated and occur within minutes of contact with allergen; and delayed hypersensitivity reactions, mediated by T cells (a type of white blood cells) and occurring hours to days after exposure.

Inhaled or ingested allergens usually cause immediate hypersensitivity reactions. Allergens bind to IgE antibodies on the surface of mast cells, which spill the contents of their granules out onto neighboring cells, including blood vessels and nerve cells. Histamine binds to the surfaces of these other cells through special proteins called histamine receptors. Interaction of histamine with receptors on blood vessels causes increased leakiness, leading to the fluid collection, swelling and increased redness. Histamine also stimulates **pain** receptors, making tissue more sensitive and irritable. Symptoms last from one to several hours following contact.

In the upper airways and eyes, immediate hypersensitivity reactions cause the runny nose and itchy, bloodshot eyes typical of **allergic rhinitis**. In the gastrointestinal tract, these reactions lead to swelling and irritation of the intestinal lining, which causes the cramping and **diarrhea** typical of food allergy. Allergens that enter the

circulation may cause **hives**, angioedema, **anaphylaxis**, or **atopic dermatitis**.

Allergens on the skin usually cause delayed hypersensitivity reaction. Roving T cells contact the allergen, setting in motion a more prolonged immune response. This type of allergic response may develop over several days following contact with the allergen, and symptoms may persist for a week or more.

Causes and symptoms

Allergens enter the body through four main routes: the airways, the skin, the gastrointestinal tract, and the circulatory system.

- Airborne allergens cause the sneezing, runny nose, and itchy, bloodshot eyes of hay **fever** (**allergic rhinitis**). Airborne allergens can also affect the lining of the lungs, causing **asthma**, or the conjunctiva of the eyes, causing **conjunctivitis** (pink eye). Exposure to cockroach allergans have been associated with the development of asthma. Airborne allergans from household pets are another common source of environmental exposure.
- Allergens in food can cause **itching** and swelling of the lips and throat, cramps, and diarrhea. When absorbed into the bloodstream, they may cause hives (urticaria) or more severe reactions involving recurrent, non-inflammatory swelling of the skin, mucous membranes, organs, and brain (angioedema). Some food allergens may cause anaphylaxis, a potentially life-threatening condition marked by tissue swelling, airway constriction, and drop in blood pressure. Allergies to foods such cow's milk, eggs, nuts, fish, and legumes (peanuts and soybeans) are common. Allergies to fruits and vegetables may also occur.
- In contact with the skin, allergens can cause reddening, itching, and blistering, called **contact dermatitis**. Skin reactions can also occur from allergens introduced through the airways or gastrointestinal tract. This type of reaction is known as atopic **dermatitis**. Dermatitis may arise from an allergic response (such as from poison ivy), or exposure to an irritant causing nonimmune damage to skin cells (such as soap, cold, and chemical agents).
- Injection of allergens, from insect **bites and stings** or drug administration, can introduce allergens directly into the circulation, where they may cause system-wide responses (including anaphylaxis), as well as the local ones of swelling and irritation at the injection site.

People with allergies are not equally sensitive to all allergens. Some may have severe allergic rhinitis but no food allergies, for instance, or be extremely sen-

sitive to nuts but not to any other food. Allergies may get worse over time. For example, childhood ragweed allergy may progress to year-round dust and pollen allergy. On the other hand, a person may lose allergic sensitivity. Infant or childhood atopic dermatitis disappears in almost all people. More commonly, what seems to be loss of sensitivity is instead a reduced exposure to allergens or an increased tolerance for the same level of symptoms.

While allergy to specific allergens is not inherited, the likelihood of developing some type of allergy seems to be, at least for many people. If neither parent has allergies, the chances of a child developing allergy is approximately 10-20%; if one parent has allergies, it is 30-50%; and if both have allergies, it is 40-75%. One source of this genetic predisposition is in the ability to produce higher levels of IgE in response to allergens. Those who produce more IgE will develop a stronger allergic sensitivity.

COMMON ALLERGENS. The most common airborne allergens are the following:

- plant pollens
- animal fur and dander
- body parts from house mites (microscopic creatures found in all houses)
- house dust
- mold spores
- cigarette smoke
- solvents
- cleaners

Common food allergens include the following:

- nuts, especially peanuts, walnuts, and brazil nuts
- fish, mollusks, and shellfish
- eggs
- wheat
- milk
- food additives and preservatives

The following types of drugs commonly cause allergic reactions:

- penicillin or other **antibiotics**
- flu vaccines
- tetanus toxoid vaccine
- gamma globulin

Common causes of contact dermatitis include the following:

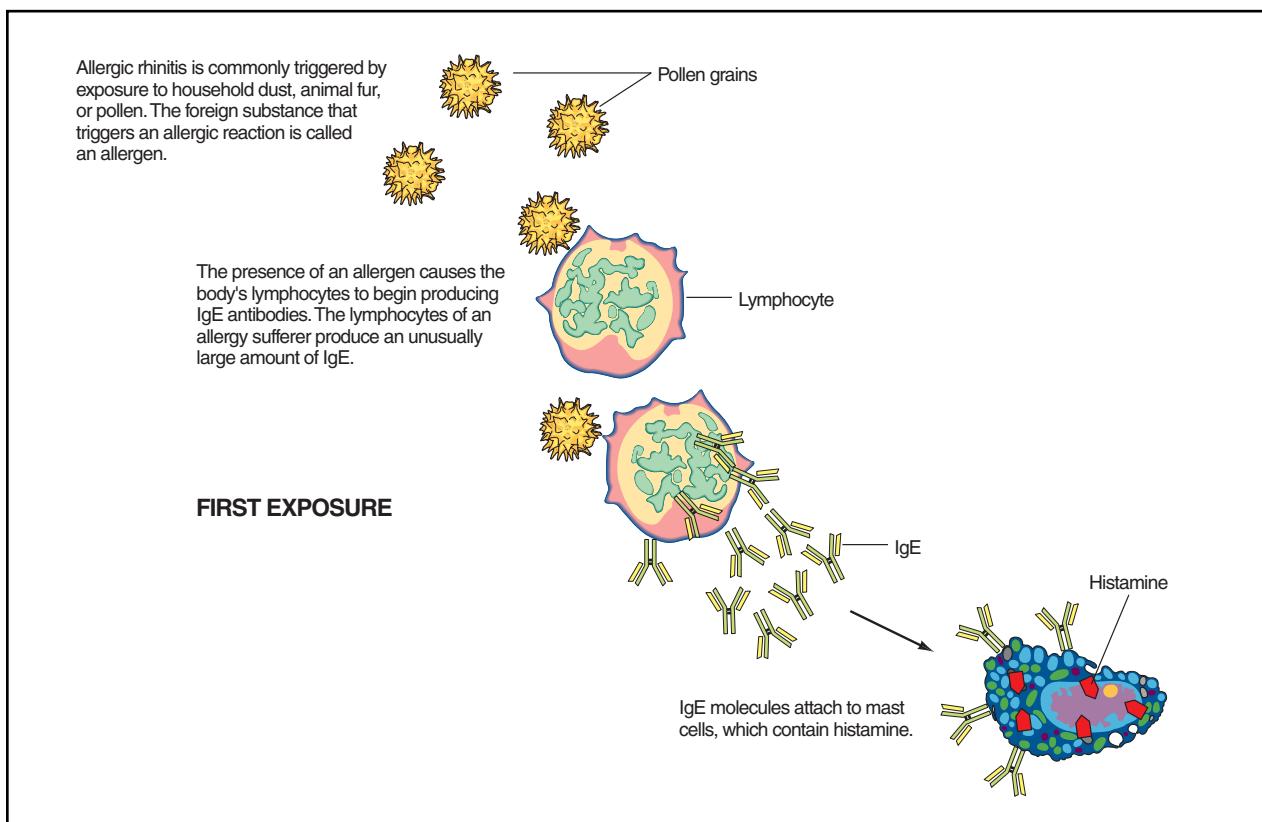
- poison ivy, oak, and sumac
- nickel or nickel alloys
- latex

Insects and other arthropods whose bites or stings typically cause allergy include the following:

- bees, wasps, and hornets
- mosquitoes
- fleas
- scabies

Symptoms depend on the specific type of allergic reaction. Allergic rhinitis is characterized by an itchy, runny nose, often with a scratchy or irritated throat due to post-nasal drip. Inflammation of the thin membrane covering the eye (allergic conjunctivitis) causes redness, irritation, and increased tearing in the eyes. Asthma causes **wheezing**, coughing, and **shortness of breath**. Symptoms of food allergies depend on the tissues most sensitive to the allergen and whether the allergen spread systemically by the circulatory system. Gastrointestinal symptoms may include swelling and tingling in the lips, tongue, palate or throat; nausea; cramping; diarrhea; and gas. Contact dermatitis is marked by reddened, itchy, weepy skin blisters, and an eczema that is slow to heal. It sometimes has a characteristic man-made pattern, such as a glove allergy with clear demarkation on the hands, wrist, and arms where the gloves are worn, or on the earlobes by wearing earrings.

Whole body or systemic reactions may occur from any type of allergen, but are more common following ingestion or injection of an allergen. Skin reactions include the raised, reddened, and itchy patches called hives that characteristically blanch with pressure and resolve within twenty-four hours. A deeper and more extensive skin reaction, involving more extensive fluid collection and pain, is called angioedema. This usually occurs on the extremities, fingers, toes, and parts of the head, neck, and face. Anaphylaxis is marked by airway constriction, blood pressure drop, widespread tissue swelling, heart rhythm abnormalities, and in some cases, loss of consciousness. Other symptoms may include, **dizziness**, weakness, seizures, coughing, flushing, or cramping. The symptoms may begin within five minutes after exposure to the allergen up to one hour or more later. Mast cells in the tissues and basophils in the blood release mediators that give rise to the clinical symptoms of this IgE-mediated hypersensitivity reaction. Commonly, this is associated with allergies to medications, foods, and insect venoms. In some individuals, anaphylaxis can occur with **exercise**, plasma exchange, hemodialysis, reaction to insulin, radiocontrast media used in certain



The allergic response. (Illustration by Hans & Cassady.)

types of medical tests, and rarely during the administration of local anesthetics.

Diagnosis

Allergies can often be diagnosed by a careful medical history, matching the onset of symptoms to the exposure to possible allergens. Allergy is suspected if the symptoms presented are characteristic of an allergic reaction and this occurs repeatedly upon exposure to the suspected allergen. **Allergy tests** can be used to identify potential allergens, but these must be supported by evidence of allergic responses in the patient's clinical history.

Skin tests

Skin tests are performed by administering a tiny dose of the suspected allergen by pricking, scratching, puncturing or injecting the skin. The allergen is applied to the skin as an aqueous extract, usually on the back, forearms, or top of the thighs. Once in the skin, the allergen may produce a classic immune wheal and flare response (a skin lesion with a raised, white, compressible area surrounded by a red flare). The tests usually begin

with prick tests or patch tests that expose the skin to small amounts of allergen to observe the response. A positive reaction will occur on the skin even if the allergen is at levels normally encountered in food or in the airways. Reactions are usually evaluated approximately fifteen minutes after exposure. Intradermal skin tests involved injection of the allergen into the dermis of the skin. These tests are more sensitive and are used for allergies associated with risk of **death**, such as allergies to antibiotics.

Allergen-Specific IgE Measurement

Tests that measure allergen-specific IgE antibodies generally follow a basic method. The allergen is bound to a solid support, either in the form of a cellulose sponge, microtiter plate, or paper disk. The patient's serum is prepared from a blood sample and is incubated with the solid phase. If allergen specific IgE antibodies are present, they will bind to the solid phase and be retained there when the rest of the serum is washed away. Next, an labeled antibody against the IgE is added and will bind to any IgE on the solid phase. The excess is washed away and the levels of IgE are determined. The commonly used RAST test (radio allergo sorbent

test) employed radio-labeled Anti-IgE antibodies. Updated methods now incorporate the use of enzyme-labeled antibodies in ELISA assays (enzyme-linked immunosorbent assays).

Total Serum IgE

The total level of IgE in the serum is commonly measured with a two-site immunometric assay. Some research indicates that there is a higher level of total serum IgE in allergic as compared to non-allergic people. However, this may not always be the case as there is considerable overlap between the two groups. This test is useful for the diagnosis of allergic fungal **sinusitis** and bronchopulmonary **aspergillosis**. Other conditions that are not allergic in nature may give rise to higher IgE levels such as **smoking**, **AIDS**, infection with parasites, and IgE myeloma.

Provocation tests

These tests involve the administration of allergen to elicit an immune response. Provocation tests, most commonly done with airborne allergens, present the allergen directly through the route normally involved. Delayed allergic contact dermatitis diagnosis involves similar methods by application of a skin patch with allergen to induce an allergic skin reaction. Food allergen provocation tests require abstinence from the suspect allergen for two weeks or more, followed by ingestion of a measured amount of the test substance administered as an opaque capsule along with a placebo control. Provocation tests are not used if anaphylaxis is a concern due to the patient's medical history.

Future diagnostic methods

As of 2000, attempts have been made for direct measurement of immune mediators such as histamine, eosinophil cationic protein (ECP), and mast cell tryptase. Another, somewhat controversial, test is electrodermal testing or electro-acupuncture allergy testing. This test has been used in Europe and is under investigation in the United States, though not approved by the Food and Drug Administration. An electric potential is applied to the skin, the allergen presented, and the electrical resistance observed for changes. This method has not been verified.

Treatment

Avoiding allergens is the first line of defense to reduce the possibility of an allergic attack. It is helpful to avoid environmental irritants such as tobacco smoke, perfumes, household cleaning agents, paints, glues, air

fresheners, and potpourri. Nitrogen dioxide from poorly vented gas stoves, woodburning stoves, and artificial fireplaces has also been linked to poor asthma control. Dust mite control is particularly important in the bedroom areas by use of allergen-impermeable covers on mattress and pillows, frequent washing of bedding in hot water, and removal of items that collect dust such as stuffed toys. Mold growth may be reduced by reducing indoor humidity, repair of house foundations to reduce indoor leaks and seepage, and installation of exhaust systems to ventilate areas where steam is generated such as the bathroom or kitchen. Allergic individuals should avoid pet allergens such as saliva, body excretions, pelts, urine, or feces. For those who insist on keeping a pet, restriction of the animal's activity to certain areas of the home may be beneficial.

Complete environmental control is often difficult to accomplish, hence therapeutic interventions may become necessary. A large number of prescription and over-the-counter drugs are available for treatment of immediate hypersensitivity reactions. Most of these work by decreasing the ability of histamine to provoke symptoms. Other drugs counteract the effects of histamine by stimulating other systems or reducing immune responses in general.

Antihistamines

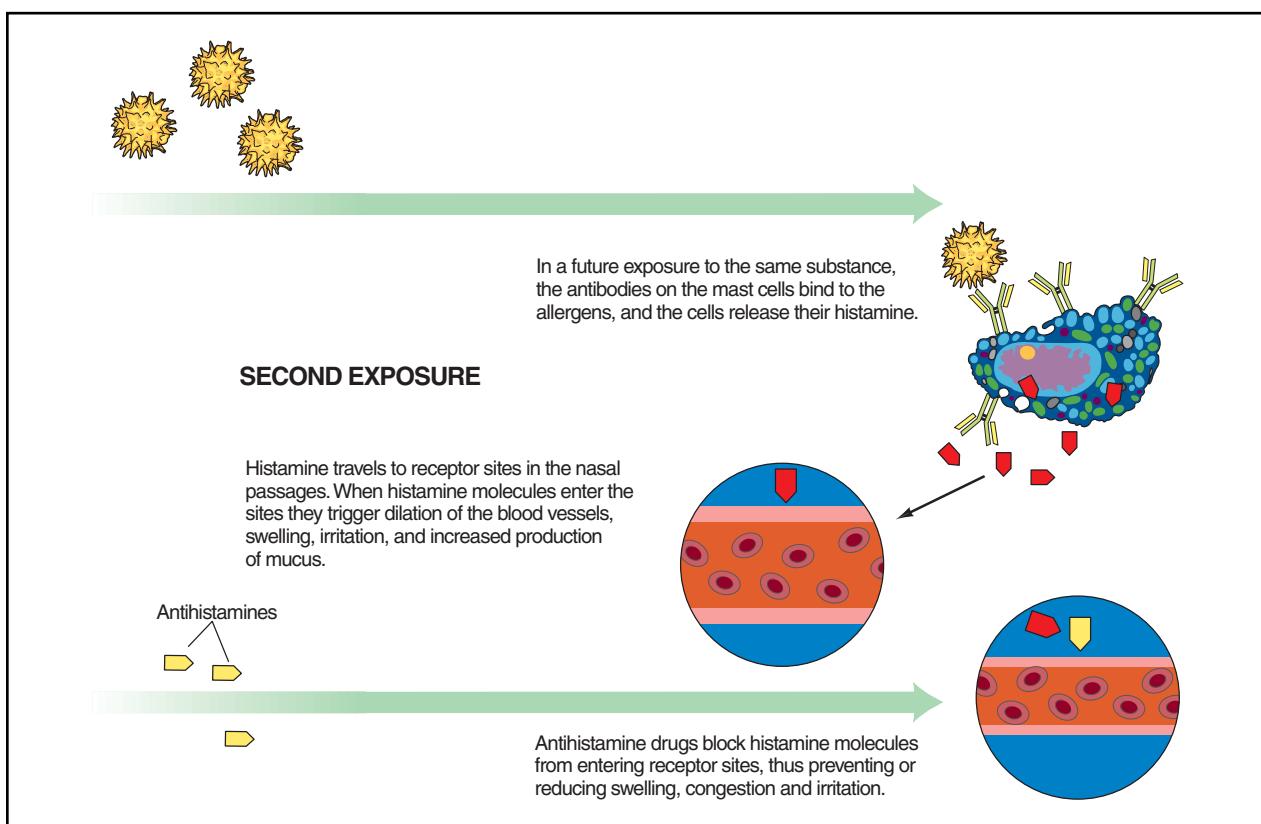
Antihistamines block the histamine receptors on nasal tissue, decreasing the effect of histamine released by mast cells. They may be used after symptoms appear, though they may be even more effective when used preventively, before symptoms appear. Antihistamines are help reduce sneezing, itching, and rhinorrhea. A wide variety of antihistamines are available.

Older, first generation antihistamines often produce drowsiness as a major side effect, as well as **dry mouth**, tachycardia, blurred vision, **constipation**, and lower the threshold for seizures. These medications also have similar effects to alcohol and care should be taken when operating motor vehicles, as individuals may not be aware that they are impaired. Such antihistamines include the following:

- diphenhydramine (Benadryl and generics)
- chlorpheniramine (Chlor-trimeton and generics)
- brompheniramine (Dimetane and generics)
- clemastine (Tavist and generics)

Newer antihistamines that do not cause drowsiness or pass the blood-brain barrier are available by prescription and include the following:

- loratadine (Claritin)



Second and subsequent exposure to allergen. (Illustration by Hans & Cassady.)

- fexofenadine (Allegra)

Hismanal has the potential to cause serious heart **arrhythmias** when taken with the antibiotic erythromycin, the antifungal drugs ketoconazole and itraconazole, or the antimalarial drug quinine. Taking more than the recommended dose of Hismanal can also cause arrhythmias. Seldane (terfenadine), the original non-drowsy antihistamine, was voluntarily withdrawn from the market by its manufacturers in early 1998 because of this potential and because of the availability of an equally effective, safer alternative drug, fexofenadine.

Decongestants

Decongestants constrict blood vessels to the mucosa to counteract the effects of histamine. This decreases the amount of blood in the nasopharyngeal and sinus mucosa and reduces swelling. Nasal sprays are available that can be applied directly to the nasal lining and oral systemic preparations are available. Decongestants are stimulants and may cause increased heart rate and blood pressure, headaches, insomnia, agitation, and difficulty emptying the bladder. Use of topical decongestants for longer than several days can cause loss of effectiveness and rebound congestion, in which

nasal passages become more severely swollen than before treatment.

Topical corticosteroids

Topical **corticosteroids** reduce mucous membrane inflammationas by decreasing the amount of fluid moved from the vascular spaces into the tissues. These medications reduce the recruitment of inflammatory cells as well as the synthesis of cytokines. They are available by prescription. Allergies tend to become worse as the season progresses because the immune system becomes sensitized to particular antigens and can produce a faster, stronger response. Topical corticosteroids are especially effective at reducing this seasonal sensitization because they work more slowly and last longer than most other medication types. As a result, they are best started before allergy season begins. Side effects are usually mild, but may include headaches, nosebleeds, and unpleasant taste sensations.

Bronchodilators or metered-dose inhalers (MDI)

Because allergic reactions involving the lungs cause the airways or bronchial tubes to narrow, as in asthma,

KEY TERMS

Allergen—A substance that provokes an allergic response.

Allergic rhinitis—Inflammation of the mucous membranes of the nose and eyes in response to an allergen.

Anaphylaxis—Increased sensitivity caused by previous exposure to an allergen that can result in blood vessel dilation and smooth muscle contraction. Anaphylaxis can result in sharp blood pressure drops and difficulty breathing.

Angioedema—Severe non-inflammatory swelling of the skin, organs, and brain that can also be accompanied by fever and muscle pain.

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.

Asthma—A lung condition in which the airways become narrow due to smooth muscle contraction, causing wheezing, coughing, and shortness of breath.

Atopic dermatitis—Infection of the skin as a result of exposure to airborne or food allergens.

Conjunctivitis—Inflammation of the thin lining of the eye called the conjunctiva.

Contact dermatitis—Inflammation of the skin as a result of contact with a substance.

Delayed hypersensitivity reactions—Allergic reactions mediated by T cells that occur hours to days after exposure.

Granules—Small packets of reactive chemicals stored within cells.

Histamine—A chemical released by mast cells that activates pain receptors and causes cells to become leaky.

Immune hypersensitivity reaction—Allergic reactions that are mediated by mast cells and occur within minutes of allergen contact.

Mast cells—A type of immune system cell that is found in the lining of the nasal passages and eyelids, displays a type of antibody called immunoglobulin type E (IgE) on its cell surface, and participates in the allergic response by releasing histamine from intracellular granules.

T cells—Immune system cells or more specifically, white blood cells, that stimulate cells to create and release antibodies.

bronchodilators, which cause the smooth muscle lining the airways to open or dilate, can be very effective. When inhalers are used, it is important that the patient be educated in the proper use of these medications. The inhaler should be shaken, and the patient should breathe out to expel air from the lungs. The inhaler should be placed at least two fingerbreadths in front of the mouth. The medication should be aimed at the back of the throat, and the inhaler activated while breathing in quite slowly 3-4 seconds. The breath should be held for at least ten seconds, and then expelled. At least thirty to sixty seconds should pass before the inhaler is used again. Care should be taken to properly wash out the mouth and brush the teeth following use, as residual medication remains in this area with only a small amount actually reaching the lungs. Some bronchodilators used to treat acute asthma attacks include adrenaline, albuterol, or other “adrenoceptor stimulants,” most often administered as aerosols. Fluticasone (Flovent) is another commonly prescribed inhaler. Some bronchodilators used to treat acute asthma attacks include

adrenaline, albuterol, Maxair, Proventil, or other “adrenoceptor stimulants,” most often administered as aerosols. Another group of medications, the long-acting beta agonists, are proving useful to reduce the use of inhalers and include salmeterol xinafoate (Serevent). Theophylline, naturally present in coffee and tea, is another drug that produces bronchodilation. It is usually taken orally, but in a severe asthma attack it may be given intravenously. Side effects include gastrointestinal disturbances, **insomnia**, headaches, and seizures.

Anticholinergics

Ipratropium bromide (atrovent) and atropine sulfate are anticholinergic drugs used for the treatment of asthma. Ipratropium is used for treating asthmatics in emergency situations with a nebulizer.

Nonsteroidal drugs

MAST CELL STABILIZERS. Cromolyn sodium prevents the release of mast cell granules, thereby prevent-

ing the release of histamine and other chemicals contained in them. It acts as a preventive treatment if it is begun several weeks before the onset of the allergy season. It can also be used for year round allergy prevention. Cromolyn sodium is available as a nasal spray for allergic rhinitis and in aerosol (a suspension of particles in gas) form for asthma.

LEUKOTRIENE MODIFIERS. These medications are useful for individuals with **aspirin** sensitivity, sinusitis, polposis, urticaria. Examples include zafirlukast (Accolate), montelukast (Singulair), and zileuton (Zyflo). When zileuton is used, care must be taken to measure liver enzymes.

Immunotherapy

In this form of therapy, allergen is injected into the skin in increasing doses over a specific period of time. This may be helpful for patients who do not respond to medications or avoidance of allergens in the environment. This type of therapy may reduce the need for medications.

Treatment of contact dermatitis

An individual suffering from contact dermatitis should initially take steps to avoid possible sources of exposure to the offending agent. Calamine lotion applied to affected skin can reduce irritation somewhat, as can cold water compresses. Side effects of topical agents may include over-drying of the skin. In the case of acute contact dermatitis, short-term oral corticosteroid therapy may be appropriate. Moderately strong corticosteroids can also be applied as a wrap for twenty-four hours. Health care workers are especially at risk for hand eruptions due to glove use.

Treatment of anaphylaxis

The emergency condition of anaphylaxis is treated with injection of adrenaline, also known as epinephrine. People who are prone to anaphylaxis because of food or insect allergies often carry an “Epi-pen” containing adrenaline in a hypodermic needle. Other medications may be given to aid the action of the epi-pen. Prompt injection can prevent a more serious reaction from developing. Particular care should be taken to assess the affected individual’s airway status, and he or she should be placed in a recumbent pose and vital signs determined. If a reaction resulted from insect sting or an injection, a tourniquet may need to be placed proximal to the area where the agent penetrated the skin. This should then be released at intervals of ten minutes at a time, for one to two minutes duration. If the individual

does not respond to such interventions, then emergency treatment is appropriate.

Alternative treatment

Any alternative treatment for allergies begins with finding the cause and then helping the patient to avoid or eliminate the allergen, although this is not always possible. As with any alternative therapy, a physician should be consulted before initiating a new form of treatment. Education on the use of alternative agents is critical, as they are still “drugs” even though they are derived from natural sources. Various categories of alternative remedies may be helpful in allergy treatment, including:

- antihistamines: vitamin C and the bioflavonoid hesperidin act as natural antihistamines.
- decongestants: vitamin C, the homeopathic remedies *Ferrum phosphoricum* and *Kali muriaticum* (used alternately), and the dietary supplement N-acetylcysteine are believed to have decongestant effects.
- mast cell stabilizers: the bioflavonoids quercetin and hesperidin may help stabilize mast cells.
- immunotherapy: the herbs **echinacea** (*Echinacea spp.*) and astragalus or milk-vetch root (*Astragalus membranaceus*) may possibly help to strengthen the immune system.
- bronchodilators: the herbal remedies ephedra (*Ephedra sinica*, also known as ma huang in **traditional Chinese medicine**), khellin (*Ammi visnaga*) and cramp bark (*Viburnum opulus*) are believed to help open the airways.

Treatment of contact dermatitis

A variety of herbal remedies, either applied topically or taken internally, may possibly assist in the treatment of contact dermatitis. A poultice (crushed herbs applied directly to the affected area) made of jewelweed (*Impatiens spp.*) or chickweed (*Stellaria media*) may soothe the skin. A cream or wash containing calendula (*Calendula officinalis*), a natural antiseptic and anti-inflammatory agent, may help heal the rash when applied topically. Homeopathic treatment may include such remedies as *Rhus toxicodendron*, *Apis mellifica*, or *Anacardium* taken internally. A qualified homeopathic practitioner should be consulted to match the symptoms with the correct remedy. Care should be taken with any agent taken internally.

Prognosis

Allergies can improve over time, although they often worsen. While anaphylaxis and severe asthma are life-

threatening, other allergic reactions are not. Learning to recognize and avoid allergy-provoking situations allows most people with allergies to lead normal lives.

Prevention

Avoiding allergens is the best means of limiting allergic reactions. For food allergies, there is no effective treatment except avoidance. By determining the allergens that are causing reactions, most people can learn to avoid allergic reactions from food, drugs, and contact allergens such as poison ivy or latex. Airborne allergens are more difficult to avoid, although keeping dust and animal dander from collecting in the house may limit exposure. Cromolyn sodium can prevent mast cell degranulation, thereby limiting the allergic response.

Immunotherapy, also known as desensitization or allergy shots, alters the balance of antibody types in the body, thereby reducing the ability of IgE to cause allergic reactions. Immunotherapy is preceded by allergy testing to determine the precise allergens responsible. Injections involve very small but gradually increasing amounts of allergen, over several weeks or months, with periodic boosters. Full benefits may take up to several years to achieve and are not seen at all in about one in five patients. Individuals receiving all shots will be monitored closely following each shot because of the small risk of anaphylaxis, a condition that can result in difficulty breathing and a sharp drop in blood pressure.

Other drugs, including steroids, are used to prevent asthma attacks and in the long-term management of asthma.

Resources

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Richard Robinson
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Allergy tests

Definition

Allergy tests indicate a person's allergic sensitivity to commonly encountered environmental substances.

Purpose

Allergy is a reaction of the immune system. Normally, the immune system responds to foreign microorganisms and particles, like pollen or dust, by producing specific proteins called antibodies that are capable of binding to identifying molecules, or antigens, on the foreign organisms. This reaction between antibody and antigen sets off a series of reactions designed to protect the body from infection. Sometimes, this same series of reactions is triggered by harmless, everyday substances. This is the condition known as allergy, and the offending substance is called an allergen. Common inhaled allergens include pollen, dust, and insect parts from tiny house mites. Common food allergens include nuts, fish, and milk.

Allergic reactions involve a special set of cells in the immune system known as mast cells. Mast cells serve as guards in the tissues where the body meets the outside world: the skin, the mucous membranes of the eyes and other areas, and the linings of the respiratory and digestive systems. Mast cells display a special type of antibody, called immunoglobulin type E (IgE), on their surface. Inside, mast cells store reactive chemicals in small packets, called granules. When the antibodies encounter allergens, they trigger the release of granules, which spill out their chemicals onto neighboring cells, including blood vessels and nerve cells. One of these chemicals, histamine, binds to the surfaces of these other cells, through special proteins called histamine receptors. Interaction of histamine with receptors on blood vessels causes neighboring cells to become leaky, leading to the fluid collection, swelling, and increased redness characteristic of a runny nose and red, irritated eyes. Histamine also stimulates **pain** receptors, causing the itchy, scratchy nose, eyes, and throat common in **allergic rhinitis**.

The particular allergens to which a person is sensitive can be determined through allergy testing. Allergy tests may be performed on the skin or using blood serum in a test tube. During skin tests, potential allergens are placed on the skin and the reaction is observed. In radio-allergosorbent allergy testing (RAST), a patient's blood serum is combined with allergen in a test tube to determine if serum antibodies react with the allergen. Provocation testing involves direct exposure to a likely aller-

gen, either through inhalation or ingestion. Positive reactions from any of these tests may be used to narrow the candidates for the actual allergen causing the allergy.

Identification of the allergenic substance may allow the patient to avoid the substance and reduce allergic reactions. In addition, allergy testing may be done in those with **asthma** that is difficult to manage, eczema, or skin **rashes** to determine if an allergy is causing the condition or making it worse. Allergy tests may also be done before allergen desensitization to ensure the safety of more extensive exposure.

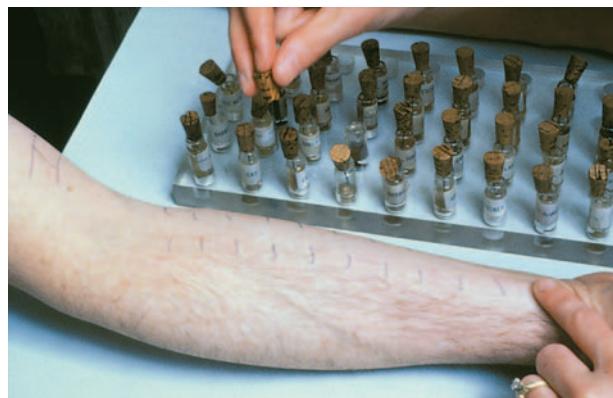
Skin testing is the most common type of allergy test. There are two forms: percutaneous and intradermal. In percutaneous or prick testing, allergen solutions are placed on the skin, and the skin is then pricked with a needle, allowing the allergen to enter the skin and become exposed to mast cells. Scratch testing, in which the skin is scratched instead of punctured, is used less often. Intradermal testing involves directly injecting allergen solutions into the skin. In both tests, a reddened, swollen spot develops at the injection site for each substance to which the person is sensitive. Skin reactivity is seen for allergens regardless of whether they usually affect the skin. In other words, airborne and food allergens cause skin reactions equally well.

The range of allergens used for testing is chosen to reflect possible sources in the environment and may include the following:

- pollen from a variety of trees, common grasses, and weeds
- mold and fungus spores
- house dust
- house mites
- animal skin cells (dander) and saliva
- food extracts
- antibiotics
- insect venoms

Radio-allergosorbent testing (RAST) is a laboratory test performed when a person may be too sensitive to risk skin testing or when medications or skin conditions prevent it.

Provocation testing is done to positively identify suspected allergens after preliminary skin testing. A purified preparation of the allergen is inhaled or ingested in increasing concentrations to determine if it will provoke a response. Food testing is much more tedious than inhalation testing, since full passage through the digestive system may take a day or more.



This patient is being exposed to certain allergens as part of an allergy test. (Custom Medical Stock Photo. Reproduced by permission.)

Precautions

While allergy tests are quite safe for most people, the possibility of a condition known as **anaphylaxis** does exist. Anaphylaxis is a potentially dangerous condition that can result in difficulty breathing and a sharp drop in blood pressure. People with a known history of anaphylaxis should inform the testing clinician. Skin tests should never include a substance known to cause anaphylaxis in the person being tested.

Provocation tests may cause an allergic reaction. Therefore, treatment medications should be available following the tests, to be administered, if needed.

Description

In prick testing, a drop of each allergen to be tested is placed on the skin, usually on the forearm or the back. A typical battery of tests may involve two dozen allergen drops, including a drop of saline solution that should not provoke a reaction (negative control) and a drop of histamine that should provoke a reaction (positive control). A small needle is inserted through the drop, and used to prick the skin below. A new needle is used for each prick. The sites are examined over the next twenty minutes for evidence of swelling and redness, indicating a positive reaction. In some instances, a tracing of the set of reactions may be made by placing paper over the tested area. Similarly, in intradermal testing, separate injections are made for each allergen tested. Observations are made over the next twenty minutes.

In RAST testing, a blood sample is taken for use in the laboratory, where the antibody-containing serum is separated from the blood cells. The serum is then exposed to allergens bound to a solid medium. If a person has antibodies to a particular allergen, those antibod-



A close-up of a patient's arm after allergy testing. (Custom Medical Stock Photo. Reproduced by permission.)

ies will bind to the solid medium and remain behind after a rinse. Location of allergen-antibody combinations is done by adding antibody-reactive antibodies, so called anti-antibodies, that are chemically linked with a radioactive dye. By locating radioactive spots on the solid medium, the reactive allergens are discovered.

Provocation testing may be performed to identify airborne or food allergens. Inhalation testing is performed only after a patient's lung capacity and response to the medium used to dilute the allergen has been determined. Once this has been determined, the patient inhales increasingly concentrated samples of a particular allergen, followed each time by measurement of the exhalation capacity. Only one allergen is tested per day. Testing for food **allergies** is usually done by removing the suspect food from the diet for two weeks, followed by eating a single portion of the suspect food and follow-up monitoring.

Preparation

Skin testing is preceded by a brief examination of the skin. The patient should refrain from using anti-allergy drugs for at least 48 hours before testing. Prior to inhalation testing, patients with asthma who can tolerate it may be asked to stop any asthma medications. Testing for food allergies requires the person to avoid all suspect food for at least two weeks before testing.

Aftercare

Skin testing does not usually require any aftercare. A generalized redness and swelling may occur in the test area, but it will usually resolve within a day or two.

Inhalation tests may cause delayed asthma attacks, even if the antigen administered in the test initially produced no response. Severe initial reactions may justify close professional observation for at least 12 hours after testing.

KEY TERMS

Allergen—A substance that provokes an allergic response.

Anaphylaxis—Increased sensitivity caused by previous exposure to an allergen that can result in blood vessel dilation (swelling) and smooth muscle contraction. Anaphylaxis can result in sharp blood pressure drops and difficulty breathing.

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.

Histamine—A chemical released by mast cells that activates pain receptors and causes cells to become leaky.

Mast cells—A type of immune system cell that is found in the lining of the nasal passages and eyelids, displays a type of antibody called immunoglobulin type E (IgE) on its cell surface, and participates in the allergic response by releasing histamine from intracellular granules.

Risks

Intradermal testing may inadvertently result in the injection of the allergen into the circulation, with an increased risk of adverse reactions. Inhalation tests may provoke an asthma attack. Exposure to new or unsuspected allergens in any test carries the risk of anaphylaxis. Because patients are monitored following allergy testing, an anaphylactic reaction is usually recognized and treated promptly. Occasionally, a delayed anaphylactic response can occur that will require immediate care. Proper patient education regarding how to recognize anaphylaxis is vital.

Normal results

Lack of redness or swelling on a skin test indicates no allergic response. In an inhalation test, the exhalation capacity should remain unchanged. In a food challenge, no symptoms should occur.

Abnormal results

Presence of redness or swelling, especially over 5 mm (1/4 inch) in diameter, indicates an allergic response.

This does not mean the substance actually causes the patient's symptoms, however, since he or she may have no regular exposure to the allergen. In fact, the actual allergen may not have been included in the test array.

Following allergen inhalation, reduction in exhalation capacity of more than 20%, and for at least 10-20 minutes, indicates a positive reaction to the allergen.

Gastrointestinal symptoms within 24 hours following the ingestion of a suspected food allergen indicates a positive response.

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Richard Robinson

Allogenic transplant see **Bone marrow transplantation**

Allopurino see **Gout drugs**



Top of balding male's head. (Photograph by Kelly A. Quin. Reproduced by permission.)

Alopecia

Definition

Alopecia simply means hair loss (baldness).

Description

Hair loss occurs for a great many reasons—from pulling it out to having it killed off by **cancer chemotherapy**. Some causes are considered natural, while others signal serious health problems. Some conditions are confined to the scalp. Others reflect disease throughout the body. Being plainly visible, the skin and its components can provide early signs of disease elsewhere in the body.

Oftentimes, conditions affecting the skin of the scalp will result in hair loss. The first clue to the specific cause is the pattern of hair loss, whether it be complete baldness (alopecia totalis), patchy bald spots, thinning, or hair loss confined to certain areas. Also a factor is the condition of the hair and the scalp beneath it. Sometimes only the hair is affected; sometimes the skin is visibly diseased as well.

Causes and symptoms

- Male pattern baldness (androgenic alopecia) is considered normal in adult males. It is easily recognized by the distribution of hair loss over the top and front of the head and by the healthy condition of the scalp.
- Alopecia areata is a hair loss condition of unknown cause that can be patchy or extend to complete baldness.
- Fungal infections of the scalp usually cause patchy hair loss. The fungus, similar to the ones that cause **athlete's foot** and **ringworm**, often glows under ultraviolet light.
- Trichotillomania is the name of a mental disorder that causes a person to pull out his/her own hair.
- Complete hair loss is a common result of cancer chemotherapy, due to the toxicity of the drugs used. Placing a tourniquet around the skull just above the ears during the intravenous infusion of the drugs may reduce or eliminate hair loss by preventing the drugs from reaching the scalp.
- Systemic diseases often affect hair growth either selectively or by altering the skin of the scalp. One example is thyroid disorders. **Hyperthyroidism** (too much thyroid hormone) causes hair to become thin and fine.

KEY TERMS

Athlete's foot—A fungal infection between the toes, officially known as tinea pedis.

Autoimmune disease—Certain diseases caused by the body's development of an immune reaction to its own tissues.

Chemotherapy—The treatment of diseases, usually cancer, with drugs (chemicals).

Hair follicles—Tiny organs in the skin, each one of which grows a single hair.

Lupus erythematosus—An autoimmune disease that can damage skin, joints, kidneys, and other organs.

Ringworm—A fungal infection of the skin, usually known as tinea corporis.

Systemic—Affecting all or most parts of the body.

Hypothyroidism (too little thyroid hormone) thickens both hair and skin.

- Several autoimmune diseases (when protective cells begin to attack self cells within the body) affect the skin, notably lupus erythematosus.

Diagnosis

Dermatologists are skilled in diagnosis by sight alone. For more obscure diseases, they may have to resort to a **skin biopsy**, removing a tiny bit of skin using a local anesthetic so that it can be examined under a microscope. Systemic diseases will require a complete evaluation by a physician, including specific tests to identify and characterize the problem.

Treatment

Successful treatment of underlying causes is most likely to restore hair growth, be it the completion of chemotherapy, effective cure of a scalp fungus, or control of a systemic disease. Two relatively new drugs—**minoxidil** (Rogaine) and **finasteride** (Proscar)—promote hair growth in a significant minority of patients, especially those with male pattern baldness and alopecia areata. While both drugs have so far proved to be quite safe when used for this purpose, **minoxidil** is a liquid that is applied to the scalp and finasteride is the first and only approved treatment in a pill form.

Minoxidil was approved for over-the-counter sales in 1996. When used continuously for long periods of

time, minoxidil produces satisfactory results in about one quarter of patients with androgenic alopecia and as many as half the patients with alopecia areata. There is also an over-the-counter extra-strength version of minoxidil (5% concentration) approved for use by men only. The treatment often results in new hair that is thinner and lighter in color. It is important to note that new hair stops growing soon after the use of minoxidil is discontinued.

Over the past few decades there have appeared a multitude of hair replacement methods performed by both physicians and non-physicians. They range from simply weaving someone else's hair in with the remains of your own to surgically transplanting thousands of hair follicles one at a time.

Hair transplantation is completed by taking tiny plugs of skin, each containing one to several hairs, from the back side of the scalp. The bald sections are then implanted with the plugs. Research completed in 2000 looked at the new technique of hair grafting, and found that micrografts (one to two hairs transplanted per follicle) resulted in fewer complications and the best results.

Another surgical procedure used to treat androgenic alopecia is scalp reduction. By stretching skin the hairless scalp can be removed and the area of bald skin decreased by closing the space with hair-covered scalp. Hair-bearing skin can also be folded over an area of bald skin with a technique called a flap.

Prognosis

The prognosis varies with the cause. It is generally much easier to lose hair than to regrow it. Even when it returns, it is often thin and less attractive than the original.

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Beth Kapes

■ Alpha-fetoprotein test

Definition

The alpha-fetoprotein (AFP) test is a blood test that is performed during **pregnancy**. This screening test measures the level of AFP in the mother's blood and indicates the probability that the fetus has one of several serious **birth defects**. The level of AFP can also be determined by analyzing a sample of amniotic fluid. This screening test cannot diagnose a specific condition; it only indicates the increase of risk for several birth defects. Outside pregnancy, the AFP test is used to detect liver disease, certain cancerous tumors, and to monitor the progress of **cancer** treatment.

Purpose

Alpha-fetoprotein is a substance produced by the liver of a fetus. The exact function of this protein is unknown. After birth, the infant's liver stops producing AFP, and an adult liver contains only trace amounts. During pregnancy, the fetus excretes AFP in urine and some of the protein crosses the fetal membranes to enter the mother's blood. The level of AFP can then be determined by analyzing a sample of the mother's blood. By analyzing the amount of AFP found in a blood or amniotic fluid sample, doctors can determine the probability that the fetus is at risk for certain birth defects. It is very important that the doctor know precisely how old the fetus is when the test is performed since the AFP level changes over the length of the pregnancy. Alone, AFP

screening cannot diagnose a birth defect. The test is used as an indicator of risk and then an appropriate line of testing (like **amniocentesis** or ultrasound) follows, based on the results.

Abnormally high AFP may indicate that the fetus has an increased risk of a neural tube defect, the most common and severe type of disorder associated with increased AFP. These types of defects include spinal column defects (**spina bifida**) and anencephaly (a severe and usually fatal brain abnormality). If the tube that becomes the brain and spinal cord does not close correctly during fetal development, AFP may leak through this abnormal opening and enter the amniotic fluid. This leakage creates abnormally high levels of AFP in amniotic fluid and in maternal blood. If the screening test indicates abnormally high AFP, ultrasound is used to diagnosis the problem.

Other fetal conditions that can raise AFP levels above normal include:

- cysts at the end of the spine
- blockage in the esophagus or intestines
- liver disease causing liver cells to die
- defects in the abdominal wall
- kidney or urinary tract defects or disease
- brittle bone disease

Levels may also be high if there is too little fluid in the amniotic sac around the fetus, more than one developing fetus, or a pregnancy that is farther along than estimated.

For unknown reasons, abnormally low AFP may indicate that the fetus has an increased risk of **Down syndrome**. Down syndrome is a condition that includes **mental retardation** and a distinctive physical appearance linked to an abnormality of chromosome 21 (called trisomy 21). If the screening test indicates an abnormally low AFP, amniocentesis is used to diagnosis the problem. Abnormally low levels of AFP can also occur when the fetus has died or when the mother is overweight.

AFP is often part of a "triple check" blood test that analyzes three substances as risk indicators of possible birth defects: AFP, estriol, and human chorionic gonadotropin (HCG). When all three substances are measured in the mother's blood, the accuracy of the test results increases.

Although AFP in human blood gradually disappears after birth, it never disappears entirely. It may reappear in liver disease, or tumors of the liver, ovaries, or testicles. The AFP test is used to screen people at high risk for these conditions. After a cancerous tumor is removed, an

KEY TERMS

Amniotic fluid—Fluid within the uterine sac in which the fetus lives until born.

Fetus—The stage in human development from the second month of pregnancy until birth.

AFP test can monitor the progress of treatment. Continued high AFP levels suggest the cancer is growing.

Precautions

It is very important that the doctor know precisely how old the fetus is when the test is performed since the AFP level considered normal changes over the length of the pregnancy. Errors in determining the age of the fetus lead to errors when interpreting the test results. Since an AFP test is only a screening tool, more specific tests must follow to make an accurate diagnosis. An abnormal test result does not necessarily mean that the fetus has a birth defect. The test has a high rate of abnormal results (either high or low) in order to prevent missing a fetus that has a serious condition.

Description

The AFP test is usually performed at week 16 of pregnancy. Blood is drawn from a vein, usually on the inside of the elbow. AFP can also be measured in the sample of amniotic fluid taken at the time of amniocentesis. Test results are usually available after about one week.

Preparation

There is no specific physical preparation for the AFP test.

Aftercare

There is no specific aftercare involved with this screening test.

Risks

The risks associated with drawing blood are minimal, but may include bleeding from the puncture site, feeling faint or lightheaded after the blood is drawn, or blood accumulating under the puncture site (hematoma).

Normal results

Alpha-fetoprotein is measured in nanograms per milliliter (ng/mL) and is expressed as a probability. The

probability (1:100, for example) translates into the chance that the fetus has a defect (a one in 100 chance, for example).

When testing for cancer or liver diseases, AFP results are reported as nanograms per milliliter. An AFP level less than or equal to 50 ng/mL is considered normal.

Abnormal results

The doctor will inform the woman of her specific increased risk as compared to the “normal” risk of a standard case. If the risk of Down syndrome is greater than the standard risk for women who are 35 years old or older (one in 270), then amniocentesis is recommended. Again, the test has a high rate of showing an abnormal AFP level in order to prevent missing a fetus that has Down’s syndrome. This screening test only predicts risk; appropriate diagnostic testing will follow after an abnormal screening result.

In tumor or liver disease testing, an AFP level greater than 50 ng/mL is considered abnormal.

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- March of Dimes Birth Defects Foundation. 1275 Mamaroneck Ave., White Plains, NY 10605. (914) 428-7100. <<http://www.modimes.org>>.
- National Cancer Institute. Building 31, Room 10A31, 31 Center Drive, MSC 2580, Bethesda, MD 20892-2580. (800) 422-6237. <<http://www.nci.nih.gov>>.

Adrienne Massel, RN

Alpha-thalassemia see **Thalassemia**

Alpha₁-adrenergic blockers

Definition

Alpha₁-adrenergic blockers are drugs that work by blocking the alpha₁-receptors of vascular smooth muscle, thus preventing the uptake of catecholamines by the smooth muscle cells. This causes vasodilation and allows blood to flow more easily.

Purpose

These drugs, called alpha blockers for short, are used for two main purposes: to treat high blood pressure (**hypertension**) and to treat benign prostatic hyperplasia (BPH), a condition that affects men and is characterized by an **enlarged prostate** gland.

High blood pressure

High blood pressure puts a strain on the heart and the arteries. Over time, hypertension can damage the blood vessels to the point of causing **stroke**, **heart failure** or kidney failure. People with high blood pressure may also be at higher risk for heart attacks. Controlling high blood pressure makes these problems less likely. Alpha blockers help lower blood pressure by causing vasodilation, meaning an increase in the diameter of the blood vessels, which allows blood to flow more easily.

Benign prostatic hyperplasia (BPH)

This condition particularly affects older men. Over time, the prostate, a donut-shaped gland below the bladder, enlarges. When this happens, it may interfere with the passage of urine from the bladder out of the body. Men who are diagnosed with BPH may have to urinate more often. Or they may feel that they can not completely empty their bladders. Alpha blockers inhibit the contraction of prostatic smooth muscle and thus relax muscles in the prostate and the bladder, allowing urine to flow more freely.

Description

Commonly prescribed alpha blockers for hypertension and BPH include doxazosin (Cardura, prazosin (Minipress) and terazosin (Hytrin). Prazosin is also used in the treatment of heart failure. All are available only with a physician's prescription and are sold in tablet form.

Recommended dosage

The recommended dose depends on the patient and the type of alpha blocker and may change over the course of treatment. The prescribing physician will gradually

increase the dosage, if necessary. Some patients may need as much as 15–20 mg per day of terazosin, 16 mg per day of doxazosin, or as much as 40 mg per day of prazosin, but most people benefit from lower doses. As the dosage increases, so does the possibility of unwanted side effects.

Alpha blockers should be taken exactly as directed, even if the medication does not seem to be working at first. It should not be stopped even if symptoms improve because it needs to be taken regularly to be effective. Patients should avoid missing any doses, and should not take larger or more frequent doses to make up for missed doses.

Precautions

Alpha blockers may lower blood pressure to a greater extent than desired. This can cause **dizziness**, lightheadedness, heart **palpitations**, and **fainting**. Activities such as driving, using machines, or doing anything else that might be dangerous for 24 hours after taking the first dose should be avoided. Patients should be reminded to be especially careful not to fall when getting up in the middle of the night. The same precautions are recommended if the dosage is increased or if the drug has been stopped and then started again. Anyone whose safety on the job could be affected by taking alpha blockers should inform his or her physician, so that the physician can take this factor into account when increasing dosage.

Dizziness, lightheadedness, and fainting are more likely to occur when people taking alpha blockers also drink alcohol, **exercise**, stand for a long time, or are exposed to hot weather. Extra care should be used under these conditions and alcohol consumption should be limited.

Some people may feel drowsy or less alert when using these drugs. They should accordingly avoid driving or performing activities that require full attention.

People diagnosed with kidney disease or liver disease may also be more sensitive to alpha blockers. They should inform their physicians about these conditions if alpha blockers are prescribed. Older people may also be more sensitive and may be more likely to have unwanted side effects, such as fainting, dizziness, and lightheadedness.

It should be noted that alpha blockers do not cure high blood pressure. They simply help to keep the condition under control. Similarly, these drugs will not shrink an enlarged prostate gland. Although they will help relieve the symptoms of prostate enlargement, the prostate may continue to grow, and it eventually may be necessary to have prostate surgery.

Alpha blockers may lower blood counts. Patients may need to have their blood checked regularly while taking this medicine.

KEY TERMS

Adrenergic—Refers to neurons (nerve cells) that use catecholamines as neurotransmitters at a synapse.

Adrenergic receptor—There are three families of adrenergic receptors, alpha₁, alpha₂ and beta, and each family contains three distinct subtypes. Each of the nine subtypes are coded by separate genes, and display specific drug specificities and regulatory properties.

Alpha blockers—Medications that bind alpha adrenergic receptors and decrease the workload of the heart and lower blood pressure. They are commonly used to treat hypertension, peripheral vascular disease, and hyperplasia.

Arteries—Blood vessels that carry oxygenated blood away from the heart to the cells, tissues, and organs of the body.

Catecholamines—Family of neurotransmitters containing dopamine, norepinephrine and epinephrine, produced and secreted by cells of the adrenal medulla in the brain. Catecholamines have excitatory effects on smooth muscle cells of the vessels that supply blood to the skin and mucous membranes and have inhibitory effects on smooth muscle cells located in the wall of the gut, the bronchial tree of the lungs, and the vessels that supply blood to skeletal muscle. There are two different main

types of receptors for these neurotransmitters, called alpha and beta adrenergic receptors. The catecholamines are therefore also known as adrenergic neurotransmitters.

Hyperplasia—The abnormal increase in the number of normal cells in a given tissue.

Hypertension—Persistently high arterial blood pressure.

Neurotransmitter—Substance released from neurons of the peripheral nervous system that travels across the synaptic clefts (gaps) of other neurons to excite or inhibit the target cell.

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

Receptor—A molecular structure in a cell or on the surface of a cell that allows binding of a specific substance that causes a specific physiologic response.

Synapse—A connection between nerve cells, by which nervous excitation is transferred from one cell to the other.

Vasodilation—The increase in the internal diameter of a blood vessel that results from relaxation of smooth muscle within the wall of the vessel thus causing an increase in blood flow.

Anyone who has had unusual reactions to alpha blockers 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.

The effects of taking alpha blockers during **pregnancy** are not fully understood. Women who are pregnant or planning to become pregnant should inform their physicians. Breastfeeding mothers who need to take alpha blockers should also talk to their physicians. These drugs can pass into breast milk and may affect nursing babies. It may be necessary to stop breastfeeding while being treated with alpha blockers.

Side effects

The most common side effects are dizziness, drowsiness, tiredness, **headache**, nervousness, irritability, stuffy or runny nose, nausea, **pain** in the arms and legs, and weakness. These problems usually go away as the

body adjusts to the drug and do not require medical treatment. If they do not subside or if they interfere with normal activities, the physician should be informed.

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

- fainting
- shortness of breath or difficulty breathing
- fast, pounding, or irregular heartbeat
- swollen feet, ankles, wrists

Other side effects may occur. Anyone who has unusual symptoms after taking alpha blockers should contact his or her physician.

Interactions

Doxazosin (Cardura) is not known to interact with any other drugs. Terazosin (Hytrin) may interact with **nonsteroidal anti-inflammatory drugs**, such as ibupro-

fen (Motrin), and with other blood pressure drugs, such as enalapril (Vasotec), and verapamil (Calan, Verelan). Prazosin (Minipress) may interact with beta adrenergic blocking agents such as propranolol (Inderal) and others, and with verapamil (Calan, Isoptin.) When drugs interact, the effects of one or both of the drugs may change or the risk of side effects may be greater.

Nancy Ross-Flanigan

Alport syndrome

Definition

A hereditary disease of the kidneys that primarily affects men, causing blood in the urine, **hearing loss** and eye problems. Eventually, **kidney dialysis** or transplant may be necessary.

Description

Alport syndrome affects about one in 5,000 Americans, striking men more often and severely than women. There are several varieties of the syndrome, some occurring in childhood and others not causing symptoms until men reach their 20s or 30s. All varieties of the syndrome are characterized by kidney disease that usually progresses to **chronic kidney failure** and by uremia (the presence of excessive amounts of urea and other waste products in the blood).

Causes and symptoms

Alport syndrome in most cases is caused by a defect in one or more genes located on the X chromosome. It is usually inherited from the mother, who is a normal carrier. However, in up to 20% of cases there is no family history of the disorder. In these cases, there appears to be a spontaneous genetic mutation causing Alport syndrome.

Blood in the urine (hematuria) is a hallmark of Alport syndrome. Other symptoms that may appear in varying combinations include:

- protein in the urine (proteinuria)
- sensorineural hearing loss
- eye problems [involuntary, rhythmic eye movements (**nystagmus**), **cataracts**, or cornea problems]
- skin problems
- platelet disorders
- abnormal white blood cells
- smooth muscle tumors

KEY TERMS

Albumin—A protein that is important in maintaining blood volume. Low albumin levels is one sign of Alport syndrome.

Dialysis—A technique of removing waste material from the blood. It is used with patients whose kidneys have stopped functioning and can no longer cleanse the blood on their own.

Diuretic—A drug that increases the amount of urine a person produces.

Hematuria—Blood in the urine, Hematuria is a hallmark of Alport syndrome.

Pulmonary edema—Excess fluid in the air spaces of the lungs.

Uremia—The presence of excessive amounts of urea and other waste products in the blood.

Not all patients with Alport syndrome have hearing problems. In general, those with normal hearing have less severe cases of Alport syndrome.

Diagnosis

Alport syndrome is diagnosed with a medical evaluation and family history, together with a **kidney biopsy** that can detect changes in the kidney typical of the condition. **Urinalysis** may reveal blood or protein in the urine. Blood tests can reveal a low platelet level.

In addition, tests for the Alport gene are now available. Although testing is fairly expensive, it is covered by many types of health insurance. DNA tests can diagnose affected children even before birth, and genetic linkage tests tracing all family members at risk for Alport syndrome are also available.

Treatment

There is no specific treatment that can “cure” Alport syndrome. Instead, care is aimed at easing the problems related to kidney failure, such as the presence of too many waste products in the blood (uremia).

To control kidney inflammation (**nephritis**), patients should:

- restrict fluids
- control high blood pressure
- manage **pulmonary edema**

- control high blood levels of potassium

Rarely patients with Alport syndrome may develop **nephrotic syndrome**, a group of symptoms including too much protein in the urine, low albumin levels, and swelling. To ease these symptoms, patients should:

- drink less
- eat a salt-free diet
- use **diuretics**
- have albumin transfusions

The treatment for chronic kidney failure is dialysis or a kidney transplant.

Prognosis

Women with this condition can lead a normal life, although they may have slight hearing loss. An affected woman may notice blood in her urine only when under stress or pregnant.

Men generally have a much more serious problem with the disease. Most will experience kidney disease in their 20s or 30s, which may eventually require dialysis or transplantation, and many develop significant hearing loss. Men with Alport syndrome often die of complications by middle age.

Prevention

Alport syndrome is a genetic disease and prevention efforts are aimed at providing affected individuals and their families with information concerning the genetic mechanisms responsible for the disease. Since it is possible to determine if a woman is a carrier, or if an unborn child has the condition, **genetic counseling** can provide helpful information and support for the decisions that affected individuals and their families may have to make.

Resources

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American Association of Kidney Patients. 100 S. Ashley Dr., #280, Tampa, FL 33602. (800) 749-2257. <<http://www.aakp.org>>.

American Kidney Fund. 6110 Executive Boulevard, Rockville, MD 20852. (800) 638-8299. <<http://216.248.130.102/Default.htm>>.

National Kidney and Urologic Disease Information Clearinghouse. 3 Information Way, Bethesda, MD 20892. (301) 654-4415. <<http://www.niddk.nih.gov>>.

National Kidney Foundation. 30 East 33rd St., New York, NY 10016. (800) 622-9010. <<http://www.kidney.org>>.

National Organization for Rare Diseases. P.O. Box 8923, Fairfield, CT 06812. (213) 745-6518. <<http://www.w2.com>>.

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Alport Syndrome Home Page. <<http://www.cc.utah.edu/~cla6202/ASHP.htm>>.

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Carol A. Turkington

Alprazolam see **Benzodiazepines**

ALS see **Amyotrophic lateral sclerosis**

Alteplase see **Thrombolytic therapy**

Altitude sickness

Definition

Altitude sickness is a general term encompassing a spectrum of disorders that occur at higher altitudes. Since the severity of symptoms varies with altitude, it is important to understand the range of the different altitudes that may be involved. High altitude is defined as height greater than 8,000 feet (2,438 m); medium altitude is defined as height between 5,000 and 8,000 feet (1,524–2,438 m); and extreme altitude is defined as height greater than 19,000 feet (5,791 m). The majority of healthy individuals suffer from altitude sickness when they reach very high altitudes. In addition, about 20% of people ascending above 9,000 (2,743 m) feet in one day will develop altitude sickness. Children under six years and women in the premenstrual part of their cycles may be more vulnerable. Individuals with preexisting medical conditions—even a minor respiratory infection—may become sick at more moderate altitudes.

Description

There are three major clinical syndromes that fall under the heading of altitude sickness: acute mountain sickness (AMS), high-altitude **pulmonary edema** (HAPE), and high-altitude cerebral **edema** (HACE). These syndromes are not separate, individual syndromes as much as they are a continuum of severity, all resulting from a decrease in oxygen in the air. AMS is the mildest, and the other two represent severe, life-threatening forms of altitude sickness.

Altitude sickness occurs because the partial pressure of oxygen decreases with altitude. (Partial pressure is a term applied to gases that is similar to the way the term concentration is applied to liquid solutions.) For instance, at 18,000 feet (5,486 m) the partial pressure of oxygen drops to one-half its value at sea level and, therefore, there is a substantially lower amount of oxygen available for the individual to inhale. This is known as hypoxia. Furthermore, since there is less oxygen to inhale, less oxygen reaches the blood. This is known as hypoxemia. These two conditions are the major factors that form the basis for all the medical problems associated with altitude sickness.

As a person becomes hypoxic, his natural response is to breathe more rapidly (hyperventilate). This is the body's attempt to bring in more oxygen at a rapid rate. This attempt at alleviating the effects of the hypoxia at higher altitudes is known as acclimatization, and it occurs during the first few days. Acclimatization is a response that occurs in individuals who travel from lower to higher altitudes. There are groups of people who have lived at high altitudes (for example, in the Himalayan and Andes mountains) for generations, and they are simply accustomed to living at such altitudes, perhaps through a genetic ability.

Causes and symptoms

Acute mountain sickness (AMS) is a mild form of altitude sickness that results from ascent to altitudes higher than 8,000 feet (2,438 m)—even 6,500 feet (1,981 m) in some susceptible individuals. Although hypoxia is associated with the development of AMS, the exact mechanism by which this condition develops has yet to be confirmed. It is important to realize that some individuals acclimatize to higher altitudes more efficiently than others. As a result, under similar conditions some will suffer from AMS while others will not. At present, the susceptibility of otherwise healthy individuals to contracting AMS cannot be accurately predicted. Of those who do suffer from AMS, the condition tends to be most severe on the second or third day after reaching the high altitude, and it usually abates after three to five days if they remain at the same altitude. However, it can recur if the individuals travel to an even higher altitude. Symptoms usually appear a few hours to a few days following ascent, and they include **dizziness**, **headache**, **shortness of breath**, nausea, vomiting, loss of appetite, and **insomnia**.

High-altitude pulmonary edema (HAPE) is a life-threatening condition that afflicts a small percentage of those who suffer from AMS. In this condition, fluid leaks from within the pulmonary blood vessels into the lung tissue. As this fluid begins to accumulate within the lung tissue (pulmonary edema), the individual begins to

KEY TERMS

Cerebral—Pertaining to the brain.

Edema—Accumulation of excess fluid in the tissues of the body.

Hypoxemia—Insufficient oxygenation of the blood.

Hypoxia—A deficiency in the amount of oxygen required for effective ventilation.

Pulmonary—Pertaining to the lungs.

become more and more short of breath. HAPE is known to afflict all types of individuals, regardless of their level of physical fitness.

Typically, the individual who suffers from HAPE ascends quickly to a high altitude and almost immediately develops shortness of breath, a rapid heart rate, a **cough** productive of a large amount of sometimes bloody sputum, and a rapid rate of breathing. If no medical assistance is provided by this point, the patient goes into a **coma** and dies within a few hours.

High-altitude cerebral edema (HACE), the rarest and most severe form of altitude sickness, involves cerebral edema, and its mechanism of development is also poorly understood. The symptoms often begin with those of AMS, but neurologic symptoms such as an altered level of consciousness, speech abnormalities, severe headache, loss of coordination, **hallucinations**, and even seizures. If no intervention is implemented, **death** is the result.

Diagnosis

The diagnosis for altitude sickness may be made from the observation of the individual's symptoms during travel to higher altitudes.

Treatment

Mild AMS requires no treatment other than an **aspirin** or ibuprofen for headache, and avoidance of further ascent. Narcotics should be avoided because they may blunt the respiratory response, making it even more difficult for the person to breathe deeply and rapidly enough to compensate for the lower levels of oxygen in the environment. Oxygen may also be used to alleviate symptoms of mild AMS.

As for HAPE and HACE, the most important course of action is descent to a lower altitude as soon as possible. Even a 1,000-2,000 -foot (305–610 m) descent can

dramatically improve one's symptoms. If descent is not possible, oxygen therapy should be started. In addition, dexamethasone (a steroid) has been suggested in order to reduce cerebral edema.

Prognosis

The prognosis for mild AMS is good, if appropriate measures are taken. As for HAPE and HACE, the prognosis depends upon the rapidity and distance of descent and the availability of medical intervention. Descent often leads to improvement of symptoms, however, recovery times vary among individuals.

Prevention

When individuals ascend from sea level, it is recommended that they spend at least one night at an intermediate altitude prior to ascending to higher elevations. In general, climbers should take at least two days to go from sea level to 8,000 feet (2,438 m). After reaching that point, healthy climbers should generally allow one day for each additional 2,000 feet (610 m), and one day of rest should be taken every two or three days. Should mild symptoms begin to surface, further ascent should be avoided. If the symptoms are severe, the individual should return to a lower altitude. Some reports indicate that acetazolamide (a diuretic) may be taken before ascent as a preventative measure for AMS.

Paying attention to diet can also help prevent altitude sickness. Water loss is a problem at higher altitudes, so climbers should drink ample water (enough to produce copious amounts of relatively light-colored or clear urine). Alcohol and large amounts of salt should be avoided. Eating frequent small, high-carbohydrate snacks (for example, fruits, jams and starchy foods) can help, especially in the first few days of climbing.

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Kapil Gupta, MD

Aluminum hydroxide see **Antacids**

Alzheimer's disease

Definition

Alzheimer's disease (AD) is the most common form of **dementia**, a neurologic disease characterized by loss of mental ability severe enough to interfere with normal activities of daily living, lasting at least six months, and not present from birth. AD usually occurs in old age, and is marked by a decline in cognitive functions such as remembering, reasoning, and planning.

Description

A person with AD usually has a gradual decline in mental functions, often beginning with slight memory loss, followed by losses in the ability to maintain employment, to plan and execute familiar tasks, and to reason and **exercise judgment**. Communication ability, mood, and personality may also be affected. Most people who have AD die within eight years of their diagnosis, although that interval may be as short as one year or as long as 20 years. AD is the fourth leading cause of **death** in adults after heart disease, **cancer**, and **stroke**.

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 21st century as the population as a whole ages. While a small number of people in their 40s and 50s develop the disease (called early-onset AD), AD predominantly affects the elderly. AD affects about 3% of all people between ages 65 and 74, about 19% of those between 75 and 84, and about 47% of those over 85. Slightly more women than men are affected with AD, but this may be because women tend to live longer, and so there is a higher proportion of women in the most affected age groups.

The costs for caring for a person with AD is considerable. The annual cost of caring for one AD patient in 1998 was estimated as about \$18,400 for a patient with mild AD, \$30,100 for a patient with moderate AD, and \$36,100 for a patient with severe AD. The annual direct and indirect costs of caring for AD patients in the United States was estimated to be as much as \$100 billion. Slightly more than half of AD patients are cared for at home, while the remainder are cared for in a variety of health care institutions.

Causes and symptoms

Causes

The cause or causes of Alzheimer's disease are unknown. Some strong leads have been found through recent research, however, and these have also given some theoretical support to several new experimental treatments.

At first AD destroys neurons (nerve cells) in parts of the brain that control memory, including the hippocampus, which is a structure deep in the deep that controls short-term memory. As these neurons in the hippocampus stop functioning, the short-term memory of the person fails, and the ability to perform familiar tasks decreases. Later AD affects the cerebral cortex, particularly the areas responsible for language and reasoning; these language skills are lost and the ability to make judgments is changed. Personality changes occur, which may include emotional outbursts, wandering, and agitation. The severity of these changes increases with the progression of the disease. Eventually many other areas of the brain become involved, the brain regions affected atrophy (shrink and lose function), and the person with AD becomes bedridden, incontinent, helpless, and non-responsive.

Autopsy of a person with AD shows that the regions of the brain affected by the disease become clogged with two abnormal structures, called neurofibrillary tangles and amyloid plaques. Neurofibrillary tangles are twisted masses of protein fibers inside nerve cells, or neurons. In AD, tau proteins, which normally help bind and stabilize parts of neurons, is changed chemically, become twisted and tangled, and no longer can stabilize the neurons. Amyloid plaques consist of insoluble deposits of beta-amyloid (a protein fragment from a larger protein called amyloid precursor protein (APP) mixed with parts of neurons and non-nerve cells. Plaques are found in the spaces between the nerve cells of the brain. While it is not clear exactly how these structures cause problems, many researchers believe that their formation is responsible for the mental changes of AD, presumably by interfering with the normal communication between neurons in the brain and later leading to the death of neurons. As of 2000, three drugs for the treatment of AD symptoms have been approved by the United States Food and Drug Administration (FDA). They act by increasing the level of chemical signaling molecules in the brain, known as neurotransmitters, to make up for this decreased communication ability. All act by inhibiting the activity of acetylcholinesterase, which is an enzyme that breaks down acetylcholine, an important neurotransmitter released by neurons that is necessary for cognitive function. These drugs modestly increase cognition and improve one's ability to perform normal activities of daily living.

What triggers the formation of plaques and tangles and the development of AD are unknown. AD likely results from many interrelated factors, including genetic, environmental, and others not yet identified. Two types of AD exist: familial AD (FAD), which is a rare autosomal dominant inherited disease, and sporadic AD, with no obvious inheritance pattern. AD is also described in terms of age at onset, with early on-set AD occurring in

people younger than 65, and late-onset occurring in those 65 and older. Early on-set AD comprises about 5-10 of AD cases and affects people aged 30 to 60. Some cases of early on-set AD are inherited and are common in some families. Early-onset AD often progresses faster than the more common late-on-set type.

All FAD, which are relatively uncommon, that have been identified so far are the early on-set type. As many as 50% of the FAD cases are known to be caused by three genes located on three different chromosomes. Some families have mutations in the APP gene located on chromosome 21, which causes the production of abnormal APP protein. Others have mutations in a gene called presenilin 1 located on chromosome 14, which causes the production of abnormal presenilin 1 protein, and others have mutations in a similar gene called presenilin 2 located on chromosome 1, which causes production of abnormal presenilin 2. Presenilin 1 may be one of the enzymes that clips APP into beta-amyloid; it may also be important in the synaptic connections between brain cells.

There is no evidence that the mutated genes that cause early on-set FAD also cause late on-set AD, but genetics does appear to play a role in this more common form of AD. Discovered by researchers at Duke University in the early 1990s, potentially the most important genetic link to AD was on chromosome 19. A gene on this chromosome, called APOE (apolipoprotein E), codes for a protein involved in transporting lipids into neurons. APOE occurs in at least three forms (alleles), called APOE e2, APOE e3, and APOE e4. Each person inherits one APOE from each parent, and therefore can either have one copy of two different forms, or two copies of one. The relatively rare APOE e2 appears to protect some people from AD, as it seems to be associated with a lower risk of AD and a later age of onset if AD does develop. APOE e3 is the most common version found in the general population, and only appears to have a neutral role in AD. However, APOE e4 appears to increase the risk of developing late onset AD with the inheritance of one or two copies of APOE e4. Compared to those without APOE e4, people with one copy are about three times as likely to develop late-onset AD, and those with two copies are almost four times as likely to do so. Having APOE e4 can also lower the age of onset by as much as 17 years. However, APOE e4 only increases the risk of developing AD and does not cause it, as not everyone with APOE e4 develops AD, and people without it can still have the disease. Why APOE e4 increases the chances of developing AD is not known with certainty. However, one theory is that APOE e4 facilitates beta-amyloid buildup in plaques, thus contributing to the lowering of the age of onset of AD; other theories involve interactions with cholesterol levels and effects on nerve

cell death independent of its effects on plaque buildup. In 2000, four new AD-related regions in the human genome were identified, where one out of several hundred genes in each of these regions may be a risk factor gene for AD. These genes, which are not yet identified, appear to make a contribution to the risk of developing late-onset AD that is at least as important as APOE e4.

Other non-genetic factors have also been studied in relation to the causes of AD. Inflammation of the brain may play a role in development of AD, and use of **nonsteroidal anti-inflammatory drugs** (NSAIDs) seems to reduce the risk of developing AD. Restriction of blood flow may be part of the problem, perhaps accounting for the beneficial effects of estrogen, which increases blood flow in the brain, among its other effects. Highly reactive molecular fragments called free radicals damage cells of all kinds, especially brain cells, which have smaller supplies of protective antioxidants thought to protect against free radical damage. Vitamin E is one such antioxidant, and its use in AD may be of possible theoretical benefit.

While the ultimate cause or causes of Alzheimer's disease are still unknown, there are several risk factors that increase a person's likelihood of developing the disease. The most significant one is, of course, age; older people develop AD at much higher rates than younger ones. There is some evidence that strokes and AD may be linked, with small strokes that go undetected clinically contributing to the injury of neurons. Blood cholesterol levels may also be important. Scientists have shown that high blood cholesterol levels in special breeds of genetically engineered (transgenic) mice may increase the rate of plaque deposition. There are also parallels between AD and other progressive neurodegenerative disorders that cause dementia, including prion diseases, Parkinson's disease, and Huntington's disease.

Numerous epidemiological studies of populations are also being conducted to learn more about whether and to what extent early life events, socioeconomic factors, and ethnicity have an impact on the development of AD. For example, results from one study indicated that rural residence in childhood, along with fewer than six years of schooling, was associated with increased AD risk. However, the low educational attainment that was identified as a risk factor might be a marker or surrogate for other deleterious socioeconomic or environmental influences in childhood, thus illustrating the difficulties in interpreting epidemiological findings, due to the complexity of the issues and the large number of variables involved.

Many environmental factors have been suspected of contributing to AD, but epidemiological population studies have not borne out these links. Among these have been pollutants in drinking water, aluminum from com-

mercial products, and metal dental fillings. To date, none of these factors has been shown to cause AD or increase its likelihood. Further research may yet turn up links to other environmental factors.

Symptoms

The symptoms of Alzheimer's disease begin gradually, usually with memory lapses. Occasional memory lapses are of course common to everyone, and do not by themselves signify any change in cognitive function. The person with AD may begin with only the routine sort of memory lapse—forgetting where the car keys are—but progress to more profound or disturbing losses, such as forgetting that he or she can even drive a car. Becoming lost or disoriented on a walk around the neighborhood becomes more likely as the disease progresses. A person with AD may forget the names of family members, or forget what was said at the beginning of a sentence by the time he hears the end.

As AD progresses, other symptoms appear, including inability to perform routine tasks, loss of judgment, and personality or behavior changes. Some patients have trouble sleeping and may suffer from confusion or agitation in the evening ("sunsetting" or Sundowner's Syndrome). In some cases, people with AD repeat the same ideas, movements, words, or thoughts, a behavior known as perseveration. In the final stages people may have severe problems with eating, communicating, and controlling their bladder and bowel functions.

The Alzheimer's Association has developed a list of ten warning signs of AD. A person with several of these symptoms should see a physician for a thorough evaluation:

- memory loss that affects job skills
- difficulty performing familiar tasks
- problems with language
- disorientation of time and place
- poor or decreased judgment
- problems with abstract thinking
- misplacing things
- changes in mood or behavior
- changes in personality
- loss of initiative

Other types of dementia, including some that are reversible, can cause similar symptoms. It is important for the person with these symptoms to be evaluated by a professional who can weigh the possibility that his or her symptoms may have another cause. Approximately 20% of those originally suspected of having AD turn out to have some other disorder; about half of these cases are treatable.

Diagnosis

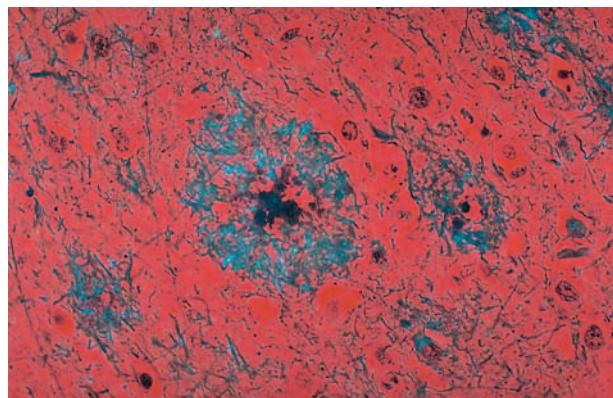
Diagnosis of Alzheimer's disease is complex, and may require office visits to several different specialists over several months before a diagnosis can be made. While a confident provisional diagnosis may be made in most cases after thorough testing, AD cannot be definitively diagnosed until autopsy examination of the brain for plaques and neurofibrillary tangles.

The diagnosis of AD begins with a thorough physical exam and complete medical history. Except in the disease's earliest stages, accurate history from family members or caregivers is essential. Since there are both prescription and over-the-counter drugs that can cause the same mental changes as AD, a careful review of the patient's drug, medicine, and alcohol use is important. AD-like symptoms can also be provoked by other medical conditions, including tumors, infection, and dementia caused by mild strokes (multi-infarct dementia). These possibilities must be ruled out as well through appropriate blood and urine tests, brain **magnetic resonance imaging (MRI)**, **positron emission tomography (PET)** or single photon emission computed tomography (SPECT) scans, tests of the brain's electrical activity (electroencephalographs or EEGs), or other tests. Several types of oral and written tests are used to aid in the AD diagnosis and to follow its progression, including tests of mental status, functional abilities, memory, and concentration. Still, the **neurologic exam** is normal in most patients in early stages.

One of the most important parts of the diagnostic process is to evaluate the patient for depression and **delirium**, since each of these can be present with AD, or may be mistaken for it. (Delirium involves a decreased consciousness or awareness of one's environment.) Depression and memory loss are both common in the elderly, and the combination of the two can often be mistaken for AD. Depression can be treated with drugs, although some antidepressants can worsen dementia if it is present, further complicating both diagnosis and treatment.

An early and accurate diagnosis of AD is important in developing strategies for managing symptoms and for helping patients and their families planning for the future and pursuing care options while the patient can still take part in the decision-making process.

A genetic test for the APOE e4 gene is available, but is not used for diagnosis, since possessing even two copies does not ensure that a person will develop AD. In addition, access to genetic information could affect the insurability of a patient if disclosed, and also affect employment status and legal rights.



Diseased tissue from the brain of an Alzheimer's patient showing senile plaques within the brain's gray matter. (Photograph by Cecil Fox, Photo Researchers, Inc. Reproduced by permission.)

Treatment

Alzheimer's disease is presently incurable, so therefore the mainstay of treatment for a person with AD is good nursing care, providing both physical and emotional support for a person who is gradually able to do less and less for himself, and whose behavior is becoming more and more erratic. Modifications of the home to increase safety and security are often necessary. The caregiver also needs support to prevent anger, despair, and burnout from becoming overwhelming. Becoming familiar with the issues likely to lie ahead, and considering the appropriate financial and legal issues early on, can help both the patient and family cope with the difficult process of the disease. Regular medical care by a practitioner with a non-defeatist attitude toward AD is important so that illnesses such as urinary or respiratory infections can be diagnosed and treated properly, rather than being incorrectly attributed to the inevitable decline seen in AD.

People with AD are also often depressed or anxious, and may suffer from sleeplessness, poor **nutrition**, and general poor health. Each of these conditions is treatable to some degree. It is important for the person with AD to eat well and continue to exercise. Professional advice from a nutritionist may be useful to provide healthy, easy-to-prepare meals. Finger foods may be preferable to those requiring utensils to be eaten. Regular exercise (supervised if necessary for safety) promotes overall health. A calm, structured environment with simple orientation aids (such as calendars and clocks) may reduce **anxiety** and increase safety. Other psychiatric symptoms, such as depression, anxiety, **hallucinations** (seeing or hearing things that aren't there), and **delusions** (false beliefs) may be treated with drugs if necessary.

Drugs

As of 2000, only three drugs—tacrine (Cognex), donepezil hydrochloride (Aricept), and rivastigmine (Exelon)—have been approved by the FDA for its treatment. Tacrine has been shown to be effective for improving memory skills, but only in patients with mild-to-moderate AD, and even then in less than half of those who take it. Its beneficial effects are usually mild and temporary, but it may delay the need for nursing home admission. The most significant side effect is an increase in a liver enzyme known as alanine aminotransferase, or ALT. Patients taking tacrine must have a weekly blood test to monitor their ALT levels. Other frequent side effects include nausea, vomiting, **diarrhea**, abdominal pain, **indigestion**, and skin rash. The cost of tacrine was about \$125 per month in early 1998, with additional costs for the weekly blood monitoring. Despite its high cost, tacrine appears to be cost-effective for those who respond to it, since it may decrease the number of months a patient needs nursing care. Donepezil is the drug most commonly used to treat mild to moderate symptoms of AD, although it only helps some patients for periods of time ranging from months to about two years. Donepezil has two advantages over tacrine: it has fewer side effects, and it can be given once daily rather than three times daily. Donepezil does not appear to affect liver enzymes, and therefore does not require weekly blood tests. The frequency of abdominal side effects is also lower. The monthly cost is approximately the same. Rivastigmine, approved for use in April of 2000, has been shown to improve the ability of patients to carry out daily activities, such as eating and dressing, decrease behavioral symptoms such as delusions and agitation, and improve cognitive functions such as thinking, memory, and speaking. The cost is similar to those of the other two drugs. However, none of these three drugs stops or reverses the progression of AD.

Estrogen, the female sex hormone, is widely prescribed for post-menopausal women to prevent **osteoporosis**. Several preliminary studies have shown that women taking estrogen have lower rates of AD, and those who develop AD have a slower progression and less severe symptoms. However, estrogen does not appear to have a beneficial effect on women who already have AD.

Preliminary studies have also suggested a reduced risk for developing AD in older people who regularly use nonsteroidal anti-inflammatory drugs (NSAIDs), including **aspirin**, ibuprofen, and naproxen, although not acetaminophen. Inflammation of the brain is a distinctive characteristic of AD, but whether it is a cause or an effect of the disease is not yet known.

Antioxidants, which act to inhibit and protect against oxidative damage caused by free radicals, have

been shown to inhibit toxic effects of beta-amyloid in tissue culture. Therefore, research is being conducted to see whether antioxidants may delay or prevent AD.

Another antioxidant, vitamin E, is also thought to delay AD onset. It is not yet clear whether this is due to the specific action of vitamin E on brain cells, or to an increase in the overall health of those taking it.

Drugs such as antidepressants, anti-psychotics, and sedatives are used to treat the behavioral symptoms (agitation, aggression, wandering, and **sleep disorders**) of AD. Research is being conducted to search for better treatments, including non-drug approaches for AD patients.

Nursing care and safety

The person with Alzheimer's disease will gradually lose the ability to dress, groom, feed, bathe, or use the toilet by himself; in the later stages of the disease, he may be unable to move or speak. In addition, the person's behavior becomes increasing erratic. A tendency to wander may make it difficult to leave him unattended for even a few minutes and make even the home a potentially dangerous place. In addition, some patients may exhibit inappropriate sexual behaviors.

The nursing care required for a person with AD is well within the abilities of most people to learn. The difficulty for many caregivers comes in the constant but unpredictable nature of the demands put on them. In addition, the personality changes undergone by a person with AD can be heartbreaking for family members, as a loved one deteriorates, seeming to become a different person. Not all AD patients develop negative behaviors: some become quite gentle, and spend increasing amounts of time in dreamlike states.

A loss of good grooming may be one of the early symptoms of AD. Mismatched clothing, unkempt hair, and decreased interest in personal hygiene become more common. Caregivers, especially spouses, may find these changes socially embarrassing and difficult to cope with. The caregiver will usually need to spend increasing amounts of time for grooming to compensate for the loss of attention from the patient, although some adjustment of expectations (while maintaining cleanliness) is often needed as the disease progresses.

Proper nutrition is important for a person with AD, and may require assisted feeding early on, to make sure the person is taking in enough nutrients. Later on, as movement and swallowing become difficult, a feeding tube may be placed into the stomach through the abdominal wall. A feeding tube requires more attention, but is generally easy to care for if the patient is not resistant to its use.

For many caregivers, incontinence becomes the most difficult problem to deal with at home, and is a principal reason for pursuing nursing home care. In the early stages, limiting fluid intake and increasing the frequency of toileting can help. Careful attention to hygiene is important to prevent skin irritation and infection from soiled clothing.

Persons with dementia must deal with six basic safety concerns: injury from falls, injury from ingesting dangerous substances, leaving the home and getting lost, injury to self or others from sharp objects, fire or **burns**, and the inability to respond rapidly to crisis situations. In all cases, a person diagnosed with AD should no longer be allowed to drive, because of the increased potential for accidents and the increased likelihood of wandering very far from home while disoriented. In the home, simple measures such as grab bars in the bathroom, bed rails on the bed, and easily negotiable passageways can greatly increase safety. Electrical appliances should be unplugged and put away when not in use, and matches, lighters, knives, or weapons should be stored safely out of reach. The hot water heater temperature may be set lower to prevent accidental scalding. A list of emergency numbers, including the poison control center and the hospital emergency room, should be posted by the phone. As the disease progresses, caregivers need to periodically reevaluate the physical safety of the home and introduce new strategies for continued safety.

Care for the caregiver

Family members or others caring for a person with AD have an extremely difficult and stressful job, which becomes harder as the disease progresses. Dementia caregivers spend significantly more time on caregiving than do people providing care for those with other types of illnesses. This type of caregiving also has a greater impact in terms of employment complications, caregiver strain, mental and physical health problems, time for leisure and other family members, and family conflict than do other types of caregiving. It is common for AD caregivers to 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 AD. Support groups are an important way to deal with the **stress** of caregiving. Becoming a member of an AD caregivers' support group can be one of the most important things a family member does, not only for him or herself, but for the person with AD as well. The location and contact numbers for AD caregiver support groups are available from the Alzheimer's Association; they may also be available through a local social service agency, the patient's physi-

cian, or pharmaceutical companies that manufacture the drugs used to treat AD. Medical treatment for depression may be an important adjunct to group support.

Outside help, nursing homes, and governmental assistance

Most families eventually need outside help to relieve some of the burden of around-the-clock care for a person with AD. Personal care assistants, either volunteer or paid, may be available through local social service agencies. Adult daycare facilities are becoming increasingly common. Meal delivery, shopping assistance, or respite care may be available as well.

Providing the total care required by a person with late-stage AD can become an overwhelming burden for a family, even with outside help. At this stage, many families consider nursing home care. This decision is often one of the most difficult for the family, since it is often seen as an abandonment of the loved one and a failure of the family. Careful counseling with a sympathetic physician, clergy, or other trusted adviser may ease the difficulties of this transition. Selecting a nursing home may require a difficult balancing of cost, services, location, and availability. Keeping the entire family involved in the decision may help prevent further stress from developing later on.

Several federal government programs may ease the cost of caring for a person with AD, including Social Security Disability, Medicare, and Supplemental Security Income. Each of these programs may provide some assistance for care, medication, or other costs, but none of them will pay for nursing home care indefinitely. Medicaid is a state-funded program that may provide for some or all of the cost of nursing home care, although there are important restrictions. Details of the benefits and eligibility requirements of these programs are available through the local Social Security or Medicaid office, or from local social service agencies.

Private long-term care insurance, special "reverse mortgages," viatical insurance, and other financial devices are other ways of paying for care for those with the appropriate financial situations. Further information on these options may be available through resources listed below.

Alternative treatment

Several substances are currently being tested for their ability to slow the progress of Alzheimer's disease. These include acetylcarinidine, a supplement that acts on the cellular energy structures known as mitochondria. Ginkgo extract, derived from the leaves of the *Ginkgo biloba* tree, appears to have antioxidant as well as anti-inflammatory and anticoagulant properties. Ginkgo

KEY TERMS

Acetylcholine—One of the substances in the body that helps transmit nerve impulses.

Dementia—Impaired intellectual function that interferes with normal social and work activities.

Ginkgo—An herb from the *Ginkgo biloba* tree that some alternative practitioners recommend for the prevention and treatment of AD.

Neurofibrillary tangle—Twisted masses of protein inside nerve cells that develop in the brains of people with AD.

Senile plaque—Structures composed of parts of neurons surrounding brain proteins called beta-amyloid deposits and found in the brains of people with AD.

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 ginkgo extract could improve their symptoms, though the study was criticized for certain flaws in its method. Large scale follow-up studies are being conducted to determine whether Ginkgo extract can prevent or delay the development of AD. Ginkgo extract is available in many health food or nutritional supplement stores. Some alternative practitioners also advise people with AD to take supplements of phosphatidylcholine, vitamin B₁₂, gotu kola, ginseng, St. John's Wort, rosemary, saiko-keishi-to-shakuyaku (A Japanese herbal mixture), and **folic acid**.

Prognosis

While Alzheimer's disease may not be the direct cause of death, the generally poorer health of a person with AD increases the risk of life-threatening infection, including **pneumonia**. In addition, other diseases common in old age—cancer, stroke, and heart disease—may lead to more severe consequences in a person with AD. On average, people with AD live eight years past their diagnosis, with a range from one to 20 years.

Prevention

There is currently no sure way to prevent Alzheimer's disease, although some of the drug treatments discussed above may eventually be proven to reduce the risk of developing the disease. The most likely current candidates are estrogen, NSAIDs, vitamin E, and **ginkgo biloba**, although this list may grow or shrink with further research.

Research on the prevention of AD is focusing on blocking the production of amyloid in the brain as well as breaking down beta-amyloid once it is released from cells but before it has a chance to aggregate into insoluble plaques. There are also promising studies being conducted to develop an AD vaccine, where immune responses may result in the elimination of the formation of amyloid plaques.

The Alzheimer's Disease Research Centers (ADCs) program promotes research, training and education, technology transfer, and multicenter and cooperative studies in AD, other dementias, and normal brain **aging**. Each ADC enrolls and performs studies on AD patients and healthy older people. Persons can participate in research protocols and clinical drug trials at these centers. Data from the ADCs as well as from other sources are coordinated and made available for use by researchers at the National Alzheimer's Coordinating Center, established in 1999.

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ORGANIZATIONS

Alzheimer's Association. 919 North Michigan Ave., Suite 1000 Chicago, IL 60611. (800) 272-3900. <<http://www.alz.org>>.

Alzheimer's Disease Education and Referral Center. P.O. Box 8250, Silver Spring, MD. (800) 438-4380. Fax: (301) 495-3334. [<adear@alzheimers.org>](mailto:adear@alzheimers.org).

Alzheimer's Research Foundation. <<http://www.alzheimers-research.org>>.

OTHER

National Institute on Aging, National Institutes of Health.
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Judith Sims

Ambiguous genitals see **Intersex states**



Man with a lazy eye. (Custom Medical Stock Photo. Reproduced by permission.)

Amblyopia

Definition

Amblyopia is an uncorrectable decrease in vision in one or both eyes with no apparent structural abnormality seen to explain it. It is a diagnosis of exclusion, meaning that when a decrease in vision is detected, other causes must be ruled out. Once no other cause is found, amblyopia is the diagnosis. Generally, a difference of two lines or more (on an eye-chart test of visual acuity) between the two eyes or a best corrected vision of 20/30 or worse would be defined as amblyopia. For example, if someone has 20/20 vision with the right eye and only 20/40 with the left, and the left eye cannot achieve better vision with corrective lenses, the left eye is said to be amblyopic.

Description

Lazy eye is a common non-medical term used to describe amblyopia because the eye with poorer vision doesn't seem to be doing its job of seeing. Amblyopia is the most common cause of impaired vision in children, affecting nearly three out of every 100 people or 2-4% of the population. Vision is a combination of the clarity of the images of the eyes (visual acuity) and the processing of those images by the brain. If the images produced by the two eyes are substantially different, the brain may not be able to fuse the images. Instead of seeing two different images or double vision (diplopia), the brain suppresses the blurrier image. This suppression can lead to amblyopia. During the first few years of life, preferring one eye over the other may lead to poor visual development in the blurrier eye.

Causes and symptoms

Some of the major causes of amblyopia are as follows:

- **Strabismus.** A misalignment of the eyes (strabismus) is the most common cause of functional amblyopia. The two eyes are looking in two different directions at the same time. The brain is sent two different images and this causes confusion. Images from the misaligned or “crossed” eye are turned off to avoid double vision.
- **Anisometropia.** This is another type of functional amblyopia. In this case, there is a difference of refractive states between the two eyes (in other words, a difference of prescriptions between the two eyes). For example, one eye may be more nearsighted than the other eye, or one eye may be farsighted and the other eye nearsighted. Because the brain cannot fuse the two dissimilar images, the brain will suppress the blurrier image, causing the eye to become amblyopic.
- **Cataract.** Clouding of the lens of the eye will cause the image to be blurrier than the other eye. The brain “prefers” the clearer image. The eye with the cataract may become amblyopic.
- **Ptosis.** This is the drooping of the upper eyelid. If light cannot enter the eye because of the drooping lid, the eye is essentially not being used. This can lead to amblyopia.
- **Nutrition.** A type of organic amblyopia in which nutritional deficiencies or chemical toxicity may result in amblyopia. Alcohol, tobacco, or a deficiency in the **B vitamins** may result in toxic amblyopia.
- **Heredity.** Amblyopia can run in families.

Barring the presence of strabismus or ptosis, children may or may not show signs of amblyopia. Children may hold their heads at an angle while trying to favor the eye with normal vision. They may have trouble seeing or reaching for things when approached from the side of the amblyopic eye. Parents should see if one side of

KEY TERMS

Anisometropia—An eye condition in which there is an inequality of vision between the two eyes. There may be unequal amounts of nearsightedness, farsightedness, or astigmatism, so that one eye will be in focus while the other will not.

Cataract—Cloudiness of the eye's natural lens.

Occlusion therapy—A type of treatment for amblyopia in which the good eye is patched for a period of time. This forces the weaker eye to be used.

Strabismus—A condition in which the eyes are misaligned and point in different directions. One eye may look straight ahead, while the other turns inward, outward, upward, or downward. This is also called crossed-eyes.

Visual acuity—Acuity is the acuteness or sharpness of vision.

approach is preferred by the child or infant. If an infant's good eye is covered, the child may cry.

Diagnosis

Because children with outwardly normal eyes may have amblyopia, it is important to have regular vision screenings performed for all children. While there is some controversy regarding the age children should have their first vision examination, their eyes can, in actuality, be examined at any age, even at one day of life.

Some recommend that children have their vision checked by their pediatrician, family physician, ophthalmologist, or optometrist at or before six months of age. Others recommend testing by at least the child's fourth birthday. There may be a "critical period" in the development of vision, and amblyopia may not be treatable after age eight or nine. The earlier amblyopia is found, the better the possible outcome. Most physicians test vision as part of a child's medical examination. If there is any sign of an eye problem, they may refer a child to an eye specialist.

There are objective methods, such as retinoscopy, to measure the refractive status of the eyes. This can help determine anisometropia. In retinoscopy, a hand-held instrument is used to shine a light in the child's (or infant's) eyes. Using hand-held lenses, a rough prescription can be obtained. Visual acuity can be determined using a variety of methods. Many different eye charts are available (e.g., tumbling E, pictures, or letters). In amblyopia, single letters are easier to recognize than when a

whole line is shown. This is called the "crowding effect" and helps in diagnosing amblyopia. Neutral density filters may also be held over the eye to aid in the diagnosis. Sometimes visual fields to determine defects in the area of vision will be performed. Color vision testing may also be performed. Again, it must be emphasized that amblyopia is a diagnosis of exclusion. Visual or life-threatening problems can also cause a decrease in vision. An examination of the eyes and visual system is very important when there is an unexplained decrease in vision.

Treatment

The primary treatment for amblyopia is occlusion therapy. It is important to alternate patching the good eye (forcing the amblyopic eye to work) and the amblyopic eye. If the good eye is constantly patched, it too may become amblyopic because of disuse. The treatment plan should be discussed with the doctor to fully understand how long the patch will be on. When patched, eye exercises may be prescribed to force the amblyopic eye to focus and work. This is called vision therapy or **vision training** (eye exercises). Even after vision has been restored in the weak eye, part-time patching may be required over a period of years to maintain the improvement.

While patching is necessary to get the amblyopic eye to work, it is just as important to correct the reason for the amblyopia. Glasses may also be worn if there are errors in refraction. Surgery or vision training may be necessary in the case of strabismus. Better nutrition is indicated in some toxic amblyopias. Occasionally, amblyopia is treated by blurring the vision in the good eye with eye drops or lenses to force the child to use the amblyopic eye.

Prognosis

The younger the person, the better the chance for improvement with occlusion and vision therapy. However, treatment may be successful in older children—even adults. Success in the treatment of amblyopia also depends upon how severe the amblyopia is, the specific type of amblyopia, and patient compliance. It is important to diagnose and treat amblyopia early because significant vision loss can occur if left untreated. The best outcomes result from early diagnosis and treatment.

Prevention

To protect their child's vision, parents must be aware of amblyopia as a potential problem. This awareness may encourage parents to take young children for vision exams early on in life—certainly before school age. Proper nutrition is important in the avoidance of toxic amblyopia.

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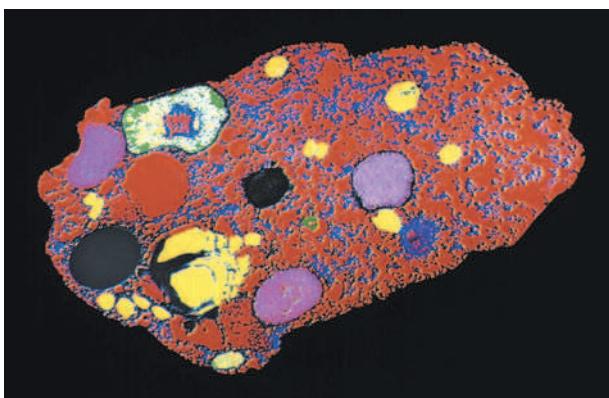
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ORGANIZATIONS

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.aovanet.org>>.

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A micrograph of *Entameoba histolytica*, a parasitic amoeba which invades and destroys the tissues of the intestines, causing amebiasis and ulceration to the intestinal wall. (Photo Researchers, Inc. Reproduced by permission.)

Amebiasis

Definition

Amebiasis is an infectious disease caused by a parasitic one-celled microorganism (protozoan) called *Entamoeba histolytica*. Persons with amebiasis may experience a wide range of symptoms, including **diarrhea**, **fever**, and cramps. The disease may also affect the intestines, liver, or other parts of the body.

Description

Amebiasis, also known as amebic dysentery, is one of the most common parasitic diseases occurring in humans, with an estimated 500 million new cases each year. It occurs most frequently in tropical and subtropical areas where living conditions are crowded, with inadequate sanitation. Although most cases of amebiasis occur in persons who carry the disease but do not exhibit any symptoms (asymptomatic), as many as 100,000 people die of amebiasis each year. In the United States, between 1 and 5% of the general population will develop amebiasis in any given year, while male homosexuals, migrant workers, institutionalized people, and recent immigrants develop amebiasis at a higher rate.

Human beings are the only known host of the amebiasis organism, and all groups of people, regardless of age or sex, can become affected. Amebiasis is primarily spread in food and water that has been contaminated by human feces but is also spread by person-to-person contact. The number of cases is typically limited, but regional outbreaks can occur in areas where human feces are used as fertilizer for crops, or in cities with water supplies contaminated with human feces.

Causes and symptoms

Recently, it has been discovered that persons with symptom-causing amebiasis are infected with *Entamoeba histolytica*, and those individuals who exhibit no symptoms are actually infected with an almost identical-looking ameba called *Entamoeba dispar*. During their life cycles, the amebas exist in two very different forms: the infective cyst or capsuled form, which cannot move but can survive outside the human body because of its protective covering, and the disease-producing form, the trophozoite, which although capable of moving, cannot survive once excreted in the feces and, therefore, cannot infect others. The disease is most commonly transmitted when a person eats food or drinks water containing *E. histolytica* cysts from human feces. In the digestive tract the cysts are transported to the intestine where the walls of the cysts are broken open by digestive secretions, releasing the mobile trophozoites. Once released within the intestine, the trophozoites multiply by feeding on intestinal bacteria or by invading the lining of the large intestine. Within the lining of the large intestine, the trophozoites secrete a substance that destroys intestinal tissue and creates a distinctive bottle-shaped sore (ulcer). The trophozoites may remain inside the intestine, in the intestinal wall, or may break through the intestinal wall and be carried by the blood to the liver, lungs, brain, or other organs. Trophozoites that remain in the intestines eventually form new cysts that are carried through the digestive tract and excreted in the feces. Under favorable temperature and humidity conditions, the cysts can survive in soil or water for weeks to months, ready to begin the cycle again.

Although 90% of cases of amebiasis in the United States are mild, pregnant women, children under two years of age, the elderly, malnourished individuals, and

people whose immune systems may be compressed, such as **cancer** or **AIDS** patients and those individuals taking prescription medications that suppress the immune system, are at a greater risk for developing a severe infection.

The signs and symptoms of amebiasis vary according to the location and severity of the infection and are classified as follows:

Intestinal amebiasis

Intestinal amebiasis can be subdivided into several categories:

ASYMPTOMATIC INFECTION. Most persons with amebiasis have no noticeable symptoms. Even though these individuals may not feel ill, they are still capable of infecting others by person-to-person contact or by contaminating food or water with cysts that others may ingest, for example, by preparing food with unwashed hands.

CHRONIC NON-DYSENTERIC INFECTION. Individuals may experience symptoms over a long period of time during a chronic amebiasis infection and experience recurrent episodes of diarrhea that last from one to four weeks and recur over a period of years. These patients may also suffer from abdominal cramps, **fatigue**, and weight loss.

AMEBIC DYSENTERY. In severe cases of intestinal amebiasis, the organism invades the lining of the intestine, producing sores (ulcers), bloody diarrhea, severe abdominal cramps, vomiting, chills, and fevers as high as 104–105°F (40–40.6°C). In addition, a case of acute amebic dysentery may cause complications, including inflammation of the appendix (**appendicitis**), a tear in the intestinal wall (perforation), or a sudden, severe inflammation of the colon (fulminating colitis).

AMEBOMA. An ameboma is a mass of tissue in the bowel that is formed by the amebiasis organism. It can result from either chronic intestinal infection or acute amebic dysentery. Amebomas may produce symptoms that mimic cancer or other intestinal diseases.

PERIANAL ULCERS. Intestinal amebiasis may produce skin infections in the area around the patient's anus (perianal). These ulcerated areas have a "punched-out" appearance and are painful to the touch.

Extraintestinal amebiasis

Extraintestinal amebiasis accounts for approximately 10% of all reported amebiasis cases and includes all forms of the disease that affect other organs.

The most common form of extraintestinal amebiasis is amebic **abscess** of the liver. In the United States, ame-

bic liver abscesses occur most frequently in young Hispanic adults. An amebic liver abscess can result from direct infection of the liver by *E. histolytica* or as a complication of intestinal amebiasis. Patients with an amebic abscess of the liver complain of **pain** in the chest or abdomen, fever, nausea, and tenderness on the right side directly above the liver.

Other forms of extraintestinal amebiasis, though rare, include infections of the lungs, chest cavity, brain, or genitals. These are extremely serious and have a relatively high mortality rate.

Diagnosis

Diagnosis of amebiasis is complicated, partly because the disease can affect several areas of the body and can range from exhibiting few, if any, symptoms to being severe, or even life-threatening. In most cases, a physician will consider a diagnosis of amebiasis when a patient has a combination of symptoms, in particular, diarrhea and a possible history of recent exposure to amebiasis through travel, contact with infected persons, or anal intercourse.

It is vital to distinguish between amebiasis and another disease, inflammatory bowel disease (IBD) that produces similar symptoms because, if diagnosed incorrectly, drugs that are given to treat IBD can encourage the growth and spread of the amebiasis organism. Because of the serious consequences of misdiagnosis, potential cases of IBD must be confirmed with multiple stool samples and blood tests, and a procedure involving a visual inspection of the intestinal wall using a thin lighted, tubular instrument (**sigmoidoscopy**) to rule out amebiasis.

A diagnosis of amebiasis may be confirmed by one or more tests, depending on the location of the disease.

Stool examination

This test involves microscopically examining a stool sample for the presence of cysts and/or trophozoites of *E. histolytica* and not one of the many other intestinal amebas that are often found but that do not cause disease. A series of three stool tests is approximately 90% accurate in confirming a diagnosis of amebic dysentery. Unfortunately, however, the stool test is not useful in diagnosing amebomas or extraintestinal infections.

Sigmoidoscopy

Sigmoidoscopy is a useful diagnostic procedure in which a thin, flexible, lighted instrument, called a sigmoidoscope, is used to visually examine the lower part of the large intestine for amebic ulcers and take tissue or fluid samples from the intestinal lining.

Blood tests

Although tests designed to detect a specific protein produced in response to amebiasis infection (antibody) are capable of detecting only about 10% of cases of mild amebiasis, these tests are extremely useful in confirming 95% of dysentery diagnoses and 98% of liver abscess diagnoses. Blood serum will usually test positive for antibody within a week of symptom onset. Blood testing, however, cannot always distinguish between a current or past infection since the antibodies may be detectable in the blood for as long as 10 years following initial infection.

Imaging studies

A number of sophisticated imaging techniques, such as **computed tomography scans (CT)**, **magnetic resonance imaging (MRI)**, and ultrasound, can be used to determine whether a liver abscess is present. Once located, a physician may then use a fine needle to withdraw a sample of tissue to determine whether the abscess is indeed caused by an amebic infection.

Treatment

Asymptomatic or mild cases of amebiasis may require no treatment. However, because of the potential for disease spread, amebiasis is generally treated with a medication to kill the disease-causing amebas. More severe cases of amebic dysentery are additionally treated by replacing lost fluid and blood. Patients with an amebic liver abscess will also require hospitalization and bed rest. For those cases of extraintestinal amebiasis, treatment can be complicated because different drugs may be required to eliminate the parasite, based on the location of the infection within the body. Drugs used to treat amebiasis, called amebicides, are divided into two categories:

Luminal amebicides

These drugs get their name because they act on organisms within the inner cavity (lumen) of the bowel. They include diloxanide furoate, iodoquinol, metronidazole, and paromomycin.

Tissue amebicides

Tissue amebicides are used to treat infections in the liver and other body tissues and include emetine, dehydroemetine, metronidazole, and chloroquine. Because these drugs have potentially serious side effects, patients given emetine or dehydroemetine require bed rest and heart monitoring. Chloroquine has been found to be the most useful drug for treating amebic liver abscess. Patients taking metronidazole must avoid alcohol because the drug-alcohol combination causes nausea, vomiting, and **headache**.

KEY TERMS

Ameboma—A mass of tissue that can develop on the wall of the colon in response to amebic infection.

Antibody—A specific protein produced by the immune system in response to a specific foreign protein or particle called an antigen.

Appendicitis—Condition characterized by the rapid inflammation of the appendix, a part of the intestine.

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.

Dysentery—Intestinal infection marked by diarrhea containing blood and mucus.

Fulminating colitis—A potentially fatal complication of amebic dysentery marked by sudden and severe inflammation of the intestinal lining, severe bleeding or hemorrhaging, and massive shedding of dead tissue.

Inflammatory bowel disease (IBD)—Disease in which the lining of the intestine becomes inflamed.

Lumen—The inner cavity or canal of a tube-shaped organ, such as the bowel.

Protozoan—A single-celled, usually microscopic organism that is eukaryotic and, therefore, different from bacteria (prokaryotic).

Most patients are given a combination of luminal and tissue amebicides over a treatment period of seven to ten days. Follow-up care includes periodic stool examinations beginning two to four weeks after the end of medication treatment to check the effectiveness of drug therapy.

Prognosis

The prognosis depends on the location of the infection and the patient's general health prior to infection. The prognosis is generally good, although the mortality rate is higher for patients with ameboma, perforation of the bowel, and liver infection. Patients who develop fulminant colitis have the most serious prognosis, with over 50% mortality.

Prevention

There are no immunization procedures or medications that can be taken prior to potential exposure to pre-

vent amebiasis. Moreover, people who have had the disease can become reinfected. Prevention requires effective personal and community hygiene.

Specific safeguards include the following:

- Purification of drinking water. Water can be purified by filtering, boiling, or treatment with iodine.
- Proper food handling. Measures include protecting food from contamination by flies, cooking food properly, washing one's hands after using the bathroom and before cooking or eating, and avoiding foods that cannot be cooked or peeled when traveling in countries with high rates of amebiasis.
- Careful disposal of human feces.
- Monitoring the contacts of amebiasis patients. The stools of family members and sexual partners of infected persons should be tested for the presence of cysts or trophozoites.

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Amebic dysentery see **Amebiasis**

Amenorrhea

Definition

The absence of menstrual periods is called amenorrhea. Primary amenorrhea is the failure to start having a

period by the age of 16. Secondary amenorrhea is more common and refers to either the temporary or permanent ending of periods in a woman who has menstruated normally in the past. Many women miss a period occasionally. Amenorrhea occurs if a woman misses three or more periods in a row.

Description

The absence of menstrual periods is a symptom, not a disease. While the average age that menstruation begins is 12, the range varies. The incidence of primary amenorrhea in the United States is just 2.5%.

Some female athletes who participate in rowing, long distance running, and cycling, may notice a few missed periods. Women athletes at a particular risk for developing amenorrhea include ballerinas and gymnasts, who typically **exercise** strenuously and eat poorly.

Causes and symptoms

Amenorrhea can have many causes. Primary amenorrhea can be the result of hormonal imbalances, psychiatric disorders, eating disorders, **malnutrition**, excessive thinness or fatness, rapid weight loss, body fat content too low, and excessive physical conditioning. Intense physical training prior to **puberty** can delay menarche (the onset of menstruation). Every year of training can delay menarche for up to five months. Some medications such as antidepressants, tranquilizers, steroids, and heroin can induce amenorrhea.

Primary amenorrhea

However, the main cause is a delay in the beginning of puberty either from natural reasons (such as heredity or poor **nutrition**) or because of a problem in the endocrine system, such as a pituitary tumor or **hypothyroidism**. An obstructed flow tract or inflammation in the uterus may be the presenting indications of an underlying metabolic, endocrine, congenital or gynecological disorder.

Typical causes of primary amenorrhea include:

- excessive physical activity
- drastic weight loss (such as occurs in anorexia or bulimia)
- extreme **obesity**
- drugs (antidepressants or tranquilizers)
- chronic illness
- turner's syndrome. (A chromosomal problem in place at birth, relevant only in cases of primary amenorrhea)
- the absence of a vagina or a uterus

- imperforate hymen (lack of an opening to allow the menstrual blood through)

Secondary amenorrhea

Some of the causes of primary amenorrhea can also cause secondary amenorrhea—strenuous physical activity, excessive weight loss, use of antidepressants or tranquilizers, in particular. In adolescents, **pregnancy** and **stress** are two major causes. Missed periods are usually caused in adolescents by stress and changes in environment. Adolescents are especially prone to irregular periods with fevers, weight loss, changes in environment, or increased physical or athletic activity. However, any cessation of periods for four months should be evaluated.

The most common cause of secondary amenorrhea is pregnancy. Also, a woman's periods may halt temporarily after she stops taking birth control pills. This temporary halt usually lasts only for a month or two, though in some cases it can last for a year or more. Secondary amenorrhea may also be related to hormonal problems related to stress, depression, **anorexia nervosa** or drugs, or it may be caused by any condition affecting the ovaries, such as a tumor. The cessation of menstruation also occurs permanently after **menopause** or a **hysterectomy**.

Polycystic ovary syndrome is another common cause of secondary amenorrhea. It is caused by ovaries containing many fluid filled sacs (cysts) with abnormal levels of male hormones (androgens). This condition is related to improper functioning of the pituitary gland, as it releases hormones necessary for pregnancy (luteinizing hormones), and can cause women to develop male characteristics, such as **acne** and coarse body hair. If the condition is not treated, some of the androgens may convert to estrogen, and chronically high levels of estrogen may increase the chance of developing **cancer** of the uterine lining.

Diagnosis

It may be difficult to find the cause of amenorrhea, but the exam should start with a pregnancy test; pregnancy needs to be ruled out whenever a woman's period is two to three weeks overdue. Androgen excess, estrogen deficiency, or other problems with the endocrine system need to be checked. Prolactin in the blood and the thyroid stimulating hormone (TSH) should also be checked.

The diagnosis usually includes a patient history and a physical exam (including a **pelvic exam**). If a woman has missed three or more periods in a row, a physician may recommend blood tests to measure hormone levels, a scan of the skull to rule out the possibility of a pituitary tumor, and ultrasound scans of the abdomen and pelvis to rule out a tumor of the adrenal gland or ovary.

Treatment

Treatment of amenorrhea depends on the cause. Primary amenorrhea often requires no treatment, but it's always important to discover the cause of the problem in any case. Not all conditions can be treated, but any underlying condition that is treatable should be treated.

If a hormonal imbalance is the problem, progesterone for one to two weeks every month or two may correct the problem. With polycystic ovary syndrome, birth control pills are often prescribed. A pituitary tumor is treated with bromocriptine, a drug that reduces certain hormone (prolactin) secretions. Weight loss may bring on a period in an obese woman. Easing up on excessive exercise and eating a proper diet may bring on periods in teen athletes. In very rare cases, surgery may be needed for women with ovarian or uterine cysts.

Prognosis

Prolonged amenorrhea can lead to **infertility** and other medical problems such as **osteoporosis** (thinning of the bones). If the halt in the normal period is caused by stress or illness, periods should begin again when the stress passes or the illness is treated. Amenorrhea that occurs with discontinuing birth control pills usually go away within six to eight weeks, although it may take up to a year.

The prognosis for polycystic ovary disease depends on the severity of the symptoms and the treatment plan. Spironolactone, a drug that blocks the production of male hormones, can help in reducing body hair. If a woman wishes to become pregnant, treatment with clomiphene may be required or, on rare occasions, surgery on the ovaries.

Prevention

Primary amenorrhea caused by a congenital condition cannot be prevented. In general, however, women should maintain a healthy diet, with plenty of exercise, rest, and not too much stress, avoiding **smoking** and substance abuse. Female athletes should be sure to eat a balanced diet and rest and exercise normally. However, many cases of amenorrhea cannot be prevented.

Resources

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KEY TERMS

- Hymen**—Membrane that stretches across the opening of the vagina.
- Hypothyroidism**—Underactive thyroid gland.
- Hysterectomy**—Surgical removal of the uterus.
- Turner's syndrome**—A condition in which one female sex chromosome is missing.

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ORGANIZATIONS

- American College of Obstetricians and Gynecologists. 409 12th Street, S.W., P.O. 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>>.

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Amikacin see **Aminoglycosides**

Amiloride see **Diuretics**

Amino acid disorders screening

Definition

Amino acid disorder screening checks for inherited disorders in amino acid metabolism. Tests are most commonly done on newborns. Two tests are available, one using a blood sample and the other a urine sample.

Purpose

Amino acid disorder screening is done in newborns, and sometimes children and adults, to detect inborn errors in metabolism of amino acids. Twenty of the 100 known amino acids are the main building blocks for human proteins. Proteins regulate every aspect of cellular

function. Of these 20 amino acids, ten are not made by the body and must be acquired through diet. Congenital (present at birth) enzyme deficiencies that affect amino acid metabolism or congenital abnormalities in the amino acid transport system of the kidneys creates a condition called aminoaciduria.

Screening is especially important in newborns. Some congenital amino acid metabolic defects cause **mental retardation** that can be prevented with prompt treatment of the newborn. One of the best known examples of this is **phenylketonuria** (PKU). This is a genetic error in metabolism of phenylalanine, an amino acid found in milk. Individuals with PKU do not produce the enzyme necessary to break down phenylalanine.

PKU occurs in about one out of 16,000 live births in the United States, but is more prevalent in Caucasians and less prevalent in Ashkenazi Jews and African Americans. Newborns in the United States are routinely screened for PKU by a blood test.

There are two types of aminoacidurias. Primary or overflow aminoaciduria results from deficiencies in the enzymes necessary to metabolize amino acids. Overflow aminoaciduria is best detected by a blood plasma test.

Secondary or renal aminoaciduria occurs because of a congenital defect in the amino acid transport system in the tubules of the kidneys. This produces increased amino acids in the urine. Blood and urine test in combination are used to determine if the aminoaciduria is of the overflow or renal type. Urine tests are also used to monitor specific amino acid disorders.

Newborns are screened for amino acid disorders. Young children with acidosis (accumulation of acid in the body), severe vomiting and **diarrhea**, or urine with an abnormal color or odor, are also screened with a urine test for specific amino acid levels.

Precautions

Both blood and urine tests are simple tests that can be done in a doctor's office or clinic. These tests can be done on even the youngest patients.

Description

Two types of amino acid screening tests are used together to diagnose amino acid disorders.

Blood plasma screening

In the blood test, a medical technician draws a small amount of blood from a baby's heel. The procedure is rapid and relatively painless. Total time for the test is less than ten minutes. The blood is sent to a laboratory where results will be available in about two days.

Urine test

In the urine test, the patient is asked to urinate into a collecting cup. For an infant, the urine is collected in a pediatric urine collector. The process is painless. The length of time the test takes is determined by how long it takes the patient to urinate. Results also take about two days.

Both these tests use thin layer chromatography to separate the amino acids present. Using this technique, the amino acids form a characteristic patterns on a glass plate coated with a thin layer of silica gel. This pattern is then compared to the normal pattern to determine if there are abnormalities.

Preparation

Before the blood test, the patient must not eat or drink for four hours. Failure to fast will alter the results of the test.

The patient should eat and drink normally before the urine test. Some drugs may affect the results of the urine test. The technician handling the urine sample should be informed of any medications the patient is taking. Mothers of breastfeeding infants should report any medications they are taking, since these can pass from mother to child in breast milk.

Aftercare

The blood screening is normally done first. Depending on the results, it is followed by the urine test. It takes both tests to distinguish between overflow and renal aminoaciduria. Also, if the results are abnormal, a 24-hour urine test is performed along with other tests to determine the levels of specific amino acids. In the event of abnormal results, there are many other tests that will be performed to determine the specific amino acid involved in the abnormality.

Risks

There are no particular risks associated with either of these tests. Occasionally minor bruising may occur at the site where the blood was taken.

Normal results

The pattern of amino acid banding on the thin layer chromatography plates will be normal.

Abnormal results

The blood plasma amino acid pattern is abnormal in overflow aminoaciduria and is normal in renal aminoaciduria. The pattern is abnormal in the urine test, suggesting additional tests need to be done to determine

KEY TERMS

Amino acid—An organic compound composed of both an amino group and an acidic carboxyl group; amino acids are the basic building blocks of proteins.

Aminoaciduria—The abnormal presence of amino acids in the urine.

Chromatography—A family of laboratory techniques that separate mixtures of chemicals into their individual components.

Enzyme—A biological catalyst that increases the rate of a chemical reaction without being used up in the reaction.

Metabolism—The sum of all the chemical and energy reactions that take place in the human body.

which amino acids are involved. In addition to PKU, a variety of other amino acid metabolism disorders can be detected by these tests, including tyrosinosis, histidinemia, maple syrup urine disease, hypervalinemia, hyperprolinemia, and homocystinuria.

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Association for Neuro-Metabolic Disorders. 5223 Brookfield Lane, Sylvania, OH 43560-1809. (419) 885-1497.

Children's PKU Network (CPN). 3790 Via De La Valle, Ste 120, Del Mar, CA 92014. (800) 377-6677. <<http://www.pkunetwork.org/>>.

National Phenylketonuria Foundation. 6301 Tejas Drive, Pasadena, TX 77503. (713) 487-4802.

Tish Davidson

Aminoglycosides

Definition

Aminoglycosides are a group of **antibiotics** that are used to treat certain bacterial infections. This group of

antibiotics includes at least eight drugs: amikacin, gentamicin, kanamycin, neomycin, netilmicin, paromomycin, streptomycin, and tobramycin. All of these drugs have the same basic chemical structure.

Purpose

Aminoglycosides are primarily used to combat infections due to aerobic, Gram-negative bacteria. These bacteria can be identified by their reaction to Gram's stain. In Gram's staining, a film of material containing the possible bacteria is placed on a glass slide and dried. The slide is stained with crystal violet for one minute, cleaned off with water and then placed into a solution of Gram's iodine solution for one minute. The iodine solution is rinsed off and the slide is immersed in 95% ethyl alcohol. The slide is then stained again with reddish carbolfuchsin or safranine for 30 seconds, rinsed in water, dried and examined. Gram-positive bacteria retain the violet purple stain. Gram-negative bacteria accept the red stain. Bacteria that can successfully be combated with aminoglycosides include *Pseudomonas*, *Acinetobacter*, and *Enterobacter* species, among others. Aminoglycosides are also effective against mycobacteria, the bacteria responsible for **tuberculosis**.

The aminoglycosides can be used against certain Gram-positive bacteria, but are not typically employed because other antibiotics are more effective and have fewer side effects. Aminoglycosides are ineffective against anaerobic bacteria (bacteria that cannot grow in the presence of oxygen), viruses, and fungi. And only one aminoglycoside, paromomycin, is used against parasitic infection.

Like all other antibiotics, aminoglycosides are not effective against **influenza**, the **common cold**, or other viral infections.

Precautions

Pre-existing medical conditions—such as kidney disease, eighth cranial nerve disease, **myasthenia gravis**, and Parkinson's disease—should be discussed prior to taking any aminoglycosides. Pregnant women are usually advised against taking aminoglycosides, because their infants may suffer damage to their hearing, kidneys, or sense of balance. However, those factors need to be considered alongside the threat to the mother's health and life in cases of serious infection. Aminoglycosides do not pass into breast milk to any great extent, so nursing mothers may be prescribed aminoglycosides without injuring their infants.

Description

Streptomycin, the first aminoglycoside, was isolated from *Streptomyces griseus* in the mid-1940s. This antibiot-

ic was very effective against tuberculosis. One of the main drawbacks to streptomycin is its toxicity, especially to cells in the inner and middle ear and the kidney. Furthermore, some strains of tuberculosis are resistant to treatment with streptomycin. Therefore, medical researchers have put considerable effort into identifying other antibiotics with streptomycin's efficacy, but without its toxicity.

Aminoglycosides are absorbed very poorly from the gastrointestinal tract; in fact, aminoglycosides taken orally are excreted virtually unchanged and undiminished in quantity. The route of drug administration depends on the type and location of the infection being treated. The typical routes of administration are by intramuscular (injection into a muscle) or intravenous injection (injection into a vein), irrigation, topical skin application, or inhalation. If the infection being treated involves the central nervous system, the drug can be injected into the spinal canal.

The bactericidal ability of aminoglycosides has not been fully explained. It is known that the drug attaches to a bacterial cell wall and is drawn into the cell via channels made up of the protein, porin. Once inside the cell, the aminoglycoside attaches to the cell's ribosomes. Ribosomes are the intracellular structures responsible for manufacturing proteins. This attachment either shuts down protein production or causes the cell to produce abnormal, ineffective proteins. The bacterial cell cannot survive with this impediment.

Antibiotic treatment using aminoglycosides may pair the drug with a second type of antibiotic, usually a beta-lactam or vancomycin, administered separately. Beta-lactams disrupt the integrity of the bacteria cell wall, making it more porous. The increased porosity allows more of the aminoglycoside into the bacteria cell.

Traditionally, aminoglycosides were administered at even doses given throughout the day. It was thought that a steady plasma concentration was necessary to combat infection. However, this administration schedule is time and labor intensive. Furthermore, administering a single daily dose can be as effective, or more effective, than several doses throughout the day.

Dosage depends on the patient's age, weight, gender, and general health. Since the drug is cleared by the kidneys, it is important to assess any underlying problems with kidney function. Kidney function is assessed by measuring the blood levels of creatinine, a protein normally found in the body. If these levels are high, it is an indication that the kidneys may not be functioning at an optimal rate and dosage will be lowered accordingly.

Risks

Aminoglycosides have been shown to be toxic to certain cells in the ears and in the kidneys. Approximately 5-

10% of the people who are treated with aminoglycosides experience some side effect, affecting their hearing, sense of balance, or kidneys. However, in most cases the damage is minor and reversible once medication is stopped.

If cells in the inner ear are damaged or destroyed, an individual may experience a loss of balance and feelings of **dizziness**. Damage to the middle ear may result in **hearing loss** or **tinnitus**. Neomycin, kanamycin, and amikacin are the most likely to cause problems with hearing, and streptomycin and gentamicin carry the greatest risk of causing vertigo and loss of balance. Kidney damage, apparent with changes in urination frequency or urine production, is most likely precipitated by neomycin, tobramycin, and gentamicin.

Young children and the elderly are at the greatest risk of suffering side effects. Excessive dosage or poor clearance of the drug from the body can be injurious at any age.

Less common side effects include skin **rashes** and **itching**. Very rarely, certain aminoglycosides may cause difficulty in breathing, weakness, or drowsiness. Gentamicin, when injected, may cause leg cramps, skin rash, **fever**, or seizures.

If side effects linger or become worse after medication is stopped, it is advisable to seek medical advice. Side effects that may be of concern include tinnitus or loss of hearing, dizziness or loss of balance, changes in urination frequency or urine production, increased thirst, appetite loss, and nausea or vomiting.

Normal results

At the proper dosage and in the presence of gram-negative enteric (intestinal) bacteria, aminoglycosides are very effective in treating an infection.

Abnormal results

In some cases, bacteria are resistant to antibiotics that would normally kill them. This resistance becomes apparent after repeated exposure to the antibiotic and arises from a mutation that alters the bacteria's susceptibility to the drug. Various degrees of resistance have been observed in bacteria that normally would be destroyed by aminoglycosides. In general, though, aminoglycoside effectiveness has held up well over time.

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KEY TERMS

Aerobic bacteria—Bacteria which require oxygen in order to grow and survive.

Anaerobic bacteria—Bacteria which cannot grow or reproduce in the presence of oxygen.

Eighth cranial nerve disease—A disorder affecting the eighth cranial nerve, characterized by a loss of hearing and/or balance.

Gram-negative—Referring to a bacteria that take on a pink color when exposed to Gram's stain.

Gram-positive—Referring to a bacteria that takes on a purplish-black color when exposed to Gram's stain.

Gram's stain—A stain used in microbiology to classify bacteria and help identify the species to which they belong. This identification aids in determining treatment.

Kidney disease—Any disorder which impairs the kidney's ability to remove waste and toxins from the body.

Myasthenis gravis—A neuromuscular disease characterized by muscle weakness in the limbs and face.

Parkinson's disease—A neurological disorder caused by deficiency of dopamine, a neurotransmitter, that is a chemical that assists in transmitting messages between the nerves within the brain. It is characterized by muscle tremor or palsy and rigid movements.

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Julia Barrett

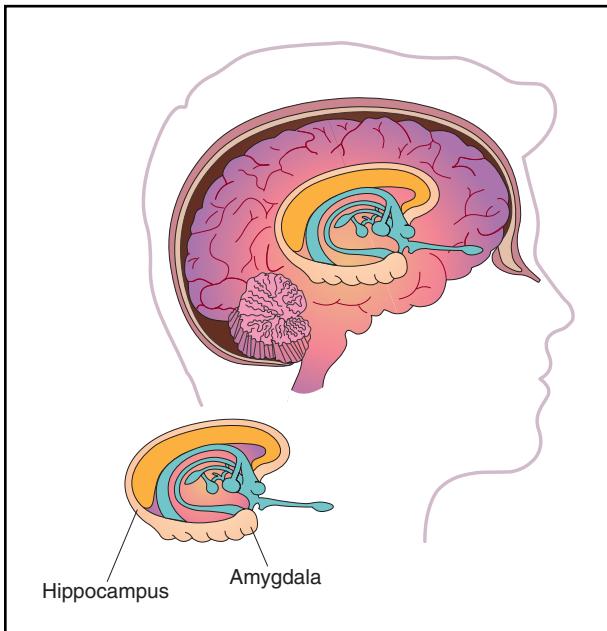
Amitriptyline see **Antidepressants, tricyclic**

Amlodipine see **Calcium channel blockers**

Amnesia

Definition

Amnesia refers to the loss of memory. Memory loss may result from two-sided (bilateral) damage to parts of



Memory loss may result from bilateral damage to the limbic system of the brain responsible for memory storage, processing, and recall. (Illustration by Electronic Illustrators Group).

the brain vital for memory storage, processing, or recall (the limbic system, including the hippocampus in the medial temporal lobe).

Description

Amnesia can be a symptom of several neurodegenerative diseases; however, people whose primary symptom is memory loss (amnesiacs), typically remain lucid and retain their sense of self. They may even be aware that they suffer from a memory disorder.

People who experience amnesia have been instrumental in helping brain researchers determine how the brain processes memory. Until the early 1970s, researchers viewed memory as a single entity. Memory of new experiences, motor skills, past events, and previous conditioning were grouped together in one system that relied on a specific area of the brain.

If all memory were stored in the same way, it would be reasonable to deduce that damage to the specific brain area would cause complete memory loss. However, studies of amnesiacs counter that theory. Such research demonstrates that the brain has multiple systems for processing, storing, and drawing on memory.

Causes and symptoms

Amnesia has several root causes. Most are traceable to brain injury related to physical trauma, disease, infec-

tion, drug and alcohol abuse, or reduced blood flow to the brain (vascular insufficiency). In Wernicke-Korsakoff syndrome, for example, damage to the memory centers of the brain results from the use of alcohol or **malnutrition**. Infections that damage brain tissue, including **encephalitis** and herpes, can also cause amnesia. If the amnesia is thought to be of psychological origin, it is termed psychogenic.

There are at least three general types of amnesia:

- **Anterograde.** This form of amnesia follows brain trauma and is characterized by the inability to remember new information. Recent experiences and short-term memory disappear, but victims can recall events prior to the trauma with clarity.
- **Retrograde.** In some ways, this form of amnesia is the opposite of anterograde amnesia: the victim can recall events that occurred after a trauma, but cannot remember previously familiar information or the events preceding the trauma.
- **Transient global amnesia.** This type of amnesia has no consistently identifiable cause, but researchers have suggested that migraines or transient ischemic attacks may be the trigger. (A **transient ischemic attack**, sometimes called “a small stroke,” occurs when a blockage in an artery temporarily blocks off blood supply to part of the brain.) A victim experiences sudden confusion and forgetfulness. Attacks can be as brief as 30-60 minutes or can last up to 24 hours. In severe attacks, a person is completely disoriented and may experience retrograde amnesia that extends back several years. While very frightening for the patient, transient global amnesia generally has an excellent prognosis for recovery.

Diagnosis

In diagnosing amnesia and its cause, doctors look at several factors. During a **physical examination**, the doctor inquires about recent traumas or illnesses, drug and medication history, and checks the patient's general health. Psychological exams may be ordered to determine the extent of amnesia and the memory system affected. The doctor may also order imaging tests such as **magnetic resonance imaging (MRI)** to reveal whether the brain has been damaged, and blood work to exclude treatable metabolic causes or chemical imbalances.

Treatment

Treatment depends on the root cause of amnesia and is handled on an individual basis. Regardless of cause, cognitive **rehabilitation** may be helpful in learning strategies to cope with memory impairment.

KEY TERMS

Classical conditioning—The memory system that links perceptual information to the proper motor response. For example, Ivan Pavlov conditioned a dog to salivate when a bell was rung.

Emotional conditioning—The memory system that links perceptual information to an emotional response. For example, spotting a friend in a crowd causes a person to feel happy.

Explicit memory—Conscious recall of facts and events that is classified into episodic memory (involves time and place) and semantic memory (does not involve time and place). For example, an amnesiac may remember he has a wife (semantic memory), but cannot recall his last conversation with her (episodic memory).

Limbic system—The brain structures involved in memory.

Magnetic resonance imaging (MRI)—MRI 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.

Motor skill learning—This memory system is associated with physical movement and activity. For example, learning to swim is initially difficult, but once an efficient stroke is learned, it requires little conscious effort.

Neurodegenerative disease—A disease in which the nervous system progressively and irreversibly deteriorates.

Priming memory—The memory system that joins perceptual and conceptual representations.

Transient ischemic attack—A sudden and brief blockage of blood flow in the brain.

Working memory—The memory system that relates to the task at hand and coordinates recall of memories necessary to complete it.

Prognosis

Some types of amnesia, such as transient global amnesia, are completely resolved and there is no permanent loss of memory. Others, such as Korsakoff syndrome, associated with prolonged alcohol abuse or amnesias caused by severe brain injury, may be permanent. Depending on the degree of amnesia and its cause, victims may be able to lead relatively normal lives. Amnesiacs can learn through therapy to rely on other memory systems to compensate for what is lost.

Prevention

Amnesia is only preventable in so far as brain injury can be prevented or minimized. Common sense approaches include wearing a helmet when bicycling or participating in potentially dangerous sports, using automobile seat belts, and avoiding excessive alcohol or drug use. Brain infections should be treated swiftly and aggressively to minimize the damage due to swelling. Victims of strokes, brain aneurysms, and transient ischemic attacks should seek immediate medical treatment.

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Amniocentesis

Definition

Amniocentesis is a procedure used to diagnose fetal defects in the early second trimester of **pregnancy**. A sample of the amniotic fluid, which surrounds a fetus in the womb, is collected through a pregnant woman's abdomen using a needle and syringe. Tests performed on fetal cells found in the sample can reveal the presence of many types of genetic disorders, thus allowing doctors and prospective parents to make important decisions about early treatment and intervention.

Purpose

Since the mid-1970s, amniocentesis has been used routinely to test for **Down syndrome**, by far the most common, nonhereditary, genetic birth defect, afflicting about one in every 1,000 babies. By 1997, approximately 800 different diagnostic tests were available, most of them for hereditary genetic disorders such as **Tay-Sachs disease**, sickle cell anemia, **hemophilia**, **muscular dystrophy** and **cystic fibrosis**.

Amniocentesis, often called amnio, is recommended for women who will be older than 35 on their due-date. It is also recommended for women who have already borne children with **birth defects**, or when either of the parents has a family history of a birth defect for which a diagnostic test is available. Another reason for the procedure is to confirm indications of Down syndrome and certain other defects which may have shown up previously during routine maternal blood screening.

The risk of bearing a child with a nonhereditary genetic defect such as Down syndrome is directly related to a woman's age—the older the woman, the greater the risk. Thirty-five is the recommended age to begin amnio testing because that is the age at which the risk of carrying a fetus with such a defect roughly equals the risk of **miscarriage** caused by the procedure—about one in 200. At age 25, the risk of giving birth to a child with this type of defect is about one in 1,400; by age 45 it increases to about one in 20. Nearly half of all pregnant women over 35 in the United States undergo amniocentesis and many younger women also decide to have the procedure. Notably, some 75% of all Down syndrome infants born in the United States each year are to women younger than 35.

One of the most common reasons for performing amniocentesis is an abnormal alpha-fetoprotein (AFP) test. Alpha-fetoprotein is a protein produced by the fetus and present in the mother's blood. A simple blood screening, usually conducted around the 15th week of pregnancy, can determine the AFP levels in the mother's blood. Levels that are too high or too low may signal possible fetal defects. Because this test has a high false-positive rate, another test such as amnio is recommended whenever the AFP levels fall outside the normal range.

Amniocentesis is generally performed during the 16th week of pregnancy, with results usually available within three weeks. It is possible to perform an amnio as early as the 11th week but this is not usually recommended because there appears to be an increased risk of miscarriage when done at this time. The advantage of early amnio and speedy results lies in the extra time for decision making if a problem is detected. Potential treatment of the fetus can begin earlier. Important, also, is the fact

that elective abortions are safer and less controversial the earlier they are performed.

Precautions

As an invasive surgical procedure, amnio poses a real, although small, risk to the health of a fetus. Parents must weigh the potential value of the knowledge gained, or indeed the reassurance that all is well, against the small risk of damaging what is in all probability a normal fetus. The serious emotional and ethical dilemmas that adverse test results can bring must also be considered. The decision to undergo amnio is always a matter of personal choice.

Description

The word amniocentesis literally means "puncture of the amnion," the thin-walled sac of fluid in which a developing fetus is suspended during pregnancy. During the sampling procedure, the obstetrician inserts a very fine needle through the woman's abdomen into the uterus and amniotic sac and withdraws approximately one ounce of amniotic fluid for testing. The relatively painless procedure is performed on an outpatient basis, sometimes using local anesthesia.

The physician uses ultrasound images to guide needle placement and collect the sample, thereby minimizing the risk of fetal injury and the need for repeated needle insertions. Once the sample is collected, the woman can return home after a brief observation period. She may be instructed to rest for the first 24 hours and to avoid heavy lifting for two days.

The sample of amniotic fluid is sent to a laboratory where fetal cells contained in the fluid are isolated and grown in order to provide enough genetic material for testing. This takes about seven to 14 days. The material is then extracted and treated so that visual examination for defects can be made. For some disorders, like Tay-Sachs, the simple presence of a telltale chemical compound in the amniotic fluid is enough to confirm a diagnosis. Depending on the specific tests ordered, and the skill of the lab conducting them, all the results are available between one and four weeks after the sample is taken.

Cost of the procedure depends on the doctor, the lab, and the tests ordered. Most insurers provide coverage for women over 35, as a follow-up to positive maternal blood screening results, and when genetic disorders run in the family.

An alternative to amnio, now in general use, is **chorionic villus sampling**, or CVS, which can be performed as early as the eighth week of pregnancy. While this allows for the possibility of a first trimester abortion, if warranted, CVS is apparently also riskier and is more expensive.



A physician uses an ultrasound monitor (left) to position the needle for insertion into the amnion when performing amniocentesis. (Photograph by Will and Deni McIntyre, Photo Researchers, Inc. Reproduced by permission.)

The most promising area of new research in prenatal testing involves expanding the scope and accuracy of maternal blood screening as this poses no risk to the fetus.

Preparation

It is important for a woman to fully understand the procedure and to feel confident in the obstetrician performing it. Evidence suggests that a physician's experience with the procedure reduces the chance of mishap. Almost all obstetricians are experienced in performing amniocentesis. The patient should feel free to ask questions and seek emotional support before, during and after the amnio is performed.

Aftercare

Necessary aftercare falls into two categories, physical and emotional.

Physical aftercare

During and immediately following the sampling procedure, a woman may experience **dizziness**, nausea, a

rapid heartbeat, and cramping. Once past these immediate hurdles, the physician will send the woman home with instructions to rest and to report any complications requiring immediate treatment, including:

- **vaginal bleeding.** The appearance of blood could signal a problem.
- **premature labor.** Unusual abdominal **pain** and/or cramping may indicate the onset of premature labor. Mild cramping for the first day or two following the procedure is normal.
- **signs of infection.** Leaking of amniotic fluid or unusual vaginal discharge, and **fever** could signal the onset of infection.

Emotional aftercare

Once the procedure has been safely completed, the **anxiety** of waiting for the test results can prove to be the worst part of the process. A woman should seek and receive emotional support from family and friends, as well as from her obstetrician and family doctor. Professional counseling may also prove necessary, particularly if a fetal defect is discovered.

KEY TERMS

Alpha-fetoprotein (AFP)—A protein normally produced by the liver of a fetus and detectable in maternal blood samples. AFP screening measures the amount of alpha-fetoprotein in the blood. Levels outside the norm may indicate fetal defects.

Anencephaly—A hereditary defect resulting in the partial to complete absence of a brain and spinal cord. It is fatal.

Chorionic villus sampling (CVS)—A procedure similar to amniocentesis, except that cells are taken from the chorionic membrane for testing. These cells, called chorionic villus cells, eventually become the placenta. The samples are collected either through the abdomen, as in amnio, or through the vagina. CVS can be done earlier in the pregnancy than amnio, but carries a somewhat higher risk.

Chromosome—Chromosomes are the strands of genetic material in a cell that occur in nearly identical pairs. Normal human cells contain 23 chromosome pairs—one in each pair inherited from the mother, and one from the father. Every human cell contains the exact same set of chromosomes.

Down syndrome—The most prevalent of a class of genetic defects known as trisomies, in which cells contain three copies of certain chromosomes rather than the usual two. Down syndrome, or trisomy 21, usually results from three copies of chromosome 21.

Genetic—The term refers to genes, the basic units of biological heredity, which are contained on the chromosomes, and contain chemical instructions which direct the development and functioning of an individual.

Hereditary—Something which is inherited—passed down from parents to offspring. In biology and medicine, the word pertains to inherited genetic characteristics.

Maternal blood screening—Maternal blood screening is normally done early in pregnancy to test for a variety of conditions. Abnormal amounts of certain proteins in a pregnant woman's blood raise the probability of fetal defects. Amniocentesis is recommended if such a probability occurs.

Tay-Sachs disease—An inherited disease prevalent among the Ashkenazi Jewish population of the United States. Infants with the disease are unable to process a certain type of fat which accumulates in nerve and brain cells, causing mental and physical retardation, and death by age four.

Ultrasound—A technique which uses high-frequency sound waves to create a visual image (a sonogram) of soft tissues. The technique is routinely used in prenatal care and diagnosis.

Risks

Most of the risks and short-term side effects associated with amniocentesis relate to the sampling procedure and have been discussed above. A successful amnio sampling results in no long-term side effects. Risks include:

- maternal/fetal hemorrhaging. While spotting in pregnancy is fairly common, bleeding following amnio should always be investigated.
- infection. Infection, although rare, can occur after amniocentesis. An unchecked infection can lead to severe complications.
- fetal injury. A very slight risk of injury to the fetus resulting from contact with the amnio needle does exist.
- miscarriage. The rate of miscarriage occurring during standard, second trimester amnio appears to be approximately 0.5%. This compares to a miscarriage rate of

1% for CVS. Many fetuses with severe genetic defects miscarry naturally during the first trimester.

- the trauma of difficult family-planning decisions. The threat posed to parental and family mental health from the trauma accompanying an abnormal test result can not be underestimated.

Normal results

Negative results from an amnio analysis indicate that everything about the fetus appears normal and the pregnancy can continue without undue concern. A negative result for Down syndrome means that it is 99% certain that the disease does not exist.

An overall “normal” result does not, however, guarantee that the pregnancy will come to term, or that the fetus does not suffer from some other defect. Laboratory tests are not 100% accurate at detecting targeted conditions, nor can every possible fetal condition be tested for.

Abnormal results

Positive results on an amnio analysis indicate the presence of the fetal defect being tested for, with an accuracy approaching 100%. Prospective parents are then faced with emotionally and ethically difficult choices regarding treatment options, the prospect of dealing with a severely affected newborn, and the option of elective abortion. At this point, the parents need expert medical advice and counseling.

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- American College of Obstetricians and Gynecologists. 409 12th Street, S.W., P.O. Box 96920

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Kurt Richard Sternlof

Amniotic fluid analysis see **Amniocentesis**

Amoxicillin see **Penicillins**

Amphetamines see **Central nervous system stimulants**

Amphotericin B see **Antifungal drugs, systemic**

Amputation

Definition

Amputation is the intentional surgical removal of a limb or body part. It is performed to remove diseased tissue or relieve pain.

Purpose

Arms, legs, hands, feet, fingers, and toes can all be amputated. Most amputations involve small body parts such as a finger, rather than an entire limb. About 65,000 amputations are performed in the United States each year.

Amputation is performed for the following reasons:

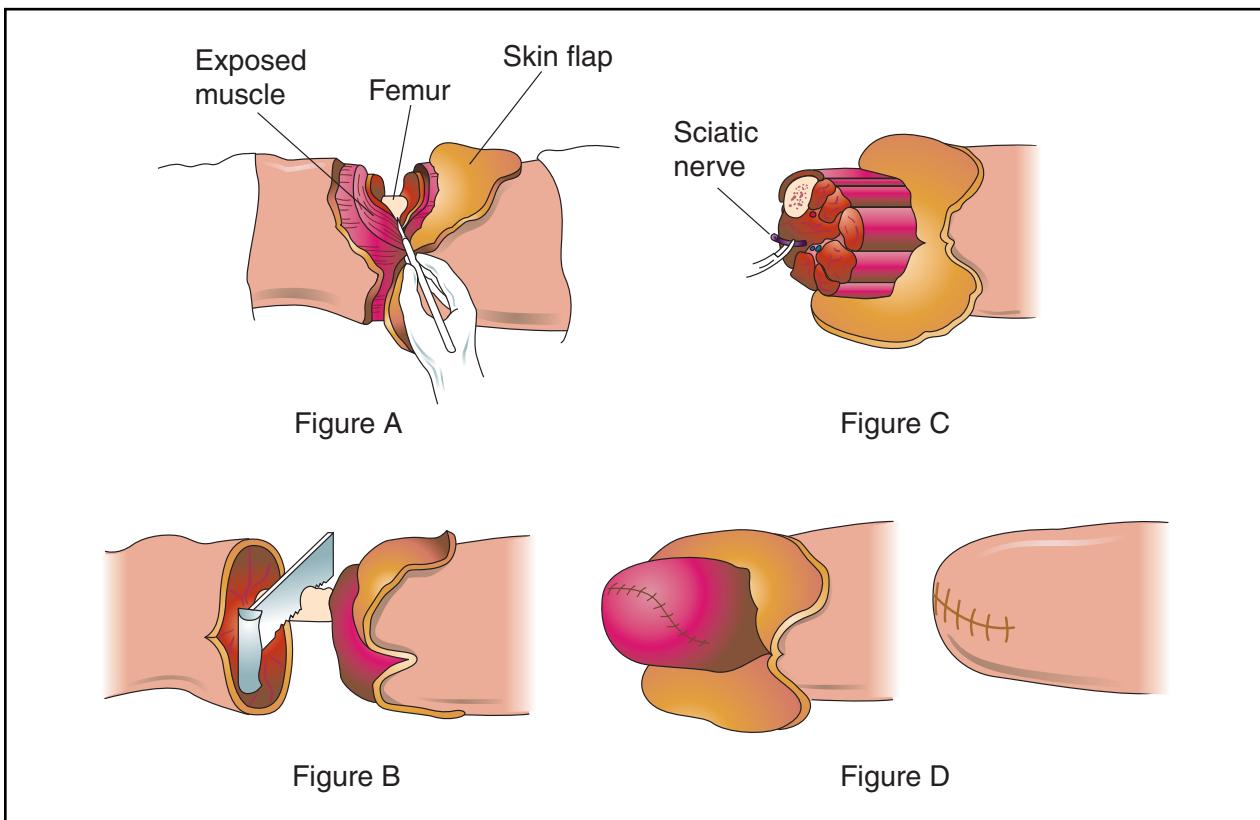
- to remove tissue that no longer has an adequate blood supply
- to remove malignant tumors
- because of severe trauma to the body part

The blood supply to an extremity can be cut off because of injury to the blood vessel, hardening of the arteries, **arterial embolism**, impaired circulation as a complication of **diabetes mellitus**, repeated severe infection that leads to **gangrene**, severe frostbite, **Raynaud's disease**, or **Buerger's disease**.

More than 90% of amputations performed in the United States are due to circulatory complications of diabetes. Sixty to eighty percent of these operations involve the legs.

Precautions

Amputations cannot be performed on patients with uncontrolled diabetes mellitus, **heart failure**, or infec-



Amputation of leg. Figure A: After the surgeon creates two flaps of skin and tissue, the muscle is cut and the main artery and veins of the femur bone are exposed. Figure B: The surgeon severs the main artery and veins. New connections are formed between them, restoring blood circulation. The sciatic nerve is then pulled down, clamped and tied, and severed. Figure C: The surgeon saws through the exposed femur bone. Figure D: The muscles are closed and sutured over the bone. The remaining skin flaps are then sutured together, creating a stump. (Illustration by Electronic Illustrators Group.)

tion. Patients with blood clotting disorders are also not good candidates for amputation.

Description

Amputations can be either planned or emergency procedures. Injury and arterial embolisms are the main reasons for emergency amputations. The operation is performed under regional or general anesthesia by a general or orthopedic surgeon in a hospital operating room.

Details of the operation vary slightly depending on what part is to be removed. The goal of all amputations is twofold: to remove diseased tissue so that the wound will heal cleanly, and to construct a stump that will allow the attachment of a prosthesis or artificial replacement part.

The surgeon makes an incision around the part to be amputated. The part is removed, and the bone is smoothed. A flap is constructed of muscle, connective tissue, and skin to cover the raw end of the bone. The flap is closed over the bone with sutures (surgical stitches) that remain

in place for about one month. Often, a rigid dressing or cast is applied that stays in place for about two weeks.

Preparation

Before an amputation is performed, extensive testing is done to determine the proper level of amputation. The goal of the surgeon is to find the place where healing is most likely to be complete, while allowing the maximum amount of limb to remain for effective **rehabilitation**.

The greater the blood flow through an area, the more likely healing is to occur. These tests are designed to measure blood flow through the limb. Several or all of them can be done to help choose the proper level of amputation.

- measurement of blood pressure in different parts of the limb
- xenon 133 studies, which use a radiopharmaceutical to measure blood flow
- oxygen tension measurements in which an oxygen electrode is used to measure oxygen pressure under the skin

If the pressure is 0, the healing will not occur. If the pressure reads higher than 40mm Hg (40 milliliters of mercury), healing of the area is likely to be satisfactory.

- laser Doppler measurements of the microcirculation of the skin
- skin fluorescent studies that also measure skin microcirculation
- skin perfusion measurements using a blood pressure cuff and photoelectric detector
- infrared measurements of skin temperature

No one test is highly predictive of healing, but taken together, the results give the surgeon an excellent idea of the best place to amputate.

Aftercare

After amputation, medication is prescribed for pain, and patients are treated with **antibiotics** to discourage infection. The stump is moved often to encourage good circulation. Physical therapy and rehabilitation are started as soon as possible, usually within 48 hours. Studies have shown that there is a positive relationship between early rehabilitation and effective functioning of the stump and prosthesis. Length of stay in the hospital depends on the severity of the amputation and the general health of the amputee, but ranges from several days to two weeks.

Rehabilitation is a long, arduous process, especially for above the knee amputees. Twice daily physical therapy is not uncommon. In addition, psychological counseling is an important part of rehabilitation. Many people feel a sense of loss and grief when they lose a body part. Others are bothered by phantom limb syndrome, where they feel as if the amputated part is still in place. They may even feel pain in this limb that does not exist. Many amputees benefit from joining self-help groups and meeting others who are also living with amputation. Addressing the emotional aspects of amputation often speeds the physical rehabilitation process.

Risks

Amputation is major surgery. All the risks associated with the administration of anesthesia exist, along with the possibility of heavy blood loss and the development of blood clots. Infection is of special concern to amputees. Infection rates in amputations average 15%. If the stump becomes infected, it is necessary to remove the prosthesis and sometimes to amputate a second time at a higher level.

Failure of the stump to heal is another major complication. Nonhealing is usually due to an inadequate blood supply. The rate of nonhealing varies from 5-30%

KEY TERMS

Arterial embolism—A blood clot arising from another location that blocks an artery.

Buerger's disease—An episodic disease that causes inflammation and blockage of the veins and arteries of the limbs. It tends to be present almost exclusively on men under age 40 who smoke, and may require amputation of the hand or foot.

Diabetes mellitus—A disease in which insufficient insulin is made by the body to metabolize sugars.

Raynaud's disease—A disease found mainly in young women that causes decreased circulation to the hands and feet. Its cause is unknown.

depending on the facility. Centers that specialize in amputation usually have the lowest rates of complication.

Persistent pain in the stump or pain in the phantom limb is experienced by most amputees to some degree. Treatment of phantom limb pain is difficult. One final complication is that many amputees give up on the rehabilitation process and discard their prosthesis. Better fitting prosthetics and earlier rehabilitation have decreased the incidence of this problem.

Normal results

The five year survival rate for all lower extremity amputees is less than 50%. For diabetic amputees, the rate is less than 40%. Up to 50% of people who have one leg amputated because of diabetes will lose the other within five years. Amputees who walk using a prosthesis have a less stable gait. Three to five percent of these people fall and break bones because of this instability. Although the **fractures** can be treated, about half the amputees who suffer them then remain wheelchair bound.

Resources

ORGANIZATIONS

American Diabetes Association. 1701 North Beauregard Street, Alexandria, VA 22311. (800) 342-2383. <<http://www.diabetes.org>>.

OTHER

Amputation Prevention Global Resource Center Page. Feb. 2001. <<http://www.diabetesresource.com>>.

Tish Davidson

Amylase tests

Definition

Amylase is a digestive enzyme made primarily by the pancreas and salivary glands. Enzymes are substances made and used by the body to trigger specific chemical reactions. The primary function of the enzyme amylase is to break down starches in food so that they can be used by the body. Amylase testing is usually done to determine the cause of sudden abdominal **pain**.

Purpose

Amylase testing is performed to diagnose a number of diseases that elevate amylase levels. **Pancreatitis**, for example, is the most common reason for a high amylase level. When the pancreas is inflamed, amylase escapes from the pancreas into the blood. Within six to 48 hours after the pain begins, amylase levels in the blood start to rise. Levels will stay high for several days before gradually returning to normal.

There are other causes of increased amylase. An ulcer that erodes tissue from the stomach and goes into the pancreas will cause amylase to spill into the blood. During a **mumps** infection, amylase from the inflamed salivary glands increases. Amylase is also found in the liver, fallopian tubes, and small intestine; inflammation of these tissues also increases levels. Gall bladder disease, tumors of the lung or ovaries, alcohol **poisoning**, ruptured **aortic aneurysm**, and intestinal strangulation or perforation can also cause unusually high amylase levels.

Precautions

This is not a screening test for future pancreatic disease.

Description

Amylase testing is done on both blood and urine. The laboratory may use any of several testing methods that involve mixing the blood or urine sample with a substance with which amylase is known to react. By measuring the end-product or the reaction time, technicians can calculate the amount of amylase present in the sample. More sophisticated methods separately measure the amylase made by the pancreas and the amylase made by the salivary glands.

Urine testing is a better long-term monitor of amylase levels. The kidneys quickly move extra amylase from the blood into the urine. Urine levels rise six to 10 hours after blood levels and stay high longer. Urine is

usually collected throughout a 2- or 24-hour time period. Results are usually available the same day.

Preparation

In most cases, no special preparation is necessary for a person undergoing an amylase blood test. Patients taking longer term urine amylase tests will be given a container and instructions for collecting the urine at home. The urine should be refrigerated until it is brought to the laboratory.

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. Applying warm packs to the puncture site relieves discomfort.

Normal results

Normal results vary based on the laboratory and the method used.

Abnormal results

Eight out of ten persons with acute pancreatitis will have high amylase levels, up to four times the normal level. Other causes of increased amylase, such as mumps, kidney failure, **pregnancy** occurring in the abdomen but outside the uterus (**ectopic pregnancy**), certain tumors, a penetrating ulcer, certain complications of diabetes, and advanced pancreatic **cancer**, are further investigated based on the person's symptoms, medical history, and the results of other tests.

In kidney disease, the kidneys are not as efficient at removing amylase from the blood. Amylase rises in the blood, but stays at normal levels in the urine.

People with macroamylasia have large clumps of amylase in their blood. These clumps are too large to move through the kidney, so they stay in the blood. Amylase levels in the blood will be high; levels in the urine will be low.

Amylase levels may be low in severe liver disease (including hepatitis), conditions in which the pancreas fails to secrete enough enzyme for proper digestions (pancreatic insufficiency), when toxic materials build up in the blood during pregnancy (pre-eclampsia), following **burns**, in thyroid disorders, and in advanced **cystic fibrosis**. Some medications can raise or lower levels.

Resources

BOOKS

A Manual of Laboratory and Diagnostic Tests. 5th ed. Ed. Francis Fishback. Philadelphia: Lippincott, 1996.

KEY TERMS

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Enzyme—A substance made and used by the body to trigger specific chemical reactions.

Pancreatitis—Inflammation of the pancreas.

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Nancy J. Nordenson

Amyloidosis

Definition

Amyloidosis is a progressive, incurable, metabolic disease characterized by abnormal deposits of protein in one or more organs or body systems.

Description

Amyloid proteins are manufactured by malfunctioning bone marrow. Amyloidosis, which occurs when accumulated amyloid deposits impair normal body function, can cause organ failure or **death**. It is a rare disease, occurring in about eight of every 1,000,000 people. It affects males and females equally and usually develops after the age of 40. At least 15 types of amyloidosis have been identified. Each one is associated with deposits of a different kind of protein.

Types of amyloidosis

The major forms of this disease are primary systemic, secondary, and familial or hereditary amyloidosis. There is also another form of amyloidosis associated with **Alzheimer's disease**.

Primary systemic amyloidosis usually develops between the ages of 50 and 60. With about 2,000 new cases diagnosed annually, primary systemic amyloidosis

is the most common form of this disease in the United States. Also known as light-chain-related amyloidosis, it may also occur in association with **multiple myeloma** (bone marrow **cancer**).

Secondary amyloidosis is a result of chronic infection or inflammatory disease. It is often associated with:

- **familial Mediterranean fever** (a bacterial infection characterized by chills, weakness, **headache**, and recurring **fever**)
- granulomatous ileitis (inflammation of the small intestine)
- Hodgkin's disease (cancer of the lymphatic system)
- leprosy
- osteomyelitis (bacterial infection of bone and bone marrow)
- rheumatoid arthritis

Familial or hereditary amyloidosis is the only inherited form of the disease. It occurs in members of most ethnic groups, and each family has a distinctive pattern of symptoms and organ involvement. Hereditary amyloidosis is thought to be autosomal dominant, which means that only one copy of the defective gene is necessary to cause the disease. A child of a parent with familial amyloidosis has a 50-50 chance of developing the disease.

Amyloidosis can involve any organ or system in the body. The heart, kidneys, gastrointestinal system, and nervous system are affected most often. Other common sites of amyloid accumulation include the brain, joints, liver, spleen, pancreas, respiratory system, and skin.

Causes and symptoms

The cause of amyloidosis is unknown. Most patients have gastrointestinal abnormalities, but other symptoms vary according to the organ(s) or system(s) affected by the disease. Usually the affected organs are rubbery, firm, and enlarged.

Heart

Because amyloid protein deposits can limit the heart's ability to fill with blood between beats, even the slightest exertion can cause **shortness of breath**. If the heart's electrical system is affected, the heart's rhythm may become erratic. The heart may also be enlarged and **heart murmurs** may be present. Congestive **heart failure** may result.

Kidneys

The feet, ankles, and calves swell when amyloidosis damages the kidneys. The kidneys become small and

KEY TERMS

Amyloid—A waxy, starch-like protein.

Peripheral nerves—Nerves that carry information to and from the spinal cord.

Stem cells—Parent cells from which other cells are made.

hard, and kidney failure may result. It is not unusual for a patient to lose 20–25 pounds and develop a distaste for meat, eggs, and other protein-rich foods. Cholesterol elevations that don't respond to medication and protein in the urine (proteinuria) are common.

Nervous system

Nervous system symptoms often appear in patients with familial amyloidosis. Inflammation and degeneration of the peripheral nerves (**peripheral neuropathy**) may be present. One of four patients with amyloidosis has **carpal tunnel syndrome**, a painful disorder that causes numbness or tingling in response to pressure on nerves around the wrist. Amyloidosis that affects nerves to the feet can cause burning or numbness in the toes and soles and eventually weaken the legs. If nerves controlling bowel function are involved, bouts of **diarrhea** alternate with periods of **constipation**. If the disease affects nerves that regulate blood pressure, patients may feel dizzy or faint when they stand up suddenly.

Liver and spleen

The most common symptoms are enlargement of these organs. Liver function is not usually affected until quite late in the course of the disease. Protein accumulation in the spleen can increase the risk of rupture of this organ due to trauma.

Gastrointestinal system

The tongue may be inflamed, enlarged, and stiff. Intestinal movement (motility) may be reduced. Absorption of food and other nutrients may be impaired (and may lead to **malnutrition**), and there may also be bleeding, abdominal **pain**, constipation, and diarrhea.

Skin

Skin symptoms occur in about half of all cases of primary and secondary amyloidosis and in all cases where there is inflammation or degeneration of the peripheral nerves. Waxy-looking raised bumps (papules)

may appear on the face and neck, in the groin, armpits, or anal area, and on the tongue or in the ear canals. Swelling, hemorrhage beneath the skin (purpura), hair loss, and **dry mouth** may also occur.

Respiratory system

Airways may be obstructed by amyloid deposits in the nasal sinus, larynx and trachea (windpipe).

Diagnosis

Blood and urine tests can reveal the presence of amyloid protein, but tissue or bone-marrow biopsy is necessary to positively diagnose amyloidosis. Once the diagnosis has been confirmed, additional laboratory tests and imaging procedures are performed to determine:

- which type of amyloid protein is involved
- which organ(s) or system(s) have been affected
- how far the disease has progressed

Treatment

The goal of treatment is to slow down or stop production of amyloid protein, eliminate existing amyloid deposits, alleviate underlying disorders (that give rise to secondary amyloidosis), and relieve symptoms caused by heart or kidney damage. Specialists in cardiology, hematology (the study of blood and the tissues that form it), nephrology (the study of kidney function and abnormalities), neurology (the study of the nervous system), and rheumatology (the study of disorders characterized by inflammation or degeneration of connective tissue) work together to assess a patient's medical status and evaluate the effects of amyloidosis on every part of the body.

Colchicine (Colestipol, Colestid), prednisone, (Prednisone), and other anti-inflammatory drugs can slow or stop disease progression. Bone-marrow and stem-cell transplants can enable patients to tolerate higher and more effective doses of melphalan (Alkeran) and other **chemotherapy** drugs prescribed to combat this non-malignant disease. Surgery can relieve nerve pressure and may be performed to correct other symptom-producing conditions. Localized amyloid deposits can also be removed surgically. Dialysis or **kidney transplantation** can lengthen and improve the quality of life for patients whose amyloidosis results in kidney failure. Heart transplants are rarely performed.

Supportive measures

Although no link has been established between diet and development of amyloid proteins, a patient whose heart or kidneys have been affected by the disease may be advised to use a diuretic or follow a low-salt diet.

Prognosis

Most cases of amyloidosis are diagnosed after the disease has reached an advanced stage. The course of each patient's illness is unique but death, usually a result of heart disease or kidney failure, generally occurs within a few years. Amyloidosis associated by multiple myeloma usually has a poor prognosis. Most patients with both diseases die within one to two years.

Prevention

Genetic counseling may be helpful for patients with hereditary amyloidosis and their families. Use of cholchicine in patients with familial Mediterranean fever has successfully prevented amyloidosis.

Resources

BOOKS

Harrison's Principles of Internal Medicine. Ed. Anthony S. Fauci, et al. New York: McGraw-Hill, 1997.

ORGANIZATIONS

Amyloidosis Network International. 7118 Cole Creek Drive, Houston, TX 77092-1421. (888) 1AMYLOID. <<http://www.health.gov/nhic/Scripts/Entry.cfm?HRCCode=HR2397>>.

National Organization for Rare Disorders. P.O. Box 8923, New Fairfield, CT 06812-8923. (800) 999-6673. <<http://www.rarediseases.org>>.

OTHER

Mayo Clinic Online. 5 March 1998. <<http://www.mayohealth.org>>.

Maureen Haggerty

Amyotrophic lateral sclerosis

Definition

Amyotrophic lateral sclerosis (ALS) is a disease that breaks down tissues in the nervous system (a neurodegenerative disease) of unknown cause that affects the nerves responsible for movement. It is also known as motor neuron disease and Lou Gehrig's disease, after the baseball player whose career it ended.

Description

ALS is a disease of the motor neurons, those nerve cells reaching from the brain to the spinal cord (upper motor neurons) and the spinal cord to the peripheral nerves (lower motor neurons) that control muscle movement. In ALS, for unknown reasons, these neurons die,

leading to a progressive loss of the ability to move virtually any of the muscles in the body. ALS affects "voluntary" muscles, those controlled by conscious thought, such as the arm, leg, and trunk muscles. ALS, in and of itself, does not affect sensation, thought processes, the heart muscle, or the "smooth" muscle of the digestive system, bladder, and other internal organs. Most people with ALS retain function of their eye muscles as well. However, various forms of ALS may be associated with a loss of intellectual function (**dementia**) or sensory symptoms.

"Amyotrophic" refers to the loss of muscle bulk, a cardinal sign of ALS. "Lateral" indicates one of the regions of the spinal cord affected, and "sclerosis" describes the hardened tissue that develops in place of healthy nerves. ALS affects approximately 30,000 people in the United States, with about 5,000 new cases each year. It usually begins between the ages of 40 and 70, although younger onset is possible. Men are slightly more likely to develop ALS than women.

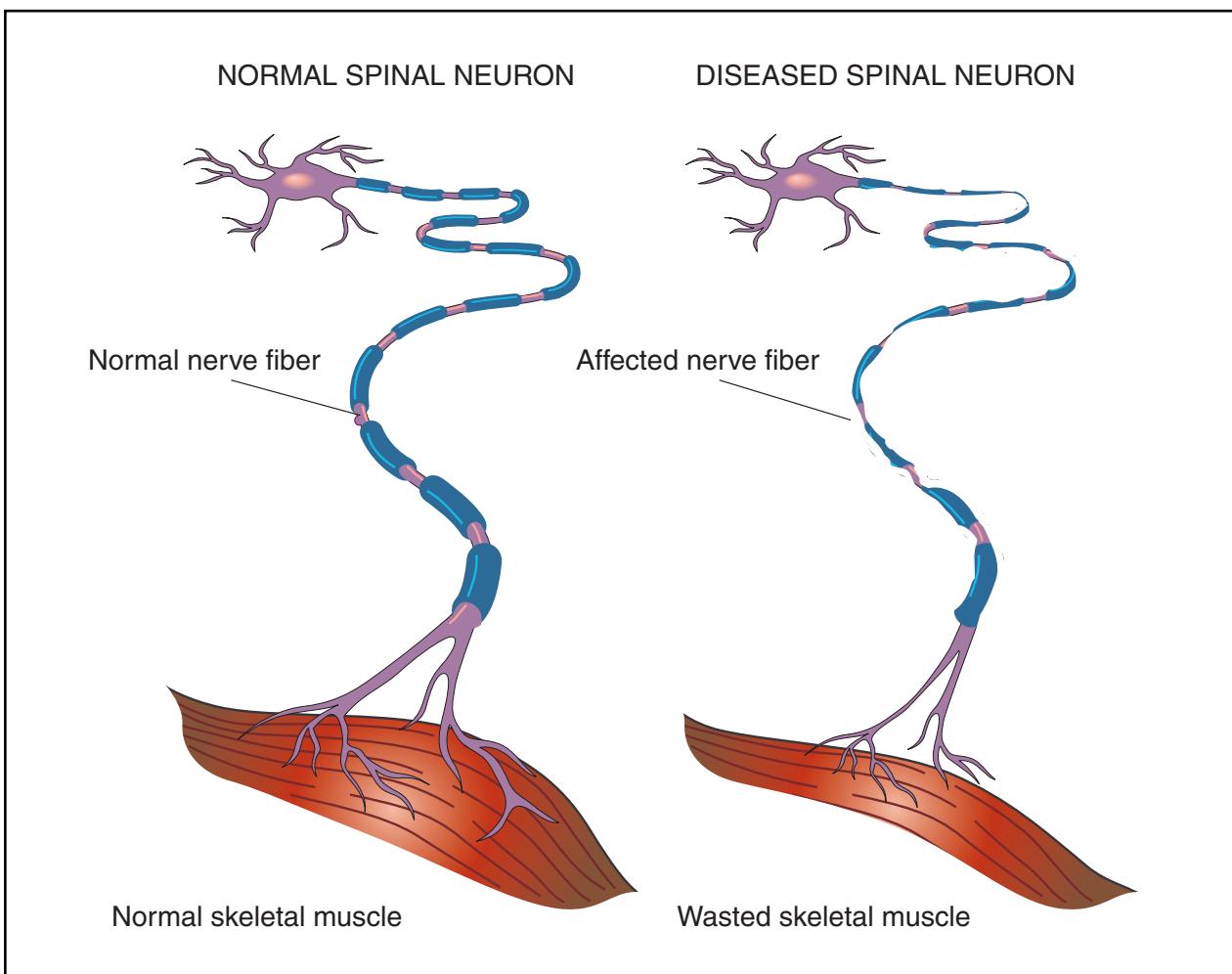
ALS progresses rapidly in most cases. It is fatal within three years for 50% of all people affected, and within five years for 80%. Ten percent of people with ALS live beyond eight years.

Causes and symptoms

Causes

The symptoms of ALS are caused by the **death** of motor neurons in the spinal cord and brain. Normally, these neurons convey electrical messages from the brain to the muscles to stimulate movement in the arms, legs, trunk, neck, and head. As motor neurons die, the muscles they innervate cannot be moved as effectively, and weakness results. In addition, lack of stimulation leads to muscle wasting, or loss of bulk. Involvement of the upper motor neurons causes spasms and increased tone in the limbs, and abnormal reflexes. Involvement of the lower motor neurons causes muscle wasting and twitching (fasciculations).

Although many causes of motor neuron degeneration have been suggested for ALS, none has yet been proven responsible. Results of recent research have implicated toxic molecular fragments known as free radicals. Some evidence suggests that a cascade of events leads to excess free radical production inside motor neurons, leading to their death. Why free radicals should be produced in excess amounts is unclear, as is whether this excess is the cause or the effect of other degenerative processes. Additional agents within this toxic cascade may include excessive levels of a neurotransmitter known as glutamate, which may over-stimulate motor neurons, thereby increasing free-radical production, and a faulty **detoxification** enzyme known as SOD-1, for



Amyotrophic lateral sclerosis (ALS) is caused by the degeneration and death of motor neurons in the spinal cord and brain. These neurons convey electrical messages from the brain to the muscles to stimulate movement in the arms, legs, trunk, neck, and head. As motor neurons degenerate, the muscles are weakened and cannot move as effectively, leading to muscle wasting. (Illustration by Electronic Illustrators Group.)

superoxide dismutase type 1. The actual pathway of destruction is not known, however, nor is the trigger for the rapid degeneration that marks ALS. Further research may show that other pathways are involved, perhaps ones even more important than this one. Autoimmune factors or premature **aging** may play some role, as could viral agents or environmental toxins.

Two major forms of ALS are known: familial and sporadic. Familial ALS accounts for about 10% of all ALS cases. As the name suggests, familial ALS is believed to be caused by the inheritance of one or more faulty genes. About 15% of families with this type of ALS have mutations in the gene for SOD-1. SOD-1 gene defects are dominant, meaning only one gene copy is needed to develop the disease. Therefore, a parent with the faulty gene has a 50% chance of passing the gene along to a child.

Sporadic ALS has no known cause. While many environmental toxins have been suggested as causes, to date no research has confirmed any of the candidates investigated, including aluminum and mercury and lead from dental fillings. As research progresses, it is likely that many cases of sporadic ALS will be shown to have a genetic basis as well.

A third type, called Western Pacific ALS, occurs in Guam and other Pacific islands. This form combines symptoms of both ALS and **Parkinson's disease**.

Symptoms

The earliest sign of ALS is most often weakness in the arms or legs, usually more pronounced on one side than the other at first. Loss of function is usually more

rapid in the legs among people with familial ALS and in the arms among those with sporadic ALS. Leg weakness may first become apparent by an increased frequency of stumbling on uneven pavement, or an unexplained difficulty climbing stairs. Arm weakness may lead to difficulty grasping and holding a cup, for instance, or loss of dexterity in the fingers.

Less often, the earliest sign of ALS is weakness in the *bulbar* muscles, those muscles in the mouth and throat that control chewing, swallowing, and speaking. A person with bulbar weakness may become hoarse or tired after speaking at length, or speech may become slurred.

In addition to weakness, the other cardinal signs of ALS are muscle wasting and persistent twitching (fasciculation). These are usually seen after weakness becomes obvious. Fasciculation is quite common in people without the disease, and is virtually never the first sign of ALS.

While initial weakness may be limited to one region, ALS almost always progresses rapidly to involve virtually all the voluntary muscle groups in the body. Later symptoms include loss of the ability to walk, to use the arms and hands, to speak clearly or at all, to swallow, and to hold the head up. Weakness of the respiratory muscles makes breathing and coughing difficult, and poor swallowing control increases the likelihood of inhaling food or saliva (aspiration). Aspiration increases the likelihood of lung infection, which is often the cause of death. With a ventilator and scrupulous bronchial hygiene, a person with ALS may live much longer than the average, although weakness and wasting will continue to erode any remaining functional abilities. Most people with ALS continue to retain function of the extraocular muscles that move their eyes, allowing some communication to take place with simple blinks or through use of a computer-assisted device.

Diagnosis

The diagnosis of ALS begins with a complete medical history and physical exam, plus a neurological examination to determine the distribution and extent of weakness. An electrical test of muscle function, called an electromyogram, or EMG, is an important part of the diagnostic process. Various other tests, including blood and urine tests, x rays, and CT scans, may be done to rule out other possible causes of the symptoms, such as tumors of the skull base or high cervical spinal cord, thyroid disease, spinal arthritis, **lead poisoning**, or severe vitamin deficiency. ALS is rarely misdiagnosed following a careful review of all these factors.

Treatment

There is no cure for ALS, and no treatment that can significantly alter its course. There are many things

KEY TERMS

Aspiration—Inhalation of food or liquids into the lungs.

Bulbar muscles—Muscles of the mouth and throat responsible for speech and swallowing.

Fasciculations—Involuntary twitching of muscles.

Motor neuron—A nerve cell that controls a muscle.

Riluzole (Rilutek)—The first drug approved in the United States for the treatment of ALS.

Voluntary muscle—A muscle under conscious control; contrasted with smooth muscle and heart muscle which are not under voluntary control.

which can be done, however, to help maintain quality of life and to retain functional ability even in the face of progressive weakness.

As of early 1998, only one drug had been approved for treatment of ALS. Riluzole (Rilutek) appears to provide on average a three-month increase in life expectancy when taken regularly early in the disease, and shows a significant slowing of the loss of muscle strength. Riluzole acts by decreasing glutamate release from nerve terminals. Experimental trials of nerve growth factor have not demonstrated any benefit. No other drug or vitamin currently available has been shown to have any effect on the course of ALS.

A physical therapist works with an affected person and family to implement **exercise** and stretching programs to maintain strength and range of motion, and to promote general health. Swimming may be a good choice for people with ALS, as it provides a low-impact workout to most muscle groups. One result of chronic inactivity is contracture, or muscle shortening. **Contractures** limit a person's range of motion, and are often painful. Regular stretching can prevent contracture. Several drugs are available to reduce cramping, a common complaint in ALS.

An occupational therapist can help design solutions to movement and coordination problems, and provide advice on adaptive devices and home modifications.

Speech and swallowing difficulties can be minimized or delayed through training provided by a speech-language pathologist. This specialist can also provide advice on communication aids, including computer-assisted devices and simpler word boards.

Nutritional advice can be provided by a nutritionist. A person with ALS often needs softer foods to prevent jaw exhaustion or **choking**. Later in the disease, **nutrition** may be provided by a **gastrostomy** tube inserted into the stomach.

Mechanical ventilation may be used when breathing becomes too difficult. Modern mechanical ventilators are small and portable, allowing a person with ALS to maintain the maximum level of function and mobility. Ventilation may be administered through a mouth or nose piece, or through a tracheostomy tube. This tube is inserted through a small hole made in the windpipe. In addition to providing direct access to the airway, the tube also decreases the risk aspiration. While many people with rapidly progressing ALS choose not to use ventilators for lengthy periods, they are increasingly being used to prolong life for a short time.

The progressive nature of ALS means that most persons will eventually require full-time nursing care. This care is often provided by a spouse or other family member. While the skills involved are not difficult to learn, the physical and emotional burden of care can be overwhelming. Caregivers need to recognize and provide for their own needs as well as those of people with ALS, to prevent depression, burnout, and bitterness.

Throughout the disease, a support group can provide important psychological aid to affected persons and their caregivers as they come to terms with the losses ALS inflicts. Support groups are sponsored by both the ALS Society and the **Muscular Dystrophy Association**.

Alternative treatment

Given the grave prognosis and absence of traditional medical treatments, it is not surprising that a large number of alternative treatments have been tried for ALS. Two studies published in 1988 suggested that amino-acid therapies may provide some improvement for some people with ALS. While individual reports claim benefits for megavitamin therapy, herbal medicine, and removal of dental fillings, for instance, no evidence suggests that these offer any more than a brief psychological boost, often followed by a more severe letdown when it becomes apparent the disease has continued unabated. However, once the causes of ALS are better understood, alternative therapies may be more intensively studied. For example, if damage by free radicals turns out to be the root of most of the symptoms, antioxidant **vitamins** and supplements may be used more routinely to slow the progression of ALS. Or, if environmental toxins are implicated, alternative therapies with the goal of detoxifying the body may be of some use.

Prognosis

ALS usually progresses rapidly, and leads to death from respiratory infection within three to five years in most cases. The slowest disease progression is seen in those who are young and have their first symptoms in the limbs. About 10% of people with ALS live longer than eight years.

Prevention

There is no known way to prevent ALS or to alter its course.

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ALS Association of America. 27001 Agoura Road, Suite 150, Calabasas Hills, CA 91301-5104. (800) 782-4747 (Information and Referral Service) or (818) 880-9007. Fax: (818) 880-9006. <<http://www.alsa.org/als/>>.

American Academy of Family Physicians. 11400 Tomahawk Creek Parkway, Leawood, KS 66211-2672. (913) 906-6000, <<http://www.aafp.org/>>. fp@aafp.org.

American Academy of Neurology. 1080 Montreal Avenue, St. Paul, Minnesota 55116. (651) 695-1940. Fax: (651) 695-2791. <<http://www.aan.com/>>. info@aan.org.

American Medical Association. 515 N. State Street, Chicago, IL 60610. (312) 464-5000. <<http://www.ama-assn.org/>>.

Centers for Disease Control and Prevention. 1600 Clifton Road, Atlanta, GA 30333. (404) 639-3534 or (800) 311-3435. <<http://www.cdc.gov/ncidod/eid/vol7no1/brown.htm>>. <http://www.cdc.gov/netinfo.htm>.

Muscular Dystrophy Association. 3300 East Sunrise Drive, Tucson AZ 85718-3208. (520) 529-2000 or (800) 572-1717. Fax: (520) 529-5300. <<http://www.mdausa.org/>>.

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ALS Society of Canada: <<http://www.als.ca/>>.

ALS Survival Guide: <<http://www.lougehrigsdisease.net/>>.

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L. Fleming Fallon, Jr., MD, DrPH

Anaerobic infections

Definition

An anaerobic infection is an infection caused by bacteria (called anaerobes) which cannot grow in the presence of oxygen. Anaerobic bacteria can infect deep **wounds**, deep tissues, and internal organs where there is little oxygen. These infections are characterized by **abscess** formation, foul-smelling pus, and tissue destruction.

Description

Anaerobic means "life without air." Anaerobic bacteria grow in places which completely, or almost completely, lack oxygen. They are normally found in the mouth, gastrointestinal tract, and vagina, and on the skin. Commonly known diseases caused by anaerobic bacteria include gas **gangrene**, **tetanus**, and **botulism**. Nearly all dental infections are caused by anaerobic bacteria.

Anaerobic bacteria can cause an infection when a normal barrier (such as skin, gums, or intestinal wall) is damaged due to surgery, injury, or disease. Usually, the immune system kills any invading bacteria, but sometimes the bacteria are able to grow and cause an infection. Body sites that have tissue destruction (necrosis) or a poor blood supply are low in oxygen and favor the growth of anaerobic bacteria. The low oxygen condition can result from blood vessel disease, **shock**, injury, and surgery.

Anaerobic bacteria can cause infection practically anywhere in the body. For example:

- Mouth, head, and neck. Infections can occur in the root canals, gums (gingivitis), jaw, tonsils, throat, sinuses, and ears.
- Lung. Anaerobic bacteria can cause **pneumonia**, lung abscesses, infection of the lining of the lung (**empyema**), and dilated lung bronchi (**bronchiectasis**).
- Intraabdominal. Anaerobic infections within the abdomen include abscess formation, **peritonitis**, and **appendicitis**.
- Female genital tract. Anaerobic bacteria can cause pelvic abscesses, **pelvic inflammatory disease**, inflammation of the uterine lining (endometritis), and pelvic infections following abortion, **childbirth**, and surgery.
- Skin and soft tissue. Anaerobic bacteria are common causes of diabetic skin ulcers, gangrene, destructive infection of the deep skin and tissues (necrotizing fascitis), and bite wound infections.
- Central nervous system. Anaerobic bacteria can cause brain and spinal cord abscesses.
- Bloodstream. Anaerobic bacteria can be found in the bloodstream of ill patients (a condition called **bacteremia**).

Causes and symptoms

People who have experienced shock, injury, or surgery, and those with blood vessel disease or tumors are at an increased risk for infection by anaerobic bacteria. There are many different kinds of anaerobic bacteria which can cause an infection. Indeed, most anaerobic infections are "mixed infections" which means that there is a mixture of different bacteria growing. The anaerobic bacteria that most frequently cause infections are *Bacteroides fragilis*, *Peptostreptococcus*, and *Clostridium* species.

The signs and symptoms of anaerobic infection can vary depending on the location of the infection. In general, anaerobic infections result in tissue destruc-

KEY TERMS

Abscess—A lump filled with pus resulting from an infection.

Anaerobic—Living and growing in the absence of oxygen.

Necrosis—Tissue death and destruction resulting from infection or disease.

tion, an abscess which drains foul-smelling pus, and possibly **fever**. Symptoms for specific infections are as follows:

- Tooth and gum infections. Swollen, tender bleeding gums, **bad breath**, and **pain**. Severe infections may produce oozing sores.
- Throat infection. An extremely **sore throat**, bad breath, a bad taste in the mouth, fever, and a sense of **choking**.
- Lung infection. Chest pain, coughing, difficulty breathing, fever, foul-smelling sputum, and weight loss.
- Intraabdominal infection. Pain, fever, and possibly, if following surgery, foul-smelling drainage from the wound.
- Pelvic infection. Foul-smelling pus or blood draining from the uterus, general or localized pelvic pain, fever, and chills.
- Skin and soft tissue infection. Infected wounds are red, painful, swollen, and may drain a foul-smelling pus. Skin infection causes localized swelling, pain, redness, and possibly a painful, open sore (ulcer) which drains foul-smelling pus. Severe skin infections may cause extensive tissue destruction (necrosis).
- Bloodstream. Bloodstream invasion causes high fever (up to 105°F [40.6°C]), chills, a general ill feeling, and is potentially fatal.

Diagnosis

The diagnosis of anaerobic infection is based primarily on symptoms, the patient's medical history, and location of the infection. A foul-smelling infection or drainage from an abscess is diagnostic of anaerobic infection. This foul smell is produced by anaerobic bacteria and occurs in one third to one half of patients late in the infection. Other clues to anaerobic infection include tissue necrosis and gas production at the infection site. A sample from the infected site may be obtained, using a swab or a needle and syringe, to determine which bacteria is (are) causing the infection. Because these bacteria can be easily killed by oxygen, they rarely grow in the laboratory cultures of tissue or pus samples.

The recent medical history of the patient is helpful in diagnosing anaerobic infection. A patient who has or recently had surgery, dental work, tumors, blood vessel disease, or injury are susceptible to this infection. The failure to improve following treatment with **antibiotics** that aren't able to kill anaerobes is another clue that the infection is caused by anaerobes. The location and type of infection also help in the diagnosis.

Diagnostic tests may include blood tests to see if bacteria are in the bloodstream and x rays to look at internal infections.

Treatment

Serious infections may require hospitalization for treatment. Immediate antibiotic treatment of anaerobic infections is necessary. Laboratory testing may identify the bacteria causing the infection and also which antibiotic will work best. Every antibiotic does not work against all anaerobic bacteria but nearly all anaerobes are killed by chloramphenicol (Chloromycetin), metronidazole (Flagyl or Protostat), and imipenem (Primaxin). Other antibiotics which may be used are clindamycin (Cleocin) or cefoxitin (Mefoxin).

Surgical removal or drainage of the abscess is almost always required. This may involve drainage by needle and syringe to remove the pus from a skin abscess (called "aspiration"). The area would be numbed prior to the aspiration procedure. Also, some internal abscesses can be drained using this procedure with the help of ultrasound (a device which uses sound waves to visualize internal organs). This type of abscess drainage may be performed in the doctor's office.

Prognosis

Complete recovery should be achieved with the appropriate surgery and antibiotic treatment. Untreated or uncontrolled infections can cause severe tissue and bone destruction, which would require plastic surgery to repair. Serious infections can be life threatening.

Prevention

Although anaerobic infections can occur in anyone, good hygiene and general health may help to prevent infections.

Resources

BOOKS

Harrison's Principles of Internal Medicine. Ed. Anthony S.

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Belinda Rowland, PhD

Anaerobic myositis see **Gangrene**

Anal atresia

Definition

The anus is either not present or it is in the wrong place.

Description

There are basically two kinds of anal atresia. In boys with high anal atresia, there may be a channel (fistula) connecting the large intestine to either the urethra (which delivers urine from the bladder) or the bladder itself. In girls, the channel may connect with the vagina. Sixty percent of children with high anal atresia have other defects, including problems with the esophagus, urinary tract, and bones. In low anal atresia, the channel may open in front of the circular mass of muscles that constrict to close the anal opening (anal sphincter) or, in boys, below the scrotum. Occasionally, the intestine ends just under the skin. It is estimated that overall abnormalities of the anus and rectum occur in about one in every 5,000 births and are slightly more common among boys. A mother who has one child with these kind of conditions has a 1% chance of having another child who suffers from this ailment.

Cause and symptoms

Anal atresia is a defect in the development of the fetus. The cause is unknown, but genetics seem to play a minor role.

Diagnosis

Usually a physician can make an obvious visual diagnosis of anal atresia right after birth. Occasionally, however, anal atresia is missed until the baby is fed and signs of intestinal obstruction appear. At the end of the first or second day, the abdomen swells and there is vomiting of fecal material. To determine the type of anal atresia and the exact position, x rays will be taken which include injecting opaque dye into the opening. **Magnetic resonance imaging (MRI)** or **computed tomography scans (CT)**, as well as ultrasound, are the imaging techniques used to determine the type and size of the anal atresia. Ultrasound uses sound waves, CT scans pass x rays through the body at different angles, and an MRI uses a magnetic field and radio waves.

KEY TERMS

Anus—The canal at the end of the large intestine through which waste is excreted to the outside of the body.

Bowel obstruction—Anything that prevents waste from moving normally to the anal opening.

Colostomy—An operation where the large intestine is diverted through an opening in the abdomen and waste is excreted.

Feces—Bodily waste material that normally passes through the anus.

Fistula—An abnormal channel that connects two organs or connects an organ to the skin.

Treatment

Surgery is the only treatment for anal atresia. For high anal atresia, immediately after the diagnosis is made, a surgical incision is made in the large intestine to make a temporary opening (**colostomy**) in the abdomen where waste is excreted. Several months later, the intestine is moved into the ring of muscle (sphincter) that is part of the anus and a hole is made in the skin. The colostomy is closed several weeks later. In low anal atresia, immediately after diagnosis, a hole is made in the skin to open the area where the anus should be. If the channel is in the wrong place, the intestine is moved into the correct position sometime during the child's first year. After surgery, the pediatric surgeon uses an instrument to dilate or widen the rectum and teaches the parents how to do this daily at home to prevent scar tissue from contracting.

Prognosis

With high anal atresia, many children have problems controlling bowel function. Most also become constipated. With low anal atresia, children generally have good bowel control, but they may still become constipated.

Prevention

There is no known way to prevent anal atresia.

Resources

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 Paidas, Charles N., and Alberto Pena. "Rectum and Anus." In *Surgery of Infants and Children*. Philadelphia: Lippincott-Raven, 1997.

Jeanine Barone, Physiologist

Anal cancer

Definition

Anal **cancer** is an uncommon form of cancer affecting the anus. The anus is the inch-and-a-half-long end portion of the large intestine, which opens to allow solid wastes to exit the body. Other parts of the large intestine include the colon and the rectum.

Description

Different cancers can develop in different parts of the anus, part of which is inside the body and part of which is outside. Sometimes abnormal changes of the anus are harmless in their early stages but may later develop into cancer. Some **anal warts**, for example, contain precancerous areas and can develop into cancer. Types of anal cancer include:

- **Squamous Cell Carcinomas.** Approximately half of anal cancers are squamous cell carcinomas, which arise from the cells lining the anal margin and the anal canal. The anal margin is the part of the anus that is half inside and half outside the body, and the anal canal is the part of the anus that is inside the body. The earliest form of squamous cell carcinoma is known as carcinoma *in situ*, or Bowen's disease.
- **Cloacogenic Carcinomas.** Approximately one-fourth to one-third of anal tumors are cloacogenic carcinomas. These tumors develop in the transitional zone, or cloaca, which is a ring of tissue between the anal canal and the rectum.
- **Adenocarcinomas.** About 15% of anal cancers are adenocarcinomas, which affect glands in the anal area. One type of adenocarcinoma that can occur in the anal area is called Paget's disease, which can also affect the vulva, breasts, and other areas of the body.
- **Skin cancers.** A small percentage of anal cancers are either basal cell carcinomas, or malignant melanomas, two types of skin cancer. Malignant melanomas, which develop from skin cells that produce the brown pigment called melanin, are far more common on areas of the body exposed to the sun.

Approximately 3,500 Americans will be diagnosed with anal cancer in 2001, and an estimated 500 individuals will die of the disease during this same interval, according to the American Cancer Society. Anal cancers are fairly rare: they make up only 1% to 2% of cancers affecting the digestive system. The disease affects women somewhat more often than men, although the number of cases among men, particularly homosexual men, seems to be increasing.

Causes and symptoms

The exact cause of most anal cancers is unknown, although certain individuals appear to have a higher risk of developing the disease. Smokers are at higher risk, as are individuals with certain types of the human papillomavirus (HPV), and those with long-term problems in the anal area, such as abnormal openings known as fistulas. Since it increases the risk of HPV infection, the practice of anal sex appears to increase the risk of anal cancer—male homosexuals who practice anal sex are about 33 times more likely to have anal cancers than heterosexual men. Those with weakened immune systems, such individuals with HIV, or transplant patients taking **immunosuppressant drugs**, are also at higher risk. Most individuals with anal cancer are over the age of 50.

Symptoms of anal cancer resemble those found in other harmless conditions. They include **pain**, **itching** and bleeding, straining during a bowel movement, change in bowel habits, change in the diameter of the stool, discharge from the anus, and swollen lymph nodes in the anal or groin area.

Diagnosis

Anal cancer is sometimes diagnosed during routine physicals, or during minor procedures such as hemorrhoid removal. It may also be diagnosed during a digital **rectal examination** (DRE), when a physician inserts a gloved, lubricated finger into the anus to feel for unusual growths. Individuals over the age of 50 who have no symptoms should have a digital rectal examination (DRE) every five to 10 years, according to American Cancer Society (ACS) guidelines for early detection of colorectal cancer.

Other diagnostic procedures for anal cancer include: **Anoscopy.** A procedure that involves use of a special device to examine the anus. **Proctoscopy.** A procedure that involves use of a lighted scope to see the anal canal. **Transrectal ultrasound.** A procedure in which sound waves are used to create an image of the anus and nearby tissues.

A biopsy is performed on any suspicious growths; that is, a tiny piece of the growth is examined under a microscope for cancer cells. The physician may also perform a procedure called a fine needle aspiration biopsy, in which a needle is used to withdraw fluid from lymph nodes located near the growth, to make sure the cancer hasn't spread to these nodes.

Anal cancer severity is categorized by the following stages:

- Stage 0 anal cancer is found only in the top layer of anal tissue.
- Stage I anal cancer has spread beyond the top layer of anal tissue, but is less than 1 inch in diameter.

- Stage II anal cancer has spread beyond the top layer of anal tissue and is larger than 1 inch in diameter, but has not spread to nearby organs or lymph nodes.
- Stage IIIA anal cancer has spread to the lymph nodes around the rectum or to nearby organs such as the vagina or bladder.
- Stage IIIB anal cancer has spread to lymph nodes in the mid-abdomen or groin, or to nearby organs and the lymph nodes around the rectum.
- Stage IV anal cancer has spread to distant lymph nodes within the abdomen or to distant organs.

Treatment

Anal cancer is treated using three methods, used either in concert or individually: surgery, **radiation therapy**, and **chemotherapy**.

Two types of surgery may be performed. A local resection, performed if the cancer has not spread, removes the tumor and an area of tissue around the tumor. An abdominoperineal resection is a more complex procedure in which the anus and the lower rectum are removed, and an opening called a **colostomy** is created for body wastes to exit. This procedure is fairly uncommon today because radiation and chemotherapy are just as effective.

Radiation therapy uses high-energy rays to fight cancer cells. It is usually delivered via a machine outside the body, but may also be delivered via surgically implanted radioactive pellets. This latter method is called internal radiation, brachytherapy, or interstitial radiation. Side effects of radiation may include tiredness, skin damage resembling **sunburn**, and damage to anal tissues.

Chemotherapy fights cancer using drugs, which may be delivered via pill or needle. Some chemotherapy types kill cancer cells directly, while others act indirectly by making cancer cells more vulnerable to radiation. The main drugs used to treat anal cancer are 5-fluorouracil (5-FU) and mitomycin or 5-FU and cisplatin. Side effects of chemotherapy, which damages normal cells in addition to cancer cells, may include **nausea and vomiting**, hair loss, loss of appetite, **diarrhea**, mouth sores, **fatigue**, **shortness of breath**, and a weakened immune system.

Alternative treatment

Research suggests **acupuncture** can help manage chemotherapy-related nausea and vomiting and control pain associated with surgery.

Prognosis

Anal cancer is often curable. The chance of recovery depends on the cancer stage and the patient's general health.

KEY TERMS

Biopsy—A procedure in which a small piece of body tissue is removed and examined under a microscope for cancer.

Chemotherapy—A cancer treatment in which drugs delivered into the blood stream kill cancer cells or make them more vulnerable to radiation therapy.

Human papillomavirus (HPV)—A virus with many subtypes, some of which cause cell changes that increase the risk of certain cancers.

Human immunodeficiency virus (HIV)—The virus that causes acquired immune deficiency syndrome (AIDS).

Lymph nodes—Bean-shaped structures found throughout the body that produce and store infection-fighting cells.

Radiation therapy—A cancer treatment that uses high-energy rays to kill or weaken cancer cells. Radiation may be delivered externally or internally via surgically implanted pellets.

Prevention

Reducing the risks of the **sexually transmitted diseases** HPV and HIV also reduces the risk of anal cancer. In addition, quitting **smoking** lowers the risk of anal cancer.

Resources

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American Joint Committee on Cancer: AJCC Cancer Staging Manual. Philadelphia, Pa: Lippincott-Raven Publishers, 1997.

PERIODICALS

Murakami, M, KJ Gurski and MA Steller. "Human Papillomavirus Vaccines For Cervical Cancer." *Journal of Immunotherapy* 1999, 22(3):212-8.

ORGANIZATIONS

American Cancer Society. (800) ACS-2345. <<http://www.cancer.org>>.

American College of Gastroenterology. <<http://www.acg.gi.org>>.

American Gastroenterological Association. 7910 Woodmont Ave., Seventh Floor, Bethesda, MD 20814. (301) 654-2055. <<http://www.gastro.org>>.

American Society of Colon and Rectal Surgeons. 85 W. Algonquin Road, Suite 550, Arlington Heights, IL 60005. (847)290-9184.

The NCI Office of Cancer Complementary and Alternative Medicine. <<http://occam.nci.nih.gov>>.

National Cancer Institute. 31 Center Drive, MSC 2580, Bethesda, MD 20892-2580. (800) 4-CANCER. <<http://www.nci.nih.gov>>.

National Coalition for Cancer Survivorship. 1010 Wayne Avenue, 5th Floor, Suite 300, Silver Spring, MD 20910. (888) 650-9127.

The NIH National Center for Complementary and Alternative Medicine. Post Office Box 8218, Silver Spring, MD 20907-8218. (888) 644-6226. <<http://nccam.nih.gov>>.

United Ostomy Association. (800) 826-0826. <<http://www.uoa.org>>.

Ann Quigley

Anal fissure see **Anorectal disorders**

Anal warts

Definition

Anal warts, also known as condyloma acuminata, are small warts that can occur in the rectum.

Description

Initially appear as tiny blemishes that can be as small as the head of a pin or grow into larger cauliflower-like protuberances. They can be yellow, pink, or light brown in color, and only rarely are painful or uncomfortable. In fact, infected individuals often are unaware that they exist. Most cases are caused by sexual transmission.

Most individuals have between one to 10 **genital warts** that range in size from roughly 0.5–1.9 cm². Some will complain of painless bumps or **itching**, but often, these warts can remain completely unnoticed.

Causes and symptoms

Condyloma acuminatum is one of the most common sexually transmitted disease (STD) in the United States. Young adults aged 17 to 33 years are at greatest risk. Risk factors include **smoking**, using **oral contraceptives**, having multiple sexual partners, and an early coital age. In addition, individuals who have a history of immunosuppression or anal intercourse are also at risk.

Roughly 90% of all anal warts are caused by the human papilloma virus (HPV) types 6 and 11, which are the least likely of over 60 types of HPV to become cancerous. Anal warts are usually transmitted through direct sexual contact with someone who is infected with condyloma acuminata anywhere in the genital area, including the penis and vagina. Studies have shown that roughly

75% of those who engage in sexual contact with someone infected with condyloma acuminata will develop these warts within three months.

Treatment

According to guidelines from the Centers for Disease Control (CDC), the treatment of all genital warts, including anal warts, should be conducted according to the methods preferred by the patient, the medications or procedures most readily available, and the experience of the patient's physician in removing anal warts.

Treatment options include electrical cauterity, surgical removal, or both. Warts that appear inside the anal canal will almost always be treated with cauterization or surgical removal. Surgical removal, also known as excision, has the highest success rates and lowest recurrence rates. Indeed, studies have shown that initial cure rates range from 63–91%.

Unfortunately, most cases require numerous treatments because the virus that causes the warts can live in the surrounding tissue. The area may seem normal and wart-free for six months or longer before another wart develops.

Laser surgery is another possibility, but requires local, general, or spinal anesthesia, depending on the number warts and where they are.

Electrocoagulation, a technique that uses electrical energy to destroy the warts, is usually the most painful of the procedures done to eliminate condyloma acuminata of the anus, and is usually reserved for larger warts. It is done with local anesthesia, and may cause discharge or bleeding from the anus.

Follow-up visits to the physician are necessary to make sure that the warts have not recurred. It is recommended that these patients see their physicians every three to six months for up to 1.5 years, which is how long the incubation period is for the HPV virus.

Carbon dioxide laser treatment and electrodesiccation are other options, but these are usually reserved for extensive warts or those that continue to recur despite numerous treatments. However, because HPV virus can be transmitted via the smoke caused by these procedures, they are usually reserved for the worst infections.

For small warts that affect only the skin around the anus, several medications are available, which can be applied directly to the surface of the warts by a physician or by the patients themselves.

Such medications include podophyllium resin (Podocon-25, Pod-Ben-25), a substance made from the cytotoxic extracts of several plants. This agent offers a

cure rate of 20–50% when used alone, and is applied by the physician weekly and then washed off 6 hours later by the patient.

Podofilox (Condylox) is another agent, and is available for patients to use at home. It can be applied twice daily for up to 4 weeks. Podofilox offers a slightly higher cure rate than podophyllin, and can also be used to prevent warts.

Trichloroacetic and bichloroacetic acids are available in several concentrations up to 80% for the treatment of condyloma acuminata. These acids work to cauterize the skin, and are quite caustic. Nevertheless, they cause less irritation and overall body effects than the other agents mentioned above. Recurrence, however, is higher with these acids.

Bleomycin (Blenoxane) is another treatment option, but it has several drawbacks. First, it must be administered by a physician into each lesion via injection, but it can have a host of side effects, and patients must be followed carefully by their physician.

Imiquimod 5% cream is also available for patients to apply themselves. It is to be applied three times weekly, for up to 16 weeks, and has been shown to clear warts within eight to 10 weeks.

Finally, the interferon drugs, which are naturally occurring proteins that have antiviral and antitumor effects, are available. These include interferon alfa 2a and 2b (Roferon, Intron A), which are to be injected into each lesion twice a week for up to eight weeks.

Prognosis

Once a diagnosis of anal warts has been made, further outbreaks can be controlled or sometimes prevented with proper care. Unfortunately, many cases of anal warts either fail to respond to treatment or recur. Patients have to undergo roughly six to nine treatments over several months to assure that the warts are completely eradicated.

Recurrence rates have been estimated to be over 50% after one year and may be due to the long incubation of HPV (up to 1.5 years), deep lesions, undetected lesions, virus present in surrounding skin that is not treated.

Prevention

Sexual abstinence and monogamous relationships can be the most effective form of prevention, and condoms may also decrease the chances of transmission of condyloma acuminata. Abstinence from sexual relations with people who have anal or genital warts can prevent infection. Unfortunately, since many people may not be aware that they have this condition, this is not always possible.

KEY TERMS

Electrocoagulation—a technique using electrical energy to destroy the warts. Usually done for warts within the anus with a local anesthesia, electrocoagulation is most painful form of therapy, and can cause both bleeding and discharge from the anus.

Individuals infected with anal warts should have follow-up checkups every few weeks after their initial treatment, after which self-exams can be done.

Sexual partners of people who have anal warts should also be examined, as a precautionary preventive measure.

Finally, 5-flourouracil (Adrucil, Efudex, Fluoroplex) may be useful to prevent recurrence once the warts have been removed. Treatment must, however, be initiated within 1 month of wart removal.

Resources

PERIODICALS

Maw, Raymond, and Geo von Krogh. "The Management of Anal Warts." *British Medical Journal*, no. 321 (October 14, 2000):910-11.

ORGANIZATIONS

Centers for Disease Control and Prevention, Sexually Transmitted Diseases Hotline: (800) 227-8922.

OTHER

<<http://www.arthritis-baldness-impotency-obesity.com/medcenter/NF009.html>>.
<<http://www.emedicine.com>>.
<<http://www.medlineplus.adam.com>>.
<<http://www.mayohealth.org>>.

Liz Meszaros

Analgesics

Definition

Analgesics are medicines that relieve **pain**.

Purpose

Analgesics are those drugs whose primary purpose is pain relief. The primary classes of analgesics are the narcotics, including additional agents that are chemically

based on the morphine molecule but have minimal abuse potential; **nonsteroidal anti-inflammatory drugs** (NSAIDs) including the salicylates; and **acetaminophen**. Other drugs, notably the tricyclic anti-depressants and anti-epileptic agents such as gabapentin, have been used to relieve pain, particularly neurologic pain, but are not routinely classified as analgesics. Analgesics provide symptomatic relief, but have no effect on causation, although clearly the NSAIDs, by virtue of their dual activity, may be beneficial in both regards.

Description

Pain has been classified as “productive” pain and “non-productive” pain. While this distinction has no physiologic meaning, it may serve as a guide to treatment. “Productive” pain has been described as a warning of injury, and so may be both an indication of need for treatment and a guide to diagnosis. “Non-productive” pain by definition serves no purpose either as a warning or diagnostic tool.

Although pain syndromes may be dissimilar, the common factor is a sensory pathway from the affected organ to the brain. Analgesics work at the level of the nerves, either by blocking the signal from the peripheral nervous system, or by distorting the interpretation by the central nervous system. Selection of an appropriate analgesic is based on consideration of the risk-benefit factors of each class of drugs, based on type of pain, severity of pain, and risk of adverse effects. Traditionally, pain has been divided into two classes, acute and chronic, although severity and projected patient survival are other factors that must be considered in drug selection.

Acute pain

Acute pain is self limiting in duration, and includes post-operative pain, pain of injury, and **childbirth**. Because pain of these types is expected to be short term, the long-term side effects of analgesic therapy may routinely be ignored. Thus, these patients may safely be treated with narcotic analgesics without concern for their addictive potential, or NSAIDs with only limited concern for their ulcerogenic risks. Drugs and doses should be adjusted based on observation of healing rate, switching patients from high to low doses, and from narcotic analgesics to non-narcotics when circumstances permit.

An important consideration of **pain management** in severe pain is that patients should not be subject to the return of pain. Analgesics should be dosed adequately to assure that the pain is at least tolerable, and frequently enough to avoid the **anxiety** that accompanies the anticipated return of pain. Analgesics should never be dosed on a “prn” (as needed) basis, but should be administered often

enough to assure constant blood levels of analgesic. This applies to both the narcotic and non-narcotic analgesics.

Chronic pain

Chronic pain, pain lasting over three months and severe enough to impair function, is more difficult to treat, since the anticipated side effects of the analgesics are more difficult to manage. In the case of narcotic analgesics this means the **addiction** potential, as well as respiratory depression and **constipation**. For the NSAIDs, the risk of gastric ulcers may be dose limiting. While some classes of drugs, such as the narcotic agonist/antagonist drugs buprenorphine, nalbuphine and pentazocine, and the selective COX-2 inhibitors celecoxib and rofecoxib represent advances in reduction of adverse effects, they are still not fully suitable for long-term management of severe pain. Generally, chronic pain management requires a combination of drug therapy, life-style modification, and other treatment modalities.

Narcotic analgesics

The narcotic analgesics, also termed opioids, are all derived from opium. The class includes morphine, codeine, and a number of semi-synthetics including meperidine (Demerol), propoxyphene (Darvon) and others. The narcotic analgesics vary in potency, but all are effective in treatment of visceral pain when used in adequate doses. Adverse effects are dose related. Because these drugs are all addictive, they are controlled under federal and state laws. A variety of dosage forms are available, including oral solids, liquids, intravenous and intrathecal injections, and transcutaneous patches.

NSAIDs, non-steroidal anti-inflammatory drugs, are effective analgesics even at doses too low to have any anti-inflammatory effects. There are a number of chemical classes, but all have similar therapeutic effects and side effects. Most are appropriate only for oral administration; however ketorolac (Toradol) is appropriate for injection and may be used in moderate to severe pain for short periods.

Acetaminophen is a non-narcotic analgesic with no anti-inflammatory properties. It is appropriate for mild to moderate pain. Although the drug is well tolerated in normal doses, it may have significant toxicity at high doses. Because acetaminophen is largely free of side effects at therapeutic doses, it has been considered the first choice for mild pain, including that of **osteoarthritis**.

Recommended dosage

Appropriate dosage varies by drug, and should consider the type of pain, as well as other risks associated

KEY TERMS

Acute pain—Pain that is usually temporary and results from something specific, such as a surgery, an injury, or an infection.

Analgesic—Medicine used to relieve pain.

Chronic pain—Pain that lasts more than three months and threatens to disrupt daily life.

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

Osteoarthritis—Joint pain resulting from damage to the cartilage.

with patient age and condition. For example, narcotic analgesics should usually be avoided in patients with a history of substance abuse, but may be fully appropriate in patients with **cancer** pain. Similarly, because narcotics are more rapidly metabolized in patients who have used these drugs for a long period, higher than normal doses may be needed to provide adequate pain management. NSAIDs, although comparatively safe in adults, represent an increased risk of gastrointestinal bleeding in patients over the age of 60.

Precautions

Narcotic analgesics may be contraindicated in patients with respiratory depression. NSAIDs may be hazardous to patients with ulcers or an ulcer history. They should be used with care in patients with renal insufficiency or **coagulation disorders**. NSAIDs are contraindicated in patients allergic to **aspirin**.

Side effects

Review adverse effects of each drug individually. Drugs within a class may vary in their frequency and severity of adverse effects.

The primary adverse effects of the narcotic analgesics are addiction, constipation, and respiratory depression. Because narcotic analgesics stimulate the production of enzymes that cause the metabolism of these drugs, patients on narcotics for a prolonged period may require increasing doses. This is not the same thing as addiction, and is not a reason for withholding medication from patients in severe pain.

NSAIDs are ulcerogenic and may cause kidney problems. Gastrointestinal discomfort is common, although in some cases, these drugs may cause ulcers

without the prior warning of gastrointestinal distress. Platelet aggregation problems may occur, although not to the same extent as if seen with aspirin.

Interactions

Interactions depend on the specific type of analgesic. See specific references.

Samuel Uretsky, PharmD

Analgesics, opioid

Definition

Opioid **analgesics**, also known as narcotic analgesics, are **pain** relievers that act on the central nervous system. Like all narcotics, they may become habit-forming if used over long periods.

Purpose

Opioid analgesics are used to relieve pain from a variety of conditions. Some are used before or during surgery (including dental surgery) both to relieve pain and to make anesthetics work more effectively. They may also be used for the same purposes during labor and delivery.

Description

Opioid analgesics relieve pain by acting directly on the central nervous system. However, this can also lead to unwanted side effects, such as drowsiness, **dizziness**, breathing problems, and physical or mental dependence.

Among the drugs in this category are codeine, propoxyphene (Darvon), propoxyphene and **acetaminophen** (Darvocet N), meperidine (Demerol), hydromorphone (Dilaudid), morphine, oxycodone, oxycodone and acetaminophen (Percocet, Roxicet), and hydrocodone and acetaminophen (Lortab, Anexsia). These drugs come in many forms—tablets, syrups, suppositories, and injections, and are sold only by prescription. For some, a new prescription is required for each new supply—refills are prohibited according to federal regulations.

Recommended dosage

Recommended doses vary, depending on the type of opioid analgesic and the form in which it is being used. Doses may be different for different patients. Check with the physician who prescribed the drug or the pharmacist

Opioid analgesics

Drug	Route of administration	Onset of action (min)	Time to peak effect (min)	Duration of action (h)
Strong agonists				
Fentanyl (Sublimaze)	IM	7–15	20–30	1–2
	IV	1–2	3–5	0.5–1
Hydromorphone (Dilaudid)	Oral	30	90–120	4
	IM	15		
	IV	10–15	30–60	2–3
	Sub-Q	30		15–30
Levorphanol (Levo-Dromoran)	Oral	10–60	90–120	4–5
	IM			
	IV	—	60	4–5
	Sub-Q	10–60	within 20	
Meperidine (Demerol)	Oral	15	60–90	2–4
	IM	10–15		
	IV		30–50	2–4
	Sub-Q	1		
Methadone (Dolophine)	Oral	30–60	90–120	4–6
	IM			
	IV	10–20	60–120	4–5
Morphine (many trade names)	Oral	—	60–120	4–5
	IM	10–30		
	IV		30–60	4–5
	Sub-Q	—		
Oxymorphone (Numorphan)	Epidural	10–30	20	4–5
	IM	10–15	30–90	3–6
	IV			
	Sub-Q	5–10	15–30	3–4
	Rectal			
Mild-to-moderate agonists				
Codiene (many trade names)	Oral	30–40	60–120	4
	IM	10–30	30–60	4
	Sub-Q	10–30		4
Hydrocodone (Hycodan)	Oral	10–30	30–60	4–6
Oxycodone (Percodan)	Oral	—	60	3–4
Propoxyphene (Darvon, Dolene)	Oral	15–60	120	4–6
Butorphanol (Stadol)	IM	10–30	30–60	3–4
	IV	2–3	30	2–4
Nalbuphine (Nubian)	IM	within 15	60	3–6
	IV	2–3	30	3–4
	Sub-Q	within 15	—	3–6
Pentazocine (Talwin)	Oral	15–30	60–90	3
	IM	15–20	30–60	2–3
	IV	2–3	15–30	2–3
	Sub-Q	15–20	30–60	2–3

who filled the prescription for correct dosages, and make sure to understand how to take the drug.

Always take opioid analgesics exactly as directed. Never take larger or more frequent doses, and do not take the drug for longer than directed. Do not stop taking the drug suddenly without checking with the physician or dentist who prescribed it. Gradually tapering the dose may reduce the chance of withdrawal symptoms.

Precautions

Anyone who uses opioid analgesics—or any narcotic—over a long time may become physically or mentally dependent on the drug. Physical dependence may lead to

withdrawal symptoms when the person stops taking the medicine. Building tolerance to these drugs is also possible when they are used for a long period. Over time, the body needs larger and larger doses to relieve pain.

Take these drugs exactly as directed. Never take more than the recommended dose, and do not take the drugs more often than directed. If the drugs do not seem to be working, consult your physician. Do not share these or any other prescription drugs with others because the drug may have a completely different effect on the person for whom it was not prescribed.

Children and older people are especially sensitive to opioid analgesics and may have serious breathing prob-

lems after taking them. Children may also become unusually restless or agitated when given these drugs.

Opioid analgesics increase the effects of alcohol. Anyone taking these drugs should not drink alcoholic beverages.

Some of these drugs may also contain **aspirin**, **caffeine**, or acetaminophen. Refer to the entries on each of these drugs for additional precautions.

Special conditions

People with certain medical conditions or who are taking certain other medicines can have problems if they take opioid analgesics. Before taking these drugs, be sure to let the physician know about any of these conditions.

ALLERGIES. Let the physician know about any **allergies** to foods, dyes, preservatives, or other substances and about any previous reactions to opioid analgesics.

PREGNANCY. Women who are pregnant or plan to become pregnant while taking opioid analgesics should let their physicians know. No evidence exists that these drugs cause **birth defects** in people, but some do cause birth defects and other problems when given to pregnant animals in experiments. Babies can become dependent on opioid analgesics if their mothers use too much during **pregnancy**. This can cause the baby to go through withdrawal symptoms after birth. If taken just before delivery, some opioid analgesics may cause serious breathing problems in the newborn.

BREAST FEEDING. Some opioid analgesics can pass into breast milk. Women who are breast feeding should check with their physicians about the safety of taking these drugs.

OTHER MEDICAL CONDITIONS. These conditions may influence the effects of opioid analgesics:

- head injury. The effects of some opioid analgesics may be stronger and may interfere with recovery in people with head injuries.
- history of convulsions. Some of these drugs may trigger convulsions.
- asthma, **emphysema**, or any chronic lung disease
- heart disease
- kidney disease
- liver disease
- underactive thyroid. The chance of side effects may be greater.
- addison's disease (a disease of the adrenal glands)
- colitis

- gallbladder disease or **gallstones**. Side effects can be dangerous in people with these conditions.
- enlarged prostate or other urinary problems
- current or past alcohol abuse
- current or past drug abuse, especially narcotic abuse
- current or past emotional problems. The chance of side effects may be greater.

USE OF CERTAIN MEDICINES. Taking opioid narcotics with certain other drugs may increase the chances of serious side effects.

Side effects

Some people experience drowsiness, dizziness, light-headedness, or a false sense of well-being after taking opioid analgesics. Anyone who takes these drugs should not drive, use machines, or do anything else that might be dangerous until they know how the drug affects them. **Nausea and vomiting** are common side effects, especially when first beginning to take the medicine. If these symptoms do not go away after the first few doses, check with the physician or dentist who prescribed the medicine.

Dry mouth is another common side effect. Dry mouth can be relieved by sucking on sugarless hard candy or ice chips or by chewing sugarless gum. Saliva substitutes, which come in liquid or tablet forms, also may help. Patients who must use opioid analgesics over long periods and who have dry mouth should see their dentists, as the problem can lead to **tooth decay** and other dental problems.

The following side effects are less common. They usually do not need medical attention and will go away after the first few doses. If they continue or interfere with normal activity, check with the physician who prescribed the medicine.

- headache
- loss of appetite
- restlessness or nervousness
- nightmares, unusual dreams, or problems sleeping
- weakness or tiredness
- mental sluggishness
- stomach pain or cramps
- blurred or double vision or other vision problems
- problems urinating, such as pain, difficulty urinating, frequent urge to urinate, or decreased amount of urine
- constipation.

Other side effects may be more serious and may require quick medical attention. These symptoms could

be signs of an overdose. Get emergency medical care immediately.

- cold, clammy skin
- bluish discoloration of the skin
- extremely small pupils
- serious difficulty breathing or extremely slow breathing
- extreme sleepiness or unresponsiveness
- severe weakness
- confusion
- severe dizziness
- severe drowsiness
- slow heartbeat
- low blood pressure
- severe nervousness or restlessness

In addition, these less common side effects do not require emergency medical care, but should have medical attention as soon as possible:

- **hallucinations** or a sense of unreality
- depression or other mood changes
- ringing or buzzing in the ears
- pounding or unusually fast heartbeat
- itching, **hives**, or rash
- facial swelling
- trembling or twitching
- dark urine, pale stools, or yellow eyes or skin (after taking propoxyphene)
- increased sweating, red or flushed face (more common after taking hydrocodone and meperidine)

Interactions

Anyone taking these drugs should notify his or her physician before taking opioid analgesics:

- Central nervous system (CNS) depressants, such as **antihistamines** and other medicines for allergies, hay **fever**, or colds; tranquilizers; some other prescription pain relievers; seizure medicines; **muscle relaxants**; sleeping pills; some anesthetics (including dental anesthetics).
- Monoamine oxidase (MAO) inhibitors, such as phenelzine (Nardil) and tranylcypromine (Parnate). The combination of the opioid analgesic meperidine (Demerol) and MAO inhibitors is especially dangerous.
- Tricyclic antidepressants, such as amitriptyline (Elavil).
- Anti-seizure medicines, such as carbamazepine (Tegretol). May lead to serious side effects, including **coma**, when combined with propoxyphene and acetaminophen (Darvocet-N) or propoxyphene (Darvon).

KEY TERMS

Analgesic—Medicine used to relieve pain.

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

Colitis—Inflammation of the colon (large bowel)

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

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

Narcotic—A drug derived from opium or compounds similar to opium. Such drugs are potent pain relievers and can affect mood and behavior. Long-term use of narcotics can lead to dependence and tolerance.

Tolerance—A decrease in sensitivity to a drug. When tolerance occurs, a person must take more and more of the drug to get the same effect.

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.

- Muscle relaxants, such as cyclobenzaprine (Flexeril).
- Sleeping pills, such as triazolam (Halcion).
- Blood-thinning drugs, such as warfarin (Coumadin).
- Naltrexone (Trexan, Revia). Cancels the effects of opioid analgesics.
- Rifampin (Rifadin).
- Zidovudine (AZT, Retrovir). Serious side effects when combined with morphine.

Nancy Ross-Flanigan

Anaphylactic shock see **Anaphylaxis**

Anaphylactoid purpura see **Allergic purpura**

Anaphylaxis

Definition

Anaphylaxis is a rapidly progressing, life-threatening allergic reaction.

Description

Anaphylaxis is a type of allergic reaction, in which the immune system responds to otherwise harmless substances from the environment. Unlike other allergic reactions, however, anaphylaxis can kill. Reaction may begin within minutes or even seconds of exposure, and rapidly progress to cause airway constriction, skin and intestinal irritation, and altered heart rhythms. In severe cases, it can result in complete airway obstruction, shock, and death.

Causes and symptoms

Causes

Like the majority of other allergic reactions, anaphylaxis is caused by the release of histamine and other chemicals from mast cells. Mast cells are a type of white blood cell and they are found in large numbers in the tissues that regulate exchange with the environment: the airways, digestive system, and skin.

On their surfaces, mast cells display antibodies called IgE (immunoglobulin type E). These antibodies are designed to detect environmental substances to which the immune system is sensitive. Substances from a genuinely threatening source, such as bacteria or viruses, are called antigens. A substance that most people tolerate well, but to which others have an allergic response, is called an allergen. When IgE antibodies bind with allergens, they cause the mast cell to release histamine and other chemicals, which spill out onto neighboring cells.

The interaction of these chemicals with receptors on the surface of blood vessels causes the vessels to leak fluid into surrounding tissues, causing fluid accumulation, redness, and swelling. On the smooth muscle cells of the airways and digestive system, they cause constriction. On nerve endings, they increase sensitivity and cause **itching**.

In anaphylaxis, the dramatic response is due both to extreme hypersensitivity to the allergen and its usually systemic distribution. Allergens are more likely to cause anaphylaxis if they are introduced directly into the circulatory system by injection. However, exposure by ingestion, inhalation, or skin contact can also cause anaphylaxis. In some cases, anaphylaxis may develop over time from less severe **allergies**.

Anaphylaxis is most often due to allergens in foods, drugs, and insect venom. Specific causes include:

- fish, shellfish, and mollusks
- nuts and seeds

- stings of bees, wasps, or hornets
- papain from meat tenderizers
- vaccines, including flu and **measles** vaccines
- penicillin
- cephalosporins
- streptomycin
- gamma globulin
- insulin
- hormones (ACTH, thyroid-stimulating hormone)
- **aspirin** and other NSAIDs
- latex, from exam gloves or condoms, for example

Exposure to cold or **exercise** can trigger anaphylaxis in some individuals.

Symptoms

Symptoms may include:

- urticaria (**hives**)
- swelling and irritation of the tongue or mouth
- swelling of the sinuses
- difficulty breathing
- wheezing
- cramping, vomiting, or **diarrhea**
- anxiety or confusion
- strong, very rapid heartbeat (**palpitations**)
- loss of consciousness

Not all symptoms may be present.

Diagnosis

Anaphylaxis is diagnosed based on the rapid development of symptoms in response to a suspect allergen. Identification of the culprit may be done with RAST testing, a blood test that identifies IgE reactions to specific allergens. Skin testing may be done for less severe anaphylactic reactions.

Treatment

Emergency treatment of anaphylaxis involves injection of adrenaline (epinephrine) which constricts blood vessels and counteracts the effects of histamine. Oxygen may be given, as well as intravenous replacement fluids. **Antihistamines** may be used for skin rash, and aminophylline for bronchial constriction. If the upper airway is obstructed, placement of a breathing tube or tracheostomy tube may be needed.

KEY TERMS

ACTH—Adrenocorticotrophic hormone, a hormone normally produced by the pituitary gland, sometimes taken as a treatment for arthritis and other disorders.

Antibody—An immune system protein which binds to a substance from the environment.

NSAIDs—Non-steroidal antiinflammatory drugs, including aspirin and ibuprofen.

Tracheostomy tube—A tube which is inserted into an incision in the trachea (tracheostomy) to relieve upper airway obstruction.

Prognosis

The rapidity of symptom development is an indication of the likely severity of reaction: the faster symptoms develop, the more severe the ultimate reaction. Prompt emergency medical attention and close monitoring reduces the likelihood of death. Nonetheless, death is possible from severe anaphylaxis. For most people who receive rapid treatment, recovery is complete.

Prevention

Avoidance of the allergic trigger is the only reliable method of preventing anaphylaxis. For insect allergies, this requires recognizing likely nest sites. Preventing food allergies requires knowledge of the prepared foods or dishes in which the allergen is likely to occur, and careful questioning about ingredients when dining out. Use of a Medic-Alert tag detailing drug allergies is vital to prevent inadvertent administration during a medical emergency.

People prone to anaphylaxis should carry an “Epi-pen” or “Ana-kit,” which contain an adrenaline dose ready for injection.

Resources

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Richard Robinson

Anemias

Definition

Anemia is a condition characterized by abnormally low levels of healthy red blood cells or hemoglobin (the component of red blood cells that delivers oxygen to tissues throughout the body).

Description

The tissues of the human body need a regular supply of oxygen to stay healthy. Red blood cells, which contain hemoglobin that allows them to deliver oxygen throughout the body, live for only about 120 days. When they die, the iron they contain is returned to the bone marrow and used to create new red blood cells. Anemia develops when heavy bleeding causes significant iron loss or when something happens to slow down the production of red blood cells or to increase the rate at which they are destroyed.

Types of anemia

Anemia can be mild, moderate, or severe enough to lead to life-threatening complications. More than 400 different types of anemia have been identified. Many of them are rare.

IRON DEFICIENCY ANEMIA. **Iron deficiency anemia** is the most common form of anemia in the world. In the United States, iron deficiency anemia affects about 240,000 toddlers between one and two years of age and 3.3 million women of childbearing age. This condition is less common in older children and in adults over 50 and rarely occurs in teenage boys and young men.

The onset of iron deficiency anemia is gradual and, at first, there may not be any symptoms. The deficiency begins when the body loses more iron than it derives from food and other sources. Because depleted iron stores cannot meet the red blood cell's needs, fewer red blood cells develop. In this early stage of anemia, the red blood cells look normal, but they are reduced in number. Then the body tries to compensate for the iron deficiency by producing more red blood cells, which are characteristically small in size. Symptoms develop at this stage.

FOLIC ACID DEFICIENCY ANEMIA. **Folic acid deficiency anemia** is the most common type of megaloblastic anemia (in which red blood cells are bigger than normal). It is caused by a deficiency of **folic acid**, a vitamin that the body needs to produce normal cells.

Folic acid anemia is especially common in infants and teenagers. Although this condition usually results from a dietary deficiency, it is sometimes due to inability to absorb enough folic acid from such foods as:

- cheese
- eggs
- fish
- green vegetables
- meat
- milk
- mushrooms
- yeast

Smoking raises the risk of developing this condition by interfering with the absorption of Vitamin C, which the body needs to absorb folic acid. Folic acid anemia can be a complication of **pregnancy**, when a woman's body needs eight times more folic acid than it does otherwise.

VITAMIN B₁₂ DEFICIENCY ANEMIA. Less common in this country than folic acid anemia, vitamin B₁₂ deficiency anemia is another type of megaloblastic anemia that develops when the body doesn't absorb enough of this nutrient. Necessary for the creation of red blood cells, B₁₂ is found in meat and vegetables.

Large amounts of B₁₂ are stored in the body, so this condition may not become apparent until as much as four years after B₁₂ absorption stops or slows down. The resulting drop in red blood cell production can cause:

- loss of muscle control
- loss of sensation in the legs, hands, and feet
- soreness or burning of the tongue
- weight loss
- yellow-blue color blindness

The most common form of B₁₂ deficiency is **pernicious anemia**. Since most people who eat meat or eggs get enough B₁₂ in their **diets**, a deficiency of this vitamin usually means that the body is not absorbing it properly. This can occur among people who have had intestinal surgery or among those who do not produce adequate amounts of intrinsic factor, a chemical secreted by the stomach lining that combines with B₁₂ to help its absorption in the small intestine.

Pernicious anemia usually strikes between the ages of 50–60. Eating disorders or an unbalanced diet increases the risk of developing pernicious anemia. So do:

- diabetes mellitus
- **gastritis, stomach cancer**, or stomach surgery
- thyroid disease
- family history of pernicious anemia

VITAMIN C DEFICIENCY ANEMIA. A rare disorder that causes the bone marrow to manufacture abnormally

small red blood cells. Vitamin C deficiency anemia results from a severe, long-standing dietary deficiency.

HEMOLYTIC ANEMIA. Some people are born with **hemolytic anemia**. Some acquire this condition, in which infection or antibodies destroy red blood cells more rapidly than bone marrow can replace them.

Hemolytic anemia can enlarge the spleen, accelerating the destruction of red blood cells (hemolysis). Other complications of hemolytic anemia include:

- pain
- shock
- gallstones and other serious health problems

THALASSEMIAS. An inherited form of hemolytic anemia, **thalassemia** stems from the body's inability to manufacture as much normal hemoglobin as it needs. There are two categories of thalassemia, depending on which of the amino acid chains is affected. (Hemoglobin is composed of four chains of amino acids.) In alpha-thalassemia, there is an imbalance in the production of the alpha chain of amino acids; in beta-thalassemia, there is an imbalance in the beta chain. Alpha-thalassemias most commonly affect blacks (25% have at least one gene); beta-thalassemias most commonly affect people of Mediterranean ancestry and Southeast Asians.

Characterized by production of red blood cells that are unusually small and fragile, thalassemia only affects people who inherit the gene for it from each parent (autosomal recessive inheritance).

AUTOIMMUNE HEMOLYTIC ANEMIAS. Warm antibody hemolytic anemia is the most common type of this disorder. This condition occurs when the body produces autoantibodies that coat red blood cells. The coated cells are destroyed by the spleen, liver, or bone marrow.

Warm antibody hemolytic anemia is more common in women than in men. About one-third of patients who have warm antibody hemolytic anemia also have lymphoma, leukemia, lupus, or connective tissue disease.

In cold antibody hemolytic anemia, the body attacks red blood cells at or below normal body temperature. The acute form of this condition frequently develops in people who have had **pneumonia**, mononeucleosis, or other acute infections. It tends to be mild and short-lived, and disappears without treatment.

Chronic cold antibody hemolytic anemia is most common in women and most often affects those who are over 40 and who have arthritis. This condition usually lasts for a lifetime, generally causing few symptoms. However, exposure to cold temperatures can accelerate

red blood cell destruction, causing **fatigue**, joint aches, and discoloration of the arms and hands.

SICKLE CELL ANEMIA. Sickle cell anemia is a chronic, incurable condition that causes the body to produce defective hemoglobin, which forces red blood cells to assume an abnormal crescent shape. Unlike normal oval cells, fragile sickle cells can't hold enough hemoglobin to nourish body tissues. The deformed shape makes it hard for sickle cells to pass through narrow blood vessels. When capillaries become obstructed, a life-threatening condition called sickle cell crisis is likely to occur.

Sickle cell anemia is hereditary. It almost always affects blacks and people of Mediterranean descent. A child who inherits the sickle cell gene from each parent will have the disease. A child who inherits the sickle cell gene from only one parent carries the sickle cell trait, but does not have the disease.

APLASTIC ANEMIA. Sometimes curable by bone marrow transplant, but potentially fatal, **aplastic anemia** is characterized by decreased production of red and white blood cells and platelets (disc-shaped cells that allow the blood to clot). This disorder may be inherited or acquired as a result of:

- recent severe illness
- long-term exposure to industrial chemicals
- use of **anticancer drugs** and certain other medications

ANEMIA OF CHRONIC DISEASE. **Cancer**, chronic infection or inflammation, and kidney and liver disease often cause mild or moderate anemia. Chronic liver failure generally produces the most severe symptoms.

Causes and symptoms

Anemia is caused by bleeding, decreased red blood cell production, or increased red blood cell destruction. Poor diet can contribute to vitamin deficiency and iron deficiency anemias in which fewer red blood cells are produced. Hereditary disorders and certain diseases can cause increased blood cell destruction. However, excessive bleeding is the most common cause of anemia, and the speed with which blood loss occurs has a significant effect on the severity of symptoms. Chronic blood loss is usually a consequence of:

- cancer
- gastrointestinal tumors
- diverticulosis
- polyposis
- heavy menstrual flow
- hemorrhoids

- nosebleeds
- stomach ulcers
- long-standing alcohol abuse

Acute blood loss is usually the result of:

- childbirth
- injury
- a ruptured blood vessel
- surgery

When a lot of blood is lost within a short time, blood pressure and the amount of oxygen in the body drop suddenly. **Heart failure** and **death** can follow.

Loss of even one-third of the body's blood volume in the space of several hours can be fatal. More gradual blood loss is less serious, because the body has time to create new red blood cells to replace those that have been lost.

Symptoms

Weakness, fatigue, and a run-down feeling may be signs of mild anemia. Skin that is pasty or sallow, or lack of color in the creases of the palm, gums, nail beds, or lining of the eyelids are other signs of anemia. Someone who is weak, tires easily, is often out of breath, and feels faint or dizzy may be severely anemic.

Other symptoms of anemia are:

- angina pectoris (chest pain, often accompanied by a **choking** sensation that provokes severe **anxiety**)
- cravings for ice, paint, or dirt
- headache
- inability to concentrate, memory loss
- inflammation of the mouth (**stomatitis**) or tongue (**glossitis**)
- insomnia
- irregular heartbeat
- loss of appetite
- nails that are dry, brittle, or ridged
- rapid breathing
- sores in the mouth, throat, or rectum
- sweating
- swelling of the hands and feet
- thirst
- tinnitus (ringing in the ears)
- unexplained bleeding or bruising

In pernicious anemia, the tongue feels unusually slick. A patient with pernicious anemia may have:

- problems with movement or balance
- tingling in the hands and feet
- confusion, depression, and memory loss

Pernicious anemia can damage the spinal cord. A doctor should be notified whenever symptoms of this condition occur.

A doctor should also be notified if a patient who has been taking iron supplements develops:

- diarrhea
- cramps
- vomiting

Diagnosis

Personal and family health history may suggest the presence of certain types of anemia. Laboratory tests that measure the percentage of red blood cells or the amount of hemoglobin in the blood are used to confirm diagnosis and determine which type of anemia is responsible for a patient's symptoms. X rays and examinations of bone marrow may be used to identify the source of bleeding.

Treatment

Anemia due to nutritional deficiencies can usually be treated at home with iron supplements or self administered injections of vitamin B₁₂. People with folic acid anemia should take oral folic acid replacements. Vitamin C deficiency anemia can be cured by taking one vitamin C tablet a day.

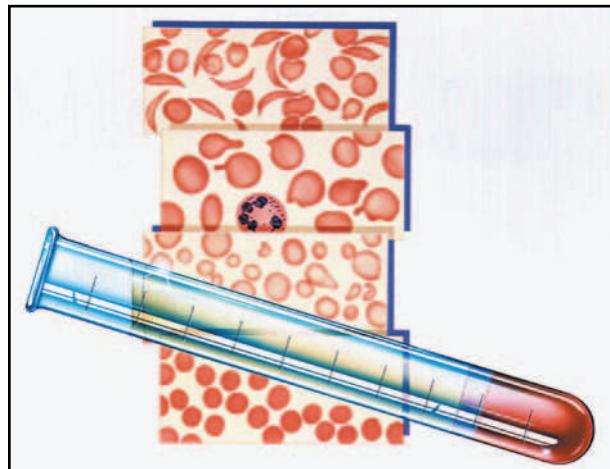
Surgery may be necessary to treat anemia caused by excessive loss of blood. Transfusions of red blood cells may be used to accelerate production of red blood cells.

Medication or surgery may also be necessary to control heavy menstrual flow, repair a bleeding ulcer, or remove polyps (growths or nodules) from the bowels.

Patients with thalassemia usually do not require treatment. However people with a severe form may require periodic hospitalization for blood transfusions and/or **bone marrow transplantation**.

SICKLE CELL ANEMIA. Treatment for sickle cell anemia involves regular eye examinations, immunizations for pneumonia and infectious diseases, and prompt treatment for sickle cell crises and infections of any kind. Psychotherapy or counseling may help patients deal with the emotional impact of this condition.

VITAMIN B₁₂ DEFICIENCY ANEMIA. A life-long regimen of B₁₂ shots is necessary to control symptoms of pernicious anemia. The patient may be advised to limit physical activity until treatment restores strength and balance.



An illustration of normal red blood cells (left) and those in three different types of anemia (from left), iron-deficiency anemia, megaloblastic anemia, and sickle cell anemia. (Illustration by John Bavosi, Custom Medical Stock Photo. Reproduced by permission.)

APLASTIC ANEMIA. People who have aplastic anemia are especially susceptible to infection. Treatment for aplastic anemia may involve blood transfusions and bone marrow transplant to replace malfunctioning cells with healthy ones.

ANEMIA OF CHRONIC DISEASE. There is no specific treatment for anemia associated with chronic disease, but treating the underlying illness may alleviate this condition. This type of anemia rarely becomes severe. If it does, transfusions or hormone treatments to stimulate red blood cell production may be prescribed.

HEMOLYTIC ANEMIA. There is no specific treatment for cold-antibody hemolytic anemia. About one-third of patients with warm-antibody hemolytic anemia respond well to large doses of intravenous and oral **corticosteroids**, which are gradually discontinued as the patient's condition improves. Patients with this condition who don't respond to medical therapy must have the spleen surgically removed. This operation controls anemia in about half of the patients on whom it's performed. Immune-system suppressants are prescribed for patients whose surgery is not successful.

Self-care

Anyone who has anemia caused by poor **nutrition** should modify his or her diet to include more **vitamins**, **minerals**, and iron. Vitamin C can stimulate iron absorption. The following foods are also good sources of iron:

- almonds
- broccoli

- dried beans
- dried fruits
- enriched breads and cereals
- lean red meat
- liver
- potatoes
- poultry
- rice
- shellfish
- tomatoes

Because light and heat destroy folic acid, fruits and vegetables should be eaten raw or cooked as little as possible.

Alternative treatment

As is the case in standard medical treatment, the cause of the specific anemia will determine the alternative treatment recommended. If the cause is a deficiency, for example iron deficiency, folic acid deficiency, B₁₂ deficiency, or vitamin C deficiency, supplementation is the treatment. For extensive blood loss, the cause should be identified and corrected. Other types of anemias should be addressed on a deep healing level with crisis intervention when necessary.

Many alternative therapies for iron-deficiency anemia focus on adding iron-rich foods to the diet or on techniques to improve circulation and digestion. Iron supplementation, especially with iron citrate (less likely to cause **constipation**), is used by alternative practitioners. This can be given in combination with herbs that are rich in iron. Some examples of iron-rich herbs are dandelion (*Taraxacum officinale*), parsley (*Petroselinum crispum*), and nettle (*Urtica dioica*). The homeopathic remedy ferrum phosphoricum can also be helpful.

An iron-rich herbal tonic can also be made using the following recipe:

- soak 1/2 oz of yellow dock root and 1/2 oz dandelion root in 1 qt of boiled water for four to 8 hours
- strain and simmer until the amount of liquid is reduced to 1 cup
- remove from heat and add 1/2 cup black strap molasses, mixing well
- store in refrigerator; take 1 tsp-2 Tbsp daily

Other herbal remedies used to treat iron-deficiency anemia aim to improve the digestion. Gentian (*Gentiana lutea*) is widely used in Europe to treat anemia and other nutritionally based disorders. The bitter qualities of gen-

tian help stimulate the digestive system, making iron and other nutrients more available for absorption. This bitter herb can be brewed into tea or purchased as an alcoholic extract (tincture).

Other herbs recommended to promote digestion include:

- anise (*Pimpinella anisum*)
- caraway (*Carum carvi*)
- cumin (*Cuminum cyminum*)
- linden (*Tilia spp.*)
- licorice (*Glycyrrhiza glabra*)

Traditional Chinese treatments for anemia include:

- acupuncture to stimulate a weakened spleen
- asian ginseng (*Panax ginseng*) to restore energy
- dong quai (*Angelica sinensis*) to control heavy menstrual bleeding
- a mixture of dong quai and Chinese foxglove (*Rehmannia glutinosa*) to clear a sallow complexion

Prognosis

Folic-acid and iron-deficiency anemias

It usually takes three to six weeks to correct folic acid or iron deficiency anemia. Patients should continue taking supplements for another six months to replenish iron reserves and should have periodic blood tests to make sure the bleeding has stopped and the anemia has not recurred.

Pernicious anemia

Although pernicious anemia is considered incurable, regular B₁₂ shots will alleviate symptoms and reverse complications. Some symptoms will disappear almost as soon as treatment begins.

Aplastic anemia

Aplastic anemia can sometimes be cured by bone marrow transplantation. If the condition is due to immunosuppressive drugs, symptoms may disappear after the drugs are discontinued.

Sickle cell anemia

Although sickle cell anemia cannot be cured, effective treatments enable patients with this disease to enjoy longer, more productive lives.

Thalassemia

People with mild thalassemia (alpha thalassemia trait or beta thalassemia minor) lead normal lives and do

KEY TERMS

Aplastic—Exhibiting incomplete or faulty development.

Diabetes mellitus—A disorder of carbohydrate metabolism brought on by a combination of hereditary and environmental factors.

Hemoglobin—An iron-containing pigment of red blood cells composed of four amino acid chains (alpha, beta, gamma, delta) that delivers oxygen from the lungs to the tissues of the body.

Megaloblast—A large erythroblast (a red marrow cell that synthesizes hemoglobin).

not require treatment. Those with severe thalassemia may require bone marrow transplantation. Genetic therapy is being investigated and may soon be available.

Hemolytic anemia

Acquired hemolytic anemia can generally be cured when the cause is removed.

Prevention

Inherited anemias cannot be prevented. **Genetic counseling** can help parents cope with questions and concerns about transmitting disease-causing genes to their children.

Avoiding excessive use of alcohol, eating a balanced diet that contains plenty of iron-rich foods, and taking a daily multivitamin can help prevent anemia.

Methods of preventing specific types of anemia include:

- avoiding lengthy exposure to industrial chemicals and drugs known to cause aplastic anemia
- not taking medication that has triggered hemolytic anemia and not eating foods that have caused hemolysis (breakdown of red blood cells)
- receiving regular B₁₂ shots to prevent pernicious anemia resulting from gastritis or stomach surgery

Resources

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Anencephaly see **Congenital brain defects**

Anesthesia, general

Definition

General anesthesia is the induction of a state of unconsciousness with the absence of **pain** sensation over the entire body, through the administration of anesthetic drugs. It is used during certain medical and surgical procedures.

Purpose

General anesthesia has many purposes including:

- pain relief (analgesia)
- blocking memory of the procedure (**amnesia**)
- producing unconsciousness
- inhibiting normal body reflexes to make surgery safe and easier to perform
- relaxing the muscles of the body

Description

Anesthesia performed with general anesthetics occurs in four stages which may or may not be observable because they can occur very rapidly:

- Stage One: Analgesia. The patient experiences analgesia or a loss of pain sensation but remains conscious and can carry on a conversation.
- Stage Two: Excitement. The patient may experience **delirium** or become violent. Blood pressure rises and becomes irregular, and breathing rate increases. This stage is typically bypassed by administering a barbiturate, such as sodium pentothal, before the anesthesia.
- Stage Three: Surgical Anesthesia. During this stage, the skeletal muscles relax, and the patient's breathing becomes regular. Eye movements slow, then stop, and surgery can begin.
- Stage Four: Medullary Paralysis. This stage occurs if the respiratory centers in the medulla oblongata of the brain that control breathing and other vital functions cease to function. **Death** can result if the patient cannot be revived quickly. This stage should never be reached. Careful control of the amounts of anesthetics administered prevent this occurrence.

Agents used for general anesthesia may be either gases or volatile liquids that are vaporized and inhaled with oxygen, or drugs delivered intravenously. A combination of inhaled anesthetic gases and intravenous drugs are usually delivered during general anesthesia; this practice is called balanced anesthesia and is used because it takes advantage of the beneficial effects of each anesthetic agent to reach surgical anesthesia. If necessary, the extent of the anesthesia produced by inhaling a general anesthetic can be rapidly modified by adjusting the concentration of the anesthetic in the oxygen that is breathed by the patient. The degree of anesthesia produced by an intravenously injected anesthetic is fixed and cannot be changed as rapidly. Most commonly, intravenous anesthetic agents are used for induction of anesthesia and then followed by inhaled anesthetic agents.

General anesthesia works by altering the flow of sodium molecules into nerve cells (neurons) through the cell membrane. Exactly how the anesthetic does this is not understood since the drug apparently does not bind to any receptor on the cell surface and does not seem to affect the release of chemicals that transmit nerve impulses (neurotransmitters) from the nerve cells. It is known, however, that when the sodium molecules do not get into the neurons, nerve impulses are not generated and the brain becomes unconscious, does not store memories, does not register pain impulses from other areas of the body, and does not control involuntary reflexes. Although anesthesia may feel like deep sleep, it is not the same. In sleep, some parts of the brain speed up while others slow down. Under anesthesia, the loss of consciousness is more widespread.

When general anesthesia was first introduced in medical practice, ether and chloroform were inhaled with the physician manually covering the patient's mouth. Since then, general anesthesia has become much more sophisticated. During most surgical procedures, anesthetic agents are now delivered and controlled by computerized equipment that includes anesthetic gas monitoring as well as patient monitoring equipment. Anesthesiologists are the physicians that specialize in the delivery of anesthetic agents. Currently used inhaled general anesthetics include halothane, enflurane, isoflurane, desflurane, sevoflurane, and nitrous oxide.

- Halothane (Fluothane) is a powerful anesthetic and can easily be overadministered. This drug causes unconsciousness but little pain relief so it is often used with other agents to control pain. Very rarely, it can be toxic to the liver in adults, causing death. It also has the potential for causing serious cardiac dysrhythmias. Halothane has a pleasant odor, and was frequently the anesthetic of choice for use with children, but since the introduction of sevoflurane in the 1990s, halothane use has declined.
- Enflurane (Ethrane) is less potent and results in a more rapid onset of anesthesia and faster awakening than halothane. In addition, it acts as an enhancer of paralyzing agents. Enflurane has been found to increase intracranial pressure and the risk of seizures; therefore, its use is contraindicated in patients with seizure disorders.
- Isoflurane (Forane) is not toxic to the liver but can cause some cardiac irregularities. Isoflurane is often used in combination with intravenous anesthetics for anesthesia induction. Awakening from anesthesia is faster than it is with halothane and enflurane.
- Desflurane (Suprane) may increase the heart rate and should not be used in patients with **aortic valve stenosis**; however, it does not usually cause heart **arrhythmias**. Desflurane may cause coughing and excitation during induction and is therefore used with intravenous anesthetics for induction. Desflurane is rapidly eliminated and awakening is therefore faster than with other inhaled agents.
- Sevoflurane (Ultane) may also cause increased heart rate and should not be used in patients with narrowed aortic valve (stenosis); however, it does not usually cause heart arrhythmias. Unlike desflurane, sevoflurane does not cause any coughing or other related side effects, and can therefore be used without intravenous agents for rapid induction. For this reason, sevoflurane is replacing halothane for induction in pediatric patients. Like desflurane, this agent is rapidly eliminated and allows rapid awakening.