KEY TERMS

Amenorrhea—Abnormal cessation of menstruation.

Bromocriptine—Also known as Parlodel, the main drug used to treat galactorrhea by reducing levels of the hormone prolactin.

Hyperlactation—Another term for galactorrhea.

Lactation—The production of breast milk.

first step in diagnosing the cause of galactorrhea. A **physical examination**, along with a breast examination, will usually be conducted. Blood and urine samples may be taken to determine levels of various hormones in the body, including prolactin and compounds related to thyroid function.

A mammogram (an x ray of the breast) or an ultrasound scan (using high frequency sound waves) might be used to determine if there are any tumors or cysts present in the breasts themselves. If a tumor of the pituitary gland is suspected, a series of computer assisted x rays called a computed tomography scan (CT scan) may be done. Another procedure that may be useful is a **magnetic resonance imaging** (MRI) scan to locate tumors or abnormalities in tissues.

Treatment

Treatment for galactorrhea will depend on the cause of the condition and the symptoms. The drug bromocriptine is often prescribed first to reduce the secretion of prolactin and to decrease the size of **pituitary tumors**. This drug will control galactorrhea symptoms and in many cases may be the only therapy necessary. Oral estrogen and progestins (hormone pills, like birth control pills) may control symptoms of galactorrhea for some women. Surgery to remove a tumor may be required for patients who have more serious symptoms of **headache** and vision loss, or if the tumor shows signs of enlargement despite drug treatment. **Radiation therapy** has also been used to reduce tumor size when surgery is not possible or not totally successful. A combination of drug, surgery, and radiation treatment can also be used.

Galactorrhea is more of a nuisance than a real threat to health. While it is important to find the cause of the condition, even if a tumor is discovered in the pituitary gland, it may not require treatment. With very small, slow-growing tumors, some physicians may suggest a "wait and see" approach.

Prognosis

Treatment with bromocriptine is usually effective in stopping milk secretion, however, symptoms may recur if drug therapy is discontinued. Surgical removal or radiation treatment may correct the problem permanently if it is related to a tumor. Frequent monitoring of hormone status and tumor size may be recommended.

Prevention

There is no way to prevent galactorrhea. If the condition is caused by the use of a particular drug, a patient may be able to switch to a different drug that does not have the side-effect of galactorrhea.

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Altha Roberts Edgren

Galactosemia

Definition

Galactosemia is an inherited disease in which the transformation of galactose to glucose is blocked, allowing galactose to increase to toxic levels in the body. If galactosemia is untreated, high levels of galactose cause vomiting, **diarrhea**, lethargy, low blood sugar, brain damage, **jaundice**, liver enlargement, **cataracts**, susceptibility to infection, and **death**.

Description

Galactosemia is a rare but potentially life-threatening disease that results from the inability to metabolize galactose. Serious consequences from galactosemia can be prevented by screening newborns at birth with a simple blood test.

Galactosemia is an inborn error of metabolism. "Metabolism" refers to all chemical reactions that take

place in living organisms. A metabolic pathway is a series of reactions where the product of each step in the series is the starting material for the next step. Enzymes are the chemicals that help the reactions occur. Their ability to function depends on their structure, and their structure is determined by the deoxyribonucleic acid (DNA) sequence of the genes that encode them. Inborn errors of metabolism are caused by mutations in these genes which do not allow the enzymes to function properly.

Sugars are sometimes called "the energy molecules," and galactose and glucose are both sugars. For galactose to be utilized for energy, it must be transformed into something that can enter the metabolic pathway that converts glucose into energy (plus water and carbon dioxide). This is important for infants because they typically get most of their nutrient energy from milk, which contains a high level of galactose. Each molecule of lactose, the major sugar constituent of milk, is made up of a molecule of galactose and a molecule of glucose, and so galactose makes up 20% of the energy source of a typical infant's diet.

Three enzymes are required to convert galactose into glucose-1-phosphate (a phosphorylated glucose that can enter the metabolic pathway that turns glucose into energy). Each of these three enzymes is encoded by a separate gene. If any of these enzymes fail to function, galactose build-up and galactosemia result. Thus, there are three types of galactosemia with a different gene responsible for each.

Every cell in a person's body has two copies of each gene. Each of the forms of galactosemia is inherited as a recessive trait, which means that galactosemia is only present in individuals with two mutated copies of one of the three genes. This also means that carriers, with only one copy of a gene mutation, will not be aware that they are carrying a mutation (unless they have had a genetic test), as it is masked by the normal gene they also carry and they have no symptoms of the disease. For each step in the conversion of galactose to glucose, if only one of the two copies of the gene controlling that step is normal (i.e. for carriers), enough functional enzyme is made so that the pathway is not blocked at that step. If a person has galactosemia, both copies of the gene coding for one of the enzymes required to convert glucose to galactose are defective and the pathway becomes blocked. If two carriers of the same defective gene have children, the chance of any of their children getting galactosemia (the chance of a child getting two copies of the defective gene) is 25% (one in four) for each **pregnancy**.

Classic galactosemia occurs in the United States about one in every 50,000–70,000 live births.

Causes and symptoms

Galactosemia I

Galactosemia I (also called classic galactosemia), the first form to be discovered, is caused by defects in both copies of the gene that codes for an enzyme called galactose-1-phosphate uridyl transferase (GALT). There are 30 known different mutations in this gene that cause GALT to malfunction.

Newborns with galactosemia I appear normal at birth, but begin to develop symptoms after they are given milk for the first time. Symptoms include vomiting, diarrhea, lethargy (sluggishness or **fatigue**), low blood glucose, jaundice (a yellowing of the skin and eyes), enlarged liver, protein and amino acids in the urine, and susceptibility to infection, especially from gram negative bacteria. Cataracts (a grayish white film on the eye lens) can appear within a few days after birth. People with galactosemia frequently have symptoms as they grow older even though they have been given a galactose-free diet. These symptoms include **speech disorders**, cataracts, ovarian atrophy and **infertility** in females, learning disabilities, and behavioral problems.

Galactosemia II

Galactosemia II is caused by defects in both copies of the gene that codes for an enzyme called galactokinase (GALK). The frequency of occurrence of galactosemia II is about one in 100,000–155,000 births.

Galactosemia II is less harmful than galactosemia I. Babies born with galactosemia II will develop cataracts at an early age unless they are given a galactose-free diet. They do not generally suffer from liver damage or neurologic disturbances.

Galactosemia III

Galactosemia III is caused by defects in the gene that codes for an enzyme called uridyl diphosphogalactose-4-epimerase (GALE). This form of galactosemia is very rare.

There are two forms of galactosemia III, a severe form, which is exceedingly rare, and a benign form. The benign form has no symptoms and requires no special diet. However, newborns with galactosemia III, including the benign form, have high levels of galactose-1-phosphate that show up on the initial screenings for elevated galactose and galactose-1-phosphate. This situation illustrates one aspect of the importance of follow-up enzyme function tests. Tests showing normal levels of GALT and GALK allow people affected by the benign form of galactosemia III to enjoy a normal diet.

KEY TERMS

Casein hydrolysate—A preparation made from the milk protein casein, which is hydrolyzed to break it down into its constituent amino acids. Amino acids are the building blocks of proteins.

Catalyst—A substance that changes the rate of a chemical reaction, but is not physically changed by the process.

Enzyme—A protein that catalyzes a biochemical reaction or change without changing its own structure or function.

Galactose—One of the two simple sugars, together with glucose, that makes up the protein, lactose, found in milk. Galactose can be toxic in high levels.

Glucose—One of the two simple sugars, together with galactose, that makes up the protein, lactose, found in milk. Glucose is the form of sugar that is usable by the body to generate energy.

Lactose—A sugar made up of of glucose and galactose. It is the primary sugar in milk.

Metabolic pathway—A sequence of chemical reactions that lead from some precursor to a product, where the product of each step in the series is the starting material for the next step.

Metabolism—The total combination of all of the chemical processes that occur within cells and tissues of a living body.

Recessive trait—An inherited trait or characteristic that is outwardly obvious only when two copies of the gene for that trait are present.

The severe form has symptoms similar to those of galactosemia I, but with more severe neurological problems, including seizures. Only two cases of this rare form had been reported as of 1997.

Diagnosis

The newborn screening test for classic galactosemia is quick and straightforward; all but three states require testing on all newborns. Blood from a baby who is two to three days old is usually first screened for high levels of galactose and galactose-1-phosphate. If either of these compounds is elevated, further tests are performed to find out which enzymes (GALT, GALK, or GALE) are present or missing. DNA testing may also be performed to confirm the diagnosis.

If there is a strong suspicion that a baby has galactosemia, galactose is removed from their diet right away. In this case, an initial screen for galactose or galactose-1-phosphate will be meaningless. In the absence of galactose in the diet, this test will be negative whether the baby has galactosemia or not. In this case, tests to measure enzyme levels must be given to find out if the suspected baby is indeed galactosemic.

In addition, galactosemic babies who are refusing milk or vomiting will not have elevated levels of galactose or galactose phosphate, and their condition will not be detected by the initial screen. Any baby with symptoms of galactosemia (for example, vomiting) should be given enzyme tests.

Treatment

Galactosemia I and II are treated by removing galactose from the diet. Since galactose is a break-down product of lactose, the primary sugar constituent of milk, this means all milk and foods containing milk products must be totally eliminated. Other foods like legumes, organ meats, and processed meats also contain considerable galactose and must be avoided. Pills that use lactose as a filler must also be avoided. Soy-based and casein hydrolysate-based formulas are recommended for infants with galactosemia.

Treatment of the severe form of galactosemia III with a galactose-restricted diet has been tried, but this disorder is so rare that the long-term effects of this treatment are unknown.

Prognosis

Early detection in the newborn period is the key to controlling symptoms. Long-term effects in untreated babies include severe **mental retardation**, **cirrhosis** of the liver, and death. About 75% of the untreated babies die within the first two weeks of life. On the other hand, with treatment, a significant proportion of people with galactosemia I can lead nearly normal lives, although speech defects, learning disabilities, and behavioral problems are common. In addition, cataracts due to galactosemia II can be completely prevented by a galactose-free diet.

Prevention

Since galactosemia is a recessive genetic disease, the disease is usually detected on a newborn screening test, since most people are unaware that they are carriers of a gene mutation causing the disease. For couples with a previous child with galactosemia, prenatal diagnosis is available to determine whether a pregnancy is similarly

affected. Families in which a child has been diagnosed with galactosemia can have DNA testing which can enable other more distant relatives to determine their carrier status. Prospective parents can then use that information to conduct family planning or to prepare for a child with special circumstances. Children born with galactosemia should be put on a special diet right away, to reduce the symptoms and complications of the disease.

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Metabolic Information Network. PO Box 670847, Dallas, TX 75367-0847. (214) 696-2188 or (800) 945-2188.

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Gallbladder cancer

Definition

Cancer of the gallbladder is cancer of the pear-shaped organ that lies on the undersurface of the liver.

Description

Bile from the liver is funneled into the gallbladder by way of the cystic duct. Between meals, the gallbladder stores a large amount of bile. To do this, it must absorb much of the water and electrolytes from the bile. In fact, the inner surface of the gallbladder is the most absorptive surface in the body. After a meal, the gallbladder's muscular walls contract to deliver the bile back through the cystic duct and eventually into the small intestine, where the bile can help digest food.

Demographics

About 5,000 people are diagnosed with gallbladder cancer each year in the United States, making it the fifth most common gastrointestinal cancer. It is more common in females than males and most patients are elderly. Southwest American Indians have a particularly high incidence—six times that of the general population.

Causes and symptoms

Gallstones are the most significant risk factor for the development of gallbladder cancer. Roughly 75 to 90 percent of patients with gallbladder cancer also have gallstones. Larger gallstones are associated with a higher chance of developing gallbladder cancer. Chronic inflammation of the gallbladder from infection also increases the risk for gallbladder cancer.

Unfortunately, sometimes cancer of the gallbladder does not produce symptoms until late in the disease. When symptoms are evident, the most common is **pain** in the upper right portion of the abdomen, underneath the right ribcage. Patients with gallbladder cancer may also report symptoms such as nausea, vomiting, weakness, **jaundice**, skin **itching**, **fever**, chills, poor appetite, and weight loss.

Diagnosis

Gallbladder cancer is often misdiagnosed because it mimics other more common conditions, such as gallstones, **cholecystitis**, and **pancreatitis**. But the imaging tests that are utilized to evaluate these other conditions can also detect gallbladder cancer. For example, ultrasound is a quick, noninvasive imaging test that reliably diagnoses gallstones and cholecystitis. It can also detect the presence of gallbladder cancer as well as show how far the cancer has spread. If cancer is suspected, a computed tomography scan is useful in confirming the presence of an abnormal mass and further demonstrating the size and extent of the tumor. Cholangiography, usually performed to evaluate a patient with jaundice, can also detect gallbladder cancer.

There are no specific laboratory tests for gallbladder cancer. Tumors can obstruct the normal flow of bile from the liver to the small intestine. Bilirubin, a component of bile, builds up within the liver and is absorbed into the bloodstream in excess amounts. This can be detected in a blood test, but it can also manifest clinically as jaundice. Elevated bilirubin levels and clinical jaundice can also occur with other conditions, such as gallstones.

On occasion, gallbladder cancer is diagnosed incidentally. About one percent of all patients who have their gallbladder removed for symptomatic gallstones are

KEY TERMS

Cholangiography—Radiographic examination of the bile ducts after injection with a special dye

Cholecystitis—Inflammation of the gallbladder, usually due to infection

Computed tomography—A radiology test by which images of cross-sectional planes of the body are obtained

Jaundice—Yellowish staining of the skin and eyes due to excess bilirubin in the bloodstream

Metastasis—The spread of tumor cells from one part of the body to another through blood vessels or lymphatic vessels

Pancreatitis—Inflammation of the pancreas

Stent—Slender hollow catheter or rod placed within a vessel or duct to provide support or maintain patency

Ultrasound—A radiology test utilizing high frequency sound waves

found to have gallbladder cancer. The cancer is found either by the surgeon or by the pathologist who inspects the gallbladder with a microscope.

Treatment

Staging of gallbladder cancer is determined by the how far the cancer has spread. The effectiveness of treatment declines as the stage progresses. Stage I cancer is confined to the wall of the gallbladder. Approximately 25% of cancers are at this stage at the time of diagnosis. Stage II cancer has penetrated the full thickness of the wall, but has not spread to nearby lymph nodes or invaded adjacent organs. Stage III cancer has spread to nearby lymph nodes or has invaded the liver, stomach, colon, small intestine, or large intestine. Stage IV disease has invaded very deeply into two or more adjacent organs or has spread to distant lymph nodes or organs by way of metastasis.

Early Stage I cancers involving only the innermost layer of the gallbladder wall can be cured by simple removal of the gallbladder. Cancers at this stage are sometimes found incidentally when the gallbladder is removed in the treatment of gallstones or cholecystitis. The majority of patients have good survival rates. Late Stage I cancers, which involve the outer muscular layers of the gallbladder wall, are generally treated in the same way as Stage II or III cancers. Removal of the gallbladder is not sufficient for these stages. The surgeon also removes nearby lymph nodes as well as a portion of the adjacent liver (radical surgery). Survival rates for these patients are considerably worse than for those with early Stage I disease. Patients with early Stage IV disease may benefit from radical surgery, but the issue is controversial. Late Stage IV cancer has spread too extensively to allow complete excision. Surgery is not an option for these patients.

Other therapies

When long-term survival is not likely, the focus of therapy shifts to improving quality of life. Jaundice and blockage of the stomach are two problems faced by patients with advanced cancer of the gallbladder. These can be treated with surgery, or alternatively, by special interventional techniques employed by the gastroenterologist or radiologist. A stent can be placed across the bile ducts in order to re-establish the flow of bile and relieve jaundice. A small feeding tube can be placed in the small intestine to allow feeding when the stomach is blocked. Pain may be treated with conventional pain medicines or a celiac **ganglion** nerve block.

Current **chemotherapy** or **radiation therapy** cannot cure gallbladder cancer, but they may offer some benefit in certain patients. For cancer that is too advanced for surgical cure, treatment with chemotherapeutic agents such as 5-fluorouracil may lengthen survival for a few months. The limited benefit of chemotherapy must be weighed carefully against its side effects. Radiation therapy is sometimes used after attempted surgical resection of the cancer to extend survival for a few months or relieve jaundice.

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Kevin O. Hwang, M.D.

Gallbladder disease *see* **Cholecystitis**

Gallbladder nuclear medicine scan

Definition

A nuclear medicine scan of the gallbladder is used to produce a set of images that look like x rays. The procedure uses a small amount of radioactive dye which is injected into the body. The dye accumulates in the organ, in this case, the gallbladder. A special camera called a scintillation or gamma camera produces images based on how the dye travels through the system and how the radiation is absorbed by the tissues. The procedure is also called cholescintigraphy or a hepatobiliary scan.

KEY TERMS

Cholecystitis—Inflammation of the gallbladder.

Cholescintigraphy—Another term for a gallbladder nuclear medicine scan.

Hepatobiliary scan—Another term for a gallbladder nuclear medicine scan.

Scintillation or gamma camera—A camera, somewhat like an x-ray machine, used to photograph internal organs after the patient has been injected with a radioactive material.

Purpose

A nuclear medicine scan can be used to diagnose disease and to find abnormalities in a body organ. A gallbladder scan can detect **gallstones**, tumors, or defects of the gallbladder. It can also be used to diagnose blockages of the bile duct that leads from the gallbladder to the small intestine. Unlike ultrasound, a gallbladder nuclear medicine scan can assess gallbladder function.

Precautions

Women who are pregnant or breastfeeding should tell their doctors before a scan is performed. Some medications or even eating a high fat meal before the procedure can interfere with the results of the scan.

Description

The gallbladder is a small pear-shaped sac located under the liver. The liver produces bile, a yellowish-green mixture of salts, acids, and other chemicals, that are stored in the gallbladder. Bile is secreted into the small intestine to help the body digest fats from foods.

Gallbladder disease, gallstones, **cancer**, or other abnormalities can cause **pain** and other symptoms. A gallbladder condition might be suspected if a patient has chronic or occasional pain in the upper right side of the abdomen. The pain may be stabbing and intense with sudden onset or it may be more of a dull, occasional ache. Loss of appetite, **nausea and vomiting** can also occur. **Fever** may indicate the presence of infection. **Jaundice**, a yellowing of the skin and whites of the eyes, may also indicate that the gallbladder is involved.

A gallbladder nuclear medicine scan may be used to diagnose gallstones, blockage of the bile duct or other abnormalities, and to assess gallbladder functioning and inflammation (**cholecystitis**). The scan is usually performed in a hospital or clinical radiology department. The patient lies on an examination table while a small amount of radioactive dye is injected into a vein in the arm. This dye circulates through the blood and collects in the gallbladder. As the dye moves through the gallbladder, a series of pictures is taken using a special camera called a *scintillation* or *gamma camera*. This procedure produces images that look like x rays. The test usually takes one to two hours to complete, but can last up to four hours.

The results of the scan are read by a radiologist, a doctor specializing in x rays and other types of scanning techniques. A report is sent, usually within 24 hours, to the doctor who will discuss the results with the patient.

Preparation

The patient may be required to withhold food and liquids for up to eight hours before the scan.

Aftercare

No special care is required after the procedure. Once the scan is complete, the patient can return to normal activities.

Risks

Nuclear medicine scans use a very small amount of radioactive material, and the risk of radiation is minimal. Very rarely, a patient may have a reaction to the dye material used.

Normal results

A normal scan shows a gallbladder without gallstones. There will be no evidence of growths or tumors, and no signs of infection or swelling. The normal gall-

bladder fills with bile and secretes it through the bile duct without blockages.

Abnormal results

An abnormal scan may show abnormal gallbladder emptying (suggesting gallbladder dysfunction or inflammation), or gallstones in the gallbladder or in the bile duct. The presence of tumors, growths or other types of blockages of the duct or the gallbladder itself could also appear on an abnormal scan.

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Altha Roberts Edgren

Gallbladder surgery *see* **Cholecystectomy**

Gallbladder x rays

Definition

This is an x-ray exam of the gallbladder (GB), a sac-like organ that stores bile that is located under the liver. The study involves taking tablets containing dye (contrast) which outline any abnormalities when x rays are taken the following day. The test was once the standard for diagnosing diseases of the GB such as **gallstones**, but is used less frequently now. This is due to advances in diagnostic ultrasound, which is quick, accurate and doesn't involve exposure to ionizing radiation. When functional parameters of the gallbladder need to be demonstrated, scintigraphy is now the study of choice. OCG, however, can be useful when a gallbladder is contracted down due to the presence of many, many gallstones. It can also help determine whether the cystic duct is clear, prior to surgical procedures such as **lithotripsy**. OCG may also be used to evaluate gallbladder disease that doesn't involve gallstones, such as adenomyomatosis of the gallbladder or cholesterolosis of the gallbladder.

Purpose

This test, also known as an oral cholecystogram or OCG, is usually ordered to help physicians diagnose disorders of the gallbladder, such as gallstones and tumors, which show up as solid dark structures. It is performed to help in the investigation of patients with upper abdominal **pain**. The test also measures gallbladder function, as the failure of the organ to visualize can signify a non-functioning or diseased gallbladder. The gallbladder may also not visualize if the bilirubin level is over 4 and the study should not be performed under these circumstances.

Precautions

Your physician must be notified if you are pregnant or allergic to iodine. Patients with a history of severe kidney damage, have an increased risk of injury or side effects from the procedure. In those cases, ultrasound is commonly used instead of the x-ray examination. Some people experience side effects from the contrast material (dye tablets), especially **diarrhea**. During preparation for the test, patients should not use any **laxatives**. Diabetics should discuss the need for any adjustment in medication with their physician.

Description

The exam is performed in the radiology department. The night before the test, patients swallow six tablets (one at a time) that contain the contrast (x-ray dye). The following day at the hospital, the radiologist examines the gallbladder with a fluoroscope (a special x ray that projects the image onto a video monitor). Sometimes, patients are then asked to drink a highfat formula that will cause the gallbladder to contract and release bile. X rays will then be taken at various intervals. There is no discomfort from the test. If the gallbladder is not seen, the patient may be asked to return the following day for x rays.

Preparation

The day before the test patients are instructed to eat a high fat lunch (eggs, butter, milk, salad oils, or fatty meats), and a fat-free meal (fruits, vegetables, bread, tea or coffee, and only lean meat) in the evening. Two hours after the evening meal, six tablets containing the contrast medium, are taken, one a time. After that, no food or fluid is permitted until after the test.

Aftercare

No special care is required after the study.

KEY TERMS

Bile—A yellow-green liquid produced by the liver, which is released through the bile ducts into the small intestines to help digest fat.

Bilirubin—A reddish-yellow pigment formed from the destruction of red blood cells, and metabolized by the liver. Levels of bilirubin in the blood increase in patients with liver disease or blockage of the bile ducts.

Ultrasound—A non-invasive procedure based on changes in sound waves of a frequency that cannot be heard, but respond to changes in tissue composition. It requires no preparation and no radiation occurs; it has become the "gold standard" for diagnosis of stones in the gallbladder, but is less accurate in diagnosing stones in the bile ducts. Gallstones as small as 2 mm can be identified.

Risks

There is a small chance of an allergic reaction to the contrast material. In addition, there is low radiation exposure. X rays are monitored and regulated to provide the minimum amount of radiation exposure needed to produce the image. Most experts feel that the risk is low compared with the benefits. Pregnant women and children are more sensitive to the risks of x rays, and the risk versus benefits should be discussed with the treating physician.

Normal results

The x ray will show normal structures for the age of the patient. The gallbladder should visualize, and be free of any solid structures, such as stones, polyps, etc.

Abnormal results

Abnormal results may show gallstones, tumors, or cholesterol polyps (a tumor growing from the lining that is usually noncancerous). Typically stones will "float" or move around as the patient changes position, whereas tumors will stay in the same place.

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Rosalyn Carson-DeWitt, MD

Gallium scan of the body

Definition

A gallium scan of the body is a nuclear medicine test that is conducted using a camera that detects gallium, a form of radionuclide, or radioactive chemical substance.

Purpose

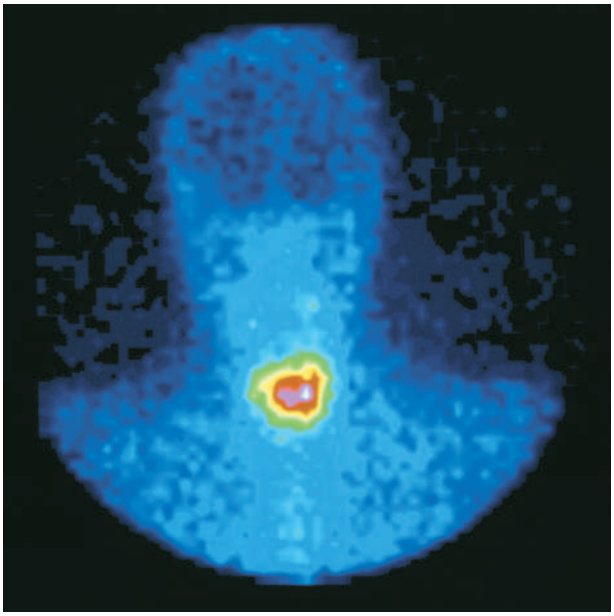
Most gallium scans are ordered to detect cancerous tumors, infections, or areas of inflammation in the body. Gallium is known to accumulate in inflamed, infected, or cancerous tissues. The scans are used to determine whether a patient with an unexplained **fever** has an infection and the site of the infection, if present. Gallium scans also may be used to evaluate **cancer** following **chemotherapy** or **radiation therapy**.

Precautions

Children and women who are pregnant or breast-feeding are only given gallium scans if the potential diagnostic benefits will outweigh the risks.

Description

The patient will usually be asked to come to the testing facility 24–48 hours before the procedure to receive the injection of gallium. Sometimes, the injection will be given only four to six hours before the study or as long as 72 hours before the procedure. The timeframe is based on the area or organs of the body being studied.



Gallium scan highlighting the thyroid gland. *(Photo Researchers. Reproduced by permission.)*

For the study itself the patient lies very still for approximately 30–60 minutes. A camera is moved across the patient's body to detect and capture images of concentrations of the gallium. The camera picks up signals from any accumulated areas of the radionuclide. In most cases, the patient is lying down throughout the procedure. Back (posterior) and front (anterior) views will usually be taken, and sometimes a side (lateral) view is used. The camera may occasionally touch the patient's skin, but will not cause any discomfort. A clicking noise may be heard throughout the procedure; this is only the sound of the scanner registering radiation.

Preparation

The intravenous injection of gallium is done in a separate appointment prior to the procedure. Generally, no special dietary requirements are necessary. Sometimes the physician will ask that the patient have light or clear meals within a day or less of the procedure. Many patients will be given **laxatives** or an enema prior to the scan to eliminate any residual gallium from the bowels.

Aftercare

There is generally no aftercare required following a gallium scan. However, women who are breastfeeding who have a scan will be cautioned against breastfeeding for four weeks following the exam.

Risks

There is a minimal risk of exposure to radiation from the gallium injection, but the exposure from one gallium scan is generally less than exposure from x rays.

Normal results

A radiologist trained in nuclear medicine or a nuclear medicine specialist will interpret the exam results and compare them to other diagnostic tests. It is normal for gallium to accumulate in the liver, spleen, bones, breast tissue, and large bowel.

Abnormal results

An abnormal concentration of gallium in areas other than those where it normally concentrates may indicate the presence of disease. Concentrations may be due to inflammation, infection, or the presence of tumor tissue. Often, additional tests are required to determine if the tumors are malignant (cancerous) or benign.

Even though gallium normally concentrates in organs such as the liver or spleen, abnormally high concentrations will suggest certain diseases and conditions. For example, Hodgkin's or non-Hodgkin's lymphoma may be diagnosed or staged if there is abnormal gallium activity in the lymph nodes. After a patient receives cancer treatment, such as radiation therapy or chemotherapy, a gallium scan may help to find new or recurring tumors or to record regression of a treated tumor. Physicians can narrow causes of liver problems by noting abnormal gallium activity in the liver. Gallium scans also may be used to diagnose lung diseases or a disease called **sarcoidosis**, in the chest.

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American College of Nuclear Medicine. PO Box 175, Landisville, PA 31906. (717) 898-6006.

American Liver Foundation. 1425 Pompton Avenue, Cedar Grove NJ 07009. (800) GO LIVER (465-4837). <http://www.liverfoundation.org>.

Society of Nuclear Medicine. 1850 Samuel Morse Drive, Reston, VA 10016. (703) 708-9000. <http://www.snm.org>.

KEY TERMS

Benign—Not cancerous. Benign tumors are not considered immediate threats, but may still require some form of treatment.

Gallium—A form of radionuclide that is used to help locate tumors and inflammation (specifically referred to as GA67 citrate).

Malignant—This term, usually used to describe a tumor, means cancerous, becoming worse and possibly growing.

Nuclear medicine—A subspecialty of radiology used to show the function and anatomy of body organs. Very small amounts of radioactive substances, or tracers, are detected with a special camera as they accumulate in certain organs and tissues.

Radionuclide—A chemical substance, called an isotope, that exhibits radioactivity. A gamma camera, used in nuclear medicine procedures, will pick up the radioactive signals as the substance gathers in an organ or tissue. They are sometimes referred to as tracers.

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Teresa G. Norris

Gallstone removal

Definition

Also known as cholelithotomy, gallstone removal is the medical procedure that rids the gallbladder of calculus buildup.

Purpose

The gallbladder is not a vital organ. Its function is to store bile, concentrate it, and release it during digestion. Bile is supposed to retain all of its chemicals in solution, but commonly one of them crystallizes and forms sand, gravel, and finally stones.

The chemistry of **gallstones** is complex and interesting. Like too much sugar in solution, chemicals in bile will form crystals as the gallbladder draws water out of the bile. The solubility of these chemicals is based on the concentration of three chemicals, not just one—bile acids, phospholipids, and cholesterol. If the chemicals are out of balance, one or the other will not remain in solution. Certain people, in particular the Pima tribe of Native Americans in Arizona, have a genetic predisposition to forming gallstones. Scandinavians also have a higher than average incidence of this disease. Dietary fat and cholesterol are also implicated in their formation. Overweight women in their middle years constitute the vast majority of patients with gallstones in every group.

As the bile crystals aggregate to form stones, they move about, eventually occluding the outlet and preventing the gallbladder from emptying. This creates symptoms. It also results in irritation, inflammation, and sometimes infection of the gallbladder. The pattern is usually one of intermittent obstruction due to stones moving in and out of the way. All the while the gallbladder is becoming more scarred. Sometimes infection fills it with pus—a serious complication.

On occasion a stone will travel down the cystic duct into the common bile duct and get stuck there. This will back bile up into the liver as well as the gallbladder. If the stone sticks at the Ampulla of Vater, the pancreas will also be plugged and will develop **pancreatitis**. These stones can cause a lot of trouble.

Bile is composed of several waste products of metabolism, all of which are supposed to remain in liquid form. The complex chemistry of the liver depends on many chemical processes, which depend in turn upon the chemicals in the diet and the genes that direct those processes. There are greater variations in the output of chemical waste products than there is allowance for their cohabitation in the bile. Incompatible mixes result in the formation of solids.

Gallstones will cause the sudden onset of **pain** in the upper abdomen. Pain will last for 30 minutes to several hours. Pain may move to the right shoulder blade. Nausea with or without vomiting may accompany the pain.

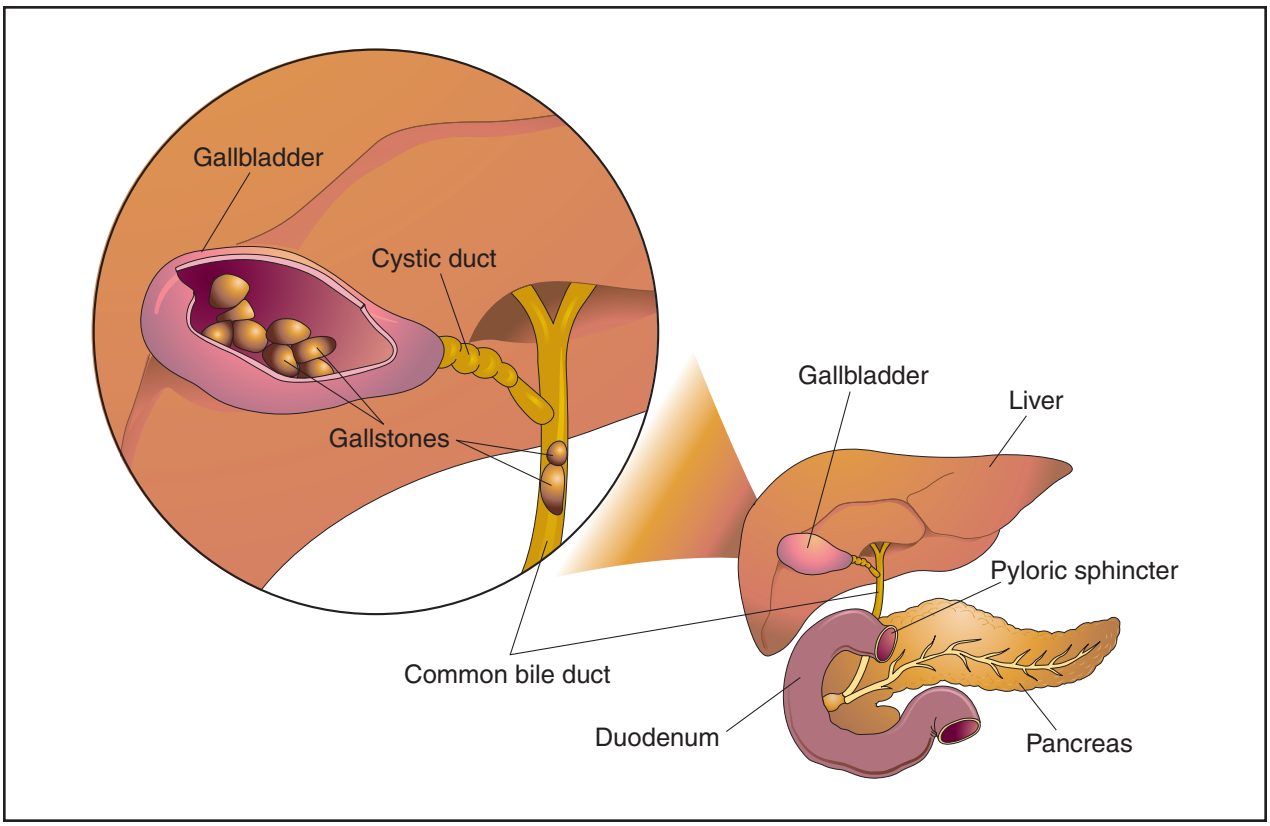
Precautions

Individuals suffering from sickle cell anemia, children, and patients with large stones may seek other treatments.

Description

Laparoscopic cholecystectomy

Surgery to remove the entire gallbladder with all its stones is usually the best treatment, provided the patient



Gallstone removal, also known as cholelithotomy, usually involves the surgical removal of the entire gallbladder, but in recent years the procedure done by laparoscopy has resulted in smaller surgical incisions and faster recovery time. *(Illustration by Electronic Illustrators Group.)*

is able to tolerate the procedure. Over the past decade, a new technique of removing the gallbladder using a laparoscope has resulted in quicker recovery and much smaller surgical incisions than the six-inch gash under the right ribs that used to be standard. Not everyone is a candidate for this approach.

If a stone is lodged in the bile ducts, additional surgery must be done to remove it. After surgery, the surgeon will ordinarily leave in a drain to collect bile until the system is healed. The drain can also be used to inject contrast material and take x rays during or after surgery.

Endoscopic retrograde cholangiopancreatoscopy (ERCP)

A procedure called endoscopic retrograde cholangiopancreatoscopy (ERCP) allows the removal of some bile duct stones through the mouth, throat, esophagus, stomach, duodenum, and biliary system without the need for surgical incisions. ERCP can also be used to inject contrast agents into the biliary system, providing superbly detailed pictures.

Cholelithotomy

Rare circumstances require different techniques. Patients too ill for a complete **cholecystectomy** (removal of the gallbladder), sometimes only the stones are removed, a procedure called cholelithotomy. But that does not cure the problem. The liver will go on making faulty bile, and stones will reform, unless the composition of the bile is altered.

Ursodeoxycholic acid

For patients who cannot receive the laparoscopic procedure, there is also a nonsurgical treatment in which ursodeoxycholic acid is used to dissolve the gallstones. Extracorporeal shock-wave **lithotripsy** has also been successfully used to break up gallstones. During the procedure, high-amplitude sound waves target the stones, slowly breaking them up.

Preparation

There are a number of imaging studies that identify gallbladder disease, but most gallstones will not show up

KEY TERMS

Cholecystectomy—Surgical removal of the gallbladder.

Cholelithotomy—Surgical incision into the gallbladder to remove stones.

Contrast agent—A substance that causes shadows on x rays (or other images of the body).

Endoscope—One of several instruments designed to enter body cavities. They combine viewing and operating capabilities.

Jaundice—A yellow color of the skin and eyes due to excess bile that is not removed by the liver.

Laparoscopy—Surgery through pencil-sized viewing instruments and tools so that incisions need be less than half an inch long.

on conventional x rays. That requires contrast agents given by mouth that are excreted into the bile. Ultrasound is very useful and can be enhanced by doing it through an endoscope in the stomach. CT (**computed tomography scans**) and MRI (**magnetic resonance imaging**) scanning are not used routinely but are helpful in detecting common duct stones and complications.

Aftercare

Without a gallbladder, stones rarely reform. Patients who have continued symptoms after their gallbladder is removed may need an ERCP to detect residual stones or damage to the bile ducts caused by the stones before they were removed. Once in a while the Ampulla of Vater is too tight for bile to flow through and causes symptoms until it is opened up.

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J. Ricker Polsdorfer, MD

Gallstones

Definition

A gallstone is a solid crystal deposit that forms in the gallbladder, which is a pear-shaped organ that stores bile salts until they are needed to help digest fatty foods. Gallstones can migrate to other parts of the digestive tract and cause severe **pain** with life-threatening complications.

Description

Gallstones vary in size and chemical structure. A gallstone may be as tiny as a grain of sand or as large as a golf ball. Eighty percent of gallstones are composed of cholesterol. They are formed when the liver produces more cholesterol than digestive juices can liquefy. The remaining 20% of gallstones are composed of calcium and an orange-yellow waste product called bilirubin. Bilirubin gives urine its characteristic color and sometimes causes **jaundice**.

Gallstones are the most common of all gallbladder problems. They are responsible for 90% of gallbladder and bile duct disease, and are the fifth most common reason for hospitalization of adults in the United States. Gallstones usually develop in adults between the ages of 20 and 50; about 20% of patients with gallstones are over 40. The risk of developing gallstones increases with age—at least 20% of people over 60 have a single large stone or as many as several thousand smaller ones. The gender ratio of gallstone patients changes with age. Young women are between two and six times more likely to develop gallstones than men in the same age group. In patients over 50, the condition affects men and women with equal frequency. Native Americans develop gallstones more often than any other segment of the population; Mexican-Americans have the second-highest incidence of this disease.

Definitions

Gallstones can cause several different disorders. Cholelithiasis is defined as the presence of gallstones within the gallbladder itself. Choledocholithiasis is the presence of gallstones within the common bile duct that leads into the first portion of the small intestine (the duodenum). The stones in the duct may have been formed inside it or carried there from the gallbladder. These gallstones prevent bile from flowing into the duodenum. Ten percent of patients with gallstones have choledocholithiasis, which is sometimes called common-duct stones. Patients who don't develop infection usually recover completely from this disorder.

Cholecystitis is a disorder marked by inflammation of the gallbladder. It is usually caused by the passage of a stone from the gallbladder into the cystic duct, which is a tube that connects the gallbladder to the common bile duct. In 5–10% of cases, however, cholecystitis develops in the absence of gallstones. This form of the disorder is called acalculous cholecystitis. Cholecystitis causes painful enlargement of the gallbladder and is responsible for 10–25% of all gallbladder surgery. Chronic cholecystitis is most common in the elderly. The acute form is most likely to occur in middle-aged adults.

Cholesterolosis or cholesterol polyps is characterized by deposits of cholesterol crystals in the lining of the gallbladder. This condition may be caused by high levels of cholesterol or inadequate quantities of bile salts, and is usually treated by surgery.

Gallstone **ileus**, which results from a gallstone's blocking the entrance to the large intestine, is most common in elderly people. Surgery usually cures this condition.

Narrowing (stricture) of the common bile duct develops in as many as 5% of patients whose gallbladders have been surgically removed. This condition is characterized by inability to digest fatty foods and by abdominal pain, which sometimes occurs in spasms. Patients with stricture of the common bile duct are likely to recover after appropriate surgical treatment.

Causes and symptoms

Gallstones are caused by an alteration in the chemical composition of bile. Bile is a digestive fluid that helps the body absorb fat. Gallstones tend to run in families. In addition, high levels of estrogen, insulin, or cholesterol can increase a person's risk of developing them.

Pregnancy or the use of birth control pills can slow down gallbladder activity and increase the risk of gallstones. So can diabetes, **pancreatitis**, and **celiac disease**. Other factors influencing gallstone formation are:

- infection
- obesity
- intestinal disorders
- coronary artery disease or other recent illness
- multiple pregnancies
- a high-fat, low-fiber diet
- smoking
- heavy drinking
- rapid weight loss

Gallbladder attacks usually follow a meal of rich, high-fat foods. The attacks often occur in the middle of the night, sometimes waking the patient with intense pain that ends in a visit to the emergency room. The pain of a gallbladder attack begins in the abdomen and may radiate to the chest, back, or the area between the shoulders. Other symptoms of gallstones include:

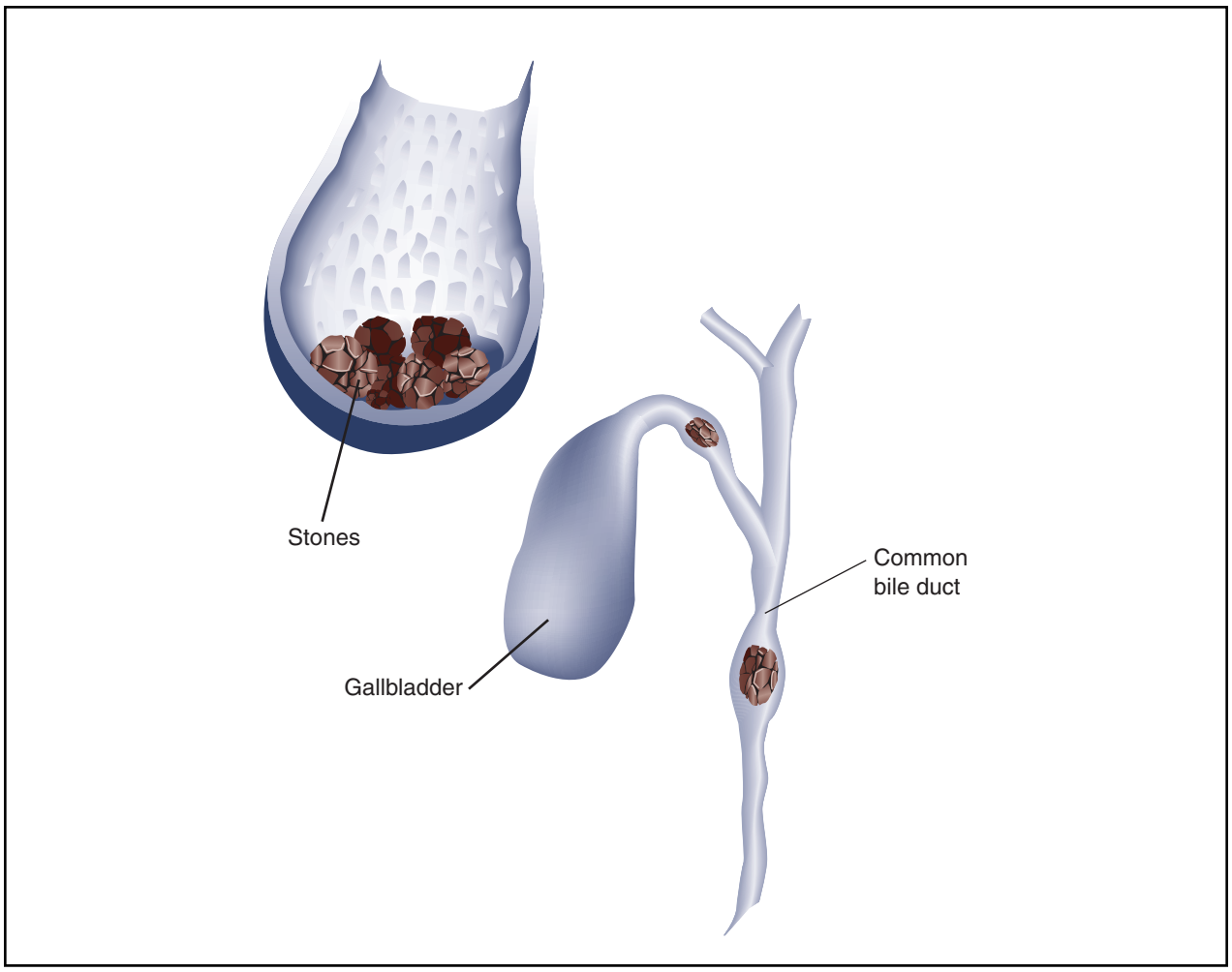
- inability to digest fatty foods
- low-grade **fever**
- chills and sweating
- nausea and vomiting
- indigestion
- gas
- belching.
- clay-colored bowel movements

Diagnosis

Gallstones may be diagnosed by a family doctor, a specialist in digestive problems (a gastroenterologist), or a specialist in internal medicine. The doctor will first examine the patient's skin for signs of jaundice and feel (palpate) the abdomen for soreness or swelling. After the basic **physical examination**, the doctor will order blood counts or blood chemistry tests to detect evidence of bile duct obstruction and to rule out other illnesses that cause fever and pain, including stomach ulcers, **appendicitis**, and heart attacks.

More sophisticated procedures used to diagnose gallstones include:

- Ultrasound imaging. Ultrasound has an accuracy rate of 96%.
- Cholecystography (cholecystogram, gallbladder series, gallbladder x ray). This type of study shows how the gallbladder contracts after the patient has eaten a high-fat meal.
- Fluoroscopy. This imaging technique allows the doctor to distinguish between jaundice caused by pancreatic **cancer** and jaundice caused by gallbladder or bile duct disorders.



Gallstones form in the gallbladder but can migrate to other parts of the body via the bile duct. *(Illustration by Argosy Inc.)*

- Endoscopy (ERCP). ERCP uses a special dye to outline the pancreatic and common bile ducts and locate the position of the gallstones.
- Radioisotopic scan. This technique reveals blockage of the cystic duct.

Treatment

Watchful waiting

One-third of all patients with gallstones never experience a second attack. For this reason many doctors advise watchful waiting after the first episode. Reducing the amount of fat in the diet or following a sensible plan of gradual weight loss may be the only treatments required for occasional mild attacks. A patient diagnosed with gallstones may be able to manage more troublesome episodes by:

- applying heat to the affected area
- resting and taking occasional sips of water
- using non-prescription forms of **acetaminophen** (Tylenol or Anacin-3)

A doctor should be notified if pain intensifies or lasts for more than three hours; if the patient's fever rises above 101°F (38.3°C); or if the skin or whites of the eyes turn yellow.

Surgery

Surgical removal of the gallbladder (**cholecystectomy**) is the most common conventional treatment for recurrent attacks. Laparoscopic surgery, the technique most widely used, is a safe, effective procedure that involves less pain and a shorter recovery period than traditional open surgery. In this technique, the doctor makes a small cut (incision) in the patient's abdomen and removes the gallbladder through a long tube called a laparoscope.

KEY TERMS

Acalculous cholecystitis—Inflammation of the gallbladder that occurs without the presence of gallstones.

Bilirubin—A reddish-yellow waste product produced by the liver that colors urine and is involved in the formation of some gallstones.

Celiac disease—Inability to digest wheat protein (gluten), which causes weight loss, lack of energy, and pale, foul-smelling stools.

Cholecystectomy—Surgical removal of the gallbladder.

Cholecystitis—Inflammation of the gallbladder.

Choledocholithiasis—The presence of gallstones within the common bile duct.

Cholelithiasis—The presence of gallstones within the gallbladder.

Cholesterolosis—Cholesterol crystals or deposits in the lining of the gallbladder.

Common bile duct—The passage through which bile travels from the cystic duct to the small intestine.

Gallstone ileus—Obstruction of the large intestine caused by a gallstone that has blocked the intestinal opening.

Lithotripsy—A nonsurgical technique for removing gallstones by breaking them apart with high-frequency sound waves.

Nonsurgical approaches

LITHOTRIPSY. Shock wave therapy (**lithotripsy**) uses high-frequency sound waves to break up the gallstones. The patient can then take bile salts to dissolve the fragments. Bile salt tablets are sometimes prescribed without lithotripsy to dissolve stones composed of cholesterol by raising the level of bile acids in the gallbladder. This approach requires long-term treatment, since it may take months or years for this method to dissolve a sizeable stone.

CONTACT DISSOLUTION. Contact dissolution can destroy gallstones in a matter of hours. This minimally invasive procedure involves using a tube (catheter) inserted into the abdomen to inject medication directly into the gallbladder.

Alternative treatment

Alternative therapies, like non-surgical treatments, may provide temporary relief of gallstone symptoms. Alternative approaches to the symptoms of gallbladder disorders include **homeopathy**, Chinese traditional herbal medicine, and **acupuncture**. Dietary changes may also help relieve the symptoms of gallstones. Since gallstones seem to develop more often in people who are obese, eating a balanced diet, exercising, and losing weight may help keep gallstones from forming.

Prognosis

Forty percent of all patients with gallstones have "silent gallstones" that produce no symptoms. Silent stones, discovered only when their presence is indicated by tests performed to diagnose other symptoms, do not require treatment.

Gallstone problems that require treatment can be surgically corrected. Although most patients recover, some develop infections that must be treated with **antibiotics**.

In rare instances, severe inflammation can cause the gallbladder to burst. The resulting infection can be fatal.

Prevention

The best way to prevent gallstones is to minimize risk factors. In addition, a 1998 study suggests that vigorous **exercise** may lower a man's risk of developing gallstones by as much as 28%. The researchers have not yet determined whether physical activity benefits women to the same extent.

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National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). Building 31, Room 9A04, 31 Center Drive, MSC 2560, Bethesda, MD 208792-2560. (301) 496-3583. <http://www.niddk.nih.gov>.

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Maureen Haggerty

Gamete intrafallopian transfer *see* **Infertility therapies**

Gamma-glutamyl transferase test *see* **Liver function tests**

Gammaglobulin

KEY TERMS

Hepatitis—Inflammation of the liver caused by a virus, chemical or drugs. There are several different types of hepatitis, including the most common forms: hepatitis A, hepatitis B, and hepatitis C.

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

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

Definition

Gammaglobulin is a type of protein found in the blood. When gammaglobulins are extracted from the blood of many people and combined, they can be used to prevent or treat infections.

Purpose

This medicine is used to treat or prevent diseases that occur when the body's own immune system is not effective against the disease. When disease-causing agents enter the body, they normally trigger the production of antibodies, proteins that circulate in the blood and help fight the disease. Gammaglobulin contains some of these antibodies. When gammaglobulins are taken from the blood of people who have recovered from diseases such as **chickenpox** or hepatitis, they can be given to other people to make them temporarily immune to those diseases. With hepatitis, for example, this is done when someone who has not been vaccinated against hepatitis is exposed to the disease.

Description

Gammaglobulin, also known as immunoglobulin, immune serum globulin or serum therapy, is injected either into a vein or into a muscle. When injected into a vein, it produces results more quickly than when injected into a muscle.

Recommended dosage

Doses are different for different people and depend on the person's body weight and the condition for which he or she is being treated.

Precautions

Anyone who has had unusual reactions to gammaglobulin 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.

People who have certain medical conditions may have problems if they take gammaglobulins. For example:

- Gammaglobulins may worsen heart problems or deficiencies of immunoglobin A (IgA, a type of antibody)
- Certain patients with low levels of gammaglobulins in the blood (conditions called agammaglobulinemia and hypogammaglobulinemia) may be more likely to have side effects when they take gammaglobulin.

Side effects

Minor side effects such as **headache**, backache, joint or muscle **pain**, and a general feeling of illness usually go away as the body adjusts to this medicine. These problems do not need medical attention unless they continue.

Other side effects, such as breathing problems or a fast or pounding heartbeat, should be brought to a physician's attention as soon as possible.

Anyone who shows the following signs of overdose should check with a physician immediately:

- unusual tiredness or weakness

- dizziness
- nausea
- vomiting
- fever
- chills
- tightness in the chest
- red face
- sweating

Interactions

Anyone who takes gammaglobulin should let the physician know all other medicines he or she is taking and should ask whether interactions with gammaglobulin could interfere with treatment.

Nancy Ross-Flanigan

Ganglion

Definition

A ganglion is a small, usually hard bump above a tendon or in the capsule that encloses a joint. A ganglion is also called a synovial **hernia** or synovial cyst.

Description

A ganglion is a non-cancerous cyst filled with a thick, jelly-like fluid. Ganglions can develop on or beneath the surface of the skin and usually occur between the ages of 20 and 40.

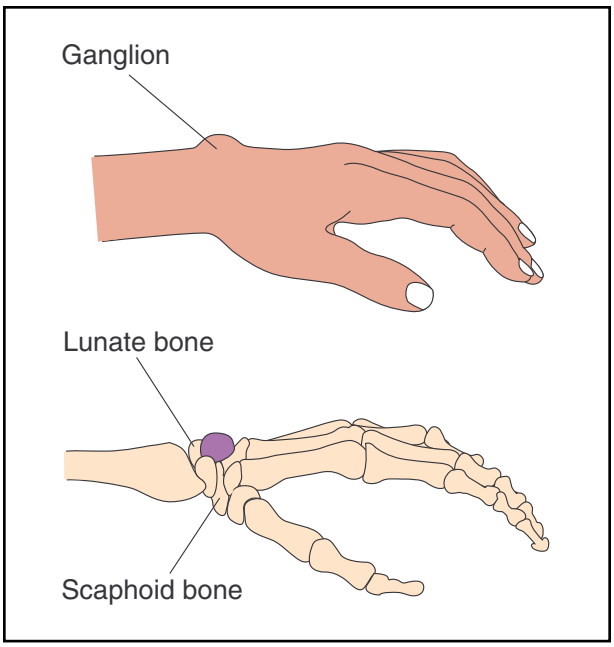
Most ganglions develop on the hand or wrist. This condition is common in people who bowl or who play handball, raquetball, squash, or tennis. Runners and athletes who jump, ski, or play contact sports often develop foot ganglions.

Causes and symptoms

Mild sprains or other repeated injuries can irritate and tear the thin membrane covering a tendon, causing fluid to leak into a sac that swells and forms a ganglion.

Ganglions are usually painless, but range of motion may be impaired. Flexing or bending the affected area can cause discomfort, as can continuing to perform the activity that caused the condition.

Cysts on the surface of the skin usually develop slowly but may result from injury or severe strain. An internal ganglion can cause soreness or a dull, aching sensation, but the mass cannot always be felt. Symptoms sometimes become evident only when the cyst causes pressure on a nerve or outgrows the membrane surrounding it.



A ganglion is a non-cancerous cyst filled with a thick, jelly-like fluid. Ganglions can develop on or beneath the surface of the skin, most likely on the hand or wrist, although runners and skiers often develop them on the foot. *(Illustration by Electronic Illustrators Group.)*

Diagnosis

Diagnosis is usually made through **physical examination** as well as such imaging studies as x ray, ultrasound, and **magnetic resonance imaging** (MRI). Fluid may be withdrawn from the cyst and evaluated.

Treatment

Some ganglions disappear without treatment, and some reappear despite treatment.

Acetaminophen (Tylenol) or other over-the-counter **analgesics** can be used to control mild **pain**. Steroids or local anesthetics may be injected into cysts that cause severe pain or other troublesome symptoms. Surgery performed in a hospital operating room or an outpatient facility, is the only treatment guaranteed to remove a ganglion. The condition can recur if the entire cyst is not removed.

A doctor should be notified if the surgical site drains, bleeds, or becomes

- inflamed

• painful

• swollen or if the patient feels ill or develops:

• head or muscle aches

• dizziness

• fever following surgery

The patient may bathe or shower as usual, but should keep the surgical site dry and covered with a bandage for two or three days after the operation. Patients may resume normal activities as soon as they feel comfortable doing so.

Prognosis

Possible complications include excessive post-operative bleeding and infection of the surgical site. Calcification, or hardening, of the ganglion is rare.

Prevention

Exercises that increase muscle strength and flexibility can prevent ganglions. Warming and cooling down before and after workouts may also decrease the rate of developing ganglions.

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Maureen Haggerty

Gangrene

Definition

Gangrene is the term used to describe the decay or **death** of an organ or tissue caused by a lack of blood supply. It is a complication resulting from infectious or inflammatory processes, injury, or degenerative changes associated with chronic diseases, such as **diabetes mellitus**.

Description

Gangrene may be caused by a variety of chronic diseases and post-traumatic, post-surgical, and spontaneous causes. There are three major types of gangrene: dry, moist, and gas (a type of moist gangrene).

Dry gangrene is a condition that results when one or more arteries become obstructed. In this type of gangrene, the tissue slowly dies, due to receiving little or no blood supply, but does not become infected. The affected area becomes cold and black, begins to dry out and wither, and eventually drops off over a period of weeks or months. Dry gangrene is most common in persons with advanced blockages of the arteries (arteriosclerosis) resulting from diabetes.

Moist gangrene may occur in the toes, feet, or legs after a crushing injury or as a result of some other factor that causes blood flow to the area to suddenly stop. When blood flow ceases, bacteria begin to invade the muscle and thrive, multiplying quickly without interference from the body's immune system.

Gas gangrene, also called myonecrosis, is a type of moist gangrene that is commonly caused by bacterial infection with *Clostridium welchii, Cl. perfringes, Cl. septicum, Cl. novyi, Cl. histolyticum, Cl. sporogenes*, or other species that are capable of thriving under conditions where there is little oxygen (anaerobic). Once present in tissue, these bacteria produce gasses and poisonous toxins as they grow. Normally inhabiting the gastrointestinal, respiratory, and female genital tract, they often infect thigh **amputationwounds**, especially in those individuals who have lost control of their bowel functions (incontinence). Gangrene, incontinence, and debility often are combined in patients with diabetes, and it is in the amputation stump of diabetic patients that gas gangrene is often found to occur.

Other causative organisms for moist gangrene include various bacterial strains, including *Streptococcus* and *Staphylococcus*. A serious, but rare form of infection with Group A *Streptococcus* can impede blood flow and, if untreated, can progress to synergistic gangrene, more commonly called necrotizing fasciitis, or infection of the skin and tissues directly beneath the skin.

Chronic diseases, such as diabetes mellitus, arteriosclerosis, or diseases affecting the blood vessels, such as **Buerger's disease** or **Raynaud's disease**, can cause gangrene. Post-traumatic causes of gangrene include compound **fractures**, **burns**, and injections given under the skin or in a muscle. Gangrene may occur following surgery, particularly in individuals with diabetes mellitus or other long-term (chronic) disease. In addition, gas gangrene can be also be a complication of dry gangrene or occur spontaneously in association with an underlying **cancer**.

In the United States, approximately 50% of moist gangrene cases are the result of a severe traumatic injury,

A close-up of gangrene in the toes of a diabetic patient. *(Photo Researchers, Inc. Reproduced by permission.)*

and 40% occur following surgery. Car and industrial accidents, crush injuries, and gunshot wounds are the most common traumatic causes. Because of prompt surgical management of wounds with the removal of dead tissue, the incidence of gangrene from trauma has significantly diminished. Surgeries involving the bile ducts or intestine are the most frequent procedures causing gangrene. Approximately two-thirds of cases affect the extremities, and the remaining one-third involve the abdominal wall.

Symptoms

Areas of either dry or moist gangrene are initially characterized by a red line on the skin that marks the border of the affected tissues. As tissues begin to die, dry gangrene may cause some **pain** in the early stages or may go unnoticed, especially in the elderly or in those individuals with diminished sensation to the affected area. Initially, the area becomes cold, numb, and pale before later changing in color to brown, then black. This dead tissue will gradually separate from the healthy tissue and fall off.

Moist gangrene and gas gangrene are distinctly different. Gas gangrene does not involve the skin as much, but usually only the muscle. In moist or gas gangrene, there is a sensation of heaviness in the affected region that is followed by severe pain. The pain is caused by swelling resulting from fluid or gas accumulation in the tissues. This pain peaks, on average, between one to four days following the injury, with a range of eight hours to several weeks. The swollen skin may initially be blistered, red, and warm to the touch before progressing to a bronze, brown, or black color. In approximately 80% of cases, the affected and surrounding tissues may produce crackling sounds (crepitus), as a result of gas bubbles accumulating under the skin. The gas may be felt beneath the skin (palpable). In wet gangrene, the pus is foul-smelling, while in gas gangrene, there is no true pus, just an almost "sweet" smelling watery discharge.

Fever, rapid heart rate, rapid breathing, altered mental state, loss of appetite, **diarrhea**, vomiting, and vascular collapse may also occur if the bacterial toxins are allowed to spread in the bloodstream. Gas gangrene can be a life-threatening condition and should receive prompt medical attention

Diagnosis

A diagnosis of gangrene will be based on a combination of the patient history, a **physical examination**, and the results of blood and other laboratory tests. A physician will look for a history of recent trauma, surgery, cancer, or chronic disease. Blood tests will be used to determine whether infection is present and determine the extent to which an infection has spread.

A sample of drainage from a wound, or obtained through surgical exploration, may be cultured with oxygen (aerobic) and without oxygen (anaerobic) to identify the microorganism causing the infection and to aid in determining which antibiotic will be most effective. The sample obtained from a person with gangrene will contain few, if any, white blood cells and, when stained (with Gram stain) and examined under the microscope, will show the presence of purple (Gram positive), rod-shaped bacteria.

X ray studies and more sophisticated imaging techniques, such as **computed tomography scans** (CT) or **magnetic resonance imaging** (MRI), may be helpful in making a diagnosis since gas accumulation and muscle death (myonecrosis) may be visible. These techniques, however, are not sufficient alone to provide an accurate diagnosis of gangrene.

Precise diagnosis of gas gangrene often requires surgical exploration of the wound. During such a procedure, the exposed muscle may appear pale, beefy-red, or in the most advanced stages, black. If infected, the muscle will fail to contract with stimulation, and the cut surface will not bleed.

Treatment

Gas gangrene is a medical emergency because of the threat of the infection rapidly spreading via the bloodstream and infecting vital organs. It requires immediate surgery and administration of **antibiotics**.

Areas of dry gangrene that remain free from infection (aseptic) in the extremities are most often left to wither and fall off. Treatments applied to the wound externally (topically) are generally not effective without adequate

blood supply to support wound healing. Assessment by a vascular surgeon, along with x rays to determine blood supply and circulation to the affected area, can help determine whether surgical intervention would be beneficial.

Once the causative organism has been identified, moist gangrene requires the prompt initiation of intravenous, intramuscular, and/or topical broad-spectrum antibiotic therapy. In addition, the infected tissue must be removed surgically (**debridement**), and amputation of the affected extremity may be necessary. Pain medications (**analgesics**) are prescribed to control discomfort. Intravenous fluids and, occasionally, blood transfusions are indicated to counteract **shock** and replenish red blood cells and electrolytes. Adequate hydration and **nutrition** are vital to wound healing.

Although still controversial, some cases of gangrene are treated by administering oxygen under pressure greater than that of the atmosphere (hyperbaric) to the patient in a specially designed chamber. The theory behind using hyperbaric oxygen is that more oxygen will become dissolved in the patient's bloodstream, and therefore, more oxygen will be delivered to the gangrenous areas. By providing optimal oxygenation, the body's ability to fight off the bacterial infection are believed to be improved, and there is a direct toxic effect on the bacteria that thrive in an oxygen-free environment. Some studies have shown that the use of hyperbaric oxygen produces marked pain relief, reduces the number of amputations required, and reduces the extent of surgical debridement required. Patients receiving hyperbaric oxygen treatments must be monitored closely for evidence of oxygen toxicity. Symptoms of this toxicity include slow heart rate, profuse sweating, ringing in the ears, **shortness of breath**, **nausea and vomiting**, twitching of the lips/cheeks/eyelids/nose, and convulsions.

The emotional needs of the patient must also be met. The individual with gangrene should be offered moral support, along with an opportunity to share questions and concerns about changes in body image. In addition, particularly in cases where amputation was required, physical, vocational, and **rehabilitation** therapy will also be required.

KEY TERMS

Aerobic—Organism that grows and thrives only in environments containing oxygen.

Anaerobic—Organism that grows and thrives in an oxygen-free environment.

Arteriosclerosis—Build-up of fatty plaques within the arteries that can lead to the obstruction of blood flow.

Aseptic—Without contamination with bacteria or other microorganisms.

Crepitus—A crackling sound.

Gram stain—A staining procedure used to visualize and classify bacteria. The Gram stain procedure allows the identification of purple (Gram positive) organisms and red (Gram negative) organisms.

Hyperbaric oxygen—Medical treatment in which oxygen is administered in specially designed chambers, under pressures greater than that of the atmosphere, in order to treat specific medical conditions.

Incontinence—A condition characterized by the inability to control urination or bowel functions.

Myonecrosis—The destruction or death of muscle tissue.

Sepsis—The spreading of an infection in the bloodstream.

Thrombosis—The formation of a blood clot in a vein or artery that may obstruct local blood flow or may dislodge, travel downstream, and obstruct blood flow at a remote location.

Prognosis

Except in cases where the infection has been allowed to spread through the blood stream, prognosis is generally favorable. Anaerobic wound infection can progress quickly from initial injury to gas gangrene within one to two days, and the spread of the infection in the blood stream is associated with a 20–25% mortality rate. If recognized and treated early, however, approximately 80% of those with gas gangrene survive, and only 15–20% require any form of amputation. Unfortunately, the individual with dry gangrene most often has multiple other health problems that complicate recovery, and it is usually those other system failures that can prove fatal.

Prevention

Patients with diabetes or severe arteriosclerosis should take particular care of their hands and feet because of the risk of infection associated with even a minor injury. Education about proper **foot care** is vital. Diminished blood flow as a result of narrowed vessels will not lessen the body's defenses against invading bacteria. Measures taken towards the reestablishment of circulation are recommended whenever possible. Any abrasion, break in the skin, or infection tissue should be cared

for immediately. Any dying or infected skin must be removed promptly to prevent the spread of bacteria.

Penetrating abdominal wounds should be surgically explored and drained, any tears in the intestinal walls closed, and antibiotic treatment begun early. Patients undergoing elective intestinal surgery should receive preventive antibiotic therapy. Use of antibiotics prior to and directly following surgery has been shown to significantly reduce the rate of infection from 20–30% to 4–8%.

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Gas embolism

Definition

Gas **embolism**, also called air embolism, is the presence of gas bubbles in the bloodstream that obstruct circulation.

Description

Gas embolism may occur with decompression from increased pressure; it typically occurs in ascending divers who have been breathing compressed air. If a diver does not fully exhale upon ascent, the air in the lungs expands as the pressure decreases, overinflating the lungs and forcing bubbles of gas (emboli) into the bloodstream. When gas emboli reach the arteries to the brain, the blood blockage causes unconsciousness. Gas embolism is second only to drowning as a cause of **death** among divers.

Gas embolism may also result from trauma or medical procedures such as catheterization and open heart surgery that allow air into the circulatory system.

Causes and symptoms

Gas embolism occurs independent of diving depth; it may occur in as little as 6 ft of water. It is frequently caused by a diver holding his breath during ascent. It may also result from an airway obstruction or other condition that prevents a diver from fully exhaling.

The primary sign of gas embolism is immediate loss of consciousness; it may or may not be accompanied by convulsions.

Diagnosis

Any unconscious diver should be assumed to be the victim of gas embolism, regardless of whether consciousness was lost during or promptly after ascent. A doctor may also find pockets of air in the chest around the lungs and sometimes a collapsed lung from overinflation and rupture. Coughing up blood or a bloody froth around the mouth are visible signs of lung injury.

Treatment

Prompt **recompression treatment** in a hyperbaric (high-pressure) chamber is necessary to deflate the gas bubbles in the bloodstream, dissolve the gases into the blood, and restore adequate oxygenated blood flow to the brain and other organs. Recompression by returning the diver to deeper water will not work, and should not be attempted. The patient should be kept lying down and given oxygen while being transported for recompression treatment.

Before the diver receives recompression treatment, other lifesaving efforts may be necessary. If the diver isn't breathing, artificial respiration (also called mouth-to-mouth resuscitation or rescue breathing) should be administered. In the absence of a pulse, **cardiopulmonary resuscitation** (**CPR**) must be performed.

Prognosis

The prognosis is dependent upon the promptness of recompression treatment and the extent of the damage caused by oxygen deprivation.

Prevention

All divers should receive adequate training in the use of compressed air and a complete evaluation of fitness for diving. People with a medical history of lung cysts or

KEY TERMS

Compressed air—Air that is held under pressure in a tank to be breathed underwater by divers. A tank of compressed air is part of a diver's scuba (self-contained underwater breathing apparatus) gear.

Compression—An increase in pressure from the surrounding water that occurs with increasing diving depth.

Decompression—A decrease in pressure from the surrounding water that occurs with decreasing diving depth.

Emboli—Plural of embolus. An embolus is something that blocks the blood flow in a blood vessel. It may be a gas bubble, a blood clot, a fat globule, a mass of bacteria, or other foreign body. It usually forms somewhere else and travels through the circulatory system until it gets stuck.

Hyperbaric chamber—A sealed compartment in which patients are exposed to controlled pressures up to three times normal atmospheric pressure. Hyperbaric treatment may be used to regulate blood gases, reduce gas emboli, and provide higher levels of oxygen more quickly in cases of severe gas poisoning.

Recompression—Restoring the elevated pressure of the diving environment to treat gas embolism by decreasing bubble size.

spontaneous collapsed lung (**pneumothorax**), and those with active **asthma** or other lung disease must not dive, for they would be at extreme risk for gas embolism. Patients with conditions such as **alcoholism** and drug abuse are also discouraged from diving. Individuals with certain other medical conditions such as diabetes may be able to dive safely with careful training and supervision.

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American College of Hyperbaric Medicine. PO Box 25914-130, Houston, Texas 77265. (713) 528-0657. <http://www.hyperbaricmedicine.org>.

Divers Alert Network. The Peter B. Bennett Center, 6 West Colony Place, Durham, NC 27705. (800) 446-2671. <http://www.diversalertnetwork.org>.

Undersea and Hyperbaric Medical Society. 10531 Metropolitan Ave., Kensington, MD 20895. (301) 942-2980. <http://www.uhms.org>.

Bethany Thivierge

Gas gangrene *see* **Gangrene**

Gastrectomy

Definition

Gastrectomy is the surgical removal of all or part of the stomach.

Purpose

Gastrectomy is performed for several reasons, most commonly to remove a malignant tumor or to cure a perforated or bleeding stomach ulcer.

Description

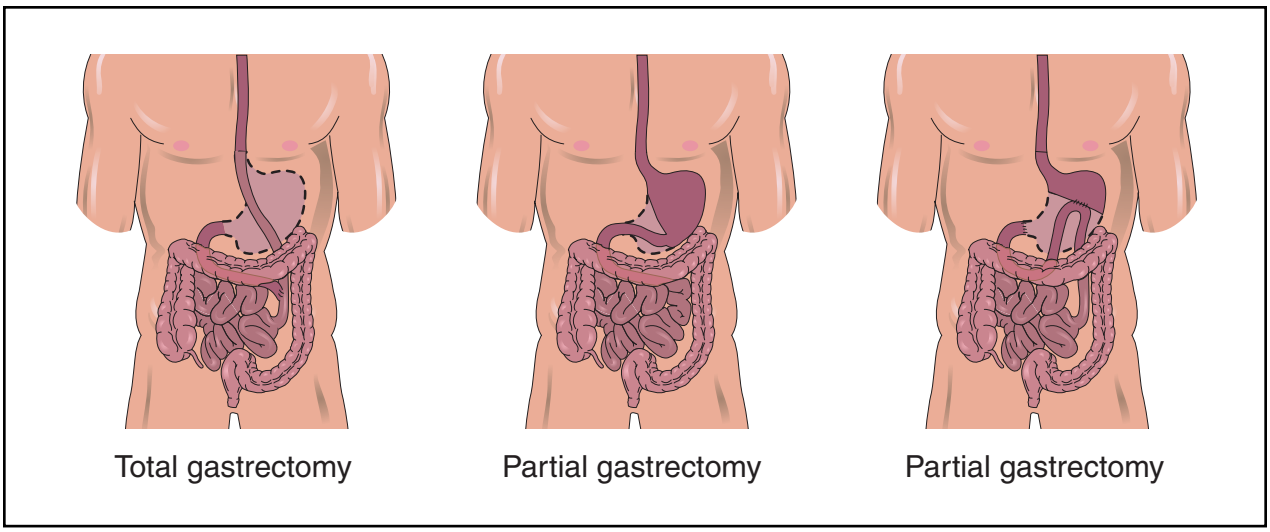
Gastrectomy for cancer

Removal of the tumor, often with removal of surrounding lymph nodes, is the only curative treatment for various forms of gastric (stomach) **cancer**. For many patients, this entails removing not just the tumor but part of the stomach as well. The extent to which lymph nodes should also be removed is a subject of some debate, but some studies show additional survival benefit associated with removal of a greater number of lymph nodes.

Gastrectomy, either total or subtotal (also called partial), is the treatment of choice for gastric adenocarcinomas, primary gastric lymphomas (originating in the stomach), and the rare leiomyosarcomas (also called gastric **sarcomas**). Adenocarcinomas are by far the most common form of **stomach cancer** and are less curable than the relatively uncommon lymphomas, for which gastrectomy offers good odds for survival.

After gastrectomy, the surgeon may "reconstruct" the altered portions of the digestive tract so that it continues to function. Several different surgical techniques are used, but, generally speaking, the surgeon attaches any remaining portion of the stomach to the small intestine.

Gastrectomy for gastric cancer is almost always done by the traditional "open" surgery technique, which requires a wide incision to open the abdomen. However, some surgeons use a laparoscopic technique that requires only a small incision. The laparoscope is connected to a



Gastrectomy, the surgical removal of all or part of the stomach, is performed primarily to remove a malignant tumor or to cure a bleeding stomach ulcer. Following the gastrectomy, the surgeon may reconstruct the altered portions of the digestive tract so that it continues to function. *(Illustration by Electronic Illustrators Group.)*

tiny video camera that projects a picture of the abdominal contents onto a monitor for the surgeon's viewing. The stomach is operated on through this incision.

The potential benefits of laparoscopic surgery include less postoperative **pain**, decreased hospitalization, and earlier return to normal activities. The use of laparoscopic gastrectomy is limited, however. Only patients with early stage gastric cancers or those whose surgery is only intended for palliation—pain and symptomatic relief rather than cure—should be considered for this minimally invasive technique. It can only be performed by surgeons experienced in this type of surgery.

Gastrectomy for ulcers

Gastrectomy is also occasionally used in the treatment of severe peptic ulcer disease or its complications. While the vast majority of peptic ulcers (gastric ulcers in the stomach or duodenal ulcers in the duodenum) are managed with medication, partial gastrectomy is sometimes required for peptic ulcer patients who have complications. These include patients who do not respond satisfactorily to medical therapy, those who develop a bleeding or perforated ulcer, and those who develop pyloric obstruction, a blockage to the exit from the stomach.

The surgical procedure for severe ulcer disease is also called an antrectomy, a limited form of gastrectomy in which the antrum, a portion of the stomach, is removed. For duodenal ulcers, antrectomy may be combined with other surgical procedures that are aimed at reducing the secretion of gastric acid, which is associated with ulcer formation. This additional surgery is commonly a **vagotomy**, surgery on the vagus nerve that disables the acid-producing portion of the stomach.

Preparation

Before undergoing gastrectomy, patients may need a variety of tests, such as x rays, **computed tomography scans** (CT scans), ultrasonography, or endoscopic biopsies (microscopic examination of tissue), to assure the diagnosis and localize the tumor or ulcer. **Laparoscopy** may be done to diagnose a malignancy or to determine the extent of a tumor that is already diagnosed. When a tumor is strongly suspected, laparoscopy is often performed immediately before the surgery to remove the tumor; this avoids the need to anesthetize the patient twice and sometimes avoids the need for surgery altogether if the tumor found on laparoscopy is deemed inoperable.

Aftercare

It is important to follow any instructions that have been given for postoperative care. Major surgery usually requires a recuperation time of several weeks.

Risks

Surgery for peptic ulcer is effective, but it may result in a variety of postoperative complications. After gastrectomy, as many as 30% of patients have significant symptoms. An operation called highly selective vagotomy is now preferred for ulcer management, and is safer than gastrectomy.

After a gastrectomy, several abnormalities may develop that produce symptoms related to food intake. This happens largely because the stomach, which serves as a food reservoir, has been reduced in its capacity by the surgery. Other surgical procedures that often accompany gastrectomy for ulcer disease can also contribute to later symptoms: vagotomy, which lessens acid production and slows stomach emptying, and **pyloroplasty**, which enlarges the opening between the stomach and small intestine to facilitate emptying of the stomach.

Some patients experience light-headedness, heart **palpitations** or racing heart, sweating, and **nausea and vomiting** after a meal. These may be symptoms of "dumping syndrome," as food is rapidly "dumped" into the small intestine from the stomach. This is treated by adjusting the diet and pattern of eating, for example, eating smaller, more frequent meals, and limiting liquids.

Patients who have abdominal bloating and pain after eating, frequently followed by nausea and vomiting, may have what is called the afferent loop syndrome. This is treated by surgical correction. Patients who have early satiety (feeling of fullness after eating), abdominal discomfort, and vomiting may have bile reflux **gastritis** (also called bilious vomiting), which is also surgically correctable. Many patients also experience weight loss.

Reactive **hypoglycemia** is a condition that results when blood sugar becomes too high after a meal, stimulating the release of insulin, about two hours after eating. A high-protein diet and smaller meals are advised.

Ulcers recur in a small percentage of patients after surgery for peptic ulcer, usually in the first few years. Further surgery is usually necessary.

Vitamin and mineral supplementation is necessary after gastrectomy to correct certain deficiencies, especially vitamin B_{12}, iron, and folate. Vitamin D and calcium are also needed to prevent and treat the bone problems that often occur. These include softening and bending of the bones, which can produce pain, and **osteoporosis**, a loss of bone mass. According to one study, the risk for spinal **fractures** may be as high as 50% after gastrectomy.

Depending on the extent of surgery, the risk for postoperative **death** after gastrectomy for gastric cancer has been reported as 1–3% and the risk of non-fatal complications as 9–18%.

Normal results

Overall survival after gastrectomy for gastric cancer varies greatly by the stage of disease at the time of surgery. For early gastric cancer, the five-year survival rate is up to 80–90%; for late-stage disease, the prognosis is bad. For gastric adenocarcinomas that are amenable to gastrectomy, the five-year survival rate is 10–30%, depending on the location of the tumor. The prognosis for patients with gastric lymphoma is better, with five-year survival rates reported at 40–60%.

Most studies have shown that patients can have an acceptable quality of life after gastrectomy for a potentially curable gastric cancer. Many patients will maintain a healthy appetite and eat a normal diet. Others may lose weight and not enjoy meals as much. Some studies show that patients who have total gastrectomies have more disease-related or treatment-related symptoms after surgery and poorer physical function than patients who have subtotal gastrectomies. There does not appear to be much difference, however, in emotional status or social activity level between patients who have undergone total versus subtotal gastrectomies.

KEY TERMS

Antrectomy—A surgical procedure for ulcer disease in which the antrum, a portion of the stomach, is removed.

Laparoscopy—The examination of the inside of the abdomen through a lighted tube, sometimes accompanied by surgery.

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Caroline A. Helwick

Gastric acid determination

Definition

Gastric acid determination, also known as stomach acid determination, gastric analysis, or basal gastric secretion, is a procedure to evaluate gastric (stomach) function.

The test specifically determines the presence of gastric acid, as well as the amount of gastric acid secreted. It is often done in conjunction with the gastric acid stimulation test, a procedure that measures gastric acid output after injection of a drug to stimulate gastric acid secretion.

Purpose

The purpose of the gastric acid determination is to evaluate gastric function by measuring the amount of acid as suctioned directly from the stomach. The complete gastric acid determination includes the basal gastric secretion test, which measures acid secretion while the patient is in a **fasting** state (nothing to eat or drink), followed by the gastric acid stimulation test, which measures the secretion of gastric acid for one hour after injection of pentagastrin or a similar drug that stimulates gastric acid output. The Gastric acid stimulation test is done when the basal secretion test suggests abnormalities in gastric secretion. It is normally performed immediately afterward.

The basal gastric secretion test is indicated for patients with obscure gastric **pain**, loss of appetite, and weight loss. It is also utilized for suspected peptic (related to the stomach) ulcer, severe stomach inflammation (**gastritis**), and Zollinger-Ellison (Z-E) syndrome (a condition in which a pancreatic tumor, called a **gastrinoma**, stimulates the stomach to secrete excessive amounts of acid, resulting in peptic ulcers). Because external factors like the sight or odor of food, as well as psychological **stress**, can stimulate gastric secretion, accurate testing requires that the patient be relaxed and isolated from all sources of sensory stimulation. Abnormal basal secretion can suggest various gastric and duodenal disorders, so further evaluation requires the gastric acid stimulation test.

The gastric acid stimulation test is indicated when abnormalities are found during the basal secretion test. These abnormalities can be caused by a number of disorders, including duodenal ulcer, **pernicious anemia**, and gastric **cancer**. The test will detect abnormalities, but x rays and other studies are necessary for a definitive diagnosis.

Precautions

Because both the basal gastric secretion test and the gastric acid stimulation test require insertion of a gastric tube (intubation) through the mouth or nasal passage, neither test is recommended for patients with esophageal problems, **aortic aneurysm**, severe gastric hemorrhage, or congestive **heart failure**. The gastric acid stimulation test is also not recommended in patients who are sensitive to pentagastrin (the drug used to stimulate gastric acid output).

Description

This test, whether performed for basal gastric acid secretion, gastric acid stimulation, or both, requires the passage of a lubricated rubber tube, either by mouth or through the nasal passage, while the patient is in a sitting or reclining position on the left side. The tube is situated in the stomach, with proper positioning confirmed by fluoroscopy or x ray.

Basal gastric acid secretion

After a wait of approximately 10–15 minutes for the patient to adjust to the presence of the tube, and with the patient in a sitting position, specimens are obtained every 15 minutes for a period of 90 minutes. The first two specimens are discarded to eliminate gastric contents that might be affected by the stress of the intubation process. The patient is allowed no liquids during the test, and saliva must be ejected to avoid diluting the stomach contents.

The four specimens collected during the test constitute the *basal acid output*. If analysis suggests abnormally low gastric secretion, the gastric acid stimulation test is performed immediately afterward.

Gastric acid stimulation test

After the basal samples have been collected, the tube remains in place for the gastric acid stimulation test. Pentagastrin, or a similar drug that stimulates gastric acid output, is injected under the skin (subcutaneously). After 15 minutes, a specimen is collected every 15 minutes for one hour. These specimens are called the *poststimulation specimens*. As is the case with the basal gastric secretion test, the patient can have no liquids during this test, and must eject saliva to avoid diluting the stomach contents.

Preparation

The patient should be fasting (nothing to eat or drink after the evening meal) on the day prior to the test, but may have water up to one hour before the test. **Antacids**, anticholinergics, cholinergics, alcohol, H_2-receptor antagonists (Tagamet, Pepcid, Axid, Zantac), reserpine, adrenergic blockers, and adrenocorticosteroids should be withheld for one to three days before the test, as the physician requests. If pentagastrin is to be administered for the gastric acid secretion test, medical supervision should be maintained, as possible side effects may occur.

Aftercare

Complications such as nausea, vomiting, and abdominal distention or pain are possible following removal of the gastric tube. If the patient has a **sore**

KEY TERMS

Achlorhydria—An abnormal condition in which hydrochloric acid is absent from the secretions of the gastric glands in the stomach.

Pernicious anemia—One of the main types of anemia, caused by inadequate absorption of vitamin B_{12}. Symptoms include tingling in the hands, legs, and feet, spastic movements, weight loss, confusion, depression, and decreased intellectual function.

Zollinger-Ellison syndrome—A rare condition characterized by severe and recurrent peptic ulcers in the stomach, duodenum, and upper small intestine, caused by a tumor, or tumors, usually found in the pancreas. The tumor secretes the hormone gastrin, which stimulates the stomach and duodenum to produce large quantities of acid, leading to ulceration. Most often cancerous, the tumor must be removed surgically; otherwise total surgical removal of the stomach is necessary.

throat, soothing lozenges may be given. The patient may also resume the usual diet and any medications that were withheld for the test(s).

Risks

There is a slight risk that the gastric tube may be inserted improperly, entering the windpipe (trachea) and not the esophagus. If this happens, the patient may have a difficult time breathing or may experience a coughing spell until the tube is removed and reinserted properly. Also, because the tube can be difficult to swallow, if a patient has an overactive gag reflex, there may be a transient rise in blood pressure due to **anxiety**.

Normal results

Reference values for the *basal gastric secretion test* vary by laboratory, but are usually within the following ranges:

- men: 1–5 mEq/h
- women: 0.2–3.8 mEq/h

Reference values for the *gastric acid stimulation test* vary by laboratory, but are usually within the following ranges:

- men: 18–28 mEq/h
- women: 11–21 mEq/h

Abnormal results

Abnormal findings in the *basal gastric secretion test* are considered nonspecific and must be evaluated in conjunction with the results of a gastric acid stimulation test. Elevated secretion may suggest different types of ulcers; when markedly elevated, Zollinger-Ellison syndrome is suspected. Depressed secretion can indicate gastric cancer, while complete absence of secretion (achlorhydria) may suggest pernicious anemia.

Elevated gastric secretion levels in the *gastric acid stimulation test* may be indicative of duodenal ulcer; high levels of secretion again suggest Zollinger-Ellison syndrome.

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Janis O. Flores

Gastric carcinoma *see* **Stomach cancer**

Gastric emptying scan

Definition

A gastric emptying scan (GES) is an x-ray exam using special radioactive material that allows physicians to identify abnormalities related to emptying of the stomach. Diseases that involve changes in the way the stomach contracts (motility disorders) are best diagnosed by this test.

Purpose

The study is used most frequently to evaluate patients who have symptoms suggestive of decreased, delayed, or rapid gastric emptying, and no visible abnormality to explain their symptoms.

Symptoms pointing to a delay in gastric emptying are non-specific, and may be due to a number of causes, such as ulcers, diabetes, tumors, and others. These symptoms include nausea, upper abdominal bloating, and at times vomiting. Another significant symptom is called "early satiety," which means feeling full after eating only a small amount of food. In some patients, weight loss is

KEY TERMS

Endoscopy—The examination of the inside of an organ with an instrument that has a light at the end of it and an optical system for examination of the organ.

Motility—Motility is spontaneous movement. One example is the automatic stomach contractions that move the food content along from the stomach into the intestines. A motility disease is one that involves changes in the way the stomach contracts.

also present. In addition to symptoms, the finding of a large amount of material in the stomach after an overnight fast suggests abnormal emptying, but does not distinguish between an actual blockage or an irregularity in gastric contractions. It is therefore essential to find out what is causing material to remain in the stomach.

Since many diseases can produce the above symptoms, structural lesions (such as tumors or regions of narrowing or scar tissue) need to be ruled out first. This is usually done by upper gastrointestinal series test or by endoscopy (examination of the inside of an organ, in this instance the stomach, with an instrument that has a light at the end of it and an optical system for examination of the organ). Once it is clear that a mechanical or physical lesion is not the cause of symptoms, attempts to document an abnormality in the nervous or muscular function of the stomach is then begun. GES is usually the first step in that evaluation.

Precautions

The exam should not be performed on pregnant women, but is otherwise quite safe. Since eggs are usually used to hold the radioactive material, patients should notify their physician if they are allergic to eggs. However, other materials can be used in place of an egg.

Description

Gastric emptying scans have undergone several changes since the initial studies in the late 1970s. During the study, patients are asked to ingest an egg sandwich containing a radioactive substance (for example, technetium) that can be followed by a special camera. The emptying of the material from the stomach is then followed and displayed both in the form of an image, as well as the percentage emptied over several hours (generally two and four hours). Studies are in progress using substances that are not radioactive, but this procedure is not available to the patient as of yet.

Preparation

The only preparation involved is for the patient to fast overnight before the test.

Risks

The radiation exposure during the study is quite small and safe, unless the patient is pregnant.

Normal results

There are several different measurements considered normal, depending on the radioactive material and solid meal used. The value is expressed as a percentage of emptying over a period of time. For a technetium-filled egg sandwich, normal emptying is 78 minutes for half the material to leave the stomach, with a variation of 11 minutes either way.

Abnormal results

GES scan studies that show emptying of the stomach in a longer than accepted period is abnormal. Severity of test results and symptoms do not always match; therefore, the physician must carefully interpret these findings. Diabetic injury to the nerves that supply the stomach (called diabetic gastroparesis) is one of the most common causes of abnormal gastric motility. However, up to 30% of patients have no obvious cause to explain the abnormal results and symptoms. These cases are called idiopathic (of unknown cause). GES is often used to follow the effect of medications used for treatment of motility disorders.

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American Pseudo-obstruction and Hirschprung's Disease Society. 158 Pleasant St., North Andover, MA 01845-2797. <http://www.tiac.net/users/aphs>.

David Kaminstein, MD

Gastric lavage *see* **Stomach flushing**
Gastric stapling *see* **Obesity surgery**
Gastric ulcers *see* **Ulcers (digestive)**

Gastrinoma

Definition

Gastrinomas are tumors associated with a rare gastroenterological disorder known as Zollinger-Ellison syndrome (ZES). They occur primarily in the pancreas and duodenum (beginning of the small intestine) and secrete large quantities of the hormone gastrin, triggering gastric acid production that produces ulcers. They may be malignant (cancerous) or benign.

Description

Gastrinomas are an integral part of the Zollinger-Ellison syndrome (ZES). In fact, ZES is also known as gastrinoma. This syndrome consists of ulcer disease in the upper gastrointestinal tract, marked increases in the secretion of gastric acid in the stomach, and tumors of the islet cells in the pancreas. The tumors produce large amounts of gastrin that are responsible for the characteristics of Zollinger-Ellison syndrome, namely severe ulcer disease. Although usually located within the pancreas, they may occur in other organs.

Gastrinomas may occur randomly and sporadically, or they may be inherited as part of a genetic condition called multiple endocrine neoplasia type 1 (MEN-1) syndrome. About half of persons with MEN-1 have gastrinomas, which tend to be more numerous and smaller than tumors in sporadic cases.

About half of ZES patients have multiple gastrinomas, which can vary in size from 1–20 mm. Gastrinomas found in the pancreas are usually much larger than duodenal gastrinomas. About two thirds of gastrinomas are malignant (cancerous). These usually grow slowly, but some may invade surrounding sites rapidly and metastasize (spread) widely. Sometimes, gastrinomas are found only in the lymph nodes, and it is uncertain whether these malignancies have originated in the lymph nodes or have metastasized from a tumor not visible in the pancreas or duodenum.

There is some evidence that the more malignant form of gastrinomas is more frequent in larger pancreatic tumors, especially in females and in persons with a shorter disease symptom duration and higher serum gastrin levels.

Causes and symptoms

Most persons with gastrinomas secrete profound amounts of gastric acid, and almost all develop ulcers, mostly in the duodenum or stomach. Early in the course of the disease, symptoms are typical of peptic ulcers, however once the disease is established, the ulcers become more persistent and symptomatic, and may respond poorly to standard anti-ulcer therapy. Abdominal **pain** is the predominant symptom of ulcer disease. About 40% of patients have **diarrhea** as well. In some patients, diarrhea is the primary symptom of gastrinoma.

Diagnosis

Persons with gastrinomas have many of the same symptoms as persons with ulcers. Their levels of gastric acid, however, are usually far greater than those in common ulcer disease. Gastrinomas are usually diagnosed by a blood test that measures the level of gastrin in the blood. Patients with gastrinomas often have gastrin levels more than 200 pg/mL, which is 4–10 times higher than normal. Serum gastrin levels as high as 450,000 pg/mL have occurred.

When the serum gastrin test does not show these extremely high levels of gastrin, patients may be given certain foods or injections in an attempt to provoke a response that will help diagnose the condition. The most useful of these provocative tests is the secretin injection test (or secretin stimulation or provocative test), which will almost always produce a positive response in persons with gastrinomas but seldom in persons without them.

Surgically, gastrinomas are often difficult to locate, even with careful inspection. They may be missed in at least 10–20% of patients with ZES. Gastrinomas are sometimes found only because they have metastasized and produced symptoms related to the spread of malignancy. Such metastasis may be the most reliable indication of whether the gastrinoma is malignant or benign.

Diagnostic imaging techniques help locate the gastrinomas. The most sophisticated is an x-ray test called radionuclide octreotide scanning (also known as somatostatin receptor scintigraphy or 111In pentetreotide SPECT). A study by the National Institutes of Health (NIH) found this test to be superior to other imaging methods, such as computed tomography scan (CT) or **magnetic resonance imaging** (MRI), in pinpointing the location of tumors and guiding physicians in treatment.

Approximately half of all gastrinomas do not show up on imaging studies. Therefore, exploratory surgery is often recommended to try to locate and remove the tumors.

KEY TERMS

Gastrin—A hormone secreted in the stomach that is involved in the production of gastric acid. Overproduction of gastric acid contributes to peptic ulcer formation.

Multiple endocrine neoplasia type 1 (MEN-1)—An inherited condition marked by multiple malignancies of the pituitary gland, parathyroid gland, and islet cells of the pancreas. About half of MEN-1 patients with pancreatic islet cell tumors will have gastrinomas, gastrin-producing tumors that lead to ulcer disease.

Peptic ulcer—An eroded area in the stomach lining or in the first part of the duodenum (beginning of the small intestine).

Serum gastrin test—A laboratory test that is performed on a blood sample to determine that level of the hormone gastrin. High levels of gastrin indicate the presence a duodenal ulcer or a gastrinoma.

Sporadic—Occurring at random or by chance, and not as a result of a genetically determined, or inherited, trait.

Treatment

Therapy for gastrinomas should be individualized, since patients tend to have varying degrees of disease and symptoms. Treatment is aimed at eliminating the overproduction of gastric acid and removing the gastrin-producing tumors.

Drugs

Gastrinomas may not be easily treated by the standard anti-ulcer approaches. The medical treatment of choice is with drugs called proton pump inhibitors, such as omeprazole or lansoprazole, daily. These drugs are potent inhibitors of gastric acid. High doses of H-2 receptor antagonists may also reduce gastric acid secretion, improve symptoms, and induce ulcer healing. These drugs must be continued indefinitely, since even a brief discontinuation will cause ulcer recurrence. **Antacids** may provide some relief, but it is usually not longlasting or healing.

Surgery

Because of the likelihood that gastrinomas may be malignant, in both sporadic tumors and those associated with the inherited MEN-1 syndrome, surgery to locate and remove gastrinomas is frequently advised. It is now known that complete surgical removal of gastrinomas can cure the overproduction of gastrin, even in patients who have metastases to the lymph nodes. Surgery in patients with MEN-1 and ZES, however, remains controversial since the benefit is less clear.

Freedom from disease after surgery is judged by improved symptoms, reduced gastric acid production, reduced need for drug therapy, normalization of serum gastrin levels, and normalization of results from the secretin stimulation test and imaging studies.

Prognosis

Medical therapy often controls symptoms, and surgery may or may not cure gastrinoma. About 50% of ZES patients in whom gastrinomas are not removed will die from malignant spread of the tumor. In patients with gastrinomas as part of MEN-1 syndrome, the cure rate is extremely low.

A NIH study of patients who had surgical removal of gastrinomas found that 42% were disease-free one year after surgery and 35% were disease-free at five years. Disease recurrences can often be detected with a serum gastrin test or secretin stimulation test.

When gastrinomas are malignant, they often grow slowly. The principal sites of metastasis are the regional lymph nodes and liver, but they may also spread to other structures. About one quarter of patients with gastrinomas have liver metastases at the time of diagnosis. This appears to be more frequent with pancreatic gastrinomas than duodenal gastrinomas.

Metastases of malignant gastrinomas to the liver is very serious. Survival five years after diagnosis is 20–30%, however patients with gastrinomas found only in the lymph nodes have been known to live as long as 25 years after diagnosis, without evidence of further tumor spread. In fact, the life expectancy of patients with gastrinomas that have spread to the lymph nodes is no different from that of patients with gastrinomas that cannot even be found at surgery for about 90%, five years after diagnosis.

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National Digestive Diseases Information Clearinghouse. 2 Information Way, Bethesda, MD 20892-3570. (800) 891-5389. <http://www.niddk.nih.gov/health/digest/nddic.htm>.

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Gastritis

Definition

Gastritis commonly refers to inflammation of the lining of the stomach, but the term is often used to cover a variety of symptoms resulting from stomach lining inflammation and symptoms of burning or discomfort. True gastritis comes in several forms and is diagnosed using a combination of tests. In the 1990s, scientists discovered that the main cause of true gastritis is infection from a bacterium called *Helicobacter pylori* (*H. pylori*).

Description

Gastritis should not be confused with common symptoms of upper abdominal discomfort. It has been associated with resulting ulcers, particularly peptic ulcers. And in some cases, chronic gastritis can lead to more serious complications.

Nonerosive H. pylori gastritis

The main cause of true gastritis is *H. pylori* infection. *H. pylori* is indicated in an average of 90% of patients with chronic gastritis. This form of nonerosive gastritis is the result of infection with *Helicobacter pylori* bacterium, a microorganism whose outer layer is resistant to the normal effects of stomach acid in breaking down bacteria.

The resistance of *H. pylori* means that the bacterium may rest in the stomach for long periods of times, even years, and eventually cause symptoms of gastritis or ulcers when other factors are introduced, such as the presence of specific genes or ingestion of **nonsteroidal anti-inflammatory drugs** (NSAIDS). Study of the role of *H. pylori* in development of gastritis and peptic ulcers has disproved the former belief that **stress** lead to most stomach and duodenal ulcers and has resulted in improved treatment and reduction of stomach ulcers. *H. pylori* is most likely transmitted between humans, although the specific routes of transmission were still under study in early 1998. Studies were also underway to determine the role of *H. pylori* and resulting chronic gastritis in development of gastric **cancer**.

Erosive and hemorrhagic gastritis

After *H. pylori*, the second most common cause of chronic gastritis is use of nonsteroidal anti-inflammatory drugs. These commonly used **pain** killers, including **aspirin**, fenoprofen, ibuprofen and naproxen, among others, can lead to gastritis and peptic ulcers. Other forms of erosive gastritis are those due to alcohol and corrosive agents or due to trauma such as ingestion of foreign bodies.

Other forms of gastritis

Clinicians differ on the classification of the less common and specific forms of gastritis, particularly since there is so much overlap with *H. pylori* in development of chronic gastritis and complications of gastritis. Other types of gastritis that may be diagnosed include:

- Acute stress gastritis—the most serious form of gastritis which usually occurs in critically ill patients, such as those in intensive care. Stress erosions may develop suddenly as a result of severe trauma or stress to the stomach lining.
- Atrophic gastritis is the result of chronic gastritis which is leading to atrophy, or decrease in size and wasting away, of the gastric lining. Gastric atrophy is the final stage of chronic gastritis and may be a precursor to gastric cancer.
- Superficial gastritis is a term often used to describe the initial stages of chronic gastritis.
- Uncommon specific forms of gastritis include granulomatous, eosiniphilic and lymphocytic gastritis.

Causes and symptoms

Nonerosive H. pylori gastritis

H. pylori gastritis is caused by infection from the *H. pylori* bacterium. It is believed that most infection occurs in childhood. The route of its transmission was still under study in 1998 and clinicians guessed that there may be more than one route for the bacterium. Its prevalence and distribution differs in nations around the world. The presence of *H. pylori* has been detected in 86–99% of patients with chronic superficial gastritis. However, physicians are still learning about the link of *H. pylori* to chronic gastritis and peptic ulcers, since many patients with *H. pylori* infection do not develop symptoms or

peptic ulcers. *H. pylori* is also seen in 90–100% of patients with duodenal ulcers.

Symptoms of *H. pylori* gastritis include abdominal pain and reduced acid secretion in the stomach. However, the majority of patients with *H. pylori* infection suffer no symptoms, even though the infection may lead to ulcers and resulting symptoms. Ulcer symptoms include dull, gnawing pain, often two to three hours after meals and pain in the middle of the night when the stomach is empty.

Erosive and hemorrhagic gastritis

The most common cause of this form of gastritis is use of NSAIDS. Other causes may be **alcoholism** or stress from surgery or critical illness. The role of NSAIDS in development of gastritis and peptic ulcers depends on the dose level. Although even low doses of aspirin or other nonsteroidal anti-inflammatory drugs may cause some gastric upset, low doses generally will not lead to gastritis. However, as many as 10–30% of patients on higher and more frequent doses of NSAIDS, such as those with chronic arthritis, may develop gastric ulcers. In 1998, studies were underway to understand the role of *H. pylori* in gastritis and ulcers among patients using NSAIDS.

Patients with erosive gastritis may also show no symptoms. When symptoms do occur, they may include **anorexia nervosa**, gastric pain, **nausea and vomiting**.

Other Forms of Gastritis

Less common forms of gastritis may result from a number of generalized diseases or from complications of chronic gastritis. Any number of mechanisms may cause various less common forms of gastritis and they may differ slightly in their symptoms and clinical signs. However, they all have in common inflammation of the gastric mucosa.

Diagnosis

Nonerosive H. pylori gastritis

H. pylori gastritis is easily diagnosed through the use of the urea breath test. This test detects active presence of *H. pylori* infection. Other serological tests, which may be readily available in a physician's office, may be used to detect *H. pylori* infection. Newly developed versions offer rapid diagnosis. The choice of test will depend on cost, availability and the physician's experience, since nearly all of the available tests have an accuracy rate of 90% or better. Endoscopy, or the examination of the stomach area using a hollow tube inserted through the mouth, may be ordered to confirm diagnosis. A biopsy of the gastric lining may also be ordered.

Erosive or hemorrhagic gastritis

Clinical history of the patient may be particularly important in the diagnosis of this type of gastritis, since its cause is most often the result of chronic use of NSAIDS, alcoholism, or other substances.

Other forms of gastritis

Gastritis that has developed to the stage of duodenal or gastric ulcers usually requires endoscopy for diagnosis. It allows the physician to perform a biopsy for possible malignancy and for *H. pylori*. Sometimes, an upper gastrointestinal x-ray study with barium is ordered. Some diseases such as Zollinger-Ellison syndrome, an ulcer disease of the upper gastrointestinal tract, may show large mucosal folds in the stomach and duodenum on radiographs or in endoscopy. Other tests check for changes in gastric function.

Treatment

H. pylori gastritis

The discovery of *H. pylori's* role in development of gastritis and ulcers has led to improved treatment of chronic gastritis. In particular, relapse rates for duodenal and gastric ulcers has been reduced with successful treatment of *H. pylori* infection. Since the infection can be treated with **antibiotics**, the bacterium can be completely eliminated up to 90% of the time.

Although *H. pylori* can be successfully treated, the treatment may be uncomfortable for patients and relies heavily on patient compliance. In 1998, studies were underway to identify the best treatment method based on simplicity, patient cooperation and results. No single antibiotic had been found which would eliminate *H. pylori* on its own, so a combination of antibiotics has been prescribed to treat the infection.

DUAL THERAPY. Dual therapy involves the use of an antibiotic and a proton pump inhibitor. Proton pump inhibitors help reduce stomach acid by halting the mechanism that pumps acid into the stomach. This also helps promote healing of ulcers or inflammation. Dual therapy has not been proven to be as effective as triple therapy, but may be ordered for some patients who can more comfortably handle the use of less drugs and will therefore more likely follow the two-week course of therapy.

TRIPLE THERAPY. As of early 1998, triple therapy was the preferred treatment for patients with *H. pylori* gastritis. It is estimated that triple therapy successfully eliminates 80–95% of *H. pylori* cases. This treatment regimen usually involves a two-week course of three drugs. An antibiotic such as amoxicillin or tetracycline, and another

antibiotic such as clarithomycin or metronidazole are used in combination with bismuth subsalicylate, a substance found in the over-the-counter medication, Pepto-Bismol, which helps protect the lining of the stomach from acid. Physicians were experimenting with various combinations of drugs and time of treatment to balance side effects with effectiveness. Side effects of triple therapy are not serious, but may cause enough discomfort that patients are not inclined to follow the treatment.

OTHER TREATMENT THERAPIES. Scientists have experimented with quadruple therapy, which adds an antisecretory drug, or one which suppresses gastric secretion, to the standard triple therapy. One study showed this therapy to be effective with only a week's course of treatment in more than 90% of patients. Short course therapy was attempted with triple therapy involving antibiotics and a proton pump inhibitor and seemed effective in eliminating *H. pylori* in one week for more than 90% of patients. The goal is to develop the most effective therapy combination that can work in one week of treatment or less.

MEASURING H. PYLORI TREATMENT EFFECTIVENESS. In order to ensure that *H. pylori* has been eradicated, physicians will test patients following treatment. The breath test is the preferred method to check for remaining signs of *H. pylori*.

Treatment of erosive gastritis

Since few patients with this form of gastritis show symptoms, treatment may depend on severity of symptoms. When symptoms do occur, patients may be treated with therapy similar to that for *H. pylori*, especially since some studies have demonstrated a link between *H. pylori* and NSAIDS in causing ulcers. Avoidance of NSAIDS will most likely be prescribed.

Other forms of gastritis

Specific treatment will depend on the cause and type of gastritis. These may include prednisone or antibiotics. Critically ill patients at high risk for bleeding may be treated with preventive drugs to reduce risk of acute stress gastritis. If stress gastritis does occur, the patient is treated with constant infusion of a drug to stop bleeding. Sometimes surgery is recommended, but is weighed with the possibility of surgical complications or **death**. Once torrential bleeding occurs in acute stress gastritis, mortality is as high as greater than 60%.

Alternative treatment

Alternative forms of treatment for gastritis and ulcers should be used cautiously and in conjunction with conventional medical care, particularly now that scientists have confirmed the role of *H. pylori* in gastritis and ulcers. Alternative treatments can help address gastritis symptoms with diet and nutritional supplements, herbal medicine and **ayurvedic medicine**. It is believed that zinc, vitamin A and beta-carotene aid in the stomach lining's ability to repair and regenerate itself. Herbs thought to stimulate the immune system and reduce inflammation include **echinacea** (*Echinacea* spp.) and goldenseal (*Hydrastis canadensis*). Ayurvedic medicine involves **meditation**. There are also certain herbs and nutritional supplements aimed at helping to treat ulcers.

KEY TERMS

Duodenal—Refers to the duodenum, or the first part of the small intestine.

Gastric—Relating to the stomach.

Mucosa—The mucous membrane, or the thin layer which lines body cavities and passages.

Ulcer—A break in the skin or mucous membrane. It can fester and pus like a sore.

Prognosis

The discovery of *H. pylori* has improved the prognosis for patients with gastritis and ulcers. Since treatment exists to eradicate the infection, recurrence is much less common. As of 1998, the only patients requiring treatment for *H. pylori* were those at high risk because of factors such as NSAIDS use or for those with ulcers and other complicating factors or symptoms. Research will continue into the most effective treatment of *H. pylori*, especially in light of the bacterium's resistance to certain antibiotics. Regular treatment of patients with gastric and duodenal ulcers has been recommended, since H. pylori plays such a consistently high role in development of ulcers. It is believed that *H. pylori* also plays a role in the eventual development of serious gastritis complications and cancer. Detection and treatment of *H. pylori* infection may help reduce occurrence of these diseases. The prognosis for patients with acute stress gastritis is much poorer, with a 60 percent or higher mortality rate among those bleeding heavily.

Prevention

The widespread detection and treatment of *H. pylori* as a preventive measure in gastritis has been discussed but not resolved. Until more is known about the routes

through which *H. pylori* is spread, specific prevention recommendations are not available. Erosive gastritis from NSAIDS can be prevented with cessation of use of these drugs. An education campaign was launched in 1998 to educate patients, particularly an **aging** population of arthritis sufferers, about risk for ulcers from NSAIDS and alternative drugs.

Resources

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OTHER

American College of Gastroenterology Page. <http://www.acg.org>.

HealthAnswers.com. <http://www.healthanswers.com>.

Teresa Norris, RN

Gastroduodenostomy (Billroth I) *see* **Ulcer surgery**

Gastroenteritis

Definition

Gastroenteritis is a catchall term for infection or irritation of the digestive tract, particularly the stomach and intestine. It is frequently referred to as the stomach or intestinal flu, although the **influenza** virus is not associated with this illness. Major symptoms include **nausea and vomiting**, **diarrhea**, and abdominal cramps. These symptoms are sometimes also accompanied by **fever** and overall weakness. Gastroenteritis typically lasts about three days. Adults usually recover without problem, but children, the elderly, and anyone with an underlying disease are more vulnerable to complications such as **dehydration**.

Description

Gastroenteritis is an uncomfortable and inconvenient ailment, but it is rarely life-threatening in the United States and other developed nations. However, an estimated 220,000 children younger than age five are hospitalized with gastroenteritis symptoms in the United States annually. Of these children, 300 die as a result of severe diarrhea and dehydration. In developing nations, diarrheal illnesses are a major source of mortality. In 1990, approximately three million deaths occurred worldwide as a result of diarrheal illness.

The most common cause of gastroenteritis is viral infection. Viruses such as rotavirus, adenovirus, astrovirus, and calicivirus and small round-structured viruses (SRSVs) are found all over the world. Exposure typically occurs through the fecal-oral route, such as by consuming foods contaminated by fecal material related to poor sanitation. However, the infective dose can be very low (approximately 100 virus particles), so other routes of transmission are quite probable.

Typically, children are more vulnerable to rotaviruses, the most significant cause of acute watery diarrhea. Annually, worldwide, rotaviruses are estimated to cause 800,000 deaths in children below age five. For this reason, much research has gone into developing a vaccine to protect children from this virus. Adults can be infected with rotaviruses, but these infections typically have minimal or no symptoms.

Children are also susceptible to adenoviruses and astroviruses, which are minor causes of childhood gastroenteritis. Adults experience illness from astroviruses as well, but the major causes of adult viral gastroenteritis are the caliciviruses and SRSVs. These viruses also cause illness in children. The SRSVs are a type of calicivirus and include the Norwalk, Southhampton, and Lonsdale viruses. These viruses are the most likely to produce vomiting as a major symptom.

Bacterial gastroenteritis is frequently a result of poor sanitation, the lack of safe drinking water, or contaminated food—conditions common in developing nations. Natural or man-made disasters can make underlying problems in sanitation and food safety worse. In developed nations, the modern food production system potentially exposes millions of people to disease-causing bacteria through its intensive production and distribution methods. Common types of bacterial gastroenteritis can be linked to *Salmonella* and *Campylobacter* bacteria; however, ***Escherichia coli*** 0157 and *Listeria monocytogenes* are creating increased concern in developed nations. **Cholera** and Shigella remain two diseases of great concern in developing countries, and research to develop long-term vaccines against them is underway.

Causes and symptoms

Gastroenteritis arises from ingestion of viruses, certain bacteria, or parasites. Food that has spoiled may also cause illness. Certain medications and excessive alcohol can irritate the digestive tract to the point of inducing gastroenteritis. Regardless of the cause, the symptoms of gastroenteritis include diarrhea, nausea and vomiting, and abdominal **pain** and cramps. Sufferers may also experience bloating, low fever, and overall tiredness. Typically, the symptoms last only two to three days, but some viruses may last up to a week.

A usual bout of gastroenteritis shouldn't require a visit to the doctor. However, medical treatment is essential if symptoms worsen or if there are complications. Infants, young children, the elderly, and persons with underlying disease require special attention in this regard.

The greatest danger presented by gastroenteritis is dehydration. The loss of fluids through diarrhea and vomiting can upset the body's electrolyte balance, leading to potentially life-threatening problems such as heart beat abnormalities (arrhythmia). The risk of dehydration increases as symptoms are prolonged. Dehydration should be suspected if a **dry mouth**, increased or excessive thirst, or scanty urination is experienced.

If symptoms do not resolve within a week, an infection or disorder more serious than gastroenteritis may be involved. Symptoms of great concern include a high fever (102° F [38.9°C] or above), blood or mucus in the diarrhea, blood in the vomit, and severe abdominal pain or swelling. These symptoms require prompt medical attention.

Diagnosis

The symptoms of gastroenteritis are usually enough to identify the illness. Unless there is an outbreak affecting several people or complications are encountered in a particular case, identifying the specific cause of the illness is not a priority. However, if identification of the infectious agent is required, a stool sample will be collected and analyzed for the presence of viruses, disease-causing (pathogenic) bacteria, or parasites.

Treatment

Gastroenteritis is a self-limiting illness which will resolve by itself. However, for comfort and convenience, a person may use over-the-counter medications such as Pepto Bismol to relieve the symptoms. These medications work by altering the ability of the intestine to move or secrete spontaneously, absorbing toxins and water, or altering intestinal microflora. Some over-the-counter medicines use more than one element to treat symptoms.

If over-the-counter medications are ineffective and medical treatment is sought, a doctor may prescribe a more powerful anti-diarrheal drug, such as motofen or lomotil. Should pathogenic bacteria or parasites be identified in the patient's stool sample, medications such as **antibiotics** will be prescribed.

It is important to stay hydrated and nourished during a bout of gastroenteritis. If dehydration is absent, the drinking of generous amounts of nonalcoholic fluids, such as water or juice, is adequate. **Caffeine**, since it increases urine output, should be avoided. The traditional BRAT diet—bananas, rice, applesauce, and toast—is tolerated by the tender gastrointestinal system, but it is not particularly nutritious. Many, but not all, medical researchers recommend a diet that includes complex carbohydrates (e.g., rice, wheat, potatoes, bread, and cereal), lean meats, yogurt, fruit, and vegetables. Milk and other dairy products shouldn't create problems if they are part of the normal diet. Fatty foods or foods with a lot of sugar should be avoided. These recommendations are based on clinical experience and controlled trials, but are not universally accepted.

Minimal to moderate dehydration is treated with oral rehydrating solutions that contain glucose and electrolytes. These solutions are commercially available under names such as Naturalyte, Pedialyte, Infalyte, and Rehydralyte. Oral rehydrating solutions are formulated based on physiological properties. Fluids that are not based on these properties—such as cola, apple juice, broth, and sports beverages—are not recommended to treat dehydration. If vomiting interferes with oral rehydration, small frequent fluid intake may be better tolerated. Should oral rehydration fail or severe dehydration occur, medical treatment in the form of intravenous (IV) therapy is required. IV therapy can be followed with oral rehydration as the patient's condition improves. Once normal hydration is achieved, the patient can return to a regular diet.

Alternative treatment

Symptoms of uncomplicated gastroenteritis can be relieved with adjustments in diet, herbal remedies, and **homeopathy**. An infusion of meadowsweet (*Filipendula ulmaria*) may be effective in reducing nausea and stomach acidity. Once the worst symptoms are relieved, slippery elm (*Ulmus fulva*) can help calm the digestive tract. Of the homeopathic remedies available, *Arsenicum album*, **ipecac**, or *Nux vomica* are three said to relieve the symptoms of gastroenteritis.

Probiotics, bacteria that are beneficial to a person's health, are recommended during the recovery phase of gastroenteritis. Specifically, live cultures of *Lactobacillus acidophilus* are said to be effective in soothing the digestive tract and returning the intestinal flora to normal. *L. aci-*

KEY TERMS

Dehydration—A condition in which the body lacks the normal level of fluids, potentially impairing normal body functions.

Electrolyte—An ion, or weakly charged element, that conducts reactions and signals in the body. Examples of electrolytes are sodium and potassium ions.

Glucose—A sugar that serves as the body's primary source of fuel.

Influenza—A virus that affects the respiratory system, causing fever, congestion, muscle aches, and headaches.

Intravenous (IV) therapy—Administration of intravenous fluids.

Microflora—The bacterial population in the intestine.

Pathogenic bacteria—Bacteria that produce illness.

Probiotics—Bacteria that are beneficial to a person's health, either through protecting the body against pathogenic bacteria or assisting in recovery from an illness.

dophilus is found in live-culture yogurt, as well as in capsule or powder form at health food stores. The use of probiotics is found in folk remedies and has some support in the medical literature. Castor oil packs to the abdomen can reduce inflammation and also reduce spasms or discomfort.

Prognosis

Gastroenteritis is usually resolved within two to three days and there are no long-term effects. If dehydration occurs, recovery is extended by a few days.

Prevention

There are few steps that can be taken to avoid gastroenteritis. Ensuring that food is well-cooked and unspoiled can prevent bacterial gastroenteritis, but may not be effective against viral gastroenteritis.

Resources

BOOKS

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Julia Barrett

Gastroesophageal reflux *see* **Heartburn**

Gastrointestinal bleeding studies *see* **GI bleeding studies**

Gastrointestinal study *see* **Liver nuclear medicine scan**

Gastrojejunostomy *see* **Ulcer surgery**

Gastroschisis *see* **Abdominal wall defects**

Gastrostomy

Definition

Gastrostomy is a surgical procedure for inserting a tube through the abdomen wall and into the stomach. The tube is used for feeding or drainage.

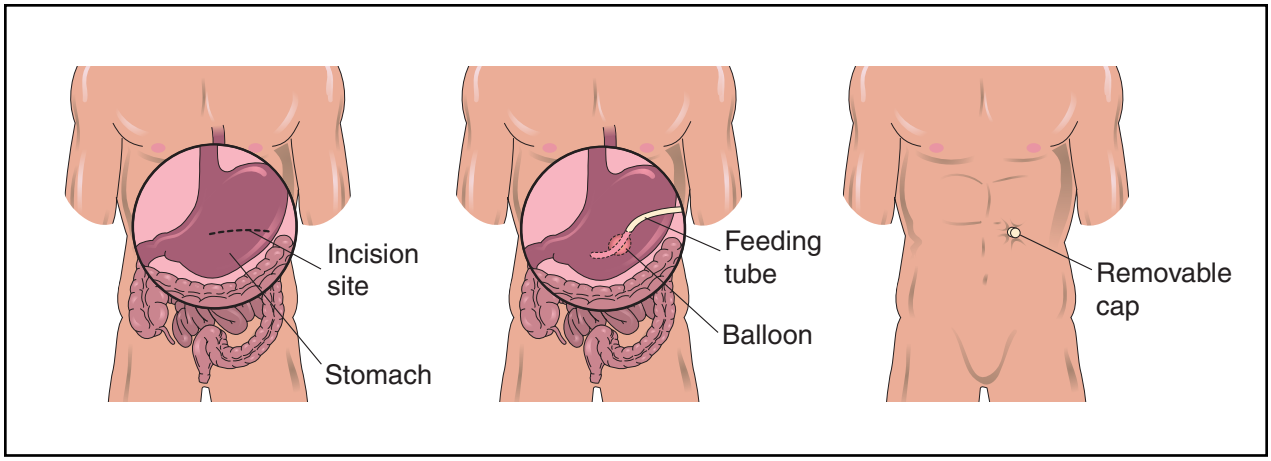
Purpose

Gastrostomy is performed because a patient temporarily or permanently needs to be fed directly through a tube in the stomach. Reasons for feeding by gastrostomy include **birth defects** of the mouth, esophagus, or stomach, and problems sucking or swallowing.

Gastrostomy is also performed to provide drainage for the stomach when it is necessary to bypass a long-standing obstruction of the stomach outlet into the small intestine. Obstructions may be caused by peptic ulcer scarring or a tumor.

Precautions

Gastrostomy is a relatively simple procedure. As with any surgery, patients are more likely to experience compli-



Gastrostomy is a procedure in which the surgeon makes an opening into the stomach and inserts a feeding tube for feeding or for drainage. *(Illustration by Electronic Illustrators Group.)*

cations if they are smokers, obese, use alcohol heavily, or use illicit drugs. In addition, some prescription medications may increase risks associated with anesthesia.

Description

Gastrostomy, also called gastrostomy tube insertion, is surgery performed by a general surgeon to give an external opening into the stomach. Surgery is performed either when the patient is under general anesthesia—where the patient feels as if he is in a deep sleep and has no awareness of what is happening—or under local anesthesia. With local anesthesia, the patient is awake, but the part of the body cut during the operation is numbed.

A small incision is made on the left side of the abdomen; then, an incision is made through the stomach. A small, flexible, hollow tube, usually made of polyvinylchloride or rubber, is inserted into the stomach. The stomach is stitched closed around the tube, and the incision is closed. The procedure is performed at a hospital or free-standing surgery center.

The length of time the patient needs to remain in the hospital depends on the age of the patient and the patient's general health. In some cases, the hospital stay can be as short as one day, but often is longer. Normally, the stomach and abdomen heal in five to seven days.

The cost of the surgery varies, depending on the age and health of the patient. Younger, sicker patients require more intensive, thus more expensive, care.

Preparation

Prior to the operation, the doctor will perform endoscopy and take x rays of the gastrointestinal tract. Blood and urine tests will also be performed, and the patient may meet with the anesthesiologist to evaluate any special conditions that might affect the administration of anesthesia.

Aftercare

Immediately after the operation, the patient is fed intravenously for at least 24 hours. Once bowel sounds are heard, indicating that the gastrointestinal system is working, the patient can begin clear liquid feedings through the tube. Gradually feedings are increased.

Patient education concerning use and care of the gastrostomy tube is very important. Patients and their families are taught how to recognize and prevent infection around the tube, how to feed through the tube, how to handle tube blockage, what to do if the tube pulls out, and what normal activities can be continued.

Risks

There are few risks associated with this surgery. The main complications are infection, bleeding, dislodgment of the tube, stomach bloating, nausea, and **diarrhea**.

Normal results

The patient is able to eat through the gastrostomy tube, or the stomach can be drained through the tube.

Resources

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KEY TERMS

Endoscopy—A procedure in which an instrument containing a camera is inserted into the gastrointestinal tract so that the doctor can visually inspect the gastrointestinal system.

OTHER

"Stomach Tube Insertion." HealthAnswers.com. <http://www.healthanswers.com>.

Tish Davidson

Gaucher disease

Definition

Gaucher disease is a rare genetic disorder that results in accumulation of fatty molecules called cerebrosides. It can have serious effects on numerous body organs including the liver, spleen, bones and central nervous system. Treatments based on molecular biology are becoming available, but are very expensive.

Description

Gaucher disease was first described by the French physician Philippe Gaucher in 1882. It is the most common of a class of diseases called lysosomal storage diseases, each of which is characterized by the accumulation of a specific chemical substance (a different substance depending on the exact disease). Gaucher disease is characterized by a wide array of different symptoms and the severity of the disease ranges from undetectable to lethal.

Three forms of the disease are recognized: Types I, II and III. Type I is by far the most common and shows the mildest symptoms. It is non-neuronopathic, meaning that the nervous system is not attacked. The onset of Type I can occur at any age in childhood or adult life with the average age of onset at about 21 years. Some affected individuals are have no symptoms throughout adult life. Type II, the infantile form, accounts for less than 1% of patients with Gaucher disease. It is neuronopathic (attacks the nervous system); nervous system effects are severe, and victims often die within the first year of life. Type III most often has its onset during childhood and has some of the features of both the adult and infantile forms. This affects less than 5% of persons with Gaucher disease.

Gaucher disease is caused by the absence, or near absence, of activity of an enzyme called glucocerebrosidase (GC). The normal action of GC is to break down a common molecule called glucocerebroside. If not broken down, glucocerebroside accumulates in certain cells to levels that can cause damage, especially in the spleen, liver, and bone. The common link among these organs is that they house a cell type called a macrophage. A macrophage is a large cell that surrounds and consumes a foreign substance (such as bacteria) in the body. The cellular structures in which glucocerebroside accumulates are called lysosomes.

The three forms of Gaucher disease also differ in their population genetics. Type I is most common in persons of eastern European (Ashkenazi) Jewish descent. Among this population, the disease occurs at a rate of one in 450 live births and about one in 10 to 15 persons are carriers, making it the most common genetic disease affecting Jewish people. The other two types are equally frequent in all ethnic groups. Type II occurs at a rate of one in 100,000 live births, while Type III is estimated to occur in one in 50,000 live births.

Causes and symptoms

Lack of the GC enzyme is caused by a mutation in the glucocerebrosidase gene. The gene is located on chromosome 1. As of 2000, there have been over 100 mutations described in this gene that causes Gaucher disease. Gaucher disease is inherited in an autosomal recessive pattern. This means that two defective gene copies must be inherited, one from each parent, for the disease to manifest itself. Persons with only one gene mutation are carriers for the disorder. A person who is a carrier for Gaucher disease does not have any symptoms and does not know he or she is a carrier unless he or she has had specific testing. When both parents are carriers for Gaucher disease, there is a one in four chance (25%) in each **pregnancy** for a child to have Gaucher disease. There is a two in three chance that a healthy sibling of an affected child is a carrier.

The results of Gaucher disease are widespread in the body and include excessive growth of the liver and spleen (hepatosplenomegaly), weakening of bones, and, in acute cases, severe nervous system damage. Many patients experience "bone crises," which are episodes of extreme **pain** in their bones.

There is a wide array of other problems that occur with Gaucher disease, such as anemia (fewer than normal red blood cells). Just how these other symptoms are caused is not known. Nor is it known why some patients have very mild disease and others have much more significant problems. Even identical twins with the disease can have differing symptoms.

Diagnosis

Diagnosis of Gaucher disease, based initially on the symptoms described above, can be confirmed by microscopic, enzymatic, and molecular tests. Biopsy (surgical removal of tissue from a problem area) of tissue is helpful for microscopic diagnosis. When biopsy tissue is examined under the microscope, cells will appear swollen and will show characteristic features of the cytoplasm (part of the cell body along with the nucleus) and nucleus. Enzyme tests will show deficiency (<30% of normal levels) of the enzyme GC. Molecular analysis of DNA samples looking at four of the more common mutations will show defects in the gene for GC in 95% of Ashkenazi Jewish individuals and in 75% of non-Jewish people. Diagnosis can be performed prenatally (before birth) if the parents' mutations are known using **amniocentesis** or **chorionic villus sampling**.

Diagnosis as to which of the three types of Gaucher disease an individual has is based on the symptoms, rather than on test results.

Treatment

Until the 1990s, only supportive therapy could be offered. **Analgesics** are used to control pain. Orthopedic treatment is used for bone **fractures**. In some cases, surgical removal of the spleen may be necessary. Several treatments for anemia have been used, including vitamin and iron supplements, blood transfusions, and bone marrow transplants.

The newest form of treatment for Gaucher disease is enzyme replacement therapy, in which GC can be administered intravenously. The enzyme can be prepared either by purification from placentas (alglucerase) or by recombinant DNA manufacturing techniques (imiglucerase). Either way, the cost of treatment ranges from $100,000 to $400,000 per year, which can prevent many from obtaining treatment.

Enzyme replacement is effective at reducing most Gaucher symptoms. The notable exception is neurologic damage in Type II disease, which remains unimproved by this treatment. This treatment is not recommended for individuals who are asymptomatic. As of 2000, the efficacy for the treatment of Type III Gaucher disease is not known. Many questions remain about enzyme replacement therapy in regard to dosage, and method and frequency of administration. The treatment program should be individualized for each patient.

Prognosis

A patient's expected lifespan varies greatly with the type of Gaucher disease. Infants with Type II disease have a life span of one to four years. Patients with Types I and III of the disease have highly variable outcomes with some patients dying in childhood and others living full lives. Little is known about the reasons for this variability.

KEY TERMS

Cerebrosides—Fatty carbohydrates that occur in the brain and nervous system.

Enzymatic replacement therapy—A treatment method used to replace missing enzymes. It is possible to synthesize enzymes and then inject them intravenously into patients.

Glucocerebroside—A cerebroside that contains glucose in the molecule.

Prevention

Genetic counseling is advised for individuals with Gaucher disease and for their relatives to accurately assess risk and discuss testing options. For couples who previously had a child with Gaucher or in situations where both parents are carriers for known Gaucher mutations, prenatal diagnosis is available to determine whether a pregnancy is affected. Families in which a person has been diagnosed with Gaucher disease can have DNA testing, which enables other relatives to determine their carrier status. Prospective parents can then use that information to conduct family planning or to prepare for a child who may have special circumstances.

Families in which both parents are known to be a carrier of a mutation for Gaucher disease could consider preimplantation genetic diagnosis. This relatively new procedure can select an embryo without both Gaucher disease mutations prior to implantation of the embryo into the uterus. This technique is only available at selected genetics centers.

As of 2000, population screening for Gaucher disease is not standard of care.

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ORGANIZATIONS

Alliance of Genetic Support Groups. 4301 Connecticut Ave. NW, Suite 404, Washington, DC 20008. (202) 966-5557. Fax: (202) 966-8553. <http://www.geneticalliance.org>.

Children's Gaucher Research Fund. PO Box 2123, Granite Bay, CA 95746-2123. (916) 797-3700. Fax: (916) 797-3707. <http://www.childrensgaucher.org>.

National Gaucher Foundation. 11140 Rockville Pike, Suite 350, Rockville, MD 20852-3106. (800) 925-8885. <http://www.gaucherdisease.org>.

National Organization for Rare Disorders (NORD). PO Box 8923, New Fairfield, CT 06812-8923. (203) 746-6518 or (800) 999-6673. Fax: (203) 746-6481. <http://www.rarediseases.org>.

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Amy Vance

Gay and lesbian health

Definition

Lesbian, gay, bisexual, and transgender (LGBT) individuals are as diverse as the general population in terms of race, ethnicity, age, religion, education, income, and family history. A number of health concerns are unique to or shared by the LGBT community, however, including an increased risk of certain cancers, infectious and **sexually transmitted diseases** (STDs), and mental health disorders; issues relating to **nutrition** and weight, tobacco use, and substance abuse; and discrimination by health care and insurance providers.

Description

The definitions of different sexual identities have shifted over the years, as have the perceptions and stereotypes of the general population. Because of the wide range of behaviors and identities that exist in the LGBT community, it is difficult to develop an inclusive definition. It is generally accepted, however, that gay men and lesbians are sexually attracted to or participate in sexual behaviors with individuals of the same gender, while bisexual men and women are sexually attracted to or participate in sexual behaviors with individuals of both genders. Transgender individuals live part- or full-time in a gender role opposite to their genetic sex.

It is estimated that approximately 2.8% of men and 1.4% of women identify as being gay, lesbian, or bisexual while 9.1% of men and 4.3% of women have participated in sexual behavior with someone of the same gender at least once. The true extent of the transgender community has not been well researched in the United States; one study from the Netherlands in 1993 found that one in 11,900 males and one in 30,400 females are transgender.

There are a number of issues that arise when trying to define sexual orientation. Many gay men and lesbians have participated in or continue to participate in sexual activities with members of the opposite sex but choose not to identify as heterosexuals or bisexuals. Others have never participated in sexual activities at all yet still identify as gay, lesbian, or bisexual. Some men and women identifying as bisexuals are in long-term, monogamous relationships with individuals of the same or opposite sex. Male-to-female (MTF) or female-to-male (FTM) transgender individuals may or may not identify themselves as gay or lesbian.

The implications of these identity issues are far-reaching. Misdiagnoses or improper medical recommendations might come from health care providers who have mistakenly assumed sexual behaviors or risks from the patient's stated identity. For example, a provider might incorrectly assume that a lesbian patient has never had sexual intercourse with a male and therefore would not have contracted STDs not normally transmitted by sexual activities between women. It has been difficult to closely estimate the numbers of LGBT individuals in the United States because of varying definitions. Likewise, the statistics in medical or social studies and surveys on LGBT issues might vary widely depending on what definitions were provided for the respondents. Because of this, many researchers have opted for the more inclusive terms of "men who have sex with men" (MSM) and "women who have sex with women" (WSW) to categorize gay, lesbian, and bisexual respondents.

Important health care issues

Many LGBT individuals have difficulty revealing their sexual identity ("coming out") to their health care providers. They may fear discrimination from providers or believe that their confidentiality might be breached. In some cases health care workers have been poorly trained to address the needs of LGBT individuals or have difficulty communicating with their LGBT patient (one study

indicated that 40% of physicians are uncomfortable providing care for gay or lesbian patients). In addition, many questions posed in questionnaires or examinations are heterosexually biased (e.g. asking a lesbian which birth control methods she uses or a gay man if he is married, single, or divorced).

Other reasons why LGBT individuals are often hesitant to share their sexual identity are more logistical. Many insurance companies deny benefits to long-term partners on the basis that they are not married. LGBT patients may have inadequate access to health care, either because they live in a remote rural area or in the crowded inner city. Some same-sex partners encounter discrimination in hospitals and clinics when they are denied the rights usually given to spouses of a patient such as visiting, making medical decisions, and participating in consultations with physicians.

Some of the health concerns and risk factors that are relevant to LBGT individuals may be shared by the general population, while others are more specific to the LGBT community, and still others are specific to different subgroups of LGBT individuals. These health concerns may be grouped into the following areas of concern:

- Sexual behavior issues: STDs such as human **immunodeficiency** virus (HIV) and acquired immune deficiency syndrome (**AIDS**), **hepatitis A** virus (HAV), **hepatitis B** virus (HBV), bacterial vaginosis, **gonorrhea**, chlamydia, and **genital warts** (human papillomavirus or HPV); anal, ovarian, and cervical **cancer**.
- Cultural issues: body image, nutrition, weight, and eating disorders; drug and alcohol abuse; tobacco use; parenting and family planning.
- Discrimination issues: inadequate medical care; harassment at work, school, or home; difficulty in obtaining housing, insurance coverage, or child custody; violence.
- Sexual identity issues: conflicts with family, friends, and work mates; psychological issues such as **anxiety**, depression, and suicide; economic hardship.

CANCER. Cancer is the second leading cause of **death** in the United States. In 2000, it was estimated that 1,220,100 individuals were diagnosed with cancer and 552,200 lost their lives as a result. LBGT individuals are at an increased risk for certain types of cancers. Some researchers believe that those who do not disclose their sexual identity live with an added **stress** that suppresses the immune system, thus leaving them with an increased risk of tumor growth.

Several studies have indicated that lesbians have higher risk for developing **breast cancer**. This is partially related to higher rates of risk factors such as **obesity**, alcohol use, tobacco use, and nulliparity (not bearing children). It has also been shown that lesbians are less likely to be screened for breast cancer than heterosexual women. Lesbians also have additional risk of developing **ovarian cancer**, due to inadequate access to health care, nulliparity, and not using **oral contraceptives** (use of oral contraceptives has been shown to decrease the risk of getting ovarian cancer).

Gay and bisexual men (or more generally, men who have sex with men [MSM]) are at higher risk of developing non-Hodgkin's lymphoma, **Hodgkin's disease**, and **anal cancer**. **Kaposi's sarcoma**, an AIDS-associated cancer, used to be found in the gay community at rates thousands of times more than the general population before more effective **antiretroviral drugs** became available for people infected with HIV. Anal cancer is associated with transmission of human papillomavirus (HPV); a 1998 study indicated 73% of HIV-positive and 23% of HIV-negative MSM were infected with more than one type of HPV. The risk factors associated with MSM are also associated with increased rates of anal cancer (i.e. **smoking**, having many sexual partners, and receiving anal intercourse).

AIDS. As of 2000, more than 753,900 individuals have been diagnosed with AIDS in the United States; of total cases, 84% are men, 16% are women, and 1% are children 12 years old or younger. The major risk groups associated with AIDS transmission are MSM who engage in high-risk sexual behaviors, intravenous drug users (IDUs) who share needles, heterosexuals who engage in high-risk sexual behaviors, inmates at correctional facilities, and neonates (newborns) whose mothers are infected with HIV.

Approximately 54% of cumulative AIDS cases are men who have sex with men. MSM also constitute 38% of newly reported HIV cases each year. An annual decrease has occurred in the number of reported AIDS-related deaths, partially attributable to the development of advanced therapies that are extending the life expectancies of AIDS patients. These new treatments, however, have inadvertently caused decreased rates of safe sex practices; one 1998 study revealed that 18% of HIV-positive men were having safe sex less often since advances in treatment.

Few studies have looked at the transmission of HIV in women who have sex with women (WSW). HIV transmission might occur in WSW because of intercourse with males or intravenous drug use. Several small studies conducted in the 1990s found no evidence of HIV transmission from sexual activities between women.

OTHER STDS. It is estimated that 333 million cases of curable STDs occur each year worldwide. Among the

most commonly found STDs in the United States are chlamydia, gonorrhea, AIDS, **syphilis**, and hepatitis B virus (HBV). Over 15 million new infections are estimated to occur each year in the United State, with approximately four million of those occurring in adolescents.

MSM are at most risk of developing **urethritis** (inflammation of the urethra), **proctitis** (inflammation of the rectum), pharyngitis (inflammation of the cavity at the back of the mouth), gonorrhea, chlamydia, HAV, HBV, syphilis, herpes, and HPV. HAV and HBV are both vaccine-preventable viruses but rates of **vaccination** among MSM are low; in 1996 the Centers for Disease Control and Prevention (CDC) found that only 3% of MSM had been vaccinated against HBV. In May 2001 the Food and Drug Administration (FDA) approved a new vaccine that combines the HAV and HBV in one, with hopes that vaccination rates will increase.

It appears that STDs are less common in women who have sex only with women than in bisexual or heterosexual women. Genital **warts**, **trichomoniasis**, and bacterial vaginosis are transmittable during sexual activity between women. Chlamydia, herpes, syphilis, gonorrhea, and HAV are also able to be transmitted between women, although at lower rates.

MENTAL HEALTH. Forty million Americans are estimated to be diagnosed with a mental disorder, a condition in which abnormalities in thought, feeling, and/or behavior cause distress or impair function. Of these, only 25% seek and obtain care from mental health professionals.

Homosexuality was labeled as a mental disorder until 1973 when it was declassified by the American Psychiatric Association; in 1986 "ego-dystonic homosexuality" was removed from the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-III). More recently, studies have shown that LGBT individuals are at increased risk of depression, panic attacks, substance abuse, and suicide. MSM have been shown to have higher rates of depression, anxiety, and **conduct disorder** than heterosexual males, although not much study has been done in this area. WSW have been shown to have increased rates of alcohol and drug abuse.

Gender identity disorder is defined as "a strong and persistent cross-gender identification...manifested by symptoms such as a stated desire to be the other sex, frequently passing as the other sex, desire to live or be treated as the other sex, or the conviction that he or she as the typical feelings and reactions of the other sex" (DSM-IV, 302.85). Transvestic fetishism is defined as involving "recurrent, intense sexually arousing fantasies, sexual urges, or behaviors involving cross-dressing" (DSM-IV, 302.3). Both disorders lead to a "disturbance that causes clinically significant distress or impairment in social, occupational, or other important areas of functioning." This last point iterates that transgender individuals not automatically considered under DSM-IV to have a mental disorder.

NUTRITION AND WEIGHT. Diet and nutritional factors are associated with a number of diseases including cancer, **stroke**, diabetes, heart disease, and **osteoporosis**. It has been shown that lesbians are more likely than heterosexual women to be obese, have a higher body mass index (BMI), and have higher rates of smoking, but are also more likely to have a healthier body image (42% compared to 21% of heterosexual women). Gay men and adolescents, on the other hand, have been shown to have increased rates of eating disorder behaviors than heterosexual men; examples are binge eating (25% compared to 11%), purging behaviors (12% to 4%), and poor body image (28% to 12%).

SUBSTANCE AND TOBACCO USE. Marijuana and **cocaine** use has been shown to be higher among lesbians than heterosexual women. The incidence of the use of some drugs is higher in gay men than heterosexual men; these include marijuana, psychedelic drugs, ecstasy, barbituates, and stimulants such as amyl or butyl nitrate ("poppers"). There is some indication that the use of some illicit drugs speeds up the replication of HIV, although more research needs to be done in this area.

Cigarette smoking is responsible for 430,000 deaths a year in the United States, with an estimated 3,000 nonsmokers dying as a result of exposure to secondhand smoke. In 1997 the rate of smoking among all adults was 25%. In contrast, 36% of gay men and lesbians were noted to be smokers. Lesbians are more than two times as likely to become heavy smokers than heterosexual women.

Prevention

There are numerous ways that health care providers can improve the access to and experience of health care services for LGBT individuals. These include:

- rewording questionnaires and examinations to be inclusive of LGBT patients
- providing referrals to social service agencies and counseling services that are LGBT-friendly
- taking educational courses that are sensitive to the needs of LGBT patients
- treating the families of LGBT patients as one would the families of heterosexual patients
- maintaining the strictest code of confidentiality
- developing and maintaining health care centers or clinics that address LGBT-specific needs

KEY TERMS

Gender identity disorder—a mental disorder in which cross-gender identification (including wanting to live and be treated as the other sex) causes distress or impairment of normal function.

Pharyngitis—inflammation of the cavity at the back of the mouth.

Proctitis—inflammation of the rectum.

Nulliparity—never having carried a pregnancy.

Transvestic fetishism—a mental disorder in which fantasies, sexual urges, or behaviors involving cross-dressing cause distress or impairment of normal function.

Urethritis—inflammation of the urethra.

- asking non-threatening questions to determine if a person is at risk of an STD
- educating patients of risk factors associated with STDs, possible vaccines, and treatments available
- providing services to individuals in the process of disclosing their sexual identity and, if applicable, their families

Resources

ORGANIZATIONS

Gay and Lesbian Medical Association. 459 Fulton Street, Suite 107, San Francisco, CA 94102. (415) 225-4547. <http://www.glma.org>.

Parents, Families, and Friends of Lesbians and Gays. 1726 M Street NW, Suite 400, Washington, DC 20036. (202) 467-8180. <http://www.pflag.org>.

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Stéphanie Islane Dionne

Gender identity disorder

Definition

The psychological diagnosis gender identity disorder (GID) is used to describe a male or female that feels a strong identification with the opposite sex and experiences considerable distress because of their actual sex.

Description

Gender identity disorder can affect children, adolescents, and adults. Individuals with gender identity disorder have strong cross-gender identification. They believe that they are, or should be, the opposite sex. They are uncomfortable with their sexual role and organs and may express a desire to alter their bodies. While not all persons with GID are labeled as transsexuals, there are those who are determined to undergo sex change procedures or have done so, and, therefore, are classified as transsexual. They often attempt to pass socially as the opposite sex. Transsexuals alter their physical appearance cosmetically and hormonally, and may eventually undergo a sex-change operation.

Children with gender identity disorder refuse to dress and act in sex-stereotypical ways. It is important to remember that many emotionally healthy children experience fantasies about being a member of the opposite sex. The distinction between these children and gender identity disordered children is that the latter experience significant interference in functioning because of their cross-gender identification. They may become severely depressed, anxious, or socially withdrawn.

Causes and symptoms

The cause of gender identity disorder is not known. It has been theorized that a prenatal hormonal imbalance may predispose individuals to the disorder. Problems in the individual's family interactions or family dynamics have also been postulated as having some causal impact.

The *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (*DSM-IV*), the diagnostic reference standard for United States mental health profes-

KEY TERMS

Cross-dressing—Dressing in clothing that is stereotypical of the opposite sex.

Gender identity disorder (GID)—A strong and lasting cross-gender identification and persistent discomfort with one's biological gender (sex) role. This discomfort must cause a significant amount of distress or impairment in the functioning of the individual.

Transsexual—A person with gender identity disorder who has an overwhelming desire to change anatomic sex; one who seeks hormonal or surgical treatment to change sex.

sionals, describes the criteria for gender identity disorder as an individual's strong and lasting cross-gender identification and their persistent discomfort with their biological gender role. This discomfort must cause a significant amount of distress or impairment in the functioning of the individual.

DSM-IV specifies that children must display at least four of the following symptoms of cross-gender identification for a diagnosis of gender identity disorder:

- a repeatedly stated desire to be, or insistence that he or she is, the opposite sex
- a preference for cross-dressing
- a strong and lasting preference to play make-believe and role-playing games as a member of the opposite sex or persistent fantasies that he or she is the opposite sex
- a strong desire to participate in the stereotypical games of the opposite sex
- a strong preference for friends and playmates of the opposite sex

Diagnosis

Gender identity disorder is typically diagnosed by a psychiatrist or psychologist, who conducts an interview with the patient and takes a detailed social history. Family members may also be interviewed during the assessment process. This evaluation usually takes place in an outpatient setting.

Treatment

Treatment for children with gender identity disorder focuses on treating secondary problems such as depression and **anxiety**, and improving self-esteem. Treatment may also work on instilling positive identifications with the child's biological gender. Children typically undergo psychosocial therapy sessions; their parents may also be referred for family or individual therapy.

Transsexual adults often request hormone and surgical treatments to suppress their biological sex characteristics and acquire those of the opposite sex. A team of health professionals, including the treating psychologist or psychiatrist, medical doctors, and several surgical specialists, oversee this transitioning process. Because of the irreversible nature of the surgery, candidates for sex-change surgery are evaluated extensively and are often required to spend a period of time integrating themselves into the cross-gender role before the procedure begins. Counseling and peer support are also invaluable to transsexual individuals.

Prognosis

Long-term follow up studies have shown positive results for many transsexuals who have undergone sex-change surgery. However, significant social, personal, and occupational issues may result from surgical sex changes, and the patient may require psychotherapy or counseling.

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Paula Anne Ford-Martin

Gene therapy

Definition

Gene therapy is a rapidly growing field of medicine in which genes are introduced into the body to treat diseases. Genes control heredity and provide the basic biological code for determining a cell's specific functions. Gene therapy seeks to provide genes that correct or supplant the disease-controlling functions of cells that are not, in essence, doing their job. Somatic gene therapy introduces therapeutic genes at the tissue or cellular level to treat a specific individual. Germ-line gene therapy inserts genes into reproductive cells or possibly into embryos to correct genetic defects that could be passed on to future generations. Initially conceived as an approach for treating inherited diseases, like **cystic fibrosis** and Huntington's disease, the scope of potential gene therapies has grown to include treatments for cancers, arthritis, and infectious diseases. Although gene therapy testing in humans has advanced rapidly, many questions surround its use. For example, some scientists are concerned that the therapeutic genes themselves may cause disease. Others fear that germ-line gene therapy may be used to control human development in ways not connected with disease, like intelligence or appearance.

The biological basis of gene therapy

Gene therapy has grown out of the science of genetics or how heredity works. Scientists know that life begins in a cell, the basic building block of all multicellular organisms. Humans, for instance, are made up of trillions of cells, each performing a specific function. Within the cell's nucleus (the center part of a cell that regulates its chemical functions) are pairs of chromosomes. These threadlike structures are made up of a single molecule of DNA (deoxyribonucleic acid), which carries the blueprint of life in the form of codes, or genes, that determine inherited characteristics.

A DNA molecule looks like two ladders with one of the sides taken off both and then twisted around each other. The rungs of these ladders meet (resulting in a spiral staircase-like structure) and are called base pairs. Base pairs are made up of nitrogen molecules and arranged in specific sequences. Millions of these base pairs, or sequences, can make up a single gene, specifically defined as a segment of the chromosome and DNA that contains certain hereditary information. The gene, or combination of genes formed by these base pairs ultimately direct an organism's growth and characteristics through the production of certain chemicals, primarily proteins, which carry out most of the body's chemical functions and biological reactions.

Scientists have long known that alterations in genes present within cells can cause inherited diseases like cystic fibrosis, sickle-cell anemia, and **hemophilia**. Similarly, errors in the total number of chromosomes can cause conditions such as **Down syndrome** or Turner's syndrome. As the study of genetics advanced, however, scientists learned that an altered genetic sequence can also make people more susceptible to diseases, like **atherosclerosis**, **cancer**, and even **schizophrenia**. These diseases have a genetic component, but are also influenced by environmental factors (like diet and lifestyle). The objective of gene therapy is to treat diseases by introducing functional genes into the body to alter the cells involved in the disease process by either replacing missing genes or providing copies of functioning genes to replace nonfunctioning ones. The inserted genes can be naturally-occurring genes that produce the desired effect or may be genetically engineered (or altered) genes.

Scientists have known how to manipulate a gene's structure in the laboratory since the early 1970s through a process called gene splicing. The process involves removing a fragment of DNA containing the specific genetic sequence desired, then inserting it into the DNA of another gene. The resultant product is called recombinant DNA and the process is genetic engineering.

There are basically two types of gene therapy. Germ-line gene therapy introduces genes into reproductive cells (sperm and eggs) or someday possibly into embryos in hopes of correcting genetic abnormalities that could be passed on to future generations. Most of the current work in applying gene therapy, however, has been in the realm of somatic gene therapy. In this type of gene therapy, therapeutic genes are inserted into tissue or cells to produce a naturally occurring protein or substance that is lacking or not functioning correctly in an individual patient.

Viral vectors

In both types of therapy, scientists need something to transport either the entire gene or a recombinant DNA to the cell's nucleus, where the chromosomes and DNA reside. In essence, vectors are molecular delivery trucks. One of the first and most popular vectors developed were viruses because they invade cells as part of the natural infection process. Viruses have the potential to be excellent vectors because they have a specific relationship with the host in that they colonize certain cell types and tissues in specific organs. As a result, vectors are chosen according to their attraction to certain cells and areas of the body.

One of the first vectors used was retroviruses. Because these viruses are easily cloned (artificially reproduced) in the laboratory, scientists have studied

them extensively and learned a great deal about their biological action. They have also learned how to remove the genetic information which governs viral replication, thus reducing the chances of infection.

Retroviruses work best in actively dividing cells, but cells in the body are relatively stable and do not divide often. As a result, these cells are used primarily for *ex vivo* (outside the body) manipulation. First, the cells are removed from the patient's body, and the virus, or vector, carrying the gene is inserted into them. Next, the cells are placed into a nutrient culture where they grow and replicate. Once enough cells are gathered, they are returned to the body, usually by injection into the blood stream. Theoretically, as long as these cells survive, they will provide the desired therapy.

Another class of viruses, called the adenoviruses, may also prove to be good gene vectors. These viruses can effectively infect nondividing cells in the body, where the desired gene product is then expressed naturally. In addition to being a more efficient approach to gene transportation, these viruses, which cause respiratory infections, are more easily purified and made stable than retroviruses, resulting in less chance of an unwanted viral infection. However, these viruses live for several days in the body, and some concern surrounds the possibility of infecting others with the viruses through sneezing or coughing. Other viral vectors include **influenza** viruses, Sindbis virus, and a herpes virus that infects nerve cells.

Scientists have also delved into nonviral vectors. These vectors rely on the natural biological process in which cells uptake (or gather) macromolecules. One approach is to use liposomes, globules of fat produced by the body and taken up by cells. Scientists are also investigating the introduction of raw recombinant DNA by injecting it into the bloodstream or placing it on microscopic beads of gold shot into the skin with a "gene-gun." Another possible vector under development is based on dendrimer molecules. A class of polymers (naturally occurring or artificial substances that have a high molecular weight and formed by smaller molecules of the same or similar substances), is "constructed" in the laboratory by combining these smaller molecules. They have been used in manufacturing Styrofoam, polyethylene cartons, and Plexiglass. In the laboratory, dendrimers have shown the ability to transport genetic material into human cells. They can also be designed to form an affinity for particular cell membranes by attaching to certain sugars and protein groups.

The history of gene therapy

In the early 1970s, scientists proposed "gene surgery" for treating inherited diseases caused by faulty genes. The idea was to take out the disease-causing gene and surgically implant a gene that functioned properly. Although sound in theory, scientists, then and now, lack the biological knowledge or technical expertise needed to perform such a precise surgery in the human body.

However, in 1983, a group of scientists from Baylor College of Medicine in Houston, Texas, proposed that gene therapy could one day be a viable approach for treating Lesch-Nyhan disease, a rare neurological disorder. The scientists conducted experiments in which an enzyme-producing gene (a specific type of protein) for correcting the disease was injected into a group of cells for replication. The scientists theorized the cells could then be injected into people with Lesch-Nyhan disease, thus correcting the genetic defect that caused the disease.

As the science of genetics advanced throughout the 1980s, gene therapy gained an established foothold in the minds of medical scientists as a promising approach to treatments for specific diseases. One of the major reasons for the growth of gene therapy was scientists' increasing ability to identify the specific genetic malfunctions that caused inherited diseases. Interest grew as further studies of DNA and chromosomes (where genes reside) showed that specific genetic abnormalities in one or more genes occurred in successive generations of certain family members who suffered from diseases like intestinal cancer, manic-depression, **Alzheimer's disease**, heart disease, diabetes, and many more. Although the genes may not be the only cause of the disease in all cases, they may make certain individuals more susceptible to developing the disease because of environmental influences, like **smoking**, pollution, and **stress**. In fact, some scientists theorize that all diseases may have a genetic component.

On September 14, 1990, a four-year old girl suffering from a genetic disorder that prevented her body from producing a crucial enzyme became the first person to undergo gene therapy in the United States. Because her body could not produce adenosine deaminase (ADA), she had a weakened immune system, making her extremely susceptible to severe, life-threatening infections. W. French Anderson and colleagues at the National Institutes of Health's Clinical Center in Bethesda, Maryland, took white blood cells (which are crucial to proper immune system functioning) from the girl, inserted ADA producing genes into them, and then transfused the cells back into the patient. Although the young girl continued to show an increased ability to produce ADA, debate arose as to whether the improvement resulted from the gene therapy or from an additional drug treatment she received.

Nevertheless, a new era of gene therapy began as more and more scientists sought to conduct clinical trial (testing in humans) research in this area. In that same

year, gene therapy was tested on patients suffering from melanoma (skin cancer). The goal was to help them produce antibodies (disease fighting substances in the immune system) to battle the cancer.

These experiments have spawned an ever growing number of attempts at gene therapies designed to perform a variety of functions in the body. For example, a gene therapy for cystic fibrosis aims to supply a gene that alters cells, enabling them to produce a specific protein to battle the disease. Another approach was used for brain cancer patients, in which the inserted gene was designed to make the cancer cells more likely to respond to drug treatment. Another gene therapy approach for patients suffering from artery blockage, which can lead to strokes, induces the growth of new blood vessels near clogged arteries, thus ensuring normal blood circulation.

Currently, there are a host of new gene therapy agents in clinical trials. In the United States, both nucleic acid based (*in vivo*) treatments and cell-based (*ex vivo*) treatments are being investigated. Nucleic acid based gene therapy uses vectors (like viruses) to deliver modified genes to target cells. Cell-based gene therapy techniques remove cells from the patient in order to genetically alter them then reintroduce them to the patient's body. Presently, gene therapies for the following diseases are being developed: cystic fibrosis (using adenoviral vector), HIV infection (cell-based), **malignant melanoma** (cell-based), Duchenne **muscular dystrophy** (cell-based), hemophilia B (cell-based), **kidney cancer** (cell-based), Gaucher's Disease (retroviral vector), **breast cancer** (retroviral vector), and lung cancer (retroviral vector). When a cell or individual is treated using gene therapy and successful incorporation of engineered genes has occurred, the cell or individual is said to be *transgenic*.

The medical establishment's contribution to transgenic research has been supported by increased government funding. In 1991, the U.S. government provided $58 million for gene therapy research, with increases in funding of $15-40 million dollars a year over the following four years. With fierce competition over the promise of societal benefit in addition to huge profits, large pharmaceutical corporations have moved to the forefront of transgenic research. In an effort to be first in developing new therapies, and armed with billions of dollars of research funds, such corporations are making impressive strides toward making gene therapy a viable reality in the treatment of once elusive diseases.

Diseases targeted for treatment by gene therapy

The potential scope of gene therapy is enormous. More than 4,200 diseases have been identified as resulting directly from abnormal genes, and countless others that may be partially influenced by a person's genetic makeup. Initial research has concentrated on developing gene therapies for diseases whose genetic origins have been established and for other diseases that can be cured or ameliorated by substances genes produce.

Early detection of cancer. The researcher's pen marks a band on a DNA sequencing autoradiogram confirming a bladder cancer. *(Custom Medical Stock Photo. Reproduced by permission.)*

The following are examples of potential gene therapies. People suffering from cystic fibrosis lack a gene needed to produce a salt-regulating protein. This protein regulates the flow of chloride into epithelial cells, (the cells that line the inner and outer skin layers) which cover the air passages of the nose and lungs. Without this regulation, patients with cystic fibrosis build up a thick mucus that makes them prone to lung infections. A gene therapy technique to correct this abnormality might employ an adenovirus to transfer a normal copy of what scientists call the cystic fibrosis transmembrane conductance regulator, or CTRF, gene. The gene is introduced into the patient by spraying it into the nose or lungs.

Familial **hypercholesterolemia** (FH) is also an inherited disease, resulting in the inability to process cholesterol properly, which leads to high levels of artery-clogging fat in the blood stream. Patients with FH often suffer heart attacks and strokes because of blocked arteries. A gene therapy approach used to battle FH is much more intricate than most gene therapies because it involves partial surgical removal of patients' livers (*ex vivo* transgene therapy). Corrected copies of a gene that serve to reduce cholesterol build-up are inserted into the liver sections, which are then transplanted back into the patients.

Gene therapy has also been tested on patients with **AIDS**. AIDS is caused by the human **immunodeficiency** virus (HIV), which weakens the body's immune system to the point that sufferers are unable to fight off diseases

like pneumonias and cancer. In one approach, genes that produce specific HIV proteins have been altered to stimulate immune system functioning without causing the negative effects that a complete HIV molecule has on the immune system. These genes are then injected in the patient's blood stream. Another approach to treating AIDS is to insert, via white blood cells, genes that have been genetically engineered to produce a receptor that would attract HIV and reduce its chances of replicating.

Several cancers also have the potential to be treated with gene therapy. A therapy tested for melanoma, or skin cancer, involves introducing a gene with an anticancer protein called tumor necrosis factor (TNF) into test tube samples of the patient's own cancer cells, which are then reintroduced into the patient. In brain cancer, the approach is to insert a specific gene that increases the cancer cells' susceptibility to a common drug used in fighting the disease.

Gaucher disease is an inherited disease caused by a mutant gene that inhibits the production of an enzyme called glucocerebrosidase. Patients with Gaucher disease have enlarged livers and spleens and eventually their bones deteriorate. Clinical gene therapy trials focus on inserting the gene for producing this enzyme.

Gene therapy is also being considered as an approach to solving a problem associated with a surgical procedure known as balloon **angioplasty**. In this procedure, a stent (in this case, a type of tubular scaffolding) is used to open the clogged artery. However, in response to the trauma of the stent insertion, the body initiates a natural healing process that produces too many cells in the artery and results in restenosis, or reclosing of the artery. The gene therapy approach to preventing this unwanted side effect is to cover the outside of the stents with a soluble gel. This gel contains vectors for genes that reduce this overactive healing response.

The Human Genome Project

Although great strides have been made in gene therapy in a relatively short time, its potential usefulness has been limited by lack of scientific data concerning the multitude of functions that genes control in the human body. For instance, it is now known that the vast majority of genetic material does not store information for the creation of proteins, but rather is involved in the control and regulation of gene expression, and is, thus, much more difficult to interpret. Even so, each individual cell in the body carries thousands of genes coding for proteins, with some estimates as high as 150,000 genes. For gene therapy to advance to its full potential, scientists must discover the biological role of each of these individual genes and where the base pairs that make them up are located on DNA.

To address this issue, the National Institutes of Health initiated the Human Genome Project in 1990. Led by James D. Watson (one of the co-discoverers of the chemical makeup of DNA) the project's 15-year goal is to map the entire human genome (a combination of the words gene and chromosomes). A genome map would clearly identify the location of all genes as well as the more than three billion base pairs that make them up. With a precise knowledge of gene locations and functions, scientists may one day be able to conquer or control diseases that have plagued humanity for centuries.

Scientists participating in the Human Genome Project have identified an average of one new gene a day, but many expect this rate of discovery to increase. By the year 2005, their goal is to determine the exact location of all the genes on human DNA and the exact sequence of the base pairs that make them up. Some of the genes identified through this project include a gene that predisposes people to **obesity**, one associated with programmed cell **death** (apoptosis), a gene that guides HIV viral reproduction, and the genes of inherited disorders like Huntington's disease, Lou Gehrig's disease, and some colon and breast cancers. In February of 2001, scientists published a rought draft of the complete human genome. With fewer than the anticipated number of genes found, between 30,000 –40,000, the consequences of this announcement are enormous. Scientists caution however, that the initial publication is only a draft of the human genome and much more work is still ahead for the completion of the project. As the human genome is completed, there will be more information available for gene therapy research and implementation.

The future of gene therapy

Gene therapy seems elegantly simple in its concept: supply the human body with a gene that can correct a biological malfunction that causes a disease. However, there are many obstacles and some distinct questions concerning the viability of gene therapy. For example, viral vectors must be carefully controlled lest they infect the patient with a viral disease. Some vectors, like retroviruses, can also enter cells functioning properly and interfere with the natural biological processes, possibly leading to other diseases. Other viral vectors, like the adenoviruses, are often recognized and destroyed by the immune system so their therapeutic effects are short-lived. Maintaining gene expression so it performs its role properly after vector delivery is difficult. As a result, some therapies need to be repeated often to provide long-lasting benefits.

One of the most pressing issues, however, is gene regulation. Genes work in concert to regulate their functioning. In other words, several genes may play a part in turning other genes on and off. For example, certain

KEY TERMS

Cell—The smallest living units of the body which group together to form tissues and help the body perform specific functions.

Chromosome—A microscopic thread-like structure found within each cell of the body and consists of a complex of proteins and DNA. Humans have 46 chromosomes arranged into 23 pairs. Changes in either the total number of chromosomes or their shape and size (structure) may lead to physical or mental abnormalities.

Clinical trial—The testing of a drug or some other type of therapy in a specific population of patients.

Clone—A cell or organism derived through asexual (without sex) reproduction containing the identical genetic information of the parent cell or organism.

Deoxyribonucleic acid (DNA)—The genetic material in cells that holds the inherited instructions for growth, development, and cellular functioning.

Embryo—The earliest stage of development of a human infant, usually used to refer to the first eight weeks of pregnancy. The term *fetus* is used from roughly the third month of pregnancy until delivery.

Enzyme—A protein that catalyzes a biochemical reaction or change without changing its own structure or function.

Eugenics—A social movement in which the population of a society, country, or the world is to be improved by controlling the passing on of hereditary information through mating.

Gene—A building block of inheritance, which contains the instructions for the production of a particular protein, and is made up of a molecular sequence found on a section of DNA. Each gene is found on a precise location on a chromosome.

Gene transcription—The process by which genetic information is copied from DNA to RNA, resulting in a specific protein formation.

Genetic engineering—The manipulation of genetic material to produce specific results in an organism.

Genetics—The study of hereditary traits passed on through the genes.

Germ-line gene therapy—The introduction of genes into reproductive cells or embryos to correct inherited genetic defects that can cause disease.

Liposome—Fat molecule made up of layers of lipids.

Macromolecules—A large molecule composed of thousands of atoms.

Nitrogen—A gaseous element that makes up the base pairs in DNA.

Nucleus—The central part of a cell that contains most of its genetic material, including chromosomes and DNA.

Protein—Important building blocks of the body, composed of amino acids, involved in the formation of body structures and controlling the basic functions of the human body.

Somatic gene therapy—The introduction of genes into tissue or cells to treat a genetic related disease in an individual.

Vectors—Something used to transport genetic information to a cell.

genes work together to stimulate cell division and growth, but if these are not regulated, the inserted genes could cause tumor formation and cancer. Another difficulty is learning how to make the gene go into action only when needed. For the best and safest therapeutic effort, a specific gene should turn on, for example, when certain levels of a protein or enzyme are low and must be replaced. But the gene should also remain dormant when not needed to ensure it doesn't oversupply a substance and disturb the body's delicate chemical makeup.

One approach to gene regulation is to attach other genes that detect certain biological activities and then react as a type of automatic off-and-on switch that regulates the activity of the other genes according to biological cues. Although still in the rudimentary stages, researchers are making headway in inhibiting some gene functioning by using a synthetic DNA to block gene transcriptions (the copying of genetic information). This approach may have implications for gene therapy.

The ethics of gene therapy

While gene therapy holds promise as a revolutionary approach to treating disease, ethical concerns over its use and ramifications have been expressed by scientists and

lay people alike. For example, since much needs to be learned about how these genes actually work and their long-term effect, is it ethical to test these therapies on humans, where they could have a disastrous result? As with most clinical trials concerning new therapies, including many drugs, the patients participating in these studies have usually not responded to more established therapies and are often so ill the novel therapy is their only hope for long-term survival.

Another questionable outgrowth of gene therapy is that scientists could possibly manipulate genes to genetically control traits in human offspring that are not health related. For example, perhaps a gene could be inserted to ensure that a child would not be bald, a seemingly harmless goal. However, what if genetic manipulation was used to alter skin color, prevent homosexuality, or ensure good looks? If a gene is found that can enhance intelligence of children who are not yet born, will everyone in society, the rich and the poor, have access to the technology or will it be so expensive only the elite can afford it?

The Human Genome Project, which plays such an integral role for the future of gene therapy, also has social repercussions. If individual genetic codes can be determined, will such information be used against people? For example, will someone more susceptible to a disease have to pay higher insurance premiums or be denied health insurance altogether? Will employers discriminate between two potential employees, one with a "healthy" genome and the other with genetic abnormalities?

Some of these concerns can be traced back to the eugenics movement popular in the first half of the twentieth century. This genetic "philosophy" was a societal movement that encouraged people with "positive" traits to reproduce while those with less desirable traits were sanctioned from having children. Eugenics was used to pass strict immigration laws in the United States, barring less suitable people from entering the country lest they reduce the quality of the country's collective gene pool. Probably the most notorious example of eugenics in action was the rise of Nazism in Germany, which resulted in the Eugenic Sterilization Law of 1933. The law required sterilization for those suffering from certain disabilities and even for some who were simply deemed "ugly." To ensure that this novel science is not abused, many governments have established organizations specifically for overseeing the development of gene therapy. In the United States, the Food and Drug Administration and the National Institutes of Health requires scientists to take a precise series of steps and meet stringent requirements before approving clinical trials.

In fact, gene therapy has been immersed in more controversy and surrounded by more scrutiny in both the health and ethical arena than most other technologies (except, perhaps, for cloning) that promise to substantially change society. Despite the health and ethical questions surrounding gene therapy, the field will continue to grow and is likely to change medicine faster than any previous medical advancement.

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Katherine Hunt, MS

General adaptation syndrome

Definition

General adaptation syndrome describes the body's short-term and long-term reaction to **stress**.

Description

Originally described by Hans De Solye in the 1920s, the general adaptation syndrome describes a three stage

reaction to stress. Stressors in humans include physical stressors, such as **starvation**, being hit by a car, or suffering through severe weather. Additionally, humans can suffer emotional or mental stress, such as the loss of a loved one, the inability to solve a problem, or even having a difficult day at work.

Stage 1: Alarm reaction

The first stage of the general adaptation stage, the alarm reaction, is the immediate reaction to a stressor. In the initial phase of stress, humans exhibit a "fight or flight" response, which causes one to be ready for physical activity. However, this initial response can also decrease the effectiveness of the immune system, making persons more susceptible to illness during this phase.

Stage 2: Stage of resistance

Stage 2 might also be named the stage of adaptation, instead of the stage of resistance. During this phase, if the stress continues, the body adapts to the stressors it is exposed to. Changes at many levels take place in order to reduce the effect of the stressor. For example, if the stressor is starvation (possibly due to anorexia), the person might experienced a reduced desire for physical activity to conserve energy, and the absorption of nutrients from food might be maximized.

Stage 3: Stage of exhaustion

At this stage, the stress has continued for some time. The body's resistance to the stress may gradually be reduced, or may collapse quickly. Generally, this means the immune system, and the body's ability to resist disease, may be almost totally eliminated. Patients who experience long-term stress may succumb to heart attacks or severe infection due to their reduced immunity. For example, a person with a stressful job may experience long-term stress that might lead to high blood pressure and an eventual **heart attack**.

Stress, a useful reaction?

Although stress can lead to disease, a researcher named Huethner has suggested that long-term stress may cause humans to better adapt to their environment. He argues that severe, long-term stress can cause persons to reject long-held assumptions or behaviors, and that stress can actually help the brain make physical changes that reflect these mental or emotional changes. In short, stress might allow persons to change the way they think and act for the better.

Causes and symptoms

Stress is the cause of general adaptation syndrome and it can manifest as **fatigue**, irritability, difficulty concentrating, and difficulty sleeping. Persons may also experience other symptoms that are signs of stress. Persons experiencing unusual symptoms, such as hair loss, without another medical explanation might consider stress as the cause.

KEY TERMS

Stressor—Any external stimuli that causes stress, ranging from starvation to test-taking.

Diagnosis

Diagnosis is difficult. Some physiological changes, such as increased cortisol levels, are characteristic of long-term stress.

Treatment

Treatment should involve **stress reduction**. Stress may be thought of as occurring in two steps. The first step is the occurrence of the external stressor, the second is the reaction to the external stressor. Stress reduction strategies generally fall into three categories: avoiding stressors, changing the reaction to the stressor(s), or relieving stress after the reaction to the stressor(s). Many strategies for stress reduction, such as exercising, listening to music, **aromatherapy**, and massage relieve stress after it occurs. Many psychotherapeutic approaches attempt to reduce the response of the patient to stressors. Persons wishing to reduce stress should consult a medical professional with whom they feel comfortable to discuss which option, or combination of options, they can use to reduce stress.

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Michael Zuck, PhD

General anesthetic *see* **Anesthesia, general**

General surgery

Definition

General surgery is the treatment of injury, deformity, and disease using operative procedures.

Purpose

General surgery is frequently performed to alleviate suffering when a cure is unlikely through medication alone. It can be used for routine procedures performed in a physician's office, such as **vasectomy**, or for more complicated operations requiring a medical team in a hospital setting, such as laparoscopic **cholecystectomy** (removal of the gallbladder). Areas of the body treated by general surgery include the stomach, liver, intestines, appendix, breasts, thyroid gland, salivary glands, some arteries and veins, and the skin. The brain, heart, eyes, and feet, to name only a few, are areas that require specialized surgical repair.

New methods and techniques are less invasive than previous practices, permitting procedures that were considered impossible in the past. For example, microsurgery has been used in reattaching severed body parts by successfully reconnecting small blood vessels and nerves.

Precautions

Patients who are obese, smoke, have bleeding tendencies, or are over 60, need to follow special precautions, as do patients who have recently experienced an illness such as **pneumonia** or a **heart attack**. Patients on medications such as heart and blood pressure medicine, blood thinners, **muscle relaxants**, tranquilizers, insulin, or sedatives, may require special lab tests prior to surgery and special monitoring during surgery. Special precautions may be necessary for patients using mind-altering drugs such as narcotics, psychedelics, hallucinogens, marijuana, sedatives, or **cocaine** since these drugs may interact with the anesthetic agents used during surgery.

Description

In earlier times, surgery was a dangerous and dirty practice. Until the middle of the 19th century, as many patients died of surgery as were cured. With the discovery and development of general anesthesia in the mid-1800s, surgery became more humane. And as knowledge about infections grew, surgery became more successful as sterile practices were introduced into the operating room. The last 50 years of the 20th century have seen continued advancements.

Types of General Surgery

General surgery experienced major advances with the introduction of the endoscope. This is an instrument for visualizing the interior of a body canal or a hollow organ. Endoscopic surgery relies on this pencil-thin instrument, capable of its own lighting system and small video camera. The endoscope is inserted through tiny incisions called portals. While viewing the procedure on a video screen, the surgeon then operates with various other small, precise instruments inserted through one or more of the portals. The specific area of the body treated determines the type of endoscopic surgery performed. For example, **colonoscopy** uses an endoscope, which can be equipped with a device for obtaining tissue samples for visual examination of the colon. Gastroscopy uses an endoscope inserted through the mouth to examine the interior of the stomach. **Arthroscopy** refers to joint surgery, and abdominal procedures are called laparoscopies.

Endoscopy is used in both treatment and diagnosis especially involving the digestive and female reproductive systems. Endoscopy has advantages over many other surgical procedures, resulting in a quicker recovery and shorter hospital stay. This non-invasive technique is being used for appendectomies, gallbladder surgery, hysterectomies and the repair of shoulder and knee ligaments. However, endoscopy does not come without limitations such as complications and high operating expense. Also, endoscopy doesn't offer advantages over conventional surgery in all procedures. Some literature states that as general surgeons become more experienced in their prospective fields, additional non-invasive surgery will be a more common option to patients.

ONE-DAY SURGERY. One-day surgery is also termed same-day, or outpatient surgery. Surgical procedures usually take two hours or less and involve minimal blood loss and a short recovery time. In the majority of surgical cases, oral medications control postoperative **pain**. Cataract removal, **laparoscopy**, tonsillectomy, repair of broken bones, **hernia repair**, and a wide range of cosmetic procedures are common same-day surgical procedures. Many individuals prefer the convenience and atmosphere of one-day surgery centers, as there is less competition for attention with more serious surgical cases. These centers are accredited by the Joint Commission on Accreditation of Healthcare Organizations or the Accreditation Association for Ambulatory Health Care.

Preparation

The preparation of patients has advanced significantly with improved diagnostic techniques and procedures. Before surgery the patient may be asked to undergo a series of tests including blood and urine studies, x

rays and specific heart studies if the patient's past medical history and/or physical exam warrants this testing. Before any general surgery the physician will explain the nature of the surgery needed, the reason for the procedure, and the anticipated outcome. The risks involved will be discussed along with the types of anesthesia utilized. The expected length of recovery and limitations imposed during the recovery period are also explained in detail before any general surgical procedure.

Surgical procedures most often require some type of anesthetic. Some procedures require only local anesthesia, produced by injecting the anesthetic agent into the skin near the site of the operation. The patient remains awake with this form of medication. Injecting anesthetic agents into a primary nerve located near the surgical site produces block anesthesia (also known as regional anesthesia), which is a more extensive local anesthesia. The patient remains conscious, but is usually sedated. General anesthesia involves injecting anesthetic agents into the blood stream and/or inhaling medicines through a mask placed over the patient's face. During general anesthesia, the patient is asleep and an airway tube is usually placed into the windpipe to help keep the airway open.

As part of the preoperative preparation, the patient will receive printed educational material and may be asked to review audio or videotapes. The patient will be instructed to shower or bathe the evening before or morning of surgery and may be asked to scrub the operative site with a special antibacterial soap. Instructions will also be given to the patient to ingest nothing by mouth for a determined period of time prior to the surgical procedure.

Aftercare

After surgery, blood studies and a laboratory examination of removed fluid or tissue are often performed especially in the case of **cancer** surgery. After the operation, the patient is brought to a recovery room and vital signs, fluid status, dressings and surgical drains are monitored. Pain medications are offered and used as necessary. Breathing exercises are encouraged to maximize respiratory function and leg exercises are encouraged to promote adequate circulation and prevent pooling of blood in the lower extremities. Patients must have a responsible adult accompany them home if leaving the same day as the surgery was performed.

Risks

One of the risks involved with general surgery is the potential for postoperative complications. These complications include—but are not limited to—pneumonia, internal bleeding, and wound infection as well as adverse reactions to anesthesia.

KEY TERMS

Appendectomy—Removal of the appendix.

Endoscope—Instrument for examining visually the inside of a body canal or a hollow organ such as the stomach, colon, or bladder.

Hysterectomy—Surgical removal of part or all of the uterus.

Laparoscopic cholecystectomy—Removal of the gallbladder using a laparoscope, a fiberoptical instrument inserted through the abdomen.

Microsurgery—Surgery on small body structures or cells performed with the aid of a microscope and other specialized instruments.

Portal—An entrance or a means of entrance.

Normal results

Advances in diagnostic and surgical techniques have increased the success rate of general surgery by many times compared to the past. Today's less invasive surgical procedures have reduced the length of hospital stays, shortened recovery time, decreased postoperative pain and decreased the size of surgical incision. On the average, a conventional abdominal surgery requires a three to six-day hospital stay and three to six-week recovery time.

Abnormal results

Abnormal results from general surgery include persistent pain, swelling, redness, drainage or bleeding in the surgical area and surgical wound infection resulting in slow healing.

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Jeffrey P. Larson, RPT

Generalized anxiety disorder

Definition

Generalized **anxiety** disorder is a condition characterized by "free floating" anxiety or apprehension not linked to a specific cause or situation.

Description

Some degree of fear and anxiety is perfectly normal. In the face of real danger, fear makes people more alert and also prepares the body to fight or flee (the so-called "fight or flight" response). When people are afraid, their hearts beat faster and they breathe faster in anticipation of the physical activity that will be required of them. However, sometimes people can become anxious even when there is no identifiable cause, and this anxiety can become overwhelming and very unpleasant, interfering with their daily lives. People with debilitating anxiety are said to be suffering from **anxiety disorders**, such as **phobias**, panic disorders, and generalized anxiety disorder. The person with generalized anxiety disorder generally has chronic (officially, having more days with anxiety than not for at least six months), recurrent episodes of anxiety that can last days, weeks, or even months.

Causes and symptoms

Generalized anxiety disorder afflicts between 2–3% of the general population, and is slightly more common in women than in men. It accounts for almost one-third of cases referred to psychiatrists by general practitioners.

Generalized anxiety disorder may result from a combination of causes. Some people are genetically predisposed to developing it. Psychological traumas that occur during childhood, such as prolonged separation from parents, may make people more vulnerable as well. Stressful life events, such as a move, a major job change, the loss of a loved one, or a divorce, can trigger or contribute to the anxiety.

Psychologically, the person with generalized anxiety disorder may develop a sense of dread for no apparent reason—the irrational feeling that some nameless catastrophe is about to happen. Physical symptoms similar to those found with **panic disorder** may be present, although not as severe. They may include trembling, sweating, heart **palpitations** (the feeling of the heart pounding in the chest), nausea, and "butterflies in the stomach."

According to the *Diagnostic and Statistical Manual of Mental Disorders,* 4th edition, a person must have at least three of the following symptoms, with some being present more days than not for at least six months, in order to be diagnosed with generalized anxiety disorder:

- restlessness or feeling on edge
- being easily fatigued
- difficulty concentrating
- irritability
- muscle tension
- sleep disturbance

While generalized anxiety disorder is not completely debilitating, it can compromise a person's effectiveness and quality of life.

Diagnosis

Anyone with chronic anxiety for no apparent reason should see a physician. The physician may diagnose the condition based on the patient's description of the physical and emotional symptoms. The doctor will also try to rule out other medical conditions that may be causing the symptoms, such as excessive **caffeine** use, thyroid disease, **hypoglycemia**, cardiac problems, or drug or alcohol withdrawal. Psychological conditions, such as depressive disorder with anxiety, will also need to be ruled out.

Since generalized anxiety disorder often co-occurs with **mood disorders** and substance abuse, the clinician may have to treat these conditions as well, and therefore must consider them in making the diagnosis.

Treatment

Over the short term, a group of tranquilizers called **benzodiazepines**, such as clonazepam (Klonipin) may help ease the symptoms of generalized anxiety disorder. Sometimes **antidepressant drugs**, such as amitryptiline (Elavil), or **selective serotonin reuptake inhibitors** (SSRIs), such as fluoxetine (Prozac) or sertraline (Zoloft), are also used.

Psychotherapy can be effective in treating generalized anxiety disorder. The therapy may take many forms. In some cases, psychodynamically-oriented psychotherapy can help patients work through this anxiety and solve problems in their lives. Cognitive behavioral therapy aims to reshape the way people perceive and react to potential stressors in their lives. Relaxation techniques have also been used in treatment, as well as in prevention efforts.

Prognosis

When properly treated, most patients with generalized anxiety disorder experience improvement in their symptoms.

KEY TERMS

Cognitive behavioral therapy—A psychotherapeutic approach that aims at altering cognitions—including thoughts, beliefs, and images—as a way of altering behavior.

Prevention

While preventive measures have not been established, a number of techniques may help manage anxiety, such as relaxation techniques, breathing exercises, and distraction—putting the anxiety out of one's mind by focusing thoughts on something else.

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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

Genetic counseling

Definition

Genetic counseling aims to facilitate the exchange of information regarding a person's genetic legacy. It attempts to:

- accurately diagnose a disorder
- assess the risk of recurrence in the concerned family members and their relatives
- provide alternatives for decision-making
- provide support groups that will help family members cope with the recurrence of a disorder

Purpose

Genetic counselors work with people concerned about the risk of an inherited disease. The counselor does not prevent the incidence of a disease in a family, but can help family members assess the risk for certain hereditary diseases and offer guidance. Many couples seek genetic counseling because there is a family history of known genetic disorders, **infertility**, **miscarriage**, still births, or early infant mortality. Other reasons for participating in genetic counseling may be the influences of a job or lifestyle that exposes a potential parent to health risks such as radiation, chemicals, or drugs. Any family history of **mental retardation** can be of concern as is a strong family history of heart disease at an early age. Recent statistics show a 3% chance of delivering a baby with **birth defects**. An additional 2% chance of having a baby with **Down syndrome** is present for women in their late thirties and older.

Precautions

Amniocentesis, one of the specific tests used to gather information for genetic counseling, is best performed between weeks 15 and 17 of a **pregnancy** and an additional one to four weeks may be required to culture skin cells and analyze them. Thus, these test data are not available to assist prospective parents in decision-making until the second trimester of the pregnancy. Individuals who participate in genetic counseling and associated testing also must be aware that there are no cures or treatments for some of the disorders that may be identified.

Description

With approximately 2,000 genes identified and approximately 5,000 disorders caused by genetic defects, genetic counseling is important in the medical discipline of obstetrics. Genetic counselors, educated in the medical and the psychosocial aspects of genetic diseases, convey complex information to help people make life decisions. There are limitations to the power of genetic counseling, though, since many of the diseases that have been shown to have a genetic basis currently offer no cure (for example, Down syndrome or Huntington's disease). Although a genetic counselor cannot predict the future unequivocally, he or she can discuss the occurrence of a disease in terms of probability.

A genetic counselor, with the aid of the patient or family, creates a detailed family pedigree that includes the incidence of disease in first-degree (parents, siblings, and children) and second-degree (aunts, uncles, and

KEY TERMS

Sickle-cell anemia—A chronic, inherited blood disorder characterized by crescent-shaped red blood cells. It occurs primarily in people of African descent, and produces symptoms including episodic pain in the joints, fever, leg ulcers, and jaundice.

Tay-Sachs disease—A hereditary disease affecting young children of eastern European Jewish descent. This disease is caused by an enzyme deficiency leading to the accumulation of gangliosides (galactose-containing cerebrosides) found in the surface membranes of nerve cells in the brain and nerve tissue. This deficiency results in mental retardation, convulsions, blindness, and, finally, death.

Thalassemia—An inherited group of anemias occurring primarily among people of Mediterranean descent. It is caused by defective formation of part of the hemoglobin molecule.

grandparents) relatives. Before or after this pedigree is completed, certain genetic tests are performed using DNA analysis, x ray, ultrasound, urine analysis, **skin biopsy**, and physical evaluation. For a pregnant woman, prenatal diagnosis can be made using amniocentesis or **chorionic villus sampling**.

Family pedigree

An important aspect of the genetic counseling session is the compilation of a family pedigree or medical history. To accurately assess the risk of inherited diseases, information on three generations, including health status and/or cause of **death**, is usually needed. If the family history is complicated information from more distant relatives may be helpful, and medical records may be requested for any family members who have had a genetic disorder. Through an examination of the family history a counselor may be able to discuss the probability of future occurrence of genetic disorders. In all cases, the counselor provides information in a non-directive way that leaves the decision-making up to the client.

Screening tests

Screening blood tests help identify individuals who carry genes for recessive genetic disorders. Screening tests are usually only done if:

- The disease is lethal or causes severe handicaps or disabilities
- The person is likely to be a carrier due to family pedigree or membership in an at-risk ethnic, geographic or racial group
- The disorder can be treated or reproductive options exist
- A reliable test is available.

Genetic disorders such as **Tay-Sachs disease**, sickle-cell anemia, and **thalassemia** meet these criteria, and screening tests are commonly done to identify carriers of these diseases. In addition, screening tests may be done for individuals with family histories of Huntington's disease (a degenerative neurological disease) or **hemophilia** (a bleeding disorder). Such screening tests can eliminate the need for more invasive tests during a pregnancy.

Another screening test commonly used in the United States in the alpha-fetoprotein (AFP) test. This test is done on a sample of maternal blood around week 16 of a pregnancy. An elevation in the serum AFP level indicates that the fetus may have certain birth defects such as neural tube defects (including **spina bifida** and anencephaly). If the test yields an elevated result, it may be run again after seven days. If the level is still elevated after repeat testing, additional diagnostic tests (e.g. ultrasound and/or amniocentesis) are done in an attempt to identify the specific birth defect present.

Ultrasound

Ultrasound is a noninvasive procedure which uses sound waves to produce a reflected image of the fetus upon a screen. It is used to determine the age and position of the fetus, and the location of the placenta. Ultrasound is also useful in detecting visible birth defects such as spina bifida (a defect in the development of the vertebrae of the spinal column and/or the spinal cord). It is also useful for detecting heart defects, and malformations of the head, face, body, and limbs. This procedure, however, cannot detect biochemical or chromosomal alterations in the fetus.

Amniocentesis

Amniocentesis is useful in determining genetic and developmental disorders not detectable by ultrasound. This procedure involves the insertion of a needle through the abdomen and into the uterus of a pregnant woman. A sample of amniotic fluid is withdrawn containing skin cells that have been shed by the fetus. The sample 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 disease, the simple presence of a

telltale chemical compound in the amniotic fluid is enough to confirm a diagnosis.

Chorionic villus sampling

Chorionic villus sampling involves the removal of a small amount of tissue directly from the chorionic villi (minute vascular projections of the fetal chorion that combine with maternal uterine tissue to form the placenta). In the laboratory, the chromosomes of the fetal cells are analyzed for number and type. Extra chromosomes, such as are present in Down syndrome, can be identified. Additional laboratory tests can be performed to look for specific disorders and the results are usually available within a week after the sample is taken. The primary benefit of this procedure is that it is usually performed between weeks 10 and 12 of a pregnancy, allowing earlier detection of fetal disorders.

Preparation

Genetic diagnosis requires that a couple share information about inherited disorders in their background with the genetic counselor, including details of any genetic diseases in either family. A couple undergoing genetic counseling also reports any past miscarriages and discusses the possibility of exposure to chemicals, radiation (including x rays), or other occupational environmental hazards. The couple also needs to disclose information about personal habits before or during pregnancy such as drug or alcohol abuse and the use of prescription or over-the-counter drugs taken by the mother since the beginning of pregnancy. The genetic counselor explains the procedures used in any testing that will be done and describes what each test can and cannot reveal.

Aftercare

Genetic counseling provides couples with information that can help them make decisions about future pregnancies. It also gives couples additional time to emotionally prepare if a disorder is detected in the fetus. The counselor discusses the results of any testing and informs the couple if a problem is apparent. The doctor or genetic counselor also discusses the treatment options available. Genetic counseling is done in a non-directive way, so that any treatment selected remains the personal choice of the individuals involved. Genetic counseling can provide information essential for family planning and pregnancy management, thus maximizing the chances of a positive outcome.

Risks

Because prenatal testing, such as amniocentesis and chorionic villus sampling, is invasive and carries a 1% risk of miscarriage it should never be considered routine.

Normal results

Screening tests and/or prenatal tests reveal no birth defects or genetic abnormalities.

Abnormal results

A birth defect or genetic disorder is detected. The early diagnosis of birth defects and genetic disorders allows a greater number of treatment options. Some disorders can be treated in utero (before birth while the fetus is still in the uterus), while others may require early delivery, immediate surgery, or **cesarean section** to minimize fetal trauma. Prior warning of fetal difficulties allows parents time to prepare emotionally for the birth of the child. In some instances, termination of the pregnancy may be chosen. Whatever the test results, this information is essential for family planning and pregnancy management.

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Jeffrey P. Larson, RPT

Genetic studies *see* **Genetic testing**

Genetic testing

Definition

A genetic test examines the genetic information contained inside a person's cells, called DNA, to determine

if that person has or will develop a certain disease or could pass a disease to his or her offspring. Genetic tests also determine whether or not couples are at a higher risk than the general population for having a child affected with a genetic disorder.

Purpose

Some families or ethnic groups have a higher incidence of a certain disease than does the population as a whole. For example, individuals from Eastern European, Ashkenazi Jewish descent are at higher risk for carrying genes for rare conditions that occur much less frequently in populations from other parts of the world. Before having a child, a couple from such a family or ethnic group may want to know if their child would be at risk of having that disease. Genetic testing for this type of purpose is called genetic screening.

During **pregnancy**, the baby's cells can be studied for certain genetic disorders or chromosomal problems such as **Down syndrome**. Chromosome testing is most commonly offered when the mother is 35 years or older at the time of delivery. When there is a family medical history of a genetic disease or there are individuals in a family affected with developmental and physical delays, genetic testing may also be offered during pregnancy. Genetic testing during pregnancy is called prenatal diagnosis.

Prior to becoming pregnant, couples who are having difficulty conceiving a child or who have suffered multiple miscarriages may be tested to see if a genetic cause can be identified.

A genetic disease may be diagnosed at birth by doing a physical evaluation of the baby and observing characteristics of the disorder. Genetic testing can help to confirm the diagnosis made by the physical evaluation. In addition, genetic testing is used routinely on all newborns to screen for certain genetic diseases which can affect a newborn baby's health shortly after birth.

There are several genetic diseases and conditions in which the symptoms do not occur until adulthood. One such example is Huntington's disease. This is a serious disorder affecting the way in which individuals walk, talk and function on a daily basis. Genetic testing may be able to determine if someone at risk for the disease will in fact develop the disease.

Some genetic defects may make a person more susceptible to certain types of **cancer**. Testing for these defects can help predict a person's risk. Other types of genetic tests help diagnose and predict and monitor the course of certain kinds of cancer, particularly leukemia and lymphoma.

Precautions

Because genetic testing is not always accurate and because there are many concerns surrounding insurance and employment discrimination for the individual receiving a genetic test, **genetic counseling** should always be performed prior to genetic testing. A genetic counselor is an individual with a master's degree in genetic counseling. A medical geneticist is a physician specializing and board certified in genetics.

A genetic counselor reviews the person's family history and medical records and the reason for the test. The counselor explains the likelihood that the test will detect all possible causes of the disease in question (known as the sensitivity of the test), and the likelihood that the disease will develop if the test is positive (known as the positive predictive value of the test).

Learning about the disease in question, the benefits and risks of both a positive and a negative result, and what treatment choices are available if the result is positive, will help prepare the person undergoing testing. During the genetic counseling session, the individual interested in genetic testing will be asked to consider how the test results will affect his or her life, family, and future decisions.

After this discussion, the person should have the opportunity to indicate in writing that he or she gave informed consent to have the test performed, verifying that the counselor provided complete and understandable information.

Description

Genes and chromosomes

Deoxyribonucleic acid (DNA) is a long molecule made up of two strands of genetic material coiled around each other in a unique double helix structure. This structure was discovered in 1953 by Francis Crick and James Watson.

DNA is found in the nucleus, or center, of most cells (Some cells, such as a red blood cell, don't have a nucleus). Each person's DNA is a unique blueprint, giving instructions for a person's physical traits, such as eye color, hair texture, height, and susceptibility to disease. DNA is organized into structures called chromosomes.

The instructions are contained in DNA's long strands as a code spelled out by pairs of bases, which are four chemicals that make up DNA. The bases occur as pairs because a base on one strand lines up with and is bound to a corresponding base on the other strand. The order of these bases form DNA's code. The order of the bases on a DNA strand is important to ensuring that we are not

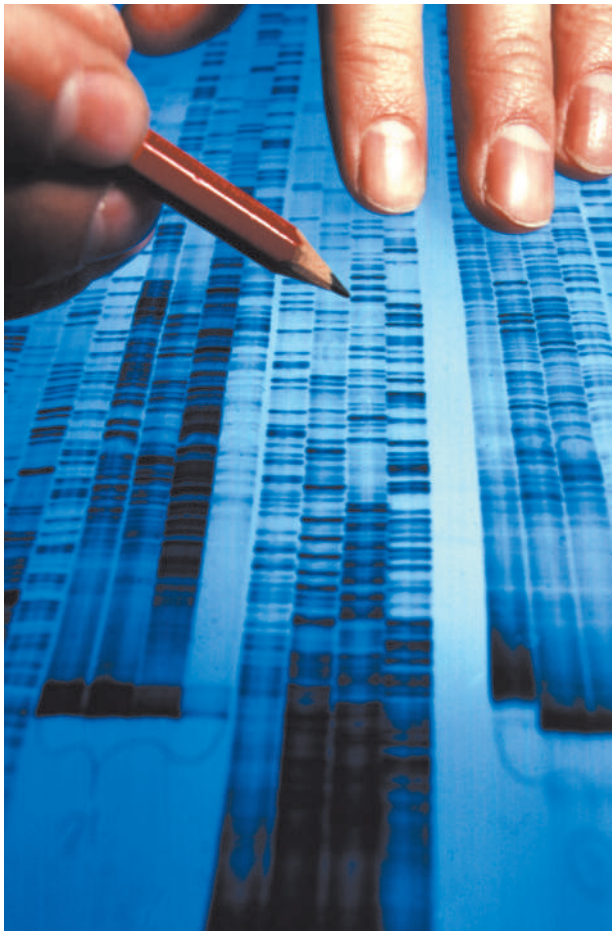
affected with any genetic diseases. When the bases are out of order, or missing, then often times, our cells do not produce important proteins which can lead to a genetic disorder. While our genes are found in every cell of our body, not every gene is functioning all of the time. Some genes are turned on during critical points in development and then remain silent for the rest of our lives. While other genes remain active all of our lives so that our cells can produce important proteins that help us digest food properly or fight off the **common cold**.

The specific order of the base pairs on a strand of DNA is important in order for the correct protein to be produced. A grouping of three base pairs on the DNA strand is called a codon. Each codon, or three base pairs, comes together to spell a word. A string of many codons together can be thought of as a series of words all coming together to make a sentence. This sentence is what instructs our cells to make a protein that helps our bodies function properly.

Our DNA strands containing a hundred to several thousand copies of genes are found on structures called chromosomes. Each cell typically has 46 chromosomes arranged into 23 pairs. Each parent contributes one chromosome to each pair. The first 22 pairs are called autosomal chromosomes, or non-sex chromosomes and are assigned a number from 1–22. The last pair are the sex chromosomes and include the X and the Y chromosomes. If a child receives an X chromosome from each parent, the child is female. If a child receives an X from the mother, and a Y from the father, the child is male.

Just as each parent contributes one chromosome to each pair, so each parent contributes one gene from each chromosome. The pair of genes produces a specific trait in the child. In autosomal dominant conditions, it takes only one copy of a gene to influence a specific trait. The stronger gene is called dominant; the weaker gene, recessive. Two copies of a recessive gene are needed to control a trait while only one copy of a dominant gene is needed. Our sex chromosomes, the X and the Y also contain important genes. Some genetic diseases are caused by missing, or altered genes on one of the sex chromosomes. Males are most often affected by sex chromosome diseases when they inherit an X chromosome with missing or mutated genes from their mother.

TYPES OF GENETIC MUTATIONS. Genetic disease results from a change, or mutation, in a chromosome or in one or several base pairs on a gene. Some of us inherit these mutations from our parents, called hereditary or germline mutations, while other mutations can occur spontaneously, or for the first time in an affected child. For many of the adult on-set diseases, genetic mutations



A scientist examines a DNA sequencing autoradiogram on a light box. *(Photo Researchers, Inc. Reproduced by permission.)*

can occur over the lifetime of the individual. This is called acquired or somatic mutations and these occur while the cells are making copies of themselves or dividing in two. There may be some environmental effects, such as radiation or other chemicals, which can contribute to these types of mutations as well.

There are a variety of different types of mutations that can occur in our genetic code to cause a disease. And for each genetic disease, there may be more than one type of mutation to cause the disease. For some genetic diseases, the same mutation occurs in every individual affected with the disease. For example, the most common form of dwarfism, called **achondroplasia**, occurs because of a single base pair substitution. This same mutation occurs in all individuals affected with the disease. Other genetic diseases are caused by different types of genetic mutations that may occur anywhere along the length of a gene. For example, **cystic fibrosis**, the most common genetic disease in the caucasian population is caused by over hundreds of different mutations along the

gene. Individual families may carry the same mutation as each other, but not as the rest of the population affected with the same genetic disease.

Some genetic diseases occur as a result of a larger mutation which can occur when the chromosome itself is either rearranged or altered or when a baby is born with more than the expected number of chromosomes. There are only a few types of chromosome rearrangements which are possibly hereditary, or passed on from the mother or the father. The majority of chromosome alterations where the baby is born with too many chromosomes or missing a chromosome, occurs sporadically or for the first time with a new baby.

The type of mutation that causes a genetic disease will determine the type of genetic test to be performed. In some situations, more than one type of genetic test will be performed to arrive at a diagnosis. The cost of genetic tests vary: chromosome studies can cost hundreds of dollars and certain gene studies, thousands. Insurance coverage also varies with the company and the policy. It may take several days or several weeks to complete a test. Research testing where the exact location of a gene has not yet been identified, can take several months to years for results.

Types of Genetic Testing

Direct DNA mutation analysis

Direct DNA sequencing examines the direct base pair sequence of a gene for specific gene mutations. Some genes contain more than 100,000 bases and a mutation of any one base can make the gene nonfunctional and cause disease. The more mutations possible, the less likely it is for a test to detect all of them. This test is usually done on white blood cells from a person's blood but can also be performed on other tissues. There are different ways in which to perform direct DNA mutation analysis. When the specific genetic mutation is known, it is possible to perform a complete analysis of the genetic code, also called direct sequencing. There are several different lab techniques used to test for a direct mutation. One common approach begins by using chemicals to separate DNA from the rest of the cell. Next, the two strands of DNA are separated by heating. Special enzymes (called restriction enzymes) are added to the single strands of DNA and then act like scissors and cut the strands in specific places. The DNA fragments are then sorted by size through a process called electrophoresis. A special piece of DNA, called a probe, is added to the fragments. The probe is designed to bind to specific mutated portions of the gene. When bound to the probe, the mutated portions appear on x-ray film with a distinct banding pattern.

Indirect DNA Testing

Family linkage studies are done to study a disease when the exact type and location of the genetic alteration is not known, but the general location on the chromosome has been identified. These studies are possible when a chromosome marker has been found associated with a disease. Chromosomes contain certain regions that vary in appearance between individuals. These regions are called polymorphisms and do not cause a genetic disease to occur. If a polymorphism is always present in family members with the same genetic disease, and absent in family members without the disease, it is likely that the gene responsible for the disease is near that polymorphism. The gene mutation can be indirectly detected in family members by looking for the polymorphism.

To look for the polymorphism, DNA is isolated from cells in the same way it is for direct DNA mutation analysis. A probe is added that will detect the large polymorphism on the chromosome. When bound to the probe, this region will appear on x-ray film with a distinct banding pattern. The pattern of banding of a person being tested for the disease is compared to the pattern from a family member affected by the disease.

Linkage studies have disadvantages not found in direct DNA mutation analysis. These studies require multiple family members to participate in the testing. If key family members choose not to participate, the incomplete family history may make testing other members useless. The indirect method of detecting a mutated gene also causes more opportunity for error.

Chromosome analysis

Various genetic syndromes are caused by structural chromosome abnormalities. To analyze a person's chromosomes, his or her cells are allowed to grow and multiply in the laboratory until they reach a certain stage of growth. The length of growing time varies with the type of cells. Cells from blood and bone marrow take one to two days; fetal cells from amniotic fluid take seven to 10 days.

When the cells are ready, they are placed on a microscope slide using a technique to make them burst open, spreading their chromosomes. The slides are stained: the stain creates a banding pattern unique to each chromosome. Under a microscope, the chromosomes are counted, identified, and analyzed based on their size, shape, and stained appearance.

A karyotype is the final step in the chromosome analysis. After the chromosomes are counted, a photograph is taken of the chromosomes from one or more cells as seen through the microscope. Then the chromo-

KEY TERMS

Autosomal disease—A disease caused by a gene located on an autosomal chromosome.

Carrier—A person who possesses a gene for an abnormal trait without showing signs of the disorder. The person may pass the abnormal gene on to offspring.

Chromosome—A microscopic thread-like structure found within each cell of the body and consists of a complex of proteins and DNA. Humans have 46 chromosomes arranged into 23 pairs. Changes in either the total number of chromosomes or their shape and size (structure) may lead to physical or mental abnormalities.

Deoxyribonucleic acid (DNA)—The genetic material in cells that holds the inherited instructions for growth, development, and cellular functioning.

Dominant gene—A gene, whose presence as a single copy, controls the expression of a trait.

Enzyme—A protein that catalyzes a biochemical reaction or change without changing its own structure or function.

Gene—A building block of inheritance, which contains the instructions for the production of a particular protein, and is made up of a molecular sequence found on a section of DNA. Each gene is found on a precise location on a chromosome.

Karyotype—A standard arrangement of photographic or computer-generated images of chromosome pairs from a cell in ascending numerical order, from largest to smallest.

Mutation—A permanent change in the genetic material that may alter a trait or characteristic of an individual, or manifest as disease, and can be transmitted to offspring.

Positive predictive value (PPV)—The probability that a person with a positive test result has, or will get, the disease.

Recessive gene—A type of gene that is not expressed as a trait unless inherited by both parents.

Sensitivity—The proportion of people with a disease who are correctly diagnosed (test positive based on diagnostic criteria). The higher the sensitivity of a test or diagnostic criteria, the lower the rate of 'false negatives,' people who have a disease but are not identified through the test.

Sex-linked disorder—A disorder caused by a gene located on a sex chromosome, usually the X chromosome.

somes are cut out and arranged side-by-side with their partner in ascending numerical order, from largest to smallest. The karyotype is done either manually or using a computer attached to the microscope. Chromosome analysis is also called cytogenetics.

Applications for Genetic Testing

Newborn screening

Genetic testing is used most often for newborn screening. Every year, millions of newborn babies have their blood samples tested for potentially serious genetic diseases.

Carrier testing

An individual who has a gene associated with a disease but never exhibits any symptoms of the disease is called a carrier. A carrier is a person who is not affected by the mutated gene he or she possesses, but can pass the gene to an offspring. Genetic tests have been developed that tell prospective parents whether or not they are carriers of certain diseases. If one or both parents are a carrier, the risk of passing the disease to a child can be predicted.

To predict the risk, it is necessary to know if the gene in question is autosomal or sex-linked. If the gene is carried on any one of chromosomes 1–22, the resulting disease is called an autosomal disease. If the gene is carried on the X or Y chromosome, it is called a sex-linked disease.

Sex-linked diseases, such as the bleeding condition **hemophilia**, are usually carried on the X chromosome. A woman who carries a disease-associated mutated gene on one of her X chromosomes, has a 50% chance of passing that gene to her son. A son who inherits that gene will develop the disease because he does not have another normal copy of the gene on a second X chromosome to compensate for the mutated copy. A daughter who inherits the disease associated mutated gene from her mother, on one of her X chromosomes will be at risk for having a son affected with the disease.

The risk of passing an autosomal disease to a child depends on whether the gene is dominant or recessive. A

prospective parent carrying a dominant gene, has a 50% chance of passing the gene to a child. A child needs to receive only one copy of the mutated gene to be affected by the disease.

If the gene is recessive, a child needs to receive two copies of the mutated gene, one from each parent, to be affected by the disease. When both prospective parents are carriers, their child has a 25% chance of inheriting two copies of the mutated gene and being affected by the disease; a 50% chance of inheriting one copy of the mutated gene, and being a carrier of the disease but not affected; and a 25% chance of inheriting two normal genes. When only one prospective parent is a carrier, a child has a 50% chance of inheriting one mutated gene and being an unaffected carrier of the disease, and a 50% chance of inheriting two normal genes.

Cystic fibrosis is a disease that affects the lungs and pancreas and is discovered in early childhood. It is the most common autosomal recessive genetic disease found in the caucasian population: one in 25 people of Northern European ancestry are carriers of a mutated cystic fibrosis gene. The gene, located on chromosome 7, was identified in 1989.

The gene mutation for cystic fibrosis is detected by a direct DNA test. Over 600 mutations of the cystic fibrosis gene have been found; each of these mutations cause the same disease. Tests are available for the most common mutations. Tests that check for the 86 of the most common mutations in the Caucasian population will detect 90% of carriers for cystic fibrosis. (The percentage of mutations detected varies according to the individual's ethnic background). If a person tests negative, it is likely, but not guaranteed that he or she does not have the gene. Both prospective parents must be carriers of the gene to have a child with cystic fibrosis.

Tay-Sachs disease, also autosomal recessive, affects children primarily of Ashkenazi Jewish descent. Children with this disease die between the ages of two and five. This disease was previously detected by looking for a missing enzyme. The mutated gene has now been identified and can be detected using direct DNA mutation analysis.

Presymptomatic testing

Not all genetic diseases show their effect immediately at birth or early in childhood. Although the gene mutation is present at birth, some diseases do-not appear until adulthood. If a specific mutated gene responsible for a late-onset disease has been identified, a person from an affected family can be tested before symptoms appear.

Huntington's disease is one example of a late-onset autosomal dominant disease. Its symptoms of mental confusion and abnormal body movements do not appear until middle to late adulthood. The chromosome location of the gene responsible for Huntington's chorea was located in 1983 after studying the DNA from a large Venezuelan family affected by the disease. Ten years later the gene was identified. A test is now available to detect the presence of the expanded base pair sequence responsible for causing the disease. The presence of this expanded sequence means the person will develop the disease.

Another late onset disease, Alzheimer's does not have as well a understood genetic cause as Huntington's disease. The specific genetic cause of **Alzheimer's disease** is not as clear. Although many cases appear to be inherited in an autosomal dominant pattern, many cases exist as single incidents in a family. Like Huntington's, symptoms of mental deterioration first appear in adulthood. Genetic research has found an association between this disease and genes on four different chromosomes. The validity of looking for these genes in a person without symptoms or without family history of the disease is still being studied.

CANCER SUSCEPTIBILITY TESTING. Cancer can result from an inherited (germline) mutated gene or a gene that mutated sometime during a person's lifetime (acquired mutation). Some genes, called tumor suppressor genes, produce proteins that protect the body from cancer. If one of these genes develops a mutation, it is unable to produce the protective protein. If the second copy of the gene is normal, its action may be sufficient to continue production, but if that gene later also develops a mutation, the person is vulnerable to cancer. Other genes, called oncogenes, are involved in the normal growth of cells. A mutation in an oncogene can cause too much growth, the beginning of cancer.

Direct DNA tests are currently available to look for gene mutations identified and linked to several kinds of cancer. People with a family history of these cancers are those most likely to be tested. If one of these mutated genes is found, the person is more susceptible to developing the cancer. The likelihood that the person will develop the cancer, even with the mutated gene, is not always known because other genetic and environmental factors are also involved in the development of cancer.

Cancer susceptibility tests are most useful when a positive test result can be followed with clear treatment options. In families with **familial polyposis** of the colon, testing a child for a mutated APC gene can reveal whether or not the child needs frequent monitoring for the disease. In families with potentially fatal familial medullary **thyroid cancer** or multiple endocrine neoplasia type 2, finding a mutated RET gene in a child provides the opportunity for that child to have preventive

removal of the thyroid gland. In the same way, MSH1 and MSH2 mutations can reveal which members in an affected family are vulnerable to familiar colorectal cancer and would benefit from aggressive monitoring.

In 1994, a mutation linked to early-onset familial breast and **ovarian cancer** was identified. BRCA1 is located on chromosome 17. Women with a mutated form of this gene have an increased risk of developing breast and ovarian cancer. A second related gene, BRCA2, was later discovered. Located on chromosome 13, it also carries increased risk of breast and ovarian cancer. Although both genes are rare in the general population, they are slightly more common in women of Ashkenazi Jewish descent.

When a woman is found to have a mutation of one of these genes, the likelihood that she will get breast or ovarian cancer increases, but not to 100%. Other genetic and environmental factors influence the outcome.

Testing for these genes is most valuable in families where a mutation has already been found. BRCA1 and BRCA2 are large genes; BRCA1 includes 100,000 bases. More than 120 mutations to this gene have been discovered, but a mutation could occur in any one of the bases. Studies show tests for these genes may miss 30% of existing mutations. The rate of missed mutations, the unknown disease likelihood in spite of a positive result, and the lack of a clear preventive response to a positive result, make the value of this test for the general population uncertain.

Prenatal and postnatal chromosome analysis

Chromosome analysis can be done on fetal cells primarily when the mother is age 35 or older at the time of delivery, experienced multiple miscarriages, or reports a family history of a genetic abnormality. Prenatal testing is done on the fetal cells from a chorionic villi sampling (from the baby's developing placenta) at 9–12 weeks or from the amniotic fluid (the fluid surrounding the baby) at 15–22 weeks of pregnancy. Cells from amniotic fluid grow for seven to 10 days before they are ready to be analyzed. Chorionic villi cells have the potential to grow faster and can be analyzed sooner.

Chromosome analysis using blood cells is done on a child who is born with or later develops signs of **mental retardation** or physical malformation. In the older child, chromosome analysis may be done to investigate developmental delays.

Extra or missing chromosomes cause mental and physical abnormalities. A child born with an extra chromosome 21 (trisomy 21) has Down syndrome. An extra chromosome 13 or 18 also produce well known syndromes. A missing X chromosome causes **Turner syndrome** and an extra X in a male causes **Klinefelter syndrome**. Other abnormalities are caused by extra or missing pieces of chromosomes. **Fragile X syndrome** is a sex-linked disease, causing mental retardation in males.

Chromosome material may also be rearranged, such as the end of chromosome 1 moved to the end of chromosome 3.This is called a chromosomal translocation. If no material is added or deleted in the exchange, the person may not be affected. Such an exchange, however, can cause **infertility** or abnormalities if passed to children.

Evaluation of a man and woman's infertility or repeated miscarriages will include blood studies of both to check for a chromosome translocation. Many chromosome abnormalities are incompatible with life; babies with these abnormalities often miscarrry during the first trimester. Cells from a baby that died before birth can be studied to look for chromosome abnormalities that may have caused the **death**.

Cancer diagnosis and prognosis

Certain cancers, particularly leukemia and lymphoma, are associated with changes in chromosomes: extra or missing complete chromosomes, extra or missing portions of chromosomes, or exchanges of material (translocations) between chromosomes. Studies show that the locations of the chromosome breaks are at locations of tumor suppressor genes or oncogenes.

Chromosome analysis on cells from blood, bone marrow, or solid tumor helps diagnose certain kinds of leukemia and lymphoma and often helps predict how well the person will respond to treatment. After treatment has begun, periodic monitoring of these chromosome changes in the blood and bone marrow gives the physician information as to the effectiveness of the treatment.

A well-known chromosome rearrangement is found in chronic myelogenous leukemia. This leukemia is associated with an exchange of material between chromosomes 9 and 22. The resulting smaller chromosome 22 is called the Philadelphia chromosome.

Preparation

Most tests for genetic diseases of children and adults are done on blood. To collect the 5–10 mL of blood needed, a healthcare worker draws blood from a vein in the inner elbow region. Collection of the sample takes only a few minutes.

Prenatal testing is done either on amniotic fluid or a **chorionic villus sampling**. To collect amniotic fluid, a physician performs a procedure called **amniocentesis**. An ultrasound is done to find the baby's position and an area filled with amniotic fluid. The physician inserts a needle

through the woman's skin and the wall of her uterus and withdraws 5–10 mL of amniotic fluid. Placental tissue for a chorionic villus sampling is taken through the cervix. Each procedures take approximately 30 minutes.

Bone marrow is used for chromosome analysis in a person with leukemia or lymphoma. The person is given local anesthesia. Then the physician inserts a needle through the skin and into the bone (usually the sternum or hip bone). One-half to 2 mL of bone marrow is withdrawn. This procedure takes approximately 30 minutes.

Aftercare

After blood collection the person can feel discomfort or bruising at the puncture site or may become dizzy or faint. Pressure to the puncture site until the bleeding stops reduces bruising. Warm packs to the puncture site relieve discomfort.

The chorionic villi sampling, amniocentesis and bone marrow procedures are all done under a physician's supervision. The person is asked to rest after the procedure and is watched for weakness and signs of bleeding.

Risks

Collection of amniotic fluid and chorionic villi sampling, have the risk of **miscarriage**, infection, and bleeding; the risks are higher for the chorionic villi sampling. Because of the potential risks for miscarriage, 0.5% following the amniocentesis and 1% following the chorionic villi sampling procedure, both of these prenatal tests are offered to couples, but not required. A woman should tell her physician immediately if she has cramping, bleeding, fluid loss, an increased temperature, or a change in the baby's movement following either of these procedures.

After bone marrow collection, the puncture site may become tender and the person's temperature may rise. These are signs of a possible infection.

Genetic testing involves other nonphysical risks. Many people fear the possible loss of privacy about personal health information. Results of genetic tests may be reported to insurance companies and affect a person's insurability. Some people pay out-of-pocket for genetic tests to avoid this possibility. Laws have been proposed to deal with this problem. Other family members may be affected by the results of a person's genetic test. Privacy of the person tested and the family members affected is a consideration when deciding to have a test and to share the results.

A positive result carries a psychological burden, especially if the test indicates the person will develop a disease, such as Huntington's chorea. The news that a person may be susceptible to a specific kind of cancer, while it may encourage positive preventive measures, may also negatively shadow many decisions and activities.

A genetic test result may also be inconclusive meaning no definitive result can be given to the individual or family. This may cause the individual to feel more anxious and frustrated and experience psychological difficulties.

Prior to undergoing genetic testing, individuals need to learn from the genetic counselor the likelihood that the test could miss a mutation or abnormality.

Normal results

A normal result for chromosome analysis is 46, XX or 46, XY. This means there are 46 chromosomes (including two X chromosomes for a female or one X and one Y for a male) with no structural abnormalities. A normal result for a direct DNA mutation analysis or linkage study is no gene mutation found.

There can be some benefits from genetic testing when the individual tested is not found to carry a genetic mutation. Those who learn with great certainty they are no longer at risk for a genetic disease, may choose not to undergo prophylactic therapies and may feel less anxious and relieved.

Abnormal results

An abnormal chromosome analysis report will include the total number of chromosomes and will identify the abnormality found. Tests for gene mutations will report the mutations found.

There are many ethical issues to consider with an abnormal prenatal test result. Many of the diseases tested for during a pregnancy, cannot be treated or cured. In addition, some diseases tested for during pregnancy, may have a late-onset of symptoms or have minimal effects on the affected individual.

Before making decisions based on an abnormal test result, the person should meet again with a genetic counselor to fully understand the meaning of the results, learn what options are available based on the test result, and what are the risks and benefits of each of those options.

Resources

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ORGANIZATIONS

Alliance of Genetic Support Groups. 4301 Connecticut Ave. NW, Suite 404, Washington, DC 20008. (202) 966-5557. Fax: (202) 966-8553. <http://www.geneticalliance.org>.
American College of Medical Genetics. 9650 Rockville Pike, Bethesda, MD 20814-3998. (301) 571-1825. <http://www.faseb.org/genetics/acmg/acmgmenu.htm>.
American Society of Human Genetics. 9650 Rockville Pike, Bethesda, MD 20814-3998. (301) 571-1825. <http://www.faseb.org/genetics/ashg/ashgmenu.htm>.
Centers for Disease Control. GDP Office, 4770 Buford Highway NE, Atlanta, GA 30341-3724. (770) 488-3235. <http://www.cdc.gov/genetics>.
March of Dimes Birth Defects Foundation. 1275 Manaroneck Ave., White Plains, NY 10605. (888) 663-4637. resourcecenter@modimes.org. <http://www.modimes.org>.
National Human Genome Research Institute. The National Institutes of Health, 9000 Rockville Pike, Bethesda, MD 20892. (301) 496-2433. <http://www.nhgri.nih.gov>.
National Society of Genetic Counselors. 233 Canterbury Dr., Wallingford, PA 19086-6617. (610) 872-1192. <http://www.nsgc.org/GeneticCounselingYou.asp>.

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Blazing a Genetic Trail. Online genetic tutorial. <http://www.hhmi.org/GeneticTrail/>.
The Gene Letter. Online newsletter. <http://www.geneletter.org>.
Online Mendelian Inheritance in Man. Online genetic testing information sponsored by National Center for Biotechnology Information. <http://www.ncbi.nlm.nih.gov/Omim/>.
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Katherine S. Hunt, MS

Genital herpes

Definition

Genital herpes is a sexually transmitted disease caused by a herpes virus. The disease is characterized by the formation of fluid-filled, painful blisters in the genital area.

Description

Genital herpes (herpes genitalis, herpes progenitalis) is characterized by the formation of fluid-filled blisters on the genital organs of men and women. The word "herpes" comes from the Greek adjective *herpestes,* meaning *creeping,* which refers to the serpent-like pattern that the blisters may form. Genital herpes is a sexually transmitted disease which means that it is spread from person-to-person only by sexual contact. Herpes may be spread by vaginal, anal, and oral sexual activity. It is not spread by objects (such as a toilet seat or doorknob), swimming pools, hot tubs, or through the air.

Genital herpes is a disease resulting from an infection by a herpes simplex virus. There are eight different kinds of human herpes viruses. Only two of these, herpes simplex types 1 and 2, can cause genital herpes. It has been commonly believed that herpes simplex virus type 1 infects above the waist (causing cold sores) and herpes simplex virus type 2 infects below the waist (causing genital sores). This is not completely true. Both herpes virus type 1 and type 2 can cause herpes lesions on the lips or genitals, but recurrent cold sores are almost always type 1. The two viruses seem to have evolved to infect better at one site or the other, especially with regard to recurrent disease.

To determine the occurrence of herpes type 2 infection in the United States, the Centers for Disease Control and Prevention (CDC) used information from a survey called the National Health and **Nutrition** Examination Survey III (1988–1994). This survey of 40,000 noninstitutionalized people found that 21.9% of persons age 12 or older had antibodies to herpes type 2. This means that 45 million Americans have been exposed at some point in their lives to herpes simplex virus type 2. More women (25.6%) than men (17.8%) had antibodies. The racial differences for herpes type 2 antibodies were whites, 17.6%; blacks, 45.9%; and Mexican Americans, 22.3%. Interestingly, only 2.6% of adults reported that they have had genital herpes. Over half (50% to 60%) of the white adults in the United States have antibodies to herpes simplex virus type 1. The occurrence of antibodies to herpes type 1 is higher in blacks.

Viruses are different from bacteria. While bacteria are independent and can reproduce on their own, viruses cannot reproduce without the help of a cell. Viruses enter human cells and force them to make more virus. A human cell infected with herpes virus releases thousands of new viruses before it is killed. The cell **death** and resulting tissue damage causes the actual sores. The highest risk for spreading the virus is the time period beginning with the appearance of blisters and ending with scab formation.

Herpes virus can also infect a cell and instead of making the cell produce new viruses, it hides inside the cell and waits. Herpes virus hides in cells of the nervous system called "neurons." This is called "latency." A latent virus can wait inside neurons for days, months, or even years. At some future time, the virus "awakens" and causes the cell to produce thousands of new viruses which causes an active infection. Sometimes an active infection occurs without visible sores. Therefore, an infected person can spread herpes virus to other people even in the absence of sores.

This process of latency and active infection is best understood by considering the genital sore cycle. An active infection is obvious because sores are present. The first infection is called the "primary" infection. This active infection is then controlled by the body's immune system and the sores heal. In between active infections, the virus is latent. At some point in the future latent viruses become activated and once again cause sores. These are called "recurrent infections" or "outbreaks." Genital sores caused by herpes type 1 recur much less frequently than sores caused by herpes type 2.

Although it is unknown what triggers latent viruses to activate, several conditions seem to bring on infections. These include illness, tiredness, exposure to sunlight, menstruation, skin damage, food allergy and hot or cold temperatures. Although many people believe that **stress** can bring on their genital herpes outbreaks, there is no scientific evidence that there is a link between stress and recurrences. However, at least one clinical study has shown a connection between how well people cope with stress and their belief that stress and recurrent infections are linked.

Newborn babies who are infected with herpes virus experience a very severe, and possibly fatal disease. This is called "neonatal herpes infection." In the United States, one in 3,000–5,000 babies born will be infected with herpes virus. Babies can become infected during passage through the birth canal, but can become infected during the **pregnancy** if the membranes rupture early. Doctors will perform a **Cesarean section** on women who go into labor with active genital herpes.

Causes and symptoms

While anyone can be infected by herpes virus, not everyone will show symptoms. Risk factors for genital herpes include: early age at first sexual activity, multiple sexual partners, and a medical history of other sexually-transmitted diseases.

Most patients with genital herpes experience a prodrome (symptoms of oncoming disease) of **pain**, burning, **itching**, or tingling at the site where blisters will

form. This prodrome stage may last anywhere from a few hours, to one to two days. The herpes infection prodrome can occur for both the primary infection and recurrent infections. The prodrome for recurrent infections may be severe and cause a severe burning or stabbing pain in the genital area, legs, or buttocks.

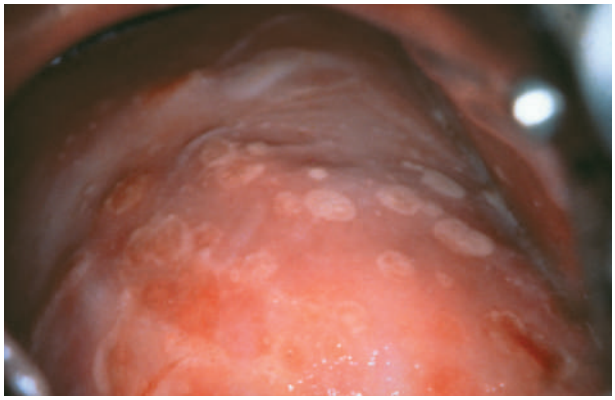
Primary genital herpes

The first symptoms of herpes usually occur within two to seven days after contact with an infected person but may take up to two weeks. Symptoms of the primary infection are usually more severe than those of recurrent infections. For up to 70% of the patients, the primary infection causes symptoms which affect the whole body (called "constitutional symptoms") including tiredness, **headache**, **fever**, chills, muscle aches, loss of appetite, as well as painful, swollen lymph nodes in the groin. These symptoms are greatest during the first three to four days of the infection and disappear within one week. The primary infection is more severe in women than in men.

Following the prodrome come the herpes blisters, which are similar on men and women. First, small red bumps appear. These bumps quickly become fluid-filled blisters. In dry areas, the blisters become filled with pus and take on a white to gray appearance, become covered with a scab, and heal within two to three weeks. In moist areas, the fluid-filled blisters burst and form painful ulcers which drain before healing. New blisters may appear over a period of one week or longer and may join together to form very large ulcers. The pain is relieved within two weeks and the blisters and ulcers heal without scarring by three to four weeks.

Women can experience a very severe and painful primary infection. Herpes blisters first appear on the labia majora (outer lips), labia minora (inner lips), and entrance to the vagina. Blisters often appear on the clitoris, at the urinary opening, around the anal opening, and on the buttocks and thighs. In addition, women may get herpes blisters on the lips, breasts, fingers, and eyes. The vagina and cervix are almost always involved which causes a watery discharge. Other symptoms that occur in women are: painful or difficult urination (83%), swelling of the urinary tube (85%), **meningitis** (36%), and throat infection (13%). Most women develop painful, swollen lymph nodes (lymphadenopathy) in the groin and pelvis. About one in ten women get a vaginal yeast infection as a complication of the primary herpes infection.

In men, the herpes blisters usually form on the penis but can also appear on the scrotum, thighs, and buttocks. Fewer than half of the men with primary herpes experience the constitutional symptoms. Thirty percent to 40% of men have a discharge from the urinary tube. Some men develop painful swollen lymph nodes (lymphadenopathy) in the groin and pelvis. Although less frequently than women, men too may experience painful or difficult urination (44%), swelling of the urinary tube (27%), meningitis (13%), and throat infection (7%).



Female cervix covered with herpes lesions *(Photo Researchers. Reproduced by permission.)*

Recurrent genital herpes

One or more outbreaks of genital herpes per year occur in 60–90% of those infected with herpes virus. About 40% of the persons infected with herpes simplex virus type 2 will experience six or more outbreaks each year. Genital herpes recurrences are less severe than the primary infection; however, women still experience more severe symptoms and pain than men. Constitutional symptoms are not usually present. Blisters will appear at the same sites during each outbreak. Usually there are fewer blisters, less pain, and the time period from the beginning of symptoms to healing is shorter than the primary infection. One out of every four women experience painful or difficult urination during recurrent infection. Both men and women may develop lymphadenopathy.

Diagnosis

Because genital herpes is so common, it is diagnosed primarily by symptoms. It can be diagnosed and treated by the family doctor, dermatologists (doctors who specialize in skin diseases), urologists (doctors who specialize in the urinary tract diseases of men and women and the genital organs of men), gynecologists (doctors who specialize in the diseases of women's genital organs) and infectious disease specialists. The diagnosis and treatment of this infectious disease should be covered by most insurance providers.

Laboratory tests may be performed to look for the virus. Because healing sores do not shed much virus, a

A close-up view of a man's penis with a blister (center of image) caused by the herpes simplex virus. *(Photograph by Dr. P. Marazzi, Custom Medical Stock Photo. Reproduced by permission.)*

sample from an open sore would be taken for viral culture. A sterile cotton swab would be wiped over open sores and the sample used to infect human cells in culture. Cells which are killed by herpes virus have a certain appearance under microscopic examination. The results of this test are available within two to ten days. Other areas which may be sampled, depending upon the disease symptoms in a particular patient, include the urinary tract, vagina, cervix, throat, eye tissues, and cerebrospinal fluid.

Direct staining and microscopic examination of the lesion sample may also be used. A blood test may be performed to see if the patient has antibodies to herpes virus. The results of blood testing are available within one day. The disadvantage of this blood test is that it usually does not distinguish between herpes type 1 and 2, and only determines that the patient has had a herpes infection at some point in his or her life. Therefore, the viral culture test must be performed to be absolutely certain that the sores are caused by herpes virus.

Because genital sores can be symptoms of many other diseases, the doctor must determine the exact cause of the sores. The above mentioned tests are performed to determine that herpes virus is causing the genital sores. Other diseases which may cause genital sores are **syphilis**, **chancroid**, **lymphogranuloma venereum**, **granuloma inguinale**, herpes zoster, erythema multiform, Behçet's syndrome, inflammatory bowel disease, **contact dermatitis**, **candidiasis**, and **impetigo**.

Because most newborns who are infected with herpes virus were born to mothers who had no symptoms of infection it is important to check all newborn babies for symptoms. Any skin sore should be sampled to determine if it is caused by herpes simplex. Babies should be checked for sores in their mouth and for signs of herpes infection in their eyes.

Treatment

There is no cure for herpes virus infections. There are **antiviral drugs** available which have some effect in lessening the symptoms and decreasing the length of herpes outbreaks. There is evidence that some may also prevent future outbreaks. These antiviral drugs work by interfering with the replication of the viruses and are most effective when taken as early in the infection process as possible. For the best results, drug treatment should begin during the prodrome stage before blisters are visible. Depending on the length of the outbreak, drug treatment could continue for up to 10 days.

Acyclovir (Zovirax) is the drug of choice for herpes infection and can be given intravenously, taken by mouth (orally), or applied directly to sores as an ointment. Acyclovir has been in use for many years and only five out of 100 patients experience side effects. Side effects of acyclovir treatment include nausea, vomiting, itchy rash, and **hives**. Although acyclovir is the recommended drug for treating herpes infections, other drugs may be used including famciclovir (Famvir), valacyclovir (Valtrex), vidarabine (Vira-A), idoxuridine (Herplex Liquifilm, Stoxil), trifluorothymidine (Viroptic), and penciclovir (Denavir).

Acyclovir is effective in treating both the primary infection and recurrent outbreaks. When taken intravenously or orally, acyclovir reduces the healing time, virus shedding period, and duration of vesicles. The standard oral dose of acyclovir for primary herpes is 200 mg five times daily or 400 mg three times daily for a period of 10 days. Recurrent herpes is treated with the same doses for a period of five days. Intravenous acyclovir is given to patients who require hospitalization because of severe primary infections or herpes complications such as aseptic meningitis or sacral ganglionitis (inflammation of nerve bundles).

Patients with frequent outbreaks (greater than six to eight per year) may benefit from long term use of acyclovir which is called "suppressive therapy." Patients on suppressive therapy have longer periods between herpes outbreaks. The specific dosage used for suppression needs to be determined for each patient and should be reevaluated every few years. Alternatively, patients may use short term suppressive therapy to lessen the chance

of developing an active infection during special occasions such as weddings or holidays.

There are several things that a patient may do to lessen the pain of genital sores. Wearing loose fitting clothing and cotton underwear is helpful. Removing clothing or wearing loose pajamas while at home may reduce pain. Soaking in a tub of warm water and using a blow dryer on the "cool" setting to dry the infected area is helpful. Putting an ice pack on the affected area for 10 minutes, followed by five minutes off and then repeating this procedure may relieve pain. A zinc sulfate ointment may help to heal the sores. Application of a baking soda compress to sores may be soothing.

Neonatal herpes

Newborn babies with herpes virus infections are treated with intravenous acyclovir or vidarabine for 10 days. These drugs have greatly reduced deaths and increased the number of babies who appear normal at one year of age. However, because neonatal herpes infection is so serious, even with treatment babies may not survive, or may suffer nervous system damage. Infected babies may be treated with long term suppressive therapy.

Alternative treatment

An imbalance in the amino acids lysine and arginine is thought to be one contributing factor in herpes virus outbreaks. A ratio of lysine to arginine that is in balance (that is more lysine than arginine is present) seems to help the immune system work optimally. Thus, a diet that is rich in lysine may help prevent recurrences of genital herpes. Foods that contain high levels of lysine include most vegetables, legumes, fish, turkey, beef, lamb, cheese, and chicken. Patients may take 500 mg of lysine daily and increase to 1,000 mg three times a day during an outbreak. Intake of the amino acid arginine should be reduced. Foods rich in arginine that should be avoided are chocolate, peanuts, almonds, and other nuts and seeds.

Clinical experience indicates a connection between high stress and herpes outbreaks. Some patients respond well to **stress reduction** and relaxation techniques. **Acupressure** and massage may relieve tiredness and stress. **Meditation**, **yoga**, **tai chi**, and **hypnotherapy** can also help relieve stress and promote relaxation.

Some herbs, including **echinacea** (*Echinacea* spp.) and garlic (*Allium sativum*), are believed to strengthen the body's defenses against viral infections. Red marine algae (family Dumontiaceae), both taken internally and applied topically, is thought to be effective in treating herpes type I and type II infections. Other topical treatments may be helpful in inhibiting the growth of the herpes virus, in minimizing the damage it causes, or in helping the sores heal. Zinc sulphate ointment seems to help sores heal and to fight recurrence. Lithium succinate ointment may interfere with viral replication. An ointment made with glycyrrhizinic acid, a component of licorice (*Glycyrrhiza glabra*), seems to inactivate the virus. Topical applications of vitamin E or tea tree oil (*Melaleuca* spp.) help dry up herpes sores. Specific combinations of homeopathic remedies may also be helpful treatments for genital herpes.

KEY TERMS

Groin—The region of the body that lies between the abdomen and the thighs.

Latent virus—A nonactive virus which is in a dormant state within a cell. Herpes virus is latent in cells of the nervous system.

Prodrome—Symptoms which warn of the beginning of disease. The herpes prodrome consists of pain, burning, tingling, or itching at a site before blisters are visible.

Recurrence—The return of an active herpes infection following a period of latency.

Ulcer—A painful, pus-draining, depression in the skin caused by an infection.

Prognosis

Although physically and emotionally painful, genital herpes is usually not a serious disease. The primary infection can be severe and may require hospitalization for treatment. Complications of the primary infection may involve the cervix, urinary system, anal opening, and the nervous system. Persons who have a decreased ability to produce an immune response to infection (called "immunocompromised") due to disease or medication are at risk for a very severe, and possibly fatal, herpes infection. Even with antiviral treatment, neonatal herpes infections can be fatal or cause permanent nervous system damage.

Prevention

The only way to prevent genital herpes is to avoid contact with infected persons. This is not an easy solution because many people aren't aware that they are infected and can easily spread the virus to others. Avoid all sexual contact with an infected person during a herpes outbreak. Because herpes virus can be spread at any

time, **condom** use is recommended to prevent the spread of virus to uninfected partners. As of early 1998 there were no herpes vaccines available, although new herpes vaccines are being tested in humans.

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Belinda Rowland, PhD

Genital warts

Definition

Genital **warts**, which are also called condylomata acuminata or venereal warts, are growths in the genital area caused by a sexually transmitted papillomavirus. A papillomavirus is a virus that produces papillomas, or benign growths on the skin and mucous membranes.

Description

Genital warts are the most common sexually transmitted disease (STD) in the general population. It is estimated that 1% of sexually active people between the ages of 18 and 45 have genital warts; however, polymerase chain reaction (PCR) testing indicates that as many as 40% of sexually active adults carry the human papillomavirus (HPV) that causes genital warts.

Genital warts vary somewhat in appearance. They may be either flat or resemble raspberries or cauliflower in appearance. The warts begin as small red or pink growths and grow as large as four inches across, interfering with intercourse and **childbirth**. The warts grow in the moist tissues of the genital areas. In women, they occur on the external genitals and on the walls of the vagina and cervix; in men, they develop in the urethra and on the shaft of the penis. The warts then spread to the area behind the genitals surrounding the anus.

Risk factors for genital warts include:

Man with genital warts. *(Custom Medical Stock Photo. Reproduced by permission.)*

- multiple sexual partners
- infection with another STD
- pregnancy
- anal intercourse
- poor personal hygiene
- heavy perspiration

Causes and symptoms

There are about 80 types of human papillomavirus. Genital warts are caused by HPV types 1, 2, 6, 11, 16, and 18. HPV is transmitted by sexual contact. The incubation period varies from one to six months.

The symptoms include bleeding, **pain**, and odor as well as the visible warts.

Diagnosis

The diagnosis is usually made by examining scrapings from the warts under a darkfield microscope. If the warts are caused by HPV, they will turn white when a 5% solution of white vinegar is added. If the warts reappear, the doctor may order a biopsy to rule out **cancer**.

Treatment

No treatment for genital warts is completely effective because therapy depends on destroying skin infected by the virus. There are no drugs that will kill the virus directly.

Medications

Genital warts were treated until recently with applications of podophyllum resin, a corrosive substance that cannot be given to pregnant patients. A milder form of podophyllum, podofilox (Condylox), has been introduced. Women are also treated with 5-fluorouracil cream,

bichloroacetic acid, or trichloroacetic acid. All of these substances irritate the skin and require weeks of treatment.

Genital warts can also be treated with injections of interferon. Interferon works best in combination with podofilox applications.

Surgery

Surgery may be necessary to remove warts blocking the patient's vagina, urethra, or anus. Surgical techniques include the use of liquid nitrogen, electrosurgery, and **laser surgery**.

Prognosis

Genital warts are benign growths and are not cancerous by themselves. Repeated HPV infection in women, however, appears to increase the risk of later **cervical cancer**. Women infected with HPV types 16 and 18 should have yearly cervical smears. Recurrence is common with all present methods of treatment—including surgery—because HPV can remain latent in apparently normal surrounding skin.

Prevention

The only reliable method of prevention is sexual abstinence. The use of condoms minimizes but does not eliminate the risk of HPV transmission. The patient's sexual contacts should be notified and examined.

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KEY TERMS

Condylomata acuminata—Another name for genital warts.

Papilloma—A benign growth on the skin or mucous membrane. Viruses that cause these growths are called human papillomaviruses (HPVs).

Podophyllum resin—A medication derived from the May apple or mandrake and used to treat genital warts.

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Rebecca J. Frey

Gentamicin *see* **Aminoglycosides**

German measles *see* **Rubella**

Gestalt therapy

Definition

Gestalt therapy is a humanistic therapy technique that focuses on gaining an awareness of emotions and behaviors in the present rather than in the past. The therapist does not interpret experiences for the patient. Instead, the therapist and patient work together to help the patient understand him/herself. This type of therapy focuses on experiencing the present situation rather than talking about what occurred in the past. Patients are encouraged to become aware of immediate needs, meet them, and let them recede into the background. The well-adjusted person is seen as someone who has a constant flow of needs and is able to satisfy those needs.

Purpose

In Gestalt therapy (from the German word meaning *form*), the major goal is self-awareness. Patients work on uncovering and resolving interpersonal issues during

therapy. Unresolved issues are unable to fade into the background of consciousness because the needs they represent are never met. In Gestalt therapy, the goal is to discover people connected with a patient's unresolved issues and try to engage those people (or images of those people) in interactions that can lead to a resolution. Gestalt therapy is most useful for patients open to working on self-awareness.

Precautions

The choice of a therapist is crucial. Some people who call themselves "therapists" have limited training in Gestalt therapy. It is important that the therapist be a licensed mental health professional. Additionally, some individuals may not be able to tolerate the intensity of this type of therapy.

Description

Gestalt therapy has developed into a form of therapy that emphasizes medium to large groups, although many Gestalt techniques can be used in one-on-one therapy. Gestalt therapy probably has a greater range of formats than any other therapy technique. It is practiced in individual, couples, and family therapies, as well as in therapy with children.

Ideally, the patient identifies current sensations and emotions, particularly ones that are painful or disruptive. Patients are confronted with their unconscious feelings and needs, and are assisted to accept and assert those repressed parts of themselves.

The most powerful techniques involve role-playing. For example, the patient talks to an empty chair as they imagine that a person associated with an unresolved issue is sitting in the chair. As the patient talks to the "person" in the chair, the patient imagines that the person responds to the expressed feelings. Although this technique may sound artificial and might make some people feel self-conscious, it can be a powerful way to approach buried feelings and gain new insight into them.

Sometimes patients use battacca bats, padded sticks that can be used to hit chairs or sofas. Using a battacca bat can help a patient safely express anger. A patient may also experience a Gestalt therapy marathon, where the participants and one or more facilitators have nonstop **group therapy** over a weekend. The effects of the intense emotion and the lack of sleep can eliminate many psychological defenses and allow significant progress to be made in a short time. This is true only if the patient has adequate psychological strength for a marathon and is carefully monitored by the therapist.

Preparation

Gestalt therapy begins with the first contact. There is no separate diagnostic or assessment period. Instead, assessment and screening are done as part of the ongoing relationship between patient and therapist. This assessment includes determining the patient's willingness and support for work using Gestalt methods, as well as determining the compatibility between the patient and the therapist. Unfortunately, some "encounter groups" led by poorly trained individuals do not provide adequate pretherapy screening and assessment.

Aftercare

Sessions are usually held once a week. Frequency of sessions held is based on how long the patient can go between sessions without losing the momentum from the previous session. Patients and therapists discuss when to start sessions, when to stop sessions, and what kind of activities to use during a session. However, the patient is encouraged and required to make choices.

Risks

Disturbed people with severe mental illness may not be suitable candidates for Gestalt therapy. Facilities that provide Gestalt therapy and train Gestalt therapists vary. Since there are no national standards for these Gestalt facilities, there are no set national standards for Gestalt therapy or Gestalt therapists.

Normal results

Scientific documentation on the effectiveness of Gestalt therapy is limited. Evidence suggests that this type of therapy may not be reliably effective.

Abnormal results

This approach can be anti-intellectual and can discount thoughts, thought patterns, and beliefs. In the hands of an ineffective therapist, Gestalt procedures can become a series of mechanical exercises, allowing the therapist as a person to stay hidden. Moreover, there is a potential for the therapist to manipulate the patient with powerful techniques, especially in therapy marathons where **fatigue** may make a patient vulnerable.

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Association for the Advancement of Gestalt Therapy. 400 East 58th St., New York, NY 10022. (212) 486-1581. <http://www.aagt.org>.

David James Doermann

Gestational diabetes

Definition

Gestational diabetes is a condition that occurs during **pregnancy**. Like other forms of diabetes, gestational diabetes involves a defect in the way the body processes and uses sugars (glucose) in the diet. Gestational diabetes, however, has a number of characteristics that are different from other forms of diabetes.

Description

Glucose is a form of sugar that is present in many foods, including sweets, potatoes, pasta, and breads. The body uses glucose to provide energy. It is stored in the liver, muscles, and fatty tissue. The pancreas produces a hormone (a chemical produced in one part of the body, which travels to another part of the body in order to exert its effect) called insulin. Insulin is required to allow glucose to enter the liver, muscles, and fatty tissues, thus reducing the amount of glucose in the blood. In diabetes, blood levels of glucose remain abnormally high. In many forms of diabetes, this is because the pancreas does not produce enough insulin.

In gestational diabetes, the pancreas is not at fault. Instead, the problem is in the placenta. During pregnancy, the placenta provides the baby with nourishment. It also produces a number of hormones that interfere with the body's usual response to insulin. This condition is referred to as "insulin resistance." Most pregnant women do not suffer from gestational diabetes, because the pancreas works to produce extra quantities of insulin in order to compensate for insulin resistance. However, when a woman's pancreas cannot produce enough extra insulin, blood levels of glucose stay abnormally high, and the woman is considered to have gestational diabetes.

About 1–3% of all pregnant women develop gestational diabetes. Women at risk for gestational diabetes include those who:

- are overweight
- have a family history of diabetes
- have previously given birth to a very large, heavy baby
- have previously had a baby who was stillborn, or born with a birth defect
- have an excess amount of amniotic fluid (the cushioning fluid within the uterus that surrounds the developing fetus)
- are over 25 years of age
- belong to an ethnic group known to experience higher rates of gestational diabetes (in the United States, these groups include Mexican-Americans, American Indians, African-Americans, as well as individuals from Asia, India, or the Pacific Islands)
- have a previous history of gestational diabetes during a pregnancy

Causes and symptoms

Most women with gestational diabetes have no recognizable symptoms. However, leaving gestational diabetes undiagnosed and untreated is risky to the developing fetus. Left untreated, a diabetic mother's blood sugar levels will be consistently high. This sugar will cross the placenta and pour into the baby's system through the umbilical cord. The unborn baby's pancreas will respond to this high level of sugar by constantly putting out large amounts of insulin. The insulin will allow the fetus's cells to take in glucose, where it will be converted to fat and stored. A baby who has been exposed to constantly high levels of sugar throughout pregnancy will be abnormally large. Such a baby will often grow so large that he or she cannot be born through the vagina, but will instead need to be born through a surgical procedure (**cesarean section**).

Furthermore, when the baby is born, the baby will still have an abnormally large amount of insulin circulating. After birth, when the mother and baby are no longer attached to each other via the placenta and umbilical cord, the baby will no longer be receiving the mother's high level of sugar. The baby's high level of insulin, however, will very quickly use up the glucose circulating in the baby's bloodstream. The baby is then at risk for having a dangerously low level of blood glucose (a condition called **hypoglycemia**).

Diagnosis

Since gestational diabetes most often exists with no symptoms detectable by the patient, and since its existence

KEY TERMS

Glucose—A form of sugar. The final product of the breakdown of carbohydrates (starches).

Insulin—A hormone produced by the pancreas that is central to the processing of sugars and carbohydrates in the diet.

Placenta—An organ that is attached to the inside wall of the mother's uterus and to the fetus via the umbilical cord. The placenta allows oxygen and nutrients from the mother's bloodstream to pass into the unborn baby.

puts the developing baby at considerable risk, screening for the disorder is a routine part of pregnancy care. This screening is usually done between the 24th and 28th week of pregnancy. By this point in the pregnancy, the placental hormones have reached a sufficient level to cause insulin resistance. Screening for gestational diabetes involves the pregnant woman drinking a special solution that contains exactly 50 grams of glucose. An hour later, the woman's blood is drawn and tested for its glucose level. A level less than 140 mg/dl is considered normal.

When the screening glucose level is over 140 mg/dl, a special three-hour glucose tolerance test is performed. This involves following a special diet for three days prior to the test. This diet is set-up to contain at least 150 grams of carbohydrate each day. Just before the test, the patient is instructed to eat and drink nothing (except water) for 10–14 hours. A blood sample is then tested to determine the **fasting** glucose level. The patient then drinks a special solution containing exactly 100 grams of glucose, and her blood is tested every hour for the next three hours. If two or more of these levels are elevated over normal, then the patient is considered to have gestational diabetes.

Treatment

Treatment for gestational diabetes will depend on the severity of the diabetes. Mild forms can be treated with diet (decreasing the intake of sugars and fats, in particular). Many women are put on strict, detailed **diets**, and are asked to stay within a certain range of calorie intake. **Exercise** is sometimes used to keep blood sugar levels lower. Patients are often asked to regularly measure their blood sugar. This is done by poking a finger with a needle called a lancet, putting a drop of blood on a special type of paper, and feeding the paper into a meter which analyzes and reports the blood sugar level. When diet and exercise do not keep blood glucose levels within an acceptable range, a patient may need to take regular shots of insulin.

Many babies born to women with gestational diabetes are large enough to cause more difficult deliveries, and they may require the use of forceps, suction, or cesarean section. Once the baby is born, it is important to carefully monitor its blood glucose levels. These levels may drop sharply and dangerously once the baby is no longer receiving large quantities of sugar from the mother. When this occurs, it is easily resolved by giving the baby glucose.

Prognosis

Prognosis for women with gestational diabetes, and their babies, is generally good. Almost all such women stop being diabetic after the birth of their baby. However, some research has shown that nearly 50% of these women will develop a permanent form of diabetes within 15 years. The child of a mother with gestational diabetes has a greater-than-normal chance of developing diabetes sometime in adulthood, also. A woman who has had gestational diabetes during one pregnancy has about a 66% chance of having it again during any subsequent pregnancies. Women who had gestational diabetes usually are tested for diabetes at the post-partum checkup or after stopping breastfeeding.

Prevention

There is no known way to actually prevent diabetes, particularly since gestational diabetes is due to the effects of normal hormones of pregnancy. However, the effects of insulin resistance can be best handled through careful attention to diet, avoiding becoming overweight throughout life, and participating in reasonable exercise.

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American Diabetes Association. 1701 North Beauregard Street, Alexandria, VA 22311. (800) 342-2383. <http://www.diabetes.org>.

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GI bleeding studies

Definition

GI bleeding studies uses radioactive materials in the investigation of bleeding from the gastrointestinal (GI) tract. These studies go under various names such as "GI bleeding scans" or "Tagged red blood cell scans." They are performed and interpreted by radiologists (physicians who specialize in diagnosis and treatment of diseases by means of x rays or related substances).

Purpose

These studies are designed to find the source of blood loss from the GI tract; that is the stomach, small bowel, or colon. They work best when bleeding is either too slow, intermittent, or too rapid to be identified by other means, such as endoscopy, upper GI series, or **barium enema**.

They are particularly useful when other methods have not been able to determine the site or cause of bleeding.

Precautions

Because of the use of radioactive materials, these studies are best avoided in pregnant patients. Another important relates to the interpretation of these tests, whether normal or abnormal. Since these studies are far from perfect, they can only be used as "guides" as to the cause or site of bleeding. In most instances, further studies must be performed to confirm their findings.

Description

Bleeding scans are based on the accumulation of radioactive material as it exits from the vessels during a bleeding episode. Blood is first withdrawn from the patient. Then, the blood, along with a radioactive substance is injected into a vein and over several hours scans measuring radioactivity are performed. The studies were initially reported to be very sensitive and accurate; however, critical evaluation of these tests have shown them to be less accurate than originally believed.

A clay model of the human digestive system. *(Custom Medical Stock Photo. Reproduced by permission.)*

Preparation

No preparation is needed for these tests. They are often done on an "emergency" basis.

Aftercare

No special care is needed after the exam.

Risks

Bleeding scans are free of any risks or side-effects, aside from the fact that they should best be avoided in **pregnancy**.

Normal results

A normal exam would fail to show any evidence of accumulation of radioactive material on the scan. However, scans may be normal in as many as 70% of patients who later turn out to have significant causes of bleeding. This is known as a false-negative result. A patient must

KEY TERMS

Endoscope, Endoscopy—An endoscope as used in the field of gastroenterology is a thin flexible tube which uses a lens or miniature camera to view various areas of the gastrointestinal tract. The performance of an exam using an endoscope is referred by the general term endoscopy. Diagnosis through biopsies or other means and therapeutic procedures can be done with these instruments.

be bleeding at the same time the scan is performed for it to be seen. Therefore, not finding evidence of a bleeding source during the study, can be misleading.

Abnormal results

The accumulation of radioactive material indicating a "leakage" of blood from the vessels is abnormal. The scan gives a rough, though not exact, guide as to the location of the bleeding. It can tell where the bleeding may be, but usually not the cause. Thus, extreme caution and skill is needed in interpreting these scans, and decisions involving surgery or other treatment should await more definitive tests.

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David Kaminstein, MD

Giant-cell arteritis *see* **Temporal arteritis**

Giardiasis

Definition

Giardiasis is a common intestinal infection spread by eating contaminated food, drinking contaminated water, or through direct contact with the organism that causes the disease, *Giardia lamblia*. Giardiasis is found throughout the world and is a common cause of traveller's **diarrhea**. In the United States it is a growing problem, especially among children in childcare centers.

Description

Giardia is one of the most common intestinal parasites in the world, infecting as much as 20% of the entire population of the earth. It is common in overcrowded developing countries with poor sanitation and a lack of clean water. Recent tests have found *Giardia* in 7% of all stool samples tested nationwide, indicating that this disease is much more widespread than was originally believed. It has been found not only in humans, but also in wild and domestic animals.

Giardiasis is becoming a growing problem in the United States, where it affects three times more children than adults. In recent years, giardiasis outbreaks have been common among people in schools or daycare centers and at catered affairs and large public picnic areas. Children can easily pass on the infection by touching contaminated toys, changing tables, utensils, or their own feces, and then touching other people. For this reason, infection spreads quickly through a daycare center or institution for the developmentally disabled.

Unfiltered streams or lakes that may be contaminated by human or animal wastes are a common source of infection. Outbreaks can occur among campers and hikers who drink untreated water from mountain streams. While 20 million Americans drink unfiltered city water from streams or rivers, giardiasis outbreaks from tainted city water have been rare. Most of these problems have occurred not due to the absence of filters, but because of malfunctions in city water treatment plants, such as a temporary drop in chlorine levels. It is possible to become infected in a public swimming pool, however, since *Giardia* can survive in chlorinated water for about 15 minutes. During that time, it is possible for an individual to swallow contaminated pool water and become infected.

Causes and symptoms

Giardiasis is spread by food or water contaminated by the *Giardia lamblia* protozoan organism found in the human intestinal tract and feces. When the cysts are ingested, the stomach acid degrades the cysts and releases the active parasite into the body. Once within the body, the parasites cling to the lining of the small intestine, reproduce, and are swept into the fecal stream. As the liquid content of the bowel dries up, the parasites form cysts, which are then passed in the feces. Once excreted, the cysts can survive in water for more than three months. The parasite is spread

further by direct fecal-oral contamination, such as can occur if food is prepared without adequate hand-washing, or by ingesting the cysts in water or food.

Giardiasis is not fatal, and about two-thirds of infected people exhibit no symptoms. Symptoms will not occur until between one and two weeks after infection. When present, symptoms include explosive, watery diarrhea that can last for a week or more and, in chronic cases, may persist for months. Because the infection interferes with the body's ability to absorb fats from the intestinal tract, the stool is filled with fat. Other symptoms include foul-smelling and greasy feces, stomach pains, gas and bloating, loss of appetite, **nausea and vomiting**. In cases in which the infection becomeschronic, lasting for months or years, symptoms might include poor digestion, problems digesting milk, intermittent diarrhea, **fatigue**, weakness, and significant weight loss.

Diagnosis

Diagnosis can be difficult because it can be easy to overlook the presence of the giardia cysts during a routine inspection of a stool specimen. In the past, the condition has been diagnosed by examining three stool samples for the presence of the parasites. However, because the organism is shed in some stool samples and not others, the infection may not be discovered using this method.

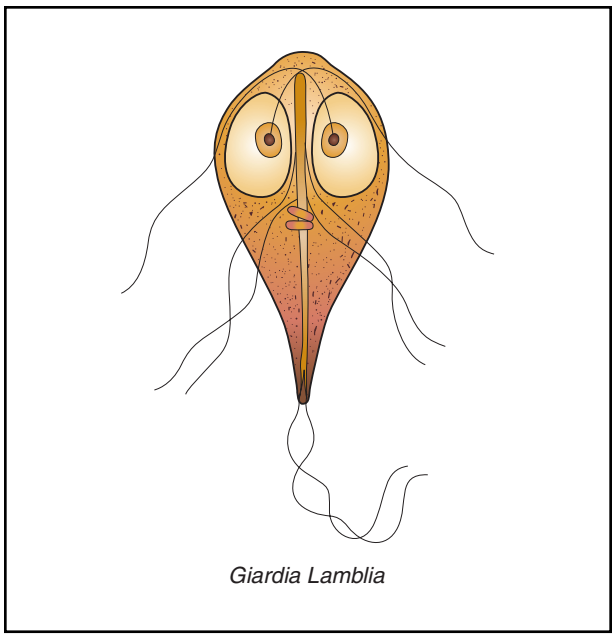
A newer, more accurate method of diagnosing the condition is the enzyme-linked immunosorbent assay (ELISA) that detects cysts and antigen in stool, and is approximately 90% accurate. While slightly more expensive, it only needs to be done once and is therefore less expensive overall than the earlier test.

Treatment

Acute giardiasis can usually be allowed to run its natural course and tends to clear up on its own. **Antibiotics** are helpful, however, in easing symptoms and preventing the spread of infection. Medications include metronidazole, furazolidone and paromomycin. Healthy carriers with no symptoms do not need antibiotic treatment. If treatment should fail, the patient should wait two weeks and repeat the drug course. Anyone with an impaired immune system (immunocompromised), such as a person with **AIDS**, may need to be treated with a combination of medications.

Prognosis

Giardiasis is rarely fatal, and when treated promptly, antibiotics usually cure the infection. While most people respond quickly to treatment, some have lingering symptoms and suffer with diarrhea and cramps for long periods, losing weight and not growing well. Those most at-risk for a course like this are the elderly, people with a weakened immune system, malnourished children, and anyone with low stomach acid.



Infection with the protozoon *Giardia lamblia*, shown above, causes diarrhea in humans. *(Illustration by Electronic Illustrators Group).*

Prevention

The best way to avoid giardiasis is to avoid drinking untreated surface water, especially from mountain streams. The condition also can be minimized by practicing the following preventive measures:

- thoroughly washing hands before handling food
- maintaining good personal cleanliness
- boiling any untreated water for at least three minutes
- properly disposing of fecal material

Children with severe diarrhea (and others who are unable to control their bowel habits) should be kept at home until the stool returns to normal. If an outbreak occurs in a daycare center, the director should notify the local health department. Some local health departments require a follow-up stool testing to confirm that the person is no longer contagious. People not in high-risk settings can return to their routine activities after recovery.

Resources

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KEY TERMS

Antibody—A specific protein produced by the immune system in response to a specific foreign protein or particle called an antigen.

Antigen—A substance (usually a protein) identified as foreign by the body's immune system, triggering the release of antibodies as part of the body's defense mechanism.

Enzyme-linked immunosorbent assay (ELISA)—A laboratory technique used to detect specific antigens or antibodies. It can be used to diagnose giardiasis.

Giardia lamblia—A type of protozoa with a whip-like tail that infects the human intestinal tract, causing giardiasis. The protozoa will not spread to other parts of the body.

Immunocompromised—A state in which the immune system is suppressed or not functioning properly.

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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 Institute of Allergies and Infectious Diseases, Division of Microbiology and Infectious Diseases. Building 31, Room. 7A-50, 31 Center Drive MSC 2520, Bethesda, MD 20892. <http://www.niaid.nih.gov>.

World Health Organization, Division of Emerging and Other Communicable Diseases Surveillance and Control. Avenue Appia 20, 1211 Geneva 27, Switzerland. (+00 41 22) 791 21 11. <http://www.who.int>.

OTHER

Centers for Disease Control. <http://www.cdc.gov/ncidod/EID/eidtext.htm>.

International Society of Travel Medicine. <http:www.istm.org>.

Carol A. Turkington

Giardia lamblia infection *see* **Giardiasis**

Gigantism *see* **Acromegaly and gigantism**

Gilchrist's disease *see* **Blastomycosis**

Gilles de la Tourette's syndrome *see* **Tourette syndrome**

Gingivitis *see* **Periodontal disease**

Ginkgo biloba

Definition

Ginkgo biloba, known as the maidenhair tree, is one of the oldest trees on Earth, once part of the flora of the Mesozoic period. The ginkgo tree is the only surviving species of the Ginkgoaceae family. This ancient deciduous tree may live for thousands of years. Ginkgo is indigenous to China, Japan, and Korea, but also thrived in North America and Europe prior to the Ice Age. This drastic climate change destroyed the wild ginkgo tree throughout much of the world. In China, ginkgo was cultivated in temple gardens as a sacred tree known as *bai gou*, thus assuring its survival there for over 200 million years. Ginkgo fossils found from the Permian period are identical to the living tree, which is sometimes called a living fossil.

Description

Ginkgo trees may grow to 122 ft (37.2 m) tall and measure 4 ft (1.2 m) in girth. The female trees have a somewhat pointed shape at the top, like a pyramid. The male trees are broader at the crown. The bark of the ornamental ginkgo tree is rough and fissured and may be an ash to dark-brown in color. Distinctive, fan-shaped leaves with long stalks emerge from a sheath on the stem. Leaves are bright green in spring and summer, and turn to golden yellow in the fall. Ginkgo trees may take as long as 30 years to flower. Ginkgo is dioecious, with male and female flowers blooming on separate trees. Blossoms grow singly from the axils of the leaf. The female flowers

appear at the end of a leafless branch. The yellow, plum-shaped fruits develop an unpleasant scent as they ripen. They contain an edible inner seed that is available in Asian country marketplaces. Ginkgo's longevity may be due, in part, to its remarkable resistance to disease, pollution, and insect damage. Ginkgo trees are part of the landscape plan in many urban areas throughout the world. Millions of ginkgo trees, grown for harvest of the medicinal leaves, are raised on plantations in the United States, France, South Korea, and Japan, and are exported to Europe for pharmaceutical processing.

Purpose

Ginkgo leaves, fresh or dry, and seeds, separated from the outer layer of the fruit, are used medicinally. Ginkgo has remarkable healing virtues that have been recorded as far back as 2800 B.C. in the oldest Chinese materia medica. Ginkgo seeds were traditionally served to guests along with alcohol drinks in Japan. An enzyme present in the ginkgo seed has been shown in clinical research to speed up alcohol metabolism in the body, underscoring the wisdom of this folk custom. The leaf extract has been used in Asia for thousands of years to treat **allergies**, **asthma**, and **bronchitis**. It is also valued in Chinese medicine as a heart tonic, helpful in the treatment of cardiac arrhythmia. Ginkgo was first introduced to Europe in 1730, and to North America in 1784 where it was planted as an exotic garden ornamental near Philadelphia. Ginkgo medicinal extracts are the primary prescription medicines used in France and Germany.

Ginkgo acts to increase blood flow throughout the body, particularly cerebral blood flow. It acts as a circulatory system tonic, stimulating greater tone in the venous system. The herb is a useful and proven remedy for numerous diseases caused by restricted blood flow. European physicians prescribe the extract for treatment of **Raynaud's disease**, a condition of impaired circulation to the fingers. It is also recommended to treat intermittent claudication, a circulatory condition that results in painful cramping of the calf muscles in the leg and impairs the ability to walk. German herbalists recommend ingesting the extract for treatment of leg ulcers, and large doses are used to treat **varicose veins**. Ginkgo is widely recommended in Europe for the treatment of **stroke**. The dried leaf extract may also act to prevent hemmorrhagic stroke by strengthening the blood capillaries throughout the body. In studies of patients with atherosclerotic clogging of the penile artery, long-term therapy with ginkgo extract has provided significant improvement in erectile function. Ginkgo extract also acts to eliminate damaging free-radicals in the body, and has been shown to be effective in treatment of **premenstrual syndrome**, relieving tender or painful breasts.

Ginkgo biloba leaves. *(Photograph by Robert J. Huffman. Field Mark Publications. Reproduced by permission.)*

Ginkgo extract has proven benefits to elderly persons. This ancient herb acts to enhance oxygen utilization and thus improves memory, concentration, and other mental faculties. The herbal extract is used to treat **Alzheimer's disease**. It has been shown to have beneficial effect on the hippocampus, an area of the brain affected by Alzheimer's disease. The herbal extract has also been shown to significantly improve long-distance vision and may reverse damage to the retina of the eye. Studies have also confirmed its value in the treatment of depression in elderly persons. The ginkgo extract may provide relief for persons with **headache**, **sinusitis**, and vertigo. It may also help relieve chronic ringing in the ears known as **tinnitus**.

The active constituents in the ginkgo tree, known as ginkgolides, interfere with a blood protein known as the platelet activating factor, or PAF. Other phytochemicals in ginkgo include flavonoids, biflavonoides, proanthocyanidins, trilactonic diterpenes (including the ginkgolides A, B, C, and M), and bilabolide, a trilactonic sesquiterpene. The therapeutic effects of this herb have not been attributed to a single chemical constituent; rather, the medicinal benefits are due to the synergy between the various chemical constituents. The standardized extract of ginkgo must be taken consistently to be effective. A period of at least 12 weeks of use may be required before the beneficial results are evident.

Preparations

Ginkgo's active principles are dilute in the leaves. The herb must be processed to extract the active phytochemicals before it is medicinally useful. It would take an estimated 50 fresh ginkgo leaves to yield one standard dose of the extract. Dry extracts of the leaf, standardized to a potency of 24% flavone glycosides and 6% terpenes, are commercially available. A standard dose is 40 mg,

three times daily, though dosages as high as 240 mg daily are sometimes indicated.

Ginkgo extracts are widely used in Europe where they are sold in prescription form or over the counter as an approved drug. This is not the case in the United States, where ginkgo extract is sold as a food supplement in tablet and capsule form.

Precautions

Ginkgo is generally safe and non-toxic in therapeutic dosages. Exceeding a daily dose of 240 mg of the dried extract may result in restlessness, **diarrhea**, and mild gastrointestinal disorders. Those on anticoagulants should have their doctor adjust their dose or should avoid ginkgo in order to avoid over-thinning their blood and hemorrhaging. Ginkgo should be avoided two days before and one to two weeks after surgery to avoid bleeding complications.

Side effects

Severe allergic skin reactions, similar to those caused by poison ivy, have been reported after contact with the fruit pulp of ginkgo. Eating even a small amount of the fruit has caused severe gastrointestinal irritation in some persons. People with persistent headaches should stop taking ginkgo. Some patients on medications for nervous system disease should avoid ginkgo. It can interact with some other medicines, but clinical information is still emerging.

Interactions

The chemically active ginkgolides present in the extract, specifically the ginkgolide B component, act to reduce the clotting time of blood and may interact with antithrombotic medicines, including **aspirin**.

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Clare Hanrahan

Ginseng, Korean

Definition

Korean ginseng is one of the most widely used and acclaimed herbs in the world. Its scientific name is *Panax ginseng*, which is the species from which Chinese, Korean, red, and white ginseng are produced. Chinese and Korean ginseng are the same plant cultivated in different regions, and have slightly different properties according to Chinese medicine. White ginseng is simply the dried or powdered root of Korean ginseng, while red ginseng is the same root that is steamed and dried in heat or sunlight. Red ginseng is said to be slightly stronger and more stimulating in the body than white, according to Chinese herbalism.

Description

Korean ginseng has had a long and illustrious history as an herb for health, and has been used for thousands of years throughout the Orient as a medicine and tonic. Early Chinese medicine texts written in the first century A.D. mention ginseng, and ginseng has long been classified by Chinese medicine as a "superior" herb. This means it is said to promote longevity and vitality. Legends around the world have touted ginseng as an aphrodisiac and sexual tonic. Researchers have found a slight connection between sex drive and consuming ginseng, although a direct link and the mechanism of action are still researched and disputed.

Korean ginseng grows on moist, shaded mountainsides in China, Korea, and Russia. It is a perennial herb that reaches heights of two or more feet, and is distinguished by its dark green leaves and red clusters of berries. The root of the plant is the part valued for its medicinal properties. The root is long and slender and sometimes resembles the shape of the human body. Asian legends claim that this "man-root" has magical powers for those lucky enough to afford or find it, and the roots bearing the closest resemblance to the human body are still the most valuable ones. The word *ren shen*

in Chinese means roughly "the essence of the earth in the shape of a man."

Korean ginseng has historically been one of the most expensive of herbs, as it has been highly in demand in China and the Far East for centuries. Wars have been fought in Asia over lands where it grew wild. Wild Korean ginseng is now nearly extinct from many regions. Single roots of wild plants have recently been auctioned in China and New York City for sums approaching $50,000. Most of the world's supply of Korean ginseng is cultivated by farmers in Korea and China.

Because of the number of herbs sold under the name of ginseng, there can be some confusion for the consumer. Korean ginseng is a member of the *Araliaceae* family of plants, which also includes closely related American ginseng (*Panax quinquefolius*) and Siberian ginseng (*Eleutherococcus senticosus*). Both American and Siberian ginseng are considered by Chinese herbalists to be different herbs than Korean ginseng, and are said to have different effects and healing properties in the body. To add more confusion, there are eight herbs in Chinese medicine which are sometimes called ginseng, including black ginseng, purple ginseng, and prince's ginseng, some of which are not at all botanically related to *Panax ginseng*, so consumers should choose ginseng products with awareness.

Dried Korean ginseng. *(Custom Medical Stock Photo. Reproduced by permission.)*

Purpose

The word *panax* is formed from Greek roots meaning "cure-all," and *Panax ginseng* has long been considered to be one of the great healing and strengthening herbs in natural medicine. Ginseng is classified as an *adaptogen*, which is a substance that helps the body adapt to **stress** and balance itself without causing major side effects. Korean ginseng is used as a tonic for improving overall health and stamina, and Chinese herbalists particularly recommend it for the ill, weak, or elderly. Korean ginseng has long been asserted to have longevity, anti-senility, and memory improvement effects in the aged population. As it helps the body to adapt to stress, athletes may use ginseng as herbal support during rigorous training. Korean ginseng generally increases physical and mental energy. It is a good tonic for the adrenal glands, and is used by those suffering from exhaustion, burnout, or debilitation from chronic illness.

Traditional Chinese medicine also prescribes Korean ginseng to treat diabetes, and research has shown that it enhances the release of insulin from the pancreas and lowers blood sugar levels. Korean ginseng has been demonstrated to lower blood **cholesterol** levels. It has also been shown to have antioxidant effects and to increase immune system activity, which makes it a good herbal support for those suffering from **cancer** and **AIDS** and other chronic conditions that impair the immune system. Further uses of Korean ginseng in Chinese medicine include treatment of **impotence**, **asthma**, and digestive weakness.

Research

Scientists have isolated what they believe are the primary active ingredients in ginseng, chemicals termed *saponin triterpenoid glycosides*, or commonly called *ginsenocides*. There are nearly 30 ginsenocides in Korean ginseng. Much research on Korean ginseng has been conducted in China, but controlled human experiments with it have not been easily accessible to the English-speaking world. Recent research in China was summarized by Dr. C. Lui in the February 1992 issue of the *Journal of Ethnopharmacology*, where he wrote that *Panax ginseng* was found to contain 28 ginsenocides that "act on the central nervous system, cardiovascular system and endocrine secretion, promote immune function, and have effects on anti-aging and relieving stress."

To summarize other research, Korean ginseng has been shown in studies to have significant effects for the following.

- Physical improvement and performance enhancement for athletes: A study performed over three years in Germany showed athletes given ginseng had favorable improvement in several categories over a control group who took a placebo. Another 1982 study showed that athletes given ginseng had improved oxygen intake and faster recovery time than those given placebos.
- Mental performance improvement and mood enhancement: In general, studies show that ginseng enhances mental performance, learning time, and memory. One study of sixteen volunteers showed improvement on a wide variety of mental tests, including mathematics. Another study showed that those performing intricate and mentally demanding tasks improved performance when given Korean ginseng. Finally, a study has shown improvement of mood in **depression** sufferers with the use of ginseng.
- Antifatigue and antistress actions: Patients with chronic **fatigue** who were given ginseng showed a statistically significant improvement in physical tests and in mental attention and concentration, when compared with those given placebos.
- Lowering blood sugar: Animal studies have shown that ginseng can facilitate the release of insulin from the pancreas and increase the number of insulin receptors in the body.
- Antioxidant properties: Scientific analysis of ginseng has shown that it has antioxidant effects, similar to the effects of vitamins A, C, and E. Thus, ginseng could be beneficial in combating the negative effects of pollution, radiation, and aging.
- Cholesterol reduction: Some studies have shown that Korean ginseng reduces total cholesterol and increases levels of good cholesterol in the body.
- Anticancer effects and immune system stimulation: Several tests have shown that Korean ginseng increases immune cell activity in the body, including the activity of T-cells and lymphocytes, which are instrumental in fighting cancer and other immune system disorders like AIDS. A Korean study indicates that taking ginseng may reduce the chances of getting cancer, as a survey of more than 1,800 patients in a hospital in Seoul showed that those who did not have cancer were more likely to have taken ginseng regularly than those patients who had contracted cancer.
- Physical and mental improvement in the elderly: One study showed significant improvement in an elderly test group in visual and auditory reaction time and cardiopulmonary function when given controlled amounts of Korean ginseng. Korean ginseng has also been shown to alleviate symptoms of menopause.
- Impotence: Studies of human sexual function and Korean ginseng have been generally inconclusive, despite the wide acclaim of ginseng as a sexual tonic. Tests with lab animals and ginseng have shown some interesting results, indicating that Korean ginseng promotes the growth of male reproductive organs, increases sperm and testoterone levels, and increases sexual activity in laboratory animals. In general, scientists believe the link between ginseng and sex drive is due to ginseng's effect of strengthening overall health and balancing the hormonal system.

Preparations

Korean ginseng can be purchased as whole roots, powder, liquid extracts, and tea. Roots should be sliced and boiled in water for up to 45 minutes to extract all the beneficial nutrients. One to five grams of dry root is the recommended amount for one serving of tea. Herbalists recommend that ginseng not be boiled in metal pots, to protect its antioxidant properties. Ginseng should be taken between meals for best assimilation.

Some high quality Korean ginseng extracts and products are standardized to contain a specified amount of ginsenosides. The recommended dosage for extracts containing four to eight percent of ginsenosides is 100 mg once or twice daily. The recommended dosage for non-standardized root powder or extracts is 1–2 g daily, taken in capsules or as a tea. It is recommended that ginseng be taken in cycles and not continuously; after each week of taking ginseng, a few days without ingesting the herb should be observed. Likewise, Korean ginseng should not be taken longer than two months at a time, after which one month's rest period should be allowed before resuming the cycle again. Chinese herbalists recommend that ginseng be taken primarily in the autumn and winter months.

Precautions

Consumers should be aware of the different kinds of ginseng, and which type is best suited for them. Red Korean ginseng is considered stronger and more stimulating than white, wild ginseng is stronger than cultivated, and Korean ginseng is generally believed to be slightly stronger than Chinese. Furthermore, American and Siberian ginseng have slightly different properties than Korean ginseng, and consumers should make an informed choice as to which herb is best suited for them. Chinese herbalists do not recommend Korean ginseng for those people who have "heat" disorders in their bodies, such as ulcers, high blood pressure, tension headaches, and symptoms associated with high stress levels. Korean ginseng is generally not recommended for

those with symptoms of nervousness, mental imbalance, inflammation, or **fever**. Korean ginseng is not recommended for pregnant or lactating women, and women of childbearing age should use ginseng sparingly, as some studies imply that it can influence estrogen levels. Also, Chinese herbalists typically only prescribe ginseng to older people or the weak, as they believe that younger and stronger people do not benefit as much from it and ginseng is "wasted on the young."

Because of the number of and demand for ginseng products on the market, consumers should search for a reputable brand, preferably with a standardized percentage of active ingredients. To illustrate the mislabeling found with some ginseng products, *Consumer Reports* magazine analyzed ten nationally-distributed ginseng products in 1995. They found that several of them lacked significant amounts of ginsenocides, despite claims on the packaging to the contrary. Ginseng fraud has led the American Botanical Council, publisher of *HerbalGram* magazine, to initiate the Ginseng Evaluation Program, a comprehensive study and standardization of ginseng products on the American market. This study and its labeling standards are still under development, and consumers should watch for it.

Side effects

Korean ginseng acts as a slight stimulant in the body, and in some cases can cause overstimulation, irritability, nervousness and **insomnia**, although strong side effects are generally rare. Taking too high a dosage of ginseng, or taking ginseng for too long without a break, can cause *ginseng intoxication*, for which symptoms might include headaches, insomnia, seeing spots, **dizziness**, shortage of breath and gastrointestinal discomfort. Long term use may cause menstrual abnormalities and breast tenderness in some women.

Interactions

Those taking hormonal drugs should use ginseng with care. Ginseng should not be taken with **caffeine** or other stimulants as these may increase its stimulatory effects and cause uncomfortable side effects.

Resources

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KEY TERMS

Adaptogen—Substance that improves the body's ability to adapt to stress.

Ginsenocide—Active substances found in ginseng.

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PERIODICALS

HerbalGram (a quarterly journal of the American Botanical Council and Herb Research Foundation). P.O. Box 144345, Austin, TX 78714-4345. (800) 373-7105.

Douglas Dupler

Glaucoma

Definition

Glaucoma is a group of eye diseases characterized by damage to the optic nerve usually due to excessively high intraocular pressure (IOP).This increased pressure within the eye, if untreated can lead to optic nerve damage resulting in progressive, permanent vision loss, starting with unnoticeable blind spots at the edges of the field of vision, progressing to tunnel vision, and then to blindness.

Description

Between two to three million people in the United States have glaucoma, and 120,000 of those are legally blind as a result. It is the leading cause of preventable blindness in the United States and the most frequent cause of blindness in African-Americans, who are at about a three-fold higher risk of glaucoma than the rest of the population. The risk of glaucoma increases dramatically with age, but it can strike any age group, even newborn infants and fetuses.

Glaucoma can be classified into two categories: open-angle glaucoma and narrow-angle glaucoma. To understand what glaucoma is and what these terms mean, it is useful to understand eye structure.

Eyes are sphere-shaped. A tough, non-leaky protective sheath (the sclera) covers the entire eye, except for the clear cornea at the front and the optic nerve at the back. Light comes into the eye through the cornea, then

passes through the lens, which focuses it onto the retina (the innermost surface at the back of the eye). The rods and cones of the retina transform the light energy into electrical messages, which are transmitted to the brain by the bundle of nerves known as the optic nerve.

The iris, the colored part of the eye shaped like a round picture frame, is between the dome-shaped cornea and the lens. It controls the amount of light that enters the eye by opening and closing its central hole (pupil) like the diaphragm in a camera. The iris, cornea, and lens are bathed in a liquid called the aqueous humor, which is somewhat similar to plasma. This liquid is continually produced by nearby ciliary tissues and moved out of the eye into the bloodstream by a system of drainage canals (called the trabecular meshwork). The drainage area is located in front of the iris, in the angle formed between the iris and the point at which the iris appears to meet the inside of the cornea.

Glaucoma occurs if the aqueous humor is not removed rapidly enough or if it is made too rapidly, causing pressure to build-up. The high pressure distorts the shape of the optic nerve and destroys the nerve. Destroyed nerve cells result in blind spots in places where the image from the retina is not being transmitted to the brain.

Open-angle glaucoma accounts for over 90% of all cases. It is called "open-angle" because the angle between the iris and the cornea is open, allowing drainage of the aqueous humor. It is usually chronic and progresses slowly. In narrow-angle glaucoma, the angle where aqueous fluid drainage occurs is narrow, and therefore may drain slowly or may be at risk of becoming closed. A closed-angle glaucoma attack is usually acute, occurring when the drainage area is blocked. This can occur, for example, if the iris and lens suddenly adhere to each other and the iris is pushed forward. In patients with very narrow angles, this can occur when the eyes dilate (e.g., when entering a dark room, or if taking certain medications).

Congenital glaucoma occurs in babies and is the result of incomplete development of the eye's drainage canals during embryonic development. Microsurgery can often correct the defects or they can be treated with a combination of medicine and surgery.

One rare form of open-angle glaucoma, normal tension glaucoma, is different. People with normal-tension glaucoma have optic nerve damage in the presence of normal IOP. As of 1998, the mechanism of this disease is a mystery but is generally detected after an examination of the optic nerve. Those at higher risk for this form of glaucoma are people with a familial history of normal tension glaucoma, people of Japanese ancestory, and people with a history of systemic heart disease such as irregular heart rhythm.

Glaucoma is also a secondary condition of over 60 widely diverse diseases and can also result from injury, inflammation, tumor, or in advanced cases of cataract or diabetes.

Causes and symptoms

Causes

The cause of vision loss in all forms of glaucoma is optic nerve damage. There are many underlying causes and forms of glaucoma. Most causes of glaucoma are not known, but it is clear that a number of different processes are involved, and a malfunction in any one of them could cause glaucoma. For example, trauma to the eye could result in the angle becoming blocked, or, as a person ages, the lens becomes larger and may push the iris forward. The cause of optic nerve damage in normal-tension glaucoma is also unknown, but there is speculation that the optic nerves of these patients are susceptible to damage at lower pressures than what is usually considered to be abnormally high.

It is probable that most glaucoma is inherited. At least ten defective genes that cause glaucoma have been identified.

Symptoms

At first, chronic open-angle glaucoma is without noticeable symptoms. The pressure build-up is gradual and there is no discomfort. Moreover, the vision loss is too gradual to be noticed and each eye fills-in the image where its partner has a blind spot. However, if it is not treated, vision loss becomes evident, and the condition can be very painful.

On the other hand, acute closed-angle glaucoma is obvious from the beginning of an attack. The symptoms are, blurred vision, severe **pain**, sensitivity to light, nausea, and halos around lights. The normally clear corneas may be hazy. This is an ocular emergency and needs to be treated immediately.

Similarly, congenital glaucoma is evident at birth. Symptoms are bulging eyes, cloudy corneas, excessive tearing, and sensitivity to light.

Diagnosis

Intraocular pressure, visual field defects, the angle in the eye where the iris meets the cornea, and the appearance of the optic nerve are all considered in the diagnosis of glaucoma. IOP is measured with an instrument known as a tonometer. One type of tonometer involves numbing the eye with an eyedrop that has a yellow coloring in it and touching the cornea with a small probe. This quick

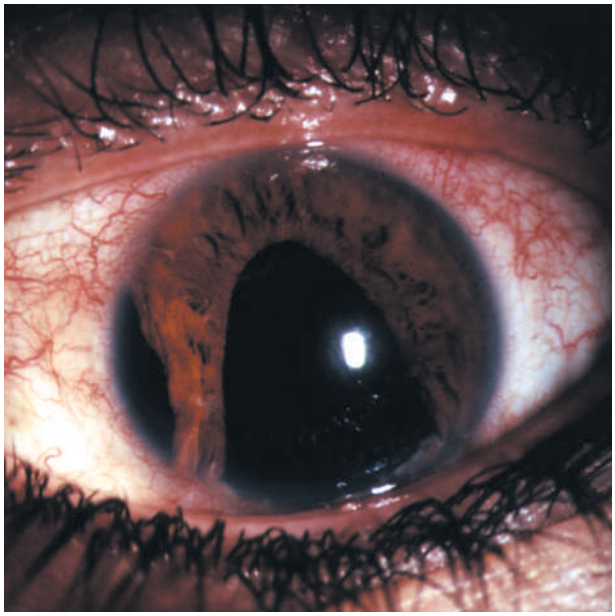
test is a routine part of an **eye examination** and is usually included without extra charge in the cost of a visit to an ophthalmologist or optometrist.

Ophthalmoscopes, hand-held instruments with a light source, are used to detect optic nerve damage by looking through the pupil. The optic nerve is examined for changes; the remainder of the back of the eye can be examined as well. Other types of lenses that can be used to examine the back of the eye may also be used. A slit lamp will allow the doctor to examine the front of the eye (i.e., cornea, iris, and lens).

Visual field tests (perimetry) can detect blind spots in a patient's field of vision before the patient is aware of them. Certain defects may indicate glaucoma.

Another test, gonioscopy, can distinguish between narrow-angle and open-angle glaucoma. A gonioscope, which is a hand-held contact lens with a mirror, allows visualization of the angle between the iris and the cornea.

Intraocular pressure can vary throughout the day. For that reason, the doctor may have a patient return for several visits to measure the IOP at different times of the day.



A close-up view of an inflamed eye with acute glaucoma and an irregularly enlarged pupil. *(Custom Medical Stock Photo. Reproduced by permission.)*

Treatment

Medications

When glaucoma is diagnosed, drugs, typically given as eye drops, are usually tried before surgery. Several classes of medications are effective at lowering IOP and thus preventing optic nerve damage in chronic and neonatal glaucoma. **Beta blockers**, like Timoptic; carbonic anhydrase inhibitors, like acetazolamide; and alpha-2 agonists, such as Alphagan, inhibit the production of aqueous humor. Miotics, like pilocarpine, and prostaglandin analogues, like Xalatan, increase the outflow of aqueous humor. Cosopt is the first eyedrop that is a combined beta blocker (Timoptic) and carbonic anhydrase inhibitor and may be helpful for patients required to take more than one glaucoma medication each day. The Food and drug administration recently approved two new prostaglandin-related drugs, Travatan and Lumigan on March 16, 2001. These drugs work by decreasing intraocular pressure and may be considered for people with glaucoma that are unable to tolerate other IOP lowering drugs. Additionally, Travatan may work best for African-Americans with glaucoma (a population at high risk for glaucoma).

It is important for patients to tell their doctors about any conditions they have or medications they are taking. Certain drugs used to treat glaucoma should not be prescribed for patients with pre-existing conditions. All of these drugs mentioned above have side effects, some of which are rare but serious and potentially life-threatening, so patients taking them should be monitored closely, especially for cardiovascular, pulmonary, and behavioral symptoms. Different medications lower IOP by different amounts, and a combination of medications may be necessary. It is important that patients take their medications and that their regimens are monitored regularly, to be sure that the IOP is lowered sufficiently. IOP should be measured three to four times per year.

As of 1998, normal-tension glaucoma is treated in the same way as chronic high-intraocular-pressure glaucoma. This reduces IOP to less-than-normal levels, on the theory that overly susceptible optic nerves are less likely to be damaged at lower pressures. Research underway may point to better treatments for this form of glaucoma.

Attacks of acute closed-angle glaucoma are medical emergencies. IOP is rapidly lowered by successive deployment of acetazolamide, hyperosmotic agents, a topical beta-blocker, and pilocarpine. Epinephrine should not be used because it exacerbates angle closure.

Surgery

There are several types of **laser surgery** used to treat glaucoma. Laser peripheral iridotomy makes an opening in the iris allowing the fluid to drain, argon laser trabeculoplasty is aimed at the fluid channel opening to help the drainage system function and laser cyclophotocoagulation is used to decrease the amount of fluid made. Microsurgery, also called "filtering surgery" has been used in many different types of glaucoma. A new opening is cre-

KEY TERMS

Agonist—A drug that mimics one of the body's own molecules.

Alpha-2 agonist (alpha-2 adrenergic receptor agonist)—A class of drugs that bind to and stimulate alpha-2 adrenergic receptors, causing responses similar to those of adrenaline and noradrenaline. They inhibit aqueous humor production and a have a wide variety of effects, including dry mouth, fatigue, and drowsiness.

Aqueous humor—A transparent liquid, contained within the eye, that is composed of water, sugars, vitamins, proteins, and other nutrients.

Betablocker (beta-adrenergic blocker)—A class of drugs that bind beta-adrenergic receptors and thereby decrease the ability of the body's own natural epinephrine to bind to those receptors, leading to inhibition of various processes in the body's sympathetic system. Betablockers can slow the heart rate, constrict airways in the lungs, lower blood pressure, and reduce aqueous secretion by ciliary tissues in the eye.

Carbonic anhydrase inhibitor—A class of diuretic drugs that inhibit the enzyme carbonic anhydrase, an enzyme involved in producing bicarbonate, which is required for aqueous humor production by the ciliary tissues in the eye. Thus, inhibitors of this enzyme inhibit aqueous humor production. Some side effects are urinary frequency, kidney stones, loss of the sense of taste, depression, and anemia.

Cornea—Clear, bowl-shaped structure at the front of the eye. It is located in front of the colored part of the eye (iris). The cornea lets light into the eye and partially focuses it.

Gonioscope—An instrument used to examine the trabecular meshwork; consists of a magnifier and a lens equipped with mirrors, which sits on the patient's cornea.

Hyperosmotic drugs—Refers to a class of drugs for glaucoma that increase the osmotic pressure in the blood, which then pulls water from the eye into the blood.

Iris—The colored part of the eye just behind the cornea and in front of the lens that controls the amount of light sent to the retina.

Lens (the crystalline lens)—A transparent structure in the eye that focuses light onto the retina.

Laser cyclophotocoagulation—A procedure used for severe glaucoma in patients who have not responded well to previous treatments. The laser partially destroys the tissues that make the fluid of the eye.

Laser peripheral iridotomy—This procedure makes a drainage hole in the iris allowing the fluid to drain from the eye

Laser Trabeculoplasty—In this procedure the laser attempts to open the normal drainage channels of the eye so fluid can drain more effectively.

Miotic—A drug that causes pupils to contract.

Ophthalmoscope—An instrument, with special lighting, designed to view structures in the back of the eye.

Optic nerve—The nerve that carries visual messages from the retina to the brain.

Prostaglandin—A group of molecules that exert local effects on a variety of processes including fluid balance, blood flow, and gastrointestinal function.

Prostaglandin analogue—A class of drugs that are similar in structure and function to prostaglandin.

Retina—The inner, light-sensitive layer of the eye containing rods and cones.

Sclera—The tough, fibrous, white outer protective covering that surrounds the eye.

Tonometry—The measurement of pressure.

Trabecular meshwork—A sponge-like tissue located near the cornea and iris that functions to drain the aqueous humor from the eye into the blood.

ated in the sclera allowing the intraocular fluid to bypass the blocked drainage canals. The tissue over this opening forms a little blister or bleb on the clear conjuctiva that Doctors monitor ensuring that fluid is draining. These surgeries are usually successful, but the effects often last less than a year. Nevertheless, they are an effective treatment for patients whose IOP is not sufficiently lowered by drugs and for those who can't tolerate the drugs. Because all surgeries have risks, patients should speak to their doctors about the procedure being performed.

Alternative treatment

Vitamin C, vitamin B_1 (thiamine), chromium, zinc,bilberry and rutin may reduce IOP.

There is evidence that medicinal marijuana lowers IOP, too. However, marijuana has serious side effects and contains carcinogens, and any IOP-lowering medication must be taken continually to avoid optic nerve damage. Although the Food and Drug Administration (FDA) and National Institutes of Health (NIH) currently recommend against treating glaucoma with marijuana, they are supporting research to learn more about it and to determine the feasibility of separating the components that lower IOP from components that produce side effects and carcinogens.

Any glaucoma patient using alternative methods to attempt to prevent optic nerve damage should also be under the care of a traditionally trained ophthalmologist or optometrist who is licensed to treat glaucoma, so that IOP and optic nerve damage can be monitored.

Prognosis

About half of the people stricken by glaucoma are not aware of it. For them, the prognosis is not good, and many of them will become blind. Sight lost due to glaucoma cannot be restored. On the other hand, the prognosis for treated glaucoma is excellent.

Prevention

Because glaucoma may not initially result in symptoms, the best form of prevention is to have regular eye exams.

Patients with narrow angles should avoid certain medications (even over-the-counter medications, such as some cold or allergy medications).Any person who is glaucoma-susceptible (i.e. narrow angles and borderline IOPs) should read the warning labels on over-the-counter medicines and inform their physicians of products they are considering taking.Steroids may also raise IOP, so patients may need to be monitored more frequently if it is necessary to use steroids for another medical condition.

Not enough is known about the underlying mechanisms of glaucoma to prevent the disease itself. However, prevention of optic nerve damage from glaucoma is essential and can be effectively accomplished when the condition is diagnosed and treated. As more is learned about the genes that cause glaucoma, it will become possible to test DNA and identify potential glaucoma victims, so they can be treated even before their IOP becomes elevated.

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American Academy of Ophthalmology. P.O. Box 7424, San Francisco, CA 94120-7424. (415) 561-8500. <http://www.eyenet.org/aao_index.html>.

Glaucoma Research Foundation. 200 Pine Street, suite 200 San Francisco,CA 94104. (415) 986-3162, (800) 826-6693. info@glaucoma.org. <http://www.glaucoma.org/.

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

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Bonny McClain

Glaucoma surgery *see* **Trabeculectomy**

Glioma *see* **Brain tumor**

Glipizide *see* **Antidiabetic drugs**

Glomerulonephritis

Definition

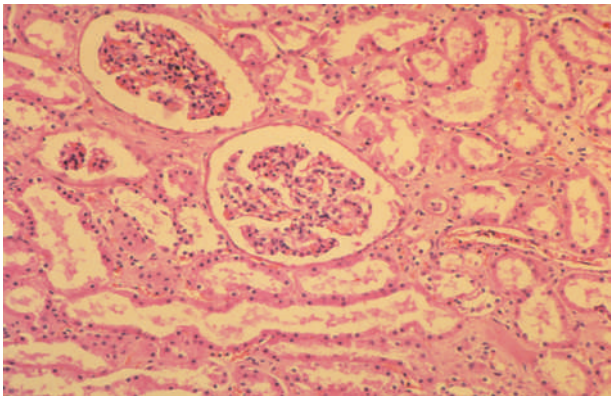
Acute glomerulonephritis is an inflammatory disease of both kidneys predominantly affecting children from ages two to 12. Chronic glomerulonephritis can develop over a period of 10–20 years and is most often associated with other systemic disease, including diabetes, **malaria**, hepatitis, or **systemic lupus erythematosus**.

Description

Acute glomerulonephritis is an inflammation of the glomeruli, bundles of tiny vessels inside the kidneys. The damaged glomeruli cannot effectively filter waste products and excess water from the bloodstream to make urine. The kidneys appear enlarged, fatty, and congested.

Causes and symptoms

Acute glomerulonephritis most often follows a streptococcal infection of the throat or skin. In children,



A close-up view of glomerulonephritis affecting the kidney. *(Custom Medical Stock Photo. Reproduced by permission.)*

it is most often associated with an upper respiratory infection, **tonsillitis**, or **scarlet fever**. Kidney symptoms usually begin two to three weeks after the initial infection. Exposure to certain paints, glue or other organic solvents may also be the causative agent. It is thought that the kidney is damaged with exposure to the toxins that are excreted into the urine.

Mild glomerulonephritis may produce no symptoms, and diagnosis is made with laboratory studies of the urine and blood. Individuals with more severe cases of the disease may exhibit:

- fatigue
- nausea and vomiting
- shortness of breath
- disturbed vision
- high blood pressure
- swelling, especially noted in the face, hands, feet, and ankles
- blood and protein in the urine, resulting in a smoky or slightly red appearance

The individual with chronic glomerulonephritis may discover their condition with a routine physical exam revealing high blood pressure, or an eye exam showing vascular or hemorrhagic changes. The kidneys may be reduced to as little as one-fifth their normal size, consisting largely of fibrous tissues.

Diagnosis

Diagnosis of glomerulonephritis is established based on medical history, combined with laboratory studies. A "dipstick" test of urine will reveal increased protein levels. A 24 hour urine collection allows measurement of the excretion of proteins and creatinine. Creatinine clearance from the bloodstream by the kidneys is considered an index of the glomerular filtration rate. Blood studies may reveal a low **blood count**, and may also be checked for the presence of a streptococcal antibody titer(a sophisticated blood test indicating presence of streptococcal infection). A **kidney biopsy** may also be performed, using ultrasound to guide the needle for obtaining the specimen.

Treatment

The main objectives in the treatment of acute glomerulonephritis are to:

- decrease the damage to the glomeruli
- decrease the metabolic demands on the kidneys
- improve kidney function

Bedrest helps in maintaining adequate blood flow to the kidney. If residual infection is suspected, antibiotic therapy may be needed. In the presence of fluid overload, **diuretics** may be used to increase output with urination. Iron and vitamin supplements may be ordered if anemia develops, and antihypertensives, if high blood pressure accompanies the illness. In order to rest the kidney during the acute phase, decreased sodium and protein intake may be recommended. The amount of protein allowed is dependent upon the amount lost in the urine, and the requirements of the individual patient. Sodium limitations depend on the amount of **edema** present. Fluid restrictions are adjusted according to the patient's urinary output and body weight.

An accurate daily record of the patient's weight, fluid intake and urinary output assist in estimating kidney function. The patient must be watched for signs of complications and recurrent infection. As edema is reduced and the urine becomes free of protein and red blood cells, the patient is allowed to increase activity. A woman who has had glomerulonephritis requires special medical attention during **pregnancy**.

Prognosis

In acute glomerulonephritis, symptoms usually subside in two weeks to several months, with 90% of children recovering without complications and adults recovering more slowly. Chronic glomerulonephritis is a disease that tends to progress slowly, so that there are no symptoms until the kidneys can no longer function. The resultant renal failure may require dialysis or kidney transplant.

Prevention

Prevention of glomerulonephritis is best accomplished by avoiding upper respiratory infections, as well

KEY TERMS

Dialysis—A process of filtering and removing waste products from the bloodstream. Two main types are hemodialysis and peritoneal dialysis. In hemodialysis, the blood flows out of the body into a machine that filters out the waste products and routes the cleansed blood back into the body. In peritoneal dialysis, the cleansing occurs inside the body. Dialysis fluid is injected into the peritoneal cavity and wastes are filtered through the peritoneum, the thin membrane that surrounds the abdominal organs.

Glomeruli—Groups of tiny blood vessels with very thin walls that function as filters in the kidney. Glomeruli become inflamed and are destroyed in the disease process of glomerulonephritis.

Renal—Relating to the kidneys, from the Latin word *renes*.

as other acute and chronic infections, especially those of a streptococcal origin. Cultures of the infection site, usually the throat, should be obtained and antibiotic sensibility of the offending organism determined. Prompt medical assessment for necessary antibiotic therapy should be sought when infection is suspected. The use of prophylactic immunizations is recommended as appropriate.

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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>.

National Kidney Foundation and Urologic Diseases Information Clearinghouse. 3 Information Way, Bethesda, MD 20892-3580. (800) 891-5390. <http://www.niddk.nih.gov/health/kidney/nkudic.htm>.

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Kathleen D. Wright, RN

Glossopharyngeal neuralgia *see* **Neuralgia**

Glucose-6-phosphate dehydrogenase deficiency

Definition

Glucose-6-phosphate dehydrogenase deficiency is an inherited condition caused by a defect or defects in the gene that codes for the enzyme, glucose-6-phosphate dehydrogenase (G6PD). It can cause **hemolytic anemia**, varying in severity from life-long anemia, to rare bouts of anemia to total unawareness of the condition. The episodes of hemolytic anemia are usually triggered by oxidants, infection, or by eating fava beans.

Description

G6PD deficiency is the most common enzyme deficiency in the world, with about 400 million people living with it. It is most prevalent in people of African, Mediterranean, and Asian ancestry. The incidence in different populations varies from zero in South American Indians to less than 0.1% of Northern Europeans to about 50% of Kurdish males. In the United States, it is most common among African American males; about 11 to 14% are G6PD-deficient.

G6PD deficiency is a recessive sex-linked trait. Thus, males have only one copy of the G6PD gene, but females have two copies. Recessive genes are masked in the presence of a gene that encodes normal G6PD. Accordingly, females with one copy of the gene for G6PD deficiency are usually normal, while males with one copy have the trait.

G6PD is present in all human cells but is particularly important to red blood cells. It is required to make NADPH in red blood cells but not in other cells. It is also required to make glutathione. Glutathione and NADPH both help protect red blood cells against oxidative damage. Thus, when G6PD is defective, oxidative damage to red blood cells readily occurs, and they break open as a result. This event is called hemolysis, and multiple hemolyses in a short time span constitute an episode of hemolytic anemia.

As of 1998, there are almost 100 different known forms of G6PD enzyme molecules encoded by defective

KEY TERMS

Bilirubin—A breakdown product derived from hemoglobin; removed from the blood by the liver.

Enzyme—A protein catalyst; one of the two kinds of biological catalysts, which are exceedingly specific; each different enzyme only catalyzes one or two specific reactions.

Enzyme activity—A measure of the ability of an enzyme to catalyze a specific reaction.

Glutathione—A molecule that acts as a co-enzyme in cellular oxidation-reduction reactions.

Hemolysis—Lysis (opening) of red blood cells, with concomitant leakage of cell contents from the cells.

Hemolytic anemia—Anemia due to hemolysis.

Jaundice—Yellowish skin color due to liver disease.

Neonatal—Describes babies just after they are born.

Recessive trait—An inherited trait that is outwardly obvious only when two copies of the gene for that trait are present—as opposed to a dominant trait where one copy of the gene for the dominant trait is sufficient to display the trait. The recessive condition is said to be masked by the presence of the dominant gene when both are present; i.e., the recessive condition is seen only in the absence of the dominant gene.

Sex-linked—Refers to genes or traits carried on one of the sex chromosomes, usually the X.

X chromosome—One of the two types of sex chromosomes, present twice in female cells and once in male cells.

G6PD genes, yet not one of them is completely inactive. This suggests that G6PD is indispensable. Many G6PD defective enzymes are deficient in their stability rather than their initial ability to function. Since red blood cells lack nuclei, they, unlike other cells, cannot synthesize new enzyme molecules to replace defective ones. Hence, we expect young red blood cells to have new, functional G6PD and older cells to have non-functioning G6PD. This explains why episodes of hemolytic anemia are frequently self-limiting; new red blood cells are generated with enzymes able to afford protection from oxidation.

The geographic distribution of G6PD deficiency, allowing for migration, coincides with the geographic distribution of **malaria**. This fact and survival statistics suggest that G6PD deficiency protects against malaria.

Glucose-6-phosphate dehydrogenase deficiency is also known as G6PD deficiency, favism, and primaquine sensitivity.

Causes and symptoms

Causes

G6PD deficiency is caused by one copy of a defective G6PD gene in males or two copies of a defective G6PD gene in females. Hemolytic anemic attacks can be caused by oxidants, infection, and or by eating fava beans.

Symptoms

The most significant consequence of this disorder is hemolytic anemia, which is usually episodic, but the vast majority of people with G6PD deficiency have no symptoms.

The many different forms of G6PD deficiency have been divided into five classes according to severity.

- Class 1—enzyme deficiency with chronic hemolytic anemia
- Class 2—severe enzyme deficiency with less than 10% of normal activity
- Class 3—moderate to mild enzyme deficiency with 10–60% of normal activity
- Class 4—very mild or no enzyme deficiency
- Class 5—increased enzyme activity Fortunately, only a small number of people fall into Class 1.

The major symptoms of hemolytic anemia are **jaundice**, dark urine, abdominal **pain**, back pain, lowered red blood cell count, and elevated bilirubin. People who suffer from severe and chronic forms of G6PD deficiency in addition may have **gallstones**, enlarged spleens, defective white blood cells, and **cataracts**.

Attacks of hemolytic anemia are serious for infants. Brain damage and **death** are possible but preventable outcomes. Newborns with G6PD deficiency are about 1.5 times as likely to get **neonatal jaundice** than newborns without G6PD deficiency.

Diagnosis

Blood tests can detect G6PD deficiency, either by measuring the G6PD enzyme activity between episodes

or by measuring bilirubin during an episode. Such tests cost about $50.00. Family histories are helpful, too.

Treatment

In a typical attack of hemolytic anemia, no treatment is needed; the patient will recover in about eight days. However, blood transfusions are necessary in severe cases. Recent success treating elevated bilirubin in newborns by exposing them to bright light has decreased the need for neonatal transfusions.

Alternative treatment

Vitamin E and **folic acid** (both anti-oxidants) may help decrease hemolysis in G6PD-deficient individuals.

Prognosis

The prognosis for almost everyone with G6PD deficiency is excellent. Large studies have shown that G6PD-deficient individuals do not acquire any illnesses more frequently than the rest of the population. In fact the opposite may be true for some diseases like ischemic heart disease and cerebrovascular disease.

Prevention

Most episodes of hemolytic anemia can be prevented by avoiding fava beans, oxidant drugs, and oxidant chemicals. All of the following oxidants can trigger attacks: acetanilid, dapsone, doxorubicin, furazolidone, methylene blue, nalidixic acid, napthalene, niridazole, nitrofurantoin, phenazopyridine, phenylhydrazine, primaquine, quinidine, quinine, sulfacetamide, sulfamethoxazole, sulfonamide, sulfapyridine, thiazolesulfone, toluidine blue, and trinitrotoluene. Since infections also trigger hemolytic attacks and have other dire consequences, sometimes it is advisable to use one of the listed drugs.

It is especially important to screen newborns who are likely to have G6PD deficiency to ensure that G6PD-deficient babies won't be subjected to any of the triggers of hemolytic anemia. Pregnant women, especially in areas where G6PD deficiency is prevalent, should avoid eating fava beans.

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Lorraine Lica, PhD

Glucosylcerebroside lipidosis *see* **Gaucher disease**

Gluten enteropathy *see* **Celiac disease**

Glyburide *see* **Antidiabetic drugs**

Glycogen storage diseases

Definition

Glycogen serves as the primary fuel reserve for the body's energy needs. Glycogen storage diseases, also known as glycogenoses, are genetically linked metabolic disorders that involve the enzymes regulating glycogen metabolism. Symptoms vary by the glycogen storage disease (GSD) type and can include muscle cramps and wasting, enlarged liver, and low blood sugar. Disruption of glycogen metabolism also affects other biochemical pathways as the body seeks alternative fuel sources. Accumulation of abnormal metabolic by-products can damage the kidneys and other organs. GSD can be fatal, but the risk hinges on the type of GSD.

Description

Most of the body's cells rely on glucose as an energy source. Glucose levels in the blood are very stringently controlled within a range or 70–100 mg/dL, primarily by hormones such as insulin and glucagon. Immediately after a meal, blood glucose levels rise and exceed the body's immediate energy requirements. In a process analogous to putting money in the bank, the body bundles up the extra glucose and stores it as glycogen in the liver and muscles. Later, as the blood glucose levels begin to dip, the body makes a withdrawal from its glycogen savings.

The system for glycogen metabolism relies on a complex system of enzymes. These enzymes are responsible for creating glycogen from glucose, transporting the glycogen to and from storage areas within cells, and extracting glucose from the glycogen as needed. Both creating and tearing down the glycogen macromolecule are multistep processes requiring a different enzyme at each step. If one of these enzymes is defective and fails to complete its step, the process halts. Such enzyme defects are the underlying cause of GSDs.

The enzyme defect arises from an error in its gene. Since the error is in the genetic code, GSDs can be passed down from generation-to-generation. However, all but one GSD are linked to autosomal genes, which means a person inherits one copy of the gene from each parent. Following a Mendelian inheritance pattern, the normal gene is dominant and the defective gene is recessive. As long as a child receives at least one normal gene, there is no risk for a GSD. GSDs appear only if a person inherits a defective gene from both parents.

The most common forms of GSD are Types I, II, III, and IV, which may account for more than 90% of all cases. The most common form is Type I, or von Gierke's disease, which occurs in one out of every 100,000 births. Other forms, such as Types VI and IX, are so rare that reliable statistics are not available. The overall frequency of all forms of glycogen storage disease is approximately one in 20,000–25,000 live births.

Causes and symptoms

GSD symptoms depend on the enzyme affected. Since glycogen storage occurs mainly in muscles and the liver, those sites display the most prominent symptoms.

There are at least 10 different types of GSDs which are classified according to the enzyme affected:

- Type Ia, or von Gierke's disease, is caused by glucose-6-phosphatase deficiency in the liver, kidney, and small intestine. The last step in glycogenolysis, the breaking down of glycogen to glucose, is the transformation of glucose-6-phosphate to glucose. In GSD I, that step does not occur. As a result, the liver is clogged with excess glycogen and becomes enlarged and fatty. Other symptoms include low blood sugar and elevated levels of lactate, lipids, and uric acid in the blood. Growth is impaired, **puberty** is often delayed, and bones may be weakened by **osteoporosis**. Blood platelets are also affected and frequent nosebleeds and easy bruising are common. Primary symptoms improve with age, but after age 20–30, liver tumors, **liver cancer**, chronic renal disease, and **gout** may appear.
- Type Ib is caused by glucose-6-phosphatase translocase deficiency. In order to carry out the final step of glycogenolysis, glucose-6-phosphate has to be transported into a cell's endoplasmic reticulum. If translocase, the enzyme responsible for that movement, is missing or defective, the same symptoms occur as in Type Ia. Additionally, the immune system is weakened and victims are susceptible to bacterial infections, such as **pneumonia**, mouth and gum infections, and inflammatory bowel disease. Types Ic and Id are also caused by defects in the translocase system.
- Type II, or Pompe's disease or acid maltase deficiency, is caused by lysosomal alpha-D-glucosidase deficiency in skeletal and heart muscles. GSD II is subdivided according to the age of onset. In the infantile form, infants seem normal at birth, but within a few months they develop muscle weakness, trouble breathing, and an enlarged heart. Cardiac failure and **death** usually occur before age 2, despite medical treatment. The juvenile and adult forms of GSD II affect mainly the skeletal muscles in the body's limbs and torso. Unlike the infantile form, treatment can extend life, but there is no cure. **Respiratory failure** is the primary cause of death.
- Type III, or Cori's disease, is caused by glycogen debrancher enzyme deficiency in the liver, muscles, and some blood cells, such as leukocytes and erythrocytes. About 15% of GSD III cases only involve the liver. The glycogen molecule is not a simple straight chain of linked glucose molecules, but rather an intricate network of short chains that branch off from one another. In glycogenolysis, a particular enzyme is required to unlink the branch points. When that enzyme fails, symptoms similar to GSD I occur; in childhood, it may be difficult to distinguish the two GSDs by symptoms alone. In addition to the low blood sugar, retarded growth, and enlarged liver causing a swollen abdomen, GSD III also causes muscles prone to wasting, an enlarged heart, and heightened levels of lipids in the blood. The muscle wasting increases with age, but the other symptoms become less severe.
- Type IV, or Andersen's disease, is caused by glycogen brancher enzyme deficiency in the liver, brain, heart, skeletal muscles, and skin fibroblasts. The glycogen constructed in GSD IV is abnormal and insoluble. As it accumulates in the cells, cell death leads to organ damage. Infants born with GSD IV appear normal at birth, but are diagnosed with enlarged livers and **failure to thrive** within their first year. Infants who survive beyond their first birthday develop **cirrhosis** of the liver by age 3–5 and die as a result of chronic liver failure.
- Type V, or McArdle's disease, is caused by glycogen phosphorylase deficiency in skeletal muscles. Under normal circumstances, muscles cells rely on oxidation of fatty acids during rest or light activity. More demanding activity requires that they draw on their glycogen stockpile. In GSD V, this form of glycogenolysis is disabled and glucose is not available. The main symptoms are muscle weakness and cramping brought on by **exercise**, as well as burgundy-colored urine after exercise due to myoglobin (a breakdown product of muscle) in the urine.
- Type VI, or Hers' disease, is caused by liver phosphorylase deficiency, which blocks the first step of

glycogenolysis. In contrast to other GSDs, Type VI seems to be linked to the X chromosome. Low blood sugar is one of the key symptoms, but it is not as severe as in some other forms of GSD. An enlarged liver and mildly retarded growth also occur.

- Type VII, or Tarui's disease, is caused by muscle phosphofructokinase deficiency. Although glucose may be available as a fuel in muscles, the cells cannot metabolize it. Therefore, abnormally high levels of glycogen are stockpiled in the muscle cells. The symptoms are similar to GSD V, but also include anemia and increased levels of uric acid.
- Types VIII and XI are caused by defects of enzymes in the liver phosphorylase activating-deactivating cascade and have symptoms similar to GSD VI.
- Type IX is caused by liver glycogen phosphorylase kinase deficiency and, symptom-wise, is very similar to GSD VI. The main differences are that the symptoms may not be as severe and may also include exercise-related problems in the muscles, such as **pain** and cramps. The symptoms abate after puberty with proper treatment. Most cases of GSD IX are linked to the X chromosome and therefore affect males.
- Type X is caused by a defect in the cyclic adenosine monophosphate-dependent (AMP) kinase enzyme and presents symptoms similar to GSDs VI and IX.

Diagnosis

Diagnosis usually occurs in infancy or childhood, although some milder types of GSD go unnoticed well into adulthood and old age. It is even conceivable that some of the milder GSDs are never diagnosed.

The four major symptoms that typically lead a doctor to suspect GSDs are low blood sugar, enlarged liver, retarded growth, and an abnormal blood biochemistry profile. A definitive diagnosis is obtained by biopsy of the affected organ or organs. The biopsy sample is tested for its glycogen content and assayed for enzyme activity. There are DNA-based techniques for diagnosing some GSDs from more easily available samples, such as blood or skin. These DNA techniques can also be used for prenatal testing.

Treatment

Some GSD types cannot be treated, while others are relatively easy to control through symptom management. In more severe cases, receiving an organ transplant is the only option. In the most severe cases, there are no available treatments and the victim dies within the first few years of life.

Of the treatable types of GSD, many are treated by manipulating the diet. The key to managing GSD I is to maintain consistent levels of blood glucose through a combination of nocturnal intragastric feeding (usually for infants and children), frequent high-carbohydrate meals during the day, and regular oral doses of cornstarch (people over age 2). Juvenile and adult forms of GSD II can be managed somewhat by a high protein diet, which also helps in cases of GSD III, GSD VI, and GSD IX. GSD V and GSD VII can also be managed with a high protein diet and by avoiding strenuous exercise.

For GSD cases in which dietary therapy is ineffective, organ transplantation may be the only viable alternative. Liver transplants have been effective in reversing the symptoms of GSD IV.

Advances in genetic therapy offer hope for effective treatment in the future. This therapy involves using viruses to deliver a correct form of the gene to affected cells. Another potential therapy utilizes transgenic animals to produce correct copies of the defective enzyme in their milk. In late 1997, a Dutch pharmaceutical company, Pharming Health Care Products, began clinical trials to treat GSD II with human alpha-glucosidase derived from the milk of transgenic rabbits. Researchers at Duke University in North Carolina are also focusing on a treatment for Pompe's disease and, aided by Synpac Pharmaceuticals Limited of the United Kingdom, plan to begin clinical trials of a recombinant form of the enzyme in 1998.

Prognosis

People with well-managed, treatable types of GSD can lead long, relatively normal lives. This goal is accomplished with the milder types of GSD, such as Types VI, IX, and X. As the GSD type becomes more severe, a greater level of vigilance against infections and other complications is required. Given current treatment options, complications such as liver disease, **heart failure**, and respiratory failure may not be warded-off indefinitely. Quality of life and life expectancy are substantially decreased.

Prevention

Because GSD is an inherited condition, it is not preventable. If both parents carry the defective gene, there is a one-in-four chance that their offspring will inherit the disorder. Other children may be carriers or they may miss inheriting the gene altogether.

Through chorionic villi sampling and **amniocentesis**, the disorder can be detected prior to birth. Some types of GSD can be detected even before conception occurs, if both parents are tested for the presence of the defective

KEY TERMS

Amniocentesis—A medical test done during pregnancy in which a small sample of the amniotic fluid is taken from around the fetus. The fluid contains fetal cells that can be examined for genetic abnormalities.

Autosomal gene—A gene found on one of the 22 autosomal chromosome pairs; i.e., not on a sex (X or Y) chromosome.

Chorionic villus sampling—A medical test done during pregnancy in which a sample of the membrane surrounding the fetus is removed for examination. This examination can reveal genetic fetal abnormalities.

Glucose—A form of sugar that serves as the body's main energy source.

Glycogen—A macromolecule composed mainly of glucose that serves as the storage form of glucose that is not immediately needed by the body.

Glycogenolysis—The process of tearing-down a glycogen molecule to free up glucose.

Glycogenosis—An alternate term for glycogen storage disease. The plural form is glycogenoses.

Gout—A painful condition in which uric acid precipitates from the blood and accumulates in joints and connective tissues.

Mendelian inheritance—An inheritance pattern for autosomal gene pairs. The genetic trait displayed results from one parent's gene dominating over the gene inherited from the other parent.

Osteoporosis—A disease in which the bones become weak and brittle.

Renal disease—Kidney disease.

Transgenic animal—Animals that have had genes from other species inserted into their genetic code.

gene. Before undergoing such testing, the prospective parents should meet with a genetic counselor and other professionals in order to make an informed decision.

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American Liver Foundation. 1425 Pompton Ave., Cedar Grove, NJ 07009. (800) 223-0179. <http://www.liverfoundation.org>.

Association for Glycogen Storage Disease. PO Box 896, Durant, Iowa 52747-9769. (319) 785-6038.

Julia Barrett

Glycosylated hemoglobin test

Definition

Glycosylated hemoglobin is a test that indicates how much sugar has been in a person's blood during the past two to four months. It is used to monitor the effectiveness of diabetes treatment.

Purpose

Diabetes is a disease in which a person cannot effectively use sugar in the blood. Left untreated, blood sugar levels can be very high. High sugar levels increase risk of complications, such as damage to eyes, kidneys, heart, nerves, blood vessels, and other organs.

A routine blood sugar test reveals how close to normal a sugar level is at the time of the test. The glycosylated **hemoglobin test** reveals how close to normal it has been during the past several months.

This information helps a physician evaluate how well a person is responding to diabetes treatment and to determine how long sugar levels have been high in a person newly diagnosed with diabetes.

KEY TERMS

Diabetes mellitus—A disease in which a person can't effectively use sugar in the blood to meet the needs of the body. It is caused by a lack of the hormone insulin.

Glucose—The main form of sugar used by the body for energy.

Glycosylated hemoglobin—A test that measures the amount of hemoglobin bound to glucose. It is a measure of how much glucose has been in the blood during the past two to four months.

Description

The Diabetes Control and Complications Trial (DCCT) demonstrated that persons with diabetes who maintained blood glucose (sugar) and total **fasting** hemoglobin levels at or close to a normal range decreased their risk of complications by 50–75%. Based on results of this study, the American Diabetes Association (ADA) recommends routine glycosylated hemoglobin testing to measure long-term control of blood sugar.

Glycosylated hemoglobin measures the percentage of hemoglobin bound to glucose. Hemoglobin is a protein found in every red blood cell. As hemoglobin and glucose are together in the red blood cell, the glucose gradually binds to the A1c form of hemoglobin in a process called glycosylation. The amount bound reflects how much glucose has been in the blood during the past average 120-day lifespan of red cells.

Several methods are used to measure the amount of bound hemoglobin and glucose. They are electrophoresis, chromatography, and immunoassay. All are based on the separation of hemoglobin bound to glucose from that without glucose.

The ADA recommends glycosylated hemoglobin be done during a person's first diabetes evaluation, again after treatment is begun and sugar levels are stabilized, then repeated semiannually. If the person does not meet treatment goals or sugar levels have not stabilized, the test should be repeated quarterly.

Other names for the test include: Hemoglobin A1c, Diabetic control index, GHb, glycosylated hemoglobin, and glycated hemoglobin. The test is covered by insurance. Results are usually available the following day.

Preparation

A person does not need to fast before 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. This test requires 5 mL of blood.

Aftercare

Discomfort or bruising may occur at the puncture site, or the person may feel dizzy or faint. Pressure to the puncture site until bleeding stops reduces bruising. Warm packs relieve discomfort.

Normal results

Diabetes treatment should achieve glycosylated hemoglobin levels of less than 7.0%. Normal values for a non-diabetic person is 4.0–6.0%.

Because laboratories use different methods, results from different laboratories can not always be compared. The National Glycosylation Standardization Program gives a certification to laboratories using tests standardized to those used in the DCCT study.

Abnormal results

Results require interpretation by a physician with knowledge of the person's clinical condition, as well as the test method used. Some methods give false high or low results if the person has an abnormal hemoglobin, such as hemoglobin S or F.

Conditions that increase the lifespan of red cells, such as a **splenectomy** (removal of the spleen), falsely increase levels. Conditions that decrease the lifespan, such as hemolysis (disruption of the red blood cell membrane), falsely decrease levels.

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Centers for Disease Control and Prevention. 1600 Clifton Rd., NE, Atlanta, GA 30333. (800) 311-3435, (404) 639-3311. <http://www.cdc.gov>.

National Diabetes Information Clearinghouse. 1 Information Way, Bethesda, MD 20892-3560. (800) 860-8747. <http://www.niddk.nih.gov/health/diabetes/ndic.htm>.

National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). Building 31, Room 9A04, 31 Center Drive, MSC 2560, Bethesda, MD 208792-2560. (301) 496-3583. <http://www.niddk.nih.gov>.

Nancy J. Nordenson

This woman's goiter may have been caused by an insufficient intake of iodine. *(Custom Medical Stock Photo. Reproduced by permission.)*

Goiter

Definition

Goiter refers to any visible enlargement of the thyroid gland.

Description

The thyroid gland sits astride the trachea (windpipe) and is shaped like a butterfly. It makes thyroxin, a hormone that regulates the metabolic activity of the body, rather like the gas pedal on a car. Too much thyroxin increases the metabolism, causing weight loss, temperature elevation, nervousness, and irritability. Too little thyroxin slows the metabolism down, deepens the voice, causes weight gain and water retention, and retards growth and mental development in children. Both conditions also alter hair and skin growth, bowel function, and menstrual flow.

Curiously, the thyroid gland is often enlarged whether it is making too much hormone, too little, or sometimes even when it is functioning normally. The thyroid is controlled by the pituitary gland, which secretes thyroid stimulating hormone (TSH) in response to the amount of thyroxin it finds in the blood. TSH increases the amount of thyroxin secreted by the thyroid and also causes the thyroid gland to grow.

- Hyperthyroid goiter—If the amount of stimulating hormone is excessive, the thyroid will both enlarge and secrete too much thyroxin. The result—hyperthyroidism with a goiter. Graves' disease is the most common form of this disorder.
- Euthyroid goiter—The thyroid is the only organ in the body to use iodine. If dietary iodine is slightly inadequate, too little thyroxin will be secreted, and the pituitary will sense the deficiency and produce more TSH. The thyroid gland will enlarge enough to make sufficient thyroxin.
- Hypothyroid goiter—If dietary iodine is severely reduced, even an enlarged gland will not be able to make enough thyroxin. The gland will keep growing under the influence of TSH, but it may never be able to make enough thyroxin.

Causes and symptoms

Excess TSH (or similar hormones), cysts, and tumors will enlarge the thyroid gland. Of these, TSH enlarges the entire gland while cysts and tumors enlarge only a part of it.

The only symptom from a goiter is the large swelling just above the breast bone. Rarely, it may constrict the trachea (windpipe) or esophagus and cause difficulty breathing or swallowing. The rest of the symptoms come from thyroxin or the lack of it.

Diagnosis

The size, shape, and texture of the thyroid gland help the physician determine the cause. A battery of blood

KEY TERMS

Cyst—A liquid-filled structure developing abnormally in the body.

Euthyroid—Having the right amount of thyroxin stimulation.

Hyperthyroid—Having too much thyroxin stimulation.

Hypothyroid—Having too little thyroxin stimulation.

Pituitary gland—The master gland, located in the middle of the head, that controls most of the other glandss by secreting stimulating hormones.

Radiotherapy—The use of ionizing radiation, either as x rays or radioactive isotopes, to treat disease.

Thyroxin—The hormone secreted by the thyroid gland.

tests are required to verify the specific thyroid disease. Functional imaging studies using radioactive iodine determine how active the gland is and what it looks like.

Treatment

Goiters of all types will regress with treatment of the underlying condition. Dietary iodine may be all that is needed. However, if an iodine deficient thyroid that has grown in size to accommodate its deficiency is suddenly supplied an adequate amount of iodine, it could suddenly make large amounts of thyroxin and cause a thyroid storm, the equivalent of racing your car motor at top speed.

Hyperthyroidism can be treated with medications, therapeutic doses of radioactive iodine, or surgical reduction. Surgery is much less common now than it used to be because of progress in drugs and radiotherapy.

Prognosis

Although goiters diminish in size, the thyroid may not return to normal. Sometimes thyroid function does not return after treatment, but thyroxin is easy to take as a pill.

Prevention

Euthyroid goiter and hypothyroid goiter are common around the world because many regions have inadequate dietary iodine, including some places in the United States. International relief groups are providing iodized salt to many of these populations. Because **mental retardation** is a common result of **hypothyroidism** in children, this is an extremely important project.

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The Micronutrient Initiative (c/o International Development Research Centre). 250 Albert St., Ottawa, Ontario, Canada K1G 3H9. (613) 236-6163, ext. 2050. <http://www.idrc.ca/mi/index.htm>.

J. Ricker Polsdorfer, MD

Gonadal dysgenesis *see* **Turner syndrome**

Gonorrhea

Definition

Gonorrhea is a highly contagious sexually transmitted disease that is caused by the bacterium *Neisseria gonorrhoeae*. The mucous membranes of the genital region may become inflamed without the development of any other symptoms. When symptoms do occur, they are different in men and women. In men, gonorrhea usually begins as an infection of the vessel that carries urine and sperm (urethra). In women, it will most likely infect the narrow part of the uterus (cervix). If untreated, gonorrhea can result in serious medical complications.

Description

Gonorrhea is commonly referred to as "the clap." The incidence of gonorrhea has steadily declined since the 1980s, largely due to increased public awareness campaigns and the risk of contracting other **sexually transmitted diseases**, such as **AIDS**. Still, current estimates range from 400,000 to as many as one million projected cases of gonorrhea in the United States each year. These estimates vary due to the private nature of the dis-

ease and the consequent underreporting that occurs. The majority of reported cases of gonorrhea come from public health clinics.

The disease affects people of all ages, races, and socioeconomic levels, but some individuals are more at-risk than others. Adolescents and young adults are the highest risk group, with more than 80% of the reported cases each year occurring in the 15–29 age group. Those individuals with multiple sexual partners and who use no barrier **contraception**, such as condoms, are most at-risk. Reported rates vary among racial and ethnic groups.

The risk factors for gonorrhea are not unlike those for all sexually transmitted diseases. Both men and women can become infected through a variety of sexual contact behaviors, including oral, anal, or vaginal intercourse. The disease is transmitted very efficiently. In fact, women run a 60–90% chance of contracting the disease after just one sexual encounter with an infected male. The disease can also be transmitted from an infected mother to her infant during delivery.

Causes and symptoms

If treated early, gonorrhea can be cured. Unfortunately, many individuals with gonorrhea, particularly women, will experience no symptoms to alert them to the possibility that they have contracted gonorrhea, and therefore, many do not seek treatment. When present, the symptoms and complications of gonorrhea are primarily limited to the genital, urinary, and gastrointestinal systems and usually begin between one day and two weeks following infection. If left untreated, serious complications can result if the disease spreads to the bloodstream and infects the brain, heart valves, and joints. Untreated gonorrhea can also result in severe damage to the reproductive system, making an individual unable to conceive a child (sterile).

Symptoms of gonorrhea in women

As many as 80% of women with gonorrhea show no symptoms. If present, symptoms may include the following:

- bleeding between menstrual periods
- chronic abdominal **pain**.
- painful urination.
- vaginal discharge, often cloudy and yellow.
- in the case of oral infection, there may be no symptoms or only a **sore throat**.
- anal infection may cause rectal **itching** or discharge.

Because women often do not show any symptoms, complications are more likely to occur as the disease progresses. The most common complication is **pelvic inflammatory disease** (PID). PID can occur in up to 40% of women with gonorrhea and may result in damage to the fallopian tubes, a **pregnancy** developing outside the uterus (**ectopic pregnancy**), or sterility. If an infected woman is pregnant, gonorrhea can be passed on to her newborn through the birth canal during delivery. These infants may experience eye infections that could lead to blindness.

Symptoms of gonorrhea in men

Men are more likely to experience the following symptoms:

- thick and cloudy discharge from the penis.
- burning or pain during urination.
- more frequent urination.
- in the case of oral infection, there may be no symptoms or only a sore throat.
- anal infection may cause rectal itching or discharge.

In men, complications can affect the prostate, testicles, and surrounding glands. Inflammation, tissue **death** and pus formation (abscesses), and scarring can occur and result in sterility.

Diagnosis

The diagnosis of gonorrhea can be made at a public health clinic or a family physician office. First, the doctor will discuss symptoms and the patient's known contact or at-risk behavior. There are three methods available to test for the presence of *Neisseria gonorrhoeae*. These include a culture, a Gram stain, and an ELISA test. Culture of secretions from the infected area is the preferred method for gonorrhea screening in patients with or without symptoms. A cotton swab can be used to collect enough sample for a culture. The sample is incubated for up to two days, providing enough time for the bacteria to multiply and be accurately identified. This test is nearly 100% accurate.

Gram stains are more accurate in the diagnosis of gonorrhea in men than in women. To perform this test, a small amount of discharge from the infected area will be placed on a slide, stained with a special dye, and examined under a microscope for the presence of the gonococcus bacteria. The advantage to this test is that results can be obtained very quickly at the initial visit. Because it requires that the physician or technician to be able to recognize and accurately identify the bacteria simply by looking at it under a microscope, however, this test is only approximately 70% accurate. As a result, one of the other methods will also probably be used to confirm the diagnosis.

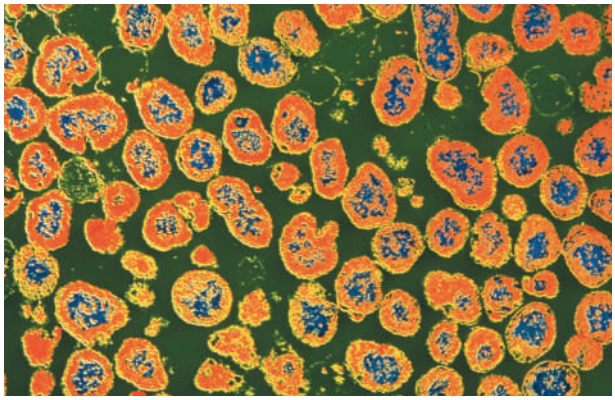
ELISA, or enzyme-linked immunosorbent assay, has emerged as a rapid and sensitive test for gonorrhea. It is much more sensitive than the gram stain and is more convenient than the culture test, which involves the transport and storage of samples. As of late 1997, several other diagnostic tests were being researched with the goal of providing a cost-effective method of screening for a variety of sexually transmitted diseases. One of the most interesting of these is a home test that can be taken by the patient themselves, allowing for a degree of privacy and confidentiality.

When a patient suspects exposure to or experiences symptoms of gonorrhea, he or she may see a public health provider or family practice physician. Physicians trained in obstetrics or gynecology may also be involved, particularly if gynecological complications occur. Men who experience complications may be referred to a urologist. There are also infectious disease doctors who specialize in the treatment and research of all infectious diseases, including those transmitted sexually. All doctors must report this highly contagious disease to public health officials, and patients are asked to provide the names of sex partners during the suspected period of infection so that they can be notified of the risk.

Treatment

Gonorrhea has become more difficult and expensive to treat since the 1970s, due to the increased resistance of gonorrhea to certain **antibiotics**. In fact, according to projections from the Centers for Disease Control and Prevention, 30% of the strains of gonorrhea were resistant to routine antibiotics in 1994, and resistance has been increasing steadily. Furthermore, many patients have both gonorrhea and chlamydial infections. Therefore, two drug treatment regimens are common. Medications used to treat gonorrhea include ceftriaxone, cefixime, spectinomycin, ciprofloxacin, and ofloxacin. Ceftriaxone and doxycycline or azithromycin are often given simultaneously to treat possible co-existing chlamydia (in pregnant women, erythromycin should be substituted for the aforementioned anti-chlamydial agents).

An extremely important consideration is to make sure that all of the prescribed medication is taken. If a course of antibiotics is not completed, the medication will only kill those organisms that are susceptible to the antibiotic, allowing those that are resistant to the effects of that particular antibiotic to multiply and possibly cause a new infection that will be more difficult to treat. Patients should refrain from sexual intercourse until treatment is complete and return for follow-up testing. Any sexual partners during the time of infection, even if those partners do not show symptoms, should be notified and treated when any sexually transmitted disease is involved.



A transmission electron microscopy (TEM) image of *Neisseria gonorrhoeae.* *(Custom Medical Stock Photo. Reproduced by permission.)*

Alternative treatment

Although there is no known alternative to antibiotics in the treatment of gonorrhea, there are herbs and **minerals** that may be used to supplement antibiotic treatment:

- *Lactobacillus acidophilus* or live-culture yogurts are helpful, while taking antibiotics, to replenish gastrointestinal flora.
- The following supplements may be used to improve the body's immune function: zinc, multivitamins and mineral complexes, vitamin C, and garlic (*Allium sativum*).
- Several herbs may reduce some symptoms or help speed healing: kelp has balanced **vitamins** and minerals. Calendula (*Calendula officinalis*), myrrh (*Commiphora molmol*), and thuja (*Thuja occidentalis*) may help reduce discharge and inflammation when used as a tea or douche.
- Hot baths may also help reduce pain and inflammation.
- A variety of herbs may help with symptoms of the reproductive and urinary systems.
- If a physician approves, **fasting**, combined with certain juices, may help cleanse the urinary and gastrointestinal systems.
- There may be **acupressure** and **acupuncture** points that will help with system cleansing. These exact pressure points can be provided and treated by an acupressurist or acupuncturist.

Prognosis

The prognosis for patients with gonorrhea varies based on how early the disease is detected and treated. If treated early and properly, patients can be entirely cured of the disease. Up to 40% of female patients who are not

KEY TERMS

Cervix—The narrow part or neck of the uterus.

Chlamydia—The most common bacterial sexually transmitted disease in the United States that often accompanies gonorrhea and is known for its lack of evident symptoms in the majority of women.

Ectopic pregnancy—A pregnancy that occurs outside the uterus, such as in the fallopian tubes. Although the fetus will not survive, in some cases, ectopic pregnancy can also result in the death of the mother.

ELISA—Enzyme-linked immunosorbent assay. This test has been used a screening test for AIDS for many years and has also been used to detect gonorrhea bacteria.

HIV—Human immunodeficiency virus, the virus that causes AIDS. The risk of acquiring AIDS is increased by the presence of gonorrhea or other sexually transmitted diseases.

Neisseria gonorrhoeae—The bacterium that causes gonorrhea. It cannot survive for any length of time outside the human body.

Pelvic inflammatory disease (PID)—An infection of the upper genital tract that is the most serious threat to a woman's ability to reproduce. At least 25% of women who contract the disease, which can be a complication of gonorrhea, will experience long-term consequences such as infertility or ectopic pregnancy.

Sexually transmitted diseases (STDs)—A group of diseases which are transmitted by sexual contact. In addition to gonorrhea, this groups generally includes chlamydia, HIV (AIDS), herpes, syphilis, and genital warts.

Sterile—Unable to conceive a child.

Urethra—The canal leading from the bladder, and in men, also a path for sperm fluid.

Urethritis—Inflammation of the urethra.

treated early may develop pelvic inflammatory disease (PID) and the possibility of resulting sterility. Although the risk of **infertility** is higher in women than in men, men may also become sterile if the urethra becomes inflamed (**urethritis**) as a result of an untreated gonorrhea infection. Following an episode of PID, a woman is six to 10 times more likely, should a pregnancy occur, to have a pregnancy develop outside the uterus (ectopic pregnancy), which can result in death. Liver infection may also occur in untreated women. In approximately 2% of patients with untreated gonorrhea, the gonococcal infection may spread throughout the body and can cause **fever**, arthritis-like joint pain, and **skin lesions**.

Prevention

Currently, there is no vaccine for gonorrhea, but several are under development. The best prevention is to abstain from having sex or to engage in sex only when in a mutually monogamous relationship in which both partners have been tested for gonorrhea, AIDS, and other sexually transmitted diseases. The next line of defense is the use of condoms, which have been shown to be highly effective in preventing disease (and unwanted pregnancies). To be 100% effective, condoms must be used properly. A female birth-control device that blocks the entry of sperm into the cervix (diaphragm) can also reduce the risk of infection. The risk of contracting gonorrhea increases with the number of sexual partners. Any man or woman who has sexual contact with more than one partner is advised to be tested regularly for gonorrhea and other sexually transmitted diseases.

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American Social Health Association. P.O. Box 13827, Research Triangle Park, NC 27709. (800) 227-8922 (National STD Hotline) or voice line at (919) 361-8400. <http://sunsite.unc.edu/ASHA/>.
National Center for HIV, STD, and TB Prevention. Centers for Disease Control and Prevention, 1600 Clifton NE, Atlanta, GA 30333. <http://www.cdc.gov/nchstp/od/nchstp.html>. NCHST@cpsod1.em.cdc.gov.
National Institute of Allergy and Infectious Diseases. National Institutes of Health, Bethesda, MD 20892.

Teresa G. Norris

Goodpasture's syndrome

Definition

An uncommon and life-threatening hypersensitivity disorder believed to be an autoimmune process related to antibody formation in the body. Goodpasture's syndrome is characterized by renal (kidney) disease and lung hemorrhage.

Description

The disorder is characterized by autoimmune reaction which deposits of antibodies in the membranes of both the lung and kidneys, causing both inflammation of kidney (**glomerulonephritis**) and lung bleeding. It is typically a disease of young males.

Causes and symptoms

The exact cause is unknown. It is an autoimmune disorder; that is, the immune system is fighting the body's own normal tissues through creating antibodies that attack the lungs and kidneys. Sometimes the disorder is triggered by a viral infection, or by the inhalation of gasoline or other hydrocarbon solvents. An association also exists between cigarette **smoking** and the syndrome. The target antigen of the Goodpasture's antibodies has been localized to a protein chain (type IV collagen).

Symptoms include foamy, bloody, or dark colored urine, decreased urine output, **cough** with bloody sputum, difficulty breathing after exertion, weakness, **fatigue**, nausea or vomiting, weight loss, nonspecific chest **pain** and/or pale skin.

Diagnosis

The clinician will perform a battery of tests to confirm a diagnosis. These tests include a complete **blood count** (CBC) to confirm anemia, iron levels to check for blood loss and blood urea nitrogen (BUN) and creatinine levels to test the kidney function. A **urinalysis** will be done to check for damage to the kidneys. A sputum test will be done to look for specific antibodies. A **chest x ray** will be done to assess the amount of fluid in the lung tissues. A lung needle biopsy and a **kidney biopsy** will show immune system deposits. The kidney biopsy can also show the presence of the harmful antibodies that attack the lungs and kidneys.

Treatment

Treatment is focused on slowing the progression of the disease. Treatment is most effective when begun early, before kidney function has deteriorated to a point where the kidney is permanently damaged, and dialysis is necessary. **Corticosteroids**, such as prednisone, or other anti-inflammatory medications may be used to reduce the immune response. Immune suppressants such as cyclophosphamide or azathioprine are used aggressively to reduce immune system effects.

A procedure whereby blood plasma, which contains antibodies, is removed from the body and replaced with fluids or donated plasma (**plasmapheresis**) may be performed daily for two or more weeks to remove circulating antibodies. It is fairly effective in slowing or reversing the disorder. Dialysis to clean the blood of wastes may be required if kidney function is poor. A kidney transplant may be successful, especially if performed after circulating antibodies have been absent for several months.

Prognosis

The probable outcome is variable. Most cases progress to severe renal failure and end-stage renal disease within months. Early diagnosis and treatment makes the probable outcome more favorable.

Prevention

No known prevention of Goodpasture's syndrome exists. People should avoid glue sniffing and the siphoning gasoline. Stopping smoking, if a family history of

KEY TERMS

Antibody—A protein molecule produced by the immune system in response to a protein that is not recognized as belonging in the body.

Antigen—Any substance that, as a result of coming in contact with appropriate cells,induces a state of sensitivity and/or immune responsiveness after a period of time and that reacts in a demonstrable way with antibodies.

Autoimmune disorder—An abnormality within the body whereby the immune system incorrectly attacks the body's normal tissues, thereby causing disease or organ dysfunction.

Blood urea nitrogen (BUN)—A test used to measure the blood level of urea nitrogen, a waste that is normally filtered from the kidneys.

Creatinine—A test used to measure the blood level of creatinine, a waste product filtered out of the blood by the kidneys. Higher than usual levels of this substance may indicate kidney disease.

Glomerulus (glomeruli)—A small tuft of blood capillaries in the kidney, responsible for filtering out waste products.

renal failure exists, may prevent some cases. Early diagnosis and treatment may slow progression of the disorder.

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American Kidney Fund. 6110 Executive Boulevard, Suite 1010, Rockville, MD 20852. (800) 638-8299. <http://www.akfinc.org.

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

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Gout

Definition

Gout is a form of acute arthritis that causes severe **pain** and swelling in the joints. It most commonly affects the big toe, but may also affect the heel, ankle, hand, wrist, or elbow. Gout usually comes on suddenly, goes away after 5–10 days, and can keep recurring. Gout is different from other forms of arthritis because it occurs when there are high levels of uric acid circulating in the blood, which can cause urate crystals to settle in the tissues of the joints.

Description

Uric acid, which is found naturally in the blood stream, is formed as the body breaks down waste products, mainly those containing purine, a substance that is produced by the body and is also found in high concentrations in some foods, including brains, liver, sardines, anchovies, and dried peas and beans. Normally, the kidneys filter uric acid out of the blood and excrete it in the urine. Sometimes, however, the body produces too much uric acid or the kidneys aren't efficient enough at filtering it from the blood, and it builds up in the blood stream, a condition known as hyperuricemia. A person's susceptibility to gout may increase because of the inheritance of certain genes or from being overweight and eating a rich diet. In some cases, another disease (such as lymphoma, leukemia, or **hemolytic anemia**) may be the underlying cause of the uric acid buildup that results in gout.

Hyperuricemia doesn't always cause gout. However, over the course of years, sharp urate crystals build up in the synovial fluid of the joints. Often, some precipitating event, such as an infection, surgery, a stubbed toe, or even a heavy drinking binge can cause inflammation. White blood cells, mistaking the urate crystals for a foreign invader, flood into the joint and surround the crystals, causing inflammation—in other words, the redness, swelling, and pain that are the hallmarks of a gout attack.

Causes and symptoms

As a result of high levels of uric acid in the blood, needle-like urate crystals gradually accumulate in the joints. Urate crystals may be present in the joint for a long time without causing symptoms. Infection, injury to the joint, surgery, drinking too much, or eating the wrong kinds of foods may suddenly bring on the symptoms, which include pain, tenderness, redness, warmth, and swelling of the joint. In many cases, the gout attack begins in the middle of the night. The pain is often so excruciating that the sufferer cannot bear weight on the

joint or tolerate the pressure of bedcovers. The inflamed skin over the joint may be red, shiny, and dry, and the inflammation may be accompanied by a mild **fever**. These symptoms may go away in about a week and disappear for months or years at a time. However, over the course of time, attacks of gout recur more and more frequently, last longer, and affect more joints. Eventually, stone-like deposits known as tophi may build up in the joints, ligaments, and tendons, leading to permanent joint deformity and decreased motion. (In addition to causing the tophi associated with gout, hyperuricemia can also cause **kidney stones**, also called renal calculi or uroliths.)

Gout affects an estimated one million Americans. It most commonly afflicts men (800,000 men versus 200,000 women). Uric-acid levels tend to increase in men at **puberty**, and, because it takes 20 years of hyperuricemia to cause gout symptoms, men commonly develop gout in their late 30s or early 40s. Women more typically develop gout later in life, starting in their 60s. According to some medical experts, estrogen protects against hyperuricemia, and when estrogen levels fall during **menopause**, urate crystals can begin to build up in the joints. Excess body weight, regular excessive alcohol intake, the use of blood pressure medications called **diuretics**, and high levels of certain fatty substances in the blood (serum triglycerides) associated with an increased risk of heart disease can all increase a person's risk of developing gout.

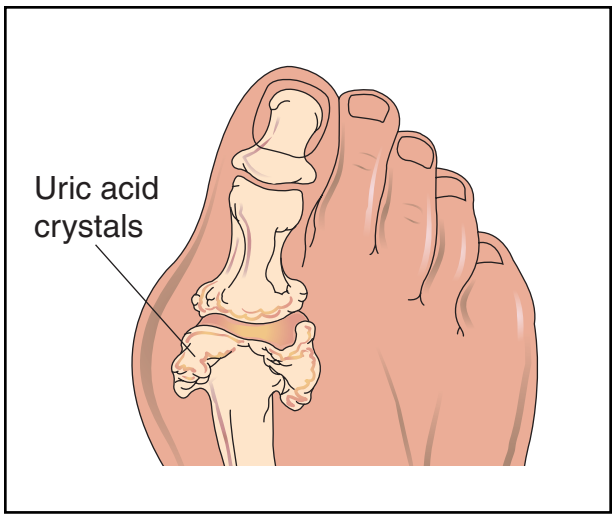
Diagnosis

Usually, physicians can diagnose gout based on the **physical examination** and medical history (the patient's description of symptoms and other information). Doctors can also administer a test that measures the level of uric acid in the blood. While normal uric acid levels don't necessarily rule out gout and high levels don't confirm it, the presence of hyperuricemia increases the likelihood of gout. The development of a tophus can confirm the diagnosis of gout. The most definitive way to diagnose gout is to take a sample of fluid from the joint and test it for urate crystals.

Treatment

The goals of treatment for gout consist of alleviating pain, avoiding severe attacks in the future, and preventing long-term joint damage. In addition to taking pain medications as prescribed by their doctors, people having gout attacks are encouraged to rest and to increase the amount of fluids that they drink.

Acute attacks of gout can be treated with nonaspirin, **nonsteroidal anti-inflammatory drugs** (NSAIDs) such as naproxen sodium (Aleve), ibuprofen (Advil), or



Gout, a form of acute arthritis, most commonly occurs in the big toe. It is caused by high levels of uric acid in the blood, in which urate crystals settle in the tissues of the joints and produce severe pain and swelling. *(Illustration by Electronic Illustrators Group.)*

indomethacin (Indocin). In some cases, these drugs can aggravate a peptic ulcer or existing kidney disease and cannot be used. Doctors sometimes also use colchicine (Colbenemid), especially in cases where nonsteroidal anti-inflammatory drugs cannot be used. Colchicine may cause **diarrhea**, which tends to go away once the patient stops taking it. **Corticosteroids** such as prednisone (Deltasone) and adrenocorticotropic hormone (Acthar) may be given orally or may be injected directly into the joint for a more concentrated effect. While all of these drugs have the potential to cause side effects, they are used for only about 48 hours and are not likely to cause major problems. However, **aspirin** and closely related drugs (salicylates) should be avoided because they can ultimately worsen gout.

Once an acute attack has been successfully treated, doctors try to prevent future attacks of gout and long-term joint damage by lowering uric acid levels in the blood. There are two types of drugs for correcting hyperuricemia. Uricosuric drugs, such as probenecid (Benemid) and sulfinpyrazone (Anturane), lower the levels of urate in the blood by increasing its removal from the body (excretion) through the urine. These drugs may promote the formation of kidney stones, and they may not work for all patients, especially those with kidney disease. Allopurinol (Zyloprim), a type of drug called a xanthine-oxidase inhibitor, blocks the production of urate in the body, and can dissolve kidney stones as well as treating gout. The potential side effects of allopurinol include rash, a skin condition known as **dermatitis**, and liver

KEY TERMS

Allopurinol—A drug that corrects hyperuricemia by inhibiting urate production.

Colchicine—A drug used to treat painful flare-ups of gout.

Corticosteroids—Medications related to a natural body hormone called hydrocortisone, which are used to treat inflammation.

Hyperuricemia—High levels of a waste product called uric acid in the blood.

Probenecid—A drug that corrects hyperuricemia by increasing the urinary excretion of urate.

Purine—A substance found in foods that is broken down into urate and may contribute to hyperuricemia and gout.

Sulfinpyrazone—A drug that corrects hyperuricemia by increasing the urinary excretion of urate.

Synovial fluid—Fluid surrounding the joints which acts as a lubricant, reducing the friction between the joints.

Urate crystals—Crystals formed by high levels of uric acid in the blood.

dysfunction. Once people begin taking these medications, they must take them for life or the gout will continue to return.

Alternative treatment

The alternative medicine approach to gout focuses on correcting hyperuricemia by losing weight and limiting the intake of alcohol and purine-rich foods. In addition, consuming garlic (*Allium sativum*) has been recommended to help prevent gout. Increasing fluid intake, especially by drinking water, is also recommended. During an acute attack, contrast **hydrotherapy** (alternating three-minute hot compresses with 30-second cold compresses) can help dissolve the crystals and resolve the pain faster.

Prognosis

Gout cannot be cured but usually it can be managed successfully. As tophi dissolve, joint mobility generally improves. (In some cases, however, medicines alone do not dissolve the tophi and they must be removed surgically.) Lowering uric acid in the blood also helps to prevent or improve the kidney problems that may accompany gout.

Prevention

For centuries, gout has been known as a "rich man's disease" or a disease of overindulgence in food and drink. While this view is perhaps a little overstated and oversimplified, lifestyle factors clearly influence a person's risk of developing gout. Since **obesity** and excessive alcohol intake are associated with hyperuricemia and gout, losing weight and limiting alcohol intake can help ward off gout. **Dehydration** may also promote the formation of urate crystals, so people taking diuretics or "water pills" may be better off switching to another type of blood pressure medication, and everyone should be sure to drink at least six to eight glasses of water each day. Since purine is broken down in the body into urate, it may also be helpful to avoid foods high in purine, such as organ meats, sardines, anchovies, red meat, gravies, beans, beer, and wine.

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ORGANIZATIONS

Arthritis Foundation.1300 W. Peachtree St., Atlanta, GA 30309. (800) 283-7800. <http://www.arthritis.org>.

Gout drugs

Definition

Gout drugs are medicines that prevent or relieve the symptoms of gout, a disease that affects the joints and kidneys.

Purpose

Gout is a disease in which uric acid, a waste product that normally passes out of the body in urine, collects

and forms crystals in the joints and the kidneys. When uric acid crystals build up in the joints, the tissue around the joint becomes inflamed, and nerve endings in the area become irritated, causing extreme **pain**. Uric acid crystals in the kidneys can lead to **kidney stones** and eventually to kidney failure.

The symptoms of gout—severe pain, usually in the hand or foot (often at the base of the big toe), but sometimes in the elbow or knee—should be reported to a health care professional. If not treated, gout can lead to high blood pressure, deformed joints, and even **death** from kidney failure. Fortunately, the condition is easily treated. For patients who have just had their first attack, physicians may prescribe only medicine to reduce the pain and inflammation, such as **nonsteroidal anti-inflammatory drugs**, **corticosteroids**, or colchicine. Patients may also be advised to change their eating and drinking habits, avoiding organ meats and other protein-rich foods, cutting out alcoholic beverages, and drinking more water. Some people never have another gout attack after the first. For those who do, physicians may prescribe additional drugs that either help the body get rid of uric acid or reduce the amount of uric acid the body produces. These drugs will not relieve gout attacks that already have started, but will help prevent attacks when taken regularly.

Description

Three main types of drugs are used in treating gout. Colchicine helps relieve the symptoms of gout by reducing inflammation. Allopurinol (Lopurin, Zyloprim) reduces the amount of uric acid produced in the body. Probenecid (Benemid, Probalan) and sulfinpyrazone (Anturane) help the body get rid of excess uric acid. Physicians may recommend that patients take more than one type of gout drug at the same time. Some of these medicines may also be prescribed for other medical conditions that are caused by too much uric acid in the body.

Recommended dosage

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

Always take gout drugs exactly as directed. Never take larger or more frequent doses than recommended. Patients who are told to take more than one gout drug should carefully follow the physician's directions for taking all medicines.

Gout drugs such as allopurinol, probenecid, and sulfinpyrazone must be taken regularly to prevent gout attacks. The medicine may take some time to begin working, so gout attacks may continue for awhile after starting to take the drug. Continuing to take the drug is important, even if it does not seem to be working at first.

Colchicine may be taken regularly in low doses to help prevent gout attacks or in high doses for only a few hours at a time to relieve an attack. The chance of serious side effects is greater when this medicine is taken in high doses for short periods.

Precautions

Seeing a physician regularly while taking gout drugs is important. The physician will check to make sure the medicine is working as it should and will watch for unwanted side effects. Blood tests may be ordered to help the physician monitor how well the drug is working.

Drinking alcohol, including beer and wine, may increase the amount of uric acid in the body and may interfere with the effects of gout medicine. People with gout (or other conditions that result from excess uric acid) may need to limit the amount of alcohol they drink or stop drinking alcohol altogether.

Some people feel drowsy or less alert when taking gout drugs. Anyone who takes this type of medicine should not drive, use machines or do anything else that might be dangerous until they have found out how the drugs affect them.

Some gout drugs may change the results of certain medical tests. Before having medical tests, anyone taking this medicine should alert the health care professional in charge.

Older people may be especially sensitive to the effects of colchicine. The drug may also stay in their bodies longer than it does in younger people. Both the increased sensitivity to the drug and the longer time for the drug to leave the body may increase the chance of side effects.

Special conditions

People who have certain medical conditions or who are taking certain other medicines can have problems if they take gout drugs. Before taking these drugs, be sure to let the physician know about any of these conditions:

ALLERGIES. Anyone who has ever had unusual reactions to gout drugs or to medicines used to relieve pain or inflammation should let his or her physician know before taking gout drugs. The physician should also be told about any **allergies** to foods, dyes, preservatives, or other substances.

DIABETES. Some gout drugs may cause false results on certain urine sugar tests, but not on others. Diabetic patients who take gout drugs should check with their

physicians to find out if their medicine will affect the results of their urine sugar tests.

PREGNANCY. The effects of taking gout drugs during **pregnancy** are not fully understood. Women who are pregnant or who may become pregnant should check with their physicians before using gout drugs.

BREASTFEEDING. Gout drugs may pass into breast milk. Women who are taking this medicine and want to breastfeed their babies should check with their physicians.

OTHER MEDICAL CONDITIONS. Gout drugs may cause problems for people with certain medical conditions. For example, the risk of severe allergic reactions or other serious side effects is greater when people with these medical conditions take certain gout drugs:

- congestive heart disease
- high blood pressure
- blood disease
- diabetes
- kidney disease or kidney stones
- cancer being treated with drugs or radiation
- stomach or intestinal problems, including stomach ulcer (now or in the past)

Before using gout drugs, people with any of medical problems listed above should make sure their physicians are aware of their conditions.

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

Side effects

A skin rash that develops during treatment with gout drugs may be a sign of a serious and possibly life-threatening reaction. If any of these symptoms occur, stop taking the medicine and check with a physician immediately:

- skin rash, **itching**, or **hives**
- scaly or peeling skin
- chills, **fever**, **sore throat**, **nausea and vomiting**, yellow skin or eyes, joint pain, muscle aches or pains—especially if these symptoms occur at the same time or shortly after a skin rash

Patients taking colchicine should stop taking it immediately if they have **diarrhea**, stomach pain, nausea, or vomiting. If these symptoms continue for 3 hours or more after the medicine is stopped, check with a physician.

Other side effects of may also need medical attention. If any of the following symptoms occur while taking gout drugs, check with the physician who prescribed the medicine as soon as possible:

- pain in the side or lower back
- painful urination
- blood in the urine

Less serious side effects, such as **headache**, loss of appetite, and joint pain and inflammation usually go away as the body adjusts to the drug and do not need medical treatment.

Other side effects may occur. Anyone who has unusual symptoms while taking gout drugs should get in touch with his or her physician.

Interactions

Gout drugs may interact with other medicines. When this happens, the effects of one or both of the drugs may change or the risk of side effects may be greater. Anyone who takes gout drugs should let the physician know all other medicines he or she is taking. Among the drugs that may interact with gout drugs are:

- **Aspirin** or other salicylates. These drugs may keep gout drugs from working properly.
- Nonsteroidal anti-inflammatory drugs such as indomethacin (Indocin) and ketoprofen (Orudis). Taking these medicines with probenecid may increase the chance of side effects from the nonsteroidal anti-inflammatory drugs.
- Blood thinners. When taken with blood thinners, such as warfarin (Coumadin), gout drugs may increase the chance of bleeding. A lower blood thinner dose may be necessary.
- Blood viscosity reducing medicines such as pentoxifylline (Trental). Taking this medicine with blood thinners may increase the chance of bleeding.
- Medicine for infections. Probenecid may increase the levels of these medicines in the blood. This may make the other medicine work better, but may also increase the risk of side effects.
- The immunosuppressant drug azathioprine (Imuran), used to prevent organ rejection in transplant patients and to treat **rheumatoid arthritis**. Taking this medicine with allopurinol can increase the risk of side effects from the azathioprine.
- Anticancer drugs such as mercaptopurine (Purinethol), plicamycin (Mithracin), and methotrexate (Rheumatrex). Taking this medicine with gout drugs may increase the risk of side effects from the anticancer drug.
- Antiretroviral drugs such as zidovudine (Retrovir). Probenecid may increase the level of this medicine in the blood. This may make side effects more likely.

KEY TERMS

Corticosteroids—Medicines that are similar to the natural hormone cortisone and belong to the family of drugs called steroids.

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

Kidney stone—A small, hard mass formed in the kidney from deposits of uric acid or other materials.

Nonsteroidal anti-inflammatory drug (NSAID)—A type of medicine used to relieve pain, swelling, and other symptoms of inflammation. Drugs in this group are not cortisone-like drugs (steroids).

Salicylates—A group of drugs that includes aspirin and related compounds. Salicylates are used to relieve pain, reduce inflammation, and lower fever.

- Antiseizure medicines such as Depakote (divalproex) and Depakene (valproic acid). Using these medicines with sulfinpyrazone may increase the chance of bleeding.

The list above does not include every drug that may interact with gout drugs. Be sure to check with a physician or pharmacist before combining gout drugs with any other prescription or nonprescription (over-the-counter) medicine.

Nancy Ross-Flanigan

Gouty arthritis *see* **Gout**

Graft-vs.-host disease

Definition

Graft-vs.-host disease is an immune attack on the recipient by cells from a donor.

Description

The main problem with transplanting organs and tissues is that the recipient host does not recognize the new tissue as its own. Instead, it attacks it as foreign in the same way it attacks germs, to destroy it.

If immunogenic cells from the donor are transplanted along with the organ or tissue, they will attack the host, causing graft vs. host disease.

The only transplanted tissues that house enough immune cells to cause graft vs. host disease are the blood and the bone marrow. Blood transfusions are used every day in hospitals for many reasons. Bone marrow transplants are used to replace blood forming cells and immune cells. This is necessary for patients whose **cancer** treatment has destroyed their own bone marrow. Because bone marrow cells are among the most sensitive to radiation and **chemotherapy**, it often must be destroyed along with the cancer. This is true primarily of leukemias, but some other cancers have also been treated this way.

Causes and symptoms

Even if the donor and recipient are well matched, graft-vs.-host disease can still occur. There are many different elements involved in generating immune reactions, and each person is different, unless they are identical twins. Testing can often find donors who match all the major elements, but there are many minor ones that will always be different. How good a match is found also depends upon the urgency of the need and some good luck.

Blood **transfusion** graft-vs.-host disease affects mostly the blood. Blood cells perform three functions: carrying oxygen, fighting infections, and clotting. All of these cell types are decreased in a transfusion graft-vs.-host reaction, leading to anemia (lack of red blood cells in the blood), a decrease in resistance to infections, and an increase in bleeding. The reaction occurs between four to 30 days after the transfusion.

The tissues most affected by bone marrow graft-vs.-host disease are the skin, the liver, and the intestines. One form or the other occurs in close to half of the patients who receive bone marrow transplants.

Bone marrow graft-vs.-host disease comes in an acute and a chronic form. The acute form appears within two months of the transplant; the chronic form usually appears within three months. The acute disease produces a skin rash, liver abnormalities, and **diarrhea** that can be bloody. The skin rash is primarily a patchy thickening of the skin. Chronic disease can produce a similar skin rash, a tightening or an inflammation of the skin, lesions in the mouth, drying of the eyes and mouth, hair loss, liver damage, lung damage, and **indigestion**. The symptoms are similar to an autoimmune disease called **scleroderma**.

Both forms of graft-vs.-host disease bring with them an increased risk of infections, either because of the process itself or its treatment with cortisone-like drugs and immunosuppressives. Patients can die of liver failure, infection, or other severe disturbances of their system.