THE ENCYCLOPEDIA OF

ENDOCRINE DISEASES AND DISORDERS

make needed adjustments to their diet, exercise plans, and medications.

Having too much circulating hormone is also possible, whether the hormone is testosterone, estrogen, thyroxine, or any other hormone that the endocrine glands produce. For example, all females produce a small amount of testosterone. However, if too much testosterone is generated by the ovaries, this leads to a virilizing effect, causing the woman's breasts to flatten, increased body hair to grow on the chest and face, and infertility. Fortunately physicians can seek the cause of this condition and then act to treat it.

Endocrine Disorders and Development in Children and Adolescents

Adults are not the only people affected by endocrine diseases; children and adolescents are susceptible as well. For example, if a child or an adolescent develops a tumor of the pituitary that secretes excess growth hormone, he or she may develop gigantism, causing the child or adolescent to grow to very tall heights. Occasionally the child can exceed seven feet in height. Conversely, a deficiency of growth hormone, due to a malfunction of either the pituitary or the hypothalamus, will lead to growth failure. As a result, the person will be significantly shorter than his or her peers.

Yet these are also conditions that physicians have begun to correct by administering specific medications or growth hormone treatments. Although such treatments may help children tremendously, both physically and psychologically, these treatments continue to be controversial among some physicians. Some experts do not want to alter nature and their philosophical view is that, for example, if a person is biologically destined to be very tall, then he or she *should* be very tall. Others argue that height will affect a person for the rest of his or her life and thus they feel that it is a parent's right to choose to do what is in the best interests of the child, including actions to limit height.

Children and adolescents with suspected or diagnosed endocrine disorders should be treated by pediatric endocrinologists, physicians who specialize in both pediatrics and endocrinology. The father of pediatric endocrinology is regarded by many as Lawson Wilkins, a physician in Baltimore, Maryland, who is said to have established the first endocrine clinic for children at Johns Hopkins in 1935. Other clinics were created, and the specialty evolved further in the mid 1950s and 1960s. By 2002, there were 65 training programs in the United States for pediatric endocrinologists.

The American Board of Pediatrics has an endocrinology board that certifies the training and competence of pediatric endocrinologists in endocrinological diseases, including diabetes. According to a 2004 article in *Pediatric Research*, 927 pediatric endocrinologists have been certified by the board since 1978.

Although most children and adolescents do not experience any disorders of the endocrine system, their endocrine systems do affect normal life changes as they grow. Such life changes include the onset of puberty and, for a female, the onset of menstruation (menarche), the growth of breasts (thelarche), the appearance of underarm hair (adrenarche) and pubic hair (pubarche), and so forth. Boys experience typical initial signs of puberty, such as facial and body hair and maturing changes in the testes and penis, as described by Dr. Tanner in 1962 and subsequently called Tanner stages.

The amazing transformation of a child into a man or woman is a major achievement orchestrated by the endocrine system, as is the decline of the hormones, no longer needed after the childbearing years are over. In some cases, however, children develop disorders that may cause either an early puberty (precocious puberty) or a delayed puberty or another growth disorder. Pediatric endocrinologists should be consulted to evaluate and treat such illnesses.

Endocrine Disorders and the Elderly

As individuals age into their senior years, they face an increased risk for developing certain endocrine disorders. These include thyroid disease, particularly hypothyroidism, and bone disorders such as osteoporosis and osteopenia. Elderly individuals also face a greater risk of developing some dangerous and often fatal forms of cancer, particularly tumors of the ovary and the pancreas. Older individuals are also more likely to develop below-normal levels of calcium in the blood (hypocalcemia), a condition that is treatable with both calcium and vitamin D supplements.

In addition, seniors face an increased risk of developing Type 2 diabetes. They urgently need

In one study of 112 patients with acromegaly, reported in a 2000 issue of the *New England Journal of Medicine,* the patients were treated with differing daily doses of pegvisomant (Somavert) over 12 weeks. (A placebo group received a pill with no medication.) A majority of the patients, 93, had previously received pituitary surgery. Of these, 57 had also been treated with radiation therapy. (Four patients withdrew from the study for varying reasons.)

The researchers found that pegvisomant worked well in most patients, successfully reducing IGF-1 concentrations within about two weeks of starting taking the drug. However, because the study was conducted for only 12 weeks, the researchers stated that further study and longer periods of treatment would be needed to determine the continued safety and effectiveness of the drug.

Because pegvisomant blocks the binding of growth hormone to the receptor, some patients begin to synthesize more growth hormone. Some reports have discussed the growth of the tumor and of visual field changes that necessitated a change in the patient's medication therapy.

Radiation therapy is often used to treat acromegaly. In most cases, 4,000–5,000 rads (40–50 Gy) are given over five weeks. The growth of the tumors is often slowed or stopped by radiation therapy. However, the effects on the secretion of growth hormone are very slow and will decrease only about 10–20 percent per year, thus making the patient's symptomatic response very slow.

A variety of helpful imaging techniques (CT and MRI) have been used to try to focus the radiation directly on the tumor and thus to limit the damage to the surrounding normal brain tissue. Proton bean therapy has also been helpful for some patients; however, it is not widely available as of this writing. Stereotactic gammaknife therapy is now also being used on some tumors.

All forms of radiation therapy can lead to the loss of other pituitary functions over the course of many years and can also increase the patient's risk of developing an intracranial malignancy. In addition, radiation may cause changes in both visual and cognitive functions, depending on the type and amount of radiation used as well as the size of the radiated field.

See also AMENORRHEA; BLOOD PRESSURE/HYPERTENSION; BONE DISEASES, CARNEY COMPLEX; DWARFISM; HYPERPHOSPHATEMIA/HYPOPHOSPHATEMIA; PITUITARY ADENOMAS; PITUITARY GLAND; PREDIABETES.

For further information about acromegaly, contact the following organization:

Pituitary Network Association
223 East Thousand Oaks Boulevard
Number 320
Thousand Oaks, CA 91360
(805) 496-4932

Baris, D., et al. "Acromegaly and Cancer Risk: A Cohort Study in Sweden and Denmark." *Cancer Causes and Control* 13, no. 5 (2002): 395–400.

Gasperi, M., et al. "Nodular Goiter Is Common in Patients with Acromegaly." *Journal of Endocrinological Investigation* 25, no. 3 (2002): 240–245.

Larsen, P. Reed, et al. *Williams Textbook of Endocrinology.* New York: W. B. Saunders Company, 2001.

LeRoith, Carel, Abeda Mulla, and Karim Meeran. "Pituitary Carcinoma as a Cause of Acromegaly." *New England Journal of Medicine* 345, no. 22 (November 29, 2001): 1,645–1,646.

Trainer, Peter J., M.D., et al. "Treatment of Acromegaly with the Growth Hormone-Receptor Antagonist Pegvisomant." *New England Journal of Medicine* 342, no. 16 (April 20, 2000): 1,171–1,177.

Addison's disease A rare endocrine disease in which the adrenal glands do not produce enough CORTISOL (hypocortisolism or primary adrenal insufficiency). Cortisol is a key hormone that helps the body respond to stress in many different ways. It regulates blood pressure, maintains adequate blood glucose levels for energy, regulates electrolytes, such as potassium and sodium, and performs many other key functions within the body. Addison's disease is also known as chronic primary adrenal insufficiency. Sometimes patients with Addison's disease are also deficient in the hormone ALDOSTERONE, which is also produced by the adrenal glands.

The disease may be first diagnosed when it is life threatening because most patients have few or no symptoms in the early stages. Addison's disease occurs in about one in 100,000 people, and it

and may actually fall into a coma. They often have severe electrolyte abnormalities with profound hyperkalemia (high potassium levels) that can cause a lethal heart arrhythmia and severe HYPONATREMIA (low sodium levels).

Often the clinical picture is clouded by the acute illness that induced the crisis, such as urosepsis, pneumonia, or heart attack. Adrenal crisis can often occur in postoperative patients who develop a bilateral adrenal hemorrhage that destroys both adrenal glands.

Individuals in an adrenal crisis need immediate emergency care with fluid and electrolyte resuscitation in addition to intravenous stress doses of steroids. Typically, 100 mg of hydrocortisone are given and then repeated every six hours for the first 24–48 hours. In addition, the underlying illness must be diagnosed and treated.

When a patient has a known case of ADDISON'S DISEASE or another cause of adrenal insufficiency, the treatment is clearer. However, when a patient presents for the first time with these symptoms, the doctor must be astute enough to consider the diagnosis of adrenal crisis and to begin therapy as soon as possible.

Individuals with Addison's disease (hypocortisolism) are the patients most likely to experience an adrenal crisis. People with Addison's disease must be educated about the appropriate stress doses of glucocorticoids they need when ill. In addition, they may need a prescription for intramuscular steroids, to be given at home, if they are unable to keep down their oral steroids due to nausea and/or vomiting. Keeping intramuscular steroids at home is also a good idea if patients live a long distance from medical care. In addition, patients need to know that they must make sure they drink fluids and consume extra salt when they begin to get ill to prevent the syndrome from progressing further. They also need to have a medical identification bracelet or necklace that identifies them as a steroid-using or Addisonian patient.

Emergency doses of cortisone or hydrocortisone are required to counteract an adrenal crisis and to meet the individual's urgent need for cortisol. If the patient remains untreated, an adrenal crisis may be fatal.

See also ADRENAL GLANDS; CORTISOL.

adrenalectomy Removal of an adrenal gland. This procedure is usually necessary because of a cancerous tumor, trauma with hemorrhage (severe bleeding), or a benign tumor (such as a PHEOCHROMOCYTOMA or aldosteronoma) that has caused the patient to experience serious physiological consequences, such as hypertension.

Some physicians have developed a means to remove the adrenal glands laparoscopically, through a small incision in the abdomen. This technique is safer than an open adrenalectomy, and it also costs less money, although it can be a longer procedure for the surgeon to perform. In addition, there is less blood loss with a laparoscopic adrenalectomy. In one published study, the length of the patient stay decreased from 7.4 days to 2.7 days with a laparoscopic adrenalectomy. However, the tumors must be small (less than six to seven centimeters in size) in order to perform this procedure. Laparoscopic surgery is more technically difficult than using a large incision to remove the adrenal gland and should be performed only by experienced surgeons.

If patients have both of their adrenal glands removed, they will develop adrenal insufficiency and require lifelong treatment with steroids in order to avoid an ADRENAL CRISIS. If only one adrenal gland is removed, patients may require only temporary treatment until the other adrenal gland begins functioning properly and handling the task of the body's entire adrenal needs.

See also ADRENAL CORTICAL CANCER; ADRENAL GLANDS; ALDOSTERONISM; CANCER.

Hansen, P., T. Bax, and L. Swanstrom. "Laparoscopic Adrenalectomy: History, Indications, and Current Techniques for a Minimally Invasive Approach to Adrenal Pathology." *Endoscopy* 29, no. 4 (1997): 309–314.

Soulie, Michel, et al. "Retroperitoneal Laparoscopic Adrenalectomy: Clinical Experience in 52 Procedures." *Urology* 56, no. 6 (2000): 921–925.

adrenal fatigue A condition of impaired adrenal function that is not severe enough to reach the level of ADDISON'S DISEASE or ADRENAL INSUFFICIENCY.

Adrenal fatigue is rare. However, some naturopaths and other unscrupulous or uneducated

Syndrome." *Endocrine Reviews* 17, no. 5 (1996): 518–532.

aldosterone A hormone synthesized by the adrenal glands (in the zona glomerulosa), that works to maintain normal electrolyte (mostly sodium and potassium) levels in the body as well as normal blood pressure. Aldosterone prevents the loss of salt and water when the patient is deficient in sodium or has low blood pressure. Aldosterone levels are regulated by the patient's potassium and sodium levels, blood pressure, angiotensin II, and renin as well as by the activity of the person's sympathetic nervous system.

A severe illness may cause the aldosterone levels to fall to very low levels. Either excessive levels of aldosterone (hyperaldosteronism) or insufficient levels of this hormone (hypoaldosteronism) will cause medical problems for the patient.

Aldosterone levels may be measured in both the blood and the urine. Patients who will be undergoing a test for their aldosterone levels may be asked to refrain from taking any diuretic medications, antihypertensive drugs, oral contraceptives, estrogens, and real licorice candy for about four hours to as long as one month before having the test to avoid invalid or confusing test results.

Patients with abnormally high aldosterone levels may have benign adrenal tumors, adrenal cancer, or liver disease, such as cirrhosis, or may have heart failure. Women in their third trimester of pregnancy may also have abnormally high levels of aldosterone.

Very low levels of aldosterone (hypoaldosteronism) may occur due to the surgical removal of the adrenal glands, ADDISON'S DISEASE, TYPE 2 DIABETES, renal tubular acidosis type 4 (TRA IV, also known as hyporeninemic hypoaldosteronism), or the toxemia that can occur in pregnancy.

See also ALDOSTERONISM; BLOOD PRESSURE; CONGENITAL ADRENAL HYPERPLASIA; HORMONES.

aldosteronism Refers to excessive levels of ALDOSTERONE within the bloodstream, a condition classified as primary aldosteronism, secondary aldosteronism, or idiopathic aldosteronism. Most cases of aldosteronism are associated with hypertension.

Primary aldosteronism, also known as primary hyperaldosteronism or Conn's syndrome, is usually caused and characterized by small benign adrenal tumors called aldosteronomas. Patients with primary aldosteronism have hypertension, hypokalemia (low potassium levels), and on occasion, muscle weakness and/or nonspecific malaise. Primary aldosteronism is also one of the few causes of hypertension that can be cured and is seen among only about 1–2 percent of all patients. Women are more likely to experience this condition than men.

Secondary hyperaldosteronism is a more common condition than primary hyperaldosteronism. Possible causes, in addition to hypertension, include heart failure, cirrhosis of the liver, or nephrotic syndrome. This ailment is caused by increased levels of aldosterone that have been induced by low blood pressure or other factors that may impair blood flow and/or the delivery of salt to the kidney. When this occurs, the kidney increases the production of aldosterone in an attempt to save salt and water and thus restore normal blood pressure and blood flow to the kidneys. Doctors can distinguish primary aldosteronism from secondary aldosteronism by measuring the patient's plasma renin levels.

Idiopathic aldosteronism is another form of the medical problem. It is found primarily among men. Patients with this condition are usually hypertensive.

Signs and Symptoms

Many patients with either primary or secondary aldosteronism have no signs or symptoms. If symptoms are present, they may include:

- Headaches
- Frequent urination
- Muscle cramps
- Muscle weakness and paresthesias (pins and needles); these symptoms are less frequently seen

Diagnosis and Treatment

Doctors who suspect aldosteronism will perform a physical examination and take a complete medical history. The patient's blood pressure is usually at least somewhat high. Routine laboratory tests for conditions such as hypokalemia or hypomagnesemia (low magnesium levels) may indicate the

range for males rather than females. In addition, levels of LUTEINIZING HORMONE (LH) will usually be high. FOLLICLE-STIMULATING HORMONE (FSH) levels will be in the normal range. An ultrasound test will reveal that no uterus is present, and it may also reveal the presence of intra-abdominal testes.

To differentiate androgen resistance from either an androgen deficiency or a deficiency of 5-alpha reductase enzyme, physicians may measure the concentrations of both testosterone and dihydrotestosterone (DHT). Individuals who have androgen resistance will have normal ratios of testosterone to dihydrotestosterone. However, with 5-alpha reductase deficiency syndrome, the DHT levels are decreased, and thus the testosterone to DHR ratio is then increased.

If doctors find the presence of intra-abdominal testes, these testes are usually removed after the individual is fully grown as they serve no purpose in an individual with a female gender identity and could later become malignant. After puberty, the individual with complete androgen resistance is given estrogen replacement therapy in order to maintain the female identity.

In rare cases, large doses of male hormone have been given to induce a normal development of the penis. For example, in an article in a 1989 issue of the *Journal of Clinical Endocrinology & Metabolism,* a baby had a very small penis and small testes that could be felt in the labialscrotal folds and had no vagina.

Laboratory tests revealed that the infant had normal 5-alpha reductase activity and androgen resistance. At the ages of $2^1/_2$ and $3^1/_2$ years, this child was given large doses of testosterone, which resulted in the further growth of the penis and also enabled the doctors to correct the child's hypospadias surgically. The doctors in this case hypothesized that the androgen receptor function causing the androgen resistance was successfully treated by the high doses of androgen. It is unknown if the boy later required any future doses of androgen.

When the androgen resistance is mild and the primary sign is infertility, treatment can be aimed at increasing testicular function with medications, such as human chorionic gonadotropin (HCG) and gonadotropin-releasing hormone (GnRH.)

See also AMENORRHEA; HERMAPHRODITISM; HYPOGONADISM; KLINEFELTER SYNDROME; OVARY; TESTES/TESTICLES; TURNER SYNDROME.

For further information on androgen resistance, contact the following organization:

Androgen Insensitivity Syndrome
Support Group (AISSG)
P.O. Box 2148
Duncan, OK 73534-2148
http://www.medhelp.org/ais

Engster, Erica A., M.D. and Antoinette M. Moran, M.D. "Sexual Determination, Sexual Differentiation and Puberty," in *Endocrine Physiology.* Madison, Conn.: Fence Creek Publishing, 1998, 1,237–1,255.

Grino, P. B., et al. "Androgen Resistance Associated with a Qualitative Abnormality of the Androgen Receptor and Responsive to High-Dose Androgen Therapy." *Journal of Clinical Endocrinology & Metabolism* 68, no. 3 (1989): 578–584.

androgens Male hormones that play a key role in sexual development, sexual interest and ability, muscle mass, weight, body hair, energy levels, bone density, and other functions. The most prominent male hormone is TESTOSTERONE, a hormone that affects sexual desire and potency, muscle mass, and the presence of body hair. Women also have some testosterone, although the testosterone levels in females are normally lower than those found in most men. Most androgens in men are produced in the TESTES. Some androgens are also produced by the ADRENAL GLANDS.

When men become androgen deficient for any reason, they will have less muscle mass, decreased bone density (which may lead to OSTEOPOROSIS), sparser body hair, and significantly decreased libido. They may develop ERECTILE DYSFUNCTION, although most men with very low androgen levels may retain a normal ability to have erections but find they have very little sex drive (as well as other medical problems). The voice will remain deep in the adult male because he has already undergone puberty. However, hypogonadal men may develop GYNECOMASTIA, or enlargements of the breast tissue.

from within the endothelium and finally ruptures into the lumen of the blood vessel, exposing lipids and other proteins directly into the bloodstream. This sets off a massive cascade of events that perpetuates the problem locally. The body harnesses the white blood cells, proteins, hormones, interleukins (hormones made by the white blood cells), and the platelets, ultimately creating an occlusive blood clot (thrombus).

This clot results in even more blocking of blood flow and also prevents sufficient oxygen from reaching the affected organ. Depending on the severity of the blood flow blockage, atherosclerosis may lead to a heart attack, stroke, or other serious medical problems.

Experts now know that most myocardial infarctions (heart attacks) occur in blood vessels that are only initially less than 50 percent blocked but, because of less stable caps on the vessel's lining, are much more likely to rupture. In contrast, vessels that have not yet ruptured but have progressed to 80–99 percent occlusion have thick, fibrous coverings which, although they limit blood flow, are much less likely to rupture and lead to a complete occlusion. In addition, as the condition has typically progressed slowly, the tissue that is endangered has often had sufficient time to develop collateral blood vessels upon which to rely. These are vessels that have bypassed the diseased area and, thus, help the organ—and the patient—to survive.

Risk Factors

Risk factors for atherosclerosis, include the following:

- High levels of "bad" cholesterol (low-density lipoproteins)
- Low levels of "good" cholesterol (high-density lipoproteins)
- Obesity
- DIABETES MELLITUS
- Hypertension
- An age of 65 and older (the risk for atherosclerosis increases with age)
- Lack of exercise
- Insulin resistance syndrome
- A family history of atherosclerosis

Diagnosis and Treatment

Atherosclerosis is diagnosed by a physician taking a complete medical history and doing a physical exam. The physician will note any history of prior heart attack, stroke, positive family history of atherosclerosis, symptoms suggesting angina, transient ischemic attack (TIA) (a mini-stroke), or claudification. During the physical examination, the doctor will check for the absence of pulses, presence of bruises, and tobacco-stained fingers and teeth. These may suggest the presence of atherosclerosis.

The doctor will also order laboratory tests to measure factors that contribute to the development of atherosclerosis, such as lipids, glucose, kidney function, C-reactive protein (CRP), homocysteine, and lipoprotein a (Lp a). Individuals who already have atherosclerosis need treatment, usually in the form of medications that improve their lipid profiles, lower their blood pressure, normalize their glucose, and make their platelets less sticky. Some individuals may respond well to taking very low doses (81 mg) of aspirin, such as a baby aspirin, each day.

Most physicians treating patients with atherosclerosis also recommend lifestyle changes. These include stopping smoking, increasing the daily intake of fiber, obtaining at least minimal exercise every day, such as walking (30 minutes, five times per week), and following a heart-healthy nutritional plan.

See also CHOLESTEROL.

of 18 years, the epiphyses are closed and the child has no further potential for growth in height.

If a child has short stature and has growth hormone deficiency, physicians may decide that growth hormone can be prescribed as long as the epiphyses are not yet fused.

See also GROWTH HORMONE.

bone diseases Illnesses that cause an underproduction of bone mass, such as osteoporosis, an overproduction of bone, such as PAGET'S DISEASE and ACROMEGALY, or abnormal bone, seen to varying extents in OSTEOPOROSIS, fibrous dysplasia, and Paget's disease. Disorders of bone may be induced by nonendocrine causes, such as cancer, infection, vitamin deficiency, disorders of cartilage production, and genetic defects.

Bone density can be measured using a variety of techniques, most commonly with dual-energy X-ray absorptiometry scan (DEXA scan). Bone biopsies are helpful in some cases. Blood and urine tests can help to determine the activities of the major cells within the bone, namely, the osteoclasts, which help to break down the bone, and the osteoblasts, which help to create the new bone.

See also CALCIUM BALANCE; OSTEOBLASTS; OSTEOCLASTS; OSTEOMALACIA; OSTEOPENIA; OSTEOPOROSIS; RICKETS.

bone mass measurement A test to determine the density of bone mass. In most cases, bone mass is measured with a dual-energy X-ray absorptiometry (DEXA) scan. Typically, bone measurements are made in the spine and the hip, but they can also be taken in other areas of the body. With primary hyperparathyroidism, cortical bone is lost prior to trabecular bone. Thus bone density is also measured at the wrist, where there is a greater preponderance of cortical bone.

An experienced clinician is needed to interpret these X-rays, because osteoarthritis can falsely elevate readings, especially in the spine. Positioning the patient for the scan is critical, especially if serial data are being compared, as there can be significant differences in bone mineral density if even slightly different areas of a bone are being measured.

Bone mass density can also be tested using what is called quantitative computerized tomography (QCT) scanning and can be estimated with forms of ultrasound. However, this technique is primarily used for screening as opposed to making serial measurements.

Low bone mass density is computed at 2.5 standard deviations versus the peak bone mass seen in a person of the same sex between the ages of 20–30 years old. This is known as the T-score. Another measure, the Z-score, compares a patient's bone density with an age-matched control.

Low bone density is known as OSTEOPOROSIS. Individuals with osteoporosis are at risk for developing serious fractures, particularly fractures of the hip. Sometimes patients have a bone mass density that is not sufficiently low to merit a diagnosis of osteoporosis but that may be low enough to fit the criteria for OSTEOPENIA. Patients with osteopenia also need to work to improve their bone density so that their condition does not further deteriorate to the level of osteoporosis.

See also BONE AGE; CALCIUM BALANCE.

breast-feeding Providing nutrition to newborns, older infants, and sometimes toddlers through milk produced by a woman's breasts. Breast-feeding is also known as lactation. Breast-feeding is strongly encouraged in the United States and other countries as a positive and nutritious way to feed a baby.

Some studies have indicated that women with HYPOCALCEMIA (below-normal levels of calcium in their blood) may actually show improvement in this condition during pregnancy and lactation, largely because of the production of PROLACTIN, a hormone linked to pregnancy, childbirth, and breast-feeding. Some women who were hypocalcemic may even become temporarily hypercalcemic while breast-feeding, as may some women with previously normal calcium blood levels.

A very small number of women, however, such as women with DIABETES MELLITUS who have proliferative retinopathy (an eye disease that may cause blindness), should consider refraining from breast-

Individuals who cannot gain sufficient calcium from their diets may take calcium supplements, usually in tablet form. In addition, prescribed vitamin D (CALCITRIOL) is usually given to such individuals to boost their blood levels of calcium. According to a 2000 article in *Alternative Therapies in Women's Health Archives,* calcium carbonate is the most popular calcium supplement, followed by calcium citrate. Some patients take bonemeal to boost their calcium levels, while others take dolomite, which is a combination of calcium carbonate and magnesium carbonate.

Less popular means of increasing calcium intake include taking supplements of calcium lactate, calcium gluconate, and calcium citrate malate. If intravenous calcium is needed, in the event of a medical emergency, calcium gluconate is usually used.

See also CALCIUM ABSORPTION; HYPERCALCEMIA; HYPOCALCEMIA; HYPOPARATHYROIDISM.

Bove, Lisa Anne. "Restoring Electrolyte Balance: Calcium & Phosphorus" 59, no. 3 (March 1996): 47–51.

Levenson, David J., M.D., and Kevin Al Dhayyat, M.A. "A Practical Analysis of Calcium Supplements." *Alternative Therapies in Women's Health Archives* 2 (April 1, 2000): 28–31.

Tordoff, Michael G. "Calcium: Taste, Intake, and Appetite." *Physiological Reviews* 81, no. 4 (October 1, 2001): 1,567–1,597.

Canadian Diabetes Association (Association Canadienne du Diabète) Formed in 1953, the Canadian Diabetes Association is a nongovernmental advocacy organization for research and education that helps an estimated 2 million Canadians who have diabetes. It has 150 branches throughout the country. The organization also funds research through the Charles H. Best Research Fund. The Canadian Diabetes Association estimates that by 2010, the number of Canadians with diabetes will increase to 3 million.

National Office:

National Life Building
1400-522 University Avenue
Toronto, Ontario M56 2R5
(416) 363-0177 or (800) BANTING (toll-free in Canada)
www.diabetes.ca

Provincial Offices:

British Columbia–Yukon Division
360-1385 West 8th Avenue
Vancouver, BC V6H 3V9
(604) 732-1331 or (800) 665-6526 (toll-free)

Alberta/Northwest Territories Division
1010-10117 Jasper Avenue NW
Edmonton, AB T5J 1W8
(780) 423-1232 or (800) 563-0032 (toll-free)

Saskatchewan Division
104-2301 Avenue C North
Saskatoon, SK S7L 5Z5
(306) 933-1238 or (800) 266-4446 (toll-free)

Manitoba Division
202-110 Broadway Avenue
Winnepeg, MB R3C 0S6
(204) 925-3800 or (800) 226-8464 (toll-free)

Ontario Division
15 Toronto Street
Suite 800
Toronto, ON M5C 2E3
(416) 363-3373 or (800) 226-8464 (toll-free)

New Brunswick Division
165 Regent Street
Suite 3
Fredericton, NB E3B 7B4
(506) 452-9009 or (800) 884-4232 (toll-free)

Nova Scotia Division
6080 Young Street
#101
Halifax, NS B3K 5L2
(902) 453-4232 or (800) 326-7712 (toll-free)

Prince Edward Island Division
Charlottetown Area Health Centre
1 Rochford Street
Charlottetown, PEI C1A 9L2
(902) 894-3005

Newfoundland and Labrador Division
354 Water Street
Suite 217
St. John's, NF A1C 1C4
(709) 754-0953

Osteoporosis is considered to be secondary if other factors have caused this medical problem. Many older people have secondary osteoporosis that was originally caused by hypogonadism, THYROTOXICOSIS, and HYPERPARATHYROIDISM. Some medications, such as GLUCOCORTICOIDS and anticonvulsants, can also cause secondary osteoporosis. Some lifestyle choices, such as alcohol abuse and smoking, can induce secondary osteoporosis as well.

With secondary osteoporosis, a variety of treatment recommendations can be made based on the underlying cause of the osteoporosis. For example, people who smoke should immediately stop smoking. Endocrine diseases and disorders such as hypogonadism, thyrotoxicosis, and hyperparathyroidism can and should be treated. If medications are inducing secondary osteoporosis, physicians may change the drug or lower the dose. For example, if glucocorticoid drugs have caused secondary osteoporosis, physicians may decide to prescribe thiazide diuretics to correct this problem.

Thyroid Disease and the Elderly

Thyroid disease, particularly hypothyroidism, is common among older people. However, as mentioned earlier, the signs and symptoms in older people may be different from those of younger people. In addition, elderly individuals may present with signs and symptoms commonly associated with other diseases of aging, such as mental confusion and paranoia (often associated with Alzheimer's disease or dementia), muscle stiffness (associated with arthritis), and heart irregularities. Older people may also present with depression, which may be masking the underlying problem of hypothyroidism. (Depression may also coexist with thyroid disease.)

Hypothyroidism in the elderly may also coexist with hypertension and hyperlipidemia. In its most severe manifestation, hypothyroidism presents as a myxedema coma, a clinical syndrome with a rapid onset that is potentially fatal to the patient. Almost all individuals who lapse into myxedema are elderly people with hypothyroidism.

Hyperthyroidism (excessive levels of thyroid hormone) is also a problem for some elderly individuals. It too may present differently in older individuals than in younger people. For example, mental decline may be one indicator of hyperthyroidism, which is not seen in middle-aged or younger adults with hyperthyroidism. Weakness is another sign of hyperthyroidism among the aged. The older person with hyperthyroidism may appear listless and depressed, unlike the younger individual with the same disease, who is overactive, nervous, and even manic.

Elderly women with hyperthyroidism have a three times greater risk of having fractures than women of the same age with normal TSH levels. Even a history of having hyperthyroidism is associated with twice the risk of developing fractures.

In general, physicians should treat patients based on their physiological age rather than their chronological age. Some patients who are 70 years old may have no illnesses and may be physically fit, at an ideal body weight, and able to tolerate most medications and/or procedures. These patients are what physicians refer to as 70 going on 50.

Obviously, the opposite is also true. A 40-year-old patient may have diabetes mellitus with multiple complications, such as diabetic nephropathy and diabetic neuropathy, and may be unable to tolerate certain medications and/or procedures well. This patient is considered by doctors to be age 40 going on age 70.

See also DIABETES MELLITUS; FRACTURES; TYPE 1 DIABETES.

Bauer, Douglas C., M.D., et al. "Risk for Fracture in Women with Low Serum Levels of Thyroid-Stimulating Hormone." *Annals of Internal Medicine* 134, no. 7 (2001): 561–568.

Boonen, S., J. Aerssens, and J. Dequeker. "Age-Related Endocrine Deficiencies and Fractures of the Proximal Femur. I. Implications of Growth Hormone Deficiency in the Elderly." *Journal of Endocrinology* 149, no. 1 (1996): 7–12.

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Patients typically have elevated triglyceride levels in the 200–500 mg/dl range with lower-than-normal high-density lipoproteins (a condition called hypoalphalipoproteinemia). They also have normal or modestly elevated total cholesterol or LDL cholesterol. Typically, LDL levels cannot be measured accurately as is done with most standard lipid profiles but, instead, must be measured directly with radioimmunoassay.

The first therapy is good medical nutrition therapy, with attention to lowering the carbohydrate content in meals. Alcohol is removed from the diet. Exercise will help tremendously as well. The intent of the nutrition and exercise is to have patients get their weight as close to ideal as possible. However, often diet and exercise are inadequate and pharmacological therapy is employed as well.

The first-line medication therapy is usually a fibric acid derivative, such as gemfibrozil (Lopid), fenofibrate (Tricor) or a form of nicotinic acid such as an intermediate-release product like Niaspan. If the patient's triglyceride level is in the lower range of 200–350, then HMG CoA reductase inhibitors are often employed, such as simvastatin (Zocor), pravastatin (Pravachol), atorvastatin (Lipitor), lovastatin (Mesvacor), or fluvastatin (Lescol-XL). Bile acid sequestrants are to be avoided in these patients, because they may actually increase the triglyceride levels.

In postmenopausal women, estrogen therapy may need to be discontinued. Younger woman taking ORAL CONTRACEPTIVES may need to discontinue them.

The aim of the doctor is for the patient to have the condition corrected as much as possible. Patients with diabetes need to attain a normal hemoglobin A1c, and patients with hypothyroidism need to achieve normal thyroid-stimulating hormone (TSH) levels.

familial hypocalciuric hypercalcemia (FHH) A hereditary (autosomal dominant) form of hypercalcemia in which the individual has high blood levels of calcium, while at the same time, he or she has low urinary calcium levels and normal levels of parathyroid hormone in the blood. Parathyroid hormone is produced by the parathyroid glands and it regulates calcium levels in the bloodstream.

The basic cause of familial hypocalciuric hypercalcemia is an inactivating mutation in the calcium-sensing receptor gene, which typically causes fewer calcium receptors that are expressed on parathyroid tissue and in the kidney. Thus, in the parathyroid glands, which are the glands located behind the thyroid, this defect causes the gland to be exposed to higher-than-normal levels of calcium to the appropriately suppressed parathyroid hormone secretion. At the same time, in the kidney, excessive calcium is absorbed.

Most people with familial hypocalciuric hypercalcemia have no signs or symptoms at all and do not require any treatment. Doctors must carefully differentiate these patients from those with true primary hyperparathyroidism, as patients with familial hypocalciuric hypercalcemia do not require surgery. If the physician does not measure the urinary calcium levels, he or she could misdiagnose patients with FHH, as patients may have high-normal or even slightly elevated intact parathyroid hormone levels.

See also HYPERCALCEMIA; HYPERPARATHYROIDISM; PARATHYROID CANCER.

feedback loops A complex process, key to the functioning of endocrine glands, in which sensors recognize changes to the individual or to the environment and, as a result, cause higher or lower levels of hormones to be secreted.

Feedback loops are analogous to a thermostat or other device that seeks to maintain a certain homeostatic level. For example, say a thermostat in a house is set at 70 degrees. When the inside temperature falls below that temperature, the change causes a sensor to order the heat to turn on. If a home has both heat and air-conditioning, the thermostat was set at 70 degrees, and the temperature rose to 71 degrees, the air-conditioning would come on.

Similarly, if the blood levels of hormones rise to a given level, feedback loops will send a message to the body to cut back on their production. If they fall below a certain level, feedback loops enable an increase in their production. For instance, cells within the pancreas measure or sense the ambient glucose concentration in the blood. Then the beta cells of the pancreas secrete an appropriate amount of insulin while the alpha cells secrete an appropriate

The cause of gestational diabetes is unknown, although experts speculate that the many hormonal changes that are experienced during pregnancy are a factor. Women who develop GDM may also have a genetic predisposition to the development of diabetes mellitus and the stress of the pregnancy may be allowing the problem to manifest itself. Another argument in favor of a genetic component to GDM is that women who were born to mothers who had GDM will present with GDM more frequently than women born to mothers not afflicted with the condition.

Women with gestational diabetes have a dramatically higher risk of developing Type 2 diabetes 15–20 years after the onset of GDM. This risk is the highest among Hispanic, Native-American, and African-American women who have had gestational diabetes.

Other risk factors for developing GDM are age (women over age 30 have a greater risk than younger woman) and the number of children that a woman has borne (the risk increases with each subsequent pregnancy).

Other risk factors for experiencing GDM include:

- A family history of diabetes
- Gestational diabetes with previous pregnancies
- Previous births of very large infants (heavier than 9 pounds)
- Prior problem pregnancies (either stillbirths or miscarriages)

Screening Pregnant Women for GDM

All pregnant women should be screened for risk factors for GDM in their first prenatal visit, according to the AMERICAN DIABETES ASSOCIATION. Physicians should consider if risk factors such as obesity, a previous history of GDM, or a family history of the disease are present. If a woman is believed to be at high risk, she should be screened prior to any planned pregnancy or very early in the pregnancy as well as at intervals throughout the pregnancy, at the discretion of the obstetrician. Typically, this screening is performed by measuring the woman's blood glucose levels or with a glucose tolerance test.

All women should be rescreened for GDM between the 24th and 28th weeks of pregnancy, unless they lack all risk factors for GDM.

Diagnosis and Treatment

The diagnosis is made either by an in-office glucose test if the glucose levels are very high or by a formal glucose tolerance test performed by a laboratory. The screening test done at 24–28 weeks of pregnancy is followed by a formal glucose tolerance test to make the diagnosis of gestational diabetes.

If testing confirms GDM, women should be referred to a diabetes care team within 48 hours of the initial diagnosis so they can receive complete information and recommendations on their particular cases. This team should include, at a minimum, the obstetrician, an endocrinologist, and a registered dietitian. Most women with GDM should also learn how to test their own blood and use the information from blood glucose testing to make appropriate meal-planning and health decisions. In very mild cases of GDM, changes in caloric and carbohydrate intake can control the diabetes. In other cases, INSULIN is required. Most experts believe that women with GDM who require insulin should test their blood at least two to four times per day.

In other cases (about 30–60 percent) insulin is required. As the pregnancy progresses, women may need higher doses of insulin. Several studies have shown the efficacy of oral hypoglycemia medications in the treatment of GDM. However, as of this writing, none of the oral medications have been approved by the Food and Drug Administration (FDA) for use in pregnancy; thus, the only approved therapy other than nutrition and exercise is injected insulin.

Lifestyle changes will also be recommended to women with GDM. Nearly all women with GDM need to eat three meals and three snacks per day at regular intervals, with a small breakfast to avoid developing a midmorning HYPERGLYCEMIA. The physician may also prescribe an exercise plan that includes non-weight-bearing types of exercises, such as walking or bicycling.

After Delivery

In most cases, women with GDM are no longer diabetic after the delivery of their babies. Only

nant woman or new mother with propylthiouricil (PTU). It is less likely to cross into the placenta than other drugs, and it is also less likely to appear in breast milk than are other antithyroid medications.

See also HASHIMOTO'S THYROIDITIS; THYROID BLOOD TESTS; THYROID-STIMULATING HORMONE; THYROID STORM.

For further information on Graves' disease, contact the following organization:

National Graves' Disease Foundation
P.O. Box 1969
Brevard, NC 28712
(828) 877-5251
http://www.ngdf.org

Imrie, Helen, et al. "Evidence for a Graves' Disease Susceptibility Locus at Chromosome Xp11 in a United Kingdom Population." *Journal of Clinical Endocrinology & Metabolism* 86, no. 2 (2001): 626–630.

Rivkees, Scott A., Charles Sklar, and Michael Freemark. "The Management of Graves' Disease in Children, With Special Emphasis on Radioiodine Treatment." *Journal of Clinical Endocrinology and Metabolism* 83, no. 11 (1998): 3,767–3,777.

Weetman, Anthony P., M.D. "Graves' Disease." *New England Journal of Medicine* 343, no. 17 (October 26, 2000): 1,236–1,248.

growth disorders Medical problems that are often caused by either inadequate or excessive levels of growth hormone. The underlying cause is often a problem with the pituitary gland.

Growth hormone deficiency refers to lower-than-normal levels of circulating growth hormone and results in short stature, such as DWARFISM. When ACROMEGALY occurs before puberty, it leads to excessive growth and GIGANTISM.

See also GENETIC SHORT STATURE; GROWTH HORMONE.

growth hormone (GH) A protein hormone synthesized by the PITUITARY GLAND that enables individuals to grow to an adult height. Of the seven anterior pituitary hormones, GH is produced in the greatest amounts. Growth hormone is secreted throughout life, although the amount that is secreted decreases as individuals age. Most of the effects of GH are mediated by insulin-like growth factor 1.

In addition to leading to the linear growth of a child, growth hormone also helps with the breakdown of fat (lipolysis), stimulates protein synthesis, and helps the body to retain needed sodium and water. Growth hormone is produced by individuals at all ages because it is also needed for the body to repair microscopic tissue damage properly. Peak levels of growth hormone production usually occur in the evening, when individuals are asleep.

A tumor of the pituitary gland may cause the excessive production of growth hormone, resulting in GIGANTISM if it occurs before puberty and is not treated and ACROMEGALY if it occurs after puberty. An insufficiency of growth hormone, on the other hand, may cause short stature, as may cause some rare cases of DWARFISM. (Dwarfism is usually caused by a genetic mutation rather than by a lack of growth hormone.)

It is controversial, but some children—especially males—who are below normal in height have been treated with growth hormone. Although growth hormone does not make them become tall, it generally allows them to achieve a greater height than they otherwise would have attained. If administered, growth hormone must be given to children prior to the onset of puberty and before the endplates in their bones (the epiphyses) close for the best effect.

Some examples of growth hormones that are used include:

- Genotropen
- Norditropen
- Humatrope
- Serostim

Growth hormone is also sometimes used in adults who have growth hormone deficiency. It will help to increase their strength and muscle mass, decrease their percentage of body fat, increase their bone density, and in general, increase their overall sense of well-being.

See also AIDS; DELAYED PUBERTY; EARLY PUBERTY; GROWTH DISORDERS; GROWTH HORMONE DEFICIENCY.

hypercalcemia have cancer. (Hyperparathyroidism and cancer together account for about 90 percent of all causes of hypercalcemia.) When a cancerous tumor is identified as the cause of hypercalcemia, it is classified as either a humoral hypercalcemia of malignancy (HHM) or as a non-HHM case.

Many diseases in which the body forms granulomas can lead to hypercalcemia. A granuloma refers to a specific clustering of white blood cell monocytes that have gone into various body tissues and have become tissue macrophages. This may occur in diseases such as tuberculosis, sarcoidosis, and histoplasmosis.

Other medical problems can sometimes cause hypercalcemia. Hyperthyroidism (overactive thyroid) from any cause can lead to mild hypercalcemia as can simple immobilization (bed rest), although this is typically seen only in young patients (such as an adolescent with paraplegia due to a car crash). Inflammatory diseases may also sometimes cause hypercalcemia. Even silicone implants may sometimes induce the condition.

Rare causes of hypercalcemia include ADDISON'S DISEASE, PHEOCHROMOCYTOMA, PAGET'S DISEASE, sarcoidosis, and rhabdomyolysis.

Sometimes medications that are taken for other medical problems can lead to the development of hypercalcemia. For example, drugs such as thiazide diuretics (hydrochlorothiazide) and lithium may cause mild cases of the condition. Excessive doses of theophylline, taken for asthma, can also lead to hypercalcemia, as can the use of tamoxifen, which is given to women with breast cancer and bone metastases. Retinoic acid given to cancer patients may also lead to the condition.

There are other causes of hypercalcemia. For example, an ingestion of excessive calcium and/or VITAMIN D can also lead to this condition. Years ago, before more potent drugs such as the histamine 2-blockers and proton pump inhibitors were available to patients with heartburn, dyspepsia, and ulcers, these medical problems were often treated with large doses of calcium-containing antacids. Many of these patients subsequently developed what was known as MILK-ALKALI SYNDROME with hypercalcemia. Now this syndrome is not seen frequently, although it can occur among patients who chronically use calcium-containing antacids. (Such patients should consult with a gastroenterologist to find out the underlying cause of their digestive disorder.)

Individuals who take very high levels of other vitamins, such as vitamin A, may also induce hypercalcemia.

Treatment of Hypercalcemia

Typically, the treatment of hypercalcemia is aimed at the underlying cause, once it has been identified. However, if the hypercalcemia is severe and has led to DEHYDRATION and mental status changes in the patient, then hospitalization and immediate treatment is usually needed. Hospitalized patients with hypercalcemia are usually given intravenous fluids in the form of normal saline (0.9 percent sodium chloride solution, which is basically salt water). They are also often given a loop diuretic such as furosemide (Lasix) and an intravenous BISPHOSPHONATE medication, usually pamidronate (Aredia). Patients with hypercalcemia may also be given steroid medications, such as prednisone. CALCITONIN may also be added to the therapy if the other medications fail or if the patient has pain that is secondary to a fracture. Calcitonin will decrease the patient's blood calcium levels. Often physicians treat patients with a combination of medications.

Once the patient has stabilized from an emergency condition, doctors seek to identify and treat the underlying cause of the hypercalcemia. Surgical removal of a parathyroid adenoma may be necessary as would be treatment of the underlying cancer or medical therapy for causal conditions such as sarcoidosis.

See also CALCIUM ABSORPTION; CALCIUM BALANCE; HYPERPARATHYROIDISM; HYPOCALCEMIA.

Bilezikian, John P. "Management of Hypercalcemia." *Journal of Clinical Endocrinology & Metabolism* 77, no. 6 (1993): 1,445–1,449.

Sanders, Leonard, R., M.D. "Hypercalcemia," in *Endocrine Secrets,* 3d ed. Philadelphia, Pa.: Hanley & Belfus, Inc., 2002, 66–71.

hypercholesterolemia See CHOLESTEROL; FAMILIAL HYPERCHOLESTEROLEMIA.

In some cases, lithium therapy that is given to patients who are bipolar (manic-depressive) may also induce hyperparathyroidism.

Secondary hyperparathyroidism is caused by a decrease in calcium levels (HYPOCALCEMIA). This may stem from any process that impairs the body's ability to absorb or retain calcium, such as an underlying kidney disease; vitamin D deficiency (as in RICKETS in children or OSTEOMALACIA in adults); malabsorption syndromes due to pancreatitis, ulcerative colitis, Crohn's disease, or other gut problems; or leakage of calcium from the kidneys into the urine (renal hypercalciuria).

Signs and Symptoms

Most patients with primary hyperparathyroidism are asymptomatic. After they are diagnosed and treated, however, some patients in retrospect will realize that they had some symptoms. Individuals vary in how they present with hyperparathyroidism, but some common signs and symptoms of this medical problem include:

- Back pain
- Joint pain
- Fatigue
- Upper abdominal pain
- Muscle weakness
- Increased thirst
- Increased urination
- Itching skin
- Bone pain
- Muscle and tongue fasciculations (tiny involuntary muscle contractions that cause the muscle to quiver)
- Band keratopathy (usually noted only by a special examination by an eye specialist)

Diagnosis and Treatment

Hyperparathyroidism is diagnosed based on the patient's medical history and physical examination as well as on laboratory tests of calcium, phosphorus, parathyroid hormone, and kidney function. Typically, total calcium or ionized calcium levels are elevated, although more frequently normocalcemic hyperparathyroidism can be diagnosed. Increased levels of protein that bind to calcium can falsely elevate the total serum calcium level, but this can be sorted out by measuring the nonbound or ionized calcium.

Serum phosphorus levels are often decreased in patients with primary hyperparathyroidism, while serum alkaline phosphatase levels may be increased. The confirmatory test is measurement of the intact parathyroid hormone level, which is nearly always elevated. Again, though, in very early cases, it may run at the upper limits of the normal level.

Patients with hyperparathyroidism may have reduced BONE DENSITY, especially of the forearm, taken in a DEXA scan. (There is more cortical bone in the forearm, and this bone decreases sooner than the other types of bone do.)

Primary hyperparathyroidism can be mistakenly diagnosed in patients with familial hypercalcemic hypocalciuria. In this condition, patients have elevated calcium levels, normal or high-normal parathyroid hormone levels, but very low excretion of calcium in the urine. This is an inherited defect in which patients' bodies do not properly sense blood calcium levels. They do not develop osteoporosis, kidney stones, myopathy, or any of the complications of hyperparathyroidism and thus do not need treatment, especially parathyroidectomy.

This condition is typically excluded by measuring a 24-hour urine for calcium. The patient collects all urine that is excreted over a 24-hour period, to be evaluated by a laboratory. Normally patients will excrete two to four milligrams per kilogram of calcium in the urine per day. Patients with hyperparathyroidism excrete at least this much and often much more than patients with familial hypercalcemic hypocalciuria, who always excrete much less.

Surgical Treatment

The best therapy for primary hyperparathyroidism is surgery. Indications for surgery include kidney stones, bone loss (especially osteoporosis), severe hypercalciuria, and total calcium levels that are greater than 11 to 12 mg/dl. On occasion, surgery may also be attempted if a patient is suffering with

aches and pains and/or cognitive dysfunction that cannot be explained by any other mechanism.

Patients must find a surgeon who has significant experience in parathyroid surgery. Using an experienced surgeon is essential because finding the offending gland may be difficult and distinguishing between a small adenoma and hyperplasia at the time of surgery is often difficult. In addition, the parathyroids' blood supply is limited. Excess damage to the area can lead to permanent hypoparathyroidism, a condition that must be treated with both calcium and vitamin D. Also, the recurrent laryngeal nerves are in this area. Damage to one or both of them can lead to chronic hoarseness or vocal cord paralysis.

In the case of parathyroid hyperplasia, the surgeon will often remove three-and-one-half of the four glands and transplant one-half of one gland into the forearm. Some of the other parathyroid tissue can be frozen and preserved for future use if needed.

In the rare cases of cancer, as much as possible of the cancer should be excised at the time of surgery, as it does not respond well to radiation or chemotherapy. An experienced surgeon will locate the offending adenoma in about 90 percent of the cases.

Preoperative imaging is not necessary, but it is being done more frequently as techniques have improved. As of this writing, the most sensitive imaging seems to be a nuclear medicine scan called a sestamibi subtraction scan. This scan may be particularly advisable in the cases of older and sicker patients, as it may help to localize the surgeon's efforts and also shorten the duration of the operation. In addition, it can lead to very directed and limited small incision surgery under local anesthesia with the use of intraoperative nuclear medicine probes, although this is not standard therapy as of this writing.

Tertiary hyperparathyroidism requires the adjustment of dosages of calcium and vitamin D supplements and often parathyroid surgery as well.

Nonsurgical Therapy

Patients who do not have any indications for surgery can be followed conservatively with close attention paid to blood calcium levels, kidney function, and bone density. Two large trials have attempted to determine which patients will require surgery, and both have failed to achieve that goal.

Some patients will go for many years without any significant signs and symptoms of hyperparathyroidism, while others will progress rapidly. Thus, patients are counseled to use a moderate amount of calcium and salt and to force fluids in order to keep the urine dilute and decrease the risk of developing kidney stones.

Patients who have secondary hyperparathyroidism may be treated with calcium and vitamin D to correct the deficiencies. They may also be treated with cinacalcet (Sensipar, Amgen). Cinacalcet is the first drug in a new class of agents called calcimimetics. Cinacalcet sensitizes calcium receptors in the parathyroid gland (the parathyroid glands perceive there is more calcium in the system) and causes direct lowering of parathyroid hormone. It is approved by the Food and Drug Administration (FDA) for the treatment of secondary hyperparathyroidism in patients with chronic kidney disease.

See also CALCIUM BALANCE; PARATHYROID GLANDS.

Dang, Devra K. "Cinacalcet." *Formulary* 39 (2004): 482–489.

Lips, Paul. "Vitamin D Deficiency and Secondary Hypoparathyroidism in the Elderly: Consequences for Bone Loss and Fractures and Therapeutic Implications." *Endocrine Reviews* 22, no. 4 (2001): 477–501.

Marx, Stephen J., M.D. "Hyperparathyroid and Hypoparathyroid Disorders." *New England Journal of Medicine* 343, no. 25 (December 21, 2000): 1,863–1,875.

hyperphosphatemia/hypophosphatemia Abnormally high levels of phosphorus in the blood (hyperphosphatemia) or abnormally low blood levels of phosphorus (hypophosphatemia). Hypophosphatemia is a rare condition that is most commonly seen in patients who suffer from starvation/malnutrition or alcoholism. Because phosphates are ubiquitous in the diets of most Americans, one meal can usually restore levels to normal. In cases of primary hypophosphatemia in which phosphorus is lost in the urine, treatments become more complicated.

es. If the hyponatremia is not resolved, patients may further worsen to the point of seizures, coma, brain damage, and even death.

Diagnosis and Treatment

Physicians will suspect that a patient may have hyponatremia based on the clinical symptoms and medical history, especially with respect to medications that were recently taken. Hyponatremia is diagnosed by blood testing that reveals a lower-than-normal serum sodium concentration.

To treat hyponatremia, the patient is typically given an intravenous sodium chloride containing solution with a concentration of sodium that is greater than what exists in the individual's bloodstream, even to the point of using very small doses of hypertonic saline (a 3 percent sodium chloride solution). On occasion, a loop diuretic, such as furosemide, may be used. Often free water must be withheld from the patient as well; patients are not allowed to drink as they wish, and water intake is limited to less than 1 L or sometimes 0.5 liter per day. If the case is a mild one, patients may be observed only, while water is withheld.

See also HYPERGLYCEMIA.

Adrogue Horacio, J., M.D., and Nicolaos E. Masias, M.D. "Hyponatremia." *New England Journal of Medicine* 342, no. 21 (May 25, 2000): 1,581–1,589.

hypoparathyroidism A condition in which there is inadequate parathyroid hormone in the bloodstream as well as in the bone, the gut, the kidneys, and other organs. Parathyroid hormone is produced by the parathyroids, which are glands embedded in the neck behind the thyroid gland.

If hypoparathyroidism becomes severe, the patient develops a condition called HYPOCALCEMIA and, in extreme cases, may have seizures. Without treatment after seizures from hypocalcemia, the patient may die. This occurs for several reasons. One is that without adequate parathyroid activity in the bloodstream, the kidneys cannot hold onto needed calcium so excessive calcium is lost via the urine. Some excess calcium may be deposited into the tissues of the kidneys and lead to calcification of the kidneys (nephrocalcinosis) or to the development of kidney stones (nephrolithiasis). Thus, ironically hypocalcemia can cause calcification.

Causes of Hypoparathyroidism

The most common cause of this condition is surgery on the thyroid or parathyroid glands or other neck surgery that causes the removal of or damage to the parathyroid glands. In some cases, hypoparathyroidism is caused by the autoimmune destruction of the parathyroid glands. Autoimmune hypoparathyroidism may exist on its own or as a part of a deficiency syndrome involving many organs. In rare cases, hypoparathyroidism results from radioactive iodine treatment given to treat hyperparathyroidism (a condition of excessively high levels of parathyroid hormone).

Rarely severe deficiencies of magnesium, a condition seen in malnourished patients and alcoholics, can lead to a state of hypoparathyroidism and hypocalcemia (abnormally low blood levels of calcium).

Signs and Symptoms of Hypoparathyroidism

Patients with hypoparathyroidism may experience some or all of the following signs and symptoms:

- Muscle cramps
- Abdominal pain
- Tingling in the feet, hands, and face
- Spasms in the hands or feet

In severe cases, patients may experience seizures or convulsions caused by TETANY, a dangerous condition of extremely low calcium blood levels.

Diagnosis and Treatment

Physicians diagnose hypoparathyroidism based on the patient's medical history, particularly any past history of any form of neck surgery, as well as the apparent presence of hypocalcemia. Patients with hypocalcemia may respond with a characteristic facial twitch when the cheekbone is tapped (CHVOSTEK'S SIGN). Others may show TROUSSEAU'S SIGN, an arm spasm and cramp that results from a test using a blood pressure cuff.

The doctor will also order laboratory tests of the patient's serum calcium levels. Low levels indicate

drier, and doughier), and slow heart rate (bradycardia), features not commonly found among people with depression alone. However, a person with hypothyroidism can also have depression, complicating the diagnosis and treatment. Treating the hypothyroidism is critical because antidepressant medications do not work optimally in an untreated hypothyroid patient.

Signs and Symptoms of Hypothyroidism

There are several common symptoms of hypothyroidism. However, children age five and under who are hypothyroid may have no apparent symptoms (although they will often have decreased growth). Adolescents may have only a few signs and symptoms, such as facial puffiness and fatigue. Doctors should not prescribe thyroid hormone to a patient without checking his or her blood to verify that the thyroid levels are too low. The patient may have another medical problem altogether, and the administration of unnecessary thyroid hormones could create other medical problems, such as iatrogenic HYPERTHYROIDISM.

The general symptoms and signs of hypothyroidism include:

- Fatigue
- Cold intolerance (patients with hypothyroidism get cold faster and the cold bothers them more than others)
- Chronic constipation
- Decreased appetite
- Apparent (or actual) depression
- Muscle cramping and weakness, especially of the proximal muscles
- Anemia
- Reduced sexual libido
- Decreased perspiration
- Paresthesias (pins and needles feelings)
- Carpal and tarsal tunnel syndromes
- Weight increase/difficulty with weight loss
- Sleepiness
- Decreased memory/concentration
- Hoarseness (thickened vocal cords)
- Slowed movements
- Thinning of the outer third of the eyebrows (also known as Queen Ann's eyebrow)
- High cholesterol levels (about 56 percent of patients experience this sign)
- Skin that is cool and dry to the touch
- Puffy face
- Failure to ovulate (ANOVULATION)
- Excessively heavy menses (menorrhagia)
- Enlarged tongue (macroglossia)

If hypothyroidism is severe and continues untreated, the following signs and symptoms may occur:

- HYPOGLYCEMIA (low blood sugar)
- Hypothermia (below-normal body temperature)
- Hypoventilation (below-normal breathing rate)
- HYPONATREMIA (inadequate levels of sodium in the blood)
- Water retention
- Bradycardia (slow heartbeat)
- Depression
- Shock
- MYXEDEMA COMA

Some studies have shown other indicators of hypothyroidism. In a 1997 issue of *The Physician and Sportsmedicine,* the authors reported on the case of a male athlete with knee and shoulder pain who had been diagnosed with tendonitis and fibromyalgia. Routine blood tests showed a highly elevated TSH level. The patient was treated with levothyroxine, and his problems resolved.

Said the authors of this study, "Previous musculoskeletal symptoms and fatigue did not recur. He has since attained personal best race times and has had his best triathlon season." They concluded that "the dramatic improvement and complete resolution of the symptoms with thyroid replacement therapy after failure with other medical treatments suggest that normal tendon healing is impaired in hypothyroidism."

diagnosing the condition is easier if there is any family history of KS. Blood tests of testosterone levels (serum testosterone) will reveal extremely low testosterone levels in males, while serum estradiol will be extremely low in females with KS. A MAGNETIC RESONANCE IMAGING (MRI) scan of the skull will reveal the presence of abnormal olfactory systems, a very common condition among as many as 75 percent of patients with KS.

Other tests that may be performed include a dual-energy X-ray absorptiometry (DEXA) scan to determine if the patient has osteoporosis and an echocardiogram to identify the presence of congenital heart disease.

Patients with KS are usually treated with hormone replacement therapy to restore normal secondary sexual characteristics and fertility and to normalize bone and muscle mass. Males are treated with testosterone replacement and females with estradiol replacement. In women, estrogen is given alone initially, to maximize breast development, and progestational agents are added later. When fertility is desired, GnRH can be used in males and women, although in men, often human chorionic gonadatropin (HCG) is used, followed by FSH.

If other conditions are present (such as osteoporosis, heart disease, and so forth), those medical problems are treated.

See also KLINEFELTER SYNDROME.

Tritos, Nicholas A., M.D. "Kallmann Syndrome and Idiopathic Hypogonadotropic Hypogonadism," Available online. URL: http://www.emedicine.com/med/topic1216.htm Downloaded on December 15, 2003.

Wynbrandt, James, and Mark D. Ludman. *The Encyclopedia of Genetic Disorders and Birth Defects,* 2d ed. New York: Facts On File, Inc., 2000.

Klinefelter syndrome An extra X chromosome that occurs in about one in 1,000 baby boys. There can be multiple X chromosomes. The greater the number of X chromosomes present, the more the physical abnormalities. Patients with Klinefelter syndrome usually develop HYPOGONADISM and INFERTILITY due to the absence of sperm in the semen (azoospermia) and other health problems. Dr. Harry Klinefelter first identified the condition in 1942.

Signs and Symptoms

The key feature for virtually all patients with Klinefelter syndrome is small and firm testes. Patients may also have GYNECOMASTIA (enlarged breasts), which is present in 50–75 percent of patients; decreased pubic hair (40–60 percent of patients); and decreased facial hair (60–80 percent). A small penis (MICROPENIS) is present in about 10–25 percent of these patients. Patients with Klinefelter syndrome do not undergo the normal changes of male puberty. Nearly 100 percent are infertile. They also have decreased muscle mass in comparison with their peers. Some males with Klinefelter syndrome are taller than average.

Associated Illnesses

Patients with Klinefelter syndrome have a high risk of developing tumors. Some experts believe that the disease itself may be caused by a tumor. Although breast cancer is rare among men, patients with Klinefelter syndrome have a 20 times greater risk of developing breast cancer than do other men. However, experts say that screening mammography for men with Klinefelter syndrome is not usually recommended since the occurrence of breast cancer is still extremely rare.

Men with Klinefelter syndrome have an increased risk for developing autoimmune disorders, such as rheumatoid arthritis, systemic lupus erythematous, and Sjögren's syndrome. Androgens may be protective against autoimmune disorders. Since men with Klinefelter syndrome have low levels of testosterone, this may be the reason for their greater incidence of autoimmune diseases. Another possible cause may be lymphocyte abnormalities found in these patients.

Patients with Klinefelter syndrome have an increased risk of learning disabilities such as dyslexia and attention deficit disorder. They may also exhibit psychiatric problems such as anxiety disorder, depression, and even psychotic disorders. Boys with Klinefelter syndrome have difficulty with peer groups and are less interested in girls than other boys. Said authors Cynthia Smyth and William Bremner in their 1998 article on

LH is secreted in a pulsatile fashion. In spite of this, the normal levels in men fall within a fairly narrow range. As with all pituitary hormones, the LH level must be interpreted in the context of the associated testosterone level or semen analysis. In women, marked variations in LH secretion occur throughout the menstrual cycle. Physicians must therefore interpret a woman's LH levels within the context of the specific time of her cycle as well as consider her concomitant estradiol levels.

Luteinizing hormone is involved in a complex FEEDBACK LOOP between the gonad (ovary or testicle), the pituitary gland, and the hypothalamus. For example, during a woman's menstrual cycle, blood LH levels increase, and this, in turn, causes the ovary to produce estradiol. When estradiol levels reach a certain point within the body, the estradiol and the gonadotropin-releasing hormone (GnRH) cause a sharp increase in LH production (the preovulatory surge). This increase causes ovulation to occur. The LH levels reach a certain point, and then they decline.

When women go through menopause, they may experience periodic HOT FLASHES, which are surges of luteinizing hormone in the bloodstream. HORMONE REPLACEMENT THERAPY (HRT) may resolve this symptom, although each woman should discuss with her own gynecologist whether or not to take HRT.

Deficiencies of LH in women of childbearing age or in men may cause INFERTILITY. If estradiol or testosterone levels are low and a concomitant measure of LH is also low, this indicates a possible hypothalamic or pituitary problem. If so, individuals who wish to have children may be treated with hormones, such as luteinizing hormone-releasing hormone (LHRH). Sometimes LH is very low or altogether absent, as in conditions such as hypogonadotropic HYPOGONADISM, KALLMANN'S SYNDROME, or other forms of secondary hypogonadism.

Tumors that secrete excessive amounts of LH are rare. However, inappropriate levels of LH in the blood are seen in a condition called POLYCYSTIC OVARY SYNDROME.

Medical science has enabled doctors to manipulate LH production to the ends of patients. For example, ORAL CONTRACEPTIVES block the LH surge that precedes the release of an egg and thus prevent pregnancy.

See also FOLLICLE-STIMULATING HORMONE.

Griffin, James E., and Ojeda, Sergio R. *Textbook of Endocrine Physiology,* 4th ed. New York: Oxford University Press, 2000.

microcephaly Unusually small head size, usually in a newborn infant. Microcephaly may be an indication of a developmental delay and always implies an abnormally small brain (microencephaly). Severe placental insufficiency due to poorly controlled DIABETES MELLITUS may lead to microcephaly. Organic acidurias such as HOMOCYSTINURIA may also lead to microcephaly.

Standard head circumferences have been developed for children between the ages of birth and 18 years old. Special head curve charts are available for children with NEUROFIBROMATOSIS TYPE 1, achondroplasia, and Williams syndrome.

See also MACROCEPHALY.

micropenis An unusually small-sized penis, often caused by a genetic disorder. The male infant with a micropenis has a penis that is less than 2.5 centimeters in length and 0.9 cm in diameter. It can be caused by decreased exposure to TESTOSTERONE in the second to third trimesters of pregnancy, insensitivity to androgens, or deficient GROWTH HORMONE or LUTEINIZING HORMONE.

Some infants are candidates for gender reassignment, which means that they are raised as girls. However, this is a highly controversial practice. Many males with Klinefelter syndrome, although not all, have very small penises.

According to Dr. C. R. J. Woodhouse in his 1998 article in *Urology,* some boys with micropenis have this problem due to an isolated growth hormone deficiency, which can be treated with human recombinant growth hormone (HRH). Although this may cause the penis to increase in size, it will still be below the average length in size for males. Another form of treatment in infants and young boys is to administer testosterone or human chorionic gonadatropin (HCG). This treatment may enable the penis to grow to a normal size.

Some physicians have treated boys with micropenis with dihydrotestosterone (DHT) cream that is applied to the penis. This hormone causes both the penis and the prostate gland to increase in size. In one study of 22 children, all of them experienced increased penile growth with DHT treatment, including four boys who had not responded to treatment with other forms of testosterone. The treatment must occur before puberty, as the response after puberty is usually poor.

Studies of the sexual function of men with micropenis indicate they can have normal sex lives. According to Woodhouse, regarding a study of 20 adult males with micropenis, "The most surprising feature of these patients was the firmness with which they were established in the male role and the success that they had in sexual relationships. In the adult group, all were heterosexual, all had erections and orgasms, and 11 of 12 ejaculated." One patient had both a wife and a mistress, and one patient had fathered a child.

See also TESTES/TESTICLES.

Woodhouse, C. R. J. "Sexual Function in Boys Born with Exstrophy, Myelomeningocele, and Micropenis." *Urology* 52, no. 1 (1998): 111.

milk-alkali syndrome The triad of very high blood calcium levels, excess alkali, and kidney insufficiency caused by a combination of an excessive amount of milk and/or alkaline antacids, particularly baking soda (bicarbonate of soda). Patients who are taking vitamin D further aggravate the problem. Milk-alkali syndrome was a common cause of HYPERCALCEMIA prior to the advent of the newer therapies for peptic ulcer disease, especially the use of histamine-2 receptor blockers such as cimetidine (Tagamet) and ranitidine (Zantac).

However, the incidence of milk-alkali syndrome has been increasing as greater numbers of patients use large amounts of calcium carbonate (Tums) supplements to help prevent or treat OSTEOPOROSIS and to decrease blood phosphorus levels among those with severe chronic renal disease. Interestingly, some patients have developed HYPOCALCEMIA when the excess calcium was removed from their diets.

Historically, milk-alkali syndrome first began in 1915 with the introduction of a regimen, by Dr. Sippy, that treated peptic ulcer disease with magnesium carbonate, sodium carbonate, and bismuth subcarbonate. The chronic form of this condition was also called Burnett's syndrome, and the subacute form was known as Cope's syndrome.

Milk-alkali syndrome can cause calcium deposits in the kidneys, which are seen in COMPUTERIZED TOMOGRAPHY (CT) scans, MAGNETIC RESONANCE IMAGING (MRI) scans, X-rays, or ultrasounds of the kidneys. The modern patient who has milk-alkali syndrome typically has no signs or symptoms of this medical problem. However, physicians may suspect the problem based on the patient's history of calcium intake and then the measurement of serum calcium levels as well as other ancillary blood findings. Patients who are heavy users of antacids are at risk for milk-alkali syndrome.

If symptoms do occur, they may include headache, nausea, and weakness. The patient may also have pain in the back or the loins and may experience excessive urination.

Most cases of milk-alkali syndrome are reversible when the patient stops drinking high levels of milk and/or consuming many antacids. In severe cases (which are rare), the kidney is damaged and the patient may experience kidney failure and may require dialysis or a kidney transplant.

See also CALCIUM BALANCE; VITAMIN D.

mineralocorticoids See ALDOSTERONE.

multiple endocrine neoplasia (MEN) A rare and serious hereditary disorder of cancer of the endocrine glands. MEN is further subdivided into MEN 1 and MEN 2.

MEN 1

MEN 1 involves multiple tumors that may occur in one or more endocrine glands. This medical problem is a hereditary disorder that occurs in an estimated three to 20 people of every 100,000 individuals. It can present at any age and affects males and females in equal numbers. MEN 1 is also known as multiple endocrine adenomatosis or Wermer's syndrome.

Researchers report that often MEN 1 affects the parathyroid glands in the neck first, causing all four parathyroid glands to become overactive and to secrete excessive levels of parathyroid hormone. This HYPERPARATHYROIDISM then causes high levels of calcium in the bloodstream (HYPERCALCEMIA), which can then cause kidney stones and renal (kidney) damage. Hyperparathyroidism may also cause constipation, bone pain, muscle pain, fatigue, indigestion, and weakness.

Patients with MEN 1 may also have abdominal pain, nausea and vomiting, vision problems, loss of coordination, lack of appetite, weight loss, and hypotension (low blood pressure). Women may experience infertility and amenorrhea and may also fail to lactate, making it impossible to breast-feed their babies. Men may have decreased libido and a loss of facial or body hair.

If MEN 1 is suspected by the physician, tests are performed on the endocrine glands to evaluate their function. A magnetic resonance imaging (MRI) scan may show a pancreatic tumor. A fasting blood sugar test may be low, while serum glucagon may be high. In evaluating the parathyroid glands, the serum parathyroid hormone and serum calcium levels are elevated if MEN 1 is present. A scan of the head may show that a pituitary tumor is present. Physicians may also check for hormone levels of cortisol, adrenocorticotropic hormone (ACTH), luteinizing hormone, and follicle-stimulating hormone.

If hyperparathyroidism is diagnosed, the usual treatment is to remove three of the four parathyroid glands and part of the fourth gland. (A portion of the fourth parathyroid gland is left in place so that it can continue to generate some parathyroid hormone.)

MEN 2

With MEN 2, patients develop thyroid cancer (medullary carcinoma of the thyroid) as well as cancer of the adrenal glands (pheochromocytoma). MEN 2 is caused by a mutation in the *RET* gene. The incidence is unknown. The cancers do not always appear at the same time. MEN 2 is also known as Sipple's syndrome.

The following symptoms are common with MEN 2:

- Chest pain
- Abdominal pain
- Weight loss
- Coughing blood

- Increased thirst
- Severe headache
- Back pain
- Increased urination

Since these symptoms are common to other disorders, the physician must perform diagnostic testing. For example, an adrenal biopsy may reveal a pheochromocytoma, while an MRI of the abdomen may show a mass in the adrenal glands. Thyroid scans may show nodules, as may an ultrasound of the thyroid gland. Laboratory tests will show elevations of urine catecholamines and urine metanephrine. Patients with MEN 2 also have elevated levels of calcitonin and serum calcium but decreased levels of serum phosphorus.

Patients with MEN 2 need surgery to remove the existing tumors and should be carefully followed up by their doctors. Thyroid tumors are removed with a total excision of the thyroid gland, and patients must take thyroid replacement hormone for the rest of their lives. The thyroid cancers found in MEN 2 are unusually aggressive, which is why the entire gland must be removed to attempt to prevent any spreading of the cancer.

Brandi, Maria Luisa, et al. "Guidelines for Diagnosis and Therapy of MEN Type 1 and Type 2." *Journal of Clinical Endocrinology and Metabolism* 86, no. 12 (2001): 5,658–5,671.

myxedema coma The metabolic syndrome of very severe HYPOTHYROIDISM with associated hypothermia (low body temperature) and other associated organ system dysfunction or failure. It is a rare syndrome with a significant mortality rate (one out of three people die), although this rate has been declining over time due to better diagnosis and supportive care.

Patients typically have long-standing hypothyroidism and have stopped taking their thyroid hormone. Some patients have never been diagnosed with hypothyroidism and thus were never treated for it. Myxedema coma is most common in elderly women and has been seen in all types of hypothyroidism. The crisis can be precipitated by an illness such as pneumonia, influenza, myocardial infarction, urinary tract infection, significant cold exposure, or exposure to narcotics.

These patients are often seen in a hospital emergency department with mental status changes (severe cases are referred to as myxedema madness), low body temperature, slow heart rate (bradycardia), low blood sodium level (HYPONATREMIA), hypoventilation, and low blood sugar (HYPOGLYCEMIA).

If the diagnosis of myxedema coma is suspected, the emergency room physicians will begin therapy before confirmatory laboratory results have been returned. Therapy includes gentle warming, appropriate intravenous fluids (with attention to sodium, glucose, and fluid volume), artificial ventilation if needed, and intravenous levothyroxine and/or triiodothyronine. In addition, if an underlying or precipitating medical illness has not been identified, the physician must still search for one and begin appropriate therapy.

The most common form of underlying hypothyroidism is primary hypothyroidism; the thyroid-stimulating hormone (TSH) is elevated and the free T4 is low. If the TSH is normal or low, the physician must suspect secondary or tertiary hypothyroidism due to pituitary or hypothalamic disease. In these cases, patients must also be tested for CORTISOL deficiency (ADDISON'S DISEASE) and begun on therapy with intravenous glucocorticoids until the testing determines that this hormone is not required.

The term *myxedema megacolon* refers to the severe dilation that can occur in the colon, especially in the cecum, and that can mimic a mechanical bowel obstruction. It usually resolves slowly with the use of thyroid hormones, intravenous fluids and nutrients, and bowel rest (avoidance of solid and liquid food). If the dilation in the cecum exceeds 15 centimeters, surgery may be needed, although in many cases, the colon can be decompressed via a tube placed under radiologic guidance.

The term pretibial myxedema refers to a brawny, nonpitting swelling of the ankles and lower shins. It is nontender, brownish orange in color, and may be plaque-like. It is only seen in patients with GRAVES' DISEASE. The name refers to the appearance of the skin under the microscope,

- A family history of osteoporosis
- Eating disorders such as ANOREXIA NERVOSA or bulimia
- Diets low in calcium
- Cigarette smoking
- Heavy alcohol consumption
- Presence of inflammatory bowel disease
- Inactive lifestyle
- Thyroid disease
- Medications such as antiseizure drugs, blood thinners, and corticosteroids

A study of 14,824 men and women in the Norfolk branch of the European Prospective Investigation into Cancer (EPIC-Norfolk) trial showed a linear relationship between the quantitative calculation of heel density by ultrasound and the risk of hip and other fractures.

Signs and Symptoms of Osteoporosis

Osteoporosis often causes no symptoms in the early stages, when it is more readily treatable. At later stages, patients with osteoporosis are at risk for developing fractures. Often the first indicator of osteoporosis is, sadly, a bone fracture. However, if physicians know that there is a family history of osteoporosis, they may screen a women younger than age 65 in an attempt to treat this medical problem before it becomes severe and before fractures occur.

A loss in height of an inch or greater is another possible indicator of osteoporosis.

Diagnosis and Treatment

If the physician suspects osteoporosis, he or she will first obtain a medical history and physical examination to elicit information on the aforementioned risk factors as well as look for the signs and symptoms of secondary causes. If there is suspicion of a secondary cause of osteoporosis, appropriate blood and urine tests will be ordered as well as X-rays. The doctor will then usually order a dual-energy X-ray absorptiometry (DEXA) scan. This test is used to measure bone density.

All patients diagnosed with osteoporosis should be taking sufficient amounts of calcium and vitamin D, 1,000–1,500 mg/day of calcium and 400–800 IU of vitamin D, in divided doses. They should also exercise regularly, a minimum of three hours per week. The best form of exercise is walking.

Other drugs that are prescribed for osteoporosis include:

- Alendronate (Fosamax)
- Risedronate (Actonel)
- Raloxifene (Evista)
- Calcitonin (Miacalcin)
- Recombinant parathyroid hormone or TERIPARATIDE (Forteo)

Alendronate decreases clinical vertebral fractures by 45–55 percent and hip fractures by up to 50 percent. Risedronate has decreased vertebral fractures by 40–70 percent and hip fractures by 30 percent. These studies cannot be compared with each other as they included different groups of women treated for different lengths of time. Both the daily and weekly preparations of these medications appear to be equally effective. Only risedronate is approved by the Food and Drug Administration (FDA) for the prevention and treatment of glucocorticoid-induced osteoporosis as of this writing.

Raloxifene has been demonstrated to decrease vertebral fractures by 30–50 percent. Calcitonin has shown a 33 percent decrease.

In the Women's Health Initiative study, in which the study subjects used hormone replacement therapy, clinical fractures were reduced by 34 percent (vertebral and hip) and 24 percent (all fractures). However, the increased risk, albeit quite small, of breast cancer, heart attack, and stroke make hormone replacement therapy less favored, given the other available medication options.

Teriparatide in a 20 mcg dose has been shown to decrease vertebral fractures by 65 percent and non-

Siris, E. S. "Epidemiological Aspects of Paget's Disease: Family History and Relationship to Other Medical Conditions." *Seminars in Arthritis and Rheumatism* 23, no. 4 (1994): 222–225.

Whyte, Michael P., M.D., et al. "Oseoprotegerin Deficiency and Juvenile Paget's Disease." *New England Journal of Medicine* 347, no. 3 (July 15, 2002): 175–184.

pancreas A gland, about six inches in length, that performs several essential functions. The pancreas has both endocrine and exocrine functions.

Endocrine Functions

For its endocrine functions, the pancreas secretes insulin from the beta cells in the islets of Langerhans. These insulin-rich beta cells make up about 50–60 percent of the pancreas.

INSULIN is a hormone that helps the body appropriately assimilate carbohydrates (sugar) so it may be stored as glycogen in the liver and muscles. It also helps to transfer fat (as fatty acids) into triglycerides and store energy, and it allows amino acids to be incorporated into protein. Without insulin, the disease known as DIABETES MELLITUS occurs. With a complete lack of insulin, individuals present with TYPE 1 DIABETES. Prior to the discovery of insulin in 1921, there was a 100 percent fatality rate among all patients with Type 1 diabetes.

The pancreas also secretes glucagon from the alpha cells (which make up about 25 percent of the pancreas). Glucagon helps release glucose from the liver when the pancreas and brain perceive that the ambient glucose level is too low. In addition, the pancreas secretes amylin, a peptide hormone that is cosecreted with insulin and helps slow the emptying of the stomach (thereby smoothing out delivery of nutrients to the bloodstream).

Amylin also decreases the amount of glucagons secreted in response to eating a meal, decreasing the rise in glucose after a meal. By acting directly on the brain, amylin helps to increase satiety (the feeling of fullness) and decrease appetite. Several amylin-like injectable products are in development for use in the treatment of diabetes.

The pancreas also secretes pancreatic polypeptide (from F cells), vasoactive intestinal polypeptide (from neurons in the gastrointestinal tract), and somatostatin and gastrin (from D cells).

Exocrine Function

In its role as an exocrine gland, the pancreas excretes a number of enzymes into the duodenum, via two ducts, in response to ingested meals. Any obstruction of these ducts or the small ducts within the pancreas, especially by gallstones and/or "sludge" from the bile, will lead to PANCREATITIS. These enzymes include lipases, pancrealipase, amylase, trypsins, and others. Most of these enzymes are stored in an inactive form to prevent the pancreas from digesting itself.

When the pancreas malfunctions, as with diabetes mellitus and pancreatitis, the results are serious. PANCREATIC CANCER is nearly always fatal unless diagnosed in the early stages.

pancreatic cancer A dangerous and usually fatal form of cancer. According to the American Cancer Society, an estimated 31,860 new cases were expected in the United States in 2004. An estimated 31,270 people were expected to die of pancreatic cancer in 2004, including 15,440 men and 15,830 women. Pancreatic cancer represents about two percent of all cancer cases in both men and women.

The five-year survival rate for pancreatic cancer is low. Only about 5 percent of patients with pancreatic cancer will survive for five years; this means 95 percent of patients with pancreatic cancer die before five years have passed.

Despite the dismal outlook with pancreatic cancer as of this writing, researchers are actively seeking information on causes and possible treatments.

Risk Factors for Developing Pancreatic Cancer

Although any individual can develop pancreatic cancer, the risk will vary depending on the following factors:

- Age: the risk increases with age and is highest among people ages 60 and older
- Smoking: people who smoke have a two to three times greater risk of developing pancreatic cancer than nonsmokers

pituitary adenomas Benign tumors of the pituitary gland. The most common pituitary adenomas secrete prolactin (PROLACTINOMA) or are nonsecreting. They are usually detected by MAGNETIC RESONANCE IMAGING (MRI) of the pituitary gland. Tumors that measure between one and nine millimeters are called microadenomas, and those that are 10 millimeters or greater are called macroadenomas. They may be detected because they make one of several hormones and cause some sort of clinical syndrome that brings the patient to medical attention. Instead of secreting complete functional hormones, some adenomas secrete only the alpha or beta subunits of pituitary hormones and they have no endocrine activity.

Sometimes pituitary adenomas are found when an MRI or COMPUTERIZED TOMOGRAPHY (CT) scan of the brain is performed for another reason. These tumors are often referred to as incidentalomas, and often they cause no symptoms.

In some autopsy series, as many as 25 percent of the deceased patients had a small pituitary adenoma, usually one that was not detected prior to death.

Treatment of these tumors is directed at the underlying disorder and can include medications, surgery, and radiation therapy. Much modern pituitary surgery is performed via the transsphenoidal approach. This surgery requires the cooperation of a neurosurgeon as well as an otorhinolaryngologist (a specialized ear, nose, and throat doctor).

With this procedure, the pituitary is approached from below, through the sinuses that are centered above the upper teeth. Mortality rates range from 0.25–3 percent, depending upon the type and size of the tumor as well as other illnesses that the patient has. Complications can include bleeding, infection (meningitis), cerebrospinal fluid leak, visual disturbance, and taste and smell changes.

See also HYPOPITUITARISM; PITUITARY FAILURE; PITUITARY GLAND.

pituitary failure A total breakdown of the pituitary gland. Pituitary failure is also known as hypopituitarism. The failure can be partial or total. This clinical syndrome is rare. The most common causes of pituitary failure are PITUITARY ADENOMAS (either due to the size of the tumor itself or secondary to therapy, including surgery, medications, or radiotherapy). It may also be caused by trauma, inflammation, or vascular problems including POSTPARTUM PITUITARY NECROSIS (Sheehan's syndrome).

There can be deficiencies of any of the six anterior pituitary hormones, including PROLACTIN, LUTEINIZING HORMONE (LH), FOLLICLE-STIMULATING HORMONE (FSH), GROWTH HORMONE, adrenocorticotropic hormone (ACTH), and THYROID-STIMULATING HORMONE (TSH). These pituitary hormones fail in a typical pattern. First, the gonadotropins (LH, FSH) will fail, then growth hormone and TSH, and finally ACTH. Prolactin deficiency is rare unless there is a vascular etiology.

More commonly, partial failure of the pituitary gland occurs. Treatment of the cause (tumor, trauma to the pituitary, and so forth) may enable the patient to recover. Because pituitary failure will result in the inability of the body to produce needed hormones, patients will need to take supplements of LEVOTHYROXINE (to replace thyroid not produced by the thyroid), hydrocortisone (to replace cortisol not produced by the adrenal glands), and other medications.

See also HYPOPITUITARISM.

pituitary gland An endocrine gland that is composed of two lobes: the anterior pituitary (the adenohypophysis) and the posterior pituitary (the neurohypophysis). Many experts call the anterior pituitary the *master gland* because it produces hormones used by another endocrine gland. For example, it releases adrenocorticotropic hormone (ACTH), which is used by the adrenal glands, and thyroid-stimulating hormone (TSH), which is used by the thyroid gland. The pituitary gland also releases luteinizing hormone (LH), follicle-stimulating hormone (FSH), prolactin (PRL), growth hormone (GH), and pro-opiomenalnocortin (POMC). These seven hormones are essential to normal functioning.

If the pituitary malfunctions, it can cause a secondary endocrine disorder in another endocrine gland, because it causes that gland to malfunction also. (A primary endocrine disorder occurs when the disease originates in the endocrine gland itself.)

See also ACROMEGALY; ACTH; FOLLICLE-STIMULATING HORMONE; GROWTH HORMONE; HYPOPITUITARISM; PROLACTIN; THYROID-STIMULATING HORMONE.

pituitary insufficiency See HYPOPITUITARISM; PITUITARY FAILURE.

polycystic ovary syndrome (PCOS) A metabolic syndrome that affects about 8 percent of women of reproductive age. Its clinical manifestations range from minimal to severe. It is characterized by menstrual irregularities, hyperandrogenism (excess male hormones, leading to acne, alopecia, and/or hirsutism), anovulation with infertility, and miscarriages. Polycystic ovary syndrome appears to be caused by or tightly associated with insulin resistance syndrome. Thus those affected with PCOS are predisposed to IMPAIRED GLUCOSE TOLERANCE, DIABETES MELLITUS, OBESITY, and HYPERLIPIDEMIA, with all the attendant risks of these health problems.

Women with PCOS also have a much greater-than-average risk of developing cardiovascular problems; the risk of a heart attack is seven times greater among patients with PCOS compared with women who do not have this syndrome. In addition, patients with PCOS have an increased risk for developing endometrial cancer and breast cancer.

Polycystic ovary syndrome was originally known as Stein-Leventhal syndrome and was first discussed in 1935. At that time, the diagnosis required hirsutism (unusual hairiness), obesity, and amenorrhea (failure to menstruate). Later, a National Institute of Health consensus revised the diagnostic criteria to include hyperandrogenism with ovulatory dysfunction as well as the exclusion of CUSHING'S SYNDROME, nonclassical CONGENITAL ADRENAL HYPERPLASIA, hyperprolactinemia, and androgen-secreting tumors. In 2004, the presence of polycystic ovaries were considered consistent with the diagnosis of PCOS but were not necessary to make the diagnosis.

The condition may present as early as puberty. Some studies indicate that women with PCOS have a low-grade chronic inflammation of the lining of their blood vessels as measured by the increased levels of high-sensitivity C-reactive protein (CRP) concentrations in their blood. This is seen in patients with insulin resistance syndrome.

Risk Factors

Women with Type 2 diabetes are at greater risk for developing PCOS than those without glucose intolerance. PCOS is also found more commonly among women who are overweight or obese. Other diseases that may present along with PCOS are ACANTHOSIS NIGRICANS and hypertension.

Many women with PCOS also have abnormal cholesterol and triglyceride levels, typically mildly increased low-density lipoprotein (LDL) levels, low high-density lipoprotein (HDL) levels, and elevated triglyceride levels (hyperlipidemia). These risk associations may significant the underlying cause is insulin resistance, as these risk factors are all associated with or caused by insulin resistance.

Signs and Symptoms

PCOS usually comes to the attention of physicians when their female patients present to them with menstrual irregularities, hirsutism, and/or infertility. As mentioned, these women are often overweight, and may have acanthosis nigricans. The two main conditions necessary to diagnose PCOS are hyperandrogenism and anovulation. In severe cases of PCOS, the physician may find large ovarian cysts during a pelvic examination, although cysts are not necessary to make the diagnosis.

Hyperandrogenism

The excessive levels of male hormones found among women with PCOS are mainly synthesized by the ovaries, although the adrenal glands may also contribute. Most women with PCOS have elevated blood levels of testosterone, with the manifestations of acne and/or hirsutism. However, some racial groups, such as Asians, may not present with acne or hirsutism. Physicians will typically measure the patient's levels of total and free testosterone as well as dehydroepiandroesterone sulfate (DHEAS) that is made by the adrenal glands.

Anovulation

Many patients with PCOS do not menstruate at all. However, some women continue to menstruate yet do not ovulate, while others have irregular men-

Prader-Willi syndrome (PWS) An inherited medical condition characterized by mental developmental delay, behavioral problems (irritability and tantrums), OBESITY, short stature, decreased muscle mass, and genital abnormalities (hypogonadatropic hypogonadism). Prader-Willi syndrome was named after the Swiss pediatricians Andrea Prader and H. Willi, who first described this condition in 1956.

Prader-Willi syndrome occurs in one in 10,000–16,000 births. Most adult patients with PWS cannot live independently. Consequently, they live with their families or in group homes.

In many patients with PWS (as many as 75 percent), the syndrome is caused by a genetic defect: the deletion of a segment on chromosome 15q11-q13, which was inherited from the father. In some cases, the genetic problem is inherited from the mother.

Signs and Symptoms of Prader-Willi Syndrome

Infants with Prader-Willi syndrome have symptoms as newborn babies. They have poor sucking reflexes and difficulties with swallowing, and they may require tube feeding. Babies with PWS also have poor muscle tone and below-normal weight, partially due to their feeding problems.

Most children and adults with Prader-Willi syndrome have small hands and feet. They often exhibit constant scratching because of a severe itching problem and may be physically scarred because of their chronic scratching behavior. Individuals with this syndrome may also have an unusually high tolerance to pain.

Most patients with Prader-Willi are also developmentally delayed, with intelligence quotients in about the 70s. (An IQ of 100 is considered normal in the general population.)

Prader-Willi syndrome is also characterized by an extreme and ravenous appetite, which leads to obesity. This excessive appetite usually starts in early childhood, around the age of three years old, and is generally attributed to a disorder in the central nervous system. The compulsive overeating (hyperphagia) is so extreme and intense that individuals with PWS will seek out food that has been left in the garbage or will eat the food of their household pets. In many households, the refrigerator and the kitchen cabinets must actually be locked up because of this complete lack of appetite control.

Short stature is another common feature of PWS. Most patients (90 percent) are below normal in height. They also generally experience a DELAYED PUBERTY due to hypogonadatropic hypogonadism. When they do experience puberty, their voices will usually not change.

Many patients with Prader-Willi also have abnormal glucose tolerance or diabetes mellitus, at least in part because of their extreme obesity. About a third of patients with this syndrome are about twice the expected normal weight for their height.

Other common characteristics of Prader-Willi syndrome include the following signs and symptoms:

- Sleep disorders, especially sleep apnea
- Poor muscle tone
- Almond-shaped eyes
- Small mouth

Some patients also have kyphosis or scoliosis (skeletal deformities), OSTEOPOROSIS, and body temperature control problems. It has also been reported that some patients are unusually adept at putting together jigsaw puzzles.

Treatment of Prader-Willi Syndrome

Until recent years, the symptoms of patients with this syndrome could not be treated but only managed, which was extremely difficult for both the individual and the families, particularly in the case of hyperphagia behavior. Some studies indicate that treatment with growth hormone may help some patients with PWS. For example, the findings of a two-year study of 54 children with the syndrome, ages four to 16 years old when they joined the study, was reported in a 2002 issue of *Pediatrics.* Some of the children (35 children) were given growth hormone, while the rest were used as a control group.

In all but one child who received growth hormone, the children showed considerable improvement. The treated children became more energetic and active, and their moods improved markedly. The memory of most of the treated children (85 percent) improved. In addition, 89 percent of the children became much more sociable. Growth hormone did not make the children become "normal," but it did dramatically improve the lives of both the

risk factors Genetic or environmental conditions that predispose an individual to illness. Race, for example, plays a role in risks for many diseases. For instance, African Americans have a higher risk for developing TYPE 2 DIABETES than Caucasians. Obesity is a condition also linked to the development of diabetes (and some experts believe that it has a genetic basis as well). Thus, if a person is African American and also obese, he or she has a higher risk for developing diabetes than Caucasians or than nonobese African Americans.

Age is another factor in the likelihood of developing a range of illnesses. The probability of developing many different endocrine diseases and disorders, such as osteoporosis, Type 2 diabetes, and other medical problems, usually increases with age.

Sometimes gender alone is a risk factor. Women or men are more likely to develop a particular endocrine disease and disorder. For example, women are more likely to develop hypothyroidism.

Family medical history is another key factor in the development of many endocrine problems. People whose parents or siblings have had thyroid disease or cancer usually face an increased risk for these diseases themselves. This is why doctors usually ask patients about other family members and their problems so they can be alert to possible signs and symptoms of this disease in the patient.

See also GENETIC RISKS.

S

secondary hypothyroidism Hypothyroidism (low thyroid levels) caused by a defect or problem at the level of the PITUITARY GLAND. If there is a problem at the level of the HYPOTHALAMUS that causes hypothyroidism, that condition is referred to as tertiary hypothyroidism.

Secondary hypothyroidism causes the same symptoms as primary hypothyroidism, although here, symptoms may be more subtle. Patients with secondary hypothyroidism must be treated as if they had primary hypothyroidism with loss or destruction of the thyroid gland. The usual treatment is the replacement of thyroid hormone with LEVOTHYROXINE (T4).

Patients with secondary hypothyroidism may have a low or a normal level of THYROID-STIMULATING HORMONE (TSH) when their blood is tested. As a result, the diagnosis must be suspected based on the totality of the patient's clinical symptoms, the physician's clinical observations, and some laboratory testing. Free thyroxine levels may be low normal or just below normal.

Once diagnosed with secondary hypothyroidism, patients are given levothyroxine supplements, starting at a low level, with the dosage titrated based on the patient's clinical symptoms as well as the free thyroxine level. Patients are evaluated clinically before any increases in the medication are prescribed. Once clinically stable levels are reached, the patient should be rechecked once every six to 12 months. The physician must also be alert to other symptoms that might indicate other pituitary deficiencies, because typically patients have more than one problem.

See also HYPOTHYROIDISM.

Sheehan's syndrome See POSTPARTUM PITUITARY NECROSIS.

skin The largest organ of the body. Many endocrine diseases and disorders have a direct and noticeable effect on the patient's skin. For example, a key feature of ADDISON'S DISEASE is to cause hyperpigmentation, typically causing the skin to change to a darker color. This color change is due to the excess of pro-opiomelanocortin (POMC) secreted from the brain, stemming from the glucocorticoid deficiency that the disease causes. Undiagnosed and poorly controlled DIABETES MELLITUS may cause the skin to itch. It may also cause a thickening of the skin (waxy contractures or scleroderma) due to excess deposits of carbohydrate/protein complexes.

People with HYPOTHYROIDISM may have very dry, coarse, and thickened skin that can be cold to the touch. The skin may also appear yellow due to excess carotene. These patients may also have decreased perspiration. Patients with HYPERTHYROIDISM may have warm, moist skin and excessive sweating.

The skin of the patient with CUSHING'S DISEASE is thin and subject to easy bruising. This is due to the effects of the excess glucocorticoids on the protein synthesis of collagen that is needed to strengthen and stabilize the subcutaneous layers of capillaries and tissues. Patients with Cushing's disease may also have severe acne, alopecia (balding), fungal infections of the skin, and HIRSUTISM (excessive hairiness). The patient with ACROMEGALY has sweaty and oily skin and may also have excessive skin tags (loose pieces of skin). Women with POLYCYSTIC OVARY SYNDROME (PCOS) often have acne.

Another condition, ACANTHOSIS NIGRICANS, causes a fine, velvety hyperpigmentation of the skin, often seen at the back of the neck, under the arms, and in the breast and groin creases. Acanthosis nigricans is often seen in patients with INSULIN RESISTANCE SYNDROME.

Patients with advanced testicular cancer may experience the following signs and symptoms:

- Abdominal pain
- Unintended weight loss
- GYNECOMASTIA (growth of excess breast tissue in men and seen in 5 percent of men with germ cell tumors and 25 percent of males who have Leydig's cell tumors)
- Urinary obstruction
- Headaches
- Seizures

Gynecomastia is the most common endocrine abnormality seen in men with testicular cancer. With the Leydig's cell form, when seen in boys ages five to 12 years old, gynecomastia is usually associated with EARLY PUBERTY. It is also seen in men ages 25–35 who have erectile dysfunction in addition to the testicular mass. The gynecomastia is often associated with increased levels of human chorionic gonadotropin (HCG). In addition, the hormone levels of prolactin, estrogens, and androgens, may be altered. Interestingly, men with very high levels of HCG may develop HYPERTHYROIDISM due to the ability of the HCG to interact with the thyroid-stimulating hormone (TSH) receptor on the surface of the thyroid gland, which then subsequently leads to an overproduction of thyroid hormone.

Diagnosis and Treatment

If the physician suspects that a man has testicular cancer, he or she will usually order an imaging test—either a COMPUTER TOMOGRAPHY (CT) scan or a MAGNETIC RESONANCE IMAGING (MRI) scan. The doctor will also order laboratory tests, such as blood tests for serum alpha-feto protein (AFP) and serum beta-HCG, both of which are markers for testicular cancer. A biopsy is usually not performed.

The treatment for testicular cancer is an inguinal orchiectomy, which is the removal of the testis and spermatic cord. If only one testis is removed, the man may continue to be fertile. It may be advisable, however, to store his sperm before the surgery so that it can be used later to create a pregnancy, if desired. In most cases, surgery is sufficient to treat and cure the cancer. If the cancer has advanced, which is unusual, chemotherapy may be necessary to extend life.

See also CANCER; TESTES/TESTICLES.

Bishop, Philippe C., and Barnett S. Kramer. "Testicular Carcinoma," in *Bethesda Handbook of Clinical Oncology.* Philadelphia, Pa.: Lippincott Williams & Wilkins, 2001.

Travis, Lois B., et al. "Risk of Second Malignant Neoplasms Among Long-term Survivors of Testicular Cancer." *Journal of the National Cancer Institute* 89, no. 19 (October 1, 1997): 1,429–1,439.

Tseng, A. Jr., et al. "Gynecomastia in Testicular Cancer Patients: Prognostic and Therapeutic Implications." *Cancer* 56, no. 10 (1985): 2,534–2,538.

testosterone The male sex hormone and the most important androgen. It is synthesized by the testes and is converted in target tissues by 5-alpha reductase to dihydrotestosterone, a more potent form of testosterone. Testosterone production increases at the beginning of puberty and contributes to the changes in androgen-dependent tissues such as beard growth, pubic hair growth, increased muscle mass, deepening of the voice, and decrease in body fat content. Testosterone is believed to be the primary determinant of libido. Testosterone affects many aspects of a man's life, including sex drive, energy levels, and physical attributes such as muscle mass and strength.

Low levels of testosterone partially define HYPOGONADISM. The other part of the definition is the inability to produce adequate levels of spermatozoa.

Women also have low levels of testosterone.

Testosterone Declines with Aging

In general, testosterone production declines with aging. The Baltimore Longitudinal Study of Aging revealed that hypogonadal levels of testosterone are present in 20 percent of men over 60 years of age, 30 percent of men over 70 years of age, and 60 percent of men over 80 years of age. The numbers are higher if the measurement is of free testosterone as opposed to total bound testosterone. Whether physiological declines in testosterone levels should be treated remains an area of controversy.

In most cases, two or three doses of Thyrogen are given to the patient intramuscularly several days prior to the RAI uptake scan and therapy. The Thyrogen increases the overall level of TSH in the system while the patient is still taking thyroid hormone replacement. Both the scan and the treatment can be done effectively without causing the patient to become hypothyroid.

For tumors that do not concentrate iodine, other forms of chemotherapy may be used, although most are fairly ineffective. Another option for patients with advanced thyroid cancer is to join a clinical study, in which they may have the opportunity to try a new drug or treatment that is under study and that otherwise would not be available to them.

See also CANCER; MULTIPLE ENDOCRINE NEOPLASIA.

For further information on thyroid cancer, contact the following organizations:

American Cancer Society
1599 Clifton Road NE
Atlanta, GA 30329
(404) 320-3333 or (800) 227-2345 (toll-free)
http://www.cancer.org

Light of Life Foundation
P.O. Box 163
Manalpan, NJ 07726
(877) 565-6325 (toll-free)
http://www.lightoflifefoundation.org

National Cancer Institute
Building 31, Room 11A16
9000 Rockville Pike
Rockville, MD 20892
(800)-4-CANCER (toll-free)
http://www.cancer.gov

ThyCa: Thyroid Cancer Survivors Association, Inc.
P.O. Box 1545
New York, NY 10159
(877) 588-7904 (toll-free)
http://www.thyca.org

Abraham, Jame, and Tito Fojo. "Endocrine Tumors." in *Bethesda Handbook of Clinical Oncology.* Philadelphia, Pa.: Lippincott Williams & Wilkins, 2001.

Gilliland, F. D., et al. "Prognostic Factors for Thyroid Carcinomas: A Population Based Study of 15,698 Cases from the Surveillance, Epidemiology and End Results (SEER) Program 1973–1991." *Cancer* 79, no. 3 (1997): 564–573.

Shoup, M., et al. "Prognostic Indicators of Outcomes in Patients with Distant Metastases from Differentiated Thyroid Carcinoma." *Journal of the American College of Surgery* 197, no. 2 (August 2003): 191–197.

thyroidectomy Partial or total surgical removal of the diseased thyroid gland, often due to nodular thyroid disease, GRAVES' DISEASE, or THYROID CANCER.

The thyroidectomy is described as partial (any part), hemi (half), isthmusectomy (excision of the isthmus), and total or near-total thyroidectomy. Thyroid surgery is best done by a surgeon with extensive experience in performing this procedure. Typically, a necklace-type incision is used. As with all surgeries, complications are possible as well as possible complications due to anesthesia, blood loss, and infection, although complications from blood loss and infection are rare.

The thyroid must be carefully excised by the surgeon because the parathyroids can be temporarily or permanently damaged or disrupted by the surgery. (If the parathyroids are damaged or destroyed, the resulting HYPOPARATHYROIDISM will necessitate the use of vitamin D and calcium, and possibly of magnesium supplement, for the remainder of the patient's life.) In addition, the recurrent laryngeal nerves are located very close to the thyroid gland and can become damaged during surgery, which would lead to partial or complete vocal cord paralysis.

If a total or near-total thyroidectomy is performed, the patient will need to take replacement thyroid medication for the rest of his or her life.

See also THYROID GLAND.

thyroid gland A very important, butterfly-shaped organ, located in the neck, that controls the body's overall METABOLISM and energy levels through its production of thyroid hormone.

The thyroid has two lobes and a connecting section called the isthmus. Embryologically, the thyroid descended from an area near the tongue. Sometimes, remnants of thyroid tissue can be left behind and can form what is known as a thy-

roglossal duct cyst in the middle of the neck. In addition, this migration of the thyroid as the fetus develops also causes the recurrent laryngeal nerves to be pulled along. A surgeon performing thyroid surgery must be very careful to avoid damaging these vital structures that control the vocal cords and the ability to speak and sing properly.

The thyroid gland can be inspected from the front of the neck. The endocrinologist will check it by palpating the thyroid from the front and often from the rear. The thyroid is fairly superficial, but it is partially covered by a thick layer of the anterior neck strap muscles.

During an examination, the physician will often want the patient to swallow to see that the thyroid moves properly up and down. Sometimes it is situated a bit lower than usual and is behind the mannerism (the top part of the sternum, or the breastbone), and thus it can be felt only when the person swallows. At times, the thyroid gland is completely behind the breastbone and can be seen only with imaging techniques.

A substantial goiter is not uncommon for the thyroid gland. The four parathyroid glands are located close to the right and left thyroid lobes and at times actually lie within the thyroid gland itself.

The thyroid gland has active transporters to take up iodine from the circulation and combine it with tyrosine, an amino acid, in order to make various thyroid hormones. The thyroid gland synthesizes T4 (LEVOTHYROXINE), T3 (tri-iodothyronine), thyroglobulin, and various other forms of thyroid hormone that are relatively unimportant. The thyroid's ability to take up iodine from the circulation actively is utilized in thyroid scanning with radioactive iodine and technetium to create images of the gland and to measure its biological activity. In addition, the ENDOCRINOLOGIST can use this ability of the gland to import iodine actively to treat patients with GRAVE'S DISEASE and THYROID CANCER with the appropriate therapeutic dosages of radioactive iodine.

When the thyroid gland functions normally, the energy levels of a person are consistent with the needs of the individual and the overall metabolism is within normal ranges. When it malfunctions, individuals may have HYPOTHYROIDISM, with low levels of thyroid hormone, or they may have HYPERTHYROIDISM, with excessively high levels of thyroid hormone. Thyroid hormone should be thought of as a permissive hormone, or one that is required in appropriate amounts to allow each cell and organ system to function properly. It is not that these systems will not function at all without thyroid hormone but, rather, that they will not function as well as they should function.

The most common forms of thyroid disease are two autoimmune disorders: Graves' disease, which causes hyperthyroidism, and HASHIMOTO'S THYROIDITIS, which causes hypothyroidism. Some individuals develop THYROID NODULES, which might need to be evaluated for the presence of thyroid cancer.

See also GOITER; THYROID BLOOD TESTS; THYROIDECTOMY; THYROIDITIS; THYROID-STIMULATING HORMONE; THYROXINE.

thyroiditis A general term indicating an inflammation of the thyroid gland. Thyroiditis may cause excessively low (hypothyroid) or high (hyperthyroid) levels of thyroid hormone. HASHIMOTO'S THYROIDITIS, the most common cause of hypothyroidism, is also the most common cause of chronic thyroiditis. Other forms of thyroiditis, which may be acute or subacute, include painless lymphocytic thyroiditis (which is the cause of the thyroiditis and is also known as painless sporadic thyroiditis and postpartum thyroiditis), subacute thyroiditis (which is painful), suppurative thyroiditis, and drug-induced thyroiditis. The treatment of the thyroiditis depends on the particular cause.

Hashimoto's Thyroiditis

An autoimmune disorder that can occur at any age, Hashimoto's thyroiditis is most common among patients between the ages of 30 and 50 years. It is more frequently found among smokers. Hashimoto's thyroiditis may also cause a GOITER (enlargement of the thyroid gland).

In the early phases of the illness, the patient maintains normal thyroid function. As the gland enlarges, portions of it become damaged and do not function as well. Thus, early on, the thyroid gland may be slightly enlarged and firmer than usual. The patient may have increased levels of antithyroid peroxidase antibodies but yet have completely normal levels of thyroid hormone.

trolling the fever. Thus, acetaminophen (Tylenol), cooling blankets, and intravenous beta-blocker medications are usually employed. Many patients may require invasive monitoring of their cardiopulmonary status and may also need mechanical ventilation (artificial breathing devices).

The underlying cause of the thyroid storm must be sought and appropriate therapy begun. If the cause is nondestructive, such as Graves' disease, then toxic nodule or goiter antithyroid drugs are begun in very high doses. Occasionally, iodine is used in the form of a supersaturated solution of potassium iodine (Lugol's solution) or iopanoic acid. If the cause of the thyroid storm is a destructive lesion of the thyroid gland, such as a form of thyroiditis, then therapy is aimed at decreasing the effects of the excess thyroid hormone.

See also HYPERTHYROIDISM.

Thyrolar (liotrix tablets) A thyroid hormone replacement medication that contains synthetic T4 and T3. The 60-mg or 1-grain tablet contains about 50 mg of T4 and 12.5 mg of T3, or about the equivalent of 100 mcg of LEVOTHYROXINE.

thyrotoxicosis The clinical syndrome resulting from an excess of thyroid hormones in the bloodstream. In extreme cases, known as THYROID STORM, the patient is in a life-threatening situation and requires immediate medical treatment. Thyroid storm is defined as thyrotoxicosis and fever plus dysfunction of one other organ system. Thyrotoxicosis is similar to HYPERTHYROIDISM but implies a more severe clinical situation with more signs and symptoms of excess thyroid hormones.

In most cases (about 80 percent) the cause of thyrotoxicosis is GRAVES' DISEASE. However, some patients with HASHIMOTO'S THYROIDITIS, a form of HYPOTHYROIDISM, can develop thyrotoxicosis. An estimated 5–10 percent of women develop thyrotoxicosis after childbirth (postpartum thyrotoxicosis), typically due to postpartum thyroiditis, also known as painless lymphocytic thyroiditis (see POSTPARTUM THYROID DISEASE). Other causes include a toxic multinodular goiter or a toxic single nodule. In rare cases, lithium therapy can cause thyrotoxicosis.

Signs and Symptoms

Patients with thyrotoxicosis typically have accentuated symptoms of hyperthyroidism, including rapid heartbeat (tachycardia), heat intolerance, nervousness, disrupted sleep, tremulousness, weight loss, and a variety of other symptoms. The patient may or may not have an enlarged thyroid GOITER. Menstruating women may have a diminished menstrual flow or may have no menstrual flow (AMENORRHEA). Elderly patients with thyrotoxicosis may present with apathy rather than with hyperactivity and may appear to have an underactive gland.

Diagnosis and Treatment

Thyrotoxicosis is usually suspected based on clinical symptoms. It is diagnosed by blood samples that test for thyroid-stimulating hormone (TSH), free thyroxine (T4), and in some cases, triiodothyronine levels (T3).

Treatment of thyrotoxicosis is directed at the underlying cause. It generally involves watchful waiting and the use of beta-blocker medications (for thyroiditis), antithyroid drugs (for Graves' disease, toxic nodule, or goiter), or surgery in any case in which the other therapies cannot be utilized safely or effectively.

Fisher, Joseph N., M.D. "Management of Thyrotoxicosis." *Southern Medical Journal* 95, no. 5 (2002): 493–505.

thyroxine (T4) Natural thyroid hormone produced by the thyroid gland. It is also known as T4 due to the four iodine molecules attached to the amino acid tyrosine that make up this hormone. Thyroxine acts as a prehormone. The body uses an enzyme to cleave one iodine and to create the more active hormone, which is T3, also known as triiodothyronine. Most of T4 that circulates in the blood is bound to proteins, mostly albumin and thyroid-binding globulin (TBG). Thyroxine can be measured as the bound hormone or total T4. A bound hormone is attached to a binding protein in the blood to be transported around the body, as well as used for storage purposes. It can also be

vasoactive intestinal peptide producing tumor (vipoma) An islet cell tumor of the pancreas that leads to severe watery diarrhea (80 percent of patients exceed three liters of diarrhea per day) and decreased potassium and chloride in the bloodstream. Also known as pancreatic cholera syndrome, Verner-Morrison syndrome, WDHA (watery diarrhea, hypokalemia, achlorhydria), or WDDH (watery diarrhea, hypokalema) syndrome. A large number (40 percent) of vipomas are malignant.

Diagnosis and Treatment

Patients present with generalized weakness and diarrhea. They have low levels of potassium, chloride, and magnesium and elevated glucose levels (likely due to the severe losses of potassium that, in turn, lead to the inability to secrete adequate insulin) and calcium. On rare occasions, vipoma is associated with MULTIPLE ENDOCRINE NEOPLASIA (MEN) syndrome. Vipoma is difficult to detect in the plasma.

Therapy is surgery to remove the tumor. If the patient has hyperplasia and not a tumor, a total pancreatectomy is considered. A drug called octreotide is quite useful in treating this syndrome.

vitamin D The vitamin that helps the body to maintain normal levels of calcium and phosphorus in the blood and bones, mainly by its effects in increasing calcium absorption from the gastrointestinal tract.

The body uses sunshine (specific ultraviolet rays) to make vitamin D (cholecalciferol or vitamin D3). It is estimated that casual sun exposure leads to the synthesis of the equivalent of ingesting about 200 IU of vitamin D. There can be wide variations in vitamin D levels of individuals, depending on the season. In some very northern countries with long winters and little sunshine, supplements of exposure to appropriate artificial ultraviolet light is critical.

Vitamin D can also be obtained from foods. Many foods are also fortified with vitamin D (vitamin D2 or ergocalciferol) such as milk and breakfast cereals. Few foods are naturally high in vitamin D. Those that are include cod liver oil, cooked salmon, cooked mackerel, sardines, and eels.

CALCIJEX is a human-made form of vitamin D that is used by people who are deficient in vitamin D and/or calcium, such as patients with HYPOPARATHRYROIDISM (a rare condition in which the parathyroid glands have been damaged by an autoimmune reaction or have been surgically damaged). Supplemental vitamin D boosts the levels of calcium in the blood and bones by increasing the absorption from the gastrointestinal tract. High doses are available by prescription only.

Deficiencies of Vitamin D (Hypovitaminosis)

Deficiencies of vitamin D may be more common than is generally realized. In one study, physicians studied 290 hospitalized patients of all ages to determine if they were deficient in vitamin D. These findings were reported in a 1998 issue of the *New England Journal of Medicine*. The researchers obtained information on diet and medical histories and also obtained measures of the serum parathyroid hormone levels of the patients. They found that 57 percent of the patients had hypovitaminosis D, or very low levels of vitamin D. The conditions most often associated with hypovitaminosis were kidney disorders, glucocorticoid (steroid) therapy, cirrhosis, anticonvulsant therapy, and gastric or bowel resections. The study also pointed out that vitamin D deficiencies are more common among acutely ill individuals than had been realized in the past.

Reichler, H., H. P. Koeffler, and A. W. Norman. "The Role of the Vitamin D Endocrine System in Health and Disease." *New England Journal of Medicine* 320, no. 15 (1989): 980–991.

Thomas, Melissa K., M.D. "Hypovitaminosis D in Medical Inpatients." *New England Journal of Medicine* 338, no. 12 (March 19, 1998): 777–783.

vitamin D resistance A medical condition in which a person has a normal level of vitamin D in the blood but the body is unable to use this vitamin D appropriately and thus develops signs and symptoms of Vitamin D deficiency. The cause may be a genetic defect that prevents CALCITRIOL (a form of Vitamin D) from binding to the vitamin D receptor. Some elderly individuals may also have vitamin D resistance, although the cause for this form is unknown.

Vitamin D resistance may lead to the development of FRACTURES stemming from OSTEOPOROSIS. Children with untreated vitamin D resistance have a rickets-like appearance, with bowed legs and weak limbs, and they may also experience balding (alopecia). Treatment may improve the condition considerably.

Vitamin D resistance syndrome cannot be completely diagnosed by blood tests alone. Researchers performing clinical studies on normal patients as well as those with Vitamin D deficiency and resistance report that measurement of fingernail thickness may correlate with each syndrome.

The treatment of vitamin D resistance is usually supplementation with calcitriol. Some patients are more responsive to supplements of calcium, while others require both calcitriol and calcium supplements.

American Federation for Aging Research (AFAR)
1414 Sixth Avenue, 18th Floor
New York, NY 10019
(212) 752-2327
http://www.afar.org

American Foundation of Thyroid Patients
P.O. Box 820195
Houston, TX 77282
(281) 496-4460
http://www.thyroidfoundation.org

American Health Assistance Foundation
15825 Shady Grove Road
Suite 140
Rockville, MD 20850
(800) 437-2423
http://www.ahaf.org

American Health Care Association (AHCA)
1201 L Street NW
Washington, DC 20005
(202) 842-4444
http://www.ahca.org

American Heart Association/American Stroke Association
7272 Greenville Avenue
Dallas, TX 75231
(800) AHA-USA1
http://www.americanheart.org

American Hospital Association (AHA)
One North Franklin
Chicago, IL 60606
(312) 422-3000
http://www.aha.org

American Fertility Association
666 Fifth Avenue
Suite 278
New York, NY 10103
(888) 917-3777
http://www.theafa.org

American Institute for Cancer Research
1759 R Street NW
Washington, DC 20009
(800) 843-8114
http://www.aicr.org

American Medical Association
515 North State Street
Chicago, IL 60610
(312) 464-5000
http://www.ama-assn.org

American Medical Women's Association
801 North Fairfax Street
Suite 400
Alexandria, VA 22314
(703) 838-0500
http://www.amwa-doc.org

American Menopause Foundation
350 Fifth Avenue
Suite 2822
New York, NY 10118
(212) 714-2398
http://www.americanmenopause.org

American Mental Health Counselor's Association
801 N. Fairfax Street, Suite 304
Alexandria, VA 22314
(703) 548-6002
http://www.amhca.org

American Nurses Association
600 Maryland Avenue SW
Suite 100 West
Washington, DC 20024
(202) 554-4444
http://www.nursingworld.org

American Obesity Association
1250 24th Street NW, Suite 300
Washington, DC 20037
(800) 98-OBESE
http://www.obesity.org

American Pharmaceutical Association
2215 Constitution Avenue NW
Washington, DC 20037
(202) 628-4410
http://www.aphanet.org

American Physical Therapy Association (APTA)
111 North Fairfax Street
Alexandria, VA 22314
(800) 999-2782, ext. 3395
http://www.apta.org

Oxalosis and Hyperoxaluria Foundation
20 E. 19th Street, #12 E
New York, NY 10003
(800) OHF-8699
http://www.ohf.org

Paget Foundation for Paget's Disease of Bone and Related Disorders
120 Wall Street
Suite 1602
New York, NY 10005
(800) 23-PAGET
http://www.paget.org

Pancreatic Cancer Action Network
2221 Rosecrans Avenue
Suite 131
El Segundo, CA 90245
(877) 272-6226
http://www.pancan.org

Pediatric Endocrinology Nursing Society
P.O. Box 2933
Gaithersburg, MD 20886
http://www.pens.org

Pedorthic Footwear Association
7150 Columbia Gateway Drive
Suite G
Columbia, MD 21046
(410) 381-7278
http://www.pedorthics.org

Pituitary Tumor Network Association
P.O. Box 1958
Thousand Oaks, CA 91358
(805) 499-9973
http://www.pituitary.org

Polycystic Ovarian Syndrome Association
P.O. Box 3403
Englewood, CO 80111
(877) 775-PCOS
http://www.pcosupport.org

Prader-Willi Alliance for Research
28 Vesey Street
Suite 2104
New York, NY 10007
(212) 332-0970
http://www.p-war.org

The Foundation for Prader-Willi Research
6407 Bardstown Road
Suite 252
Louisville, KY 40291
(502) 254-9375

President's Council on Physical Fitness and Sports
701 Pennsylvania Avenue NW
Suite 250
Washington, DC 20004
(202) 272-3421
http://www.fitness.gov

RESOLVE: The National Infertility Association
1310 Broadway
Somerville, MA 02144
(888) 623-0744
http://www.resolve.org

Social Security Administration (SSA)
Office of Public Inquiries
Windsor Park Building
6401 Security Boulevard
Baltimore, MD 21235
(800) 772-1213
http://www.ssa.gov

Society for Inherited Metabolic Disorders
Oregon Health Sciences University/L473
3181 Southwest Sam Jackson Park Road
Portland, OR 97201
(503) 494-5400
http://www.simd.org

Society for Neuroscience
11 Dupont Circle NW
Suite 500
Washington, DC 20036
(202) 462-6688
http://www.sfn.org

Substance Abuse and Mental Health Services Administration (SAMSHA)
Department of Health and Human Services
Room 12-105 Parklawn Building
5600 Fishers Lane
Rockville, MD 20857
(800) 729-6686
http://www.samhsa.gov

APPENDIX V
MEDICATIONS TO TREAT DIABETES

I. INSULIN SECRETAGOGUES		
	1st Generation	**2nd Generation**
A. Sulfonylureas	Tolbutamide	Glyburide/ Micronized Glyburide
	Tolazamide	Glipizide
	Chlorpropramide	Glimepiride
B. Meglitinide	Repaglinide (Prandin)	
C. Phenylalanine Derivatives	Nateglinide (Starlix)	
II. Thiazolidinediones (TZDs)	Rosiglitazone (Avandia)	
	Pioglitazone (Actos)	
III. Alpha Glucosidase Inhibitors	Acarbose (Precose)	
	Miglitol (Glyset)	
IV. Biguanide	Metformin (Glucophage)	

SULFONYLUREA MEDICATIONS AND TYPICAL DOSING			
Generic Name	**Trade Name**	**Number of Daily Doses**	**Typical Daily Dose**
Tolbutamide	Orinase	2–3	500–3000 mg/day
Acetohexamide	Dymelor	1–2	250–500 mg/1–2 a day
Tolazamide	Tolinase	1–2	100–1000 mg/day
Chlorpropamide	Diabinese	1	100–500 mg/day
Glyburide	Diabeta Micronase	1	1.25–20 mg/day
Micronized glyburide	Glynase PresTab	1	1.5–12 mg/day
Glipizide	Glucotrol	1–2	2.5–40 mg/day
Glipizide GITS	Glucotrol XL	1	2.5–20 mg/day
Glimepiride	Amaryl	1	0.5–8 mg/day

SECRETAGOGUE MEDICATIONS AND TYPICAL DOSING		
Generic Name	**Trade Name**	**Typical Dosing**
Repaglinide	Prandin	1.5–16 mg, 3 or 4/day
Nateglinide	Starlix	180–360 mg/day

these issues. Contact the American Diabetes Association for further information.)

10. Some hypoglycemic adults (and children) may appear to be in a drunken state when they are, in fact, in serious need of glucose. Wearing a medical bracelet can help alert medical experts and other authorities to the presence of diabetes and other chronic medical problems and may also help to increase the probability of fast and effective treatment.

Paget Foundation for Paget's Disease of Bone and Related Disorders
http://www.paget.org

Pancreatic Cancer Action Network
http://www.pancan.org

Pituitary Tumor Network Association
http://www.pituitary.com

Power of Prevention (A Diabetes Web Site)
www.powerofprevention.com

Prader-Willi Alliance for Research
http://www.pwsresearch.org

Prader-Willi Syndrome Association
http://www.pwsausa.org

RESOLVE: The National Infertility Association
http://www.resolve.org

Society for Neuroscience
http://www.sfn.org

ThyCa: Thyroid Cancer Survivors' Association, Inc.
http://www.thyca.org

Thyroid-Cancer.net
http://www.thyroid-cancer.net

Thyroid Foundation of America, Inc.
http://www.allthyroid.org

Transplant Recipient International Organization
http://www.trio.org

United Network for Organ Sharing
http://www.unos.org

Wilson's Disease Association
http://www.wilsonsdisease.org

APPENDIX XII

PERCENT DISTRIBUTIONS OF BODY MASS INDEX AMONG PERSONS 18 YEARS OF AGE AND OVER, BY SELECTED CHARACTERISTICS: UNITED STATES, 1999

UNITED STATES, 1999

Selected Characteristic	Total	Underweight	Healthy Weight	Overweight	Obese
Sex					
Male	100.0	0.9	34.2	43.5	21.7
Female	100.0	4	48.3	.7	20.6
Age					
18–44 years	100.0	2.2	45.7	32.4	19.3
45–64 years	100.0	1.1	33.4	39.4	26.1
65 years and older	100.0	2.9	41.4	37.4	18.3
Race and Ethnicity					
Caucasian	100.0	2.2	41.9	35.5	20.4
Black or African American	100.0	1.5	33.6	36.4	28.5
American Indian or Alaska Native	100.0	1.0	27.1	34.9	37.0
Asian	100.0	3.9	68.9	21.6	5.6
Native Hawaiian or other Pacific Islander	100.0	2.0	17.6	34.3	46.1
Hispanic or Latino					
Education					
Less than a high school diploma	100.0	2.3	35.3	36.8	25.5
High school graduate/GED recipient	100.0	1.5	36.8	37.0	24.7
Some college	100.0	1.9	37.7	36.7	23.7
Bachelor of Arts, science degree, or professional degree	100.0	1.9	45.3	37.2	15.6
Family Income					
Less than $20,000	100.0	3.1	42.4	32.3	22.2
$20,000–$34,999	100.0	2.2	40.4	33.8	23.7
$35,000–$54,999	100.0	1.9	39.7	35.5	22.9
$55,000–$74,999	100.0	1.8	40.7	36.5	21.1
$75,000 or more	100.0	2.2	42.5	37.9	17.5
Marital status					
Married	100.0	1.6	38.1	37.9	22.4
Widowed	100.0	3.7	42.5	33.6	20.1
Divorced or separated	100.0	2.2	40.4	35.3	22.1
Never married	100.0	3.3	50.7	27.9	18.0
Living with a partner	100.0	2.8	46.3	33.5	17.4
Region					
Northeast	100.0	2.2	42.9	35.8	19.1
Midwest	100.0	1.9	40.6	34.9	22.5
South	100.0	2.4	39.9	35.2	22.5
West	100.0	2.0	44.0	35.2	18.7

(continues)

APPENDIX XV
STATE CANCER REGISTRIES

ALABAMA

Alabama Statewide Cancer Registry
Alabama Department of Public Health
P.O. Box 303017
Montgomery, AL 36130
(334) 206-5552
http://www.adph.org/cancer_registry

ALASKA

Alaska Cancer Registry
3601 C Street, Suite 540
P.O. Box 240249
Anchorage, AK 99524
(907) 269-8000
http://www.epi.hss.state.ak.us

ARIZONA

Arizona Cancer Registry
Arizona Department of Health Services
1740 West Adams Room 410
Phoenix, AZ 85007
(602) 542-7308
http://www.hs.state.az.us/phs/phstats/acr/index.htm

ARKANSAS

Arkansas Central Cancer Registry
Arkansas Department of Health
Division of Chronic Disease/Disability Prevention
4815 West Markham Street, Slot 7
Little Rock, AR 72295
(501) 661-2392
http://www.healthyarkansas.com/arkcancer/arkcancer.html

CALIFORNIA

California Department of Human Services
Cancer Surveillance Section
1700 Tribute Road, Suite 100
Sacramento, CA 95815
(916) 779-0303
http://www.ccrcal.org/index.htm

COLORADO

Colorado Department of Public Health and Environment
Colorado Central Cancer Registry
PPD-CR-A5
4300 Cherry Creek Drive South
Denver, CO 80246
(303) 692-2542
http://www.cdphe.state.co.us/pp/cccr.cccrhom.asp

CONNECTICUT

Connecticut Tumor Registry
410 Capitol Avenue
P.O. Box 340308 MS #13-TMR
Hartford, CT 06134
(860) 509-7163
http://www.dph.state.ct.us/OPPE/hptumor.htm

DELAWARE

Delaware Department of Health and Social Services
Division of Public Health
P.O. Box 637
Dover, DE 19903
(302) 739-5617
http://www.state.de.us/dhss/dph

DISTRICT OF COLUMBIA

District of Columbia Cancer Registry
District of Columbia Department of Health
825 North Capitol Street NE
Room 3145

Washington, DC 20002
(202) 442-5910
http://www.dchealth.dc.gov/services/special_programs/cancer_control/index.shtm

FLORIDA

Florida Cancer Data System
University of Miami School of Medicine
P.O. Box 016960 (D4-11)
Miami, FL 33101
(305) 243-4600
http://fcds.med.miami.edu

GEORGIA

Georgia Department of Human Services
Division of Public Health/Cancer Control Section
Two Peachtree Street NW
14th Floor, 14.283
Atlanta, GA 30303
(404) 657-1943
http://www.phr.state.ga.us/programs/cancer

HAWAII

Hawaii Tumor Registry
1236 Lauhala Street
Honolulu, HI 96813
(808) 586-9750
http://planet-hawaii.com/htr

IDAHO

Idaho Hospital Association
Cancer Data Registry of Idaho
615 North Seventh Street
Boise, ID 83702
(208) 338-5100
http://www.idcancer.org

ILLINOIS

Illinois State Cancer Registry
Illinois Department of Public Health
605 West Jefferson Street
Springfield, IL 62761
(217) 785-1873
http://www.idph.state.il.us/about/epi/cancer.htm

INDIANA

Indiana State Department of Health
State Cancer Registry
Two North Meridian Street
Section 7-D
Indianapolis, IN 46204
(317) 233-7158
http://www.in.gov/isdh/dataandstast/cancer.htm

IOWA

State Health Registry of Iowa
250 FB Building
Iowa City, IA 52242
(319) 335-8609
http://www.public-health.uiowa.edu/shri

KANSAS

Kansas Cancer Registry
University of Kansas Medical Center
3901 Rainbow Boulevard
Kansas City, KS 66160
(913) 588-2744
http://www.kumc.edu/som/kcr

KENTUCKY

Kentucky Cancer Registry
2365 Harrodsburg Road
Suite A230
Lexington, KY 40504
(859) 219-0773
http://www.kcr.uky.edu

LOUISIANA

Louisiana Tumor Registry
Louisiana State University Health Sciences Center—New Orleans
1600 Canal Street
Suite 1104
New Orleans, LA 70112
(504) 568-4283
http://www.lcltfb.org/registry.html

MAINE

Maine Cancer Registry
Division of Family and Community Health

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