Hypopituitarism

Clinical features of hypopituitarism develop slowly and vary with the severity of the disorder and the number of deficient hormones. Signs and symptoms of hypopituitarism in adults may include gonadal failure (secondary amenorrhea, impotence, infertility, decreased libido), diabetes insipidus, hypothyroidism (fatigue, lethargy, sensitivity to cold, menstrual disturbances), and adrenocortical insufficiency (hypoglycemia, anorexia, nausea, abdominal pain, orthostatic hypotension). Postpartum necrosis of the pituitary (Sheehan's syndrome) characteristically causes failure of lactation, menstruation, and growth of pubic and axillary hair; and symptoms of thyroid and adrenocortical failure. In children, hypopituitarism causes retarded growth or delayed puberty. Dwarfism usually isn't apparent at birth but early signs begin to appear during the first few months of life; by age 6 months, growth retardation is obvious. Although these children generally enjoy good health, pituitary dwarfism may cause chubbiness due to fat deposits in the lower trunk, delayed secondary tooth eruption and, possibly, hypoglycemia. Growth continues at less than half the normal rate— sometimes extending into the patient's 20s or 30s—to an average height of 4′ (122 cm), with normal proportions. P When hypopituitarism strikes before puberty, it prevents development of secondary sex characteristics (including facial and body hair). In males, it produces undersized testes, penis, and prostate gland; absent or minimal libido; and the inability to initiate and maintain an erection. In females, it usually causes immature development of the breasts, sparse or absent pubic and axillary hair, and primary amenorrhea. Panhypopituitarism may induce a host of mental and physiologic abnormalities, including lethargy, psychosis, orthostatic hypotension, bradycardia, anemia, and anorexia. However, clinical manifestations of hormonal deficiencies resulting from pituitary destruction don't become apparent until 75% of the gland is destroyed. Total loss of all hormones released by the anterior pituitary is fatal unless treated. Neurologic signs associated with hypopituitarism and produced by pituitary tumors include headache, bilateral temporal hemianopia, loss of visual acuity and, possibly, blindness. Acute hypopituitarism resulting from surgery or infection is often associated with fever, hypotension, vomiting, and hypoglycemia—all characteristic of adrenal insufficiency.

Hyperpituitarism

Acromegaly develops slowly and typically produces diaphoresis, oily skin, hypermetabolism, and hypertrichosis. Severe headache, central nervous system impairment, bitemporal hemianopia, loss of visual acuity, and blindness may result from the intrasellar tumor compressing the optic chiasm or nerves. Hypersecretion of hGH produces cartilaginous and connective tissue overgrowth, resulting in a characteristic hulking appearance, with an enlarged supraorbital ridge and thickened ears and nose. Prognathism, projection of the jaw, becomes marked and may interfere with chewing. Laryngeal hypertrophy, paranasal sinus enlargement, and thickening of the tongue cause the voice to sound deep and hollow. Distal phalanges display an arrowhead appearance on X-rays, and the fingers are thickened. Irritability, hostility, and various psychological disturbances may occur. Prolonged effects of excessive hGH secretion include bowlegs, barrel chest, arthritis, osteoporosis, kyphosis, hypertension, and arteriosclerosis. Both gigantism and acromegaly may also cause signs of glucose intolerance and clinically apparent diabetes mellitus because of the insulinantagonistic character of hGH. If acromegaly is left untreated, the patient is at risk for

premature cardiovascular disease, colon polyps, and colon cancer. Gigantism develops abruptly, producing some of the same skeletal abnormalities seen in acromegaly. As the disease progresses, the pituitary tumor enlarges and invades normal tissue, resulting in the loss of other trophic hormones, such as thyroid-stimulating hormone, luteinizing hormone, follicle-stimulating hormone, and corticotropin, thus causing the target organ to stop functioning.

Diabetes insipidus

The patient's history typically shows an abrupt onset of extreme polyuria (usually 4 to 16 L/day of dilute urine but sometimes as much as 30 L/day). As a result, the patient is extremely thirsty and drinks great quantities of water to compensate for the body's water loss. This disorder may also result in nocturia. In severe cases, it may lead to extreme fatigue from inadequate rest caused by frequent voiding and excessive thirst. Other characteristic features of diabetes insipidus include signs and symptoms of dehydration (poor tissue turgor, dry mucous membranes, constipation, muscle weakness, dizziness, and hypotension). These symptoms usually begin abruptly, commonly appearing within 1 to 2 days after a basal skull fracture, a stroke, or surgery. Relieving cerebral edema or increased intracranial pressure may cause all of these symptoms to subside just as rapidly as they began.

Hypothyroidism in adults

Typically, the early clinical features of hypothyroidism are vague: fatigue, menstrual changes, hypercholesterolemia, forgetfulness, sensitivity to cold, unexplained weight gain, and constipation. As the disorder progresses, characteristic myxedematous signs and symptoms appear: decreasing mental stability; dry, flaky, inelastic skin; puffy face, hands, and feet; hoarseness; periorbital edema; upper eyelid droop; dry, sparse hair; and thick, brittle nails. (See Facial signs of myxedema.) Cardiovascular involvement leads to decreased cardiac output, slow pulse rate, signs of poor peripheral circulation and, occasionally, an enlarged heart. Other common effects include anorexia, abdominal distention, menorrhagia, decreased libido, infertility, ataxia, intention tremor, and nystagmus. Reflexes show delayed relaxation time (especially in the Achilles tendon).

Hypothyroidism in children

The weight and length of an infant with infantile cretinism appear normal at birth, but characteristic signs of hypothyroidism develop by the time he's 3 to 6 months old. In a breast-fed infant the onset of most symptoms may be delayed until weaning because breast milk contains small amounts of thyroid hormone. Typically, an infant with cretinism sleeps excessively, seldom cries (except for occasional hoarse crying), and is inactive. Because of this, his parents may describe him as a “good baby—no trouble at all.” However, such behavior actually results from lowered metabolism and progressive mental impairment. The infant with cretinism also exhibits abnormal deep tendon reflexes, hypotonic abdominal muscles, a protruding abdomen, and slow, awkward movements. He has feeding difficulties, develops constipation and, because his immature liver can't conjugate bilirubin, becomes jaundiced. His large, protruding tongue obstructs respiration, making breathing loud and

noisy and forcing him to open his mouth to breathe. He may have dyspnea on exertion, anemia, abnormal facial features— such as a short forehead; puffy, wide-set eyes (periorbital edema); wrinkled eyelids; and a broad, short, upturned nose—and a dull expression, resulting from mental retardation. His skin is cold and mottled because of poor circulation, and his hair is dry, brittle, and dull. Teeth erupt late and tend to decay early; body temperature is below normal; and pulse rate is slow. In the child who acquires hypothyroidism after age 2, appropriate treatment can prevent mental retardation. However, growth retardation becomes apparent in short stature (due to delayed epiphyseal maturation, particularly in the legs), obesity, and a head that appears P abnormally large because the arms and legs are stunted. An older child may show delayed or accelerated sexual development.

Thyroiditis

Autoimmune thyroiditis is usually asymptomatic and commonly occurs in females, with peak incidence in middle age. It's the most prevalent cause of spontaneous hypothyroidism. In subacute granulomatous thyroiditis, moderate thyroid enlargement may follow an upper respiratory tract infection or a sore throat. The thyroid may be painful and tender, and dysphagia may occur. In Riedel's thyroiditis, the gland enlarges slowly as it's replaced by hard, fibrous tissues. This fibrosis may compress the trachea or the esophagus. The thyroid feels firm. Clinical effects of miscellaneous thyroiditis are characteristic of pyogenic infection: fever, pain, tenderness, and reddened skin over the gland.

Simple goiter

Thyroid enlargement may range from a mildly enlarged gland to a massive, multinodular goiter. (See Massive goiter.) Because simple goiter doesn't alter the patient's metabolic state, clinical features arise solely from enlargement of the thyroid gland. The patient may complain of respiratory distress and dysphagia from compression of the trachea and esophagus, and swelling and distention of the neck. In addition, large goiters may obstruct venous return, produce venous engorgement and, in rare cases, induce development of collateral venous circulation in the chest. Obstruction may cause dizziness or syncope (Pemberton's sign) when the patient raises her arms above her head.

Hyperthyroidism

The classic features of hyperthyroidism are an enlarged thyroid (goiter), nervousness, heat intolerance, weight loss despite increased appetite, sweating, diarrhea, tremor, and palpitations. Exophthalmos is considered most characteristic but is absent in many patients with hyperthyroidism. Many other symptoms are common because hyperthyroidism profoundly affects virtually every body system. Central nervous system—difficulty in concentrating because increased T4 secretion accelerates cerebral function; excitability or nervousness due to increased basal metabolic rate; fine tremor, shaky handwriting, and clumsiness from increased activity in the spinal cord area that controls muscle tone; emotional instability and mood swings, ranging from occasional outbursts to overt psychosis Skin, hair, and nails—smooth, warm, flushed skin (patient sleeps with minimal covers and little clothing); fine, soft hair; premature graying and increased hair loss in both sexes; friable

nails and onycholysis (distal nail separated from the bed); pretibial myxedema (dermopathy), producing thickened skin, accentuated hair follicles, raised red patches of skin that are itchy and sometimes painful, with occasional nodule formation (Microscopic examination shows increased mucin deposits.) P Cardiovascular system—tachycardia; full, bounding pulse; wide pulse pressure; cardiomegaly; increased cardiac output and blood volume; visible point of maximal impulse; paroxysmal supraventricular tachycardia and atrial fibrillation (especially in the elderly); and occasionally, systolic murmur at the left sternal border Respiratory system—dyspnea on exertion and at rest, possibly from cardiac decompensation and increased cellular oxygen utilization GI system—possible anorexia; nausea and vomiting due to increased GI mobility and peristalsis; increased defecation; soft stools or, with severe disease, diarrhea; and liver enlargement Musculoskeletal system—weakness, fatigue, and muscle atrophy; rare coexistence with myasthenia gravis; generalized or localized paralysis associated with hypokalemia may occur; and occasional acropachy —soft-tissue swelling, accompanied by underlying bone changes where new bone formation occurs Reproductive system—in women, oligomenorrhea or amenorrhea, decreased fertility, higher incidence of spontaneous abortions; in men, gynecomastia due to increased estrogen levels; in both sexes, diminished libido Eyes—exophthalmos (from the combined effects of accumulation of mucopolysaccharides and fluids in the retroorbital tissues that force the eyeball outward, and of lid retraction that produces the characteristic staring gaze); occasional inflammation of conjunctivae, corneas, or eye muscles; diplopia; and increased tearing.

Hypoparathyroidism

Although mild hypoparathyroidism may be asymptomatic, it usually produces hypocalcemia and high serum phosphate levels that affect the P central nervous system (CNS) as well as other body systems. Chronic hypoparathyroidism typically causes neuromuscular irritability, increased deep tendon reflexes, Chvostek's sign (hyperirritability of the facial nerve, producing a characteristic spasm when it's tapped), dysphagia, organic mental syndrome, psychosis, mental deficiency in children, and tetany. Acute (overt) tetany begins with a tingling in the fingertips, around the mouth and, occasionally, in the feet. This tingling spreads and becomes more severe, producing muscle tension and spasms and consequent adduction of the thumbs, wrists, and elbows. Pain varies with the degree of muscle tension but seldom affects the face, legs, and feet. Chronic tetany is usually unilateral and less severe; it may cause difficulty in walking and a tendency to fall. Both forms of tetany can lead to laryngospasm, stridor and, eventually, cyanosis. They may also cause seizures. These CNS abnormalities tend to be exaggerated during hyperventilation, pregnancy, infection, withdrawal of thyroid hormone, therapy with loop diuretics, and before menstruation. Other clinical effects include abdominal pain; dry, lusterless hair; spontaneous hair loss; brittle fingernails that develop ridges or fall out; dry, scaly skin; cataracts; and weakened tooth enamel, which causes teeth to stain, crack, and decay easily. Hypocalcemia may induce cardiac arrhythmias and may eventually lead to heart failure.

Hyperparathyroidism

Clinical effects of primary hyperparathyroidism result from hypercalcemia and are typically present in several body systems. Renal system—nephrocalcinosis due to elevated levels of calcium and, possibly, recurring nephrolithiasis, which may lead to renal insufficiency. Renal

manifestations, including polyuria, are the most common effects of hyperparathyroidism. Skeletal and articular system—chronic low back pain and easy fracturing due to bone degeneration, bone tenderness, chondrocalcinosis, occasional severe osteopenia, especially on the vertebrae, erosions of the juxta-articular surface, subchondral fractures, traumatic synovitis, and pseudogout GI system—pancreatitis, causing constant, severe epigastric pain radiating to the back; peptic ulcers, causing abdominal pain, anorexia, nausea, and vomiting Neuromuscular system—marked muscle weakness and atrophy, particularly in the legs Central nervous system—psychomotor and personality disturbances, depression, overt psychosis, stupor and, possibly, coma Other—skin necrosis, cataracts, calcium microthrombi to lungs and pancreas, polyuria, anemia, and subcutaneous calcification. Similarly, in secondary hyperparathyroidism, decreased serum calcium levels may produce the same features of calcium imbalance, with skeletal deformities of the long bones (rickets, for example) as well as symptoms of the underlying disease.

Adrenal hypofunction

Adrenal hypofunction typically produces such effects as weakness, fatigue, weight loss, and various GI disturbances, such as nausea, vomiting, anorexia, and chronic diarrhea. When primary, the disorder usually causes a conspicuous bronze coloration of the skin. The patient appears to be deeply suntanned, especially in the creases of the hands and over the metacarpophalangeal joints, the elbows, and the knees. He may also exhibit a darkening of scars, areas of vitiligo (absence of pigmentation), and increased pigmentation of the mucous membranes, especially the gingival mucosa. Abnormal skin and mucous membrane coloration results from decreased secretion of cortisol (one of the glucocorticoids), which causes the pituitary gland to simultaneously secrete excessive amounts of corticotropin and melanocyte-stimulating hormone (MSH). Associated cardiovascular abnormalities in adrenal hypofunction include orthostatic hypotension, decreased cardiac size and output, and a weak, irregular pulse. Other clinical effects include decreased tolerance for even minor stress, poor coordination, fasting hypoglycemia (due to decreased gluconeogenesis), and a craving for salty food. Adrenal hypofunction may also retard axillary and pubic hair growth in females, decrease the libido (from decreased androgen production) and, in severe cases, cause amenorrhea. Secondary adrenal hypofunction produces similar clinical effects but without hyperpigmentation because corticotropin and MSH levels are low. Because aldosterone secretion may continue at fairly normal levels in secondary adrenal hypofunction, this condition doesn't necessarily cause accompanying hypotension and electrolyte abnormalities.

Cushing's syndrome

Like other endocrine disorders, Cushing's syndrome induces changes in multiple body systems, depending on the adrenocortical hormone involved. Clinical effects may include the following. Endocrine and metabolic systems—diabetes mellitus, with decreased glucose tolerance, fasting hyperglycemia, and glycosuria Musculoskeletal system—muscle weakness due to hypokalemia or to loss of muscle mass from increased catabolism, pathologic fractures due to decreased bone mineral, and skeletal growth retardation in children Skin—purplish striae; fat pads above the clavicles, over the upper back (buffalo hump), on the face (moon face), and throughout the trunk, with slender arms and legs; little

or no scar formation; poor wound healing; acne and hirsutism in females GI system—peptic ulcer, resulting from increased gastric secretions and pepsin production, and decreased gastric mucus Central nervous system (CNS)—irritability and emotional lability, ranging from euphoric behavior to depression or psychosis; insomnia Cardiovascular system—hypertension due to sodium and water retention; left ventricular hypertrophy; capillary weakness due to protein loss, which leads to bleeding, petechiae, and ecchymosis Immune system—increased susceptibility to infection due to decreased lymphocyte production and suppressed antibody formation; decreased resistance to stress (Suppressed inflammatory response may mask even a severe infection.) Renal and urologic systems—sodium and secondary fluid retention, increased potassium excretion, inhibited antidiuretic hormone P secretion, ureteral calculi from increased bone demineralization with hypercalciuria Reproductive system—increased androgen production with clitoral hypertrophy, mild virilism, and amenorrhea or oligomenorrhea in women. Sexual dysfunction also occurs.

Hyperaldosteronism

Most clinical effects of hyperaldosteronism result from hypokalemia, which increases neuromuscular irritability and produces muscle weakness; intermittent, flaccid paralysis; fatigue; headaches; paresthesia; and, possibly, tetany (resulting from metabolic alkalosis), which can lead to hypocalcemia. Diabetes mellitus is common, perhaps because hypokalemia interferes with normal insulin secretion. Hypertension and its accompanying complications are also common. Other characteristic findings include visual disturbances and loss of renal concentrating ability, resulting in nocturnal polyuria and polydipsia. Azotemia indicates chronic potassium depletion nephropathy.

Adrenogenital syndrome

The neonatal female with simple virilizing CAH has ambiguous genitalia (enlarged clitoris, with urethral opening at the base; some labioscrotal fusion) but normal genital tract and gonads. As she grows older, signs of progressive virilization develop: early appearance of pubic and axillary hair, deep voice, acne, and facial hair. The neonatal male with this condition has no obvious abnormality; however, at prepuberty he shows accentuated masculine characteristics, such as deepened voice and an enlarged phallus, with frequent erections. At puberty, females fail to begin menstruation, and males have small testes. Both males and females with this condition may be taller than other children their age as a result of rapid bone and muscle growth, but because excessive androgen levels hasten epiphyseal closure, abnormally short adult stature results. (See Acquired adrenal virilism.)

Pheochromocytoma

The cardinal sign of pheochromocytoma is persistent or paroxysmal hypertension. Common clinical effects include palpitations, tachycardia, headache, diaphoresis, pallor, warmth or flushing, paresthesia, tremor, excitation, fright, nervousness, feelings of impending doom, abdominal pain, tachypnea, nausea, and vomiting. Orthostatic hypotension and paradoxical response to antihypertensive drugs are common, as are associated glycosuria, hyperglycemia, and hypermetabolism. Patients with hypermetabolism may show marked

weight loss but some patients with pheochromocytomas are obese. Symptomatic episodes may recur as seldom as once every 2 months or as often as 25 times a day. They may occur spontaneously or may follow certain precipitating events, such as postural change, exercise, laughing, smoking, induction of anesthesia, urination, or a change in environmental or body temperature. Pheochromocytoma is commonly diagnosed during pregnancy, when uterine pressure on the tumor induces more frequent attacks; such attacks can prove fatal for both mother and fetus as a result of a stroke, acute pulmonary edema, cardiac arrhythmias, or hypoxia. In such patients, the risk of spontaneous abortion is high but most fetal deaths occur during labor or immediately after birth.

Multiple endocrine neoplasia

Clinical effects of MEN may develop in various combinations and orders, depending on the glands involved. The most common manifestation of MEN I is hyperparathyroidism, followed by ulcer due to Zollinger-Ellison syndrome (marked by increased gastrin production from non-beta islet cell tumors of the pancreas). Hypoglycemia may result from pancreatic beta islet cell tumors, with increased insulin production. When MEN I affects the parathyroids, it produces signs of hyperparathyroidism, including hypercalcemia (because the parathyroids are primarily responsible for the regulation of calcium and phosphorus levels). When MEN causes pituitary tumor, it's most commonly a prolactinoma, but can be a growth hormone or corticotropin, or even a nonsecretory adenoma. Characteristic features of MEN II with medullary carcinoma of the thyroid include enlarged thyroid mass, with resultant increased calcitonin and, occasionally, ectopic corticotropin, causing Cushing's syndrome. With tumors of the adrenal medulla, symptoms include headache, tachyarrhythmias, and hypertension; with adenomatosis or hyperplasia of the parathyroids, symptoms result from renal calculi.

Diabetes mellitus

Diabetes may begin dramatically with ketoacidosis or insidiously. Its most common symptom is fatigue from energy deficiency and a catabolic state. Insulin deficiency causes hyperglycemia, which pulls fluid from body tissues, causing osmotic diuresis, polyuria, dehydration, polydipsia, dry mucous membranes, poor skin turgor and, in most patients, unexplained weight loss.In ketoacidosis and hyperosmolar hyperglycemic nonketotic syndrome, dehydration may cause hypovolemia and shock. Wasting of glucose in the urine usually produces weight loss and hunger in type 1 diabetes, even if the patient eats voraciously. (See Understanding ketoacidosis and hyperosmolar coma, pages 646 and 647.) Long-term effects of diabetes may include retinopathy, nephropathy, atherosclerosis, and peripheral and autonomic neuropathy. Peripheral neuropathy usually affects the hands and feet and may cause numbness or pain. Autonomic neuropathy may manifest itself in several ways, including gastroparesis (leading to delayed gastric emptying and a feeling of nausea and fullness after meals), nocturnal diarrhea, impotence, and orthostatic hypotension. Because hyperglycemia impairs the patient's resistance to infection, diabetes may result in skin and urinary tract infections (UTIs) and vaginitis. Glucose content of the epidermis and urine encourages bacterial growth.

Otitis externa

Acute otitis externa characteristically produces moderate to severe pain that's exacerbated by manipulating the auricle or tragus, clenching the teeth, opening the mouth, or chewing. Its other clinical effects may include fever, foul-smelling discharge, crusting in the external ear, regional cellulitis, partial hearing loss, and itching. It's usually difficult to view the tympanic membrane because of pain in the external canal.Hearing acuity is normal unless complete occlusion has occurred.Fungal otitis externa may be asymptomatic, although A. niger produces a black or gray, blotting, paperlike growth in the ear canal. In chronic otitis externa, pruritus replaces pain, and scratching may lead to scaling and skin thickening. Aural discharge may also occur.

Benign tumors of the ear canal

A benign ear tumor is usually asymptomatic, unless it becomes infected, in which case pain, fever, or inflammation may result. (Pain is usually a sign of a malignant tumor.) If the tumor grows large enough to obstruct the ear canal by itself or through accumulated cerumen and debris, it may cause hearing loss and the sensation of pressure.

Otitis media

Clinical features of acute suppurative otitis media include severe, deep, throbbing pain (from pressure behind the tympanic membrane); signs of upper respiratory tract infection (sneezing or coughing); mild to very high fever; hearing loss (usually mild and conductive); tinnitus; dizziness; nausea; and vomiting. Other possible effects include bulging of the tympanic membrane, with concomitant erythema, and purulent drainage in the ear canal from tympanic membrane rupture. However, many patients are asymptomatic.Acute secretory otitis media produces a severe conductive hearing loss—which varies from 15 to 35 dB, depending on the thickness and amountof fluid in the middle ear cavity—and, possibly, a sensation of fullness in the ear and popping, crackling, or clicking sounds on swallowing or with jaw movement. Accumulation of fluid may also cause the patient to hear an echo when he speaks and to experience a vague feeling of top-heaviness.The cumulative effects of chronic otitis media include thickening and scarring of the tympanic membrane, decreased or absent tympanic membrane mobility, cholesteatoma (a cystlike mass in the middle ear) and, in chronic suppurative otitis media, a painless, purulent discharge.The extent of associated conductive hearing loss varies with the size and type of tympanic membrane perforation and ossicular destruction. If the tympanic membrane has ruptured, the patient may state that the pain has suddenly stopped. Complications may include abscesses (brain, subperiosteal, and epidural), sigmoid sinus or jugular vein thrombosis,septicemia, meningitis, suppurative labyrinthitis, facial paralysis, andotitis externa.

Mastoiditis

Primary clinical features include a dull ache and tenderness in the area of the mastoid process, low-grade fever, headache, and a thick, purulent discharge that gradually becomes more profuse, possibly leading to otitis externa. Postauricular erythema and edema may push the auricle out from the head;

pressure within the edematous mastoid antrum may produce swelling and obstruction of the external ear canal, causing conductive hearing loss.

Otosclerosis

Spongy bone in the otic capsule immobilizes the footplate of the normally mobile stapes, disrupting the conduction of vibrations from the tympanic membrane to the cochlea. This causes progressive unilateral hearing loss, which may advance to bilateral deafness. Other symptoms include tinnitus and paracusis of Willis (hearing conversation better in a noisy environment than in a quiet one).

Infectious myringitis

Acute infectious myringitis begins with severe ear pain, commonly accompanied by tenderness over the mastoid process. Small, reddened, inflamed blebs form in the canal, on the tympanic membrane and, with bacterial invasion, in the middle ear. Fever and hearing loss are rare unless fluid accumulates in the middle ear, or a large bleb totally obstructs the external auditory meatus. Spontaneous rupture of these blebs may cause bloody discharge. Chronic granular myringitis produces pruritus, purulent discharge, and gradual hearing loss.

Ménière's disease

Ménière's disease produces three characteristic effects: severe episodic vertigo, tinnitus, and sensorineural hearing loss. A feeling of fullness or blockage in the ear is also common. Violent paroxysmal attacks last from 10 minutes to several hours. During an acute attack, other symptoms include severe nausea, vomiting, sweating, giddiness, and nystagmus. Vertigo may cause loss of balance and falling to the affected side. Symptoms tend to wax and wane as the endolymphatic pressure rises and falls. To lessen these symptoms, the patient may assume a characteristic posture—lying on the side of the unaffected ear and looking in the direction of the affected ear. Initially, the patient may be asymptomatic between attacks, except for residual tinnitus that worsens during an attack. Such attacks may occur several times a year, or remissions may last as long as several years. These attacks become less frequent as hearing loss progresses (usually unilaterally); they may cease when hearing loss is total. All symptoms are aggravated by motion.

Labyrinthitis

Because the inner ear controls both hearing and balance, this infection typically produces severe vertigo (with any movement of the head) and sensorineural hearing loss. Vertigo begins gradually but peaks within 48 hours, causing loss of balance and falling in the direction of the affected ear. Other associated signs and symptoms include spontaneous nystagmus, with jerking movements of the eyes toward the unaffected ear, and nausea, vomiting, and giddiness. With cholesteatoma, signs of middle ear disease may appear. With severe bacterial infection, purulent drainage, increased salivation, generalized malaise, and perspiration can occur. To minimize symptoms such as giddiness and nystagmus, the patient may assume a characteristic posture —lying on the side of the unaffected ear and looking in the direction of

the affected ear.

Hearing loss

Sudden deafness may be conductive, sensorineural, or mixed, depending on etiology. Associated clinical features depend on the underlying cause. Noise-induced hearing loss causes sensorineural damage, the extent of which depends on the duration and intensity of the noise. Initially, the patient loses perception of certain frequencies (around 4,000 Hz) but, with continued exposure, eventually loses perception of all frequencies.

Motion sickness

Typically, motion sickness induces nausea, vomiting, headache,dizziness, fatigue, diaphoresis and, occasionally, difficulty in breathing,leading to a sensation of suffocation. These symptoms usually subside when the precipitating stimulus is removed, but they may persist for several hours or days.

Epistaxis

Blood oozing from the nostrils usually originates in the anterior nose and is bright red. Blood from the back of the throat originates in the posterior area and may be dark or bright red (commonly mistaken for hemoptysis due to expectoration). Epistaxis is generally unilateral, except when it's due to dyscrasia or severe trauma. In severe epistaxis, blood may seep behind the nasal septum; it may also appear in the middle ear and in the corners of the eyes. Associated clinical effects depend on the severity of bleeding. Moderate blood loss may produce light-headedness, dizziness, and slight respiratory difficulty; severe hemorrhage causes hypotension, rapid and bounding pulse, dyspnea, and pallor. Bleeding is considered severe if it persists longer than 10 minutes after pressure is applied and causes blood loss as great as 1 L/hour in adults. Exsanguination (bleeding to death) from epistaxis is rare.

Septal perforation and deviation

A small septal perforation is usually asymptomatic but may produce a whistle on inspiration. A large perforation causes rhinitis, epistaxis, nasal crusting, and watery discharge.The patient with a deviated septum may develop a crooked nose, as the midline deflects to one side. The predominant symptom of severe deflection, however, is nasal obstruction. Other manifestations include a sensation of fullness in the face, shortness of breath, stertor (snoring or laborious breathing), nasal discharge, recurring epistaxis, infection, sinusitis, and headache.

Sinusitis

The primary indication of acute sinusitis is nasal congestion, followed by a gradual buildup of pressure in the affected sinus. For 24 to 48 hours after onset, nasal discharge may be present and later may become purulent. Associated symptoms include malaise, sore throat, headache,and low-grade fever of 99° to 99.5° F [37.2° to 37.5° C]).Characteristic pain depends on the affected sinus: maxillary sinusitis causes pain over the cheeks and upper teeth; ethmoid sinusitis, pain over the eyes; frontal sinusitis, pain over

the eyebrows; and sphenoid sinusitis (rare), pain behind the eyes. (See Locating the paranasal sinuses.) Purulent nasal drainage that continues for longer than 3 weeks after an acute infection subsides suggests subacute sinusitis. Other clinical features of the subacute form include nasal congestion, vague facial discomfort, fatigue, and a nonproductive cough. The effects of chronic sinusitis are similar to those of acute sinusitis, but the chronic form causes continuous mucopurulent discharge.

Nasal polyps

Nasal obstruction is the primary indication of nasal polyps. Such obstruction causes anosmia, a sensation of fullness in the face, nasal discharge, headache, and shortness of breath. Associated clinical features are usually the same as those of allergic rhinitis.

Nasal papillomas

Both inverted and exophytic papillomas typically produce symptoms related to unilateral nasal obstruction—congestion, postnasal drip,headache, shortness of breath, dyspnea and, rarely, severe respiratory distress, nasal drainage, and infection. Epistaxis is most likely to occur with exophytic papillomas. Occasionally hemorrhage may be the presenting symptom.

Adenoid hyperplasia

Typically, adenoid hyperplasia produces symptoms of respiratory obstruction, especially mouth breathing, snoring at night, and frequent, prolonged nasal congestion. Persistent mouth breathing during the formative years produces voice alteration and distinctive changes in facial features—a slightly elongated face, open mouth, highly arched palate, shortened upper lip, and vacant expression.

Velopharyngeal insufficiency

Generally, this condition causes unintelligible speech, marked by hypernasality, nasal emission, poor consonant definition, and a weak voice. The patient experiences dysphagia and, if velopharyngeal insufficiency is severe, he may regurgitate through the nose.

Pharyngitis

Pharyngitis produces a sore throat and slight difficulty in swallowing. Swallowing saliva is usually more painful than swallowing food. Pharyngitis may also cause the sensation of a lump in the throat as well as a constant, aggravating urge to swallow. Associated features may include mild fever, headache, muscle and joint pain, coryza, and rhinorrhea. Uncomplicated pharyngitis usually subsides in 3 to 10 days.

Tonsillitis

Acute tonsillitis commonly begins with a mild to severe sore throat. A very young child, unable to describe a sore throat, may stop eating.Tonsillitis may also produce dysphagia, fever, swelling and tenderness of the lymph glands in the submandibular area, muscle and joint pain, chills, malaise,

headache, and pain (frequently referred to the ears).Excess secretions may elicit the complaint of a constant urge to swallow; the back of the throat may feel constricted. Such discomfort usually subsides after 72 hours. Chronic tonsillitis produces a recurrent sore throat and purulent drainage in the tonsillar crypts. Frequent attacks of acute tonsillitis may also occur. Complications include obstruction from tonsillar hypertrophy and peritonsillar abscess.

Throat abscesses

Key symptoms of peritonsillar abscess include severe throat pain,occasional ear pain on the same side as the abscess, and tenderness of the submandibular gland. Dysphagia causes drooling. Trismus may occur as a result of the spread of edema and infection from the peritonsillar space to the pterygoid muscles. Other effects include fever, chills,malaise, rancid breath, nausea, muffled speech, dehydration, cervical adenopathy, and localized or systemic sepsis. Clinical features of retropharyngeal abscess include pain, dysphagia, fever and, when the abscess is located in the upper pharynx, nasal obstruction; with a lowpositioned abscess, dyspnea, progressive inspiratory stridor (from laryngeal obstruction), neck hyperextension and, in children, drooling and muffled crying occur. Other symptoms in children may include gurgling respirations, dyspnea and dysphagia, respiratory symptoms, and fever. A very large abscess may press on the larynx, causing edema, or may erode into major vessels, causing sudden death from asphyxia or aspiration.

Vocal cord paralysis

Unilateral paralysis, the most common form, may cause vocal weakness and hoarseness. Bilateral paralysis typically produces vocal weakness and incapacitating airway obstruction if the cords become paralyzed in the adducted position.

Vocal cord nodules and polyps

Nodules and polyps inhibit the approximation of vocal cords and produce painless hoarseness. The voice may also develop a breathy or husky quality

Laryngitis

Acute laryngitis typically begins with hoarseness, ranging from mild to complete loss of voice. Associated clinical features include pain (especially when swallowing or speaking), a persistent dry cough, fever, laryngeal edema, and malaise. In chronic laryngitis, persistent hoarseness is usually the only symptom.

Juvenile angiofibroma

Juvenile angiofibroma produces unilateral or bilateral nasal obstruction and severe recurrent epistaxis, usually between ages 7 and 21. Recurrent epistaxis eventually causes secondary anemia. Associated effects include purulent rhinorrhea, facial deformity, and nasal speech. Serous otitis media and hearing loss may result from eustachian tube obstruction.

Blepharitis

Clinical features of blepharitis include itching, burning, foreign-body sensation, and sticky, crusted eyelids on waking. This constant irritation results in unconscious rubbing of the eyes (causing reddened rims) or continual blinking. Other signs include waxy scales in seborrheic blepharitis; and flaky scales on lashes, loss of lashes, and ulcerated areas on lid margins in ulcerative blepharitis. In association with KCS, dry eyes may also be a problem.

Exophthalmos

The obvious effect is a bulging eyeball, commonly with diplopia, if extraocular muscle edema causes misalignment. (See Recognizing exophthalmos.) A rim of the sclera may be visible below the upper lid as lid retraction occurs, and the patient may blink infrequently. Other symptoms depend on the cause: pain may accompany traumatic exophthalmos; a tumor may produce conjunctival hyperemia or chemosis; retraction of the upper lid predisposes to exposure keratitis. If exophthalmos is associated with cavernous sinus thrombosis, the patient may exhibit paresis of the muscles supplied by cranial nerves III, IV, and VI; limited ocular movement; and a septictype (high) fever.

Ptosis

An infant with congenital ptosis has a smooth, flat upper eyelid, without the eyelid fold normally caused by the pull of the levator muscle; associated weakness of the superior rectus muscle isn't uncommon. The child with unilateral ptosis that covers the pupil can develop an amblyopic eye from disuse or lack of eye stimulation. In bilateral ptosis, the child may elevate his brow in an attempt to compensate, wrinkling his forehead in an effort to raise the upper lid. Also, the child may tilt his head backward to see. In myasthenia gravis, ptosis results from fatigue and characteristically appears in the evening, but is relieved by rest. Ptosis due to oculomotor nerve damage produces a fixed, dilated pupil; divergent strabismus; and slight depression of the eyeball.

Orbital cellulitis

Orbital cellulitis generally produces unilateral eyelid edema, hyperemia of the orbital tissues, reddened eyelids, and matted lashes. Although the eyeball is initially unaffected, proptosis develops later (because of edematous tissues within the bony confines of the orbit). Other indications include extreme orbital pain, impaired eye movement, chemosis, and purulent discharge from indurated areas. The severity of associated systemic symptoms (chills, fever, and malaise) varies according to the cause. Complications include posterior extension, causing cavernous sinus thrombosis, panophthalmitis, meningitis, or brain abscess and, rarely, atrophy and subsequent loss of vision secondary to optic neuritis.

Dacryocystitis

Dacryocystitis is extremely painful for the patient. The hallmark of both the acute and chronic forms of dacryocystitis is constant tearing. Other symptoms of dacryocystitis include inflammation and tenderness over the nasolacrimal sac; pressure over this area may fail to produce purulent discharge

from the punctum.

Chalazion

A chalazion occurs as a painless, hard lump that usually points toward the conjunctival side of the eyelid. Eversion of the lid reveals a red or red-yellow elevated area on the conjunctival surface. Otherwise, it's seen as an indurated bump under the skin of the upper eyelid.

Stye

Typically, a stye produces redness, swelling, and pain. An abscess frequently forms at the lid margin, with an eyelash pointing outward from its center. A stye is a localized red, swollen, and tender abscess of the lid glands.

Inclusion conjunctivitis

Inclusion conjunctivitis develops 5 to 12 days after contamination (it takes longer to develop than gonococcal ophthalmia). In a neonate, reddened eyelids and tearing with moderate mucoid discharge are presenting symptoms. In neonates, pseudomembranes may form, which can lead to conjunctival scarring. In adults, follicles appear inside the lower eyelids; such follicles don't form in infants because the lymphoid tissue isn't yet well developed. Children and adults also develop preauricular lymphadenopathy, and children may develop otitis media as a complication. Inclusion conjunctivitis may persist for weeks or months, possibly with superficial corneal involvement.

Conjunctivitis

Conjunctivitis commonly produces hyperemia of the conjunctiva, sometimes accompanied by discharge, tearing and, with corneal involvement, pain and photophobia. It generally doesn't affect vision. Conjunctivitis usually begins in one eye and rapidly spreads to the other by contamination of towels, washcloths, or the patient's own hand. Acute bacterial conjunctivitis (pinkeye) usually lasts only 2 weeks. The patient typically complains of itching, burning, and the sensation of a foreign body in his eye. The eyelids show a crust of sticky, mucopurulent discharge. If the disorder is due to N. gonorrhoeae, however, the patient exhibits a profuse, purulent discharge. Viral conjunctivitis produces copious tearing with minimal exudate, and enlargement of the preauricular lymph node. Some viruses follow a chronic course and produce severe disabling disease; others last 2 to 3 weeks and are self-limiting.Itching is the hallmark of allergy. Giant papillae resembling cobblestones may be seen on the palpebral conjunctiva

Trachoma

Trachoma begins with a mild infection resembling bacterial conjunctivitis (visible conjunctival follicles, red and edematous eyelids, pain, photophobia, tearing, and exudation). After about 1 month, if the infection is untreated, conjunctival follicles enlarge into inflamed papillae that later become yellow or gray. At this stage, small blood vessels invade the cornea under the upper lid.Eventually, severe scarring and contraction of the eyelids cause entropion; the eyelids turn inward and the lashes rub against the cornea, producing corneal scarring and visual distortion. In late stages, severe conjunctival scarring may

obstruct the lacrimal ducts and cause dry eyes.

Keratitis

Keratitis is usually unilateral. The patient presents with decreased vision, discomfort ranging from mild irritation to acute pain, tearing, and photophobia. On gross examination with a penlight, the corneal light reflex may appear distorted. When keratitis results from exposure, it usually affects the lower portion of the cornea.

Corneal abrasion

A corneal abrasion typically produces redness, increased tearing, discomfort with blinking, a sensation of "something in the eye" and, because the cornea is richly endowed with nerve endings from the trigeminal nerve (cranial nerve V), pain disproportionate to the size of the injury. It may also affect visual acuity, depending on the size and location of the injury.

Corneal ulcers

Typically, corneal ulceration begins with pain (aggravated by blinking) and photophobia, followed by increased tearing. Eventually, central corneal ulceration produces pronounced visual blurring. The eye may appear injected. If a bacterial ulcer is present, purulent discharge is possible.

Uveitis

Anterior uveitis produces moderate to severe unilateral eye pain; severe ciliary injection; photophobia; tearing; a small, nonre-active pupil; and blurred vision (due to the increased number of cells in the aqueous humor). It sometimes produces deposits called keratic precipitates on the back of the cornea, which may be seen in the anterior chamber. The iris may adhere to the lens, causing posterior synechiae and pupillary distortion; pain and photophobia may occur. Onset may be acute or insidious. Posterior uveitis begins insidiously, with complaints of slightly decreased or blurred vision or floating spots. Posterior uveitis may be acute or chronic, and it may affect one or both eyes. Retinal damage caused by lesions from toxoplasmosis and retinal detachments may occur. Refer the patient to an ophthalmologist for dilated fundus examination and treatment for local systemic diseases

Retinal detachment

Initially, the patient may complain of floating spots and recurrent flashes of light (photopsia). However, as detachment progresses, gradual, painless vision loss may be described as a veil, curtain, or cobweb that eliminates a portion of the visual field.

Vascular retinopathies

Central retinal artery occlusion produces sudden, painless, unilateral loss of vision (partial or complete). It may follow amaurosis fugax or transient episodes of unilateral loss of vision lasting from a few seconds to minutes, probably due to vasospasm. This condition typically causes permanent blindness. However,

some patients experience spontaneous resolution within hours and regain partial vision. Central retinal vein occlusion causes reduced visual acuity, allowing perception of only hand movement and light. This condition is painless, except when it results in secondary neovascular glaucoma (uncontrolled proliferation of weak blood vessels). The prognosis is poor—some patients with this condition develop secondary glaucoma within 3 to 4 months after occlusion. Nonproliferative diabetic retinopathy produces changes in the lining of the retinal blood vessels that cause the vessels to leak plasma or fatty substances, which decrease or block blood flow (nonperfusion) within the retina. This disorder may also produce microaneurysms and small hemorrhages. Nonproliferative retinopathy causes no symptoms in some patients; in others, leakage of fluid into the macular region causes significant loss of central visual acuity (necessary for reading and driving) and diminished night vision.

Age-related macular degeneration

The patient notices a change in central vision. Initially, straight lines (for example, of buildings) become distorted; later, a blank area appears in the center of a printed page (central scotoma).

Cataract

Characteristically, a patient with a cataract experiences painless, gradual blurring and loss of vision. As the cataract progresses, the normally black pupil appears hazy, and when a mature cataract develops, the white lens may be seen through the pupil. Some patients complain of blinding glare from headlights when they drive at night; others complain of poor reading vision, and of an unpleasant glare and poor vision in bright sunlight. Patients with central opacities report better vision in dim light than in bright light because the cataract is nuclear and, as the pupils dilate, patients can see around the lens opacity.

Retinitis pigmentosa

Typically, night blindness occurs while the patient is in his teens. As the disease progresses, his visual field gradually constricts, causing tunnel or “gun-barrel” vision. Many people retain this tunnel of useful vision until quite late in life. The speed of vision loss varies considerably from person to person. However, blindness follows invasion of the macular region.

Optic atrophy

Optic atrophy causes abrupt or gradual painless loss of visual field or visual acuity, with subtle changes in color vision.

Extraocular motor nerve palsies

The most characteristic clinical effect of extraocular motor nerve palsies is diplopia of recent onset, which varies in different visual fields, depending on the muscles affected. Typically, the patient with third nerve palsy exhibits ptosis, exotropia (eye looks outward), pupil dilation, and unresponsiveness to light; the eye is unable to move and can't accommodate. The patient with fourth nerve palsy displays diplopia and an inability to rotate the eye downward or upward. The head is tilted to the side opposite the involved area in superior oblique palsy. Sixth nerve palsy causes one eye to turn; the eye can't abduct

beyond the midline. To compensate for diplopia, the patient turns his head to the unaffected side and can develop torticollis.

Glaucoma

Chronic open-angle glaucoma is usually bilateral, with insidious onset and a slowly progressive course. Symptoms appear late in the disease and include mild aching in the eyes, loss of peripheral vision, seeing halos around lights, and reduced visual acuity (especially at night) that isn't correctable with glasses. Acute angle-closure glaucoma typically has a rapid onset, constituting an ophthalmic emergency. Symptoms include acute pain in a unilaterally inflamed eye, with pressure over the eye, moderate pupil dilation that's nonreactive to light, a cloudy cornea, blurring and decreased visual acuity, photophobia, and seeing halos around lights. Increased IOP may induce nausea and vomiting, which may cause glaucoma to be misinterpreted as GI distress. Unless treated promptly, this acute form of glaucoma produces blindness in 3 to 5 days.

Stomatitis and other oral infections

Acute herpetic stomatitis begins suddenly with mouth pain, malaise, lethargy, anorexia, irritability, and fever, which may persist for 1 to 2 weeks. Gums are swollen and bleed easily, and the mucous membrane is extremely tender. Papulovesicular ulcers appear in the mouth and throat and eventually become punched-out lesions with reddened areolae. Submaxillary lymphadenitis is common. Pain usually disappears 2 to 4 days before healing of ulcers is complete. If the child with stomatitis sucks his thumb, these lesions spread to the hand. P A patient with aphthous stomatitis typically reports burning, tingling, and slight swelling of the mucous membrane. Single or multiple shallow ulcers with whitish centers and red borders appear and heal at one site and then reappear at another.

Gastroesophageal reflux

GERD doesn't always cause symptoms, and in patients showing clinical effects, it isn't always possible to confirm physiologic reflux. The most common feature of GERD is heartburn, which may become more severe with vigorous exercise, bending, or lying down, and may be relieved by antacids or sitting upright. The pain of esophageal spasm resulting from reflux esophagitis tends to be chronic and may mimic angina pectoris, radiating to the neck, jaws, and arms. Other symptoms include odynophagia, which may be followed by a dull substernal ache from severe, long-term reflux; dysphagia from esophageal spasm, stricture, or esophagitis; and bleeding (bright red or dark brown). Rarely, nocturnal regurgitation wakens the patient with coughing, choking, and a mouthful of saliva. Reflux may be associated with hiatal hernia. Direct hiatal hernia becomes clinically significant only when reflux is confirmed. Pulmonary symptoms result from reflux of gastric contents into the throat and subsequent aspiration; they include chronic pulmonary disease or nocturnal wheezing, bronchitis, asthma, morning hoarseness, and cough. In children, other signs consist of failure to thrive and forceful vomiting from esophageal irritation. Such vomiting sometimes causes aspiration pneumonia.

Tracheoesophageal fistula and esophageal atresia

A neonate with type C tracheoesophageal fistula with esophageal atresia appears to swallow normally but soon after swallowing coughs, struggles, becomes cyanotic, and stops breathing as he aspirates fluids returning from the blind pouch of the esophagus through his nose and mouth. Stomach distention may cause respiratory distress; air and gastric contents (bile and gastric secretions) may reflux through the fistula into the trachea, resulting in chemical pneumonitis. An infant with type A esophageal atresia appears normal at birth. The infant swallows normally, but as secretions fill the esophageal sac and overflow into the oropharynx, he develops mucus in the oropharynx and drools excessively. When the infant is fed, regurgitation and respiratory distress follow aspiration. Suctioning the mucus and secretions temporarily relieves these symptoms. Excessive secretions and drooling in the neonate strongly suggest esophageal atresia. Repeated episodes of pneumonitis, pulmonary infection, and abdominal distention may signal type E (or H-type) tracheoesophageal fistula. When a child with this disorder drinks, he coughs, chokes, and becomes cyanotic. Excessive mucus builds up in the oropharynx. Crying forces air from the trachea into the esophagus, producing abdominal distention. Because such a child may appear normal at birth, this type of P tracheoesophageal fistula may be overlooked, and diagnosis may be delayed as long as 1 year. Type B (proximal fistula) and type D (fistula to both segments) cause immediate aspiration of saliva into the airway and bacterial pneumonitis.

Corrosive esophagitis and stricture

Effects vary from none at all to intense pain and edema n the mouth, anterior chest pain, marked salivation, inability to swallow, and tachypnea. Bloody vomitus containing pieces of esophageal tissue signals severe damage. Signs of esophageal perforation and mediastinitis, especially crepitation, indicate destruction of the entire esophagus. Inability to speak implies laryngeal damage. The acute phase subsides in 3 to 4 days, enabling the patient to eat again. Fever suggests secondary infection. Symptoms of dysphagia return P if stricture develops, usually within weeks; rarely, stricture is delayed and develops several years after the injury.

Mallory-Weiss syndrome

Mallory-Weiss syndrome typically begins with vomiting of blood or passing large amounts of blood rectally a few hours to several days after forceful vomiting. The bleeding, which may be accompanied by epigastric or back pain, may range from mild to massive, but is usually more profuse than in esophageal rupture. In Mallory-Weiss syndrome, the blood vessels are only partially severed, preventing retraction and closure of the lumen.

Esophageal diverticula

Midesophageal and epiphrenic diverticula with an associated motor disturbance (achalasia or spasm) seldom produce symptoms, although the patient may experience dysphagia and heartburn. Zenker's diverticulum, however, produces distinctly staged symptoms, beginning with initial throat irritation followed by dysphagia and near-complete obstruction. In early stages, regurgitation occurs soon after eating; in later stages, regurgitation after eating is delayed and may even occur during sleep, leading to food aspiration and pulmonary infection. ELDER TIP Hoarseness, asthma, and pneumonitis may be the only signs of esophageal diverticula in elderly patients. Other signs and symptoms include noise when liquids are swallowed, chronic cough, hoarseness, a bad taste in the mouth or foul breath and, rarely, bleeding.

Hiatal hernia

Typically, a paraesophageal hernia produces no symptoms; it's usually an incidental finding during a barium swallow or when testing for occult blood. Because this type of hernia leaves the closing mechanism of the cardiac sphincter unchanged, it rarely causes acid reflux or reflux esophagitis. Symptoms result from displacement or stretching of the stomach and may include a feeling of fullness in the chest or pain resembling angina pectoris. Even if it produces no symptoms, this type of hernia needs surgical treatment because of the high risk of strangulation that can occur when a large portion of stomach becomes caught above the diaphragm. A sliding hernia without an incompetent sphincter produces no reflux or symptoms and, consequently, doesn't require treatment. When a sliding hernia causes symptoms, they are typical of gastric reflux, resulting from the incompetent lower esophageal sphincter (LES), and may include the following: P Pyrosis (heartburn) occurs 1 to 4 hours after eating (especially overeating) and is aggravated by reclining, belching, and increased intra-abdominal pressure. It may be accompanied by regurgitation or vomiting. Retrosternal or substernal chest pain results from reflux of gastric contents, stomach distention, and spasm or altered motor activity. Chest pain usually occurs after meals or at bedtime and is aggravated by reclining, belching, and increased intra-abdominal pressure. Other common symptoms reflect possible complications: Dysphagia occurs when the hernia produces esophagitis, esophageal ulceration, or stricture, especially with ingestion of very hot or cold foods, alcoholic beverages, or a large amount of food. Bleeding may be mild or massive, frank or occult; the source may be esophagitis or erosions of the gastric pouch. Severe pain and shock result from incarceration,

in which a large portion of the stomach is caught above the diaphragm (usually occurs with paraesophageal hernia). Incarceration may lead to perforation of the gastric ulcer and strangulation and gangrene of the herniated portion of the stomach. It requires immediate surgery.

Gastritis

After exposure to the offending substance, the patient with acute gastritis typically reports a rapid onset of symptoms, such as epigastric discomfort, indigestion, cramping, anorexia, nausea, vomiting, and hematemesis. The symptoms last from a few hours to a few days. The patient with chronic gastritis may describe similar symptoms or may have only mild epigastric discomfort, or his complaints may be vague, such as an intolerance for spicy or fatty foods or slight pain relieved by eating. The patient with chronic atrophic gastritis may be asymptomatic.

Gastroenteritis

Signs and symptoms vary depending on the pathologic organism and on the level of GI tract involved. However, gastroenteritis in adults is usually an acute, self-limiting, nonfatal disease producing diarrhea, abdominal discomfort (ranging from cramping to pain), nausea, and vomiting. Other possible signs and symptoms include fever, malaise, and borborygmi. In children, the elderly, and the debilitated, gastroenteritis produces the same symptoms, but these patients' intolerance to electrolyte and fluid losses leads to a higher mortality.

Peptic ulcers

Heartburn and indigestion usually signal the beginning of a gastric ulcer attack. Eating stretches the gastric wall and may cause or, in some cases, relieve pain and feelings of fullness and distention. Other typical effects include weight loss and repeated episodes of massive GI bleeding. Duodenal ulcers produce heartburn, well-localized midepigastric pain (relieved by food), weight gain (because the patient eats to relieve discomfort), and a peculiar sensation of hot water bubbling in the back of the throat. Attacks usually occur about 2 hours after meals, whenever the stomach is empty, or after consumption of orange juice, coffee, aspirin, or alcohol. Exacerbations tend to recur several times per year and then fade into remission. Vomiting and other digestive disturbances are rare. Ulcers may penetrate the pancreas and cause severe back pain. Other complications of peptic ulcers include perforation, hemorrhage, and pyloric obstruction. Ulcers may, on occasion, produce no symptoms.

Ulcerative colitis

The hallmark of ulcerative colitis is recurrent attacks of bloody diarrhea, in many cases containing pus and mucus, interspersed with asymptomatic remissions. The intensity of these attacks varies with the extent of inflammation. It isn't uncommon for a patient with ulcerative colitis to have as many as 15 to 20 liquid, bloody stools daily. Other symptoms include spastic rectum and anus, abdominal pain, irritability, weight loss, weakness, anorexia, nausea, and vomiting. Ulcerative colitis may lead to complications, such as hemorrhage, stricture, or perforation of the colon. Other complications include joint inflammation, ankylosing spondylitis, eye lesions, mouth ulcers, liver disease, and pyoderma gangrenosum. Scientists think that these complications occur when the immune system triggers inflammation in other parts of the body. These disorders are usually mild and disappear when the colitis is treated. Patients with ulcerative colitis have an increased risk of developing colorectal cancer; children with ulcerative colitis may experience impaired growth and sexual development.

Necrotizing enterocolitis

Neonates who have suffered from perinatal hypoxemia have the potential for developing NEC. A distended (especially tense or rigid) abdomen with gastric retention is the earliest and most common sign of oncoming NEC, which usually appears 1 to 10 days after birth. Other clinical features are increasing residual gastric contents (which may contain bile), bile-stained vomitus, and occult blood in the stool. About 25% of patients have bloody diarrhea. A red or shiny, taut abdomen may indicate peritonitis. Nonspecific signs and symptoms include thermal instability, lethargy, metabolic acidosis, jaundice, and DIC. The major complication is perforation, which requires surgery. Recurrence of NEC and mechanical and functional abnormalities of the intestine, especially stricture, are P the usual cause of residual intestinal malfunction in any infant who survives acute NEC; this complication may develop as late as 3 months postoperatively.

Crohn's disease

Clinical effects may be mild and nonspecific initially; they vary according to the location and extent of the lesion. Acute inflammatory signs and symptoms mimic appendicitis and include steady, colicky pain in the right lower quadrant, cramping, tenderness, flatulence, nausea, fever, and diarrhea. Bleeding may occur and, although usually mild, may be massive. Bloody stools may also occur. Chronic symptoms, which are more typical of the disease, are more persistent and less severe; they include diarrhea (four to six stools per day) with pain in the right lower abdominal quadrant, steatorrhea (excess fat in feces), marked weight loss and, rarely, clubbing of fingers. The patient may complain of weakness and fatigue. Complications include intestinal obstruction, fistula formation between the small bowel and the bladder, perianal and perirectal abscesses and fistulas, intra-abdominal abscesses, and perforation.

Pseudomembranous enterocolitis

Pseudomembranous enterocolitis begins suddenly with copious watery or bloody diarrhea that may contain pus or mucus, abdominal pain, and fever. Serious complications, including severe dehydration, electrolyte imbalance, hypotension, shock, and colonic perforation, may occur in this disorder.

Irritable bowel syndrome

IBS characteristically produces lower abdominal pain (usually relieved by defecation or passage of gas) and diarrhea that typically occurs during the day. These symptoms alternate with constipation or normal bowel function. Stools are commonly small and contain visible mucus. Dyspepsia and abdominal distention may occur. Symptoms of IBS are two to three times more common in women than in men, with women comprising 80% of patients with a more severe form of the disorder.

Celiac disease

Celiac disease produces clinical effects on many body systems: GI symptoms include recurrent attacks of diarrhea, steatorrhea, abdominal distention due to flatulence, stomach cramps, weakness, anorexia and, occasionally, increased appetite without weight gain. Atrophy of intestinal villi leads to malabsorption of fat, carbohydrates, and protein as well as loss of calories, fat-soluble vitamins (A, D, and K), calcium, and essential minerals and electrolytes. In adults, celiac disease produces multiple nonspecific ulcers in the small bowel, which may perforate or bleed. Hematologic effects include normochromic, hypochromic, or macrocytic anemia due to poor absorption of folate, iron, and vitamin B12 and to hypoprothrombinemia from jejunal loss of vitamin K. Osteomalacia, osteoporosis, tetany, and bone pain (especially in the lower back, rib cage, and pelvis) are some of

the musculoskeletal symptoms of celiac disease. These signs and symptoms are due to calcium loss and vitamin D deficiency, which weakens the skeleton, causing rickets in children and compression fractures in adults. Neurologic effects may include peripheral neuropathy, seizures, or paresthesia. Dry skin, eczema, psoriasis, dermatitis herpetiformis, and acne rosacea are some of the dermatologic effects of celiac disease. Deficiency of sulfur-containing amino acids may cause generalized fine, sparse, prematurely gray hair; brittle nails; and localized hyperpigmentation on the face, lips, or mucosa. Endocrine symptoms include amenorrhea, hypometabolism and, possibly, with severe malabsorption, adrenocortical insufficiency. Psychosocial effects include mood changes and irritability. Symptoms may develop during the first year of life, when gluten is introduced into the child's diet as cereal. Clinical effects may disappear during adolescence and reappear in adulthood. One theory proposes that the age at which symptoms first appear depends on the strength of the genetic factor: A strong factor produces symptoms during the child's first 4 years; a weak factor, in late childhood or adulthood.

Diverticular disease

Diverticulosis usually produces no symptoms but may cause recurrent left lower quadrant pain, which is commonly accompanied by alternating constipation and diarrhea and is relieved by defecation or the passage of flatus. Symptoms resemble irritable bowel syndrome (IBS) and suggest that both disorders may coexist. Mild diverticulitis produces moderate left lower abdominal pain, mild nausea, gas, irregular bowel habits, low-grade fever, and leukocytosis. In severe diverticulitis, the diverticula can rupture and produce abscesses or peritonitis, which occurs in up to 20% of such patients. Symptoms of rupture include abdominal rigidity and left lower quadrant pain. Peritonitis follows release of fecal material from the rupture site and causes signs of sepsis and shock (high fever, chills, and hypotension). Rupture of the diverticulum near a vessel may cause microscopic or massive hemorrhage, depending on the vessel's size. Chronic diverticulitis may cause fibrosis and adhesions that narrow the bowel's lumen and lead to bowel obstruction. Symptoms of incomplete obstruction are constipation, ribbonlike stools, intermittent diarrhea, and abdominal distention. Increasing obstruction causes abdominal rigidity and pain, diminishing or absent bowel sounds, nausea, and vomiting.

Appendicitis

Typically, appendicitis begins with generalized or localized abdominal pain in the right upper abdomen, followed by anorexia, nausea, and vomiting (rarely profuse). Pain eventually localizes in the right lower abdomen (McBurney's point) with abdominal “boardlike” rigidity, retractive respirations, increasing tenderness, increasingly severe abdominal spasms and, almost invariably, rebound tenderness. (Rebound tenderness on the opposite side of the abdomen suggests peritoneal inflammation.) Later signs and symptoms include constipation or diarrhea, slight fever, and tachycardia. The patient may walk bent over or lie with his right knee flexed to reduce pain.

Peritonitis

The key symptom of peritonitis is sudden, severe, and diffuse abdominal pain that tends to intensify and localize in the area of the underlying disorder. For instance, if appendicitis causes the rupture, pain eventually localizes in the right lower quadrant. Many patients display weakness, pallor, excessive sweating, and cold skin as a result of excessive loss of fluid, electrolytes, and protein into the abdominal cavity. Decreased intestinal motility and paralytic ileus result from the effect of bacterial toxins on the intestinal muscles. Intestinal obstruction causes nausea, vomiting, and abdominal rigidity. Other clinical characteristics include hypotension, tachycardia, signs and

symptoms of dehydration (oliguria, thirst, dry swollen tongue, and P pinched skin), an acutely tender abdomen associated with rebound tenderness, temperature of 103° F (39.4° C) or higher, and hypokalemia. Inflammation of the diaphragmatic peritoneum may cause shoulder pain and hiccups. Abdominal distention and resulting upward displacement of the diaphragm may decrease respiratory capacity. Typically, the patient with peritonitis tends to breathe shallowly and move as little as possible to minimize pain. He may lie on his back, with his knees flexed, to relax abdominal muscles.

Intestinal obstruction

Colicky pain, nausea, vomiting, constipation, and abdominal distention characterize small-bowel obstruction. It may also cause drowsiness, intense thirst, malaise, and aching and may dry up oral mucous membranes and the tongue. Auscultation reveals bowel sounds, borborygmi, and rushes; occasionally, these are loud enough to be heard without a stethoscope. Palpation elicits abdominal tenderness, with moderate distention; rebound tenderness occurs when obstruction has caused strangulation with ischemia. In late stages, signs of hypovolemic shock result from progressive dehydration and plasma loss.

Inguinal hernia

Inguinal hernia usually causes a lump to appear over the herniated area when the patient stands or strains. The lump disappears when the patient is supine. Tension on the herniated contents may cause a sharp, steady pain in the groin, which fades when the hernia is reduced. Strangulation produces severe pain and may lead to partial or complete bowel obstruction and even intestinal necrosis. Partial bowel obstruction may cause anorexia, vomiting, pain and tenderness in the groin, an irreducible mass, and diminished bowel sounds. Complete obstruction may cause shock, high fever, absent bowel sounds, and bloody stools.

Intussusception

In an infant or child, intussusception produces four cardinal clinical effects: Intermittent attacks of colicky pain cause the child to scream, draw his legs up to his abdomen, turn pale and diaphoretic and, possibly, display grunting respirations. Vomiting of stomach contents may occur initially, followed by further vomiting of bilestained or fecal material. “Currant-jelly” stools, containing a mixture of blood and mucus, may be observed. The patient will have a tender, distended abdomen, with a palpable, sausage-shaped abdominal mass; the viscera are usually absent from the right lower quadrant. In adults, intussusception produces nonspecific, chronic, and intermittent symptoms, including colicky abdominal pain and tenderness, vomiting, diarrhea (occasionally constipation), bloody stools, and weight loss. Abdominal pain usually localizes in the right lower quadrant, radiates to the back, and increases with eating. Adults with severe intussusception may develop strangulation with excruciating pain, abdominal distention, and tachycardia.

Volvulus

Vomiting and rapid, marked abdominal distention follow sudden onset of severe abdominal pain. Nausea, vomiting, bloody stools, constipation, and shock may occur. Without immediate treatment, volvulus can lead to strangulation of the twisted bowel loop, ischemia, infarction, perforation, and fatal peritonitis.

Inactive colon

The primary symptom of inactive colon is chronic constipation. The patient commonly strains to produce hard, dry stools accompanied by mild abdominal discomfort. Straining can aggravate other rectal conditions such as hemorrhoids.

Pancreatitis

In many patients, the first and only symptom of mild pancreatitis is steady epigastric pain centered close to the umbilicus, radiating between the tenth thoracic and sixth lumbar vertebrae, and unrelieved by vomiting. However, a severe attack causes extreme pain, persistent vomiting, abdominal rigidity, diminished bowel activity (suggesting peritonitis), crackles at lung bases, and left pleural effusion. Progression produces extreme malaise and restlessness, with mottled skin, tachycardia, low-grade fever (100° to 102° F [37.7° to 38.8° C]), and cold, sweaty extremities. The proximity of the inflamed pancreas to the bowel may cause ileus. If pancreatitis damages the islets of Langerhans, complications may include diabetes mellitus. Fulminant pancreatitis causes massive hemorrhage and total destruction of the pancreas, resulting in diabetic acidosis, shock, or coma.

Hemorrhoids

Although hemorrhoids may be asymptomatic, they characteristically cause painless, intermittent bleeding, which occurs on defecation. Bright red blood appears on stool or on toilet paper due to injury of the fragile mucosa covering the hemorrhoid. These first-degree hemorrhoids may itch because of poor anal hygiene. When second-degree hemorrhoids prolapse, they're usually painless and spontaneously return to the anal canal following defecation. Third-degree hemorrhoids cause constant discomfort and prolapse in response to any increase in intra□abdominal pressure. They must be manually reduced. Thrombosis of external hemorrhoids produces sudden rectal pain and a subcutaneous, large, firm lump that the patient can feel. If hemorrhoids cause severe or recurrent bleeding, they may lead to secondary anemia with significant pallor, fatigue, and weakness; however, such systemic complications are rare.

Anorectal abscess and fistula

Characteristics are throbbing pain and tenderness at the site of the abscess. A hard, painful lump develops on one side, preventing comfortable sitting. Discharge of pus may occur from the rectum, and there may be constipation or pain associated with bowel movements.

Rectal polyps

Because rectal polyps don't generally cause symptoms, they're usually discovered incidentally during a digital examination or rectosigmoidoscopy. Rectal bleeding is a common sign; high rectal polyps leave a streak of blood on the stool, whereas low rectal polyps bleed freely. Rectal polyps vary in appearance. Common polypoid adenomas are small, multiple lesions that are redder than normal mucosa. They're commonly pedunculated (attached to rectal mucosa by a long, thin stalk) and granular, with a red, lobular, or eroded surface. Villous adenomas are usually sessile (attached to the mucosa by a wide base) and vary in size from 0.5 to 12 cm. They are soft, friable, and finely lobulated. They may grow large and cause painful defecation; however, because adenomas are soft, they rarely cause bowel obstruction. Sometimes adenomas prolapse outside the anus, expelling parts of the adenoma with feces. These polyps may cause diarrhea, bloody stools, and subsequent fluid and electrolyte depletion, with hypotension and oliguria. In hereditary polyposis, rectal polyps resemble benign adenomas but occur as hundreds of small (0.5 cm) lesions carpeting the entire mucosal surface. Associated signs include diarrhea, bloody stools, and secondary anemia. In patients

with hereditary polyposis, changes in bowel habits with abdominal pain usually signal rectosigmoid cancer. P Juvenile polyps are large, inflammatory lesions, commonly without an epithelial covering. Mucus-filled cysts cover their usually smooth surface. Focal polypoid hyperplasia produces small (less than 3 mm), granular, sessile lesions, similar to the colon in color, or gray or translucent. They usually occur at the rectosigmoid junction.

Pilonidal disease

Generally, a pilonidal cyst produces no symptoms until it becomes infected, causing local pain, tenderness, swelling, or heat. Other clinical features include continuous or intermittent purulent drainage, followed by development of an abscess, chills, fever, headache, and malaise.

Rectal prolapse

In rectal prolapse, protrusion of tissue from the rectum may occur during defecation or walking. Other symptoms include a persistent sensation of rectal fullness, bloody diarrhea, pain in the lower abdomen due to ulceration, a feeling of incomplete evacuation, and rectal incontinence. Hemorrhoids or rectal polyps may coexist with a prolapse.

Anal fissure

Onset of an acute anal fissure is characterized by tearing, cutting, or burning pain during or immediately after a bowel movement. A few drops of blood may streak toilet paper or underclothes. Painful anal sphincter spasms result from ulceration of a “sentinel pile” (swelling at the lower end of the fissure). A fissure may heal spontaneously and completely or it may partially heal and break open again. Chronic fissure produces scar tissue that hampers normal bowel evacuation.

Pruritus ani

The key symptom of pruritus ani is perianal itching or burning after a bowel movement, during stress, or at night. In acute pruritus ani, scratching produces reddened skin, with weeping excoriations; in chronic pruritus ani, skin becomes thick and leathery, with excessive pigmentation.

Proctitis

Key symptoms include tenesmus, constipation, a feeling of rectal fullness, and abdominal cramps on the left side. The patient feels an intense urge to defecate, which produces a small amount of stool that may contain blood and mucus.

Neurofibromatosis

Signs and symptoms of NF-1 vary greatly from one family to another and within members of the same family. A patient who initially seems to have mild symptoms may develop more severe problems later. An infant with this form may present with only café-au-lait spots or may also have congenital glaucoma, plexiform neurofibromas, or pseudoarthrosis. About 90% of patients have Lisch nodules on the iris; as many as 15% develop optic pathway gliomas, which may cause a significant loss of vision. Cutaneous and other neurofibromas may begin to develop or become more prominent at puberty; pregnancy may exacerbate tumor growth. Some tumors become malignant; about 8% of patients develop neurofibrosarcoma (cancer of the nerve sheath). Other less-specific features may include other types of tumors (such as meningiomas), short stature, seizures, speech and learning disabilities, mental retardation (occasionally), and abnormalities of the cerebral, GI, and renal arteries. The first sign of NF-2 is usually a central nervous system tumor, such as a spinal or intracranial meningioma, an acoustic neuroma, and occasionally a schwannoma or spinal astrocytoma. Cutaneous neurofibromas may be less conspicuous in this form, and café-au-lait spots may be minimal or even absent. Learning disabilities and other less-specific features characteristic of NF-1 aren't typically seen in NF-2.

Osteogenesis imperfecta

Clinical severity varies, depending on the type. In type I, fractures characteristically occur from minimal trauma. The sclerae are a deep blue-black color, and the teeth may be yellow or even grayish blue from opalescent dentin. Patients with dental abnormalities are shorter and have more fractures at birth, more frequent fractures, and more severe skeletal deformities than type I patients with normal teeth. Bowing of the lower limbs is common in this type, as is kyphosis in adults. About 40% of all adults with type I have severely impaired hearing, and virtually all adults have some degree of hearing impairment by age 50. The number of fractures may spontaneously decrease in adolescence.

Type II is characterized by intrauterine fractures due to extreme bone fragility, leading to intrauterine or early infant death. Death usually results from complications of bone fragility, heart failure, pulmonary hypertension, or respiratory failure. Therapeutic intervention doesn't usually increase survival. Type III is generally nonlethal. Fractures are usually present at birth and occur frequently in childhood; they typically lead to progressive skeletal deformity and, eventually, impaired mobility. Patients have a poor growth rate; most fall below the third percentile in height for their age. Their sclerae are usually normal or light blue, and their teeth aren't usually opalescent. Type IV is characterized by osteoporosis, which leads to increased bone fragility. The sclerae may be light blue at birth but appear normal in adolescents and adults. Bowed limbs may be present at birth, but only 25% of patients have fractures at birth. The number of fractures may decrease spontaneously at puberty, but the majority of patients are short. A few have a skull deformity.

Marfan syndrome

The most common signs and symptoms of this disorder are skeletal abnormalities, particularly excessively long tubular bones and an arm span that exceeds the patient's height. The patient is usually taller than average for his family (in the 95th percentile for his age), with the upper half of his body

shorter than average and the lower half, longer. His fingers are long and slender (arachnodactyly). Weakness of ligaments, tendons, and joint capsules results in joints that are loose, hyperextensible, and habitually dislocated. Excessive growth of the rib bones gives rise to chest deformities such as pectus excavatum (funnel chest). Eye problems are also common; 75% of patients have crystalline lens displacement (ectopia lentis), the ocular hallmark of Marfan syndrome. Quivering of the iris with eye movement (iridodonesis) typically suggests this disorder. Most patients are severely myopic, many have retinal detachment, and some have glaucoma. The most serious complications occur in the cardiovascular system and include weakness of the aortic media, which leads to progressive dilation or dissecting aneurysm of the ascending aorta. Such dilation appears first in the coronary sinuses and is commonly preceded by aortic insufficiency. Less-common cardiovascular complications include mitral valve prolapse and endocarditis. Other associated problems include sparsity of subcutaneous fat, frequent hernias, cystic lung disease, recurrent spontaneous pneumothorax, and scoliosis or kyphosis.

Stickler's syndrome

The clinical phenotype can consist of ocular, auditory, craniofacial, and skeletal abnormalities. The number of organ systems involved and the specific phenotypic features expressed can vary significantly between affected family members and, in particular, between unrelated affected persons. Ocular symptoms, particularly high myopia, are common in persons with Stickler's syndrome, with the exception of those who have COLIJA2 mutations. Vitreal abnormalities are considered a hallmark of Stickler's syndrome, although the abnormalities in the vitreous differ in persons with a COL2AI mutation from those with a COLIIAI mutation. Retinal detachment resulting in blindness is the most serious ocular complication. The vitreoretinal degeneration that leads to retinal detachment is much more common in persons with a COL2AI mutation. Persons with Stickler's syndrome can also have congenital cataracts and develop glaucoma. Ocular symptoms are typically absent in persons with linkage to COLIJA2. Auditory symptoms include conductive hearing loss secondary to Eustachian tube dysfunction in children with cleft palate or collagen defects in the inner ear apparatus. Sensorineural hearing loss has an earlier onset and tends to be more progressive in persons with a COLIJAI mutation. Craniofacial features may include micrognathia (small lower jaw) and a flattened midface and nasal bridge. Micrognathia may be associated with some degree of cleft palate (bifid uvula to complete cleft of the palate). Micrognathia associated with glossoptosis places neonates and infants with Stickler's syndrome at significant risk for episodic obstructive apnea during feeding and when lying flat. Skeletal symptoms can include joint hypermobility in young children, spondyloepiphyseal dysplasia, and, later, degenerative arthropathy during early adult years. Also related to the collagen defect, scoliosis and mitral valve prolapse can develop in some persons with Stickler's syndrome.

Cystic fibrosis

The clinical effects of cystic fibrosis may become apparent soon after birth or may take years to develop. They include major aberrations in sweat gland, respiratory, and GI function. Sweat gland dysfunction is the most consistent abnormality. Increased concentrations of sodium and chloride in the sweat lead to hyponatremia and hypochloremia and can eventually induce fatal shock and arrhythmias, especially in hot weather. Respiratory symptoms reflect obstructive changes in the lungs: wheezy respirations; a dry, nonproductive paroxysmal cough; dyspnea; and tachypnea. These changes stem from thick, tenacious

secretions in the bronchioles and alveoli and eventually lead to severe atelectasis and emphysema. Children with cystic fibrosis display a barrel chest, cyanosis, and clubbing of the fingers and toes. They suffer recurring bronchitis and pneumonia as well as associated nasal polyps and sinusitis. Death typically results from pneumonia, emphysema, or atelectasis. The GI effects of cystic fibrosis occur mainly in the intestines, pancreas, and liver. One early symptom is meconium ileus; the neonate with cystic fibrosis doesn't excrete meconium, a dark green mucilaginous material found in the intestine at birth. He develops symptoms of intestinal obstruction, such as abdominal distention, vomiting, constipation, dehydration, and electrolyte imbalance. As the child gets older, obstruction of the pancreatic ducts and resulting deficiency of trypsin, amylase, and lipase prevent the conversion and absorption of fat and protein in the GI tract. The undigested food is then excreted in frequent, bulky, foul-smelling, pale stools with a high fat content. This malabsorption induces poor weight gain, poor growth, ravenous appetite, distended abdomen, thin extremities, and sallow skin with poor turgor. The inability to absorb fats results in a deficiency of fatsoluble vitamins (A, D, E, and K), leading to clotting problems, retarded bone growth, and delayed sexual development. Males may experience azoospermia and sterility; females may experience secondary amenorrhea but can reproduce. A common complication in infants and children is rectal prolapse secondary to malnutrition and wasting of perirectal supporting tissues. In the pancreas, fibrotic tissue, multiple cysts, thick mucus, and eventually fat replace the acini (small, saclike swellings normally found in this gland), producing symptoms of pancreatic insufficiency: insufficient insulin production, abnormal glucose tolerance, and glycosuria. About 15% of patients have adequate pancreatic exocrine function for normal digestion and, therefore, have a better prognosis. Biliary obstruction and fibrosis may prolong neonatal jaundice. In some patients, cirrhosis and portal hypertension may lead to esophageal varices, episodes of hematemesis and, occasionally, hepatomegaly.

Tay-Sachs disease

A neonate with classic Tay-Sachs disease appears normal at birth, although he may have an exaggerated Moro reflex. By age 3 to 6 months, he becomes apathetic and responds only to loud sounds. His neck, trunk, arm, and leg muscles grow weaker, and soon he can't sit up or lift his head. He has difficulty turning over, can't grasp objects, and has progressive vision loss. By age 18 months, the infant is usually deaf and blind and has seizures, generalized paralysis, and spasticity. His pupils are dilated and don't react to light. Decerebrate rigidity and a vegetative state follow. The child suffers recurrent bronchopneumonia after age 2 and usually dies before age 5. A child who survives may develop ataxia and progressive motor retardation between ages 2 and 8. The “ juvenile” form of Tay-Sachs disease generally appears between ages 2 and 5 as a progressive deterioration of psychomotor skills and gait. Patients with this type can survive to adulthood.

Phenylketonuria

An infant with undiagnosed and untreated PKU appears normal at birth but by 4 months begins to show signs of arrested brain development, including mental retardation and, later, personality disturbances (schizoid and antisocial personality patterns and uncontrollable temper). Such a child may have a lighter complexion than unaffected siblings and typically has blue eyes. He may also have microcephaly; eczematous skin lesions or dry, rough skin; and a musty (mousy) odor due to skin and urinary excretion

of phenylacetic acid. About 80% of these children have abnormal EEG patterns, and about one-third have seizures, usually beginning between ages 6 and 12 months. Children with PKU show a precipitous decrease in IQ in their first year, are usually hyperactive and irritable, and exhibit purposeless, repetitive motions. They have increased muscle tone and an awkward gait. Although blood phenylalanine levels are near normal at birth, they begin to rise within a few days. By the time they reach significant levels (about 30 mg/dl), cerebral damage has begun. Such irreversible damage probably is complete by age 2 or 3. However, early detection and treatment can minimize cerebral damage, and children under strict dietary control can lead normal lives.

Albinism

Light-skinned Whites with tyrosinase-negative albinism have pale skin and hair color ranging from white to yellow; their pupils appear red because of translucent irides. Blacks with the same disorder have hair that may be white, faintly tinged with yellow, or yellow-brown. Both Whites and Blacks with tyrosinase-positive albinism grow darker as they age. For instance, their hair may become straw-colored or light brown and their skin cream-colored or pink. People with tyrosinase-positive albinism may also have freckles and pigmented nevi that may require excision. In tyrosinase-variable albinism, at birth the child's hair is white, his skin is pink, and his eyes are gray. As he grows older, though, his hair becomes yellow, his irides may become darker, and his skin may even tan slightly. The skin of a person with albinism is easily damaged by the sun. It may look weather-beaten and is highly susceptible to precancerous and cancerous growths. The patient may also have photophobia, myopia, strabismus, and congenital horizontal nystagmus.

Sickle cell anemia

Characteristically, sickle cell anemia produces tachycardia, cardiomegaly, systolic and diastolic murmurs, pulmonary infarctions (which may result in cor pulmonale), chronic fatigue, unexplained dyspnea or dyspnea on exertion, hepatomegaly, jaundice, pallor, joint swelling, aching bones, chest pains, ischemic leg ulcers (especially around the ankles), and increased susceptibility to infection. Such symptoms usually don't develop until after age 6 months because large amounts of fetal Hb protect infants for the first few months after birth. Low socioeconomic status and related problems, such as poor nutrition and education, may delay diagnosis and supportive treatment. Infection, stress, dehydration, and conditions that provoke hypoxia— strenuous exercise, high altitude, unpressurized aircraft, cold, and vasoconstrictive drugs—may all provoke periodic crises. A painful crisis (vasoocclusive crisis, infarctive crisis), the most common crisis and the hallmark of the disease, usually appears periodically after age 5. It results from blood vessel obstruction by rigid, tangled sickle cells, which causes tissue anoxia and possible necrosis. This type of crisis is characterized by severe abdominal, thoracic, muscular, or bone pain and possibly worsening jaundice, dark urine, and a low-grade fever. Autosplenectomy, in which splenic damage and scarring is so extensive that the spleen shrinks and becomes impalpable, occurs in patients with longterm disease. This can lead to increased susceptibility to Streptococcus pneumoniae sepsis, which can be fatal without prompt treatment.

Infection may develop after the crisis subsides (in 4 days to several weeks), so watch for lethargy, sleepiness, fever, or apathy. An aplastic crisis (megaloblastic crisis) results from bone marrow depression

and is associated with infection, usually viral. It's characterized by pallor, lethargy, sleepiness, dyspnea, possible coma, markedly decreased bone marrow activity, and RBC hemolysis. In infants between ages 8 months and 2 years, an acute sequestration crisis may cause sudden massive entrapment of RBCs in the spleen and liver. This rare crisis causes lethargy and pallor and, if untreated, commonly progresses to hypovolemic shock and death. A hemolytic crisis is quite rare and usually occurs in patients who also have glucose-6-phosphate dehydrogenase deficiency. It probably results from complications of sickle cell anemia, such as infection, rather than from the disorder itself. Hemolytic crisis causes liver congestion and hepatomegaly as a result of degenerative changes. It worsens chronic jaundice, although increased jaundice doesn't always point to a hemolytic crisis. Suspect any of these crises in a sickle cell anemia patient with pale lips, tongue, palms, or nail beds; lethargy; listlessness; sleepiness with difficulty awakening; irritability; severe pain; a fever over 104° F (40° C); or a fever of 100° F (37.8° C) that persists for 2 days. Sickle cell anemia also causes long-term complications. Typically, the child is small for his age and has delayed puberty. (However, fertility isn't impaired.) If he reaches adulthood, his body build tends to be spiderlike — narrow shoulders and hips, long extremities, curved spine, barrel chest, and elongated skull. An adult usually has complications from organ infarction, such as retinopathy and nephropathy. Premature death commonly results from infection or from repeated occlusion of small blood vessels and consequent infarction or necrosis of major organs (such as cerebral blood vessel occlusion causing stroke).

Hemophilia

Hemophilia produces abnormal bleeding, which may be mild, moderate, or severe, depending on the degree of factor deficiency. Mild hemophilia commonly goes undiagnosed until adulthood because the patient doesn't bleed spontaneously or after minor trauma but has prolonged bleeding if challenged by major trauma or surgery. Postoperative bleeding continues as a slow ooze or ceases and starts again, up to 8 days after surgery. Severe hemophilia causes spontaneous bleeding. In many cases, the first sign of severe hemophilia is excessive bleeding after circumcision. Later, spontaneous bleeding or severe bleeding after minor trauma may produce large subcutaneous and deep intramuscular hematomas. Bleeding into joints (hemarthrosis) and muscles causes pain, swelling, extreme tenderness and, possibly, permanent deformity. Moderate hemophilia causes symptoms similar to severe hemophilia but produces only occasional spontaneous bleeding episodes. Bleeding near peripheral nerves may cause peripheral neuropathy, pain, paresthesia, and muscle atrophy. If bleeding impairs blood flow through a major vessel, it can cause ischemia and gangrene. Pharyngeal, lingual, intracardial, intracerebral, and intracranial bleeding may all lead to shock and death.

Fragile X syndrome

Small children may have relatively few identifiable physical characteristics; behavioral or learning difficulties may be the initial presenting features. Many adult male patients display a prominent jaw and forehead and a head circumference exceeding the 90th percentile. A long, narrow face with long or large ears that may be posteriorly rotated can be a helpful finding at all ages. Connective tissue abnormalities—including hyperextension of the fingers, a floppy mitral valve (in 80% of adults), and mild to severe pectus excavatum—have also been reported. Unusually large testes, found in most affected males after puberty, are an important identifying factor of the disorder. The average IQ of a person with

fragile X syndrome is comparable to that of a person with Down syndrome; however, the behavioral characteristics are quite different. Hyperactivity, speech difficulties, language delay, and autistic-like behaviors may be attributed to other disorders, such as attention deficit hyperactivity disorder, and thus delay the diagnosis. About 50% of females with the FMR1 full mutation will have clinical symptoms, although the degree of severity and number of symptoms vary widely among females with fragile X syndrome. Those who are symptomatic typically have a much milder clinical presentation than males due to having an unaffected X chromosome in addition to the one with an FMR1 full mutation. Some degree of cognitive impairment is usually present in symptomatic females. Learning disabilities—math difficulties, language deficits, and attentional problems—are most common. Some females can have IQ scores in the mental retardation range. Although affected females can have autistic-like features, excessive shyness or social anxiety are the more common behavioral symptoms. Prominent ears and the connective tissue manifestations may be as significant as in males. Although males with the FMR1 permutation are asymptomatic, some female carriers of an FMR1 premutation can have associated symptoms. These symptoms include significantly earlier menopause and a low normal performance IQ.

Down syndrome

The physical signs of Down syndrome (especially hypotonia) as well as some dysmorphic facial features and heart defects may be apparent at birth. The degree of mental retardation may not become apparent until the infant grows older. People with Down syndrome typically have craniofacial anomalies, such as slanting, almond-shaped eyes with epicanthic folds; a flat face; a protruding tongue; a small mouth and chin; a single transverse palmar crease (simian crease); small white spots (Brushfield's spots) on the iris; strabismus; a small skull; a flat bridge across the nose; slow dental development, with abnormal or absent teeth; small ears; a short neck; and cataracts. Other physical effects may include dry, sensitive skin with decreased elasticity; umbilical hernia; short stature; short extremities, with broad, flat, and squarish hands and feet; clinodactyly (small little finger that curves inward); a wide space between the first and second toe; and abnormal fingerprints and footprints. Hypotonic limb muscles impair reflex development, posture, coordination, and balance. Congenital heart disease (septal defects or pulmonary or aortic stenosis), duodenal atresia, megacolon, and pelvic bone abnormalities are common. The incidence of leukemia and thyroid disorders (particularly hypothyroidism) may be increased. Frequent upper respiratory infections can be a serious problem. Genitalia may be poorly developed and puberty delayed. Females may menstruate and be fertile. Males are infertile with low serum testosterone levels; many have undescended testicles. Patients with Down syndrome may have an IQ between 30 and 70; however, social performance is usually beyond that expected for mental age and fewer than 10% will have severe mental retardation. The level of intellectual function depends greatly on the environment and the amount of early stimulation received in addition to the IQ.

Trisomy 18 syndrome

Growth retardation begins in utero and remains significant after birth. Initial hypotonia may soon give way to hypertonia. Common findings include microcephaly and dolichocephaly, micrognathia, genital and perineal abnormalities (including imperforate anus), diaphragmatic hernia, and various renal defects. Congenital heart defects, such as ventricular septal defect, tetralogy of Fallot, transposition of the great vessels, and coarctation of the aorta, occur in 80% to 90% of patients and may be the cause of

death in many infants. Other findings may include a short and narrow nose with upturned nares; unilateral or bilateral cleft lip and palate; low-set, slightly pointed ears; a short neck; a conspicuous clenched hand with overlapping fingers (usually seen on ultrasound as well); neural tube defects; omphalocele; cystic hygroma; choroid plexus cysts (also seen in some healthy infants); and oligohydramnios.

Trisomy 13 syndrome

Infants with trisomy 13 syndrome may present with microcephaly, varying degrees of holoprosencephaly, sloping forehead with wide sutures and fontanel, and a scalp defect at the vertex. Microophthalmia, cataracts, and other eye abnormalities are seen in most patients with full trisomy 13. Bilateral cleft lip with associated cleft palate is seen in at least 45% of patients. Most are born with a congenital heart defect, especially hypoplastic left heart, ventricular septal defect, patent ductus arteriosus, or dextroposition, which may significantly contribute significantly to the cause of death. Other possible findings include a flat and broad nose, low-set ears and inner ear abnormalities, polydactyly of the hands and feet, club feet, omphaloceles, neural tube defects, cystic hygroma, genital abnormalities, cystic kidneys, hydronephrosis, and musculoskeletal abnormalities. Affected infants may also experience failure to thrive, seizures, apnea, and feeding difficulties.

Turner's syndrome

Turner's syndrome produces obvious characteristic signs. At birth, 50% of infants with this syndrome measure below the third percentile in length. Commonly, they have swollen hands and feet, a wide chest, and a low hairline that becomes more obvious as they grow. They may have severe webbing of the neck, and some have coarse, enlarged, prominent ears. Gonadal dysgenesis is seen at birth. Other signs and symptoms include pigmented nevi, lymphedema, hypoplasia, or malformed nails. As the child grows, short stature is common. The patient may exhibit average to slightly below-average intelligence. Developmental problems include right-left disorientation for extrapersonal space and defective figure drawing. The patient is typically immature and socially naive. Auscultation of the infant's chest indicates cardiovascular malformations, such as coarctation of the aorta and ventricular septal defects.

Klinefelter's syndrome

Klinefelter's syndrome may not be apparent until puberty or later in mild cases. Because many of these patients aren't mentally retarded, behavioral problems in adolescence or infertility may be the only presenting features initially. The syndrome's characteristic features include a small penis and prostate gland, small testicles, sparse facial and abdominal hair, feminine distribution of pubic hair (triangular shape), sexual dysfunction (impotence, lack of libido) and, in fewer than 50% of patients, gynecomastia. Aspermatogenesis and infertility result from progressive sclerosis and hyalinization of the seminiferous tubules in the testicles and from testicular fibrosis during and after puberty. In the mosaic form of Klinefelter's syndrome, such pathologic changes and resulting infertility may be delayed. Klinefelter's syndrome may also be associated with osteoporosis, abnormal body build (long legs with short, obese trunk), tall stature, learning disabilities characterized by poor verbal skills and, in some individuals, behavioral problems beginning in adolescence. It's also associated with an increased incidence of

pulmonary disease and varicose veins and a significantly increased rate of breast cancer because of the extra X chromosome.

Velocardiofacial syndrome

Clinical features of VCFS vary greatly among affected persons. Neonates with complex heart malformations, dysmorphic features, hypocalcemia, missing thymus, and renal anomalies represent the severe end of the VCFS clinical presentation. On the other hand, the clinical features can be so mild that an affected parent isn't identified until an offspring is diagnosed and genetic testing is subsequently done on the parents. Symptoms have been reported in the cardiac, craniofacial, neuropsychological, renal, ocular, neurologic, skeletal, endocrine, immune, and hematologic systems. The most common symptoms can be classified as cardiac, craniofacial, and neuropsychological. Clinical studies indicate that 70% to 85% of persons with VCFS have cardiac anomalies, of which conotruncal defects (for example, tetralogy of Fallot, interrupted aortic arch, truncus arteriosis) are the most common. This incidence may decrease over time as persons with only mild symptoms, such as learning difficulties in school or subtle dysmorphic features, are tested and found to be deletion positive. Craniofacial features include palatal abnormalities, dysmorphic facial features, and dysphagia usually due to velopharyngeal incompetence with or without pharyngoesophageal dysmotility. Therefore, feeding problems during infancy are common. The palate may be hypotonic and hypoplastic or have a midline cleft (ranging from bifid uvula to complete clefts of the palate). Related to palate problems are speech delays and abnormalities—particularly hypernasal speech and dyspraxia. Typical dysmorphic features include malformed ears, narrow palpebral fissures, hooded upper eyelids, ptosis, a broad square nasal root, a bulbous nasal tip (typically with a midline vertical crease), and micrognathia. Neuropsychological symptoms are present to some degree in most persons with VCFS. Hypotonia during the neonatal stage through early childhood period has been reported in more than 75% of cases. Even as hypotonia resolves with maturation, coordination and balance remain problematic. Cognitive symptoms, which can range from learning difficulties to varying levels of mental retardation, have been reported in over 80% of persons with VCFS. Children with VCFS typically have difficulties in visual-spatial activities, planning, attention, and concentration. Their strengths tend to be in rote verbal memory skills. Reading skills usually exceed math skills; however, reading comprehension tends to be problematic. The behavior of children with VCFS can be either shy and withdrawn or disinhibited and impulsive. Thought problems can be recognized during childhood and adolescence. Adults with VCFS are at risk for psychiatric disorders, particularly schizophrenia.

Neural tube defects

Spina bifida occulta is usually accompanied by a depression or dimple, tuft of hair, soft fatty deposits, port wine nevi, or a combination of these abnormalities on the skin over the spinal defect; however, such signs may be absent. Spina bifida occulta doesn't usually cause neurologic dysfunction but occasionally is associated with foot weakness or bowel and bladder disturbances. Such disturbances are especially likely during rapid growth phases, when the spinal cord's ascent within the vertebral column may be impaired by its abnormal adherence to other tissues. In both myelomeningocele and meningocele, a saclike structure protrudes over the spine. Like spina bifida occulta, meningocele seldom causes neurologic deficit. But myelomeningocele, depending on the level of the defect, causes

permanent neurologic dysfunction, such as flaccid or spastic paralysis and bowel and bladder incontinence. Associated disorders include trophic skin disturbances (ulcerations, cyanosis), clubfoot, knee contractures, hydrocephalus (in about 90% of patients), and possibly mental retardation, Arnold-Chiari syndrome (in which part of the brain protrudes into the spinal canal), and curvature of the spine.

Cleft lip and cleft palate

Orofacial cleft defects are divided into two major groups: cleft lip with or without cleft palate or cleft palate only. Cleft of the lip may involve the alveolus (premaxilla) and may extend through the palate (hard and soft). Congenital clefts of the face occur most commonly in the upper lip. They can range from a simple notch to a complete cleft from the lip edge, through the floor of the nostril and through the alveolus. Cleft lip can occur on either or both sides of the midline but rarely along the midline itself. A cleft lip involving only one side is a unilateral cleft lip, and a cleft on both sides of the midline is a bilateral cleft lip. When a bilateral cleft lip involves clefting of the alveolus on both sides of the premaxilla, the premaxilla is separated from the maxilla into a freely moving segment. A cleft of the palate only may be partial or complete, involving only the soft palate or extending from the soft palate completely through the hard palate. A cleft palate can occur alone or with a cleft lip. Isolated cleft palate is more commonly associated with congenital defects other than isolated cleft lip with or without cleft palate. (See Variations of cleft lip and cleft palate.) The constellation of U-shaped cleft palate, mandibular hypoplasia, and glossoptosis is known as Pierre Robin syndrome, or Robin syndrome. Robin syndrome can occur as an isolated defect or one feature of many different syndromes; therefore, a comprehensive genetic evaluation is suggested for infants with Robin syndrome. Because of the mandibular hypoplasia and glossoptosis, careful evaluation and management of the airway are mandatory for infants with Robin syndrome.

Asthma

An asthma attack may begin dramatically, with simultaneous onset of many severe symptoms, or insidiously, with gradually increasing respiratory distress. It typically includes progressively worsening shortness of breath, cough, wheezing, and chest tightness or some combination of these signs or symptoms. During an acute attack, the cough sounds tight and dry. As the attack subsides, tenacious mucoid sputum is produced (except in young children, who don't expectorate). Characteristic wheezing may be accompanied by coarse rhonchi, but fine crackles aren't heard unless associated with a related complication. Between acute attacks, breath sounds may be normal. The intensity of breath sounds in symptomatic asthma is typically reduced. A prolonged phase of forced expiration is typical of airflow obstruction. Evidence of lung hyperinflation (use of accessory muscles, for example) is particularly common in children. Acute attacks may be accompanied by tachycardia, tachypnea, and diaphoresis. In severe attacks, the patient may be unable to speak more than a few words without pausing for breath. Cyanosis, confusion, and lethargy indicate the onset of respiratory failure.

Allergic rhinitis

In seasonal allergic rhinitis, the key signs and symptoms are paroxysmal sneezing, profuse watery rhinorrhea, nasal obstruction or congestion, and pruritus of the nose and eyes. It's usually accompanied by pale, cyanotic, edematous nasal mucosa; red and edematous eyelids and conjunctivae; excessive lacrimation; and headache or sinus pain. Some patients also complain of itching in the throat and malaise. In perennial allergic rhinitis, conjunctivitis and other extranasal effects are rare, but chronic nasal obstruction is common. In many cases, this obstruction extends to eustachian tube obstruction, particularly in children. In both types of allergic rhinitis, dark circles may appear under the patient's eyes (“allergic shiners”) because of venous congestion in the maxillary sinuses. The severity of signs and symptoms may vary from season to season and from year to year.

Atopic dermatitis

Scratching the skin causes vasoconstriction and intensifies pruritus, resulting in erythematous, weeping lesions. Eventually, the lesions become scaly and lichenified. Usually, they're located in areas of flexion and extension, such as the neck, antecubital fossa, popliteal folds, and behind the ears. Patients with atopic dermatitis are prone to unusually severe viral infections, bacterial and fungal skin infections, ocular complications, and allergic contact dermatitis.

Latex allergy

Early signs that a life-threatening hypersensitivity reaction may be occurring include hypotension, tachycardia, and oxygen desaturation. Other clinical findings include urticaria, flushing, bronchospasm, difficulty breathing, pruritus, palpitations, abdominal pain, and syncope. Mild signs and symptoms may include itchy skin, swollen lips, nausea, diarrhea, and red, swollen, teary eyes.

Anaphylaxis

An anaphylactic reaction produces sudden physical distress within seconds or minutes (although a delayed or persistent reaction may occur for up to 24 hours) after exposure to an allergen. The reaction's severity is inversely related to the interval between exposure to the allergen and the onset of symptoms. Usually, the first symptoms include a feeling of impending doom or fright, weakness, sweating, sneezing, shortness of breath, nasal pruritus, urticaria, and angioedema, followed rapidly by symptoms in one or more target organs. Cardiovascular symptoms include hypotension, shock and, sometimes, cardiac arrhythmias. If untreated, arrhythmia may precipitate circulatory collapse. Respiratory symptoms can occur at any level in the respiratory tract and commonly include nasal mucosal edema, profuse watery rhinorrhea, itching, nasal congestion, and sudden sneezing attacks. Edema of the upper respiratory tract results in hypopharyngeal and laryngeal obstruction (hoarseness, stridor, and dyspnea). This is an early sign of acute respiratory failure, which can be fatal. GI and genitourinary symptoms include severe stomach cramps, nausea, diarrhea, and urinary urgency and incontinence.

Urticaria and angioedema

The characteristic features of urticaria are distinct, raised, evanescent (temporary) dermal wheals surrounded by an erythematous flare. These lesions may vary in size. In cholinergic urticaria, the wheals may be tiny and blanched, surrounded by erythematous flares. Angioedema characteristically produces nonpitted swelling of deep subcutaneous tissue, usually on the eyelids, lips, genitalia, and mucous membranes. These swellings don't usually itch but may burn and tingle.

Blood transfusion reaction

Immediate effects of a hemolytic transfusion reaction develop within a few minutes or hours after the start of the transfusion and may include chills, fever, urticaria, tachycardia, dyspnea, nausea, vomiting, tightness in the chest, chest and back pain, hypotension, bronchospasm, angioedema, and signs and symptoms of anaphylaxis, shock, pulmonary edema, heart failure, and renal failure. In a surgical patient under anesthesia, these symptoms are masked, but blood oozes from mucous membranes or the incision site. Delayed hemolytic reactions can occur up to several weeks after a transfusion, causing fever, an unexpected fall in serum hemoglobin (Hb) level, and jaundice. Allergic reactions are typically afebrile and characterized by urticaria and angioedema, possibly progressing to cough, respiratory distress, nausea, vomiting, diarrhea, abdominal cramps, vascular instability, shock, and coma. The hallmark of febrile nonhemolytic reactions is mild to severe fever that may begin at the start of transfusion or within 2 hours after its completion. Bacterial contamination produces a high fever, nausea, vomiting, diarrhea, abdominal cramps and, possibly, shock. Symptoms of viral contamination may not appear for several weeks after transfusion.

Rheumatoid arthritis

RA usually develops insidiously and initially produces nonspecific signs and symptoms, such as fatigue, malaise, anorexia, persistent low-grade fever, weight loss, lymphadenopathy, and vague articular symptoms. Later, more specific localized articular symptoms develop, commonly in the fingers at the proximal interphalangeal, metacarpophalangeal, and metatarsophalangeal joints. These symptoms usually occur bilaterally and symmetrically and may extend to the wrists, knees, elbows, and ankles. The affected joints stiffen after inactivity, especially upon rising in the morning. The fingers may assume a spindle shape from marked edema and joint congestion. The joints become tender and painful, at first only when the patient moves them, but eventually even at rest. They commonly feel hot to the touch. Ultimately, joint function is diminished. Deformities are common if active disease continues. Proximal interphalangeal joints may develop flexion deformities or become hyperextended. Metacarpophalangeal joints may swell dorsally, and volar subluxation and stretching of tendons may pull the fingers to the ulnar side (“ulnar drift”). The fingers may become fixed in a characteristic “swan's neck” appearance, or “boutonnière” deformity. The hands appear foreshortened, the wrists boggy; carpal tunnel syndrome from synovial pressure on the median nerve causes tingling paresthesia in the fingers. The most common extra-articular finding is the gradual appearance of rheumatoid nodules — subcutaneous, round or oval, nontender masses — usually on pressure areas such as the elbows. Vasculitis can lead to skin lesions, leg ulcers, and multiple systemic complications. Peripheral neuropathy may produce numbness or tingling in the feet or weakness and loss of sensation in the fingers. Stiff, weak, or painful muscles are common. Other common extra-articular effects include pericarditis, pulmonary nodules or fibrosis, pleuritis, scleritis, and episcleritis. Another complication is destruction of the odontoid process, part of the second cervical vertebra. Rarely, cord compression may occur, particularly in patients with long-standing deforming disease. Upper P motor neuron signs and symptoms, such as a positive Babinski's sign and muscle weakness, may also develop. RA can also cause temporomandibular joint disease, which impairs chewing and causes earaches. Other extra-articular findings may include infection, osteoporosis, myositis, cardiopulmonary lesions, lymphadenopathy, and peripheral neuritis.

Juvenile rheumatoid arthritis

Signs and symptoms vary with the type of JRA. Affecting boys and girls almost equally, systemic JRA accounts for about 10% of cases. The affected children may have mild, transient arthritis or frank polyarthritis with fever and rash. Joint involvement may not be evident at first, but the child's behavior may clearly suggest joint pain. Such a child may constantly want to sit in a flexed position, may not walk much, or may P refuse to walk at all. Young children with JRA are noticeably irritable and listless. Fever in systemic JRA occurs suddenly and spikes to 103° F (39.4° C) or higher once or twice daily, usually in the late afternoon, then rapidly returns to normal or subnormal. (This “sawtooth” or intermittent spiking fever pattern helps differentiate JRA from other inflammatory disorders.) When fever spikes, an evanescent rheumatoid rash commonly appears, consisting of small pale or salmon pink macules, usually on the trunk and proximal extremities and occasionally on the face, palms, and soles. Massaging or applying heat intensifies this rash. It's usually most conspicuous where the skin has been rubbed or subjected to pressure such as the areas of

skin covered by underclothing. Other signs and symptoms of systemic JRA may include hepatosplenomegaly, lymphadenopathy, pleuritis, pericarditis, myocarditis, and nonspecific abdominal pain. Polyarticular JRA accounts for about 40% of cases and is three times more common in females than in males; affected children may be seronegative or seropositive for rheumatoid factor (RF). It involves five or more joints and usually develops insidiously. Most commonly involved joints are the wrists, elbows, knees, ankles, and small joints of the hands and feet. Polyarticular JRA can also affect larger joints, including the temporomandibular joints, cervical spine, hips, and shoulders. These joints become swollen, tender, and stiff. Usually, the arthritis is symmetrical; it may be remittent or indolent. The patient may run a low-grade fever with daily peaks. Listlessness and weight loss can occur, possibly with lymphadenopathy and hepatosplenomegaly. Other signs of polyarticular JRA include subcutaneous nodules on the elbows or heels and noticeable developmental retardation. Seropositive polyarticular JRA, the more severe type, usually occurs late in childhood and can cause destructive arthritis that mimics adult rheumatoid arthritis. Pauciarticular JRA involves few joints (usually no more than four), typically affecting the knees and other large joints. This form accounts for 50% of cases and has major subtypes. The first, pauciarticular JRA with chronic iridocyclitis, most commonly strikes females younger than age 6 and involves the knees, elbows, ankles, or iris. Inflammation of the iris and ciliary body is commonly asymptomatic but may produce pain, redness, blurred vision, and photophobia. The second subtype, pauciarticular JRA with sacroiliitis, usually strikes males (9:1) older than age 8, who tend to test positive for human leukocyte antigen (HLA)-B27. This subtype is characterized by lower extremity arthritis that produces hip, sacroiliac, heel, and foot pain as well as Achilles' tendinitis. These patients may later develop the sacroiliac and lumbar arthritis characteristic of ankylosing spondylitis. Some also experience acute iritis, but not as many as those with the first subtype. The third subtype includes patients with joint involvement who are antinuclear antibody (ANA) and HLA-B27 negative and don't develop iritis. These patients have a better prognosis than those with the first or second subtype. Common to all types of JRA is joint stiffness in the morning or after periods of inactivity. Back pain and limited range of motion is common. Growth disturbances may also occur, resulting in uneven length of arms or legs due to overgrowth or undergrowth adjacent to inflamed joints.

Psoriatic arthritis

Psoriatic lesions usually precede the arthritic component; however, after the full syndrome is established, joint and skin lesions recur simultaneously. Arthritis may involve one joint or several joints symmetrically. Spinal involvement occurs in some patients. Peripheral joint involvement is most common in the distal interphalangeal joints of the hands, which have a characteristic sausage-like appearance. Nail changes include pitting, transverse ridges, onycholysis, keratosis, yellowing, and destruction. The patient may experience general malaise, fever, and eye involvement.

Ankylosing spondylitis

The first indication of ankylosing spondylitis is intermittent low back pain that's usually most severe in the morning or after a period of inactivity. Other signs and symptoms depend on the disease stage and may include: hip deformity and associated limited range of motion

kyphosis in advanced stages, caused by chronic stooping to relieve symptoms mild fatigue, fever, anorexia, or weight loss; occasional iritis; aortic insufficiency and cardiomegaly; and upper lobe pulmonary fibrosis (mimics tuberculosis) pain and limited expansion of the chest due to involvement of the costovertebral joints peripheral arthritis involving shoulders, hips, and knees stiffness and limited motion of the lumbar spine tenderness over the inflammation site. These signs and symptoms progress unpredictably, and the disease can go into remission, exacerbation, or arrest at any stage.
Sjögren's syndrome

About 50% of patients with Sjögren's syndrome have confirmed RA and a history of slowly developing sicca complex. However, some patients seek medical help for rapidly progressive and severe oral and ocular dryness, in many cases accompanied by periodic parotid gland enlargement. Ocular dryness (xerophthalmia) leads to foreign body sensation (gritty, sandy eye), redness, burning, photosensitivity, eye fatigue, itching, and mucoid discharge. The patient may also complain of a film across his field of vision. Oral dryness (xerostomia) leads to difficulty swallowing and talking; abnormal taste or smell sensation or both; thirst; ulcers of the tongue, buccal mucosa, and lips (especially at the corners of the mouth); and severe dental caries. Dryness of the respiratory tract leads to epistaxis, hoarseness, chronic nonproductive cough, recurrent otitis media, and increased incidence of respiratory infections. Other effects may include dyspareunia and pruritus (associated with vaginal dryness), generalized itching, fatigue, recurrent low-grade fever, and arthralgia or myalgia. Lymph node enlargement may be the first sign of malignant lymphoma or pseudolymphoma. Specific extraglandular findings in Sjögren's syndrome include interstitial pneumonitis; interstitial nephritis, which results in renal tubular acidosis in 25% of patients; Raynaud's phenomenon (20%); and vasculitis, usually limited to the skin and characterized by palpable purpura on the legs (20%). About 50% of patients show signs of hypothyroidism related to autoimmune thyroid disease. A few patients develop systemic necrotizing vasculitis.

Lupus erythematosus

The onset of SLE may be acute or insidious and produces no characteristic clinical pattern. However, its symptoms commonly include fever, weight loss, malaise, and fatigue as well as rashes and polyarthralgia. SLE may involve every organ system. In 90% of patients, joint involvement is similar to that in rheumatoid arthritis. Skin lesions are most commonly erythematous rashes in areas exposed to light. The classic butterfly rash over the nose and cheeks occurs in fewer than 50% of the patients. (See Butterfly rash, page 468.) Ultraviolet rays often provoke or aggravate skin eruptions. Vasculitis can develop (especially in the digits), possibly leading to infarctive lesions, necrotic leg ulcers, or digital gangrene. Raynaud's phenomenon appears in about 20% of P patients. Patchy alopecia and painless ulcers of the mucous membranes are common. Constitutional symptoms of SLE include aching, malaise, fatigue, lowgrade or spiking fever, chills, anorexia, and weight loss. Lymph node enlargement (diffuse or local, and nontender), abdominal pain, nausea, vomiting, diarrhea, and constipation may occur. Females may experience irregular menstrual periods or amenorrhea during the active phase of SLE. About 50% of SLE patients develop signs of cardiopulmonary abnormalities, such as pleuritis, pericarditis, and dyspnea. Myocarditis, endocarditis, tachycardia, parenchymal infiltrates, and pneumonitis may occur. Renal effects may include hematuria, proteinuria, urine sediment, and cellular casts, which may progress

to total kidney failure. Urinary tract infections may result from heightened susceptibility to infection. Seizure disorders and mental dysfunction may indicate neurologic damage. Central nervous system (CNS) involvement may produce emotional instability, psychosis, and organic mental syndrome. Headaches, irritability, and depression are common. (See Signs of systemic lupus erythematosus.)

Fibromyalgia syndrome

The primary symptoms is diffuse, dull, aching pain that's typically concentrated across the neck and shoulders and in the lower back and proximal limbs. It can involve all body quadrants (bilateral upper trunk and arms, and bilateral lower trunk and legs) and typically is worse in the morning, when it's associated with stiffness. The pain can vary form day to day and be exacerbated by stress, lack of sleep, weather changes, and inactivity. Sleep disturbance and fatigue are commonly reported. The patient awakens feeling fatigued and remains so throughout the day. Fatigue is commonly present from a half hour to several hours after rising in the morning and can last for the rest of the day. Other associated features that can occur with FMS include irritable bowel syndrome, tension headaches, puffy hands (sensation of hand swelling, especially in the morning), and paresthesia.

Goodpasture's syndrome

Goodpasture's syndrome may initially cause malaise, fatigue, and pallor associated with severe iron deficiency anemia. Pulmonary findings range from slight dyspnea and cough with blood-tinged sputum to hemoptysis and frank pulmonary hemorrhage. Subclinical pulmonary bleeding may precede overt hemorrhage and renal disease by months or years. Usually, renal findings are subtler, although some patients note hematuria and peripheral edema.

Reiter's syndrome

The patient with Reiter's syndrome may complain of dysuria, hematuria, urgent and frequent urination, and mucopurulent penile discharge, with swelling and reddening of the urethral meatus. Small painless ulcers may erupt on the glans penis (balanitis). These coalesce to form irregular patches that cover the penis and scrotum. He may also experience suprapubic pain, fever, anorexia with weight loss, and other genitourinary (GU) complications, such as prostatitis and hemorrhagic cystitis. Arthritic symptoms usually follow GU or enteric symptoms and last from 2 to 4 months. Asymmetrical and extremely variable polyarticular P arthritis is most common, with a tendency to develop in weight-bearing joints of the legs and sometimes in the low back or sacroiliac joints. The arthritis is usually acute, with warm, erythematous, and painful joints, but it may be mild, with minimal synovitis. Muscle wasting is common near affected joints. Fingers and toes may swell and appear sausagelike. Ocular symptoms include mild bilateral conjunctivitis, possibly complicated by keratitis, iritis, retinitis, or optic neuritis. In severe cases, burning, itching, and profuse mucopurulent discharge are possible. In 30% of patients, skin lesions (keratoderma blennorrhagicum) develop 4 to 6 weeks after onset of other symptoms and may last for several weeks. These macular to hyperkeratotic lesions commonly resemble those of psoriasis. They usually occur on the palms and soles but can develop anywhere on the trunk, extremities, or scalp. Nails become

thick, opaque, and brittle; keratic debris accumulates under the nails. In many patients, painless, transient ulcerations erupt on the buccal mucosa, palate, and tongue.

Scleroderma

Scleroderma typically begins with Raynaud's phenomenon — blanching, cyanosis, and erythema of the fingers and toes in response to stress or exposure to cold. Progressive phalangeal resorption may shorten the fingers. Compromised circulation, which results from abnormal thickening of the arterial intima, may cause slowly healing ulcerations on the tips of the fingers or toes that may lead to gangrene. Raynaud's phenomenon may precede scleroderma by months or years. Later symptoms include pain, stiffness, and finger and joint swelling. Skin thickening produces taut, shiny skin over the entire hand and forearm. Facial skin also becomes tight and inelastic, causing a masklike appearance and “pinching” of the mouth. As tightening progresses, contractures may develop. GI dysfunction causes frequent reflux, heartburn, dysphagia, and bloating after meals. These symptoms may cause the patient to decrease food intake and lose weight. Other GI effects include abdominal distention, diarrhea, constipation, and malodorous floating stools.

Polymyositis and dermatomyositis

Polymyositis begins acutely or insidiously with muscle weakness, tenderness, and discomfort. It affects proximal muscles more than distal muscles and impairs performance of ordinary activities. The patient may have trouble getting up from a chair, combing his hair, reaching into a high cupboard, climbing stairs, or even raising his head from a pillow. Other muscular symptoms include inability to move against resistance, proximal dysphagia, dysphonia, and difficulty breathing. In dermatomyositis, an erythematous rash usually erupts on the face, neck, upper back, chest, and arms as well as around the nail beds. A characteristic heliotropic rash appears on the eyelids, accompanied by periorbital edema. Gottron's papules (violet, flat-topped lesions) may appear on the interphalangeal joints.

X-linked infantile hypogammaglobulinemia

Typically, the infant with X-linked hypogammaglobulinemia is asymptomatic until age 6 months, when transplacental maternal immunoglobulins that provided immunity have been depleted. He then develops recurrent bacterial otitis media, pneumonia, dermatitis, bronchitis, and meningitis — usually caused by pneumococci, streptococci, Haemophilus influenzae, or other gram-negative organisms. Purulent conjunctivitis, abnormal dental caries, and polyarthritis resembling rheumatoid arthritis may also occur. Severe malabsorption associated with infestation by Giardia lamblia may retard development. Despite recurrent infections, lymphadenopathy and splenomegaly are usually absent.

Common variable immunodeficiency

In common variable immunodeficiency, pyogenic bacterial infections are characteristic but tend to be chronic rather than acute (as in X-linked hypogammaglobulinemia). Recurrent sinopulmonary infections, chronic bacterial conjunctivitis, and malabsorption (commonly associated with infestation by Giardia lamblia) are usually the first clues to

immunodeficiency. Common variable immunodeficiency may be associated with autoimmune diseases, such as systemic lupus erythematosus, rheumatoid arthritis, hemolytic anemia, and pernicious anemia, and with cancers, such as leukemia and lymphoma.

IgA deficiency

Some IgA-deficient patients have no symptoms, possibly because they have extra amounts of low-molecular-weight IgM. This immunoglobulin takes over IgA function and helps maintain immunologic defenses. Among patients who develop symptoms, chronic sinopulmonary infection is the most common. Other effects are respiratory allergy, often triggered by infection; GI tract diseases, such as celiac disease, ulcerative colitis, and regional enteritis; autoimmune diseases, such as rheumatoid arthritis, systemic lupus erythematosus, immunohemolytic anemia, and chronic hepatitis; and malignant tumors, such as squamous cell carcinoma of the lungs, reticulum cell sarcoma, and thymoma. Age of onset varies. Some IgA-deficient children with recurrent respiratory disease and middle ear inflammation may begin to synthesize IgA spontaneously as recurrent infections subside and their condition improves.

DiGeorge syndrome

Symptoms are usually obvious at birth or shortly thereafter. An infant with DiGeorge syndrome may have low-set prominent ears, notched ear pinnae, a mouth without the usual bow-shaped lip, an undersized jaw, and abnormally wide-set eyes (hypertelorism) that are low-set and posteriorly angulated. Additionally, an infant may have a bifid uvula and a high, arched palate. Congenital heart anomalies are common. Cardiovascular abnormalities include great blood vessel anomalies (these may also develop soon after birth) and tetralogy of Fallot. An infant with thymic hypoplasia (rather than aplasia) may experience a spontaneous return of cell-mediated immunity but can develop severe Tcell deficiencies later in life. This allows exaggerated susceptibility to viral, fungal, or bacterial infections, which may be overwhelming. Hypoparathyroidism, usually associated with DiGeorge syndrome, typically causes tetany, hyperphosphatemia, and hypocalcemia. Hypocalcemia (calcium levels less than 7 mg/dl) develops early and is unusually resistant to treatment. It can lead to tetany, seizures, central nervous system damage, and early heart failure. Rare cases of partial immunoglobulin (Ig) A deficiency have been linked to chromosome 1 and deletions of the IgA1 or IgA2 genes. Alterations in chromosome 6 suggest altered major histocompatibility complex, which is reflected in decreased T-cell responses. Aberrations in chromosome 18 are linked to facial abnormalities, nystagmus, hypotonia, atretic or stenotic ear canals, hearing loss, and mental retardation.

Acquired immunodeficiency syndrome

A person with HIV may remain asymptomatic for months or years. Initially, laboratory evidence or seroconversion to HIV antibodies may be the only clinical evidence of infection. However, as the disease progresses, the patient may develop generalized adenopathy and nonspecific signs and symptoms, such as weight loss, fatigue, night sweats, and fevers. As the patient's T-cell count lowers further, neurologic symptoms, opportunistic infections, and

certain normally rare P cancers may develop. HIV also destroys lymph nodes and immunologic organs, leading to major dysfunctions of the immunological system. Eventually, HIV advances to AIDS. (Some individuals, termed nonprogressors, develop AIDS very slowly or not at all. They seem to have genetic differences that prevent the virus from attaching to certain immune receptors.)

Chronic mucocutaneous candidiasis

Chronic candidal infections can affect the skin, mucous membranes, nails, and vagina, usually causing large, circular lesions. These infections seldom produce systemic symptoms but in late stages may be associated with recurrent respiratory tract infections. Other associated conditions include severe viral infections that may precede the onset of endocrinopathy and, sometimes, hepatitis. Involvement of the mouth, nose, and palate may cause speech and eating difficulties. Symptoms of endocrinopathy are peculiar to the organ involved. Tetany and hypocalcemia are most common and are associated with hypoparathyroidism. Addison's disease, hypothyroidism, diabetes, and pernicious anemia are also connected with chronic mucocutaneous candidiasis. Psychiatric disorders are likely because of disfigurement and multiple endocrine aberrations.

Chronic fatigue syndrome

CFS has specific symptoms and signs, based on the exclusion of other possible causes. Its characteristic symptom is prolonged, often overwhelming fatigue that's commonly associated with a varying complex of other symptoms that are similar to those of many infections, including myalgia and cephalgia. It may develop within a few hours and can last for 6 months or more. Fatigue isn't relieved by rest and is severe enough to restrict activities of daily living by at least 50%.

Chronic granulomatous disease

Usually, the patient with CGD displays signs and symptoms associated with infections of the skin, lymph nodes, lung, liver, and bone by age 2. Skin infection is characterized by small, well-localized areas of tenderness. Seborrheic dermatitis of the scalp and axilla is also common. Lymph node infection typically causes marked lymphadenopathy with draining lymph nodes and hepatosplenomegaly. Many patients develop liver abscess, which may be recurrent and multiple; abdominal tenderness, fever, anorexia, and nausea point to abscess formation. Other common infections include osteomyelitis, which causes localized pain and fever, pneumonia, and gingivitis with severe periodontal disease.

Severe combined immunodeficiency disease

An extreme susceptibility to infection becomes obvious in the infant with SCID in the first months of life. The infant fails to thrive and develops chronic otitis; sepsis; watery diarrhea (associated with Salmonella or Escherichia coli); recurrent pulmonary infections (usually caused by Pseudomonas, cytomegalovirus, or Pneumocystis jiroveci [formerly carinii]); persistent oral candidiasis, sometimes with esophageal erosions; and possibly fatal viral infections such as chickenpox. P. jiroveci pneumonia usually strikes a severely

immunodeficient infant in the first 3 to 5 weeks after birth. Onset is typically insidious, with gradually worsening cough, low-grade fever, tachypnea, and respiratory distress. Chest X-ray characteristically shows bilateral pulmonary infiltrates.

Complement deficiencies

Clinical effects vary with the specific deficiency. C2 and C3 deficiencies and C5 familial dysfunction increase susceptibility to bacterial infection (which may involve several body systems simultaneously). C2 and C4 deficiencies are also associated with collagen vascular disease such as lupus erythematosus and with chronic renal failure. C5 dysfunction, a familial defect in infants, causes failure to thrive, diarrhea, and seborrheic dermatitis. C1 esterase inhibitor deficiency (hereditary angioedema) may cause periodic swelling in the face, hands, abdomen, or throat, with potentially fatal laryngeal edema.

Malignant brain tumors

General ▪ Headache; mental activity changes ▪ Decreased motor strength and coordination ▪ Seizures; scanning speech ▪ Altered vital signs Localizing ▪ Third ventricle: changes in mental activity and level of consciousness, nausea, pupillary dilation and sluggish light reflex; later—paresis or ataxia ▪ Brain stem and pons: early—ipsilateral trigeminal, abducens, and facial nerve palsies; later—cerebellar ataxia, tremors, other cranial nerve deficits ▪ Third or fourth ventricle or aqueduct of Sylvius: secondary hydrocephalus ▪ Thalamus or hypothalamus: various endocrine, metabolic, autonomic, and behavioral changes ▪ Increased ICP, papilledema) ▪ Mental and behavioral changes ▪ Altered vital signs (increased systolic pressure; widened pulse pressure, respiratory changes) ▪ Speech and sensory disturbances ▪ In children, irritability, projectile vomiting : headache (bifrontal or bioccipital); worse in the morning; intensified by coughing, straining, or sudden head movements abnormal reflexes, motor responses : papilledema, nystagmus, hearing loss, flashing lights, dizziness, ataxia, paresthesia of face, cranial nerve palsies (V, VI, VII, IX, X, primarily sensory), hemiparesis, suboccipital tenderness; compression of supratentorial area produces other general and focal signs and symptoms Skull changes (bony bulge) over tumor ▪ Sphenoidal ridge, indenting optic nerve: unilateral visual changes and papilledema ▪ Prefrontal parasagittal: personality and behavioral changes ▪ Motor cortex: contralateral motor changes ▪ Anterior fossa compressing both optic nerves and frontal lobes: bilateral vision loss ▪ Pressure on cranial nerves causing varying symptom ▪ Decreased visual acuity and other vision disturbances Stiff neck and suboccipital discomfort

Pituitary tumors

As pituitary adenomas grow, they replace normal glandular tissue and enlarge the sella turcica, which houses the pituitary gland. The resulting pressure on adjacent intracranial structures produces these typical clinical manifestations: Neurologic: frontal headache visual symptoms, beginning with blurring and progressing to field cuts (hemianopsias) and then unilateral blindness P cranial nerve involvement (III, IV, VI) from lateral extension of the tumor, resulting in strabismus; double vision, with compensating head tilting and dizziness; conjugate deviation of gaze; nystagmus; lid ptosis; and limited eye movements increased intracranial pressure (ICP) (secondary hydrocephalus) personality changes or dementia, if the tumor breaks through to the frontal lobes seizures rhinorrhea, if the tumor erodes the base of the skull pituitary apoplexy secondary to hemorrhagic infarction of the adenoma. Such hemorrhage may lead to both cardiovascular and adrenocortical collapse. Endocrine: hypopituitarism, to some degree, in all patients with adenoma, becoming more obvious as the tumor replaces normal gland tissue (signs and symptoms include amenorrhea, decreased libido and impotence in men, skin changes [waxy appearance, decreased wrinkles, and pigmentation], loss of axillary and pubic hair, lethargy, weakness, increased fatigability, intolerance to cold, and constipation [because of decreased corticotropin and thyroid-stimulating hormone production]) addisonian crisis, precipitated by stress and resulting in nausea, vomiting, hypoglycemia, hypotension, and circulatory collapse diabetes insipidus, resulting from extension to the hypothalamus prolactin-

secreting adenomas (in 70% to 75%), with amenorrhea and galactorrhea GH-secreting adenomas, with acromegaly corticotropin-secreting adenomas, with Cushing's syndrome.

Laryngeal cancer

In intrinsic laryngeal cancer, the dominant and earliest symptom is hoarseness that persists longer than 3 weeks; in extrinsic cancer, it's a lump in the throat or pain or burning in the throat when drinking citrus juice or hot liquid. Later clinical effects of metastasis include dysphagia, dyspnea, cough, enlarged cervical lymph nodes, and pain radiating to the ear.

Thyroid cancer

The primary sign of thyroid cancer is a painless nodule, a hard nodule in an enlarged thyroid gland, or palpable lymph nodes with thyroid enlargement. Eventually, the pressure of such a nodule or enlargement causes hoarseness, dysphagia, dyspnea, and pain on palpation. If the tumor is large enough to destroy the gland, hypothyroidism follows, with its typical symptoms of low metabolism (mental apathy and sensitivity to cold). However, if the tumor stimulates excess thyroid hormone production, it induces symptoms of hyperthyroidism (sensitivity to heat, restlessness, and hyperactivity). Other clinical features include diarrhea, anorexia, irritability, vocal cord paralysis, and symptoms of distant metastasis.

Malignant spinal neoplasms

Extramedullary tumors produce symptoms by pressing on nerve roots, the spinal cord, and spinal vessels; intramedullary tumors, by destroying the parenchyma and compressing adjacent areas. Because intramedullary tumors may extend over several spinal cord segments, their symptoms are more variable than those of extramedullary tumors. The following clinical effects are likely with all malignant spinal cord neoplasms: Pain—Most severe directly over the tumor, radiates around the trunk or down the limb on the affected side and is unrelieved by bed rest. It may worsen when lying down or with straining, coughing, or sneezing. Pain can be diffuse, occurring over all extremities. Generally, it progressively worsens and isn't relieved by medication. Motor symptoms—Asymmetric spastic muscle weakness, decreased muscle tone, exaggerated reflexes, and a positive Babinski's sign. If the tumor is at the level of the cauda equina, muscle flaccidity, muscle wasting, weakness, and progressive diminution in tendon reflexes are characteristic. Sensory deficits—Contralateral loss of pain, temperature, and touch sensation (Brown-Séquard's syndrome). These losses are less obvious to the patient than functional motor changes. Caudal lesions invariably produce paresthesia in the nerve distribution pathway of the involved roots. Bowel and bladder symptoms—Urine retention is an inevitable late sign with cord compression. Early signs include incomplete emptying or difficulty with the urine stream, which is usually unnoticed or ignored. Cauda equina tumors cause bladder and bowel incontinence due to flaccid paralysis.

Lung cancer

Because early-stage lung cancer usually produces no symptoms, this disease is usually in an advanced state at diagnosis. These late-stage symptoms commonly lead to diagnosis: Epidermoid and small cell carcinomas —smoker's cough, hoarseness, wheezing, dyspnea,

hemoptysis, and chest pain Adenocarcinoma and large cell carcinoma —fever, weakness, weight loss, anorexia, and shoulder pain. In addition to their obvious interference with respiratory function, lung tumors may also alter the production of hormones that regulate body function or homeostasis. Clinical conditions that result from such changes are known as hormonal paraneoplastic syndromes: Gynecomastia may result from large cell carcinoma. Hypertrophic pulmonary osteoarthropathy (bone and joint pain from cartilage erosion due to abnormal production of growth hormone) may result from large cell carcinoma and adenocarcinoma. Cushing's and carcinoid syndromes may result from small cell carcinoma. Hypercalcemia may result from epidermoid tumors. Metastatic signs and symptoms vary greatly, depending on the effect of tumors on intrathoracic and distant structures: bronchial obstruction: hemoptysis, atelectasis, pneumonitis, dyspnea cervical thoracic sympathetic nerve involvement: miosis, ptosis, exophthalmos, reduced sweating chest wall invasion: piercing chest pain, increasing dyspnea, severe shoulder pain, radiating down arm esophageal compression: dysphagia local lymphatic spread: cough, hemoptysis, stridor, pleural effusion pericardial involvement: pericardial effusion, tamponade, arrhythmias P phrenic nerve involvement: dyspnea, shoulder pain, unilateral paralyzed diaphragm, with paradoxical motion recurrent nerve invasion: hoarseness, vocal cord paralysis vena caval obstruction: venous distention and edema of face, neck, chest, and back. Distant metastasis may involve any part of the body, most commonly the central nervous system, liver, and bone.

Breast cancer

Warning signals of possible breast cancer include: a lump or mass in the breast (a hard, nontender stony mass is usually malignant) change in symmetry or size of the breast change in skin, thickening, scaly skin around the nipple, dimpling, edema (peau d'orange), or ulceration change in skin temperature (a warm, hot, or pink area; suspect cancer in a nonlactating woman older than childbearing age until proven otherwise) unusual drainage or discharge (a spontaneous discharge of any kind in a nonbreast-feeding, nonlactating woman warrants thorough investigation; so does any discharge produced by breast manipulation (greenish black, white, creamy, serous, or bloody.) (If a breast-fed infant rejects one breast, this may suggest possible breast cancer.) change in the nipple, such as itching, burning, erosion, or retraction pain (not usually a symptom of breast cancer unless the tumor is advanced, but it should be investigated) bone metastasis, pathologic bone fractures, and hypercalcemia edema of the arm.

Gastric cancer

Early clues to gastric cancer are chronic dyspepsia and epigastric discomfort, followed in later stages by weight loss, anorexia, feeling of fullness after eating, anemia, and fatigue. If the cancer is in the cardia, the first sign or symptom may be dysphagia and, later, vomiting (commonly coffeeground vomitus). Affected patients may also have blood in their stools. The course of gastric cancer may be insidious or fulminating. Unfortunately, the patient typically treats himself with antacids or histamine blockers until the symptoms of advanced stages appear.

Esophageal cancer

Dysphagia and weight loss are the most common presenting symptoms. Dysphagia is mild and intermittent at first, but it soon becomes constant. Pain, hoarseness, coughing, and esophageal obstruction follow. Cachexia usually develops.

Pancreatic cancer

The most common features of pancreatic cancer are weight loss, abdominal or low back pain, jaundice, and diarrhea. Other generalized effects include fever, loss of appetite, nausea, vomiting, weakness, indigestion, clay-colored stools, paleness, depression, skin lesions (usually on the legs), and fatigue.

Colorectal cancer

Signs and symptoms of colorectal cancer result from local obstruction and, in later stages, from direct extension to adjacent organs (bladder, prostate, ureters, vagina, sacrum) and distant metastasis (usually liver). In the early stages, signs and symptoms are typically vague and depend on the anatomic location and function of the bowel segment containing the tumor. Later signs or symptoms usually include pallor, cachexia, ascites, hepatomegaly, or lymphangiectasis. ELDER TIP Older patients may ignore bowel symptoms, believing that they result from constipation, poor diet, or hemorrhoids. Evaluate your older patient's responses to your questions carefully. On the right side of the colon (which absorbs water and electrolytes), early tumor growth causes no signs of obstruction because the tumor tends to grow along the bowel rather than surround the lumen, and the fecal content in this area is normally liquid. It may, however, cause black, tarry stools; anemia; and abdominal aching, pressure, or dull cramps. As the disease progresses, the patient develops weakness, fatigue, exertional dyspnea, vertigo and, eventually, diarrhea, obstipation, anorexia, weight loss, vomiting, and other signs or symptoms of intestinal obstruction. In addition, a tumor on the right side may be palpable. On the left side, a tumor causes signs of an obstruction even in early stages because in this area stools are of a formed consistency. It commonly causes rectal bleeding (in many cases ascribed to hemorrhoids), intermittent abdominal fullness or cramping, and rectal pressure. As the disease progresses, the patient develops obstipation, P diarrhea, or “ribbon” or pencil-shaped stools. Typically, he notices that passage of stools or flatus relieves the pain. At this stage, bleeding from the colon becomes obvious, with dark or bright red blood in the feces and mucus in or on the stools. With a rectal tumor, the first symptom is a change in bowel habits, in many cases beginning with an urgent need to defecate on arising (morning diarrhea) or obstipation alternating with diarrhea. Other signs are blood or mucus in stools and a sense of incomplete evacuation. Late in the disease, pain begins as a feeling of rectal fullness that later becomes a dull, and sometimes constant, ache confined to the rectum or sacral region.

Kidney cancer

Kidney cancer produces a classic clinical triad (hematuria, pain, and a palpable mass), but any one may be the first sign of cancer. Microscopic or gross hematuria (which may be intermittent) suggests that the cancer has spread to the renal pelvis. Constant abdominal or

flank pain may be dull or, if the cancer causes bleeding or blood clots, acute and colicky. The mass is generally smooth, firm, and nontender. All three signs coexist in only about 10% of patients. Other signs include fever (perhaps from hemorrhage or necrosis), hypertension (from compression of the renal artery with renal parenchymal ischemia), rapidly progressing hypercalcemia (possibly from ectopic parathyroid hormone production by the tumor), and urine retention. Weight loss, edema in the legs, nausea, and vomiting signal advanced disease.

Liver cancer

Clinical effects of liver cancer include: a mass in the right upper quadrant tender, nodular liver on palpation severe pain in the epigastrium or the right upper quadrant bruit, hum, or rubbing sound if tumor involves a large part of the liver weight loss, weakness, anorexia, fever occasional jaundice or ascites occasional evidence of metastasis through venous system to lungs, from lymphatics to regional lymph nodes, or by direct invasion of portal veins dependent edema.

Bladder cancer

In early stages, about 25% of patients with bladder tumors have no symptoms. Commonly, the first sign is gross, painless, intermittent hematuria (in many cases with clots in the urine). Many patients with invasive lesions have suprapubic pain after voiding. Other signs and symptoms include bladder irritability, urinary frequency, nocturia, and dribbling.

Gallbladder and bile duct cancer

Clinically, gallbladder cancer is almost indistinguishable from cholecystitis—pain in the epigastrium or right upper quadrant, weight loss, anorexia, nausea, vomiting, and jaundice. However, chronic, progressively severe pain in an afebrile patient suggests malignancy. In patients with simple gallstones, pain is sporadic. Another telling clue to malignancy is palpable gallbladder (right upper quadrant), with obstructive jaundice. Some patients may also have hepatosplenomegaly. Progressive profound jaundice is commonly the first sign of obstruction due to extrahepatic bile duct cancer. The jaundice is usually accompanied by chronic pain in the epigastrium or the right upper quadrant, radiating to the back. Other common signs or symptoms, if associated with active cholecystitis, include pruritus, skin excoriations, anorexia, weight loss, chills, and fever.

Prostate cancer

Signs and symptoms of prostate cancer appear only in the advanced stages and include difficulty initiating a urine stream, dribbling, urine retention, unexplained cystitis and, rarely, hematuria. Pain may be present in the lower back, with urination, ejaculation, and bowel movement.

Testicular cancer

The first sign is usually a firm, painless, and smooth testicular mass, varying in size and sometimes producing a sense of testicular heaviness. When such a tumor causes chorionic gonadotropin or estrogen production, gynecomastia and nipple tenderness may result. In

advanced stages, signs and symptoms include ureteral obstruction, abdominal mass, cough, hemoptysis, shortness of breath, weight loss, fatigue, pallor, and lethargy.

Penile cancer

In a circumcised man, early signs of penile cancer include a small circumscribed lesion, a pimple, or a sore on the penis. In an uncircumcised man, however, such early symptoms may go unnoticed, so penile cancer first becomes apparent when it causes late-stage signs or symptoms, such as pain, hemorrhage, dysuria, purulent discharge, and obstruction of the urinary meatus. Rarely is metastasis the first sign of penile cancer.

Cervical cancer

Preinvasive cervical cancer produces no symptoms or other clinically apparent changes. Early invasive cervical cancer causes abnormal vaginal bleeding, persistent vaginal discharge, and postcoital pain and bleeding. In advanced stages, it causes pelvic pain, vaginal leakage of urine and feces from a fistula, anorexia, weight loss, and anemia.

Uterine cancer

Uterine enlargement, and persistent and unusual premenopausal bleeding, or any postmenopausal bleeding, are the most common indications of uterine cancer. The discharge may at first be watery and bloodstreaked, but it gradually becomes more bloody. Other signs or symptoms, such as pain and weight loss, don't appear until the cancer is well advanced.

Vaginal cancer

Commonly, the patient with vaginal cancer has experienced abnormal bleeding and discharge. Also, she may have a small or large, in many cases firm, ulcerated lesion in any part of the vagina. As the cancer progresses, it commonly spreads to the bladder (producing frequent voiding and bladder pain), the rectum (bleeding), vulva (lesion), pubic bone (pain), or other surrounding tissues.

Ovarian cancer

Typically, symptoms vary with the size of the tumor. An ovary may grow to considerable size before it produces overt symptoms. Occasionally, in the early stages, ovarian cancer causes vague abdominal discomfort, dyspepsia, and other mild GI disturbances. As it progresses, it causes urinary frequency, constipation, pelvic discomfort, distention, and weight loss. Tumor rupture, torsion, or infection may cause pain, which, in young patients, may mimic appendicitis. Granulosa cell tumors have feminizing effects (such as bleeding between periods in premenopausal women); conversely, arrhenoblastomas have virilizing effects. Advanced ovarian cancer causes ascites, rarely postmenopausal bleeding and pain, and symptoms relating to metastatic sites (most commonly pleural effusions).

Cancer of the vulva

In 50% of patients, cancer of the vulva begins with vulval pruritus, bleeding, or a small vulval mass (which may start as a small ulcer on the surface; eventually, it becomes infected and

painful), so such symptoms call for immediate diagnostic evaluation. Seventy percent of lesions develop on the labia, but tumors can be found on the clitoris, Bartholin's P glands, and perineum. Less common indications include a mass in the groin or abnormal urination or defecation.

Fallopian tube cancer

Generally, early stage fallopian tube cancer produces no symptoms. Late-stage disease is characterized by an enlarged abdomen with a palpable mass, amber-colored vaginal discharge, excessive bleeding during menstruation or, at other times, abdominal cramps, frequent urination, bladder pressure, persistent constipation, weight loss, and unilateral colicky pain produced by hydrops tubae profluens. (This last symptom occurs when the abdominal end of the fallopian tube closes, causing the tube to become greatly distended until its accumulated P secretions suddenly overflow into the uterus.) Metastasis develops by local extension or by lymphatic spread to the abdominal organs or to the pelvic, aortic, and inguinal lymph nodes. Extra-abdominal metastasis is rare.

Primary malignant bone tumors

Bone pain is the most common indication of primary malignant bone tumors. It's generally more intense at night; isn't usually associated with mobility. The pain is dull and usually localized, although it may be referred from the hip or spine and result in weakness or a limp. Another common sign is a mass or tumor. The tumor site may be tender and may swell; the tumor itself is often palpable. Pathologic fractures are common. In late stages, patient may be cachectic, with fever and impaired mobility.

Multiple myeloma

The earliest indication of multiple myeloma is severe, constant back and rib pain that increases with exercise and may be worse at night. Arthritic symptoms may also occur: achiness, joint swelling, and tenderness, possibly from vertebral compression. Other effects include fatigue, fever, malaise, slight evidence of peripheral neuropathy (such as peripheral paresthesia), and pathologic fractures. As multiple myeloma progresses, symptoms of vertebral compression may become acute, accompanied by anemia, weight loss, thoracic deformities (ballooning), and loss of body height (5” [12.7 cm] or more) due to vertebral collapse. Renal complications such as pyelonephritis (caused by tubular damage from large amounts of Bence Jones protein, hypercalcemia, and hyperuricemia) may occur. Severe, recurrent infection such as pneumonia may follow damage to nerves associated with respiratory function.

Basal cell epithelioma

Three types of basal cell epithelioma occur: Noduloulcerative lesions usually occur on the face, particularly the forehead, eyelid margins, and nasolabial folds. In early stages, these lesions are small, smooth, pinkish, and translucent papules. Telangiectatic vessels cross the surface, and the lesions are occasionally pigmented. As the lesions enlarge, their centers become depressed and their borders become firm and elevated. Ulceration P and local invasion eventually occur. These ulcerated tumors, known as rodent ulcers, rarely

metastasize; however, if untreated, they can spread to vital areas and become infected or cause massive hemorrhage if they invade large blood vessels. Superficial basal cell epitheliomas are multiple in many cases and commonly occur on the chest and back. They're oval or irregularly shaped, lightly pigmented plaques, with sharply defined, slightly elevated threadlike borders. Due to superficial erosion, these lesions appear scaly and have small, atrophic areas in the center that resemble psoriasis or eczema. They're usually chronic and don't tend to invade other areas. Superficial basal cell epitheliomas are related to ingestion of or exposure to arsenic-containing compounds. Sclerosing basal cell epitheliomas (morphea-like epitheliomas) are waxy, sclerotic, yellow to white plaques without distinct borders. Occurring on the head and neck, sclerosing basal cell epitheliomas commonly look like small patches of scleroderma.

Squamous cell carcinoma

Squamous cell carcinoma commonly develops on the skin of the face, the ears, the dorsa of the hands and forearms, and other sun-damaged areas. Lesions on sun-damaged skin tend to be less invasive and less likely to metastasize than lesions on unexposed skin. Notable exceptions to this tendency are squamous cell lesions on the lower lip and the ears. P These are almost invariably markedly invasive metastatic lesions with a generally poor prognosis. Transformation from a premalignant lesion to squamous cell carcinoma may begin with induration and inflammation of the preexisting lesion. When squamous cell carcinoma arises from normal skin, the nodule grows slowly on a firm, indurated base. If untreated, this nodule eventually ulcerates and invades underlying tissues. (See Staging squamous cell carcinoma, page 874.) Metastasis can occur to the regional lymph nodes, producing characteristic systemic symptoms of pain, malaise, fatigue, weakness, and anorexia.

Malignant melanoma

Common sites for melanoma are on the head and neck in men, on the legs in women, and on the backs of persons exposed to excessive sunlight. Up to 70% arise from a preexisting nevus. It rarely appears in the conjunctiva, choroid, pharynx, mouth, vagina, or anus. Suspect melanoma when any skin lesion or nevus enlarges, changes color, becomes inflamed or sore, itches, ulcerates, bleeds, undergoes textural changes, or shows signs of surrounding pigment regression (halo nevus or vitiligo). (See Recognizing potentially malignant nevi, page 876.) Each type of melanoma has special characteristics: Superficial spreading melanoma, the most common, usually develops between ages 40 and 50. Such a lesion arises on an area of chronic irritation. In women, it's most common between the knees and ankles; in Blacks and Asians, on the toe webs and soles (lightly pigmented areas subject to trauma). Characteristically, this melanoma has a red, white, and blue color over a brown or black background and an irregular, notched margin. Its surface is irregular, with small, elevated tumor nodules that may ulcerate and bleed. Horizontal growth may continue for many years; when vertical growth begins, prognosis worsens. Nodular melanoma usually develops between ages 40 and 50, grows vertically, invades the dermis, and metastasizes early. Such a lesion is usually a polypoidal nodule, with uniformly dark discoloration (it may be grayish), and looks like a blackberry. Occasionally, this melanoma is fleshcolored, with flecks of pigment around its base (possibly inflamed). Lentigo maligna

melanoma is relatively rare. It arises from a lentigo maligna on an exposed skin surface and usually occurs between ages 60 and 70. This lesion looks like a large (3- to 6-cm) flat freckle of tan, brown, black, whitish, or slate color and has irregularly scattered black nodules on the surface. It develops slowly, usually over P many years, and eventually may ulcerate. This melanoma commonly develops under the fingernails, on the face, and on the back of the hands.

Kaposi's sarcoma

The initial sign of Kaposi's sarcoma is one or more obvious lesions in various shapes, sizes, and colors (ranging from red-brown to dark purple) appearing most commonly on the skin, buccal mucosa, hard and soft palates, lips, gums, tongue, tonsils, conjunctiva, and sclera. In advanced disease, the lesions may join, becoming one large plaque. Untreated lesions may appear as large, ulcerative masses. Other signs and symptoms include: health history of AIDS pain (if the sarcoma advances beyond the early stages or if a lesion breaks down or impinges on nerves or organs) edema from lymphatic obstruction dyspnea (in cases of pulmonary involvement), wheezing, hypoventilation, and respiratory distress from bronchial blockage. The most common extracutaneous sites are the lungs and GI tract (esophagus, oropharynx, and epiglottis). Signs and symptoms of disease progression and metastasis include severe pulmonary involvement and GI involvement leading to digestive problems.

Hodgkin's lymphoma

The first sign of Hodgkin's lymphoma is usually a painless swelling of one of the cervical lymph nodes (but sometimes the axillary, mediastinal, or inguinal lymph nodes), occasionally in a patient who gives a history of recent upper respiratory infection. In older patients, the first signs and symptoms may be nonspecific—persistent fever, night sweats, fatigue, P weight loss, and malaise. Rarely, if the mediastinum is initially involved, Hodgkin's lymphoma may produce respiratory symptoms. Another early and characteristic indication of Hodgkin's lymphoma is pruritus, which, although mild at first, becomes acute as the disease progresses. Other symptoms depend on the degree and location of systemic involvement. Lymph nodes may enlarge rapidly, producing pain and obstruction, or enlarge slowly and painlessly for months or years. It isn't unusual to see the lymph nodes “wax and wane,” but they usually don't return to normal. Sooner or later, most patients develop systemic manifestations, including enlargement of retroperitoneal nodes and nodular infiltrations of the spleen, the liver, and bones. At this late stage other symptoms include edema of the face and neck, progressive anemia, possible jaundice, nerve pain, and increased susceptibility to infection.

Non-Hodgkin's lymphoma

Usually, the first indication of non-Hodgkin's lymphoma is swelling of the lymph glands, enlarged tonsils and adenoids, and painless, rubbery nodes in the cervical supraclavicular areas. In children, these nodes are usually in the cervical region, and the disease causes dyspnea and coughing. As the lymphoma progresses, the patient develops symptoms specific to the area involved and systemic complaints of fatigue, malaise, weight loss, fever, and night sweats.

Mycosis fungoides

The first sign of MF may be generalized erythroderma, possibly associated with itching. Eventually, MF evolves into varied combinations of infiltrated, thickened, or scaly patches, tumors, or ulcerations.

Acute leukemia

Signs of acute leukemia may be gradual or abrupt; they include high fever accompanied by thrombocytopenia and abnormal bleeding (such as nosebleeds), gingival bleeding, purpura, ecchymoses, petechiae, easy bruising after minor trauma, and prolonged menses. Nonspecific signs and symptoms, such as low-grade fever, weakness, and lassitude, may persist for days or months before visible symptoms appear. Other insidious signs and symptoms include pallor, chills, and recurrent infections. In addition, ALL, AML, and acute monoblastic leukemia may cause dyspnea, anemia, fatigue, malaise, tachycardia, palpitations, systolic ejection murmur, and abdominal or bone pain. Specific AML symptoms include local infections (laryngitis, pharyngitis, meningitis) or septicemia. Joint arthralgias and abdominal fullness (from enlarged spleen) may occur. Specific ALL symptoms include night sweats, shortness of breath, anorexia, weight loss, kepatosplenomegaly, and lymph adenopathy. When leukemic cells cross the blood-brain barrier and thereby escape the effects of systemic chemotherapy, the patient may develop meningeal leukemia (confusion, lethargy, headache).

Chronic myelogenous leukemia

Typically, during the chronic phase, CML induces the following clinical effects: anemia (fatigue, weakness, decreased exercise tolerance, pallor, dyspnea, tachycardia, and headache) thrombocytopenia, with resulting bleeding and clotting disorders (retinal hemorrhage, ecchymoses, hematuria, melena, bleeding gums, nosebleeds, and easy bruising) hepatosplenomegaly, with abdominal discomfort and pain in splenic infarction from leukemic cell infiltration. Other signs and symptoms include sternal and rib tenderness from leukemic infiltrations of the periosteum; low-grade fever; weight loss; anorexia; renal calculi or gouty arthritis from increased uric acid excretion; occasionally, prolonged infection and ankle edema; and, rarely, priapism and vascular insufficiency. Acceleration of the disease process results in fever, night sweats, splenomegaly, and bone pain.

Chronic lymphocytic leukemia

CLL is the most benign and the most slowly progressive form of leukemia. Clinical signs derive from the infiltration of leukemic cells in bone marrow, lymphoid tissue, and organ systems. In early stages, patients usually complain of fatigue, malaise, fever, and nodal enlargement. They're particularly susceptible to infection. In advanced stages, patients may experience severe fatigue and weight loss, with liver or spleen enlargement, bone tenderness, and edema from lymph node obstruction. Pulmonary infiltrates may appear when lung parenchyma is involved. Skin infiltrations, manifested by macular to nodular eruptions, occur in about one-half of the cases of CLL. As the disease progresses, bone marrow involvement may lead to anemia, pallor, weakness, dyspnea, tachycardia,

palpitations, bleeding, and infection. Opportunistic fungal, viral, and bacterial infections commonly occur in late stages

Cerebral palsy

Spastic cerebral palsy is characterized by hyperactive deep tendon reflexes, increased stretch reflexes, rapid alternating muscle contraction and relaxation, muscle weakness, underdevelopment of affected limbs, muscle contraction in response to manipulation, and a tendency to contractures. Typically, a child with spastic CP walks on his toes with a scissors gait, crossing one foot in front of the other. In athetoid cerebral palsy, involuntary movements—grimacing, wormlike writhing, dystonia, and sharp jerks—impair voluntary movement. Usually, these involuntary movements affect the arms more severely than the legs; involuntary facial movements may make speech difficult. These athetoid movements become more severe during stress, decrease with relaxation, and disappear entirely during sleep. Ataxic cerebral palsy is characterized by disturbed balance, incoordination (especially of the arms), hypoactive reflexes, nystagmus, muscle weakness, tremor, lack of leg movement during infancy, and a widebased gait as the child begins to walk. Ataxia makes sudden or fine movements almost impossible. Some children with CP display a combination of these clinical features. In most, impaired motor function makes eating (especially swallowing) difficult and retards growth and development. Up to 40% of these children are mentally retarded, about 25% have seizure disorders, and about 80% have impaired speech. Many also have dental abnormalities, vision and hearing defects, and reading disabilities.

Hydrocephalus

In infants, the unmistakable sign of hydrocephalus is rapidly increasing head circumference, clearly disproportionate to the infant's growth. Other characteristic changes include widening and bulging of the fontanels; distended scalp veins; thin, shiny, and fragile-looking scalp skin; and underdeveloped neck muscles. (See Signs of hydrocephalus.) In severe hydrocephalus, the roof of the orbit is depressed, the eyes are displaced downward, and the sclerae are prominent. Sclera seen above the iris is called the “setting-sun sign.” A high-pitched, shrill cry, abnormal muscle tone of the legs, irritability, anorexia, and projectile vomiting commonly occur. In adults and older children, indicators of hydrocephalus include decreased level of consciousness (LOC), ataxia, incontinence, loss of coordination, and impaired intellect.

Cerebral aneurysm

Occasionally, rupture of a cerebral aneurysm causes premonitory symptoms that last several days, such as headache, nuchal rigidity, stiff back and legs, and intermittent nausea. Usually, however, onset is abrupt and without warning, causing a sudden severe headache, nausea, vomiting and, depending on the severity and location of bleeding, altered consciousness (including deep coma). Bleeding causes meningeal irritation, resulting in nuchal rigidity, back and leg pain, fever, restlessness, irritability, occasional seizures, and blurred vision. Bleeding into the brain tissues causes hemiparesis, hemisensory defects, dysphagia, and visual defects. If the aneurysm is near the internal carotid artery, it compresses the oculomotor nerve and causes diplopia, ptosis, dilated pupil, and inability to rotate the eye. The severity of symptoms varies considerably from patient to patient, depending on the site and amount of bleeding. To better describe their conditions, patients with ruptured cerebral aneurysms are grouped as follows:

Grade I (minimal bleed): Patient is alert with no neurologic deficit; he may have a slight headache and

nuchal rigidity. Grade II (mild bleed): Patient is alert, with a mild to severe headache, nuchal rigidity and, possibly, third-nerve palsy. Grade III (moderate bleed): Patient is confused or drowsy, with nuchal rigidity and, possibly, a mild focal deficit. Grade IV (severe bleed): Patient is stuporous, with nuchal rigidity and, possibly, mild to severe hemiparesis. Grade V (moribund; commonly fatal): If nonfatal, patient is in deep coma or decerebrate. Generally, cerebral aneurysm poses three major threats: Death from increased ICP: Increased ICP may push the brain downward, impair brain stem function, and cut off blood supply to the part of the brain that supports vital functions. Rebleed: Generally, after the initial bleeding episode, a clot forms and seals the rupture, which reinforces the wall of the aneurysm for 7 to 10 days. However, after the 7th day, fibrinolysis begins to dissolve the clot and increases the risk of rebleeding. Signs and symptoms are similar to those accompanying the initial hemorrhage. Rebleeds during the first 24 hours after initial hemorrhage aren't uncommon, and they contribute to cerebral aneurysm's high mortality. Vasospasm: Why this occurs isn't clearly understood. Usually, vasospasm occurs in blood vessels adjacent to the cerebral aneurysm, but it may extend to major vessels of the brain, causing ischemia and altered brain function. Other complications of cerebral aneurysm include pulmonary embolism (a possible adverse effect of deep vein thrombosis or aneurysm treatment) and acute hydrocephalus, occurring as CSF accumulates in the cranial cavity because of blockage by blood or adhesions.

Arteriovenous malformations

An AVM may be asymptomatic until complications occur; these may include rupture and a resulting sudden bleed in the brain, known as a hemorrhagic stroke. Arteriovenous malformations vary in size and location within the brain. Systolic bruit may be auscultated over the carotid artery, mastoid process, or orbit on examination. Symptoms that occur prior to an AVM rupture are related to smaller and slower bleeding from the abnormal vessels, which are usually fragile because their structure is abnormal.

In more than half of patients with AVM, hemorrhage from the malformation is the first symptom. Depending on the location and the severity of the bleed, the hemorrhage can be profoundly disabling or fatal. The risk of bleeding from an AVM is approximately 2% to 4% per year. The first symptoms often include headache, seizure, or other sudden neurological problems, such as vision problems, weakness, inability to move a limb or a side of the body, lack of sensation in part of the body, or abnormal sensations, such as ringing and numbness. Symptoms are the same as for stroke. The individual with an AVM may complain of chronic mild headache, a sudden and severe headache, or a localized or general headache. The headache may resemble migraine and vomiting may occur. Seizures may result from focal neurologic deficits (depending on the location of the AVM) resulting from compression and diminished perfusion. Symptoms of intracranial (intracerebral, subarachnoid, or subdural) hemorrhage result. Muscle weakness and decreased sensation can occur in any part of the body. Mental status change can occur where the individual appears sleepy, stuporous, lethargic, confused, disoriented, or irritable. Additional symptoms may include stiff neck, speech or sense of smell impairment, dysfunctional movement, fainting, facial paralysis, eyelid drooping, tinnitus, dizziness, and decreased level of consciousness (LOC). If an AVM bleeds once, the risk is greater that it will bleed again in the future. Intracerebral or subarachnoid hemorrhages are the most common first symptoms of cerebral arteriovenous malformation. In some cases, symptoms may also occur due to lack of blood flow to an area of the brain (ischemia), compression or distortion of brain tissue by large AVMs, or abnormal brain

development in the area of the malformation. Progressive loss of nerve cells in the brain may occur, caused by mechanical (pressure) and ischemic (lack of blood supply) factors.

Headache

Initially, migraine headaches usually produce unilateral, pulsating pain, which later becomes more generalized. They're commonly preceded by a scintillating scotoma, hemianopsia, unilateral paresthesia, or speech disorders. The patient may experience irritability, anorexia, nausea, vomiting, and photophobia. (See Clinical features of migraine headaches.) Both muscle contraction and tractioninflammatory vascular headaches produce a dull, persistent ache, tender spots on the head and neck, and a feeling of tightness around the head, with a characteristic “hatband” distribution. The pain is usually severe and unrelenting. If caused by intracranial bleeding, these headaches may result in neurologic deficits, such as paresthesia and muscle weakness; narcotics may fail to relieve pain in these cases. If caused by a tumor, pain is most severe when the patient awakens.

Seizure disorder

The hallmarks of seizure disorder are recurring seizures, which can be classified as partial or generalized (some patients may be affected by more than one type). Partial seizures arise from a localized area of the brain, causing specific symptoms. In some patients, partial seizure activity may spread to the entire brain, causing a generalized seizure. Partial seizures include simple partial (jacksonian) and complex partial seizures (psychomotor or temporal lobe). A simple partial motor-type seizure begins as a localized motor seizure characterized by a spread of abnormal activity to adjacent areas of the brain. It typically produces stiffening or jerking in one extremity, accompanied by a tingling sensation in the same area. For example, it may start in the thumb and spread to the entire hand and arm. The

patient seldom loses consciousness, although the seizure may progress to a generalized seizure. A simple partial sensory-type seizure involves perceptual distortion, which can include hallucinations. The symptoms of a complex partial seizure vary but usually include purposeless behavior. The patient experiences an aura immediately before the seizure. An aura represents the beginning of abnormal electrical discharges within a focal area of the brain and may include a pungent smell, GI distress (nausea or indigestion), a rising or sinking feeling in the stomach, a dreamy feeling, an unusual taste, or a visual disturbance. Overt signs of a complex partial seizure include a glassy stare, picking at one's clothes, aimless wandering, lipsmacking or chewing motions, and unintelligible speech; these signs may last for just a few seconds or as long as 20 minutes. Mental confusion may last several minutes after the seizure; as a result, an observer may mistakenly suspect intoxication with alcohol or drugs or psychosis. Generalized seizures, as the term suggests, cause a generalized electrical abnormality within the brain and include several distinct types: Absence (petit mal) seizures occur most commonly in children, although they may affect adults as well. They usually begin with a brief change in level of consciousness, indicated by blinking or rolling of the eyes, a blank stare, and slight mouth movements. There's little or no tonic-clonic movement. The patient retains his posture and continues preseizure activity without difficulty. Typically, each seizure lasts from 1 to 10 seconds. If not properly treated, seizures can recur as often as 100 times per day. An absence seizure may progress to generalized tonic-clonic seizures. A myoclonic (bilateral massive epileptic myoclonus) seizure is characterized by brief, involuntary muscular

jerks of the body or extremities, which may occur in a rhythmic fashion and may precede generalized tonic-clonic seizures by months or years. A generalized tonic-clonic (grand mal) seizure typically begins with a loud cry, precipitated by air rushing from the lungs through the vocal cords. The patient then falls to the ground, losing consciousness. The body stiffens (tonic phase) and then alternates between episodes of muscular spasm and relaxation (clonic phase). Tongue-biting, incontinence, labored breathing, apnea, and subsequent cyanosis may also occur. The seizure stops in 2 to 5 minutes, when abnormal electrical conduction of the neurons is completed. The patient then regains consciousness but is somewhat confused and may have difficulty talking. If he can talk, he may complain of drowsiness, fatigue, headache, muscle soreness, and arm or leg weakness. He may fall into deep sleep after the seizure. These seizures may start as facial seizures and spread to become generalized. An akinetic seizure is characterized by a general loss of postural tone (the patient falls in a flaccid state) and a temporary loss of consciousness. It occurs in young children and is sometimes called a “drop attack” because it causes the child to fall. Status epilepticus is a continuous seizure state that can occur in all seizure types. The most life-threatening example is generalized tonicclonic status epilepticus, a continuous generalized tonic-clonic seizure without intervening return of consciousness. Status epilepticus is accompanied by respiratory distress. It can result from abrupt withdrawal of anticonvulsant medications, hypoxic encephalopathy, acute head trauma, metabolic encephalopathy, or septicemia secondary to encephalitis or meningitis.

Stroke

Clinical features of stroke vary with the artery affected (and, consequently, the portion of the brain it supplies), the severity of damage, and the extent of collateral circulation that develops to help the brain compensate for decreased blood supply. If the stroke occurs in the left hemisphere, it produces symptoms on the right side; if in the right hemisphere, symptoms are on the left side. However, a stroke that causes cranial nerve damage produces signs of cranial nerve dysfunction on the same side as the hemorrhage. Symptoms are usually classified according to the artery affected: Middle cerebral artery: aphasia, dysphasia, visual field cuts, and hemiparesis on affected side (more severe in the face and arm than in the leg) Carotid artery: weakness, paralysis, numbness, sensory changes, and visual disturbances on affected side; altered level of consciousness (LOC), bruits, headaches, aphasia, and ptosis Vertebrobasilar artery: weakness on affected side, numbness around lips and mouth, visual field cuts, diplopia, poor coordination, dysphagia, slurred speech, dizziness, amnesia, and ataxia Anterior cerebral artery: confusion, weakness, and numbness (especially in the leg) on affected side, incontinence, loss of coordination, impaired motor and sensory functions, and personality changes Posterior cerebral arteries: visual field cuts, sensory impairment, dyslexia, coma, and cortical blindness; typically, paralysis is absent.

Symptoms can also be classified as premonitory, generalized, and focal. Premonitory symptoms, such as drowsiness, dizziness, headache, and mental confusion, are rare. Generalized symptoms, such as headache, vomiting, mental impairment, seizures, coma, nuchal rigidity, fever, and disorientation, are typical. Focal symptoms, such as sensory and reflex changes, reflect the site of hemorrhage or infarct and may worsen.

Meningitis

The cardinal signs of meningitis are infection (fever, chills, and malaise) and increased intracranial pressure (ICP; headache, vomiting and, rarely, papilledema). Signs of positive Brudzinski's and Kernig's signs, exaggerated and symmetrical deep tendon reflexes, and opisthotonos (a spasm in which the back and extremities arch backward so that the body rests on the head and heels). (See Two signs of meningitis, pages 198 and 199.) Other manifestations of meningitis are irritability; sinus arrhythmias; photophobia, diplopia, and other visual problems; and delirium, deep stupor, and coma. An infant may not show clinical signs of infection but may be fretful and refuse to eat. Such an infant may vomit often, leading to dehydration; this prevents a bulging fontanel and thus masks this important sign of increased ICP. As the illness progresses, twitching, seizures (in 30% of infants), or coma may develop. Most older children have the same symptoms as adults. In subacute meningitis, the onset may be insidious.

Encephalitis

All viral forms of encephalitis have similar clinical features, although certain differences do occur. Usually, the acute illness begins with sudden onset of fever, headache, and vomiting and progresses to include signs and symptoms of meningeal irritation (stiff neck and back) and neuronal damage (drowsiness, coma, paralysis, seizures, ataxia, tremors, nausea, vomiting, and organic psychoses). After the acute phase of the illness, coma may persist for days or weeks. The severity of arbovirus encephalitis may range from subclinical to rapidly fatal necrotizing disease. Herpes encephalitis also produces signs and symptoms that vary from subclinical to acute and commonly fatal fulminating disease. Associated effects include disturbances of taste or smell.

Brain abscess

Onset varies according to cause, but generally brain abscess produces clinical effects similar to those of a brain tumor. Early symptoms result from increased intracranial pressure (ICP) and include constant intractable headache, worsened by straining; nausea; vomiting; and focal or generalized seizures. Typical later symptoms include ocular disturbances, such as nystagmus, decreased vision, and unequal pupil size. Other features differ with the site of the abscess: temporal lobe abscess: auditory-receptive dysphasia, central facial weakness, and hemiparesis cerebellar abscess: dizziness, coarse nystagmus, gaze weakness on lesion side, tremor, and ataxia frontal lobe abscess: expressive dysphasia, hemiparesis with unilateral motor seizure, drowsiness, inattention, and mental function impairment. Signs of infection, such as fever, pallor, and bradycardia, are absent until late stages unless they result from the predisposing condition. If the abscess is encapsulated, they may never appear. Depending on abscess size and location, level of consciousness (LOC) varies from drowsiness to deep stupor.

Huntington's disease

Onset is insidious. The patient eventually becomes totally dependent— emotionally and physically—through loss of musculoskeletal control, and he develops progressively severe choreic movements. Such movements are rapid, usually violent, and purposeless. Initially, they're unilateral and more prominent in the face and arms than in the legs, progressing from mild fidgeting to grimacing, tongue smacking, dysarthria (indistinct speech), athetoid movements (especially of the hands) related to emotional state, and torticollis. Ultimately, the patient with Huntington's disease develops progressive

dementia, although the dementia doesn't always progress at the same rate as the chorea. Dementia can be mild at first, but eventually causes severe disruption of the personality. Personality changes include obstinacy, carelessness, untidiness, moodiness, apathy, inappropriate behavior, loss of memory and concentration and, occasionally, paranoia.

Parkinson's disease

The cardinal symptoms of Parkinson's disease are muscle rigidity and akinesia and an insidious resting tremor that begins in the fingers (unilateral pill-roll tremor), increases during stress or anxiety, and decreases with purposeful movement and sleep. Muscle rigidity results in resistance to passive muscle stretching, which may be uniform (leadpipe rigidity) or jerky (cogwheel rigidity). Akinesia causes the patient to walk with difficulty (gait lacks normal parallel motion and may be retropulsive or propulsive) and produces a high-pitched, monotone voice; drooling; a masklike facial expression; loss of posture control (the patient walks with body bent forward); and dysarthria, dysphagia, or both. Occasionally, akinesia may also cause oculogyric crises (eyes are fixed upward, with involuntary tonic movements) or blepharospasm (eyelids are completely closed). Parkinson's disease itself doesn't impair the intellect, but a coexisting disorder, such as arteriosclerosis, may do so.

Myelitis and acute transverse myelitis

In acute transverse myelitis, onset is rapid, with motor and sensory dysfunctions below the level of spinal cord damage appearing in 1 to 2 days. Patients with acute transverse myelitis develop flaccid paralysis of the legs (sometimes beginning in just one leg) with loss of sensory and sphincter functions. Such sensory loss may follow pain in the legs or trunk. Reflexes disappear in the early stages but may reappear later.

The extent of damage depends on the level of the spinal cord affected; transverse myelitis seldom involves the arms. If spinal cord damage is severe, it may cause shock (hypotension and hypothermia).

Alzheimer's disease

Onset is insidious. Initially, the patient undergoes almost imperceptible changes, such as forgetfulness, recent memory loss, difficulty learning and remembering new information, deterioration in personal hygiene and appearance, and an inability to concentrate. Gradually, tasks that require abstract thinking and activities that require judgment become more difficult. Progressive difficulty in communication and severe deterioration in memory, language, and motor function result in a loss of coordination and an inability to write or speak. Personality changes (restlessness, irritability) and nocturnal awakenings are common. Patients also exhibit loss of eye contact, a fearful look, wringing of the hands, and other signs of anxiety. When a patient with Alzheimer's disease is overwhelmed with anxiety, he becomes dysfunctional, acutely confused, agitated, compulsive, or fearful. Eventually, the patient becomes disoriented, and emotional lability and physical and intellectual disability progress. The patient becomes susceptible to infection and accidents. Usually, death results from infection.

Creutzfeldt-Jakob disease

Early signs and symptoms of mental impairment may include slowness in thinking, difficulty

concentrating, impaired judgment, and memory loss. Dementia is progressive and occurs early. Involuntary movements, such as muscle twitching, trembling, and peculiar body movements, and visual disturbances, appear with disease progression and advancing mental deterioration. Hallucinations are also common. Duration of the typical illness is 4 months.

Reye's syndrome

The severity of the child's signs and symptoms varies with the degree of encephalopathy and cerebral edema. In any case, Reye's syndrome develops in five stages. After the initial viral infection, a brief recovery period follows when the child doesn't seem seriously ill.

A few days later, he develops intractable vomiting; lethargy; rapidly changing mental status (mild to severe agitation, confusion, irritability, and delirium); rising blood pressure, respiratory rate, and pulse rate; and hyperactive reflexes. Reye's syndrome commonly progresses to coma. As coma deepens, seizures develop, followed by decreased tendon reflexes and, usually, respiratory failure. Increased ICP, a serious complication, is now considered the result of an increased cerebral blood volume causing intracranial hypertension. Such swelling may develop as a result of acidosis, increased cerebral metabolic rate, and an impaired autoregulatory mechanism.

Guillain-Barré syndrome

About 50% of patients with Guillain-Barré syndrome have a history of minor febrile illness (10 to 14 days before onset), usually an upper respiratory tract infection or, less commonly, gastroenteritis with Camphylobacter jejuni. When infection precedes onset of Guillain-Barré syndrome, signs of infection subside before neurologic features appear. Other possible precipitating factors include surgery, rabies or swine influenza vaccination, viral illness like Epstein-Barr virus, cytomegalovirus, hepatitis, and HIV, Hodgkin's or other malignant disease, and lupus erythematosus. Symmetrical muscle weakness, the major neurologic sign, usually appears in the legs first (ascending type) and then extends to the arms and facial nerves in 24 to 72 hours. Sometimes, muscle weakness develops in the arms first (descending type) or in the arms and legs simultaneously. (See Testing for thoracic sensation.) In milder forms of this disease, muscle weakness may affect only the cranial nerves or may not occur at all. Another common neurologic sign is paresthesia, which sometimes precedes muscle weakness but tends to vanish quickly. However, some patients with this disorder never develop this symptom. Other clinical features may include facial diplegia (possibly with ophthalmoplegia), dysphagia or dysarthria and, less commonly, weakness of the muscles supplied by cranial nerve XI. Muscle weakness develops so quickly that muscle atrophy doesn't occur, but hypotonia and areflexia do. Stiffness and pain in the form of a severe “charley horse” commonly occur.

Myasthenia gravis

The dominant symptoms of myasthenia gravis are skeletal muscle weakness and fatigability. In the early stages, easy fatigability of certain muscles may appear with no other findings. Later, it may be severe enough to cause paralysis. Typically, myasthenic muscles are strongest in the morning but weaken throughout the day, especially after exercise. Short rest periods temporarily restore muscle function.

Muscle weakness is progressive; more and more muscles become weak, and eventually some muscles may lose function entirely. Resulting symptoms depend on the muscle group affected; they become more intense during menses and after emotional stress, prolonged exposure to sunlight or cold, or infections.

Amyotrophic lateral sclerosis

Progressive loss of muscle strength and coordination eventually interfere with everyday activities. Patients with ALS develop fasciculations, accompanied by atrophy and weakness, especially in the muscles of the feet and the hands. Other signs include impaired speech; difficulty chewing, swallowing, and breathing and, occasionally, choking and excessive drooling. Mental deterioration doesn't occur, but patients may become depressed as a reaction to the disease.

Multiple sclerosis

Clinical findings in MS depend on the extent and site of myelin destruction, the extent of remyelination, and the adequacy of subsequent restored synaptic transmission. Signs and symptoms in MS may be transient, or they may last for hours or weeks. They may wax and wane with no predictable pattern, vary from day to day, and be bizarre and difficult for the patient to describe. In most patients, visual problems and sensory impairment, such as numbness and tingling sensations (paresthesia), are the first signs that something may be wrong. Other characteristic changes include: ocular disturbances—optic neuritis, diplopia, ophthalmoplegia, blurred vision, and nystagmus muscle dysfunction—weakness, paralysis ranging from monoplegia to quadriplegia, spasticity, hyperreflexia, intention tremor, and gait ataxia urinary disturbances—incontinence, frequency, urgency, and frequent infections emotional lability—characteristic mood swings, irritability, euphoria, and depression. Associated signs and symptoms include poorly articulated or scanning speech and dysphagia. Clinical effects may be so mild that the patient is unaware of them or so bizarre that he appears hysterical.

Trigeminal neuralgia

Typically, the patient reports a searing or burning pain that occurs in lightninglike jabs and lasts from 1 to 15 minutes (usually 1 to 2 minutes) in an area innervated by one of the divisions of the trigeminal nerve, primarily the superior mandibular or maxillary division. The pain rarely affects more than one division and seldom the first division (ophthalmic) or both sides of the face. It affects the second (maxillary) and third (mandibular) divisions of the trigeminal nerve equally.

Bell's palsy

Bell's palsy usually produces unilateral facial weakness, occasionally with aching pain around the angle of the jaw or behind the ear. On the weak side, the mouth droops (causing the patient to drool saliva from the corner of his mouth), and taste perception is distorted over the affected anterior portion of the tongue. The forehead appears smooth, and the patient's ability to close his eye on the weak side is markedly impaired. When he tries to close this eye, it rolls upward (Bell's phenomenon) and shows excessive tearing. Although Bell's phenomenon occurs in normal people, it isn't apparent because the

eyelids close completely and cover this eye motion. In Bell's palsy, incomplete eye closure makes this upward motion obvious. Other symptoms may include loss of taste and ringing in the ear.

Peripheral neuritis

The clinical effects of peripheral neuritis develop slowly, and the disease usually affects the motor and sensory nerve fibers. Symptoms vary according to which type of nerve is affected (sensory, motor, or autonomic). Neuropathy can affect any one or be a combination of all three types. Sensory changes: Damage to sensory fibers results in changes in sensation, ranging from abnormal sensations, such as burning, nerve pain, or tingling, to numbness or an inability to determine joint position in the area. Sensation changes often begin in the feet and progress toward the center of the body with involvement of other areas as the condition worsens. Motor changes: Damage to the motor fibers interferes with muscle control and can cause weakness, loss of muscle bulk, and loss of dexterity. Muscle cramping may be a sign of motor nerve involvement. Other muscle-related symptoms include lack of muscle control, difficulty or inability to move a part of the body (paralysis), muscle atrophy, muscle twitching (fasciculation) or cramping, difficulty breathing or swallowing, falling (from legs buckling or tripping over toes), or lack of dexterity (such as the inability to button a shirt). Autonomic changes: The autonomic nerves control involuntary or semivoluntary functions, such as control of internal organs and blood pressure. Damage to autonomic nerves can cause blurred vision, decreased ability to sweat (anhidrosis), dizziness that occurs when standing up or fainting associated with a fall in blood pressure, heat intolerance with exertion (decreased ability to regulate body temperature), nausea or vomiting after meals, abdominal bloating (swelling), feeling full after eating a small amount (early satiety), diarrhea, constipation, unintentional weight loss (more than 5% of body weight), urinary incontinence, feeling of incomplete bladder emptying, difficulty beginning to urinate (urinary hesitancy), and male impotence.

Complex regional pain syndrome

Patients usually report severe and constant pain; severe pain is common with CRPS2 in particular. The affected area may have altered blood flow, feeling either warm or cool to the touch, with discoloration, sweating, or swelling. In time, skin, hair, and nail changes may occur along with impaired mobility and muscle wasting, especially if adequate treatment is delayed.

Premenstrual syndrome

Clinical effects vary widely among patients and may include any combination of the following: behavioral—mild to severe personality changes, nervousness, hostility, irritability, agitation, sleep disturbances, fatigue, lethargy, and depression somatic—breast tenderness or swelling, abdominal tenderness or bloating, joint pain, headache, edema, diarrhea or constipation, and exacerbations of skin problems (such as acne or rashes), respiratory problems (such as asthma), or neurologic problems (such as seizures). PMS may need to be differentiated from premenstrual dysphoric disorder, which is a more severe form of PMS that's marked by severe depression, irritability, and tension before menstruation. (See Premenstrual dysphoric disorder.)

Dysmenorrhea

Dysmenorrhea produces sharp, intermittent, cramping, lower abdominal pain, which usually radiates to the back, thighs, groin, and vulva. Such pain—sometimes compared to labor pains—typically starts with or immediately before menstrual flow and peaks within 24 hours. Dysmenorrhea may also be associated with the characteristic signs and symptoms of premenstrual syndrome (urinary frequency, nausea, vomiting, diarrhea, headache, chills, abdominal bloating, painful breasts, depression, and irritability).

Vulvovaginitis

In trichomonal vaginitis, vaginal discharge is thin, bubbly, green-tinged, and malodorous. This infection causes marked irritation and itching, and urinary symptoms, such as burning and frequency. Candidal vaginitis produces a thick, white, cottage cheese-like discharge and red, edematous mucous membranes, with white flecks adhering to the vaginal wall, and is often accompanied by intense itching. G. vaginalis produces a gray, foul, “fishy” smelling discharge. Acute vulvitis causes a mild to severe inflammatory reaction, including edema, erythema, burning, and pruritus. Severe pain on urination and dyspareunia may necessitate immediate treatment. Herpes infection may cause painful ulceration or vesicle formation during the active phase.

Ovarian cysts

Small ovarian cysts (such as follicular cysts) usually don't produce symptoms unless torsion or rupture causes signs of an acute abdomen (vomiting, abdominal tenderness, distention, and rigidity). Large or multiple cysts may induce mild pelvic discomfort, low back pain, dyspareunia, or abnormal uterine bleeding secondary to a disturbed ovulatory pattern. Ovarian cysts with torsion induce acute abdominal pain similar to that of appendicitis. Granulosa-lutein cysts that appear early in pregnancy may grow as large as 2″ to 2½″ (5 to 6 cm) in diameter and produce unilateral pelvic discomfort and, if rupture occurs, massive intraperitoneal hemorrhage. In nonpregnant women, these cysts may cause delayed menses, followed by prolonged or irregular bleeding. Polycystic ovarian disease may also produce secondary amenorrhea, oligomenorrhea, or infertility.

Polycystic ovary syndrome

Signs and symptoms of PCOS include mild pelvic discomfort, lower back pain, and dyspareunia caused by multiple ovarian cysts, abnormal uterine bleeding secondary to disturbed ovulatory pattern, hirsutism and male-pattern hair loss that result from abnormal patterns of estrogen secretion, obesity caused by abnormal hormone regulation, and acne caused by excess sebum production that results from disturbed androgen secretion.

Endometriosis

The classic symptom of endometriosis is acquired dysmenorrhea, which may produce constant pain in the lower abdomen and in the vagina, posterior pelvis, and back. This pain usually begins from 5 to 7 days before menses reaches its peak and lasts for 2 to 3 days. It differs from primary dysmenorrheal pain, which is more cramplike and concentrated in the abdominal midline. However, the pain's severity doesn't necessarily indicate the extent of the disease. Other clinical features depend on the location of the ectopic tissue: ovaries and oviducts: infertility and profuse menses ovaries or cul-de-sac: deep-thrust dyspareunia bladder: suprapubic pain, dysuria, hematuria small bowel and appendix: nausea and vomiting, which worsen before menses, and abdominal cramps cervix, vagina, and perineum: bleeding from endometrial deposits in these areas during menses. The primary complications of endometriosis are infertility and chronic pelvic pain.

Uterine leiomyomas

Leiomyomas may be located within the uterine wall or may protrude into the endometrial cavity or from the serosal surface of the uterus. Most leiomyomas produce no symptoms. The most common symptom is abnormal bleeding, which typically presents clinically as menorrhagia. Uterine leiomyomas probably don't cause pain directly except when associated with torsion of a pedunculated subserous tumor. Pelvic pressure and impingement on adjacent viscera are common indications for treatment. Other symptoms may include urinary retention, constipation, or dyspareunia.

Precocious puberty

The usual pattern of precocious puberty in females is a rapid growth spurt, thelarche (breast development), pubarche (pubic hair development), and menarche—all before age 9. These changes may occur independently or simultaneously.

Menopause

Many menopausal women are asymptomatic but some have severe symptoms. The decline in ovarian function and consequent decreased estrogen level produce menstrual irregularities: a decrease in the amount and duration of menstrual flow, spotting, and episodes of amenorrhea and polymenorrhea (possibly with hypermenorrhea). Irregularities may last a few months or persist for several years before menstruation ceases permanently. The following body system changes may occur (usually after the permanent cessation of menstruation): Reproductive system: Menopause may cause shrinkage of vulval structures and loss of subcutaneous fat, possibly leading to atrophic vulvitis; atrophy of vaginal mucosa and flattening of vaginal rugae, possibly causing bleeding after coitus or douching; vaginal itching and discharge from bacterial invasion; and loss of capillaries in the atrophying vaginal wall, causing the pink, rugal lining to become smooth and white. Menopause may also produce excessive vaginal dryness and dyspareunia due to decreased lubrication from the vaginal walls and decreased secretion from Bartholin's glands; smaller ovaries and oviducts; and progressive pelvic relaxation as the supporting structures lose their tone due to the absence of estrogen. ELDER TIP As a woman ages, atrophy causes the vagina to shorten and the mucous lining to become thin, dry, less elastic, and pale as a result of decreased vascularity. In addition, the pH of vaginal secretions increases, making the P 0 vaginal environment more alkaline. The type of flora also changes, increasing the older woman's chance of vaginal infections. Urinary system: Atrophic cystitis due to the effects of decreased estrogen levels on bladder mucosa and related structures may cause pyuria, dysuria, and urinary frequency, urgency, and incontinence. Urethral carbuncles from loss of urethral tone and mucosal thinning may cause dysuria, meatal tenderness, and

hematuria. Mammary system: Breast size decreases. Integumentary system: The patient may experience loss of skin elasticity and turgor due to estrogen deprivation, loss of pubic and axillary hair and, occasionally, slight alopecia. Autonomic nervous system: The patient may exhibit hot flashes and night sweats (in 75% of women), vertigo, syncope, tachycardia, dyspnea, tinnitus, emotional disturbances (irritability, nervousness, crying spells, fits of anger), and exacerbation of pre-existing depression, anxiety, and compulsive, manic, or schizoid behavior. Menopause may also induce atherosclerosis, and a decrease in estrogen level contributes to osteoporosis. Ovarian activity in younger women is believed to provide a protective effect on the cardiovascular system, and the loss of this function at menopause may partly explain the increased death rate from myocardial infarction in older women. Also, estrogen has been found to increase levels of high-density lipoprotein cholesterol.

Female infertility

Pelvic inflammatory disease

Clinical features of PID vary with the affected area but generally include a profuse, purulent vaginal discharge, sometimes accompanied by low□grade fever and malaise (particularly if gonorrhea is the cause). The patient experiences lower abdomen pain; movement of the cervix or palpation of the adnexa may be extremely painful. Frequent, painful urination is also commonly reported. Additional signs and symptoms include irregular or absent menstruation, dyspareunia, low back pain, and nausea and vomiting.

Amenorrhea

Secondary amenorrhea can be diagnosed when a change is noted in a previously established menstrual pattern (absence of menstruation for 3 months). A thorough physical and pelvic examination rules out pregnancy, as well as anatomic abnormalities such as cervical stenosis that may cause false amenorrhea (cryptomenorrhea), in which menstruation occurs without external bleeding. Onset of menstruation within 1 week after administration of pure progestational agents, such as medroxyprogesterone and progesterone, indicates a functioning uterus. If menstruation doesn't occur, special diagnostic studies are appropriate. Blood and urine studies may reveal hormonal imbalances, such as lack of ovarian response to gonadotropins (elevated pituitary gonadotropins), failure of gonadotropin secretion (low pituitary gonadotropin levels), and abnormal thyroid levels. Tests for identification of dominant or missing hormones include cervical mucus ferning, vaginal cytologic examinations, basal body temperature, endometrial biopsy (during dilatation and curettage), urinary 17-ketosteroids, and plasma progesterone, testosterone, and androgen levels. A complete medical workup, including X-rays, laparoscopy, and a biopsy, may detect ovarian, adrenal, and pituitary tumors.

Abnormal premenopausal bleeding

Bleeding not associated with abnormal pregnancy is usually painless, but it may be severely painful. When bleeding is associated with abnormal pregnancy, other symptoms include nausea, breast tenderness, bloating, and fluid retention. Severe or prolonged bleeding causes anemia, especially in patients with underlying disease such as blood dyscrasia and in patients receiving anticoagulants.

Dysfunctional uterine bleeding

DUB usually occurs as metrorrhagia (episodes of vaginal bleeding between menses); it may also occur as hypermenorrhea (heavy or prolonged menses, longer than 8 days) or chronic

polymenorrhea (menstrual cycle of less than 18 days). Such bleeding is unpredictable and can cause anemia.

Postmenopausal bleeding

Vaginal bleeding, the primary symptom, ranges from spotting to outright hemorrhage; its duration also varies. Other symptoms depend on the cause. Excessive estrogen stimulation, for example, may also produce copious cervical mucus; estrogen deficiency may cause vaginal mucosa to atrophy.

Abortion

Prodromal signs of spontaneous abortion may include a pink discharge for several days or a scant brown discharge for several weeks before the onset of cramps and increased vaginal bleeding. For a few hours, the cramps intensify and occur more frequently; then the cervix dilates to expel uterine contents. If the entire contents are expelled, cramps and bleeding subside. However, if any contents remain, cramps and bleeding continue.

Ectopic pregnancy

Ectopic pregnancy sometimes produces symptoms of normal pregnancy or no symptoms other than mild abdominal pain, making diagnosis difficult. Characteristic clinical effects after fallopian tube implantation include amenorrhea or abnormal menses, followed by slight vaginal bleeding, and unilateral pelvic pain over the mass. Rupture of the tube causes life-threatening complications, including hemorrhage, shock, and peritonitis. The patient experiences sharp lower abdominal pain, possibly radiating to the shoulders and neck, often precipitated by activities that increase abdominal pressure, such as a bowel movement; she feels extreme pain upon motion of the cervix and palpation of the adnexa during a pelvic examination.

Hyperemesis gravidarum

The cardinal symptoms of hyperemesis gravidarum are unremitting nausea and vomiting. The vomitus initially contains undigested food and mucus as well as small amounts of bile; later, only bile and mucus; and finally, blood and material that resembles coffee grounds. Persistent vomiting causes substantial weight loss and eventual emaciation. Associated effects may include pale, dry, waxy, and possibly jaundiced skin; subnormal or elevated temperature; rapid pulse; a fetid, fruity breath odor from acidosis; and central nervous system symptoms, such as confusion, delirium, headache, lassitude, stupor and, possibly, coma.

Gestational hypertension

Mild preeclampsia generally produces the following clinical effects: hypertension, proteinuria (less than 5 g/24 hours), generalized edema, and sudden weight gain of more than 3 lb (1.4 kg) per week during the second trimester or more than 1 lb (0.5 kg) a week during the third trimester. Severe preeclampsia is marked by increased hypertension and proteinuria, eventually leading to the development of oliguria. Hemolysis, elevated liver enzymes, and low platelets (the HELLP P 7 syndrome) is a severe variant. Other symptoms that may indicate worsening preeclampsia include blurred vision due to retinal arteriolar spasms, epigastric pain or heartburn, and severe frontal headache. In eclampsia, all the clinical manifestations of preeclampsia are magnified and are associated with seizures and, possibly, coma, premature labor, stillbirth, renal failure, and hepatic damage.

Hydatidiform mole

The early stages of a pregnancy in which a hydatidiform mole develops typically seem normal, except that the uterus may grow more rapidly than usual. The first obvious signs of trouble—absence of fetal heart tones, vaginal bleeding (from spotting to hemorrhage), and lower abdominal cramps—mimic those of spontaneous abortion. The blood may contain hydatid vesicles; hyperemesis is possible, and signs and symptoms of preeclampsia are also possible. Other complications of P 9 hydatidiform mole may include anemia, infection, trophoblast embolism, uterine rupture, and choriocarcinoma.

Placenta previa

Placenta previa usually produces painless third-trimester bleeding (often the first complaint). Various malpresentations occur because of the placenta's location and interfere with proper descent of the fetal head. P 0 (The fetus remains active, however, with good heart tones.) Complications of placenta previa include shock or maternal and fetal death.

Abruptio placentae

Abruptio placentae produces a wide range of clinical effects, depending on the extent of placental separation and the amount of blood lost from maternal circulation. (See Degrees of placental separation in abruptio placentae, page 1192.) Mild abruptio placentae (marginal separation) develops gradually and produces mild to moderate bleeding, vague lower abdominal discomfort, mild to moderate abdominal tenderness, and uterine irritability. Fetal heart tones remain strong and regular. Moderate abruptio placentae (about 50% placental separation) may develop gradually or abruptly and produces continuous abdominal pain, moderate dark red vaginal bleeding, a tender uterus that remains firm between contractions, barely audible or irregular and bradycardiac fetal heart tones and, possibly, signs of shock. Labor usually starts within 2 hours and often proceeds rapidly.

Cardiovascular disease in pregnancy

Typical clinical features of cardiovascular disease during pregnancy include distended jugular veins, diastolic murmurs, moist basilar pulmonary crackles, cardiac enlargement (discernible on percussion or as a cardiac shadow on chest X-ray), and cardiac arrhythmias (other than sinus or paroxysmal atrial tachycardia). Other characteristic abnormalities may include cyanosis, pericardial friction rub, pulse delay, and pulsus alternans. P 4 Decompensation may develop suddenly or gradually, with persistent crackles at the lung bases. As it progresses, edema, increasing dyspnea on exertion, palpitations, a smothering sensation, and hemoptysis may occur.

Adolescent pregnancy

Clinical manifestations of adolescent pregnancy are the same as those of adult pregnancy (amenorrhea, nausea, vomiting, breast tenderness, fatigue). However, the pregnant adolescent is much more likely to develop complications, such as poor weight gain during pregnancy, premature labor, and pregnancy-induced hypertension. In addition, the neonate is more likely to be of low birth weight. Some of these complications are related to the pregnant adolescent's physical immaturity, rapid growth, interest in fad diets, and generally poor nutrition; other complications may stem from the adolescent's need to deny her condition or to her ignorance of early signs of pregnancy, which often delays initiation of prenatal care.

Diabetic complications during pregnancy

Indications for diagnostic screening for maternal diabetes mellitus during pregnancy include obesity, excessive weight gain, excessive hunger or thirst, polyuria, recurrent monilial infections, glycosuria, previous delivery of a large neonate, polyhydramnios, maternal hypertension, and a family history of diabetes.

Preterm labor

Like labor at term, preterm labor produces rhythmic uterine contractions, cervical dilation and effacement, possible rupture of the membranes, expulsion of the cervical mucus plug, and a bloody discharge.

Premature rupture of membranes

Typically, PROM causes blood-tinged amniotic fluid containing vernix particles to gush or leak from the vagina. Maternal fever, fetal tachycardia, and foul□smelling vaginal discharge indicate infection.

Puerperal infection

A characteristic sign of puerperal infection is fever (at least 100.4° F [38° C]) that occurs in the first 24 hours in the first 9 days postpartum. This fever can spike as high as 105° F (40.6° C) and is commonly associated with chills, headache, malaise, restlessness, and anxiety. Abortion or miscarriage isn't usually associated with this infection and fever. Accompanying signs and symptoms depend on the infection's extent and site and may include: endometritis: heavy, sometimes foul-smelling lochia; tender, enlarged uterus; backache; severe uterine contractions persisting after childbirth parametritis (pelvic cellulitis): vaginal tenderness and abdominal pain and tenderness (pain may become more intense as infection spreads). The inflammation may remain localized, may lead to abscess formation, or may spread through the blood or lymphatic system. Widespread inflammation may cause: pelvic thrombophlebitis: severe, repeated chills and dramatic swings in body temperature; lower abdominal or flank pain; and, possibly, a palpable tender mass over the affected area, which usually develops near the second postpartum week femoral thrombophlebitis: pain, stiffness, or swelling in a leg or the groin; inflammation or shiny, white appearance of the affected leg; malaise; fever; and chills, usually beginning 10 to 20 days postpartum (these signs may precipitate pulmonary embolism) peritonitis: body temperature usually elevated, accompanied by tachycardia (greater than 140 beats/minute), weak pulse, hiccups, nausea, vomiting, and diarrhea; constant and possibly excruciating abdominal pain.

Mastitis and breast engorgement

Mastitis may develop anytime during lactation but usually begins 1 to 2 weeks postpartum with fever (101° F [38.3° C] or higher in acute mastitis), malaise, and flulike symptoms. The breast (or, occasionally, both breasts) becomes tender, hard, swollen, and warm. Unless mastitis is treated adequately, it may progress to breast abscess. Breast engorgement generally starts with onset of lactation (day 2 to day 5 postpartum). The breasts undergo changes similar to those in mastitis, and body temperature may be elevated. Engorgement may be mild, causing only slight discomfort, or severe, causing considerable pain. A severely engorged breast can interfere with the infant's capacity to feed because of his inability to position his mouth properly on the swollen, rigid breast.

Galactorrhea

In the female with galactorrhea, milk continues to flow after the 21-day period that's normal after weaning. Galactorrhea may also be spontaneous and unrelated to normal lactation, or it may be

caused by manual expression. Such abnormal flow is usually bilateral and may be accompanied by amenorrhea.

Hyperbilirubinemia

The primary sign of hyperbilirubinemia is jaundice, which doesn't become clinically apparent until serum bilirubin levels reach about 7 mg/dl. Physiologic jaundice develops 24 hours after delivery in 50% of term neonates (usually day 2 to day 3) and 48 hours after delivery in 80% of premature neonates (usually day 3 to day 5). It generally disappears by day 7 in term neonates and by day 10 in premature neonates. Throughout physiologic jaundice, serum unconjugated bilirubin levels don't exceed 12 mg/dl. Pathologic jaundice may appear anytime after the first day of life and persists beyond 7 days with serum bilirubin levels greater than 12 mg/dl in a term neonate, 15 mg/dl in a premature neonate, or increasing more than 5 mg/dl in 24 hours.

Erythroblastosis fetalis

Jaundice usually isn't present at birth but may appear as soon as 30 minutes later or within 24 hours. The mildly affected neonate shows mild to moderate hepatosplenomegaly and pallor. In severely affected neonates who survive birth, erythroblastosis fetalis usually produces pallor, edema, petechiae, hepatosplenomegaly, grunting respirations, pulmonary crackles, poor muscle tone, neurologic unresponsiveness, possible heart murmurs, a bilestained umbilical cord, and yellow or meconium-stained amniotic fluid. About 10% of untreated neonates develop kernicterus from hemolytic disease and show symptoms such as anemia, lethargy, poor sucking ability, retracted head, stiff limbs, squinting, a high-pitched cry, and seizures. Hydrops fetalis causes extreme hemolysis, fetal hypoxia, heart failure (with possible pericardial effusion and circulatory collapse), edema (ranging from mild peripheral edema to anasarca), peritoneal and pleural effusions (with dyspnea and pulmonary crackles), and green- or browntinged amniotic fluid (usually indicating a stillbirth). Other distinctive characteristics of the neonate with hydrops fetalis include enlarged placenta, marked pallor, hepatosplenomegaly, cardiomegaly, and ascites. Petechiae and widespread ecchymoses are present in severe cases, indicating concurrent disseminated intravascular coagulation. This disorder retards intrauterine growth, so the neonate's lungs, kidneys, brain, and thymus are small, and despite edema, his body size is smaller than that of neonates of comparable gestational age.

Medullary sponge kidney

Symptoms usually appear only as a result of complications and are seldom present before adulthood. Complications include formation of calcium oxylate stones, which lodge in the dilated cystic collecting ducts or pass through a ureter, and infection secondary to dilation of the ducts. These complications, which occur in about 30% of patients, are likely to produce severe colic, hematuria, lower urinary tract infection ([UTI]; burning on urination, urgency, frequency), and pyelonephritis. Secondary impairment of renal function from obstruction and infection occurs in only about 10% of patients.

Polycystic kidney disease

Adult polycystic kidney disease is commonly asymptomatic through the patient's 40s, but may induce nonspecific symptoms, such as hypertension, polyuria, and recurrent UTIs. Later, the patient develops overt symptoms related to the enlarging kidney mass, such as lumbar pain, widening girth, and swollen or tender abdomen. Abdominal pain is usually worsened by exertion and relieved by lying down. In advanced stages, this disease may cause recurrent hematuria, life-threatening retroperitoneal bleeding resulting from cyst rupture, proteinuria, and colicky abdominal pain from the ureteral passage of clots or calculi. Generally, about 10 years after symptoms appear, progressive compression of kidney structures by the enlarging mass produces renal failure and uremia. Hypertension is found in about 20% to 30% of children and up to 75% of adults due to intrarenal ischemia, which activates the renin-angiotensin system.

Acute renal failure

Acute renal failure is a critical illness. Its early signs are oliguria, azotemia and, rarely, anuria. Electrolyte imbalance, metabolic acidosis, and other severe effects follow, as the patient becomes increasingly uremic and renal dysfunction disrupts other body systems: GI: anorexia, nausea, vomiting, diarrhea or constipation, stomatitis, bleeding, hematemesis, dry mucous membranes, uremic breath P Central nervous system (CNS): headache, drowsiness, irritability, confusion, peripheral neuropathy, seizures, coma Cutaneous: dryness, pruritus, pallor, purpura and, rarely, uremic frost Cardiovascular: early in the disease, hypotension; later, hypertension, arrhythmias, fluid overload, heart failure, systemic edema, anemia, altered clotting mechanisms Respiratory: pulmonary edema, Kussmaul's respirations. Fever and chills indicate infection, a common complication.

Acute pyelonephritis

Typical clinical features include urgency, frequency, burning during urination, dysuria, nocturia, and hematuria (usually microscopic but may be gross). Urine may appear cloudy and have an ammonia-like or fishy odor. Other common symptoms include a temperature of 102° F (38.9° C) or higher, shaking chills, flank pain, anorexia, and general fatigue. These symptoms characteristically develop rapidly over a few hours or a few days. Although these symptoms may disappear within days, even without treatment, residual bacterial infection is likely and may cause symptoms to recur later.

Acute poststreptococcal glomerulonephritis

APSGN begins within 1 to 3 weeks after untreated pharyngitis. Symptoms include mild to moderate edema, oliguria (less than 400 ml/24 hours), proteinuria, azotemia, hematuria, and fatigue. Mild to severe hypertension may result from either sodium or water retention (due to decreased GFR) or inappropriate renin release. Heart failure from hypervolemia leads to pulmonary edema.

Acute tubular necrosis

Nephrotoxic injury causes multiple symptoms similar to those of renal failure, particularly azotemia, anemia, acidosis, overhydration, and hypertension. Some patients may also experience fever, rash, and eosinophilia. However, ATN is usually difficult to recognize in its early stages because effects of the critically ill patient's primary disease may mask the symptoms of ATN. The first recognizable effect may be decreased urine output. Generally, hyperkalemia and the characteristic uremic syndrome soon follow, with oliguria (or, rarely, anuria) and confusion, which may progress to uremic coma. Other possible complications may include heart failure, uremic pericarditis, pulmonary edema, uremic lung, anemia, anorexia, intractable vomiting, and poor wound healing due to debilitation.

Renal infarction

Although renal infarction may be asymptomatic, typical symptoms include severe upper abdominal pain or gnawing flank pain and tenderness, costovertebral tenderness, fever, anorexia, nausea, and vomiting. Gross hematuria may be present. When arterial occlusion causes infarction, the affected kidney is small and not palpable. Renovascular hypertension, a frequent complication that may occur several days after infarction, results from reduced blood flow, which stimulates the renin-angiotensin mechanism.

Renal calculi

Clinical effects vary with size, location, and etiology of the calculi. Pain, the key symptom, usually results from obstruction; large, rough calculi occlude the opening to the ureter and increase the frequency and force of peristaltic contractions. The pain of classic renal colic travels from the costovertebral angle to the flank, to the suprapubic region and external genitalia. The intensity of this pain fluctuates and may be excruciating at its peak. If calculi are in the renal pelvis and calyces, pain may be more constant and dull. Back pain (from calculi that produce an obstruction within a kidney) and severe abdominal pain (from calculi traveling down a ureter) may also occur. (See Types of renal calculi.) Nausea and vomiting usually accompany severe pain.

Renal vein thrombosis

Clinical features of renal vein thrombosis vary with speed of onset. Rapid onset of venous obstruction produces severe lumbar pain and tenderness in the epigastric region and the costovertebral angle. Other characteristic features include fever, leukocytosis, pallor,

hematuria, proteinuria, peripheral edema and, when the obstruction is bilateral, oliguria and other uremic signs. The kidneys enlarge and become easily palpable. Hypertension is unusual but may develop. Gradual onset causes symptoms of nephrotic syndrome. Peripheral edema is possible but pain is generally absent. Other clinical signs include proteinuria, hypoalbuminemia, and hyperlipidemia. Infants with this disease have enlarged kidneys, oliguria, and renal insufficiency that may progress to acute or chronic renal failure.

Nephrotic syndrome

The dominant clinical feature of nephrotic syndrome is mild to severe dependent edema of the ankles or sacrum, or periorbital edema, especially in children. Edema may lead to ascites, pleural effusion, and swollen external genitalia. Accompanying symptoms may include orthostatic hypotension, lethargy, anorexia, depression, and pallor. Major complications are malnutrition, infection, coagulation disorders, thromboembolic vascular occlusion, and accelerated atherosclerosis.

Chronic glomerulonephritis

Chronic glomerulonephritis typically develops insidiously and asymptomatically, usually over many years. At any time, however, it may suddenly become progressive, producing nephrotic syndrome, hypertension, proteinuria, and hematuria. In late stages of progressive chronic glomerulonephritis, it may accelerate to uremic symptoms, such as azotemia, nausea, vomiting, pruritus, dyspnea, malaise, and fatigability. Mild to severe edema and anemia may accompany these symptoms. Severe hypertension may cause cardiac hypertrophy, leading to heart failure, and may accelerate the development of advanced renal failure, eventually necessitating dialysis or transplantation.

Renovascular hypertension

In addition to elevated systemic blood pressure, renovascular hypertension usually produces symptoms common to hypertensive states, such as headache, palpitations, tachycardia, anxiety, lightheadedness, decreased tolerance of temperature extremes, retinopathy, and mental sluggishness. Significant complications include heart failure, myocardial infarction, stroke and, occasionally, renal failure.

Hydronephrosis

Clinical features of hydronephrosis vary with the cause of the obstruction. In some patients, hydronephrosis produces no symptoms or only mild pain and slightly decreased urinary flow; in others, it may produce severe, colicky renal pain or dull flank pain that may radiate to the groin, and gross urinary abnormalities, such as hematuria, pyuria, dysuria, alternating oliguria and polyuria, or complete anuria. Other symptoms of hydronephrosis include nausea, vomiting, abdominal fullness, pain on urination, dribbling, or hesitancy. Unilateral obstruction may cause pain on only one side, usually in the flank area. The most common complication of an obstructed kidney is infection (pyelonephritis) due to stasis that exacerbates renal damage and may create a life-threatening crisis. Paralytic ileus frequently accompanies acute obstructive uropathy.

Renal tubular acidosis

In children and adults, RTA may lead to urinary tract infection, rickets, and growth problems. Possible complications of RTA include nephrocalcinosis and pyelonephritis.

Chronic renal failure

Chronic renal failure produces major changes in all body systems: Renal and urologic: Initially, salt-wasting and consequent hyponatremia produce hypotension, dry mouth, loss of skin turgor, listlessness, fatigue, and nausea; later, somnolence and confusion P develop. As the number of functioning nephrons decreases, so does the kidneys' capacity to excrete sodium, resulting in salt retention and overload. Accumulation of potassium causes muscle irritability, then muscle weakness as the potassium level continues to rise. Fluid overload and metabolic acidosis also occur. Urinary output decreases; urine is very dilute and contains casts and crystals. Cardiovascular: Renal failure leads to hypertension, arrhythmias (including life-threatening ventricular tachycardia or fibrillation), cardiomyopathy, uremic pericarditis, pericardial effusion with possible cardiac tamponade, heart failure, and periorbital and peripheral edema. Respiratory: Pulmonary changes include reduced pulmonary macrophage activity with increased susceptibility to infection, pulmonary edema, pleuritic pain, pleural friction rub and effusions, crackles, thick sputum, uremic pleuritis and uremic lung (or uremic pneumonitis), dyspnea due to heart failure, and Kussmaul's respirations as a result of acidosis. GI: Inflammation and ulceration of GI mucosa cause stomatitis, gum ulceration and bleeding and, possibly, parotitis, esophagitis, gastritis, duodenal ulcers, lesions on the small and large bowel, uremic colitis, pancreatitis, and proctitis. Other GI symptoms include a metallic taste in the mouth, uremic fetor (ammonia smell to breath), anorexia, nausea, and vomiting. Cutaneous: Typically, the skin is pallid, yellowish bronze, dry, and scaly. Other cutaneous symptoms include severe itching; purpura; ecchymoses; petechiae; uremic frost (most often in critically ill or terminal patients); thin, brittle fingernails with characteristic lines; and dry, brittle hair that may change color and fall out easily. Neurologic: Restless leg syndrome, one of the first signs of peripheral neuropathy, causes pain, burning, and itching in the legs and feet, which may be relieved by voluntarily shaking, moving, or rocking them. Eventually, this condition progresses to paresthesia and motor nerve dysfunction (usually bilateral footdrop) unless dialysis is initiated. Other signs and symptoms include muscle cramping and twitching, shortened memory and attention span, apathy, drowsiness, irritability, confusion, coma, and seizures. EEG changes indicate metabolic encephalopathy. Endocrine: Common endocrine abnormalities include stunted growth patterns in children (even with elevated growth hormone levels), infertility and decreased libido in both sexes, amenorrhea and cessation of menses in females, and impotence, decreased sperm production, and testicular atrophy in males. Increased aldosterone secretion (related to increased renin production) and impaired carbohydrate metabolism (increased blood glucose levels similar to diabetes mellitus) may also occur. Hematopoietic: Anemia, decreased red blood cell (RBC) survival time, blood loss from dialysis and GI bleeding, mild thrombocytopenia, and platelet defects occur. Other problems include increased bleeding and clotting disorders, demonstrated by purpura, hemorrhage

from body orifices, easy bruising, ecchymoses, and petechiae. Skeletal: Calcium-phosphorus imbalance and consequent parathyroid hormone imbalances cause muscle and bone pain, skeletal demineralization, pathologic fractures, and calcifications in the brain, eyes, gums, joints, myocardium, and blood vessels. Arterial calcification may produce coronary artery disease. In children, renal osteodystrophy (renal rickets) may develop.

Lower urinary tract infection

Lower UTI usually produces urgency, frequency, dysuria, cramps or spasms of the bladder, itching, a feeling of warmth during urination, nocturia, and possibly urethral discharge in males. Inflammation of the bladder wall also causes hematuria and fever. Other common features include low back pain, malaise, nausea, vomiting, abdominal pain or tenderness over the bladder area, chills, and flank pain.

Vesicoureteral reflux

Vesicoureteral reflux typically manifests itself as the signs and symptoms of UTI: frequency, urgency, burning on urination, hematuria, foul- P smelling urine and, in infants, dark, concentrated urine. With upper urinary tract involvement, signs and symptoms usually include high fever, chills, flank pain, vomiting, and malaise.

Neurogenic bladder

Neurogenic bladder produces a wide range of clinical effects, depending on the underlying cause and its effect on the structural integrity of the bladder. Usually, this disorder causes some degree of incontinence, changes in initiation or interruption of micturition, and the inability to empty the bladder completely. Other effects of neurogenic bladder include vesicoureteral reflux, deterioration or infection in the upper urinary tract, and hydroureteral nephrosis. Depending on the site and extent of the spinal cord lesion, spastic neurogenic bladder may produce involuntary or frequent scanty urination, without a feeling of bladder fullness, and possibly spontaneous spasms of the arms and legs. Anal sphincter tone may be increased. Tactile stimulation of the abdomen, thighs, or genitalia may precipitate voiding and spontaneous contractions of the arms and legs. With cord lesions in the upper thoracic (cervical) level, bladder distention can trigger hyperactive autonomic reflexes, resulting in severe hypertension, bradycardia, and headaches. Flaccid neurogenic bladder may be associated with overflow incontinence, diminished anal sphincter tone, and a greatly distended bladder (evident on percussion or palpation), but without the accompanying feeling of bladder fullness due to sensory impairment.

Prostatitis

Acute prostatitis begins with fever, chills, low back pain, myalgia, perineal fullness, and arthralgia. Urination is frequent and urgent. Dysuria, nocturia, and urinary obstruction may also occur. The urine may appear cloudy. When palpated rectally, the prostate is tender, indurated, swollen, firm, and warm. Chronic bacterial prostatitis sometimes produces no symptoms but usually elicits the same urinary symptoms as the acute form but to a lesser

degree. UTI is a common complication. Other possible signs include painful ejaculation, hemospermia, persistent urethral discharge, and sexual dysfunction.

Epididymitis

The key symptoms are pain, extreme tenderness, and swelling in the groin and scrotum with erythema, high fever, malaise, and a characteristic waddle—an attempt to protect the groin and scrotum during walking. An acute hydrocele may also result from inflammation.

Benign prostatic hyperplasia

Clinical features of BPH depend on the extent of prostatic enlargement and the lobes affected. Characteristically, the condition starts with a group of symptoms known as prostatism: reduced urine stream caliber and force, urinary hesitancy, and difficulty starting micturition (resulting in straining, feeling of incomplete voiding, and an interrupted stream). As the obstruction increases, it causes frequent urination with nocturia, dribbling, urine retention, incontinence, and possibly hematuria. Physical examination indicates a visible midline mass above the symphysis pubis that represents an incompletely emptied bladder; rectal palpation discloses an enlarged prostate. Examination may detect secondary anemia and, possibly, renal insufficiency secondary to obstruction. P As BPH worsens, complete urinary obstruction may follow infection or use of decongestants, tranquilizers, alcohol, anti-depressants, or anticholinergics. Complications include infection, renal insufficiency, hemorrhage, and shock.

Respiratory distress syndrome

Although a neonate with RDS may breathe normally at first, he usually develops rapid, shallow respirations within minutes or hours of birth, with intercostal, subcostal, or sternal retractions; nasal flaring; and audible expiratory grunting. This grunting is a natural compensatory mechanism designed to produce positive end-expiratory pressure (PEEP) and prevent further alveolar collapse. Severe disease is marked by apnea, bradycardia, and cyanosis (from hypoxemia, left-to-right shunting through the foramen ovale, or right-to□left intrapulmonary shunting through atelectatic regions of the lung). Other clinical features include pallor, frothy sputum, and low body temperature as a result of an immature nervous system and the absence of subcutaneous fat.

Sudden infant death syndrome

Although parents find some victims wedged in crib corners or with blankets wrapped around their heads, autopsies rule out suffocation as the cause of death. Autopsy shows a patent airway, so aspiration of vomitus isn't the cause of death. Typically, SIDS babies don't cry out and show no signs of having been disturbed in their sleep. However, their positions or tangled blankets may suggest movement just before death, perhaps due to terminal spasm. Depending on how long the infant has been dead, a SIDS baby may have a mottled complexion with extreme cyanosis of the lips and fingertips or pooling of blood in the legs and feet that may be mistaken for bruises. Pulse and respirations are absent, and the diaper is wet and full of stool.

Croup

The onset of croup usually follows an upper respiratory tract infection. Clinical features include inspiratory stridor, hoarse or muffled vocal sounds, varying degrees of laryngeal obstruction and respiratory distress, and a characteristic sharp, barking, seal-like cough. These symptoms may last only a few hours or persist for a day or two. As it progresses, croup causes inflammatory edema and, possibly, spasm, which can obstruct the upper airway and severely compromise ventilation. (See How croup affects the upper airway.) Each form of croup has additional characteristics: In laryngotracheobronchitis, the symptoms seem to worsen at night. Inflammation causes edema of the bronchi and bronchioles as well as increasingly difficult expiration that frightens the child. Other characteristic features include fever, diffusely decreased breath sounds, expiratory rhonchi, and scattered crackles. Laryngitis, which results from vocal cord edema, is usually mild and produces no respiratory distress except in infants. Early signs include a sore throat and cough, which, rarely, may progress to marked hoarseness, suprasternal and intercostal retractions, inspiratory stridor, dyspnea, P diminished breath sounds, restlessness and, in later stages, severe dyspnea and exhaustion. Acute spasmodic laryngitis affects a child between ages 1 and 3, particularly one with allergies and a family history of croup. It typically begins with mild to moderate hoarseness and nasal discharge, followed by the characteristic cough and noisy inspiration (that usually awaken the child at night), labored breathing with retractions, rapid pulse, and clammy skin. The child understandably becomes anxious, which may lead to increasing dyspnea and transient cyanosis. These severe symptoms diminish after several hours but reappear in a milder form on the next one or two nights.

Epiglottiditis

Sometimes preceded by an upper respiratory infection, epiglottiditis may rapidly progress to complete upper airway obstruction within 2 to 5 hours. Laryngeal obstruction results from inflammation and edema of the epiglottis. Accompanying symptoms include high fever, stridor, sore throat, dysphagia, irritability, restlessness, and drooling. To relieve severe respiratory distress, the child with epiglottiditis may hyperextend his neck, sit up, and lean forward with his mouth open, tongue protruding, and nostrils flaring as he tries to breathe. He may develop inspiratory retractions and rhonchi.

Acute respiratory distress syndrome

ARDS initially produces rapid, shallow breathing and dyspnea within hours to days of the initial injury (sometimes after the patient's condition appears to have stabilized). Hypoxemia develops, causing an increased drive for ventilation. Because of the effort required to expand the stiff lung, intercostal and suprasternal retractions result. Fluid accumulation produces crackles and rhonchi; worsening hypoxemia causes restlessness, apprehension, mental sluggishness, motor dysfunction, and tachycardia (possibly with transient increased arterial blood pressure). Severe ARDS causes overwhelming hypoxemia. If uncorrected, this results in hypotension, decreasing urine output, respiratory and metabolic acidosis, and eventually ventricular fibrillation or standstill. ELDER TIP The older patient may appear to do well following an initial episode of ARDS. Symptoms commonly appear 2 to 3 days later.

Acute respiratory failure in COPD

In patients who have COPD with ARF, increased ventilation-perfusion mismatch and reduced alveolar ventilation decrease PaO_2 (hypoxemia) and increase $PaCO_2$ (hypercapnia). This rise in carbon dioxide (CO_2) lowers the pH. The resulting hypoxemia and acidemia affect all body organs, especially the CNS and the respiratory and cardiovascular systems. Specific symptoms vary with the underlying cause of ARF but may include these systems: Respiratory—Rate may be increased, decreased, or normal depending on the cause; respirations may be shallow, deep, or alternate between the two; and air hunger may occur. Cyanosis may or may not be present, depending on the hemoglobin (Hb) level and arterial oxygenation. Auscultation of the chest may reveal crackles, rhonchi, wheezing, or diminished breath sounds. CNS—When hypoxemia and hypercapnia occur, the patient may show evidence of restlessness, confusion, loss of concentration, irritability, tremulousness, diminished tendon reflexes, and papilledema; he may slip into a coma. Cardiovascular—Tachycardia, with increased cardiac output and mildly elevated blood pressure secondary to adrenal release of catecholamine, occurs early in response to low PaO_2 . With myocardial hypoxia, arrhythmias may develop. Pulmonary hypertension, secondary to pulmonary capillary vasoconstriction, may cause increased pressures on the right side of the heart, elevated jugular veins, an enlarged liver, and peripheral edema. Stresses on the heart may precipitate cardiac failure.

Pulmonary edema

The early symptoms of pulmonary edema reflect interstitial fluid accumulation and diminished lung compliance: dyspnea on exertion, paroxysmal nocturnal dyspnea, orthopnea, and coughing. Clinical features include tachycardia, tachypnea, dependent crackles, jugular vein distention, and a diastolic (S_3) gallop. With severe pulmonary edema, the alveoli and bronchioles may fill with fluid and intensify the early symptoms. Respiration becomes labored and rapid, with more diffuse crackles and coughing that produces frothy, bloody sputum. Tachycardia increases, and arrhythmias may

occur. Skin becomes cold, clammy, diaphoretic, and cyanotic. Blood pressure falls and the pulse becomes thready as cardiac output falls. Symptoms of severe heart failure with pulmonary edema may also include signs of hypoxemia, such as anxiety, restlessness, and changes in the patient's level of consciousness.

Cor pulmonale

As long as the heart can compensate for the increased pulmonary vascular resistance, clinical features reflect the underlying disorder and occur mostly in the respiratory system. They include chronic productive cough, exertional dyspnea, wheezing respirations, fatigue, and weakness. Progression of cor pulmonale is associated with dyspnea (even at rest) that worsens on exertion, tachypnea, orthopnea, edema, weakness, and right upper quadrant discomfort. Chest examination reveals findings characteristic of the underlying lung disease. Signs of cor pulmonale and right-sided heart failure include dependent edema; distended jugular veins; prominent parasternal or epigastric cardiac impulse; hepatojugular reflux; an enlarged, tender liver; ascites; and tachycardia. Decreased cardiac output may cause a weak pulse and hypotension. Chest examination yields various findings, depending on the underlying cause of cor pulmonale. In COPD, auscultation reveals wheezing, rhonchi, and diminished breath sounds. When the disease is secondary to upper airway obstruction or damage to central nervous system respiratory centers, chest findings may be normal, except for a right ventricular lift, gallop rhythm, and loud pulmonic component of S2. Tricuspid insufficiency produces a pansystolic murmur heard at the lower left sternal border; its intensity increases on inspiration, distinguishing it from a murmur due to mitral valve disease. A right ventricular early murmur that increases on inspiration can be heard at the left sternal border or over the epigastrium. A systolic pulmonic ejection click may also be heard. Alterations in the patient's level of consciousness may occur.

Legionnaires' disease

The multisystem clinical features of Legionnaires' disease follow a predictable sequence, although the onset of the disease may be gradual or sudden. After a 2- to 10-day incubation period, nonspecific, prodromal signs and symptoms appear, including diarrhea, anorexia, malaise, diffuse myalgias and generalized weakness, headache, and recurrent chills. An unremitting fever develops within 12 to 48 hours with a temperature that may reach 105° F (40.6° C). A cough then develops that's nonproductive initially but eventually may produce grayish, nonpurulent, and occasionally blood-streaked sputum. Other characteristic features include nausea, vomiting, disorientation, mental sluggishness, confusion, mild temporary amnesia, pleuritic chest pain, tachypnea, dyspnea, and fine crackles. Patients who develop pneumonia may also experience hypoxia. Other complications include hypotension, delirium, heart failure, arrhythmias, acute respiratory failure, renal failure, and shock (usually fatal)

Atelectasis

Clinical effects vary with the cause of collapse, the degree of hypoxemia, and any underlying disease but generally include some degree of dyspnea. Atelectasis of a small area of the lung may produce only minimal symptoms that subside without specific treatment. However, massive collapse can produce severe dyspnea, anxiety, cyanosis, diaphoresis, peripheral circulatory collapse, tachycardia, and substernal or intercostal retraction. Also, atelectasis may result in compensatory hyperinflation

of unaffected areas of the lung, mediastinal shift to the affected side, and elevation of the ipsilateral hemidiaphragm.

Respiratory acidosis

Acute respiratory acidosis produces CNS disturbances that reflect changes in the pH of cerebrospinal fluid rather than increased CO2 levels in cerebral circulation. Effects range from restlessness, confusion, and apprehension to somnolence, with a fine or flapping tremor (asterixis), or coma. The patient may complain of headaches as well as exhibit dyspnea and tachypnea with papilledema and depressed reflexes. Unless the patient is P receiving O2 , hypoxemia accompanies respiratory acidosis. This disorder may also cause cardiovascular abnormalities, such as tachycardia, hypertension, atrial and ventricular arrhythmias and, in severe acidosis, hypotension with vasodilation (bounding pulses and warm periphery).

Respiratory alkalosis

The cardinal sign of respiratory alkalosis is deep, rapid breathing, possibly exceeding 40 breaths/minute. This pattern of breathing is similar to Kussmaul's respirations that characterize diabetic acidosis. Such hyperventilation usually leads to CNS and neuromuscular disturbances, such as light-headedness or dizziness (due to below-normal CO2 levels that decrease cerebral blood flow), agitation, circumoral and peripheral paresthesias, carpopedal spasms, twitching (possibly progressing to tetany), and muscle weakness. Severe respiratory alkalosis may cause cardiac arrhythmias (that may fail to respond to conventional treatment), seizures, or both.

Pneumothorax

The cardinal features of pneumothorax are sudden, sharp, pleuritic pain (exacerbated by movement of the chest, breathing, and coughing); asymmetrical chest wall movement; and shortness of breath. Additional signs of tension pneumothorax are weak and rapid pulse, pallor, jugular vein distention, and anxiety. Tracheal deviations may be present with mediastinal shift. Tension pneumothorax produces the most severe respiratory symptoms; a spontaneous pneumothorax that releases only a small amount of air into the pleural space may cause no symptoms. In a nontension pneumothorax, the severity of symptoms is usually related to the size of the pneumothorax and the degree of preexisting respiratory disease.

Pneumonia

The main symptoms of pneumonia are coughing, sputum production, pleuritic chest pain, shaking chills, shortness of breath, rapid shallow breathing, and fever. Physical signs vary widely, ranging from diffuse, fine crackles to signs of localized or extensive consolidation and pleural effusion. There may also be associated symptoms of headache, sweating, loss of appetite, excess fatigue, and confusion (in older people). Complications include hypoxemia, respiratory failure, pleural effusion, empyema, lung abscess, and bacteremia, with spread of infection to other parts of the body, resulting in meningitis, endocarditis, and pericarditis.

Idiopathic bronchiolitis obliterans with organizing pneumonia

The presenting symptoms of BOOP are usually subacute, with a flulike syndrome of fever, persistent and nonproductive cough, dyspnea (especially with exertion), malaise, anorexia, and weight loss

lasting for several weeks to several months. Physical assessment findings may reveal dry crackles as the only abnormality. Less common symptoms include a productive cough, hemoptysis, chest pain, generalized aching, and night sweats.

Pulmonary embolism

Total occlusion of the main pulmonary artery is rapidly fatal; smaller or fragmented emboli produce symptoms that vary with the size, number, and location of the emboli. Usually, the first symptom of pulmonary embolism is dyspnea, which may be accompanied by anginal or pleuritic chest pain. Other clinical features include tachycardia, productive cough (sputum may be blood-tinged), low-grade fever, and pleural effusion. Less common signs include massive hemoptysis, chest splinting, leg edema and, with a large embolus, cyanosis, syncope, and distended jugular veins. In addition, pulmonary embolism may cause pleural friction rub and signs of circulatory collapse (weak, rapid pulse and hypotension) and hypoxia P (restlessness and anxiety).

Sarcoidosis

Initial symptoms of sarcoidosis include arthralgia (in the wrists, ankles, and elbows), fatigue, malaise, and weight loss. Other clinical features vary according to the extent and location of the fibrosis: Respiratory—breathlessness, cough (usually nonproductive), substernal pain; complications in advanced pulmonary disease include pulmonary hypertension and cor pulmonale Cutaneous—erythema nodosum, subcutaneous skin nodules with maculopapular eruptions, and extensive nasal mucosal lesions Ophthalmic—anterior uveitis (common), glaucoma, and blindness (rare) Lymphatic—bilateral hilar and right paratracheal lymphadenopathy and splenomegaly P Musculoskeletal—muscle weakness, polyarthralgia, pain, and punched-out lesions on phalanges Hepatic—granulomatous hepatitis, usually asymptomatic Genitourinary—hypercalciuria Cardiovascular—arrhythmias (premature beats, bundle-branch or complete heart block) and, rarely, cardiomyopathy Central nervous system—cranial or peripheral nerve palsies, basilar meningitis, seizures, and pituitary and hypothalamic lesions producing diabetes insipidus.

Severe acute respiratory syndrome

The incubation period for SARS is typically 3 to 5 days but may last as long as 14 days. Initial signs and symptoms include fever, shortness of breath and other minor respiratory symptoms, general discomfort, headache, rigors, chills, myalgia, sore throat, and dry cough. Some individuals may develop diarrhea or a rash. Later complications include respiratory failure, liver failure, heart failure, myelodysplastic syndromes, and death

Lung abscess

The clinical effects of lung abscess include a cough that may produce bloody, purulent, or foul-smelling sputum, pleuritic chest pain, dyspnea, excessive sweating, chills, fever, headache, malaise, diaphoresis, and weight loss. Chronic lung abscess may cause localized bronchiectasis. Failure of an abscess to improve with antibiotic treatment suggests possible underlying neoplasm or other causes of obstruction.

Hemothorax

The patient with hemothorax may experience chest pain, tachypnea, and mild to severe dyspnea, depending on the amount of blood in the pleural cavity and associated pathologic conditions. If respiratory failure results, the patient may appear anxious, restless, possibly stuporous, and

cyanotic; marked blood loss produces hypotension and shock. The affected side of the chest expands and stiffens, whereas the unaffected side rises and falls with the patient's breaths.

Pulmonary hypertension

Most patients complain of increasing dyspnea on exertion, weakness, syncope, and fatigability. Many also show signs of right-sided heart failure, including peripheral edema, ascites, jugular vein distention, and hepatomegaly. Other clinical effects vary with the underlying disorder.

Pleural effusion and empyema

Patients with pleural effusion characteristically display symptoms relating to the underlying pathologic condition. Most patients with large effusions, particularly those with underlying pulmonary disease, complain of dyspnea. Those with effusions associated with pleurisy complain of pleuritic chest pain. Other clinical features depend on the cause of the effusion. Patients with empyema also develop fever and malaise.

Pleurisy

Sharp, stabbing pain that increases with deep breathing may be so severe that it limits movement on the affected side. Dyspnea also occurs. Other symptoms vary according to the underlying pathologic process.

Chronic obstructive pulmonary disease

The typical patient, a long-term cigarette smoker, has no symptoms until middle age. His ability to exercise or do strenuous work gradually starts to decline, and he begins to develop a productive cough. These signs are subtle at first but become more pronounced as the patient gets older and the disease progresses. Eventually the patient may develop dyspnea on minimal exertion, frequent respiratory infections, intermittent or continuous hypoxemia, and grossly abnormal pulmonary function studies. Advanced COPD may cause severe dyspnea, overwhelming disability, cor pulmonale, severe respiratory failure, and death.

Bronchiectasis

Initially, bronchiectasis may be asymptomatic. When symptoms do arise, they're commonly attributed to other illnesses. The patient usually P complains of frequent bouts of pneumonia or hemoptysis. The classic symptom, however, is a chronic cough that produces foul-smelling, mucopurulent secretions in amounts ranging from less than 10 ml/day to more than 150 ml/day. Cough and sputum production are observed in greater than 90% of bronchiectasis patients. Characteristic findings include coarse crackles during inspiration over involved lobes or segments, occasional wheezing, dyspnea, sinusitis, weight loss, anemia, malaise, clubbing, recurrent fever, chills, and other signs of infection.

Idiopathic pulmonary fibrosis

The usual presenting symptoms of IPF are dyspnea and a dry, hacking, and typically paroxysmal cough. Most patients have had these symptoms for several months to 2 years before seeking medical help. End-expiratory crackles, especially in the bases of the lungs, are usually heard early in the disease. Bronchial breath sounds appear later, when airway consolidation develops. Rapid, shallow breathing occurs, especially with exertion, and clubbing has been noted in more than 40% of patients. Late in the disease, cyanosis and evidence of pulmonary hypertension (augmented S2 and

S3 gallop) commonly occur. As the disease progresses, profound hypoxemia and severe, debilitating dyspnea are the hallmark signs.

Tuberculosis

After an incubation period of 4 to 8 weeks, TB is usually asymptomatic in primary infection but may produce nonspecific symptoms, such as fatigue, weakness, anorexia, weight loss, night sweats, and low-grade fever. ELDER TIP Fever and night sweats, the typical hallmarks of TB, may not be present in elderly patients, who instead may exhibit a change in activity or weight. Assess older patients carefully. In reactivation, symptoms may include a cough that produces mucopurulent sputum, occasional hemoptysis, and chest pains.

Silicosis

Initially, silicosis may be asymptomatic or may produce dyspnea on exertion, usually attributed to being “out of shape” or “slowing down.” If the disease progresses to the chronic and complicated stage, dyspnea on exertion worsens, and other symptoms—usually tachypnea and an insidious dry cough that's most pronounced in the morning—appear. Progression to the advanced stage causes dyspnea on minimal exertion, worsening cough, and pulmonary hypertension, which in turn leads to right-sided heart failure and cor pulmonale. Patients with silicosis have a high incidence of active TB, which should be considered when evaluating patients with this disease. Central nervous system changes—confusion, lethargy, and a decrease in the rate and depth of respiration as the partial pressure of arterial carbon dioxide increases—also occur in advanced silicosis. Other clinical features include malaise, disturbed sleep, and hoarseness. The severity of these symptoms may not correlate with chest X-ray findings or the results of pulmonary function tests.

Asbestosis

Clinical features may appear before chest X-ray changes. The first symptom is usually dyspnea on exertion, typically after 10 years' exposure. As fibrosis extends, dyspnea on exertion increases until, eventually, dyspnea occurs even at rest. Advanced disease also causes a dry cough (may be productive in smokers), chest pain (commonly pleuritic), recurrent respiratory infections, and tachypnea. Cardiovascular complications include pulmonary hypertension, right ventricular hypertrophy, and cor pulmonale. Finger clubbing commonly occurs.

Coal worker's pneumoconiosis

Simple CWP produces no symptoms, especially in nonsmokers. Symptoms of complicated CWP include exertional dyspnea and a cough that occasionally produces inky-black sputum (when fibrotic changes undergo avascular necrosis and their centers cavitate). Other clinical features of CWP include increasing dyspnea and a cough that produces milky, gray, clear, or coal-flecked sputum. Recurrent bronchial and pulmonary infections produce yellow, green, or thick sputum. Complications include pulmonary hypertension, right ventricular hypertrophy and cor pulmonale, and pulmonary tuberculosis (TB). In cigarette smokers, chronic bronchitis and emphysema may also complicate the disease.

Impetigo

Common nonbullous impetigo typically begins with a small red macule that turns into a vesicle or pustule. When the vesicle breaks, a thick yellow crust forms from the exudate. (See Recognizing impetigo, page 736.) Autoinoculation may cause satellite lesions. Although it can occur anywhere, impetigo usually occurs around the mouth and nose and on the knees and elbows. Other features include pruritus, burning, and regional lymphadenopathy. A rare but serious complication of streptococcal impetigo is glomerulonephritis, which is more likely to occur when many members of the same family have impetigo.

Folliculitis, furunculosis, and carbunculosis

Pustules of folliculitis usually appear in a hair follicle on the scalp, arms, and legs in children; on the face of bearded men (sycosis barbae); and on the eyelids (styes). Deep folliculitis may be painful. Folliculitis may progress to the hard, painful nodules of furunculosis, which commonly develop on the neck, face, axillae, and buttocks. For several days these nodules enlarge, and then rupture, discharging pus and necrotic material. After the nodules rupture, pain subsides, but erythema and edema may persist for days or weeks. Carbunculosis is marked by extremely painful, deep abscesses that drain through multiple openings onto the skin surface, usually around several hair follicles. Fever and malaise may accompany these lesions.

Staphylococcal scalded skin syndrome

SSSS can usually be traced to a prodromal upper respiratory tract infection, possibly with concomitant purulent conjunctivitis. Cutaneous changes progress through three stages: Erythema: Erythema, which may begin diffusely or as a scarlatiniform rash, usually becomes visible around the mouth and other orifices and may spread in widening circles over the entire body surface. The skin becomes tender; Nikolsky's sign (sloughing of the skin when friction is applied) may appear. Exfoliation (24 to 48 hours later): In the more common, localized form of this disease, superficial erosions with a red, moist base and minimal crusting occur, generally around body orifices, and may spread to exposed areas of the skin. (See Identifying staphylococcal scalded skin syndrome, page 740.) In the more severe forms of this disease, large, flaccid bullae erupt and may spread to cover extensive areas of the body. These bullae eventually rupture, revealing sections of denuded skin; mucous membranes are spared. Desquamation: In this final stage, affected areas dry up, and powdery scales form. Normal skin replaces these scales in 5 to 7 days.

Tinea versicolor

Tinea versicolor typically produces raised or macular, round or oval, slightly scaly lesions on the upper trunk, which may extend to the lower abdomen, neck, arms, groin, thigh, genitalia and, rarely, the face. These lesions are usually tawny but may range from hypopigmented (white) patches in dark-skinned patients to hyperpigmented (brown) patches in fair-skinned patients. Some areas don't tan when exposed to sunlight, causing the cosmetic defect for which most people seek medical help. Inflammation, burning, and itching are possible but usually absent.

Dermatophytosis

Lesions vary in appearance depending on the site of invasion (inside or outside the hair shaft), duration of infection, level of host resistance, and amount of inflammatory response. Tinea capitis ranges in appearance from broken-off hairs with little scaling to severe painful, inflammatory, pus-filled masses (kerions) covering the entire scalp. Partial hair loss occurs in all cases. The cardinal clue is broken-off hairs. Tinea corporis produces flat lesions on the skin at any site except the scalp, bearded skin, hands,

or feet. These lesions may be dry and scaly or moist and crusty; as they enlarge, their centers heal, causing the classic ring-shaped appearance. In tinea unguium (onychomycosis), infection typically starts at the tip of one or more toenails (fingernail infection is less common) and produces gradual thickening, discoloration, and crumbling of the nail, with accumulation of subungual debris. Eventually, the nail may be destroyed completely. Tinea pedis, or athlete's foot, causes scaling and blisters between the toes. Severe infection may result in inflammation, with severe itching and pain on walking. A dry, squamous inflammation may affect the entire sole. (See Athlete's foot.) Tinea manuum produces scaling patches and hyperkeratosis on the palmar surface. It's usually unilateral and associated with tinea pedis. Tinea cruris (jock itch) produces red, raised, sharply defined, itchy or burning lesions in the groin that may extend to the buttocks, inner thighs, and the external genitalia. Warm weather, obesity, and tight clothing encourage fungus growth. Tinea barbae is an uncommon infection that affects the bearded facial area of men.

Scabies

Typically, scabies causes itching, which intensifies at night. Characteristic lesions are usually excoriated and may appear as erythematous nodules. These threadlike lesions are approximately 1 cm long and generally occur between fingers, on flexor surfaces of the wrists, on elbows, in axillary folds, at the waistline, on nipples and buttocks in females, and on genitalia in males.

Cutaneous larva migrans

A transient rash, tingling, or, possibly, a small vesicle appears at the point of penetration, usually on an exposed area that has come in contact with the ground, such as the feet, legs, or buttocks. The incubation period is typically 1 to 6 days. The parasite may be active almost as soon as it enters the skin. Local pruritus begins within hours following penetration. As the parasite migrates, it etches a noticeable thin, raised, red line on the skin, which may become vesicular and encrusted. Pruritus quickly develops, often with crusting and secondary infection following excoriation. Onset is usually characterized by slight itching that develops into intermittent stinging pain as the thin, red lines develop. The larva's apparently random path can cover from 1 mm to 1 cm a day. Penetration of more than one larva may involve a much larger area of the skin, marking it with many tracks.

Pediculosis

Clinical features of pediculosis capitis include itching; excoriation (with severe itching); matted, foul-smelling, lusterless hair (in severe cases); occipital and cervical lymphadenopathy (posterior cervical lymphadenopathy without obvious disease is characteristic); and a rash on the trunk, probably due to sensitization. Adult lice migrate from the scalp and deposit oval, gray-white nits on the proximal one-third of hair shafts. Pediculosis corporis initially produces small, red papules (usually on the shoulders, trunk, or buttocks). Later, wheals (probably a sensitivity reaction) may develop. Untreated pediculosis corporis may lead to vertical excoriations and ultimately to dry, discolored, thickly encrusted, scaly skin, with bacterial infection and scarring. In severe cases, headache, fever, and malaise may accompany cutaneous symptoms. Pediculosis pubis causes skin irritation from scratching, which is usually more obvious than the bites. Small gray-blue spots (maculae caeruleae) may appear on the thighs or upper body. Small red spots are often seen in the underclothing.

Acne vulgaris

The acne plug may appear as a closed comedo, or whitehead (if it doesn't protrude from the follicle and is covered by the epidermis), or as an open comedo, or blackhead (if it does protrude and isn't covered by the epidermis). The black coloration is caused by the melanin or pigment of the follicle.

Rupture or leakage of an enlarged plug into the dermis produces inflammation and characteristic acne pustules, papules or, in severe forms, acne cysts or abscesses.

Hirsutism

Hirsutism typically produces enlarged hair follicles as well as enlargement and hyperpigmentation of the hairs themselves. Excessive facial hair growth is the complaint for which most patients seek medical help. Generally, hirsutism involves appearance of thick, pigmented hair in the beard area, upper back, shoulders, sternum, axillae, and pubic area. Frontotemporal scalp hair recession is often a coexisting condition. Patterns of hirsutism vary widely, depending on the patient's race and age. ELDER TIP Elderly women commonly show increased hair growth on the chin and upper lip. In secondary hirsutism, signs of masculinization may appear—eepening of the voice, increased muscle mass, increased size of genitalia, menstrual irregularity, and decreased breast size

Alopecia

In male-pattern alopecia, hair loss is gradual and usually affects the thinner, shorter, and less pigmented hairs of the frontal and parietal portions of the scalp. In women, hair loss is generally more diffuse; completely bald areas are uncommon but may occur. Alopecia areata affects small patches of the scalp but may also occur as alopecia totalis, which involves the entire scalp and eyebrows, or as alopecia universalis, which involves the entire body. Although mild erythema may occur initially, affected areas of scalp or skin appear normal. “Exclamation point” hairs (loose hairs with dark, rough, brushlike tips on narrow, less pigmented shafts) occur at the periphery of new patches. Regrowth hairs are thin and may be white or gray. They're usually replaced by normal hair. In trichotillomania, patchy, incomplete areas of hair loss with many broken hairs appear on the scalp but may occur on other areas such as the eyebrows.

Rosacea

Rosacea generally begins with periodic flushing across the central oval of the face, accompanied later by telangiectasia, papules, pustules, and nodules. Rhinophyma is commonly associated with severe untreated rosacea but may occur alone. Rhinophyma usually appears first on the lower half of the nose, and produces red, thickened skin and follicular enlargement. It's found almost exclusively in men older than age 40. Related ocular lesions are uncommon.

Vitiligo

Vitiligo produces depigmented or stark-white patches on the skin; on fair skinned whites, these are almost imperceptible. Lesions are usually bilaterally symmetrical with sharp borders, which occasionally are hyperpigmented. Lesions that are small initially can enlarge and even progress to total depigmentation (universal vitiligo). These unique patches generally appear over bony prominences on the back of the hands; on the face, the axillae, genitalia, nipples, or umbilicus; around orifices (such as the eyes, mouth, and anus); within P body folds; and at sites of trauma. The hair within these lesions may also turn white. Because hair follicles and certain parts of the eyes also contain pigment cells, vitiligo may be associated with premature gray hair and ocular pigmentary changes.

Melasma

Typically, melasma produces large, brown, irregular patches, symmetrically distributed on the forehead, cheeks, and sides of the nose. Less commonly, these patches may occur on the neck, upper lip, temples and, occasionally, on the dorsa of the forearms.

Photosensitivity reactions

Immediately after sun exposure, a phototoxic reaction causes a burning sensation followed by erythema (sunburn-type reaction), edema, desquamation, and hyperpigmentation. Berlock dermatitis produces an acute reaction with erythematous vesicles that later become hyperpigmented. Photoallergic reactions may take one of two forms. Developing 2 hours to 5 days after light exposure, polymorphous light eruption (PMLE) produces erythema, papules, vesicles, urticaria, and eczematous lesions on exposed areas; pruritus may persist for 1 to 2 weeks. Solar urticaria begins minutes after exposure and lasts about an hour; erythema and wheals follow itching and burning sensations.

Dermatitis

Atopic skin lesions generally begin as erythematous areas on excessively dry skin. PEDIATRIC TIP In children, lesions typically appear on the forehead, cheeks, and extensor surfaces of the arms and legs. In adults, lesions appear at flexion points (antecubital fossa, popliteal area, and neck). During flare-ups, pruritus and scratching cause edema, crusting, and scaling. Eventually, chronic atopic lesions lead to multiple areas of dry, scaly skin, with white dermatographia, blanching, and lichenification. Common secondary conditions associated with atopic dermatitis include viral, fungal, or bacterial infections, and ocular disorders. Because of intense pruritus, the upper eyelid is commonly hyperpigmented and swollen, and a double fold occurs under the lower lid (Morgan-Dennie folds, Morgan folds, Dennie pleats, or Mongolian lines). Atopic cataracts are unusual but may develop between ages 20 and 40. Kaposi's varicelliform eruption, a potentially fatal, generalized viral infection, may develop if the patient with atopic dermatitis comes in contact with a person who's infected with herpes simplex.

Toxic epidermal necrolysis

Early symptoms include inflammation of the mucous membranes, a burning sensation in the conjunctivae, malaise, fever, and generalized skin tenderness. After such prodromal symptoms, TEN erupts in three phases: diffuse, erythematous rash vesiculation and blistering large-scale epidermal necrolysis and desquamation. Large, flaccid bullae that rupture easily expose extensive areas of denuded skin, permitting both loss of tissue fluids and electrolytes and widespread systemic involvement.

Warts

Clinical manifestations depend on the type of wart and its location: common (verruca vulgaris): rough, elevated, rounded surface; appears most frequently on extremities, particularly hands and fingers; most prevalent in children and young adults condyloma acuminatum (moist wart or genital wart): usually small, pink to red, moist, and soft; may occur singly or in large cauliflower-like clusters on the penis, scrotum, vulva, cervix, vagina, and anus; can also occur on oral mucosa following oral-genital exposure; considered a sexually transmitted disease digitate: fingerlike, horny projection arising from a pea-shaped base; occurs on scalp or near hairline filiform: single, thin, threadlike projection; commonly occurs around the face and neck P flat (also known as juvenile or verruca plana): multiple groupings of up to several hundred slightly raised lesions with smooth, flat, or slightly rounded tops; common on the face, neck, chest, knees, dorsa of hands, wrists, and flexor surfaces of the forearms; usually occur in children but can affect adults; often linear distribution because of spread from scratching or shaving periungual: rough, irregularly shaped, elevated surface; occurs around edges of fingernails and toenails; when severe, may extend under nail and lift it off nail bed, causing pain plantar: slightly elevated or flat; occur singly or in large clusters (mosaic warts), primarily at pressure points of feet.

Psoriasis

The most common complaint of the patient with psoriasis is itching and, occasionally, pain from dry, cracked, encrusted lesions. Psoriatic lesions are erythematous and usually form well-defined plaques, sometimes covering large areas of the body. (See Psoriatic plaques.) Such lesions most commonly appear on the scalp, chest, elbows, knees, shins, back, and buttocks. The plaques consist of characteristic silver scales that either flake off easily or can thicken, covering the lesion. Removal of psoriatic scales frequently produces fine bleeding points (Auspitz sign). Occasionally, small guttate lesions appear, either alone or with plaques; these lesions are typically thin and erythematous, with few scales. Widespread shedding of scales is common in exfoliative or erythrodermic psoriasis and may also develop in chronic psoriasis. Rarely, psoriasis becomes pustular, taking one of two forms. In localized pustular (Barber's) psoriasis, pustules appear on the palms and soles and remain sterile until opened. In generalized pustular (von Zumbusch's) psoriasis, which often occurs with fever, leukocytosis, and malaise, groups of pustules coalesce to form lakes of pus on red skin. These pustules also remain sterile until opened and commonly involve the tongue and oral mucosa. In about 30% of patients, psoriasis spreads to the fingernails, producing small indentations and yellow or brown discoloration. In severe cases, the accumulation of thick, crumbly debris under the nail, causes it to separate from the nail bed. Some patients with psoriasis develop arthritic symptoms (psoriatic arthritis), usually in one or more joints of the fingers or toes, or sometimes in the sacroiliac joints, which may progress to spondylitis. Such patients may complain of morning stiffness. Joint symptoms show no consistent linkage to the course of the cutaneous manifestations of psoriasis; they demonstrate remissions and exacerbations similar to those of rheumatoid arthritis.

Lichen planus

Lichen planus may develop suddenly or insidiously. Initial lesions commonly appear on the arms or legs (generally on the wrist and medial sides of the thighs) and evolve into the generalized eruption of flat, glistening, purple papules marked with white lines or spots (Wickham's striae). These lesions may be linear from scratching or may coalesce into plaques. Lesions often affect the mucous membranes (especially the buccal mucosa), male genitalia and, less often, the nails. These lesions are painful, especially when ulcers develop. Mild to severe pruritus is common.

Corns and calluses

Both corns and calluses cause pain through pressure placed on underlying tissue by localized thickened skin. Corns contain a central keratinous core, are smaller and more clearly defined than calluses, and are usually more painful. The pain they cause may be dull and constant or sharp when pressure is applied. “Soft” corns are caused by the pressure of a bony prominence. They appear as whitish thickenings and are commonly found between the toes, most often in the fourth interdigital web. “Hard” corns are sharply delineated and conical, and appear most frequently over the dorsolateral aspect of the fifth toe. Calluses have indefinite borders and may be quite large. They usually produce dull pain on pressure, rather than constant pain. Although calluses commonly appear over plantar warts, they're distinguished from these warts by normal skin markings.

Pityriasis rosea

Pityriasis typically begins with an erythematous “herald” patch, which may appear anywhere on the body, although it occurs most commonly on the trunk. Although this slightly raised, oval lesion is about 2 to 6 cm in diameter, approximately 25% of patients don't notice it. A few days to several weeks later, yellow-tan or erythematous patches with scaly edges (about 0.5 to 1 cm in diameter) erupt on the trunk and extremities—and, rarely, on the face, hands, and feet in adolescents. Eruption continues for 7 to 10 days, and the patches persist for 2 to 6 weeks. Occasionally, these patches are macular,

vesicular, or urticarial. A characteristic of this disease is the arrangement of lesions, which produces a pattern similar to that of a pine tree. Accompanying pruritus, if present, is usually mild but may be severe.

Hyperhidrosis

Axillary hyperhidrosis frequently produces such extreme sweating that patients often ruin their clothes in 1 day and develop contact dermatitis from clothing dyes; similarly, hyperhidrosis of the soles can easily damage a pair of shoes. Profuse sweating from both the soles and palms hinders the patient's ability to work and interact socially. Patients with this condition often report increased emotional strain.

Pressure ulcers

Pressure ulcers commonly develop over bony prominences. Early features of superficial lesions are shiny, erythematous changes over the compressed area, caused by localized vasodilation when pressure is relieved. Superficial erythema progresses to small blisters or erosions and, ultimately, to necrosis and ulceration. An inflamed area on the skin's surface may be the first sign of underlying damage when pressure is exerted between deep tissue and bone. Bacteria in a compressed site cause inflammation and, eventually, infection, which leads to further necrosis. A foul-smelling, purulent discharge may seep from a lesion that penetrates the skin from beneath. Infected, necrotic tissue prevents healthy granulation of scar tissue; a black eschar may develop around and over the lesion.