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.