Recent studies have shown that dopamine agonists may be safely withdrawn in patients who have maintained normal prolactin levels for 2 years and who have no visible tumor remnant on tapering doses of dopamine agonist. Once the dopamine agonist is discontinued, prolactin levels should be checked every 3 months for 1 year and then annually. An MRI should be obtained only if the prolactin level becomes elevated again. Recurrence risk after drug withdrawal ranges from 26% to 69% and is predicted by the initial prolactin level and tumor size.

GROWTH HORMONE

Definition

GH is a single-chain polypeptide hormone consisting of 191 amino acids that is synthesized, stored, and secreted by the anterior pituitary somatotrophs. GH secretion is regulated by two factors derived from the hypothalamus: growth hormone–releasing hormone (GHRH) and somatostatin. GHRH stimulates somatotroph GH release, and somatostatin inhibits it. GH stimulates secretion of insulin-like growth factor-I (IGF-I) by the liver. IGF-I circulates in the blood attached to binding proteins; although there are six binding proteins in serum, more than 80% of IGF-I is bound to a protein called IGFBP3. Postnatally and through puberty, GH and IGF-I are critical in determining longitudinal skeletal growth, skeletal maturation, and acquisition of bone mass. In adulthood, they are instrumental in the maintenance of skeletal architecture and bone mass. GH also has effects on the metabolism of carbohydrates, lipids, and proteins by antagonizing insulin action, increasing lipolysis and free fatty acid production, and increasing protein synthesis.

Growth Hormone Deficiency

Epidemiology

Childhood-onset GH deficiency is most commonly idiopathic, but it may be genetic or associated with congenital anatomic malformations in the brain or sellar region. The most common cause of GH deficiency in adults is a pituitary macroadenoma and its treatment; deficiency of one or more pituitary hormones occurs in 30% to 60% of such cases. The incidence of hypopituitarism 10 years after irradiation of the sellar region is approximately 50%.

Clinical Presentation

Children with GH deficiency exhibit growth retardation, short stature, and fasting hypoglycemia. Manifestations of adult GH deficiency include reduced bone mineralization, decreased muscle strength and exercise performance, decreased lean body mass with increase in fat mass and abdominal adiposity, glucose intolerance and insulin resistance, abnormal lipid profile including elevated low-density lipoprotein and triglyceride levels with decreased high-density lipoprotein, depressed mood, and impaired psychosocial well-being.

Diagnosis and Differential Diagnosis

Because of the pulsatile nature of pituitary GH secretion, a single random measurement of serum GH is not helpful to diagnose GH deficiency. In adults with GH deficiency due to a pituitary tumor and concomitant hypopituitarism involving any three other pituitary hormones, a low IGF-I level is sufficient to diagnose GH deficiency, and provocative testing is not warranted. Falsely low IGF-I levels are also seen in malnutrition, acute illness, celiac disease, poorly controlled diabetes mellitus, liver disease, and estrogen ingestion. In children, there tends to be greater variation in IGF-I levels that do not correspond to the true GH status, so provocative testing is required.

The historical "gold standard" stimulatory test is insulin-induced hypoglycemia (insulin tolerance test or ITT). Symptomatic hypoglycemia with a serum glucose level lower than 45 mg/dL is a potent stimulus for GH secretion; the normal GH response is greater than 10 ng/mL in children and greater than 5 ng/mL in adults. Because of the unavailability in the United States of GHRH, which is as sensitive and specific as the ITT in stimulating GH secretion, glucagon stimulation is being used, especially in adults with ischemic heart disease or seizures. A normal response with the glucagon stimulation test is defined as a GH peak greater than 3 ng/mL.

Treatment and Prognosis

Recombinant human growth hormone (hGH) is administered to promote linear growth in short children. The U.S. Food and Drug Administration (FDA) has approved GH treatment for conditions involving complete absence of GH associated with severe growth retardation or partial GH deficiency resulting in short stature. Short stature is defined as height more than 2.5 standard deviations below the mean for age-matched normal children, growth velocity less than the 25th percentile, delayed bone age, and predicted adult height less than the mean parental height. The conditions approved by the FDA to use GH include GH deficiency, idiopathic short stature, Turner's syndrome, Prader-Willi syndrome, chronic kidney disease, AIDS-associated muscle wasting, *SHOX* gene deficiency, Noonan's syndrome, and children born small for gestational age. Combined clinical evaluations, along with an inadequate pituitary GH response to provocative testing, are used in the assessment of childhood GH deficiency. Higher doses of GH are recommended for children without GH deficiency disorders or with partial GH deficiency.

In adults, GH is administered as a daily subcutaneous injection starting at 0.1 to 0.3 mg, with dose increases at 6-week intervals based on clinical response, side effects, and IGF-I levels. Absolute contraindications to GH therapy in adults include active neoplasm, intracranial hypertension, and proliferative diabetic retinopathy; uncontrolled diabetes and untreated thyroid disease are relative contraindications. Side effects of GH therapy are usually transient and include arthralgias, fluid retention, carpal tunnel syndrome, and glucose intolerance. Additional side effects in children include slipped capital femoral epiphysis and hydrocephalus.

Acromegaly or Growth Hormone Hypersecretion

Definition and Epidemiology

Acromegaly is literally translated as abnormal enlargement of the extremities of the skeleton. It is caused by hypersecretion of GH in adulthood. In children, excessive GH secretion before closure of the epiphyseal growth plate leads to gigantism. In both cases, the cause is almost always a GH-secreting pituitary tumor.