Growth Hormone Deficiency

Growth hormone (GH) is a protein made by the pituitary gland and released into the blood in brief pulses. The major way that GH promotes growth is by increasing levels of the hormone, insulin-like growth factor-1 (IGF-1), and its carrier protein, IGF binding protein-3 (IGFBP-3), in the blood. GH and IGF-1 work together on the cartilage cells of the growth plate in long bones to increase bone length leading to increased height.

Growth hormone deficiency (GHD) in children is defined as growth failure associated with inadequate growth hormone production. Growth failure should be evaluated in children whose length or height remains below the normal range (i.e. <3rd percentile) or whose length or height percentile is falling and is crossing major percentile landmarks over time. Before considering growth hormone deficiency as a possible diagnosis, a child with growth failure needs to be evaluated for more common conditions that can impact growth. Growth failure can occur in children who have inflammation (recurrent illnesses, arthritis, inflammatory bowel disease, etc.), poor nutrition (inadequate intake or malabsorption conditions such as celiac disease, cystic fibrosis, etc.), other chronic conditions (psychosocial short stature, chronic renal insufficiency, liver disease, hypothyroidism, etc.) and genetic conditions that impact growth (skeletal dysplasias, familial short stature, Russell-Silver Syndrome, Turner Syndrome, etc.). Children receiving stimulant therapy for attention deficit and hyperactivity disorder may have impairment of growth, particularly if caloric intake is significantly affected. However, stimulant therapy does not cause GHD. Chronic glucocorticoid therapy (inhaled or oral) can cause significant growth failure. Children with constitutional delay of growth and puberty ("late-bloomers") can have growth failure that may be difficult to separate from GHD.

Screening tests for GHD in children with growth failure with no identified cause include bone age X-ray and serum IGF-1 and IGFBP-3 levels. A delayed bone age is more common in children with GHD. An IGF-1 in the low part of the normal range or below normal increases the likelihood of GHD. An MRI picture of the brain showing a small or ectopic (misplaced) pituitary gland supports a diagnosis of GHD. The gold standard for diagnosing GHD is failure to increase GH levels in a growth hormone stimulation test (GHST). A GHST is performed in children after an overnight fast by giving a medication or medications (such as insulin, clonidine, arginine, glucagon, L-Dopa, etc.) to cause release of growth hormone into the blood and drawing blood frequently. If the highest growth hormone level obtained following two separate stimuli is less than 10 ng/mL, this is diagnostic of GHD. However, GHST is not required for diagnosis of GHD if other clinical parameters are present. Isolated congenital GHD may be associated with low blood sugars in infants and a small penis in male infants. Congenital GHD may be also be associated with multiple other pituitary deficiencies in infants and is increased in children with optic nerve hypoplasia and midline defects including cleft palate.

Children diagnosed with GHD benefit from GH replacement therapy with improved linear growth until the growth plates fuse. rhGH therapy is given by daily subcutaneous injections. Children and their families are taught to self-inject rhGH at home. The rhGH starting dose is based upon the child's weight and may be adjusted during therapy based upon weight gain, growth response and IGF-1 levels. Children receiving rhGH therapy should be seen by the pediatric endocrinologist every 3 to 6 months for monitoring of growth and adjustment of the rhGH dose. The earlier a child is diagnosed with GHD, the better the final height attained and the higher the likelihood that the child will reach a height that is normal for an adult. Some children with severe GHD will require rhGH therapy as adults due to the metabolic effects of GH.

In addition to growth, growth hormone regulates the metabolism. As calories are consumed, growth hormone controls whether those calories are used to build bone, muscle and cartilage or stored as fat. Between meals, growth hormone regulates mobilization of fat for use as energy. Growth hormone deficiency is a condition that involves impaired linear growth and significant metabolic differences including changes in body composition (decreased bone mass, decreased lean mass and increased visceral adiposity) and lipid profile (elevated LDL cholesterol and triglycerides). In children with growth hormone deficiency, growth hormone replacement therapy is important to normalize the metabolism and maximize these metabolic benefits. If a child stops growth hormone prematurely, he/she will not be able to gain the benefits of maximal bone mineral accrual and lean body mass during his pubertal growth spurt and will have increased visceral adiposity and abnormal lipid profile; this can have a negative long-term impact on his/her bone and cardiovascular health.

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Major
Aspects of
Growth
In
Children

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