Growth hormone deficiency diagnosis

There is uncertainty about the appropriate cut-off for the diagnosis of Growth hormone deficiency and little data about the yield of significant abnormal findings in patients with peak growth hormone (GH) of 7-10 ng/mL.

A study could not identify a marker of increased risk of pituitary dysfunction that could guide routine screening. However, data demonstrate the need for systematic follow-up of pituitary function after moderate or severe TBI or SAH [1)].

Clinical evaluation, including growth criteria and other medical histories

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Imaging studies

Insulin-like growth factor 1 (IGF-1) levels and IGF binding protein type 3 (IGFBP-3) levels

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Usually confirmation by provocative testing

Evaluation of other pituitary hormones and for other causes of poor growth

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Current consensus guidelines for the diagnosis of growth hormone deficiency require integration of growth criteria, medical history, laboratory testing, and imaging results.

Growth is assessed; data for height and weight should be plotted on a growth chart (auxologic assessment) for all children. (For children 0 to 2 years, see World Health Organization [WHO] Growth Charts; for children 2 years and older, see Centers for Disease Control and Prevention [CDC] Growth Charts.)

Measurement of IGF-1 and IGFBP-3 levels

Begins the assessment of the GH/IGF-1 axis. IGF-1 reflects GH activity, and IGFBP-3 is the major carrier of IGF peptides. Levels of IGF-1 and IGFBP-3 are measured because GH levels are pulsatile, highly variable, and difficult to interpret.

IGF-1 levels vary by age and should be interpreted relative to bone age rather than to chronologic age. IGF-1 levels are lowest in infancy and early childhood (< 5 years) and thus do not reliably discriminate between normal and subnormal in these age groups. However, IGFBP-3 levels, unlike IGF-1, are less affected by undernutrition and allow discrimination between normal and subnormal in younger children. At puberty, IGF-1 levels rise and normal levels help exclude GH deficiency. Low IGF-1 levels in older children suggest GH deficiency; however, IGF-1 levels are low in conditions other than GH deficiency (eg, psychosocial deprivation, undernutrition, celiac disease, hypothyroidism) and these disorders must be excluded.

In children with low levels of IGF-1 and IGFBP-3, GH deficiency is usually confirmed by measuring GH levels. Because basal GH levels are typically low or undetectable (except after the onset of sleep), random GH levels are not useful and assessment of GH levels requires provocative testing. However, provocative testing is nonphysiologic, subject to laboratory error, and poorly reproducible. Also, the definition of a normal response varies by age, sex, and testing center and is based on limited evidence.

Screening laboratory tests

Screening laboratory tests are done to look for other possible causes of poor growth, including

Hypothyroidism (eg, thyroid-stimulating hormone, thyroxine)

Renal disorders (eg, electrolytes, creatinine levels)

Inflammatory and immune conditions (eg, tissue transglutaminase antibodies, C-reactive protein)

Hematologic disorders (eg, complete blood count with differential)

Genetic testing for specific syndromes (eg, Turner syndrome) may be indicated by physical findings or if growth pattern differs significantly from family. If GH deficiency is highly suspected, additional tests of pituitary function are done (eg, ACTH, 8 AM serum cortisol level, LH, FSH, and prolactin levels).

Provocative testing

Because GH responses are typically abnormal in patients with diminished thyroid or adrenal function, provocative testing should be done in these patients only after adequate hormone replacement therapy.

The insulin tolerance test is the best provocative test for stimulating GH release but is rarely done because it is risky. Other provocative tests are less dangerous but also less reliable. These include tests using arginine infusion (500 mg/kg IV given over 30 minutes), clonidine (0.15 mg/m2 orally [maximum 0.25 mg]), levodopa (10 mg/kg orally for children; 500 mg orally for adults), and glucagon (0.03 mg/kg IV [maximum 1 mg]). GH levels are measured at different times after drug administration depending on the drug.

Because no single test is 100% effective in eliciting GH release, two GH provocation tests are done (typically on the same day). GH levels generally peak 30 to 90 minutes after administration of insulin

or the onset of arginine infusion, 30 to 120 minutes after levodopa, 60 to 90 minutes after clonidine, and 120 to 180 minutes after glucagon. The GH response that is considered normal is somewhat arbitrary. Generally, any stimulated GH level > 10 ng/mL (> 10 mcg/L) is sufficient to rule out GH deficiency. GH deficiency may be considered for responses < 10 ng/mL (< 10 mcg/L; some centers use a lower cutoff, eg, 7 ng/mL [7 mcg/L]) to two pharmacologic stimuli, but results must be interpreted in the context of auxologic data. Because GH levels rise during puberty, many children who fail provocative GH stimulation testing before puberty may have normal results after puberty or when primed with gonadal steroids.

Provocative testing may not detect subtle defects in the regulation of GH release. For example, in children with short stature secondary to GH secretory dysfunction, results of provocative testing for GH release are usually normal. However, serial measurements of GH levels over 12 to 24 hours indicate abnormally low 12- or 24-hour integrated GH secretion. However, this test is expensive and uncomfortable and thus is not the test of choice for GH deficiency.

If diminished GH release is confirmed, tests of secretion of other pituitary hormones and (if abnormal) hormones of their target peripheral endocrine glands along with pituitary imaging studies must be done if not done previously.

Imaging

Growth hormone deficiency Imaging.

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Tölli A, Borg J, Bellander BM, Johansson F, Höybye C. Pituitary function within the first year after traumatic brain injury or subarachnoid hemorrhage. J Endocrinol Invest. 2017 Feb;40(2):193-205. doi: 10.1007/s40618-016-0546-1. Epub 2016 Sep 26. PubMed PMID: 27671168; PubMed Central PMCID: PMC5269462.