

Growth Hormone Deficiency

Clinical Background

Growth hormone deficiency is not uncommon in childhood and is usually acquired in adulthood.

Childhood growth hormone deficiency

- Epidemiology
 - Prevalence – not uncommon
 - Age – recognized by slow linear growth <1%
 - Sex – M>F
- Etiology
 - Growth hormone deficiency
 - Inborn errors of the Pit-1 gene
 - Prop-1 mutations
 - Growth hormone releasing hormone (GHRH) gene defects
 - Genetic insensitivity to GH
- Pathophysiology
 - GH is secreted by the anterior pituitary
 - Binding of GH to the transmembrane receptor leads to the production of insulin-like growth factor 1 (IGF-1) and insulin-like growth factor binding protein 3 (IGFBP-3)
 - Secreted in a pulsatile fashion, natural impetus for secretion is sleep (rises at night and sporadically during the day, may be related to meals)
 - GH levels increase in response to hypoglycemia
- Clinical Presentation
 - Short stature (defined as height more than 2 standard deviations below the mean), severe growth failure, delayed bone age
- Treatment
 - FDA indications for GH replacement
 - GH deficiency
 - No GH deficiency but other indications
 - Idiopathic (ISS) short stature – most controversial indication
 - Small for gestational age (SGA) infants
 - 90% SGA infants catch up in growth by age 2 years and do not require GH supplementation
 - Chronic renal insufficiency
 - Causes in children – structural (usually congenital), metabolic (oxalosis, cystinosis), acquired (infection)
 - The younger the age of onset, the greater the stature loss
 - Dialysis/transplant often do not normalize growth
 - Turner syndrome
 - Prader-Willi syndrome

Adult GH deficiency

- Epidemiology
 - Prevalence – uncommon
- Etiology
 - Acquired pituitary damage – surgery, tumor, granulomas, cranial irradiation, trauma, hypophysitis

- Acquired hypothalamic damage
- Usually a sequential loss in anterior pituitary function – loss of GH, follicle stimulating hormone and leuteinizing hormone (FSH and LH) may be followed by loss of thyroid stimulating hormone (TSH) and loss of adrenocorticotrophic hormone (ACTH)
- Pathophysiology
 - Almost always acquired damage to pituitary or rarely hypothalamus
- Clinical Presentation
 - Constitutional – fatigue, low self-esteem
 - Increased body fat, reduced lean mass
 - Reduced exercise capacity
 - Dyslipidemia
 - Complications – coronary artery disease (CAD), hypertension, insulin resistance, osteopenia
- Treatment
 - GH replacement

Diagnosis

Childhood growth hormone deficiency

- Indications for testing – severe short status (>2 standard deviations below mean), severe growth deceleration, history of brain tumor, cranial irradiation, radiologic evidence of abnormality of pituitary
- Diagnosis
 - Must rule out all other causes of short stature
 - Hypothyroidism
 - Chromosomal disorders
 - Prader-Willi syndrome
 - Genetic disorder involving deletion of long arm of chromosome 15
 - Incidence – 1/15,000
 - Infants – hypotonic with poor feeding
 - Age 2 – hyperphagic, short stature
 - Adults – prone to diabetes mellitus type 2 and morbid obesity, hypogonadism
 - Turner syndrome
 - Chromosomal abnormality (XO)
 - Incidence – 1/2000 live births
 - Short stature and infertility
 - Chronic systemic disease
 - Renal failure is most common
 - Malabsorption (celiac disease)
 - Skeletal disorders
 - Idiopathic short stature
- Evaluation for growth hormone (GH) deficiency may be initiated in a child whose height is more than 2 standard deviations below the mean
- Laboratory testing
 - GH levels alone cannot diagnose GH deficiency due to pulsatile nature of GH release
 - GH levels after stimulation (low); 1GF-1 cannot be used as a single test to diagnose GH deficiency
 - Best test is insulin-induced hypoglycemia

- Method – 0.1 units of insulin/kg of body weight and measure GH at 0, 15, 30, 60 and 90 minutes
- Other agents are L dopa, arginine, clonidine and glucagon
 - GHRH plus arginine
- Normal stimulation result is GH >10 ng/mL in children, >5 ng/mL in adults
- IGF-1 measurements – low
- IGFBP-3 – low

Adult GH deficiency

- Indications for testing – evidence of hypothalamic-pituitary disease
- Diagnosis
 - Laboratory testing
 - Diagnosis usually requires 2 positive stimulation tests
 - GH stimulation – insulin-induced hypoglycemia (ITT) or GHRH and arginine stimulation are the best test for adults
 - Arginine stimulation test
 - 0.5 g/kg body weight IV given over 30 minutes with serum GH at 0, 30, 60, 90 minutes; positive test is GH <3 ng/mL and hypoglycemia
 - This test is not as accurate as ITT in adults
 - IGF-1 (normal low), IGFBP-3 (normal to low)
 - Severely low levels of IGF-1 can be used as evidence for GH deficiency
 - 3 or more pituitary hormone deficiencies occur
 - Consider testing other anterior pituitary hormones (LH/FSH, TSH, ACTH)
 - Imaging studies
 - If no obvious etiology of deficiency, then do CT or MRI to rule out tumor

Monitoring

- Linear height velocity usually accelerates with GH replacement
 - May not occur in ISS
- Repeat GH testing – only necessary after puberty to assess if lifelong GH supplementation is necessary

Lab Tests

Indications for Laboratory Testing

Tests generally appear in the order most useful for common clinical situations. For test-specific information, refer to the test number in the ARUP Laboratory Test Directory on the ARUP Web site at www.aruplab.com.

Test Name and Number	Recommended Use	Limitations	Follow Up
Growth Hormone 0070080 Method: Chemiluminescent Immunoassay	Determine level of GH in a timed sample	Low or normal levels do not rule out GH deficiency	

IGF-1 (Insulin-Like Growth Factor I) 0070125 Method: Chemiluminescent Immunoassay	Used in assessment of GH deficiency	Increased in pubertal and pregnant patients Normal value does not rule out GH deficiency	Use in conjunction with IGF Binding Protein-3
IGF Binding Protein-3 0070060 Method: Chemiluminescent Immunoassay	Used in assessment of GH deficiency	Normal value does not rule out GH deficiency	Use in conjunction with Insulin-Like Growth Factor 1
Growth Hormone, 0 Minutes 0070081 Method: Chemiluminescent Immunoassay	Used in GH stimulation testing		
Growth Hormone, 30 Minutes 0070082 Method: Chemiluminescent Immunoassay	Used in GH stimulation testing		
Growth Hormone, 60 Minutes 0070083 Method: Chemiluminescent Immunoassay	Used in GH stimulation testing		
Growth Hormone, 90 Minutes 0070084 Method: Chemiluminescent Immunoassay	Used in GH stimulation testing		

Additional Tests Available

Test Name and Number	Comments
IGF Binding Protein 2 0098842 Method: Radioimmunoassay	
IGF Binding Protein-1 0098843 Method: Radioimmunoassay	

<p>Growth Hormone Antibody 0092142</p> <p>Method: Radiobinding Assay</p>	
<p>Growth Hormone, 15 Minutes 0070048</p> <p>Method: Chemiluminescent Immunoassay</p>	
<p>Growth Hormone, 45 Minutes 0070049</p> <p>Method: Chemiluminescent Immunoassay</p>	
<p>Growth Hormone, 120 Minutes 0070164</p> <p>Method: Chemiluminescent Immunoassay</p>	
<p>Insulin, 30 Minutes 0070064</p> <p>Method: Chemiluminescent Immunoassay</p>	
<p>Insulin, 60 Minutes 0070066</p> <p>Method: Chemiluminescent Immunoassay</p>	
<p>Insulin, 120 Minutes 0070068</p> <p>Method: Chemiluminescent Immunoassay</p>	
<p>Luteinizing Hormone and Follicle Stimulating Hormone 0070193</p> <p>Method: Electrochemiluminescent Immunoassay</p>	
<p>Thyroid Stimulating Hormone 0070145</p> <p>Method: Electrochemiluminescent Immunoassay</p>	
<p>Adrenocorticotrophic Hormone 0070010</p> <p>Method: Chemiluminescent Immunoassay</p>	

Guidelines

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