Growth Disorders
Supporting patients, TOGETHER

Definition, prevalence, and etiology
Selected growth disorders associated with short stature
Partnering with a pediatric endocrinologist
Short stature associated with growth disorders

Suspect a growth disorder if you notice a slowdown in your patient’s growth rate

Variation from normal growth pattern could indicate a pathological condition

Most common pathological causes
- Growth Hormone Deficiency (GHD)
- Hypothyroidism
- Celiac disease
- Turner syndrome (TS)

Other causes
- Renal, hepatic, and gastrointestinal diseases
- Other genetic syndromes

A height >2 SD below the mean for age, or less than the 3rd percentile.
### Selected growth disorders associated with short stature

<table>
<thead>
<tr>
<th>DESCRIPTION</th>
<th>ETIOLOGY</th>
<th>MAJOR CLINICAL SIGNS</th>
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<tbody>
<tr>
<td><strong>Growth Hormone Deficiency (GHD)</strong></td>
<td>Condition may be congenital or acquired. Acquired cause of GHD can be due to a history of head trauma, central nervous system infection, birth trauma, or cranial irradiation.¹</td>
<td>Physical exam may reveal microphallus or midline craniofacial abnormalities. Growth may initially be normal but then fall progressively off the growth curve. Typically, children with this condition have¹:</td>
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<td>• Short stature, which is often the only clinical manifestation of GHD²</td>
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<td>• A delayed bone age with a preserved or increased weight for age¹</td>
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<td><strong>Noonan Syndrome (NS)</strong></td>
<td>May affect between ≈1/1000 and 1/2500 live births.³</td>
<td>Usually birth weight and length are normal³</td>
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<td>• Most often the genetic defect is identified by PTPN11 gene sequencing³</td>
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<td>• KRAS, SHOC2, RAF1, and SOS1 gene sequencing also may help identify the genetic defect associated with a specific case of NS³</td>
<td>• Short stature (&lt;2 SD below mean)</td>
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<td>• Based on the underlying genetic defect, manifestations of NS may vary, but right sided cardiac findings are common³</td>
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<td>• In about 50% to 70% of NS cases, developmental delays, growth failure, and short stature are frequently observed³</td>
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<td>• In up to 10%–15% of children with NS, scoliosis and other spinal abnormalities are present³</td>
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<td><strong>Turner Syndrome (TS)</strong></td>
<td>A chromosomal disorder that affects phenotypic females who have one intact X chromosome and complete or partial absence of the second sex chromosome with one or more clinical manifestations.⁴</td>
<td>Some common abnormalities associated with Turner Syndrome are⁴:</td>
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<td></td>
<td></td>
<td>• Short Stature</td>
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<tr>
<td></td>
<td></td>
<td>• Pterygium colli (webbed neck)</td>
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<td></td>
<td></td>
<td>• Low hairline at the back of the neck</td>
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<td></td>
<td></td>
<td>• Lymphedema</td>
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<td></td>
<td></td>
<td>• Skeletal abnormalities</td>
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<td>• Heart defects</td>
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</table>

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## Small for Gestational Age (SGA)

Children with birth weight and/or length less than 2 SD below the mean for gestational age are classified as born SGA. There are several causes, including fetal, placental, maternal, and environmental factors, but the specific etiology is frequently unknown. In SGA infants where an etiology is identified, about 50% involve maternal factors, 5% involve fetal abnormalities, and less than 5% are felt to be due to placental pathology. SGA can occur alongside intrauterine growth restriction (IUGR) and/or premature birth or be diagnosed at term without any prenatal complications.

Heterogeneous and characterized by broad spectrum of clinical characteristics, including:
- Endocrine and metabolic disturbances
- Potential cognitive impairment
- Low lean mass and potentially increased central adiposity
- Some children born SGA have inadequate catch-up growth in first 2 years

## Idiopathic Short Stature (ISS)

Unknown. However, children with ISS should be considered growth hormone sufficient. They have normal body proportions, no history of a low birth size, no chromosomal abnormalities, no dysmorphic syndromes, and no systemic, endocrine, or nutritional diseases. In absence of pathological causes, children with height >2 SD below the mean can be considered to have ISS.

- Often short stature is the only clinical feature

## Prader-Willi Syndrome (PWS)

Due to lack of expression of paternally inherited genes in the region of chromosome 15q11.2-q13. 70% have a deletion of the paternally inherited region, while 25% have maternal uniparental disomy in which the individual has inherited 2 copies of the critical region on chromosome 15 from the mother. 5% of cases have abnormal imprinting or methylation that silences paternal genes in the PWS region.

The most distinctive characteristics:
- In infancy
  - Poor muscle tone; lethargy; difficulty feeding; poor suck; poor reflexes
- In early childhood
  - Facial features such as a narrow forehead and almond-shaped eyes; puffy hands and fingers; delays in motor and language skills; learning disabilities; behavior problems; increased appetite; obesity; short stature
- In late childhood/adolescence
  - Abnormally increased appetite; lack of satiety after eating; food-seeking behavior; obesity-related complications such as diabetes and sleep apnea
A pediatric endocrinologist can:

- Determine a differential diagnosis
- Tailor treatment if necessary
- Optimize outcomes

If you suspect short stature due to a growth disorder, partnering with a pediatric endocrinologist may help.