Assessment and Management of Growth Issues

Objectives

• Differentiate between normal growth variants and growth variants that are linked to a disorder
• Describe the process of identifying representative growth variants in pediatric patients
• Discuss the management of representative growth variants in pediatric patients

Defining Short and Tall Stature

• Both short stature and tall stature are statistical definitions
• While a child may have “abnormal” stature from a purely statistical point of view, this does not imply that the child’s stature is abnormal in the sense of a pathological condition

| Short stature | Stature >2 SD below mean value for children of that age, sex, and population group | Often described as <3rd percentile for height (actually <2.3rd percentile) |
| Tall stature  | Stature >2 SD above mean value for children of that age, sex, and population group | Often described as >97th percentile for height (actually >97.7th percentile) |

SD = standard deviation(s)
Growth Variants: Short Stature

- Familial Short Stature
  - Not Linked to Disorder
  - Early/Late Puberty
- Constitutional Delay of Growth and Puberty

Growth Variants: Tall Stature

- Constitutional Tall Stature
  - Not Linked to Disorder
- Extra Growth Cases
  - >2 SHOX genes
  - >3.5 IGF1R

Case 1: Carla

- 9 years old
- At birth
  - Length: 49.3 (50th PCTL; 0 SDS)
  - Weight: 3.3 kg (50th PCTL; 0 SDS)
- At presentation
  - Height: >118.5 cm (1st PCTL; -2.5 SDS)
  - Weight: 22.7 kg (5th PCTL; -1.6 SDS)
- Growth velocity normal
- Medical history normal
- Physical examination normal

What questions would you ask?
Case 1: Genetic Target Height

- Carla lives with her biological parents
- Parents' heights were measured
  - Mother: 148.5 cm (<3rd PCTL)
  - Father: 162.6 cm (<3rd PCTL)
- Calculation of genetic target height based on midparental height
  - 13 cm is subtracted from father's height and averaged with mother's height
  - 149.6 cm
  - 149.6 + 148.5 = 298.1 cm
  - 298.1 ÷ 2 = 149.1 cm
- Carla's predicted adult height is 149.1 cm (> -2 SDS)

What is the probable diagnosis?

Case 1: Laboratory and Radiology Results

- Lab values*
  - Hb: 13.2 g/dL (11–16);
  - Hct: 36% (34–40%)
  - IgA: 38 mg/dL (24–120);
  - IgA tTG: undetectable (<7 U/mL)
  - ESR: 5 mm/h (3–13)
  - FT4: 1.1 ng/dL (0.9–1.6);
  - TSH: 2.3 μU/mL (0.5–4.3)
  - IGF-1: 49 ng/mL (28–155);
  - IGFBP-3: 1.7 mg/dL (0.8–3.9)
- Bone age assessment: 9.0 years

Case 1: FSS and Growth

- Most common cause of short stature in US
- Family history of short stature
- Normal birth length and weight
- Current and predicted height >2 SD below mean for age and sex
- Bone age consistent with chronological age
- Normal annual growth rate
- Normal timing of onset of puberty
- No other cause of short stature
Case 1: Resolution

• Continue to observe Carla’s growth patterns and pubertal development over time
• Reassure Carla and her parents
  – She is healthy and growing normally
  – Growth is consistent with the familial pattern
  – No further testing is necessary
  – Treatment is not desirable
• Carla likely to have short stature as an adult


Case 2: Kyle

• 14 years old
• At birth
  – Length: 49.5 cm (50th PCTL)
  – Weight: 3.1 kg (50th PCTL)
• At presentation
  – Height: 152.5 cm (3rd PCTL; -3.5 SDS)
  – Weight: 30.2 kg (3rd PCTL; -2.8 SDS)
• Mother: 163.3 cm; father: 176.9 cm (both 50th PCTL); father was “late bloomer”
• Genetic target height based on midparental height: 176.6 cm (50th PCTL)
• Normal health history, above-average student
• Increasingly distressed about his short stature and youthful appearance


Case 2: Physical Examination

• Short, thin boy
• Little muscle mass
• Appeared younger than his chronological age
• Erupting 12-year molars
• Tanner Stage II
  – Thinned, reddened scrotum with 4-mL testes
  – No pubic hair
• No abnormalities detected

What do these findings suggest?
Case 2: Laboratory and Radiology Results

- **Lab values**
  - Hb: 14.6 g/dL (11–16); Hct: 39% (34–40%)
  - IgA: 51 mg/dL (24–120); IgA tTG: undetectable (<7 U/mL)
  - ESR: 6 mm/h (3–13)
  - FT4: 1.2 ng/dL (0.9–1.6); TSH: 2.9 μU/mL (0.5–4.3)
  - IGF-1: 44 ng/mL (28–155); IGFBP-3: 2.3 mg/dL (0.8–3.9)

- **Bone age assessment: 12.5 years**

*Reference ranges are shown in parentheses. Green type = finding of particular significance.

[Green type = finding of particular significance.]

Constitutional Delay of Growth and Puberty

- Normal growth variant
- Usually at least 1 parent had a similar pattern of growth and delayed puberty
- Normal length and weight at birth
- Slow growth during first 2–3 years of life, followed by normal growth rate during prepubertal years
- Delayed pubertal growth spurt, resulting in increased shortness relative to contemporaries during early teenage years
- Sexual development normal but delayed
- Delayed bone age
- Genetic target height is usually attained

Management of CDGP

- Can be managed with expectant observation or sex steroid hormone therapy
- Main objective of drug treatment is to reduce psychosocial difficulties; does not increase adult height
- Drug therapy options
  - Low-dose testosterone (boys)
  - Low-dose estrogen (girls)
- Usual treatment criteria
  - ≥14 years old
  - Height below 3rd PCTL
  - Tanner Stage I or II
  - Predicted adult height in normal range

Case 2: Resolution

• Kyle receives depot injection of testosterone enanthate
  – Dose is 100 mg every 4 weeks
  – Total of 4 injections
• Sexual development
  – Pubic hair present by 4th injection
  – Early Tanner Stage IV one year after starting treatment
• Growth by age 15.0 years
  – Height: 147.5 cm (<1st PCTL; –2.7 SDS)
  – Weight: 38.3 kg (<1st PCTL; –2.4 SDS)

Case 3: Olivia

• 8 years old
• At birth
  – Length: 50.4 cm (75th PCTL)
  – Weight: 3.6 kg (75th PCTL)
• At presentation
  – Height: 145.1 cm (99th PCTL)
  – Weight: 34.2 kg (75th PCTL)
• Mother: 180.3 cm; father: 188.0 cm
• Genetic target height based on midparental height: 177.7 cm (99th PCTL; >2 SDS)
• Normal health history
• Good student

What questions would you ask?


Case 3: Physical Exam and Test Results

• Physical exam
  – Tall and thin
  – Long arms and legs
  – Tanner Stage I
• Lab values*
  – Hb: 13.8 g/dL (11–16); Hct: 38% (34–40%)
  – IgA: 51 mg/dL (24–120); IgA TTG: undetectable (<7 U/mL)
  – ESR: 4 mm/h (1–15)
  – FT4: 1.4 ng/dL (0.9–1.6); TSH: 2.6 μU/mL (0.5–4.3)
  – IGF-1: 123 ng/mL (28–155); IGFBP-3: 3.4 mg/dL (0.8–3.9)
• Bone age assessment: 8.2 years

What is the probable diagnosis?

*Reference ranges are shown in parentheses.
Green type = finding of particular interest.
Constitutional Tall Stature

- Normal weight and length at birth
- Growth velocity abnormally increased during first 4 years of life
- Normal growth rates by 4 or 5 years of age
- Body proportions generally normal, but arms and legs may be somewhat long
- Normal or slightly advanced skeletal maturation
- Normal timing of puberty
- IGF-1 and IGFBP-3 levels often high normal
- Treatment of CTS is now uncommon
- Polymorphisms in genes associated with tall stature: GH-1, IGF-1, IGFBP-3, or HMG-A2

Case 3: Resolution

- Continue to observe Olivia’s growth patterns over time
- Reassure Olivia and her parents
  - She is healthy and growing normally
  - Growth is consistent with the familial pattern
  - Further testing would be unproductive
  - Treatment is not desirable
- Olivia is likely to have tall stature as an adult

Check Point 1

The accurate statement is: __________.

a. children with familial short stature (FSS) usually have decreased growth velocity
b. bone age is generally delayed in children with FSS and constitutional delay of growth and puberty (CDGP)
c. short-term testosterone therapy usually increases the adult height of boys with CDGP
d. many children with constitutional tall stature (CTS) have abnormally increased growth velocity during the first 4 years of life
Answer to Check Point 1

The correct answer is d.

a. Children with familial short stature (FSS) usually have decreased growth velocity.

b. Bone age is generally delayed in children with FSS and constitutional delay of growth and puberty (CDGP).

c. Short-term testosterone therapy usually increases the adult height of boys with CDGP.

d. Many children with constitutional tall stature (CTS) have abnormally increased growth velocity during the first 4 years of life.

Case 4: Robert

- 4 years old
- Born at 38 weeks gestation
- Pregnancy complicated by placental insufficiency
- At birth:
  - Length: 45.1 cm (1st PCTL; > –2 SDS)
  - Weight: 2.3 kg (1st PCTL; > –2 SDS)
- At presentation:
  - Height: 89.1 cm (1st PCTL; > –3.2 SDS)
  - Weight: 12.5 kg (1st PCTL; > –2.5 SDS)
  - Head circumference between 3rd and 10th PCTL from birth to 36 months
- Mild developmental delay, easily distracted

*Genetic target height based on midparental height = 182 cm (75th PCTL).

What is the probable diagnosis?

Case 4: Physical Exam and Lab Values

- Physical exam:
  - Short and thin
  - Slightly protuberant abdomen
  - Tanner Stage I
  - Limited verbal ability

- Lab values:
  - Hb: 12.5 g/dL (11–16); Hct: 37% (34–40%)
  - IgG: 46 mg/dL (24–120); IgA TTG: undetectable (<7 U/mL)
  - ESR: 5 mm/h (1–15)
  - FT4: 1.2 ng/dL (0.9–1.6); TSH: 2.4 μU/mL (0.5–4.3)
  - IGF-1: 38 ng/mL (28–155); IGFBP3: 1.5 mg/dL (0.8–3.9)
- Bone age assessment: not performed

What do these findings suggest?
SGA and Growth

- Weight and/or length < -2 SD
- May/may not have history of IUGR
- Increased risk for perinatal morbidity
- Often have period of accelerated linear growth during first 12 months
- ~90% have stature above -2 SD by age 2 y
- Typical adult height is -1 SD below mean
- Children of tall parents may reach normal adult height
- Pubertal timing usually within normal limits

Case 4: Growth Hormone Therapy

- rhGH indicated for treatment of growth failure in children born SGA who fail to manifest catch-up growth by 2 years of age
- GH testing is not required
- Recommended dose ≤0.48 mg/kg/wk
- Continuous treatment recommended until growth rate falls to <2 cm/y during adolescence
- Most treated individuals achieve height in normal range

Case 4: Resolution

- At 5 years of age
  - Height: 102.1 cm (7th PCTL; -1.5 SDS)
  - Weight: 15.5 kg (7th PCTL; -1.4 SDS)
- If height gain is maintained, will be in normal range as adult
- Some improvement noted in school performance
Case 5: Ethan

• 12 years old
• At birth
  - Length: 50.3 cm (50th PCTL)
  - Weight: 3.5 kg (50th PCTL)
• At presentation
  - Height: 140.1 cm (10th PCTL; –1.2 SDS)
  - Weight: 29.0 kg (2nd PCTL; –2.0 SDS)
• Genetic target height based on midparental height = 176.5 cm (50th PCTL)
• Medical history normal
• Normal systems review except for occasional constipation and fatigue

What questions would you ask?

Case 5: Physical Examination

• Short, thin child
• Pale skin
• Slightly enlarged liver
• Tanner Stage I

What do these findings suggest?

Case 5: Lab Values and Biopsy

• Lab values*
  - IgA: 56 mg/dL (24–120); IgA tTG: 12 U/mL (<7 U/mL)
  - Hb: 9.5 g/dL (11–16); Hct: 29% (34–40%)
  - ESR: 6 mm/h (3–13)
  - FT4: 1.3 ng/dL (0.9–1.6); TSH: 2.8 μU/mL (0.5–4.3)
  - IGF-1: 61 ng/mL (28–155); IGFBP3: 1.7 mg/dL (0.8–3.9)
• Small bowel biopsy confirms CD

*Reference ranges are shown in parentheses. Red type = abnormal value.
CD = celiac disease.

*Reference ranges are shown in parentheses. Red type = abnormal value.
Celiac Disease and Growth

- Chronic autoimmune disorder caused by permanent sensitivity to gluten
- Atrophy of villi lining small intestine causes malabsorption
- Affects 1 in every 80 to 300 US children
- Age at presentation and range of signs/symptoms highly variable
- Poor weight gain followed by slow growth may be first signs
  - Up to 8.3% of children with short stature and no GI symptoms have CD
- Delayed puberty may occur

Case 5: Resolution

- Ethan referred to pediatric gastroenterologist and registered dietitian
- After 3 months of GFD
  - Serologic conversion
  - Anemia resolved
  - Histologic improvement
- After 6 months
  - Marked increases in linear growth and weight
  - Progression to Tanner Stage II

GI Disorders and Growth

- Disorders often linked to growth failure
  - CD
  - Inflammatory bowel disorder
    - Crohn disease (growth failure especially common)
    - Ulcerative colitis
  - Insulin-treated diabetes mellitus (with suboptimal control)
- Generally characterized by drop-off in weight percentile before decrease in height percentile
- Growth failure may be first symptom
- Comorbidities may exacerbate growth failure
Some Other Systemic Disorders That Impair Growth

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Mechanisms of Growth Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cystic fibrosis</td>
<td>Pancreatic dysfunction, hypoxia, malabsorption, inadequate nutritional intake, frequent infections, corticosteroids, comorbid diabetes</td>
</tr>
<tr>
<td>Cystic heart disease</td>
<td>Hypoxia, inadequate nutritional intake to meet increased energy demands of failing heart</td>
</tr>
<tr>
<td>Chronic anemia (eg, sickle cell disease)</td>
<td>Hypoxia, increased work by CV system, nutritional intake inadequate to meet demands of increased hematopoiesis</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>Decreased caloric intake, electrolyte loss, metabolic acidosis, protein wasting, insulin resistance, chronic anemia, compromised cardiac function</td>
</tr>
<tr>
<td>Systemic juvenile inflammatory arthritis</td>
<td>Chronic inflammation, corticosteroids</td>
</tr>
</tbody>
</table>

Case 6: Emma

- 14 years old
- At birth
  - Length: 48.2 kg (50th PCTL)
  - Weight: 3.1 kg (50th PCTL)
- At presentation
  - Height: 150.0 cm (10th PCTL; -1.7 SDS)
  - Weight: 33.0 kg (1st PCTL; -2.6 SDS)
- At 50th percentile for weight until age 10 and for height until age 12
- Tanner Stage II (not consistent with family history)
- Genetic target height based on midparental height = 163.5 cm (50th PCTL)
- Medical history normal
- “High achiever”

What questions would you ask?

Case 6: Physical Exam and Lab Values

- Physical exam
  - Short and very thin
  - Tanner Stage II
  - Pale skin
  - Thin, somewhat brittle hair
- Lab values*
  - Hb: 6.5 g/dL (11–16); Hct: 22% (34–40%)
  - IgA: 48 mg/dL (24–120); IgA TTG: undetectable (<7 U/mL)
  - ESR: 6 mm/h (3–13)
  - FT4: 1.1 ng/dL (0.8–1.6); TSH: 2.8 μU/mL (0.5–4.3)
  - IGF-1: 41 ng/mL (28–155); IGFBP3: 1.8 mg/dL (0.8–3.9)
- Bone age assessment: 12 years, 6 months

What do these findings suggest?

*Normal ranges shown in parentheses. Red type = abnormal finding.
Case 6: Nutritional Evaluation

- Typical dietary intake on school day
  - Breakfast: 1 cup oatmeal
  - No lunch (bag lunch from home discarded)
  - Dinner: salad dressed with vinegar
- No induced vomiting or laxative abuse
- No compulsive exercising
- Normal body image
- Excessive fear of becoming obese

Nutritional Growth Retardation

- Caused by voluntary undernutrition (less severe than eating disorder)
- Usually seen in adolescents with fear of obesity
- Patients have delayed linear growth ± puberty or menarche secondary to inadequate weight gain
- Catch-up growth usually begins 1–3 months after start of nutritional therapy
- If epiphyses fuse before corrective action is taken, patient is likely to have permanent height deficit
- Sexual maturation resumes soon after initiation of nutritional therapy

Case 6: Resolution

- Brief course of counseling
- Consultation with registered dietitian
- After beginning nutritional therapy
  - Weight returned to 50th PCTL within 3 months
  - Catch-up linear growth began within 6 weeks
    - First menstrual period at 14 years, 8 months
- Emma is likely to attain genetic target height
Check Point 2

The accurate statement is:

a. children born small for gestational age (SGA) usually have delayed puberty
b. about 90% of children born SGA have stature above –2 SD by the time they are 2 years old
c. in patients with an underlying gastrointestinal disorder, linear growth velocity is usually impacted before weight
d. as long as they adhere to their nutritional therapy regimen, patients with nutritional growth retardation will reach their genetic target height

Answer to Check Point 2

The correct answer is b.

a. children born small for gestational age (SGA) usually have delayed puberty
b. about 90% of children born SGA have stature above –2 SD by the time they are 2 years old
c. in patients with an underlying gastrointestinal disorder, linear growth velocity is usually impacted before weight
d. as long as they adhere to their nutritional therapy regimen, patients with nutritional growth retardation will reach their genetic target height

Case 7: Mia

• 3 years old
• At birth
  – Length: 46.7 cm (10th PCTL)
  – Weight: 2.7 kg (10th PCTL)
• 3 otitis media episodes during first year
• Parents at 75th PCTL for height
• Genetic target height based on midparental height: 167.6 cm (75th PCTL)

What questions would you ask?
Case 7: WHO and CDC Growth Charts

Case 7: Physical Examination

- Short, thin child
- Alert, good verbal skills
- Ears somewhat low-set, with slight posterior rotation
- Atrophic scarring of right tympanum
- Mild conductive hearing loss in right ear
- Other findings normal

What diagnostic tests should be ordered?

Case 7: Diagnostic Tests

- **Karyotype:** 45, X
- **Lab values***
  - Hb: 13.5 g/dL (11–16); Hct: 38% (34–40%)
  - IgA: 51 mg/dL (24–120); IgA tTG: undetectable (<7 U/mL)
  - ESR: 6 mm/h (3–13)
  - FT4: 1.1 ng/dL (0.9–1.6); TSH: 2.8 μU/mL (0.5–4.3)
  - IGF-1: 30 ng/mL (28–155); IGFBP3: 1.1 mg/dL (0.8–3.9)

*Reference ranges shown in parentheses. Green type = finding of special interest. Red type = abnormality.
**Features of Turner Syndrome**

- Short stature
- Multiple nevi
- Low posterior hairline
- Increased carrying angle
- Webbed neck
- Broad chest ("shield chest")
- Widely spaced nipples
- Small lower jaw
- Low-set ears with posterior rotation; OM history
- Cardiac abnormalities
  - Aortic coarctation
  - Left-sided defects
- Renal abnormalities
  - Horseshoe kidney
  - Duplicated collecting system
- Ovarian insufficiency

*Except for short stature, some/all features may not be present.

OM = otitis media.


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**Screening Recommendations at Diagnosis of TS**

- All patients
  - Cardiovascular evaluation by specialist
  - Renal ultrasound
  - Hearing evaluation by audiologist
  - Evaluation for scoliosis/kyphosis
  - Evaluation for knowledge of TS; referral to support groups
  - Evaluation for growth and pubertal development
- Ages 0–4
  - Evaluation for hip dislocation
  - Eye exam by pediatric ophthalmologist (if age ≥ 1 y)


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**Case 7: TS Growth Chart**

- At 84.0 cm, Mia’s height is
  - Below the 3rd percentile on the CDC growth chart
  - At the 50th percentile on the TS-specific growth chart


Growth Hormone Therapy in TS

- Effective as early as 9 months of age
- Start treatment as soon as growth failure is apparent
- Early initiation of treatment allows for
  - Normalizing childhood growth
  - Beginning estrogen replacement at physiologically appropriate age
- Often increases adult height by ~10 cm
- Taller adult stature predicted by
  - Relatively young age and tall height at start of therapy
  - Tall parental heights
  - Long duration of therapy
  - GH given at maximum recommended dose (varies with product)

Estrogen Replacement Therapy in TS

- >90% of girls with TS require ERT
- Single determination of plasma FSH and LH is usually sufficient to document need for ERT
- Start at appropriate age for onset of puberty (~12 y)
- Begin with low doses to avoid bone age acceleration
- Transdermal delivery is preferred
- ERT usually continues until time of normal menopause

Case 7: Resolution

- Mia's growth velocity after beginning GH therapy
  - 12.5 cm during first year
  - 9.1 cm during second year
- Consistent with findings of Toddler Turner Study
- Growth velocity suggests that Mia's adult height may be in normal range
Case 8: Jacob

- 30 months old
- At birth
  - Length: 50.1 cm (50th PCTL)
  - Weight: 3.5 kg (50th PCTL)
- At presentation
  - Height: 82.0 cm (1st PCTL)
  - Weight: 13.5 kg (25th PCTL)
  - BMI: 20.1 kg/m² (99th PCTL, obese)
- Parents and 2 older brothers at 50th PCTL for height
- Genetic target height based on midparental height, 176.9 cm (50th PCTL)

Case 8: WHO and CDC Growth Charts

What would you be alert for during the physical exam?

Case 8: Physical Examination

- Short, obese child
- Moderately hypotonic
- Poor muscle development
- Fair hair and skin
- Small penis
- Irritable and uncooperative
- Speech difficult to understand

What diagnostic tests should be ordered?
Case 8: Diagnostic Tests

- Molecular testing
  - DNA methylation analysis: results abnormal
  - FISH: PWS due to paternal deletion of 15q11-13

- Lab values*
  - Hb: 14.5 g/dL (11–16);
    Hct: 39% (34–40%)
  - IgA: 32 mg/dL (24–120);
    IgA tTG: undetectable (<7 U/mL)
  - ESR: 4 mm/h (3–13)
  - FT4: 0.8 ng/dL (0.9–1.6);
    TSH: 0.4 μU/mL (0.5–4.3)
  - IGF-1: 18 ng/mL (28–155);
    IGFBP3: 0.6 mg/dL (0.8–3.9)

*Reference ranges shown in parentheses. Red type = abnormality.
FISH = fluorescence in situ hybridization; PWS = Prader-Willi syndrome.

Features of PWS

- Severe neonatal hypotonia
- Poor suck in infancy
- Small penis, cryptorchidism
- Small hands and feet
- Scoliosis
- Head/facial abnormalities
- Hyopigmentation
- Poor gross and fine motor coordination
- Mild–moderate mental retardation
- Speech-articulation problems
- Behavior issues
- Mild prenatal growth retardation or normal size at birth
- Feeding problems with/without FTT (<0–6 months)
- Steady growth along growth curve at normal rate (~6–18 months)
- Body weight steadily increases, linear growth falls off (~18–36 months)
- Aggressive food seeking, low linear growth velocity (>3 years)

GH Therapy for PWS

- Benefits
  - Increased linear growth
  - Greater lean mass, improved lean-to-fat ratio
  - Improved pulmonary function
  - Improved lipid parameters
  - Increased motor strength
- Initiate treatment (0.24 mg/kg/wk) as soon as growth failure is detected (~2 years of age); monitor using IGF-1 levels
- Contraindicated in patients who are severely obese, have a history of upper airway obstruction or sleep apnea, or have severe respiratory impairment

*Reference ranges shown in parentheses. Red type = abnormality.
PWS = Prader-Willi syndrome; PWSD = Prader-Willi syndrome due to deletion.
Case 8: Resolution

- Linear growth after starting GH therapy
  - 9 cm in year 1
  - 7.5 cm in year 2
- At 4 yr, 6 mo of age
  - Height: 98.5 cm (2nd percentile)
  - Weight: 15.0 kg (25th percentile)
  - BMI: 15.5 kg/m^2 (48th percentile, normal)
- With ongoing treatment for hypothyroidism and GH therapy, final adult height likely to be normal

Some Other Genetic Disorders Associated With Short Stature

<table>
<thead>
<tr>
<th>Category</th>
<th>Syndrome</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Numeric chromosomal abnormalities</td>
<td>SHOX</td>
<td>Heterogeneous; increased BMI; muscular hypertrophy; short limbs compared to trunk; bowed forearms and lower legs</td>
</tr>
<tr>
<td></td>
<td>Down</td>
<td>Height deficit of ~20 cm; mild GH insufficiency in ~50% of children; hypothyroidism and CD may exacerbate short stature</td>
</tr>
<tr>
<td>Clinically defined syndromes with no known chromosomal abnormality</td>
<td>Noonan</td>
<td>Abnormalities of head and neck, possible heart defects; height deficit of ~15 cm; pubertal growth delay, especially in boys with hypogonadism</td>
</tr>
<tr>
<td></td>
<td>Russell-Silver</td>
<td>Poor fetal growth; feeding difficulties during infancy; short stature persists throughout childhood; adult height often ~3 to ~4 SDS because puberty occurs at age but not height-appropriate time</td>
</tr>
</tbody>
</table>

Check Point 3

The accurate statement is: ________.

a. A karyotype analysis should be ordered for all girls at the 5th percentile or less for height unless their parents and other family members are very short
b. When started early, growth hormone (GH) treatment usually increases the adult height of girls with Turner syndrome by about 20 cm
c. Molecular testing for Prader-Willi syndrome (PWS) should begin with a fluorescence in situ hybridization (FISH) assay
d. A case-control study showed that even when GH therapy is begun at an early age, few children with PWS attain a normal adult height
Answer to Check Point 3

The correct answer is a.

a. A karyotype analysis should be ordered for all girls at the 5th percentile or less for height unless their parents and other family members are very short.

b. When started early, growth hormone (GH) treatment usually increases the adult height of girls with Turner syndrome by about 20 cm.

c. Molecular testing for Prader-Willi syndrome (PWS) should begin with a fluorescence in situ hybridization (FISH) assay.

d. A case-control study showed that even when GH therapy is begun at an early age, few children with PWS attain a normal adult height.

Summary (1)

- FSS and CDGP, the most common growth variants associated with short stature, as well as CTS, the most prevalent growth variant associated with tall stature, are normal growth variants that are not linked to a disorder.
- The process of identifying growth variants in pediatric patients begins with the accurate measurement of height (or length), as well as a thorough health history and physical examination and an appropriate battery of laboratory tests.

Summary (2)

- Depending on patient characteristics, the process of identifying the growth variant associated with short or tall stature may also involve a bone age assessment, a karyotype, and other specialized tests.
- Based on the nature of the variant and patient characteristics, the management of growth variants may involve expectant observation, medical nutrition therapy, treatment of an underlying disorder, administration of sex steroids, and/or treatment with rhGH.
Photo Credits

• Slide 42: Courtesy of Turner Syndrome Society of the United States
• Slide 52: Courtesy of Prader-Willi Syndrome Association (USA)