Different From My Friends
Delayed Puberty

Materials for Learners

Packet should include the following:

- Handout #1: Sequence of Events in Puberty
- Handout #2: Tanner Stages of Secondary Sexual Characteristics (Female)
- Clinical Pearls
- Knowledge questions and answers
- References
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Handout/Figure #1: Sequence of Events in Puberty

The sequence of events at puberty in British females.

(With permission from S.J. Emans and M.R. Laufer, Emans, Laufer, Goldstein’s Pediatric and Adolescent Gynecology, 6th ed. Lippincott, Williams & Wilkins; Wolters Kluwer, 2012)
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Handout #2: Tanner Stages of Secondary Sexual Characteristics (Female)
TANNER STAGES

**Female pubic hair development.** *Tanner stage 1:* Prepubertal, with no pubic hair. *Tanner stage 2:* Sparse growth of long, straight hair extending along the labia. *Tanner stage 3:* Pubic hair has increased in quantity, is darker, and is present in the typical female triangle, but in smaller quantity. *Tanner stage 4:* Pubic hair is more dense, curled, and adult in distribution, but is less abundant. *Tanner stage 5:* Abundant, adult-type pattern; hair may extend on to the medial aspect of the thighs.

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Handout #2 continued: Tanner Stages of Secondary Sexual Characteristics (Female)

Female breast development. **Tanner stage 1**: Prepubertal, with elevation of papilla only. **Tanner stage 2**: Breast buds appear. Areola is slightly widened and projects as a small mound. **Tanner stage 3**: Enlargement of the entire breast with no protrusion of the papilla or of secondary mound. **Tanner stage 4**: Enlargement of the areola and papilla as a secondary mound. **Tanner stage 5**: Adult configuration of the breast with protrusion of the nipple. Areola no longer projects separately from remainder of breast.

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Clinical Pearls:

- A girl who had not experienced breast development by age 13 years or has had arrest of pubertal development has pubertal delay.
- The differential diagnosis of delayed puberty includes central causes (nutritional deficiency, hypopituitarism, tumors, and chronic disease such as inflammatory bowel disease or celiac disease), thyroid disorders (hypothyroidism), adrenal disorders, and POI. Constitutional delay is a diagnosis of exclusion.
- Pubertal arrest in a girl who is underweight for height or has lost weight should prompt an evaluation for systemic disease associated with undernutrition including IBD, malabsorption (i.e. celiac), anorexia nervosa or other chronic disease.
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Knowledge questions:

1. Which of the following statements is the most correct?
   a. The growth spurt occurs during late adolescence in a girl, typically before Tanner breast stage 4-5
   b. The onset of puberty is more closely related to an individual’s bone age than chronologic age.
   c. Menarche usually occurs about 3-4 years after the onset of breast development
   d. Menarche usually precedes the upslope of the height velocity curve

2. A 14 year old female presents with Tanner 2 breast and Tanner 2 pubic hair development. She notes that she began breast development 2-3 years prior. Her height and weight had previously tracked along the 25% curve but over the last several years, height has fallen to below the 3rd percentile and weight has increased to the 40%. Based on the information provided so far, which of the following is least likely on the list of possible etiologies?
   a. Acquired hypothyroidism
   b. Cushing’s syndrome
   c. Inflammatory bowel disease
   d. Growth hormone deficiency

3. In which of the following adolescents presenting with delayed puberty would you be suspicious of finding an elevated FSH level?
   a. 16 year old female with a history of malignancy treated with chemotherapy
   b. 14 year old female with strong family history of intellectual disability
   c. 13 year old female with short stature (148 cm), overweight for height, and history of hearing impairment.
   d. all of the above

4. A 14 year old female is referred for evaluation of delayed puberty. She has always been “small” compared with classmates. The family has just moved to the area and they do not have growth charts. She has no past medical history. Mom had menarche at age 13. Comprehensive 10 point ROS is negative. She does well in school and does not engage in regular exercise. No history of sexual activity. On examination, her height is 61 inches and weight is 96 pounds. She is Tanner 1 for both pubic hair and breast development but otherwise has a normal examination with no dysmorphic features. The most appropriate test to include in the initial workup is:
   a. Karyotype
   b. FSH
   c. DXA scan
   d. Cranial MRI
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Answers to Knowledge Questions

1. Which of the following statements is the most correct?

Preferred response: b “The onset of puberty is more closely related to an individual’s bone age than chronologic age.”

Because bone age is more closely related to onset of puberty than chronological age, a bone age assessment can be helpful in determining the cause and extent of delayed puberty.

The growth spurt occurs during early adolescence in a girl, typically occurring between Tanner breast stage 2 and 3 with peak height velocity at 11.5 years. Menarche occurs at a mean age of 12.7 years, about 2-2.5 years after the onset of breast development. Menarche usually occurs on a downslope of the height velocity curve.

2. A 14 year old female presents with Tanner 2 breast and Tanner 2 pubic hair development. She notes that she began breast development 2-3 years prior. Her height and weight had previously tracked along the 25% curve but over the last several years, height has fallen to below the 3rd percentile and weight has increased to the 40%. Based on the information provided so far, which of the following is least likely on the list of possible etiologies?

Preferred response: c “Inflammatory bowel disease”

In this patient, there has been recent fall-off in her height curve, while weight curve has moved up to the 40% percentile (from the 25%). Growth charts that show a fall off in height but not weight, or patients who are overweight for height, suggest potential endocrinopathies. Acquired hypothyroidism, cortisol excess (iatrogenic or cushing’s syndrome), and growth hormone deficiency are all examples of conditions with which patients would present with similar growth curves and delayed puberty. In contrast, weight is typically more affected in height in inflammatory bowel disease with afflicted patients often underweight for their height.

3. In which of the following adolescents presenting with delayed puberty, would you be suspicious of finding an elevated FSH level?

Preferred response: d “All of the above”

Persistently elevated FSH levels are consistent with primary ovarian insufficiency (POI). An adolescent with a history of delayed puberty and a history of malignancy treated with chemotherapy (particularly alkylating agents) and/or radiation to the pelvis or abdomen is at risk for POI. Fragile X premutation carriers are also associated with POI; a strong family history of mental retardation, developmental delay, or autism should raise concern for Fragile X. Finally, short stature, characteristic physical stigmata (webbed neck, low hairline, lymphedema, broad chest, etc) and other problems (including cardiac anomalies, renal anomalies, hypertension, thyroid dysfunction, and hearing impairment) have been found to be associated with Turner syndrome (45,X). Adolescents with Turner syndrome
have a normal uterus and vagina but no ovarian function secondary to bilateral streak gonads.

4. A 14 year old female is referred for evaluation of delayed puberty. She has always been “small” compared with classmates. The family has just moved to the area and they do not have growth charts. She has no past medical history. Mom had menarche at age 13. Comprehensive 10 point ROS is negative. She does well in school and does not engage in regular exercise. No history of sexual activity. On examination, her height is 61 inches and weight is 96 pounds. She is Tanner 1 for both pubic hair and breast development but otherwise has a normal examination with no dysmorphic features. The most appropriate test to include in the initial workup is:

Preferred response: b “FSH”
An FSH level will help determine if etiology is hypothalamic-pituitary (low or normal FSH) or secondary to ovarian insufficiency (high FSH). Unless a high FSH level is expected (prior radiation or chemotherapy), a single elevated FSH level should be repeated 2-4 weeks later for confirmation.

A karyotype would be helpful to determine etiology of ovarian insufficiency if FSH level is high or the adolescent is suspected to have Turner Syndrome (significant short stature or other physical stigmata). Similarly other testing for Fragile X premutation carrier and anti-mullerian hormone for ovarian reserve is indicated if FSH level is elevated.

Although girls with delayed puberty and low weight may not acquire normal bone mass and DXA scan should be considered in a patient with delayed puberty or long-standing amenorrhea, it is usually not a typical part of baseline evaluation. In adolescents with low to normal FSH levels and delayed puberty with suspicion of hypothalamic or pituitary tumor (e.g. elevated prolactin level, neurologic symptoms, unexplained poor growth), evaluation should include cranial MRI during as part of second line testing.
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References