Facilitator Preparation: Facilitators should thoroughly review this module. They should also prepare or photocopy handouts to distribute during the course of the case presentation and the "Materials for Learners" packet.

Open the Discussion: Introduce the case title and the objectives of the session. Explain that this will be an interactive case discussion prompted by a series of multiple choice questions and not a lecture. Distribute Part I of the case and ask one or more of the participants to read it aloud.

A 13 year old Female with Poor Growth
Delayed Puberty

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Objectives:
- o Define normal puberty and the stages of pubertal development in girls.
- o Describe the differential diagnosis for pubertal delay.
- o Initiate the evaluation of an adolescent with pubertal delay.

Part 1
Introduction:

A 13-and-a-half-year old female, Sarah, comes to your office for her annual physical examination. She has been in good health with no chronic medical problems and no acute illnesses.

Sarah has no concerns today but is accompanied by her mother who is worried that her daughter has not grown very much in the past year, and thinks her height and weight are the same as last year. Sarah reports that she thinks she's the only girl in her class who hasn't gotten her period.

Following this reading, ask all participants "*So what do you think about this case? What would you like to focus on during our discussion today*?" List agenda items on a blackboard or flipchart. Then use the questions below to guide the discussion. Remember that the key to successfully leading a small group is facilitation of the discussion rather than lecture. Draw as many participants as possible into the

discussion. Allow silences while group members think about questions. Present material from the discussion guide only when needed to complement or redirect the group discussion.

Potential Discussion Questions:

What additional information would you like to know?
- Growth chart: Are the patient's concerns regarding growth and development accurate? A *growth chart* needs to be constructed with as many data points as are available (to determine if growth ceased at a specific point or if she has remained consistently on a single, delayed curve).
- Is Sarah on any medications that might affect her metabolism and her growth?
- Is there a history of head trauma or a surgery that might have affected the hypothalamic-pituitary area, and growth hormone (GH)-secreting neurons?
- Is she having headaches, visual changes, vomiting, neurologic symptoms, or other signs of a central process? Does she have a history of chronic disease, abdominal pain, or diarrhea?
- Are there other stressors (family, school) that might be affecting weight and nutritional intake? Does she participate in competitive athletics or hyperexercise?
- Relevant family history: History of short stature, history of miscarriages, age of pubertal onset in each parent, pubertal delay in other family members?
- Mid-parental height (MPH): The heights of both parents should be determined in order to calculate MPH (father's height - 5 inches, averaged with mother's height for a girl) to see how closely she is following her genetic potential.
- Age at which patient began pubertal development (if any) and rate of development.
- Physical exam findings to assess for stigmata of chronic disease (e.g. Turner's syndrome) or signs of a central process (e.g. papilledema).

What is considered normal growth?
- Normal growth velocity is 5-6 cm/year up until puberty.
- There is a peak in height velocity (and weight gain) during puberty; females average 9 cm/year during PHV.
- Adolescents should be evaluated if:
    - there is a linear growth rate of less than 4 cm/year
    - there is no peak in linear growth by age 14 in girls.
- Short stature is defined as a target height that is two standard deviations below the mean height for age and sex (<3%).

What physiologic changes happen during puberty?
Puberty results from activation of the hypothalamic-pituitary-ovarian axis
- Pulses of GnRH from the hypothalamus stimulate pulsatile gonadotropin (LH & FSH) release from the pituitary gland;
    - LH stimulates ovarian theca cells to synthesize androgen precursors;
    - FSH increases aromatase enzyme which converts precursors to E2 (estradiol).

- E2 from ovary accounts for most of the circulating estrogen, although there is a small amount of extra-ovarian conversion from androstenedione and testosterone.
- Estrogen stimulates breast growth and maturation of vaginal mucosa, and increase in growth hormone and IGF-1, all of which contribute to growth spurt.

What is the normal sequence of puberty in a female patient?
Ask learners to refer to Figure 1: Sequence of Puberty in their packet.
- Breast development (thelarche) usually begins first before pubic hair development
    o Stimulated predominantly by ovarian estrogen secretion.
- Pubic hair (pubarche) follows (usually lags behind by six months) although it is the first sign of pubertal developmental in 15-30% of girls
    o Pubic hair development precedes breast development more commonly in African-American girls than in Caucasian girls.
    o Stimulated by secretion of adrenal androgenic hormones.
- Other signs: Growth of uterus, estrogenization of vaginal mucosa, physiologic vaginal discharge.
- Pubertal growth spurt follows shortly after onset of puberty.
- Menarche: Towards the end of pubertal changes and growth spurt

Figure 1: Sequence of Puberty
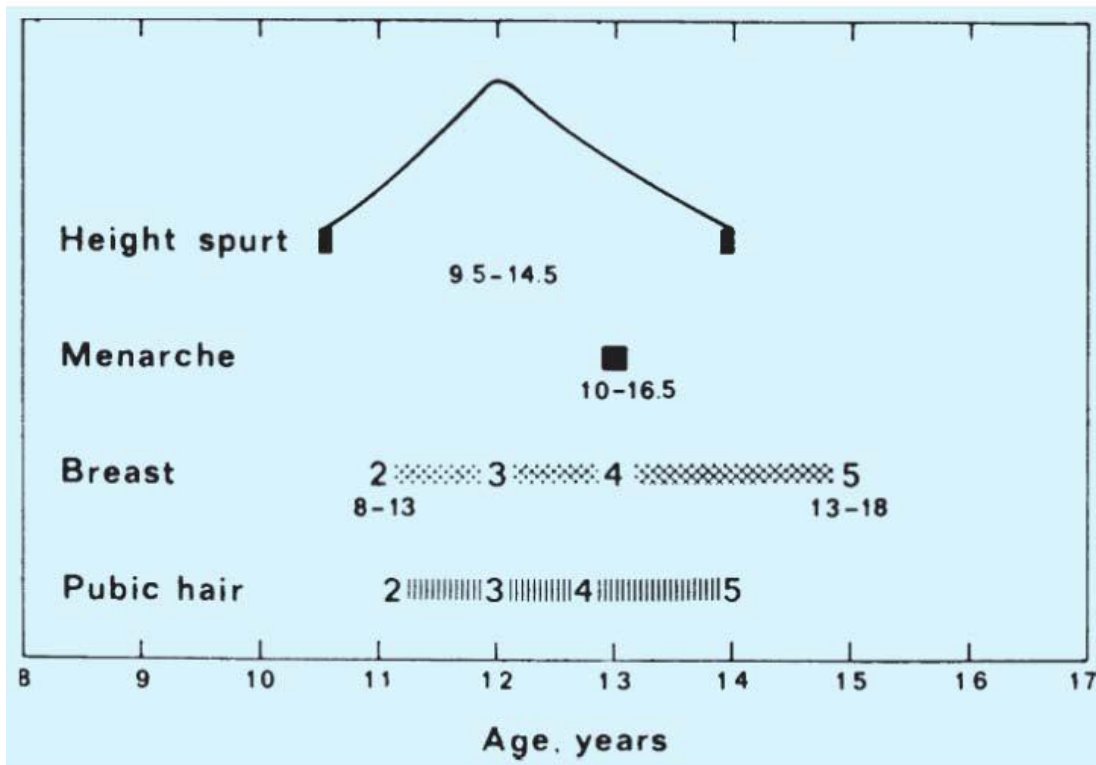
(With permission from S.J. Emans and M.R. Laufer, *Emans, Laufer, Goldstein's Pediatric and Adolescent Gynecology*, 6th ed. Lippincott, Williams & Wilkins; Wolters Kluwer, 2012)

What is normal versus abnormal puberty?

Normal puberty:
- Mean age at onset of breast development in Non-Hispanic White: 10.3 years (9.5 yrs in Black, 9.8 yrs in Hispanic).
- Mean age for onset of pubic hair development in Non-Hispanic White: 10.5 years (9.5 yrs in Black, 10.3 yrs in Hispanic).
- Mean age at onset of menarche in Non-Hispanic White: 12.7 years (12.1 yrs in Black, 12.2 years in Hispanic).
- The mean duration of complete pubertal development is 4.2 years in a girl (range of 1.5 - 6 years), and menarche typically occurs 2½ years after thelarche (onset of breast buds).

Delayed Puberty:
- Absence of any sign of puberty at a chronologic age 2-2.5 SDs above the mean age of pubertal development
  - In females, no breast development by age 13.
- Abnormal or halt in progression through puberty once initial pubertal changes have begun.
- More than four years have elapsed between onset of breast development and menarche.

Distribute Part II of the case and growth chart #1 and have participant(s) read it aloud.

Part II:

Current History:

Sarah says that she likes to eat and remarks that her appetite has increased over the past two years. She eats a good variety of foods with no restrictions. She is active in sports, playing field hockey during the fall and tennis during the spring usually for 1-2 hours a day.

On comprehensive ROS, she denies abdominal pain, nausea, vomiting, bloating and diarrhea. Her bowel movements are formed and often hard every other day. She has had no skin, joint, or visual complaints. Your records show that one year ago, Sarah's breast and pubic hair development were both Tanner stage 2.

Past Medical History:

Sarah's past medical history is unremarkable. She was a full-term gestational infant. She is on no medications and has had no operations or hospital admissions. She developed breast buds at age 11 years, followed by development of scant pubic hair.

Family History:

Her mother's height is 64 inches and the father's height 69 inches; therefore, her mid-parental height is ~64" (father's height – 5 inches, averaged with mother's height). Her mother had menarche at age 13.

No history of short stature or pubertal delay.

Physical examination:
Sarah is a thin, but otherwise well-appearing adolescent girl.
Height: 62 ¼ inches, weight: 84 pounds, BMI: 15.2.
Vital signs: blood pressure 95/54, pulse 72.
No obvious skeletal disproportion.
Skin: clear, without comedones or other lesions.
HEENT: pupils rounds and equally reactive. Sclerae clear. Extraocular muscles intact. Oropharynx clear. No midline facial defects.
Neck: no goiter or lymphadenopathy.
Chest: Tanner 2 breast development. Lungs clear.
Heart: normal sinus rhythm, without murmur, gallop or rub.
Abd: soft, no hepatosplenomegaly or masses.
GU: Tanner 2 pubic hair. Normal external genitalia. Reddened, thin vaginal mucosa.
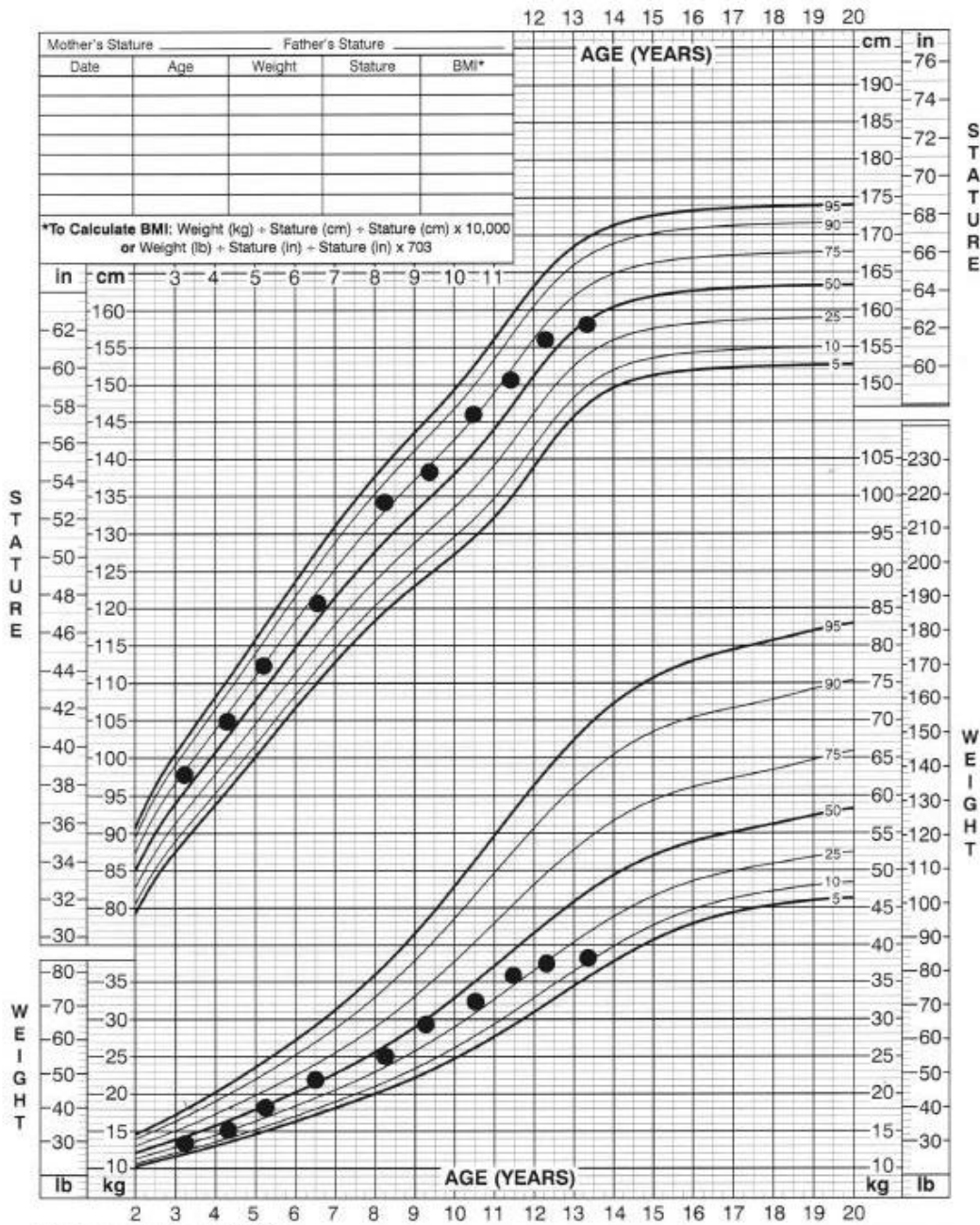Stool - negative for occult blood.
Neuro: nonfocal, normal reflexes, without delayed relaxation.
Spine: no scoliosis.

SARAH'S GROWTH CHART

2 to 20 years: Girls
Stature-for-age and Weight-for-age percentiles

NAME Sarah

RECORD # Before treatment

Pause and begin next set of discussion questions.
Potential discussion questions:

What are the tanner stages in females?
Tanner staging, also known as sexual maturity rating, describes the onset and progression of physical pubertal changes. Females are rated for both breast development and pubic hair growth; there are five stages.

Ask learners to refer to Handout #2: Tanner Stages of Secondary Sexual Characteristics (Female) in their packet. Allow a few minutes for learners to review the content

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.

(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)
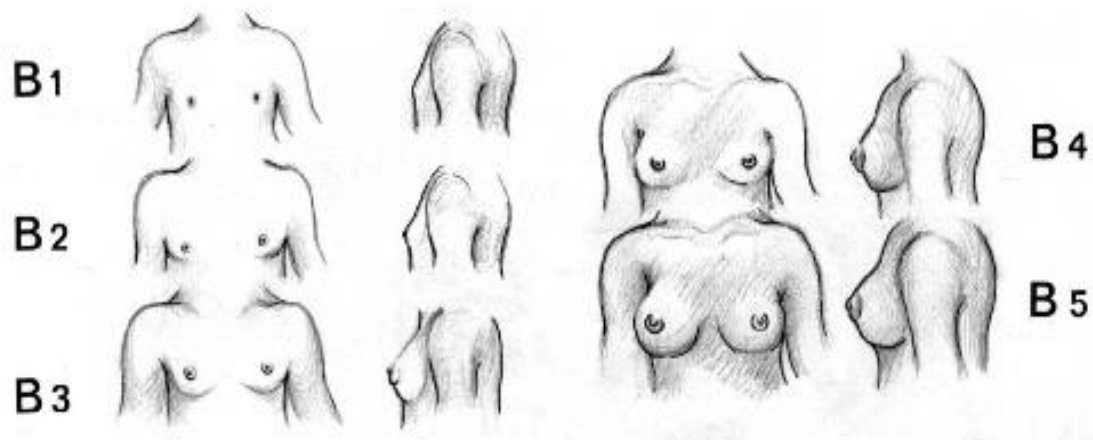
Female breast development. *Tanner stage 1*: Prepubertal, with elevation of papilla only. *Tanner stage 2:* Breast buds appear. Areola is slightly widened and projects as a small mound. *Tanner stage 3:* Enlargement of the entire breast with no protrusion of the papilla or of secondary mound. *Tanner 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.

(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)

What is your assessment of Sarah's pubertal development?
- Sarah underwent thelarche at a normal time, but her development has not continued to progress.
- Her past medical records reveal that her puberty has been completely *arrested* since the age of 11 years (when breast buds were noted).
- Both Sarah's weight and linear growth have been interrupted with a fall-off in weight before height.

Does Sarah need a pelvic examination?
- In the girl with delayed puberty, an internal examination is not needed because the differential diagnosis is largely between a hypothalamic-pituitary cause (*e.g.* slowing of GnRH pulses from a systemic illness) or an ovarian cause.
- An external genital examination is important to assure a normal clitoris, labia, hymen and presence or absence of estrogen effect on the vaginal mucosa.
- A recto-abdominal examination may be helpful to confirm normal internal anatomy and in this patient particularly to check stool for occult blood, but it is an optional examination if stool samples can be obtained for testing.
- In contrast, the patient with full pubertal development and no menses needs an internal examination to exclude a genital anomaly (mullerian anomaly or androgen insensitivity syndrome) or obstruction (imperforate hymen, transverse vaginal septum).

What is the differential diagnosis for Sarah's pubertal delay? (Then, can you narrow down the differential based on the information you have obtained?)
It is often helpful to put a stick figure on the board (see below) to help students organize their differential diagnosis of delayed puberty (with no signs of virilization or androgen excess).

Differential Diagnosis for Pubertal Delay

Central Nervous System (CNS) causes
Hypogonadotropic hypogonadism (low to normal FSH, LH levels)
- Chronic disease, especially those associated with malnutrition (cystic fibrosis, Crohn's, celiac disease, HIV, renal disease)
- Inherited defects in GnRH (e.g., Kallmann's syndrome), GnRH receptors
- CNS tumors (e.g., craniopharyngiomas)
- Genetic syndromes: Lawrence-Moon-Biedl, Prader-Willi syndromes
- Pituitary causes: tumor (*e.g.,* prolactinoma, germinoma, etc.)
infiltrative disease (sarcoid, tuberculosis, eosinophilic germinoma, CNS leukemia), hemochromatosis, head trauma, postpartum necrosis, "empty sella," infarction, cranial radiation, surgery, genetic mutations, panhypopituitarism
- Depression, substance use, stress
- Physiologic (constitutional) delay
- Eating disorders, athletic competition
- Inadequate nutrition from food insecurity
- Drugs, especially those associated with hyperprolactinemia (e.g. antipsychotics)
Thyroid
- Hypothyroidism
Adrenal
- Cushing syndrome (including iatrogenic)
- Addison's disease
Ovaries
Hypergonadotropic hypogonadism (high FSH and LH levels)
- Primary ovarian insufficiency (POI)
- Turner syndrome
- Pure gonadal dysgenesis (46, XX or 46, XY)
- Fragile X premutation carriers
- Autoimmune oophoritis
- Radiation or chemotherapy
- Other: galactosemia, myotonia dystrophica, Trisomy 21, sarcoidosis, ataxia telangiectasia; ovarian hemorrhage, torsion, removal or destruction; mumps or CMV oophoritis; idiopathic;17-hydroxylase deficiency, aromatase deficiency, FSH or LH receptor mutations; mutations in X chromosome

Sarah has a process that has interrupted both weight gain and linear growth. Self-induced

weight loss (e.g. anorexia nervosa) and systemic diseases (e.g. Crohn's disease, celiac disease) need to be considered. As the patient appeared to be previously healthy, the learner should consider the processes that either develop in early to middle adolescence or that fail to manifest themselves during childhood.

Example Drawing:

CNS

Thyroid

Adrenals

Ovaries
Uterus
Vagina
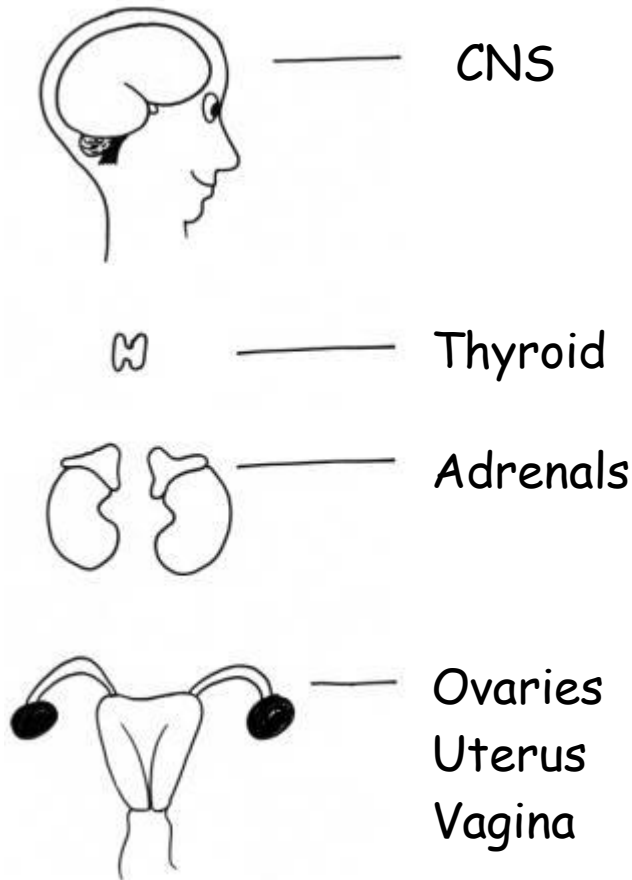
As a primary health care provider, what baseline tests would you order (if any)?
Students should generate a list of tests they would order using the differential diagnosis outlined. It is helpful to first list all the possible tests and then ask students which they should obtain first (as opposed to second or third steps of the workup).
- A screening CBC, ESR, LFTs, chemistries should be obtained to exclude a chronic illness. Consider celiac screen (TTG antibody, IgA), in patient with delayed puberty and underweight for height.
- A thyrotropin stimulating hormone (TSH) level and free T4.
- A follicle stimulating hormone (FSH) level to determine if the etiology is hypothalamic-pituitary (low or normal FSH) or secondary to ovarian insufficiency (high FSH).
- Prolactin.

- If the FSH level is high, karyotype and other studies (e.g., Fragile X premutation carrier testing, antibodies against thyroid and adrenal glands, and AMH for ovarian reserve) to determine the etiology of ovarian insufficiency.
- A hand and wrist radiograph for determination of bone age helps to estimate final height and extent of delay.
- An estradiol level may be helpful to confirm absence or presence of estrogen effect although levels vary over time
- Consider IGF-1 and IGF-BP3 to screen for growth hormone deficiency in girls with poor linear growth. Note that IGF levels may also be low in malnutrition and are not diagnostic of GH deficiency.

Distribute Lab results. Ask participants to evaluate for abnormalities.

Sarah's Lab results

- CBC - HCT 31% with MCV of 74 (other indices within normal limits), normal WBC and platelets
- ESR, liver function tests, electrolytes, BUN, creatinine, glucose, albumin, total protein, Ca, phosphorus all within normal limits
- Bone age (chronologic age 13 years) = 12 years (one standard deviation is 10 months)
- Thyroid function tests: free T4 1.02 ng/dl, TSH 1.8 uU/ml
- FSH 2.3 IU/L
- Tissue transglutaminase (TTG) > 112 EU/ml (negative < 20 EU/ml), IgA 182 mg/dL (normal 70-312 mg/dL)

What is your diagnosis? What do you do you know about celiac disease?
- Autoimmune mediated enteropathy triggered by ingestion of the gliadin fraction of wheat gluten, barley, and rye in genetically susceptible people
- Female > male; increasingly recognized with atypical manifestations
- Common presentations include constipation, irritable bowel syndrome, short stature, delayed puberty, iron deficiency anemia
- Initial screening with IgA level and TTG antibodies
    - IgA deficiency is more common in patients with celiac than in the general population
    - TTG antibodies are highly sensitive and specific for the diagnosis of celiac disease but can be falsely negative in untreated celiac patients with IgA deficiency
    - Thus, total serum IgA should be measured with TTG antibodies to ensure TTG antibody screen is accurate
- Small bowel biopsy remains gold standard (villous atrophy)
- Treatment is gluten free diet

As is seen in Sarah's case, the most consistent features are decreased rates of weight gain and linear growth which may persist without gastrointestinal symptoms.

What is the management plan for Sarah?

- Nutritional issues: After confirmatory biopsy, a gluten-free diet is the mainstay of therapy for patients with celiac disease. Symptomatic improvement typically occurs within a few weeks, and tests of absorptive function and small-bowel histologic changes improve typically after a few months.
- Growth: Normal growth velocity will likely resume after this patient is placed on an appropriate nutritional regimen. This is accomplished by initiation of a gluten-free diet.
- Sex hormone replacement: Sex steroid replacement (estrogen) is not needed in this case because normal GnRH and accompanying LH and FSH secretion will resume after the patient's nutritional status improves.

Distribute Epilogue and growth chart #2. Ask someone to real the epilogue out loud.

Epilogue
Sarah is currently age 14 6/12 years. She was referred to GI and had a small bowel biopsy following baseline lab testing which confirmed diagnosis of celiac disease. Sarah started a gluten-free diet following biopsy results. She has shown a good response to therapy with a marked acceleration of her growth velocity. Her breast and pubic hair development resumed within 6 months of initiation of this modified diet, and she just experienced menarche. Her repeat TTG was 18 EU/ml

Sarah's growth chart after initiating gluten free diet

2 to 20 years: Girls
Stature-for-age and Weight-for-age percentiles

NAME Sarah
RECORD # After Treatment
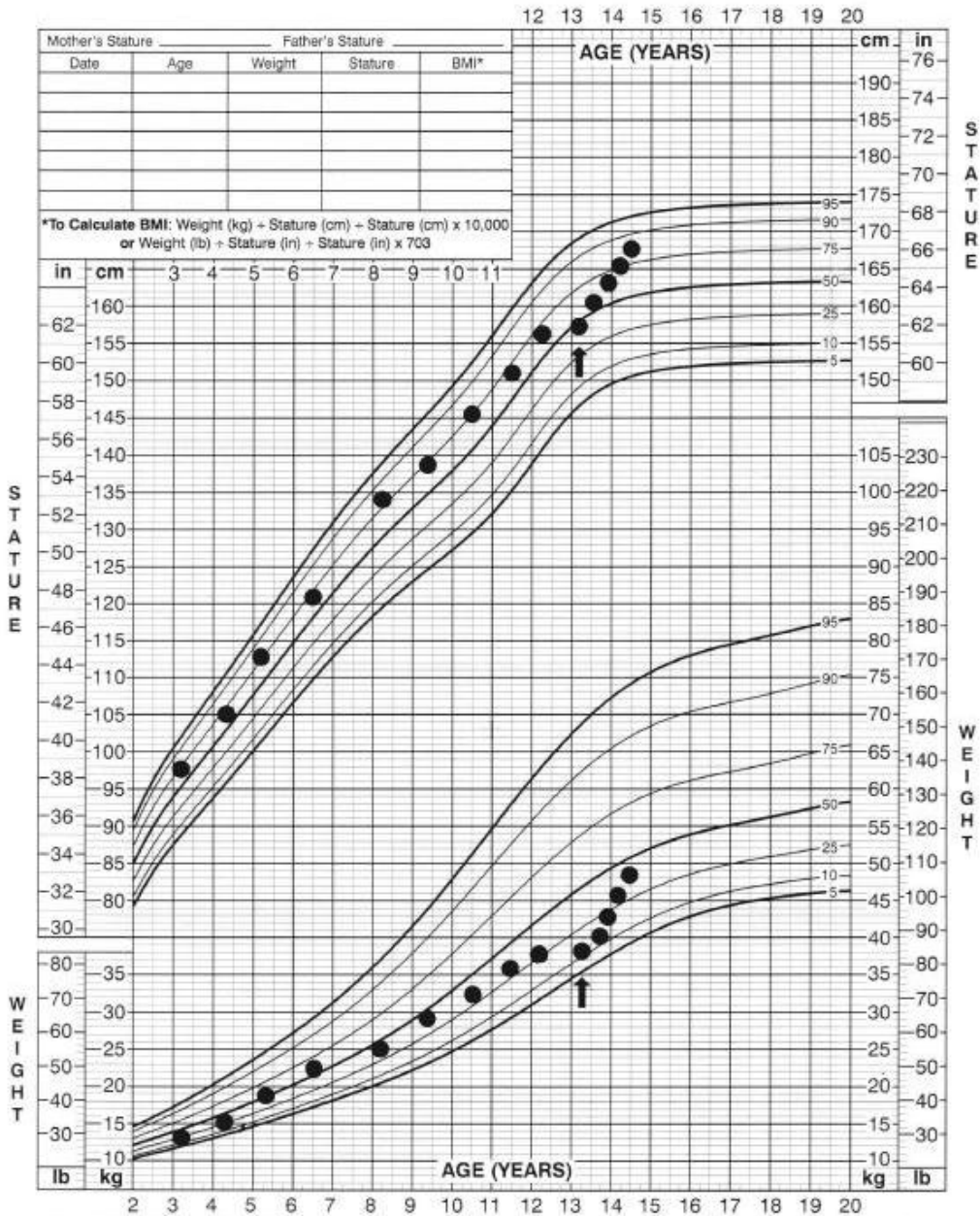
Refer back to group's learning agenda and summarize the key teaching points that were made. This will give the group a sense of accomplishment, and emphasize the important messages.

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.

Knowledge questions:

Distribute knowledge questions to group. Ask learners to complete the knowledge questions in their packet. If time allows, questions and answers can be discussed as a group, or learners can complete and review answers on their own.

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 61inches 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

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 the 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 61inches 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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8. Nelson LM. Primary Ovarian Insufficiency. *New England Journal of Medicine.* 2009. 360(6): 606-614

Materials for Learners:

Packet should include the following:
- Handout #1: Sequence of Puberty
- Handout #2: Tanner Stages of Secondary Sexual Characteristics (Female)
- Clinical Pearls
- Knowledge questions and answers
- References

A 13 year old Female with Poor Growth
Delayed Puberty

<u>Part 1</u>
Introduction:

A 13-and-a-half-year old female, Sarah, comes to your office for her annual physical examination. She has been in good health with no chronic medical problems and no acute illnesses.

Sarah has no concerns today but is accompanied by her mother who is worried that her daughter has not grown very much in the past year, and thinks her height and weight are the same as last year. Sarah reports that she thinks she's the only girl in her class who hasn't gotten her period.

A 13 year old Female with Poor Growth
Delayed Puberty

Part II:
Current History:

Sarah says that she likes to eat and remarks that her appetite has increased over the past two years. She eats a good variety of foods with no restrictions. She is active in sports, playing field hockey during the fall and tennis during the spring usually for 1-2 hours a day.

On comprehensive ROS, she denies abdominal pain, nausea, vomiting, bloating and diarrhea. Her bowel movements are formed and often hard every other day. She has had no skin, joint, or visual complaints. Your records show that one year ago, Sarah's breast and pubic hair development were both Tanner stage 2.

Past Medical History:

Sarah's past medical history is unremarkable. She was a full-term gestational infant. She is on no medications and has had no operations or hospital admissions. She developed breast buds at age 11 years, followed by development of scant pubic hair.

Family History:

Her mother's height is 64 inches and the father's height 69 inches; therefore, her mid-parental height is ~64" (father's height – 5 inches, averaged with mother's height). Her mother had menarche at age 13.

No history of short stature or pubertal delay.

Physical examination:
Sarah is a thin, but otherwise well-appearing adolescent girl.
Height: 62 ¼ inches, weight: 84 pounds, BMI: 15.2.
Vital signs: blood pressure 95/54, pulse 72.
No obvious skeletal disproportion.
Skin: clear, without comedones or other lesions.
HEENT: pupils rounds and equally reactive. Sclerae clear. Extraocular muscles intact. Oropharynx clear. No midline facial defects.
Neck: no goiter or lymphadenopathy.
Chest: Tanner 2 breast development. Lungs clear.
Heart: normal sinus rhythm, without murmur, gallop or rub.
Abd: soft, no hepatosplenomegaly or masses.
GU: Tanner 2 pubic hair. Normal external genitalia. Reddened, thin vaginal mucosa.
Stool - negative for occult blood.
Neuro: nonfocal, normal reflexes, without delayed relaxation.
Spine: no scoliosis.
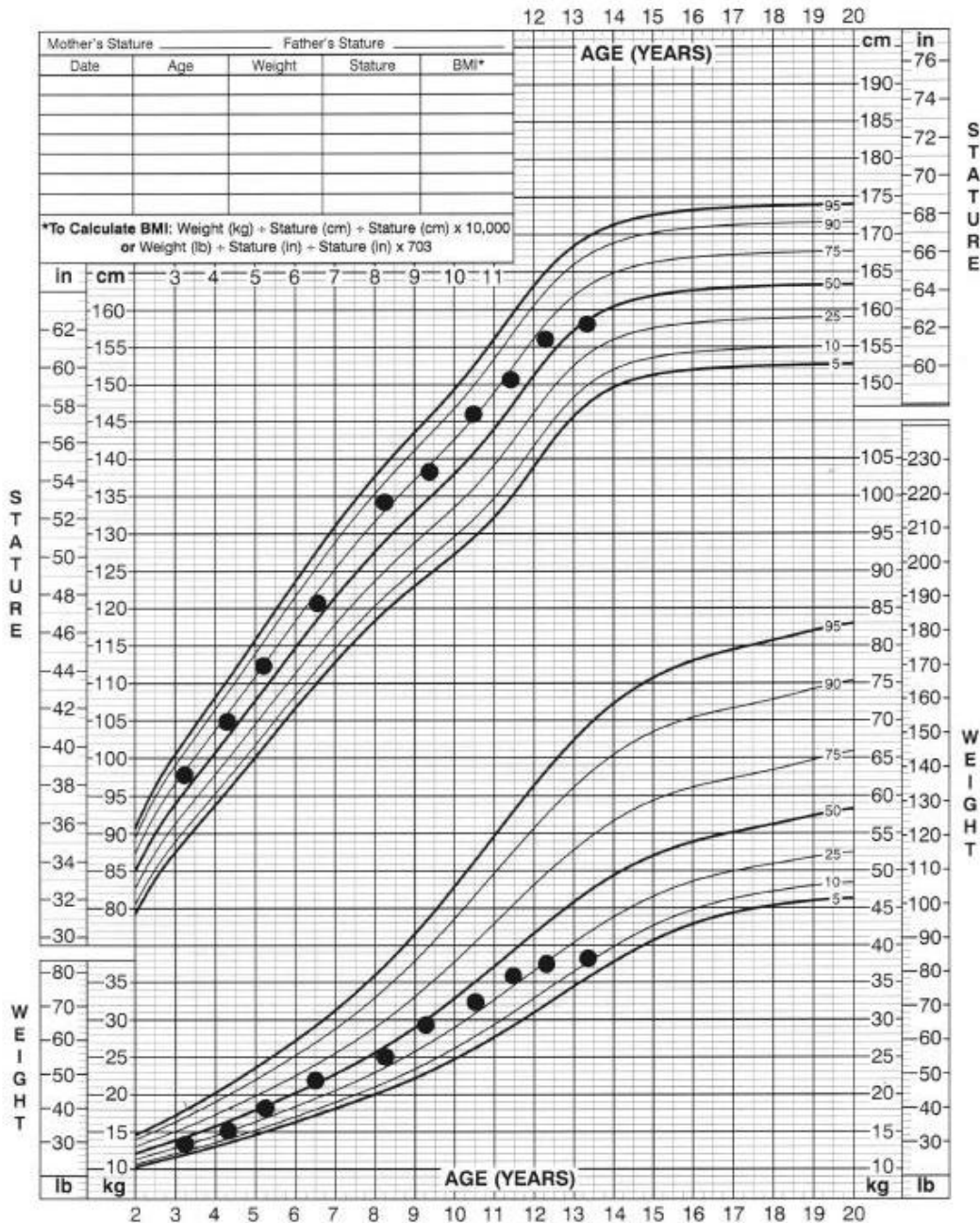
A 13 year old Female with Poor Growth
Delayed Puberty

Sarah's Growth Chart (#1)

2 to 20 years: Girls
Stature-for-age and Weight-for-age percentiles

NAME _Sarah_

RECORD # _Before treatment_

A 13 year old Female with Poor Growth
Delayed Puberty

Sarah's Lab results

- CBC - HCT 31% with MCV of 74 (other indices within normal limits), normal WBC and platelets
- ESR, liver function tests, electrolytes, BUN, creatinine, glucose, albumin, total protein, Ca, phosphorus all within normal limits
- Bone age (chronologic age 13 years) = 12 years (one standard deviation is 10 months)
- Thyroid function tests: free T4 1.02 ng/dl, TSH 1.8 uU/ml
- FSH 2.3 IU/L
- Tissue transglutaminase (TTG) > 112 EU/ml (negative < 20 EU/ml), IgA 182 mg/dL (normal 70-312 mg/dL)

A 13 year old Female with Poor Growth
Delayed Puberty

Epilogue

Sarah is currently age 14 6/12 years. She was referred to GI and had a small bowel biopsy following baseline lab testing which confirmed diagnosis of celiac disease. Sarah started a gluten-free diet following biopsy results. She has shown a good response to therapy with a marked acceleration of her growth velocity. Her breast and pubic hair development resumed within 6 months of initiation of this modified diet, and she just experienced menarche. Her repeat TTG was 18 EU/ml

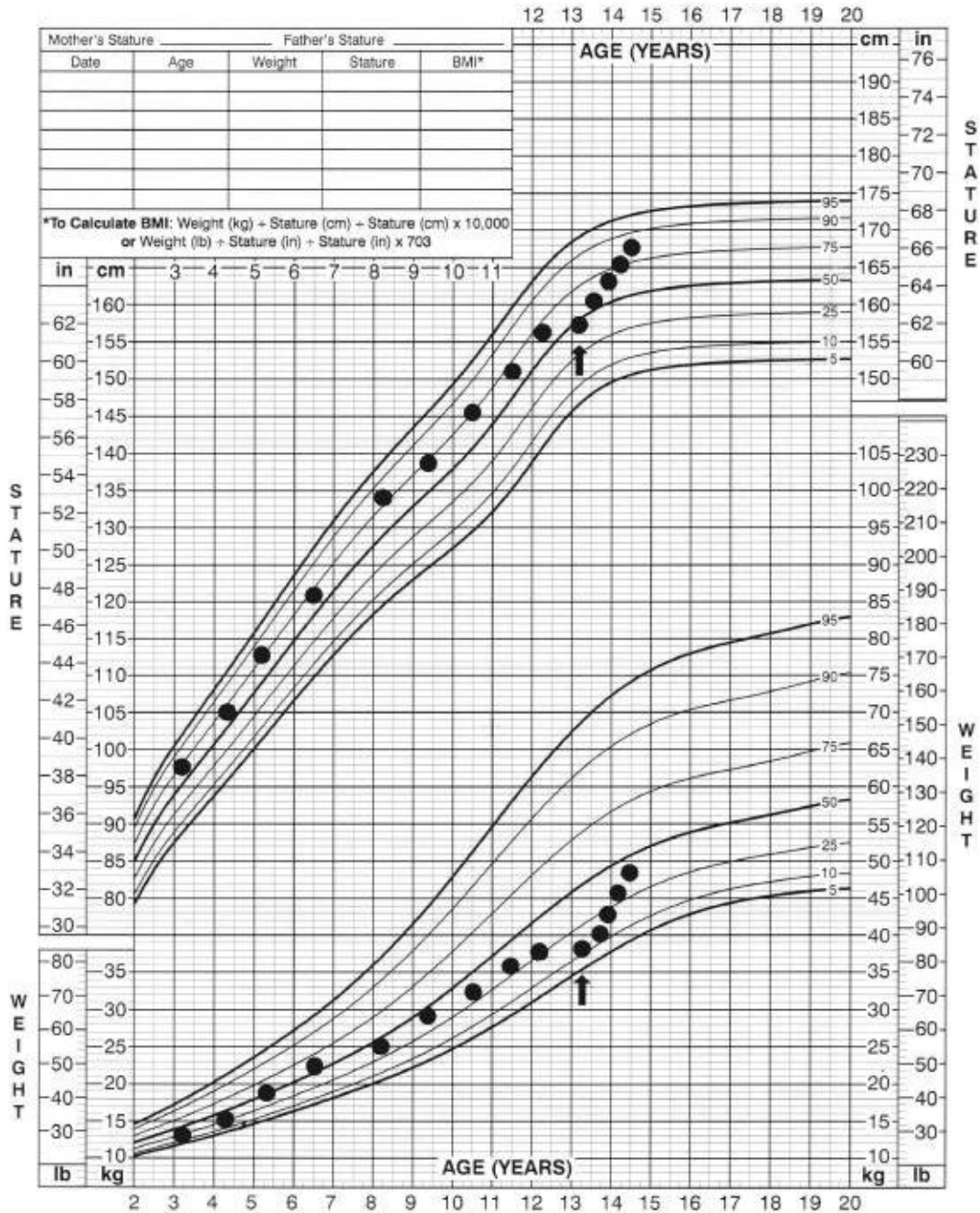# A 13 year old Female with Poor Growth
Delayed Puberty

Sarah's growth chart (#2)

CDC 2 to 20 years: Girls Stature-for-age and Weight-for-age percentiles growth chart. NAME Sarah. RECORD # After treatment.

Revised and corrected November 28, 2000.
SOURCE: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000).
http://www.cdc.gov/growthcharts