The Shortest in the Class  
Facilitator’s Guide

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Topic: Turner’s Syndrome and Short Stature

Abstract:  
Questions about short stature are common in primary care practice. Health care providers need to know how to approach a child with short stature. This case presents the story of Marybeth, a nearly 13 year-old girl who is short and also has no signs of pubertal development. Her story will promote a discussion of the differential diagnosis and primary care management of short stature and delayed puberty, including hormonal therapies.

Goal:  
To provide learners with a basic understanding of the evaluation of short stature.

Objectives:  
By the end of the session, learners will be able to:  
1. List the differential diagnosis for short stature  
2. Begin the evaluation of an adolescent with short stature.

Prerequisite Case: N/A

Related Cases:  
“Different From My Friends” (Turner’s Syndrome and Delayed Puberty)**  
“Normal vs. Abnormal Patterns” (Understanding Growth)  
“Timmy and the ‘Big Kids’” (Constitutional Short Stature)  
“Will I Ever Get My Period?” (Growth and Chronic Disease)

Themes:  
Adolescent Health, Growth in Children and Adolescents

**Editor’s note: The case narratives of the two Turner’s syndrome cases are similar, but “Different From My Friends” focuses on the evaluation of delayed puberty while “The Shortest in the Class” focuses on the assessment of short stature. Facilitators should choose the case most appropriate for their group of learners.

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Key Words:
Short stature, puberty, growth disorders, normal pubertal development, Turner’s syndrome, breast development, pubertal delay

Bright Futures Core Concepts:
While all of the Core Concepts are included in each case, this particular case can be used to highlight communication, partnership, and prevention/health promotion.

Materials Provided:
• Facilitator’s Guide
• 3-part Case Narrative: Part I, Part II, Epilogue
• Handout #1: Normal Pubertal Development
• Handout #2: Marybeth’s Growth Chart
• Bibliography

Facilitator Preparation:
Facilitators should thoroughly review this guide and the other materials provided. At the end of the guide we have included a section entitled, “Independent Learning/Prevention Exercises,” that will further stimulate group and individual education on this topic.

Suggested Format for a One Hour Session:
We anticipate that case facilitators will modify implementation of the case session to best fit their educational setting and learners. For detailed recommendations on case facilitation, please see the previous chapter entitled, “A Brief Guide to Facilitating Case Discussion.”

Open the Discussion: Introduce the case title and the session goal. Explain that this will be an interactive case discussion and not a lecture.

Introduction: Marybeth is a nearly 13 year-old girl with short stature and no signs of pubertal development. A challenge is that there is little documentation of her past growth velocity or previous medical care as she has not seen a pediatrician in several years. The clinician is forced to rely on information from the parents and current clues from today’s history and physical examination.

The constellation of short stature and no pubertal development should prompt a consideration of Turner’s syndrome. The clinician should seek to identify features consistent with that diagnosis through the history and physical examination, though patients with Turner’s syndrome, depending on the age of presentation, can have none of the stigmata except for short stature. Girls with Turner’s Syndrome may have the karotype 45, X, a mosaic karotype (e.g. 46, XX/ 45, X) or an isochromosome of X. Slightly over half of patients with dysgenetic gonads have a 45, X karotype. The classic stigmata of the syndrome are short stature, widely spaced nipples, low hairline, short (4th, 5th) metacarpals, ptosis, low-set ears, high-arched palate, lymphedema, and multiple
pigmented nevi. Associated problems include cardiac abnormalities, hearing impairment, otitis media, mastoiditis, renal anomalies and an increased incidence of hypertension, achlorhydria, diabetes mellitus and autoimmune thyroiditis. An untreated adolescent with Turner’s Syndrome typically has bilateral streak (dysgenetic) gonads, prepubertal female genitalia, and a normal uterus and vagina. Girls with a mosaic karotype, particularly involving loss of only the short arm of the X chromosome, are more likely to have experienced pubertal maturation.

The clinician should elicit a thorough history, plot the height and weight on a growth chart, calculate the midparental height, and perform an exam. The differential will ultimately reveal a patient with Turner’s mosaic who will need growth hormone and sex steroid replacement to complete optimal growth and development.

Distribute Part I of the case and ask one or more of the participants to read it aloud.

Part I

Marybeth is a 12 year 11 month old girl whose parents are concerned about her short stature. They claim that she has always been “the shortest in the class,” but “eats well” and is not underweight for her height. She has not yet had any breast or pubic hair development and has not started her menses. A review of systems is unremarkable. She has a good energy level and appetite. She is a B+ student and active in sports. She has been healthy overall, and has not seen a physician in 4 years. Marybeth appears as a well nourished, but somewhat short, adolescent.

After talking to Marybeth and her parents together, you glance toward her parents, “I’m now going to spend a few minutes with Marybeth to discuss her health concerns. If you would go back to the waiting room, I’ll come and get you in a few minutes. We’ll make a final plan together.”

As her parents’ exit, Marybeth begins by saying that even though she wants to be a “little taller,” she is not extremely concerned about her height. But over the course of the interview, she becomes increasing open with her feelings.

She tells you, “I am never picked for basketball teams during gym class at school” and “I always have to use a stool or chair to reach anything.” “All of my friends are taller than me and have started their periods.” You ask Marybeth if she has shared these concerns with anyone. She responds that “only my best friend knows how I really feel.”

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.
Guiding Questions for Discussion:

**What additional information would like to know?** To assess whether the parents’ concerns regarding the short stature are accurate and legitimate, you would need to find out more information about the patient’s past medical history. Has the patient had stigmata of a chronic illness that might be affecting her growth? 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). In this case only one point is available for the past four years. Is she 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, or other signs of a central nervous system process?

The assessment should also include questions about other stressors, family constellation, intensity of sports participation, concerns about weight and nutritional intake, and how much discussion she has had at home about her pubertal development. The *Bright Futures Guidelines for Health Supervision* list screening questions that clinicians may find useful:

- Who do you live with?
- How do you get along with family members?
- How often do you miss school?
- What activities and sports are you involved in?
- How do you feel about your weight? Are you trying to change your weight? How?
- What do you usually eat in the morning? At noon? In the afternoon? In the evening?
- Has anyone talked with you about what to expect as your body develops? Have you read about it?
- Have you started your period yet?

*Family history* is also important (e.g. history of short stature, history of miscarriages, age of pubertal onset in each parent, pubertal delay in other family members, etc.). The heights of both parents should be ascertained in order to calculate a mid-parental height (MPH) (for girls=father’s height - 5 inches, averaged with mother’s height). The MPH will enable you to see how closely Marybeth is following her genetic potential. Lastly, she needs a thorough physical examination to assess for stigmata of a chronic disease, a known syndrome (e.g. chondrodysplasia or Turner’s syndrome), or signs of a central process (e.g. papilledema, etc.)

**What is the differential diagnosis of short stature?**

Growth deficiencies may be divided into two broad categories: Primary growth deficiency and secondary growth deficiency. *Primary growth deficiency* may be defined as an intrinsic defect in the skeletal system as a result of either a genetic defect or prenatal damage to the system. Examples include: skeletal dysplasia, chromosomal abnormalities,
congenital errors of metabolism, intrauterine growth retardation, and genetic or familial short stature. Secondary growth deficiency is growth that is retarded because of factors, generally outside the skeletal system, which delay osseous maturation. These factors include: endocrine (e.g., growth hormone deficiency, hypothyroidism), nutritional (e.g., protein-calorie malnutrition), metabolic (e.g., disorders of carbohydrate, lipid or protein metabolism), psychosocial (e.g., psychosocial or deprivation dwarfism), specific organ failure or dysfunction (e.g., bowel - Crohn disease; kidney - nephrotic syndrome, heart - congestive heart failure; lungs, bowel - cystic fibrosis), or unknown/idiopathic (e.g., constitutional delay). Learners can expand on examples of any of the above.

Distribute Handout #1: Normal Pubertal Development. Review the contents.

Is Marybeth’s puberty delayed? This is an important question to answer as pubertal development (specifically, the stage of pubertal development) can affect growth. Breast development is typically the first sign of puberty in a female. A girl who has experienced no breast development or other signs of puberty by age 13 years is 2 standard deviations from the normal age and has delayed development. The average age with standard deviation (SD) for attainment of pubertal milestones in North American girls is age 10.9 ± 1.0 years for breast budding (Tanner II) and 11.2 ± 1.1 years for pubic hair development (Tanner II), although a recent study suggested that girls may be achieving these milestones earlier. Marybeth is close to meeting the definition of delayed puberty and in the setting of short stature, concern is raised even further.

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

Part II

From your discussion with Marybeth and her parents, you learn that her past medical history is remarkable for recurrent otitis media as a child. She appears to have a good relationship with her family. She was born at full-term after an uncomplicated pregnancy; birthweight was over 7 lbs and length 21”. She met normal developmental milestones, and her only surgery was placement of tympanostomy tubes at age 2 years for recurrent otitis media. She had one hospital admission at age 1 year for observation after a febrile seizure. She is on no medications or vitamins. Her mother’s height is 62” and the father’s height 69”.

On physical exam, she is young-appearing and healthy.
   Weight: 35 kg (77 pounds)
   Height: 132.4 cm (52 inches)

Vital Signs: BP 100/64, Pulse 76.
Skin: pigmented nevi on back, anterior neck, and right axilla
HEENT: benign
Neck: no goiter or lymphadenopathy
Breast: Tanner I
Lungs: clear
Heart: normal sinus rhythm, I/VI systolic ejection murmur along left sternal border. No gallop or rub.
Abdominal: soft, no hepatosplenomegaly
Neurologic: nonfocal, normal reflexes, without delayed relaxation.
What parts of the physical examination/health assessment are particularly important?

Distribute Handout #2: Growth Chart for Girls: 2 to 20 years (Physical Growth NCHS Percentiles)

Her height is <5%; her weight is 5-10% and her BMI (kg/m²) is 20. She is not underweight for her height and thus the differential diagnosis should focus on endocrinologic rather than nutritional causes of her short stature.

Her midparental height = \((69-5) + 62 \over 2\)

= 63 inches

What is the most likely diagnosis now? The combination of short stature, lack of pubertal development, and several characteristic stigmata including multiple nevi and recurrent otitis media point to Turner’s Syndrome. Rotated ears and a narrow Eustachian tube are also common, associated with frequent bouts of otitis media. Additionally, in Lippe’s series the incidence of gonadal failure was 96% and short stature 100%. This data has been verified by other investigators, as well. The differential includes diagnoses noted in Part I.

As a primary health provider, what baseline tests would you want to order (if any)? The learners should generate a list of tests they would order using the differential diagnosis generated. It is helpful to list all of the possible tests and ask participants to vote on the top four tests they would obtain first. Then reveal the lab results for those tests, and decide what second and third steps are. Besides screening CBC and chemistries to exclude an unsuspected chronic illness, the most important endocrine tests are a TSH level (to exclude hypothyroidism) and a FSH level to determine if the etiology is hypothalamic-pituitary (low or normal FSH) or secondary to ovarian failure (high FSH). If hypothyroidism could occur because of a CNS process, then other thyroid function tests (e.g. T₄, TBGI) should be obtained. Prolactin level is drawn if the FSH level is low. If FSH level is high, a karyotype and other studies are drawn to determine the etiology of ovarian failure. Hand and wrist radiograph for bone age helps to estimate final height and to ascertain if the bone age is delayed more than height age (common with hypothyroidism). Give out the diagnostic karyotype data last.

Baseline initial tests:
- **Bone age** is 10 years (standard deviation is 10 months). With a chronologic age of nearly 13 years, the bone age is DELAYED. Determination of bone age allows an estimate of final adult height and the comparison with height age and weight age. The clinician should consider speaking with a pediatric endocrinologist upon receipt of the delayed bone age. This finding is a hint that there is a hormonal deficit.
- **Thyroid function tests**: T₄ 8.8 µg/dl, TSH 2.6 µIU/ml, TBGI 0.93 NORMAL. Hypothyroidism is frequently accompanied by poor linear growth and bone age is delayed more than height age.
• CBC, liver function tests, electrolytes, BUN, creatinine, glucose, albumin, total protein, Ca, phosphorus, sedimentation rate (ESR) – NORMAL. These tests help to exclude a systemic illness.

• FSH 167.3 IU/L - MARKEDLY ELEVATED. A high FSH level is consistent with gonadal failure. It should be noted that FSH may not be elevated between age 3 and 10 years but rises in girls with Turner’s Syndrome at the age of normal puberty.

Impression:
Investigations are consistent with gonadal failure. Turner’s syndrome or variant are highest on differential.

Secondary work-up:
• Karyotype: 45, X/ 46, XX  Mosaic karyotype with two cell lines, consistent with diagnosis of Turner’s variant or mosaic.

Discuss the management plan for this patient.
Growth: The timely management of growth failure will affect many aspects of Turner’s syndrome, including the age at which estrogen replacement is begun, socialization and academic achievement. Height should be plotted on growth curves specific for Turner’s syndrome patients. Though these patients are not GH-deficient, they respond well to exogenous GH (recombinant human GH). GH therapy should be initiated by a pediatric endocrinologist as soon as the patient falls beneath the 5th percentile. Recent studies have documented short-term growth acceleration following treatment with GH, either alone or in combination with low doses of oxandrolone (an oral anabolic steroid). Rosenfield et al.7 followed 62 American girls with Turner’s syndrome over a 6-year period. Of the 17 recipients of GH alone, 14 (82%) exceeded their original projected adult height. Of the 45 recipients of combination GH plus oxandrolone, 41 (92%) exceeded their projected adult height. The mean height of the patients at the study’s conclusion was 151.7 cm or 5 feet. Based on this data, combined with equally impressive outcomes from other studies, GH therapy has become the standard of care for these patients in this and many other countries. An adult height of > 150 cm, the lower limit of normal for American women, is now an attainable goal for most girls with Turner’s syndrome who are treated for a minimum of 6 years with GH therapy during childhood.

Sex hormone replacement: Sex steroid replacement (estrogen) is typically begun at the age of 14-15 years and will promote secondary sex characteristic development. One must initiate this therapy cautiously as estrogen will accelerate maturation of the epiphyses and if begun prematurely can decrease a patient’s final height. A physician should discuss the issue of estrogen replacement with each patient and her family as psychological issues around puberty also contribute to the decision of when estrogen is initiated.

Distribute the Bibliography page and Epilogue. Ask someone to read the Epilogue aloud.
Epilogue

Marybeth was begun on growth hormone therapy at age 13. She showed a good response to therapy with a marked acceleration of her growth velocity. She is a good student and has many friends. However, she has become quite self-conscious as her “body is different from all of my classmates.” Because of her age and concern about lack of pubertal development, low-dose estrogen therapy was begun at 14 years 6 months.

At age 15, Marybeth now enters the examination room by herself, while her parents wait outside. She appears to be more confident. When asked how she is, she responds that “Gym class is better now. I actually even get picked for sports teams! I can also reach things on shelves which I could never do before.” When asked how she was getting along with peers, she replies, “I have two close friends that I hang out with a lot. Before, I always felt like their little sister. I’m really happy that I don’t stick out like I used to.”

You congratulate Marybeth on how well she is doing and for being adherent with her medical regimen.

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. Suggest further sources of reading or other information if there are agenda items that were not covered in the discussion.

**Independent Learning/Prevention Exercises:** Facilitators may wish to assign “Independent Learning/Prevention Exercises” to the group, particularly if time constraints hinder the completion of the case. The following list includes suggestions to explore the available community resources that focus on Turner’s Syndrome, as well as other areas of pertinent interest that can be integrated during or after the session. If the exercise is done in the absence of the facilitator, learners should take notes on their experience, then discuss with a faculty member for feedback.

1. Find out about the Turner’s Society and explore their web site, newsletter, and consumer guides.
2. Invite the parents and/or patient (older adolescent or adult) with Turner’s Syndrome to speak to the group.
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Part I

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Part II

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| Weight: 35 kg (77 pounds) | Height: 132.4 cm (52 inches) |

Vital Signs: BP 100/64, Pulse 76.
Skin: pigmented nevi on back, anterior neck, and right axilla.
HEENT: benign
Neck: no goiter or lymphadenopathy
Breast: Tanner I
Lungs: clear
Heart: normal sinus rhythm, I/VI systolic ejection murmur along left sternal border. No gallop or rub.
Abdominal: soft, no hepatosplenomegaly
Genitourinary: Tanner I pubic hair. Normal external genitalia
Neurologic: nonfocal, normal reflexes, without delayed relaxation
The Shortest in the Class

Epilogue

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The Shortest in the Class
Handout #1: Normal Pubertal Development

Sequence Of Pubertal Events
Average American Female/Male

From: Wildey LS, Byrd GM, Biro FM, *Pubertal Growth and Maturation*, Center for Continuing Education in Adolescent Health, Division of Adolescent Medicine, Children’s Hospital Medical Center, Cincinnati, Ohio, 1996.
The Shortest in the Class
Handout #2: Marybeth’s Growth Chart

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

Mother’s Stature Father’s Stature
Date Age Weight Stature BMI

"To Calculate BMI: Weight (kg) = Stature (cm) + Stature (cm) x 10,000
or Weight (lb) = Stature (in) + Stature (in) x 703"

NAME Marybeth
RECORD #

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
The Shortest in the Class

Bibliography


Suggested Readings (Annotated)


*Both articles are excellent reviews, providing an overview of issues surrounding the diagnosis and management of a child/adolescent with short stature.

These are guidelines for general health supervision of children and adolescents with Turner’s Syndrome. The type of imaging recommended and the periodicity of cardiac screening is likely to be changed.

Suggested Informational Resource