CASE FOUR

Short case number: 3_06_04
Category: Children & Young People
Discipline: Paediatrics Medicine
Setting: General Practice_Urban
Topic: Growth_Short Stature

Case

Justin Witherspoon is 8 years old, his parents are concerned that Justin is the shortest child in his class and does not seem to have grown much in the last 2 years.
"He is still wearing the same school uniform since last year"
Justin does not say much during the consultation, but when asked he says that he hates being called names by the other children because he is so short.
Justin "has always been on the small side" but he is otherwise healthy.
His current height is: 116cm, Weight is 22.5kg.

Questions

1. What are the key features of your history and examination of Justin and why?
2. What features of history and examination would concern you that Justin had a pathological cause for his short stature? Outline the investigations that you would undertake in assessing these possible causes.
3. As part of your assessment of Justin you calculate Justin's height age, midparental height and height velocity, explain the meaning of these terms and how you would calculate them.
4. Your assessment of Justin suggests that he has familial [genetic] short stature, while explaining this to his mother, she asks about Growth hormone injections and whether they would help Justin grow. What would you explain to Justin's mother?
5. Justin's mother enquires about puberty and whether his short stature will also mean that he will be a "late developer". In your explanation to Justin's mother outline the stages of pubertal development, the definitions of early and late puberty and how this can be assessed clinically.

Resources

- South M, Isaacs D editors. Practical Paediatrics. 7th edition. Edinburgh: Churchill Livingstone; 2012.

ANSWERS

Question 1
What are the key features of your history and examination of Justin and why?

History

- What is the height compared to peers? How long has the child been short? Who is concerned about the short stature and is there teasing at school? What is the school performance?
- What are the birth details and past medical history? Was there unexplained neonatal hypoglycaemia (suggesting pituitary hormone deficiency) or early illnesses? Determine the dental and milestone development, specific disease symptoms and nutritional status. Has puberty commenced? Are previous growth measurements available (child health record or measurements from local doctor or school)?
- What are the heights and ages of pubertal onset of the parents and siblings? Is there a family history of short stature or specific diseases?

Examination

- Accurate height and weight (using a reliable measuring device, particularly for height); body proportions (span, upper and lower segments).
- Assessment of pubertal status.
- General physical examination including evidence of chronic disease, nutritional state and dysmorphic features suggesting a syndrome.
- Any sign of goitre or clinical signs of hypothyroidism, including dry hair and skin, bradycardia and delayed reflexes.
- Evidence of 'midline brain development syndromes' which may result in hypopituitarism. This includes cleft palate, single central incisor and small male genitalia (associated with gonadotrophin deficiency in utero). The combination of neonatal hypoglycaemia and small genitalia suggests hypopituitarism.
- Examination of visual fields and optic fundi to exclude the possibility of a pituitary lesion, in particular craniopharyngioma.

Note

- There is a wide variation of normal growth
- 3% of normal children will be above the 97th percentile or below the 3rd percentile
- Assessment of growth velocity (growth over time) is of more value than a single growth measurement
- The average growth rate during childhood is 5 cm/year (but be aware of height velocity charts for different rates of growth by age)
- To maintain a height percentile, height velocity needs to be $\geq$ 50%

Question 2:
What features of history and examination would concern you that Justin had a pathological cause for his short stature? Outline the investigations that you would undertake in assessing these possible causes.

The single most important aspect of the management of short stature is to plot the current and previous heights and weights and parental heights on a percentile chart in order to answer the following questions

- Is the child short and below the 3rd height centile? Is this appropriate for midparental height?
- Is the child growing slowly and is there evidence that the height is falling across the percentile lines? This can be further plotted on a height velocity chart.

Investigations should be performed if there is any evidence of specific chronic disease, if there is a suggestion of chromosomal abnormality or if the growth velocity is subnormal. The following investigations may be performed:

- bone age X-ray
- full blood count, CRP and ESR
- urea, creatinine and electrolytes
- urinalysis ± microscopy and culture
- calcium and phosphate
- thyroid function tests
- chromosomes (girls only)
- screening test for coeliac disease (total IgA and endomysial antibodies or tissue transglutaminase antibodies).
- IGF-1 (+ IGFBP3)

Question 3
As part of your assessment of Justin you calculate Justin's height age, midparental height and height velocity, explain the meaning of these terms and how you would calculate them.

The midparental height (MPH), also known as the target height, allows the height of any individual child to be considered in relation to the heights of his/her biological parents. The midparental height can be calculated using the following formulae:

Boys: MPH = (Fathers Height + Mothers height) +13/2,
Girls: MPH = (Mothers Height +Fathers height) – 13)/2,

Height velocity = Growth over time

A velocity below the 25th centile for bone age is potentially abnormal in a short child. A reliable height velocity requires at least 6 months of growth data, and preferably 12 months with consistent measurements at 3-4-monthly intervals over that time. Examination of the growth data plus the points obtained in history and examination should allow distinction between a variation of normal or a pathological cause of short stature.

Question 4

Your assessment of Justin suggests that he has familial [genetic] short stature, while explaining this to his mother, she asks about Growth hormone injections and whether they would help Justin grow. What would you explain to Justin's mother?

Short stature is considered by some children and their families to be a physical and psychosocial disability. Extreme short stature can certainly be considered as a disadvantage in both a social and medical sense. Many paediatricians and paediatric endocrinologists consider that, if the estimated final height of a female will be less than 152.4 cm (5 ft) or a male less than 162.6 cm (5 ft 4 in), then consideration should be given to the use of a growth promoting agent. The major growth promoting agent used in the treatment of short stature is biosynthetic growth hormone. Biosynthetic growth hormone has been available commercially in Australia since 1985. In 1988, the *Guidelines for the Use of Growth Hormone in Australia* were liberalized, allowing the use of growth hormone in short children who are growing poorly but are not growth-hormone-deficient.

Growth hormone can be administered only daily by subcutaneous injections, usually given 6-7 days per week. Despite the availability of biosynthetic growth hormone, the annual cost of growth hormone therapy remains very high. Growth hormone should therefore only be used for children who have short stature and who could potentially benefit from the therapy.

A child must have abnormally short stature (height less than the 1st percentile) with an abnormally low growth rate (height velocity < 25%), measured over a minimum period of 1 year at intervals of not greater than 6 months. The child should be growing at a height velocity below the 25th centile for skeletal age and sex.

Question 5

Justin's mother enquires about puberty and whether his short stature will also mean that he will be a "late developer". In your explanation to Justin's mother outline the stages of pubertal development, the definitions of early and late puberty and how this can be assessed clinically.

<u>Tanner Stages of Puberty</u>

Males: genital (penis) development
• *Stage 1:* Preadolescent, testes, scrotum and penis are of about the same size and proportion as in early childhood • *Stage 2:* Enlargement of scrotum and testes. Skin of scrotum reddens and changes in texture. Little or no enlargement of penis at this stage • *Stage 3:* Enlargement of the penis, which occurs at first mainly in length. Further growth of the testes and scrotum • *Stage 4:* Increased size of penis with growth in breadth and development of glans. Testes and scrotum larger; scrotal skin darkened • *Stage 5:* Genitalia adult in size and shape
Females: breast development
• *Stage 1:* Preadolescent: elevation of papilla only • *Stage 2:* Breast bud stage: elevation of breast and papilla as small mound. Enlargement of areola diameter • *Stage 3:* Further enlargement and elevation of breast and areola, with no separation of their contours • *Stage 4:* Projection of areola and papilla to form a secondary mound above the level of the breast

- *Stage 5:* Mature stage: projection of papilla only, due to recession of the areola to the general contour of the breast

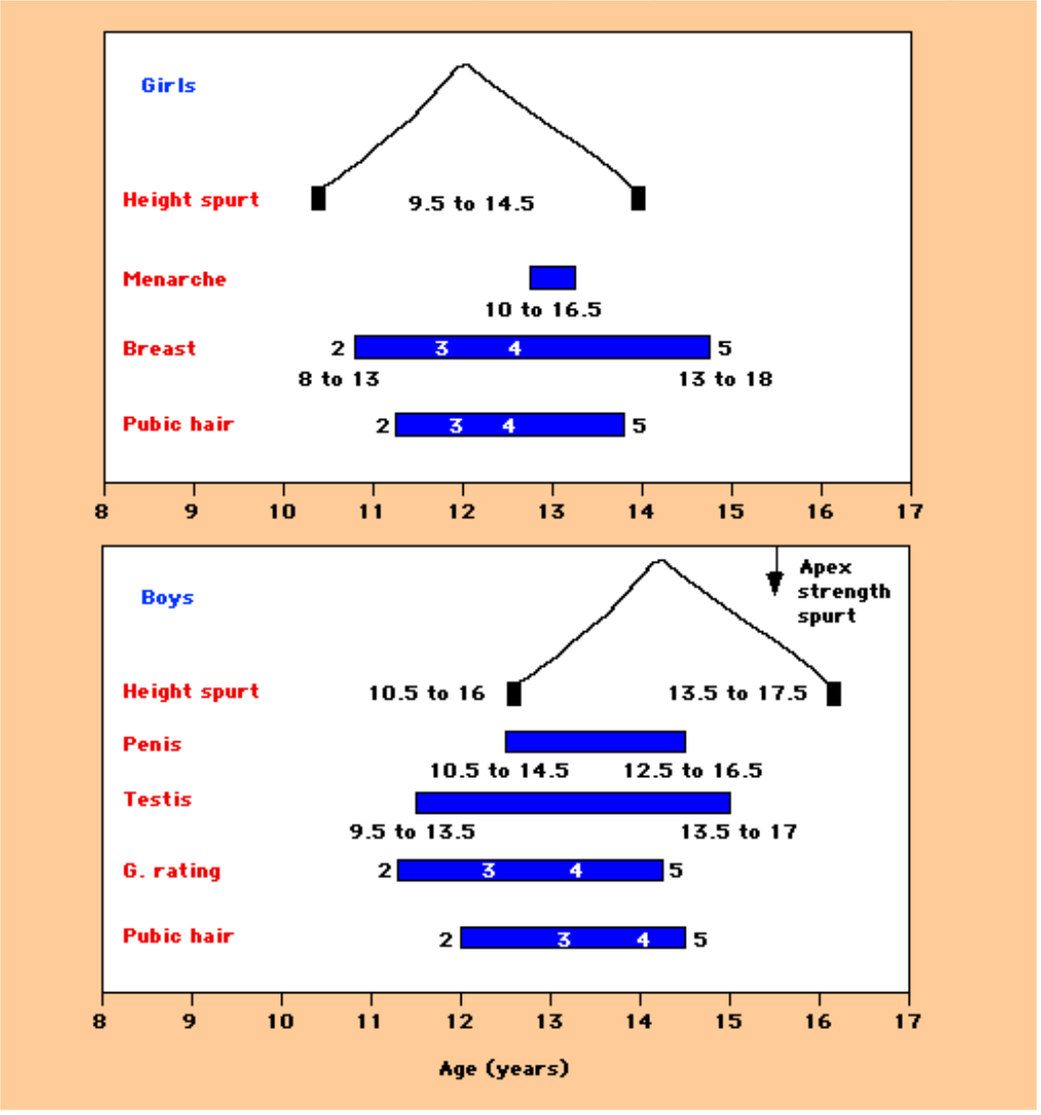
Both sexes: pubic hair

- *Stage 1:* Preadolescent: the vellus over the pubes is not further developed than that over the abdominal wall, that is, no pubic hair
- *Stage 2:* Sparse growth of long, slightly pigmented downy hair, straight or slightly curled at the base of the penis in boys, or chiefly along labia in girls
- *Stage 3:* Considerably darker, coarser and more curled. The hair spreads sparsely over the junction of the pubes
- *Stage 4:* Hair now adult in type, but area covered is still considerably smaller than in adult. No spread to the medial surface of thighs
- *Stage 5:* Adult in quantity and type with distribution of the horizontal (or classic 'feminine') pattern. Spread to medial surface of thighs but not up linea alba or elsewhere above the base of the inverse triangle (spread up linea alba occurs late and is rated stage 6)

Normal Puberty Development.

Normal ages for onset of puberty are 8-13 years in girls, with the mean age being 11 years and 9-14 years in boys, with a mean age of 11.5 years.

The table below shows the different age ranges for pubertal milestones in girls and boys.



Timing of pubertal milestones In girls, the first sign of puberty is the onset of breast development (thelarche) which occurs at a mean age of approximately 11 years; this is followed by pubic hair growth and menarche. In boys, the first sign is testicular enlargement which occurs at a mean age of approximately 11.5 years; this is followed by penile and pubic hair growth. In The diagrams above demonstrate the sequence of events at puberty. An average boy and girl are represented in relation to the scale of ages. The range of ages within which some of the changes occur is indicated by the figures below them. (Data from Marshall, WA, Tanner, JM. Arch Dis Child 1969; 44:291.)

Late Puberty

Delayed puberty (late puberty) is failure to develop secondary sexual characteristics by a certain age, usually set as two standard deviations from the mean. By this definition, 2.5% of the population will be considered to have pubertal delay. Pubertal arrest, which is defined as no progress in puberty over two years, is also included in the definition of pubertal delay. In girls, delayed puberty is defined as lack of breast development by age 13 years (some authors use a cut-

off of 12 years), lack of pubic hair by age 14 years, lack of menarche by age 16 years, or greater than five years between thelarche and menarche.
In boys, puberty is considered delayed if testicular enlargement does not occur by 14 years of age, there is lack of pubic hair by age 15 years, or more than five years are required to complete genital enlargement.4

Early Puberty
Precocious puberty refers to the appearance of physical and hormonal signs of pubertal development at an earlier age than is considered normal. For many years, puberty was considered precocious in girls younger than 8 years; however, recent studies indicate that signs of early puberty (breasts and pubic hair) are often present in girls (particularly black girls) aged 6-8 years. For boys, onset of puberty before age 9 years is considered precocious.[5]

In many countries, including Australia, children appear to be going through puberty at an age which is much younger than children in previous generations. This is called the secular trend in growth and development. The earlier age of puberty is probably due to effects of improved nutrition and living circumstances and absence of chronic disease. This seems to be particularly true for girls, with many girls showing early signs of breast development just before 8 years of age and starting to have menstrual periods while still in primary school. In most cases this early puberty is just a variation of normal.

Bone Age is a useful indicator of timing of puberty. Delayed bone age suggests late onset of puberty.

[4] http://pediatrics.uchicago.edu/chiefs/ClinicCurriculum/documents/RWPubertyNormalanddelayed.pdf
[5] http://emedicine.medscape.com/article/924002-overview