Clinical Algorithms

Delayed puberty

A J CHAPMAN

Puberty is a period of changing patterns of hormone secretion culminating in sexual maturity and fertility. An increase in adrenal androgen output and an altered hypothalamic pituitary sensitivity to circulating steroids are its earliest manifestations. A pulsatile pattern of gonadotrophin secretion, initially nocturnal, develops with a consequent rise in gonadal steroid synthesis. The somatic features that follow from these hormonal stimuli have been described and staged by Tanner.¹

In girls the appearance of subareolar breast budding (thelarche) marks the onset of puberty. Secondary sexual hair growth (adrenarche) and an increased rate of growth follow closely. First menstruation (menarche) is a late pubertal feature. In boys testicular enlargement to more than 2 ml, as assessed by a Prader orchidometer (figure), constitutes the earliest pubertal sign. There is a gradual increase in sexual hair and penile length. The pubertal increase in rate of growth occurs later in boys than in girls.

A Prader orchidometer for measuring size of testes in genital development. Models are marked according to their volume in cubic centimetres.

The age of onset of puberty varies within a wide range. Delayed puberty is therefore a somewhat arbitrary term, but 97% of boys and girls would be expected to show some signs of puberty by their 15th or 16th year. Complete lack of pubertal development in girls by their 14th birthday and boys by their 15th birthday warrants investigation. The causes of delayed puberty are many (algorithm), but it must be emphasised that most are rare. Constitutional delayed puberty is the most common type and is more common in boys than girls. In practice, girls presenting with delayed puberty on the basis

of absent menarche, or boys presenting because they have not started a growth spurt, are often found to have early signs of puberty.

Diagnosis

History and examination will often show the cause of delayed puberty. The most useful aid to diagnosing delayed puberty is a Tanner growth chart. On this is represented the third to 97th percentile distribution of normal height and weight between the ages of 9 and 18 years. The stages of puberty are also summarised. Separate charts are available for boys and girls.

HISTORY

The patient's history will often show the cause of delayed puberty. Chronic childhood diseases of renal, cardiorespiratory, or gastrointestinal systems will all result in delayed development. Insult to the hypothalamic pituitary gonadal axis from irradiation or chemotherapy is an increasingly recognised problem as children with previously fatal disease are now surviving into their teens. Psychiatric history is relevant to delayed puberty: emotional deprivation has been reported to delay puberty, though this is difficult to assess, and anorexia nervosa is an important illness that may prevent pubertal development. Intellectual impairment may be associated with hypogonadism as in Klinefelter's syndrome. There is no evidence that constitutional delayed puberty is familial, although a history of delayed development in an older brother or sister often helps to reassure the patient that he or she is progressing normally, albeit slowly, into puberty. The age at which the father or mother entered puberty may be a relevant factor in determining the age of onset of puberty in their children. Certainly the heights of the parents are important in determining the expected final height of a patient. Various familial diseases are, however, associated with delayed puberty, such as the many syndromes of spinocerebellar degeneration.

EXAMINATION

General—Examination should always start with assessment of height and weight. Accurate measurements should be plotted on a growth and development record chart. Height and weight can also usefully be plotted against bone age as well as chronological age, bone age showing a better correlation with pubertal development. Excess weight is a feature of growth hormone deficiency, often associated with gonadotrophin deficiency. Conversely, a relatively low weight results from malabsorption. A patient in his or her late teens who is excessively tall may show the eunuchoid proportions of primary or secondary hypogonadism. The webbed neck and wide carrying angle of Turner's syndrome are also noted during inspection of body habitus. Detection of cardiovascular abnormalities

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such as septal defects or aortic coarctation during systematic examination should alert the examiner to the possible diagnosis of Turner's or Noonan's syndrome.

Specific—Examination of the genitalia and secondary sexual features includes inspection of hernial orifices and, if indicated by initial examination and investigation, rectal examination. If examination shows genitalia appropriate to the gender of the patient the pubertal stage must be accurately recorded. Inappropriate or ambiguous genitalia, testes in hernial orifices or labia, or a blind ending vagina necessitate consideration of the various hermaphrodite and pseudohermaphrodite conditions. Abnormalities of the cranial nerves should be looked for. Visual field defects result from suprasellar extension of pituitary tumours. Anosmia is a variable feature of hypothalamic hypogonadism (Kallmann's syndrome). Congenital deafness is associated with pure gonadal dysgenesis.

Investigation and treatment

The algorithm shows a scheme for investigating delayed puberty. Its investigation and treatment are properly matters for the specialist, and early referral should be the rule. As stated above, however, most boys and girls will turn out to be normal. In the presence of an unremarkable history and examination, particularly if early signs of puberty are apparent, an expectant policy may be adopted. In such cases assessment of bone age is the single most useful investigation, and it is to this that height, weight, and pubertal state should be correlated. If there is no discrepancy between these indices and the patient's bone age, observation over six months is reasonable. If by the end of this time the patient has not started to develop or grow at a normal rate he or she should be referred for a specialist opinion.

In practice, children referred for an endocrine opinion are

often subjected to "screening," which includes estimation of bone age, radiography of the pituitary fossa, and combined pituitary function tests. Chromosomal abnormalities underlie a number of conditions, particularly in phenotypic girls, and this should be an early investigation. Patients with a relatively low weight should be investigated for malabsorption. It is important to reach a correct diagnosis as quickly as possible in order to minimise the distress that delayed puberty produces in teenagers. Treatment of the many rare conditions often requires collaboration between endocrinologist, surgeon, and, sometimes, psychiatrist and is outside the scope of this article. The most common diagnostic and therapeutic problem is isolated gonadotrophin deficiency. Serum and urinary gonadotrophin concentrations, response to luteinising hormone releasing hormone stimulation, and sleeping patterns of luteinising hormone secretion do not consistently distinguish between the two conditions. It has recently been suggested that prolactin responses to thyrotrophin releasing hormone differ sufficiently in these two conditions to allow a distinction to be made.² An expectant policy to resolve the problem is not always acceptable to the patient. In such cases puberty may be induced with human chorionic gonadotrophin or testosterone in boys and oestrogens in girls. Once puberty has been started using agents, they may be withdrawn. The patient with constitutional delayed puberty is usually able thereafter to continue through puberty unaided.

References

- 1 Tanner JM. Cited in: Marshall WA. *Human growth and its disorders*. London: Academic Press, 1977:61-85.
- 2 Spitz IM, Hirsh HJ, Trestian S. The prolactin response to thyrotrophin-releasing hormone differentiates isolated gonadotrophin deficiency from delayed puberty. *N Engl J Med* 1983;308:575-9.
- 3 London DR. Disorders of the reproductive system. In: Weatherall DJ, Ledingham JGG, Warrell DA, eds. *Oxford textbook of medicine*. Oxford: Oxford University Press, 1983:10.69-10.90.

MATERIA NON MEDICA

Paths of prehistory

Why do it? Why walk 80 miles in freezing December weather on the South Downs Way? Get cold and wet . . . madness or masochism? And yet I had a few days' holiday owing and I tried to persuade my wife we should go somewhere warm or artistic—Paris, Rome, or Athens. "No," she said, "we have just moved into a new house and I want to just relax peacefully at home. Why don't you go for one of your long walks? You know you like them." So off I went with waterproofs and spare clothing. I didn't go so far as to offer to sleep in a tent, preferring to find bed and breakfast as I went along.

The South Downs Way stretches from just south of Petersfield in Hampshire to Eastbourne in East Sussex, and for most of its path follows the edge of the escarpment, with superb views (when you could see them) across the Weald as far as the North Downs. It is one of the old trackways which iron and bronze age people used to move across country, avoiding the bogs and robbers of the lowlands. They also built banks and ditches and in some places large settlements on the downs—remains of their burial mounds line the route.

So here I was for six days treading the paths of prehistory. I wondered what kind of people had travelled this way, what they looked like, what kind of animals they had, what they were carrying, where they came from and where they were going. As the miles passed I built a picture in my mind's eye, a vision of what it might have been like on the track or in one of their fortified villages. I saw the tents of skin, the wood fires with food cooking, the lookouts and defenders. The picture became particularly strong when I stopped to munch some cheese, celery, and apple in one of those hilltop camps. I saw the families, the old and young, helping and working together. I could almost hear them talking . . . their spirits were certainly close at hand the whole week.

There were other companions on the downs, some more readily seen than others. Birds of all kinds were plentiful and rabbits too scampered through the woods or out of the hedgerows and across the fields. A fox or two

appeared on the path in the early morning or evening and roe deer were seen in the little copses or larger woods.

Early morning and evening were best, the former cold and foggy with the sun breaking through the mist as the path climbed the hill, shining with diamond like light on the frosted ground. Above the mist I was in a different Arcadian world of blue sky and immeasurable space.

I stayed in pubs or people's homes via the *Ramblers' Guide*—a surprise guest often at this time of the year. I had the pleasure of watching other people's families, and was taken willingly to two primary schools' Christmas plays. Sometimes I just relaxed by a cheerful log fire with a pint of beer. The surgery and the problems of inner cities were far away.—JOHN COHEN, general practitioner, London.

Faithful followers

The late Very Reverend Dr George Johnstone Jeffrey DD, a moderator of the general assembly of the Church of Scotland and a man of great good will and wit, was seldom caught out in matters of instant question and answer. But he told me how once, at least, he came very near to defeat. He had spoken to a group of children about the great metrical version of the 23rd psalm—*The Lord's my shepherd*—a piece of sacred music greatly, even excessively, revered in Scotland. He asked the children what they thought of it. "Not much," said a brisk little girl; "here is a psalm about a shepherd but it never mentions his dog." Dr Jeffrey confessed that he was momentarily stumped. "Let us read it through carefully," he suggested, "I'm sure we'll find something about the dog." As the reading went on he was at a loss until the first two lines of the last verse saved the day: "Goodness and Mercy all my life shall surely follow me." "There!" he exclaimed, "the names of not just one dog but of two; Goodness and Mercy, following the shepherd through all the days of his life, just as a shepherd's dogs always do."—J W HOWIE, Edinburgh.