Mode of Presentation

The general public are becoming increasingly aware that hormones are sometimes given to limit growth, and the number of tall children being brought to doctors' surgeries for advice is apparently increasing. There are three principal ways in which they present:

1. Tall parents are sometimes worried that their baby will grow to an excessive stature and seek medical advice in its infancy, although at that stage the child may not be unduly big (Figure 1).
2. Early in school life it is noticed that the patient is considerably taller than his or her classmates (Figure 2).
3. At puberty, when the adolescent growth spurt increases, the difference in size between a child who is already tall and his or her friends (Figure 3).

Usually the only presenting symptom is tallness, although in some adolescent girls the primary complaint is big feet. This complaint arises from the fact that the feet usually reach their adult size before the rest of the body, and there is a period during adolescence when the feet are almost full size and further growth in stature is still to come. The parents' fear that their daughter's feet will continue to grow very quickly is rarely justified.

Assessment

The objects of assessment are to exclude abnormality; to estimate the patient's final stature; and to decide whether or not treatment with hormones or by other means is desirable.

A routine history is taken and particular attention should be paid to the child's earlier growth, attainment of paediatric milestones and performance at school. Any history of ophthalmic or cardiovascular disorder in the patient or the family should be carefully noted. The statures, not only of the child's parents but of as many other adult relatives and forebears as possible, should be recorded and the statures of siblings should be plotted on a standard centile chart. In the case of adolescent girls it is important to ask whether or not menstruation has begun, and if so when.

The clinical examination should include accurate measurement of stature, assessment of pubertal development, if any, and the observation of any unusual features such as linearity of body-build, a narrow palate, and hands and feet which are disproportionately big or unduly long in relation to their breadth.

The child's stature is plotted on a centile chart together with that of the parents, In the case of boys 5 in. (12.7 cm.) should be added to the mother's stature before it is plotted, and in the case of girls 5 in. (12.7 cm.) should be subtracted from their father's stature before it is plotted. These adjustments allow for the difference between the adult centiles for the two sexes, and enable us to plot an adult's stature at the correct centile on a chart for the opposite sex. If the child is between two and nine years of age, then the charts of Tanner et al., (1970) may be used. These charts which were reproduced in an earlier article of this series show the distribution of the heights of normal children in relation to the sizes of their parents.

Most children who seek medical advice because of their tallness are perfectly normal and healthy. The object of further assessment is then to decide whether the patient's final stature will be within the limits which he or she will find acceptable. Basically we have to distinguish between the tall child who will become an unduly tall adult and the one who is tall only because he or she is an early maturer and will reach a quite acceptable final height (Figures 3 and 4).

At the age of six or seven it usually becomes possible to predict the child's adult stature from his present stature and skeletal age, as estimated from a radiograph of the hand and wrist. The estimation of skeletal maturity and the prediction of adult height are discussed in an earlier article. Predictions carried out in this way are probably not so accurate in the case of tall children as they are in the case of those who are nearer to average height, but in most normal individuals, the predicted adult stature is within 1.5 in. on either side of the true value. Sometimes, however skeletal maturation does not proceed at a uniform rate and a temporary slowing

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of skeletal development will falsely increase the prediction, or a temporary acceleration will lower it. Where possible therefore judgment should be based on a series of predictions over a period of time rather than on a single observation.

Before considering treatment it is necessary to exclude certain conditions which are associated with tallness but which may require management different from that of the normal tall child.

**Cerebral Gigantism (Sotos’ Syndrome)**

Excessive size is evident at birth and growth is especially rapid in the first three or four years, but final height may not be excessive. The hands, feet and cranium are large, with a long skull. There is a rather characteristic facial appearance due to an elongated chin and relatively thick subcutaneous tissues, with full lips. There is usually frontal bossing and the eyes are rather far apart with an antimongoloid slant. Radiographs of the skull show enlarged frontal sinuses. The sella turcica is usually large but within normal limits.

Skeletal age is usually advanced. Occasional non-specific EEG abnormalities and seizures have been reported. Low intelligence is common but not invariably present. This, in combination with poor co-ordination and large size in childhood, make social adjustment difficult. Treatment with androgens or oestrogens is not always desirable because it does not reduce the patient’s relative size in childhood and may even increase it. Only in those cases where it is apparent that the adult height will be unusually great should treatment be given.

**Marfan’s Syndrome**

This syndrome consists of long narrow hands with long fingers (arachnodactyly) hyperextensibility, lens subluxation and aortic dilation. There is a tendency towards tall stature with long slim limbs and little subcutaneous fat. Associated with joint laxity there may be scoliosis and kyphosis. The face and palate are usually narrow. In the eye, in addition to lens subluxation with defect in the suspensory ligament,
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Figure 1 (Left). Supine length at age 1 - 2 years and stature at age 2 - 4 years of the daughter of tall parents. The measurements are at the 90th centile, and the skeletal age (indicated by crosses) is approximately equal to the chronological age. The child is, in fact, quite small in relation to her parents, but is too young for any prediction of her final stature.

Figure 2 (Below). Repeated measurements of stature in a very tall but normal boy. The points show stature plotted against chronological age and the crosses show stature plotted against skeletal age. Skeletal age has remained consistently about three years in advance of chronological age. On the basis of the points he would appear to be heading for a final stature of about 6 ft. 6 in. but height predictions, taking his skeletal maturity into account, have varied from 6 ft. 3 in. to 6 ft. 5 in.

there may be retinal detachment. The ascending aorta may be dilated with or without dissecting aneurysm. Less commonly the thoracic or abdominal aorta or the pulmonary artery is dilated. There may be secondary aortic regurgitation. The syndrome is hereditary and its occurrence in the family history is a factor in diagnosis. Serious vascular complications may develop at any age and are the chief cause of death. The mean age of survival is 43 years for men and 46 years for women. Intelligence is normal. The ophthalmic and vascular complications of this syndrome are more important than the patient’s final stature and must be borne in mind if hormonal treatment is considered. It may be difficult to distinguish clinically between Marfan’s syndrome and homocystinuria, in which subluxation of the lens, mental defect and slim build with arachnodactyly are also found. There may be medial degeneration of the aorta and elastic arteries. The distinction can be made by biochemical estimation of homocystine in the urine. A completely satisfactory therapy has not yet been developed. Stature is rarely great enough to justify steps to limit growth and, in girls, oestrogen treatment is positively contraindicated as thromboembolic phenomena constitute the most dangerous feature of the disease.

Excessive Growth Hormone Production

This is rare in childhood but, when it occurs, it leads to excessive growth which may be accompanied by signs of acromegaly before growth has stopped. It almost invariably leads to acromegaly later. A pituitary adenoma of sufficient size to produce neurological symptoms is seldom found in children or adolescents, but there may be one which is detectable radiographically. The skull should therefore be X-rayed to exclude enlargement of the pituitary fossa and paranasal sinuses, which would strongly suggest this condition. The hand and wrist X-rays taken for height predictions should also be examined for acromegalic features.

In adult acromegals there is an abnormally high concentration of growth hormone in the blood. In normal subjects

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the serum growth hormone concentration is reduced by raising the blood glucose whereas in some acromegals this does not occur. There is a raised serum insulin concentration. Estimates of serum growth hormone and insulin in the course of a glucose tolerance test are therefore useful as part of the assessment of acromegaly. It is not yet possible to interpret this test satisfactorily during childhood as insufficient comparative data are available and in the absence of other evidence of pituitary hyperfunction or tumour, this test should not be taken as a basis for deciding to ablate all or part of the pituitary gland by surgical or radiotherapeutic means. When the clinical and radiographic evidence indicates that there is an adenoma such treatment may be considered but should be avoided, as far as the other circumstances of the case permit, until puberty is complete.

Other Rare Conditions

Other rare conditions to be considered include Berardinelli's lipodystrophy syndrome in which there is accelerated growth and hyperlipemia in early childhood and hyperglycaemia may develop later. There is also enlargement of the hands, feet, penis and liver, hypertrophy of muscle and lack of adipose tissue from early life. Death may result from cirrhosis of the liver with oesophageal varices. In Wiedermann-
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Figure 4. Growth of a child with constitutional precocious sexual development. This was accompanied by rapid maturation of the skeleton and early attainment of adult height. The joined up points indicate her stature and the crosses indicate her skeletal age. 'M' indicates menarche. Note that she was a very tall child, but after she had begun to menstruate, just after her sixth birthday her growth slowed down and had very nearly ceased when she was last seen at the age of 111 years. It is unlikely that her final stature will be above the tenth centile.

Beckwith syndrome, macroglossia, omphalocoele, macrosomia and cytomegaly of the foetal adrenal are found. Early postnatal growth may in fact be slow but later stature is usually in the region of the 90th centile and skeletal maturation is advanced. General growth may allow adequate room in the mouth for the large tongue. Partial glossectomy has been successfully performed. Prognosis beyond childhood is unknown at present. Hyperthyroidism may cause tallness and should be excluded.

During the period of assessment parents should be asked to consider and, where possible, to discuss with the child the maximum adult height which they would find acceptable. At the same time the advantages and disadvantages of the possible treatments should be explained to them.

Treatment of Normal Tall Children

If the child has no clinical abnormalities and a stature below the 97th centile then no further immediate action is indicated but the child should be remeasured and X-rayed at annual intervals, to ensure that it is not growing at above the average rate, as this would increase its centile status. Even if the child's stature is a little above the 97th centile but fully compatible with that of the parents the same course may be adopted. When the stature is well above the 97th centile or is
not in keeping with that of the parents then the patient should be referred to a specialist.

Both medical and surgical treatments may be applied to limit the growth of normal children. The medical treatment is to give androgens to boys or oestrogens to girls.

The earlier the age at which treatment begins, the greater is the reduction in final height which is likely to be achieved. However, as the treatment causes development of the secondary sex characters, too early a start would cause undue psychological problems and in extreme cases, might cause too much limitation of growth. It is rarely desirable, in practice, to begin treatment before a chronological age of about ten years. At this time, of course, the skeletal age may be either more or less than ten. In girls whose skeletal age is less than 13 years when treatment begins it is not unreasonable to hope that the final stature may be about two inches below the predicted value, but it is not yet possible to predict how effective the treatment will be in an individual case. If the skeletal age is more than 11 2/3 years, the treatment is unlikely to be very effective. The upper age limit for the effective treatment of boys is not known, but it seems improbable that any significant result would be obtained at a skeletal age of more than 14 years.

Androgens usually cause an initial acceleration of growth but oestrogens seldom do so. An initial acceleration is more likely if treatment begins early in the child’s natural puberty than if it is given later. Both treatments cause development of the secondary sex characters and are usually accompanied by an early development of skeletal maturation although this may not be apparent for the first six months. The object of treatment is to accelerate skeletal maturation to such an extent that the amount of time it takes for the child’s stature to increase is greatly diminished and, even though growth may be accelerated in the first instance, the ultimate stature attained should be less than that which would have been attained without the treatment.

It is difficult to assess the value of such treatment because we can compare the final height achieved only with the prediction of height which was made before treatment began. As we have already stated, these predictions in tall children are not always as accurate as one would like. However, there have been cases in whom the difference between the predicted and final height has been sufficiently great to leave little doubt that the treatment has had some effect. Generally, the earlier the treatment the rather the success.

The use of testosterone to limit growth in boys has the disadvantages that initial acceleration of growth, combined with the early development of the secondary sex characters, may only accentuate the boy’s psychological and social difficulties if he is already self-conscious about his stature. If treatment is long there is a risk of impaired fertility.

The administration of oestrogens to girls presumably carries with it the same risks as accompany the use of oral contraceptives in adults, and most authorities agree that a much higher dosage of oestrogen than is used for contraceptive purposes must be used for effective limitation of growth. There have been reports of venous thrombosis in girls taking oestrogens to limit their growth but there is at least a theoretical possibility that this might occur. Cyclic menstrual bleeding is induced by the oestrogen but treatment is not infrequently followed by a period of amenorrhea. If some cases this probably means only that the central nervous system has not yet reached that stage of maturity at which cycles are normally established and the 'periods' which occur during treatment are only the result of the direct action of oestrogen on the uterus. In these cases we are simply waiting for the natural menarche to occur at its proper time. It is however possible that in some cases the treatment interferes with the onset of normal cycles and there is the possibility that there might be some long-term loss of fertility although, again, there is no evidence that this has ever occurred. Also oestrogens may increase risk of carcinoma in later life.

There are some who argue that the risk of any of these misfortunes occurring is so small that it can for practical purposes be ignored. The author, on the other hand, takes the view that even this slight risk is not justified unless there are good grounds for believing that the patient is heading for an adult height which will be a serious handicap. It is seldom justifiable to give oestrogens to a girl whose height prediction does not exceed 6 ft., although of course all the circumstances of the case must be considered and there can be no absolute rules. If medical treatment is given, it should be under specialist supervision.

Surgical treatment can take the form either of limitation of growth of the epiphyses or actual shortening of the shaft of the bone. Surgery has the advantage that its end results are rather more predictable than in the case of hormonal treatment. It has the further advantage that it can be carried out later in life when the patient can make up his or her own mind about whether or not treatment is necessary and need not rely on the judgments of parents or doctors. As it is sometimes possible to shorten the legs by as much as 5 inches, the effectiveness of surgical treatment as far as stature is concerned cannot be denied. Fortunately many tall children have legs which are relatively long in relation to the trunk, and a reduction in their length does not lead to any obvious disproportion. It is however possible that the arms, hands and feet might seem unduly large. Surgery inevitably involves a period of incapacity, but once over, the results are apparent and there is little likelihood of after effects.

Even if the predicted height is not great enough to justify medical or surgical treatment, reassurance and psychological support may be required. Tall girls often tend to slouch and may need encouragement to maintain a good posture.

Reference


In Dr. W. A. Marshall’s article, ‘Understanding Growth Rates’, published in November 1971 issue of Update, an error occurred on Figure 4b, page 1427. The arrows labelled ‘M’ indicating age of menarche should be at the same ages as in Figure 4a on page 1426. The red arrow should be at age 11.8 years on the red curve, and the green arrow at age 13.8 years on the green curve.