Conclusion

Obviously our service as organised in Poole would not be suitable for all diabetic clinics. Such a service must be tailor-made to suit local conditions. The mini clinics organised in Wolverhampton² would be unsuitable here because most local family practitioners prefer to look after their own patients.

The service has been criticised as being just a way of relieving the heavy work load for a consultant in a diabetic clinic, but it is also important to see it as a means of providing better and improved care for the diabetic within the community and allowing the consultant to deal with the difficult problems for which he has been trained.

I would like to acknowledge the help and advice given by my colleagues at Poole General Hospital, in particular by Dr C E Upton, the clinical assistant. I would also like to thank all the general practitioners in the area, without whose support the scheme could not operate. My thanks are also due to Winthrop Laboratories and Hoechst Pharmaceuticals Ltd for their continued help. I would also like to thank Mr R Stanton, computer manager, Basingstoke District Hospital.

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Problems of Childhood

Short stature

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British Medical Journal, 1976, **1**, 1139-1141

Short stature may be a sign of treatable disease and a cause of distress by itself. Assessment is essential as early as possible in childhood for two reasons: firstly, treatment, if appropriate, is effective only if started well before the epiphyses fuse; and, secondly, when no specific treatment is available, an informed prognosis at an early stage may allay anxiety and enable advice and support to be given to the child.

Definition

There is no clear demarcation between normal and abnormal stature and so the definition of short stature is arbitrary. As a general rule, however, any child whose height falls below the third centile line for his community is considered to be short. In Britain the most appropriate and recent standards are the centile charts* prepared by Professor Tanner and his colleagues.^{1 2} The most useful ones have an extra line indicating three standard deviations below the mean (the third centile line is -1.9 SD).

Children with heights above the third centile may have disorders restraining their growth, but in such patients short stature is unlikely to be the presenting symptom. Occasionally, however, the parents of a child whose height falls above the third centile line will feel that he is short for their family. In these circumstances special charts that make allowance for parents' heights are of value.³

*These and the other charts prepared by Tanner and referred to in this article are available commercially from Creaseys Ltd, Castlemead, Gascoyne Way, Hertford.

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Causes of short stature

The characteristic features of the main causes of short stature, their treatment, and the degree of stunting of adult stature that they produce are given in the table. In patients without disease the expected adult height may be reasonably estimated with a knowledge of present height and bone age and the help of special tables or growth charts.^{5 6}

Accurate figures of the incidence of most of the conditions in the table are not available, though most are very uncommon—for example, the approximate incidence of growth hormone deficiency is 1/10 000 and that of Turner's syndrome 1/3000 girls. In a recent urban community study only 16% of children whose heights were below the third centile had organic disease, and in most instances the nature of this was an obvious general disease, such as Down's syndrome, cyanotic congenital heart disease, or cystic fibrosis. Among the 84% "short normal" children at least a third came from severely depriving backgrounds and these children were not only stunted physically but also retarded in tests of intellectual function. Thus social deprivation is the most common pathological cause of retarded growth in this country.

Although the other conditions are uncommon causes of short stature, some are particularly important because specific treatment is available. Thus the approach to children who are short must take into consideration both the most likely causes and the treatable causes.

Diagnosis

SCREENING

Not all mothers of short children seek advice. In our experience 70% of mothers of children whose heights were below the third centile recognised that their child was short, though only 10% sought medical advice. Therefore routine measurement of all children should be done at some stage. There are obvious administrative advantages in this being done at school entry at the age of 4 or 5, although clearly children who are brought at an earlier age with short stature as a clinical problem should be investigated then.

All children whose heights are below the third centile should be seen by the school or family doctor when particular attention should be paid to the following points.

History—The history should include the parents' heights; the weight and gestational age of the child at birth; the pattern of growth since birth—for instance, from child welfare clinic records; the appetite, energy, and well-being of the child; any specific symptoms; and the social history, possibly from the health visitor who knows the family.

Causes of short stature

Main types	Clinical features	Bone age	Specific treatment	Adult stature
Disproportionate				
Short limbed: Achondroplasia	Inherited as a dominant; large cranium, lumbar lordosis	Normal but characteristic radiological appearances	None	Very short
Diastrophic dwarfism	Inherited as a recessive; club feet, scoliosis			
Short trunk: Morquio syndrome For other examples see Smith ⁴	Short spine			
Genetic				
Short adult stature	Family history of short stature. No other symptom or sign. Height usually not far below third centile	Normal	None	Near third centile
Delayed maturation	Family history of delayed maturation. Delayed puberty. Shortness of stature most definite just before puberty growth spurt begins	Delayed	Occasionally short courses of anabolic steroids justified	Normal for family
Combined	May be very short	Delayed	Occasionally short courses of anabolic steroids justified	Usually near third centile
Low birth weight				
Result of prolonged restraint of intrauterine growth	Low birth weight for gestational age	Often slightly delayed	None	Usually near third centile
Russell-Silver syndrome	Slim. Asymmetrical; comparatively large cranium	Often slightly delayed	Growth hormone has slight but clinically insignificant effect	Usually significantly below the third centile
Nutritional				
Celiac disease	Usually large abdomen or tendency to diarrhoea or anaemia	Delayed	Gluten-free diet	Normal if treated
Disease of major organ or metabolism				
Cyanotic congenital heart disease Chronic renal failure Chronic infection Mental retardation	Usually present either with symptom of underlying disease or with obvious ill health, poor appetite, and lack of energy	Often slightly delayed	Appropriate for underlying disease	Varies with underlying disease
Syndromes				
Chromosomal: Turner's syndrome	Characteristic features of webbed neck and wide carrying angle may not be present, but primary amenorrhoea is invariable. Height progressively falls below normal throughout childhood	Delayed increasingly with age	Replacement oestrogen and progesterone near usual age of puberty	Usually very short
Other: See Smith 1970 ⁴	Worth considering possibility of a syndrome if short stature is associated with more than one other abnormality	Varies, often delayed	None	Variable but often very short
Endocrine disease				
Growth hormone deficiency: Idiopathic	Normal birth weight. Slow rate of growth evident after the age of 2. Tendency to increased amount of subcutaneous fat	Moderate retardation	Human growth hormone by injection 2 or 3 times a week from age of diagnosis until growth ceases	Within normal range if treatment started early in life
Secondary to intracranial pathology especially craniopharyngioma	Usually associated with other hormone deficiency such as diabetes insipidus. Slow growth may not occur until after primary disease has been treated			
Thyroid deficiency	In juvenile hypothyroidism classical symptoms and signs (constipation, cold sensitivity, dry skin and sparse hair, and delayed deep tendon reflex relaxation) may not be obvious	Marked retardation	Thyroxine	Within normal range if treatment started early in life
Cortisol excess	Cushing's syndrome in childhood whether the result of pituitary or adrenal disease or of steroids given therapeutically is invariably associated with short stature	Retarded	Treat cause	Normal
Precocious puberty	Before the epiphyses fuse children with precocious puberty are tall for their age. Premature fusion of the epiphyses result in stunted final height	Advanced	Treat cause	Usually stunted
Social				
Multiple deficiencies in poor overcrowded families	Parents may be short as a result of poor environment during their childhood. Child often thin physically and delayed educationally	Retarded	Material or social help to family. Extra food and support at school	May be permanent though not gross stunting
Gross emotional deprivation	Clinically and biochemically may resemble true growth hormone deficiency. There is often a history of voracious appetite or excessive thirst	Retarded sometimes grossly	Social and psychiatric help to family and child. Permanent separation of child from family may be necessary	Permanent stunting may occur

Examination—During a general physical examination note should be made of the child's proportions, in order to recognise any child whose limbs are unusually short; the standard of nutrition; the presence of any minor abnormality or abnormal facies; the child's colour, size of the abdomen, and appearance of the optic discs and routine examination of the urine.

As a result of this initial assessment it should be possible to place each child into one of the following four groups.

(1) Those who should be referred for further investigation. Indications for this are: (a) a height that is further than three standard deviations below the mean (the shaded area on the charts (2)) or (b) any abnormal symptoms or sign, such as lack of energy, a tendency to diarrhoea, signs of anaemia, abnormality in the urine, or (c) a slow rate of growth (see 4).

(2) Those who are normal and short for genetic reasons. This diagnosis may be made confidently in children who are well, who have no abnormal symptom or sign, whose heights are near the third centile line (not more than 3 standard deviations from the mean), and those who have one parent whose height is near or below the third centile (162 cm (5 ft 4 in) in boys and 151 cm (4 ft 11½ in) in girls).

(3) Those who have no physical disease but are suffering as a result of social problems or deprivation. Children whose heights fall between the third centile and the -3 SD line, who have no other abnormal signs and whose home circumstances are very poor fall into this group. It is important to recognise these children early in their school careers as extra help physically, socially, and intellectually at school may partly compensate for early deficiencies. The progress of these children during their early years at school should be watched carefully and their heights and weights remeasured occasionally.

(4) Those who should be remeasured a year later. Children whose heights fall between the third centile line and the -3 SD line, in whom there is no obvious explanation for shortness and who are well, should be remeasured after one year at school. If their growth rate during that time has been slow (5 cm or less) they should be referred for further investigation (see 1).

FURTHER INVESTIGATION

The children referred for investigation should be those who are very short, who are growing slowly, and with symptoms or signs of ill health. In addition it is entirely appropriate for children, usually older ones, who are worried about their lack of height, to be referred. The purpose of investigation is to diagnose the reason for the short stature, particularly the possibility of a treatable cause, and to enable an informed prognosis of adult stature to be given, which is particularly important for normal, slow maturing children.

At hospital the paediatrician will carry out a careful physical examination including measurements of sitting as well as of standing height. These measures (plotted on the appropriate chart) will enable the group of children with disproportionate short stature to be recognised and referred for detailed radiological investigations. Children in whom there is no obvious cause for short stature should have their bone age estimated and an x-ray film of the skull taken and should have investigations to exclude the following diagnoses: (a) Turner's syndrome, in all girls, preferably by chromosomal analysis, (b) severe renal disease by urine culture and blood urea or creatinine, (c) hypothyroidism by protein bound iodine, free thyroxine index, and if possible thyroid stimulating hormone estimations, (d) malabsorption syndrome; if there is any clinical suspicion of this condition jejunal biopsy should be done, and (e) growth hormone deficiency; it is not appropriate to consider growth hormone deficiency until the other diagnoses have been excluded because some of them may lead to confusingly low serum growth hormone levels.

Growth hormone deficiency is unlikely to be confirmed in children without the classical clinical features of normal birth weight, slow growth rate, and plumpness (a skinfold measurement above the average). Nevertheless, now that safe and simple screening investigations have been developed it is appropriate to consider this diagnosis in all very short children in whom no other explanation can be found. The easiest outpatient screening method is the exercise test, a single blood specimen for growth hormone analysis being taken 30 minutes after the beginning of a ten-minute period of hard exercise. This is most easily done by using a stationary exercise bicycle. In children of 8 or more the necessary exercise is roughly equivalent to riding two miles uphill. The most important feature however is that the amount of exercise should be tiring for the child; a fit child requires to exercise harder than a less athletic one.

An alternative screening test, the method of choice in young children, is a sleep test. There is a pulse of growth hormone release during the first half-hour of the initial phase of deep, slow wave sleep. This test clearly is best done with electroencephalogram control but this is seldom practicable. A reasonable alternative is to take two or three samples of blood through an indwelling catheter during the first hour of sleep.

A serum growth hormone level of 20 IU/l excludes growth hormone deficiency. If a lower level is found during screening, the test should be repeated or a more powerful stimulus to growth hormone release employed. Several tests have been devised (Bovril, glucagon, arginine, levodopa) but these are less satisfactory than insulin-induced hypoglycaemia, and except in very unusual circumstances (for instance, a child who gets dangerous or severe spontaneous hypoglycaemia) have little place. Before subjecting a child to an insulin tolerance test, it is right to be sure that other causes of low serum growth hormone (emotional deprivation, obesity, hypothyroidism, and coeliac disease) have been excluded.

To be effective an insulin tolerance test should lead to a fall in blood glucose to half the fasting level and cause symptoms of hypoglycaemia. The usual dose of insulin needed is 0.1 U/kg by intravenous injection, but occasionally up to twice this dose may be given. Whenever an insulin tolerance test is done an intravenous infusion of normal saline should be running, to enable intravenous glucose to be given urgently if needed, and a member of staff should stay with the patient throughout the test. Usually half-hourly blood samples for blood glucose, cortisol, and growth hormone are taken over a two-hour period. Failure of growth hormone to reach 10 IU/l during a satisfactory insulin tolerance test is good confirmatory evidence of growth hormone deficiency and a level of 10 to 20 IU/l is compatible with a diagnosis of partial growth hormone deficiency. In either case a trial of treatment with human growth hormone should be given. This treatment, which inevitably is in very short supply, and incidentally is effective only in patients who are growth-hormone deficient, is at present prepared and distributed by the Medical Research Council, through a series of growth clinics or measurement centres.²

Conclusion

The scheme of assessment and investigation outlined in this article could result in all children whose short stature can be treated being recognised and on treatment by the age of 7. Short children who present at other times than the school medical examination should, of course, be assessed similarly: younger children because the earlier the treatment is started the better the results; and older children because treatment started before puberty has some worthwhile effect. At any age, especially when specific treatment will not help, an informed prognosis and discussion will.

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Is there any useful or effective treatment for an elderly man with primary amyloid disease?

There is no effective treatment for primary amyloidosis. Corticosteroids are contraindicated and immunosuppressive drugs are ineffective. All that can be done is to treat symptoms while remembering that patients with amyloid disease may be sensitive to drugs such as digitalis. It is perhaps worth pointing out that amyloid may be detected in tissues from over half of elderly people by sensitive techniques and its presence does not necessarily constitute disease. Even when its presence interferes with function the course of the illness is variable and may be prolonged.