values make interpretation of coagulation tests unreliable, but our diagnosis of dysfibrinogenaemia was based on the grossly prolonged reptilase time compared with the thrombin time. If simple hypofibrinogenaemia were responsible, we would have expected both times to have been similarly prolonged. Furthermore, the coagulation factor assays are independent of the patient's fibrinogen value.

As regards the diagnosis of congenital or hereditary tyrosinaemia, the record needs to be put right. It is correct to say that tyrosinaemia (with abnormally excretion of phenolic acids) and hypermethioninaemia alone, do not indicate the diagnosis. In all three infants reported, not only was there evidence of acute liver necrosis but also of severe proximal renal tubular disease characterised by proteinuria, gross generalised aminoaciduria, phosphaturia, hypophosphataemia, and early rickets accompanied by considerably raised serum alkaline phosphatase, mainly of bone origin. The galactose-1-phosphate uridyl transferase deficiency galactosaemia was excluded in all, and none of the infants received fructose in the diet or in medication. 

These observations strongly favour the diagnosis of congenital or hereditary tyrosinaemia of acute variety; unfortunately necropsy examination in the first two patients was not available. As for galactokinase deficiency galactosaemia, liver disease does not occur in this disorder.

References

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Lest we forget

Sirs,

Your editorial1 was a splendid reminder to us to be primarily people-oriented. Your question, 'How often do we in our postgraduate and in-service training discuss the problems of children in hospital, their psychological needs, and the needs and the problems of unrestricted access for parents?' is timely.

Now we are in the third decade of 'deinstitutionalisation' of the severely mentally handicapped, do we need to ask a similar question? 'How often do we in our postgraduate and in-service training discuss the problems of severely subnormal children living at home, the physical and psychological needs, and all the problems of parents continuing to care for over grown toddlers who are extraordinarily slow to learn?'

How often do we reflect on the needs of the mothers of the severely handicapped? How often do we consider her fourfold role as: (a) Mother of the handicapped child; (b) Mother of the other children; (c) Wife; (d) Needing time/space to be 'herself'.

If we are to support the severely subnormal in the community then we must be acutely aware of the needs and stresses of those who provide day and night care, too often, without a break.

Reference
1 Anonymous. Lest we forget. [Editorial]. Arch Dis Child 1985;60:93.

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Who should get growth hormone?

Sir,

The four papers on the assessment of potential candidates for growth hormone treatment1-4 contain some contradictions that may lead to misunderstandings among readers. These contradictions originate mainly from different definitions of growth hormone deficiency.

The two papers on exercise tests2 3 emphasise the latter half of the classic definition, that is the combination of a growth velocity below the 25th centile for age or bone age and a growth hormone response to adequate insulin hypoglycaemia under 15 mU/l. The commentary4 emphasises the first half of this definition. Low growth velocity is considered as an absolute requisite for the diagnosis, but no indication is given as to which growth velocity is abnormally low. If the classic 25th centile were used, 25% of the children would have to be tested.

There is increasing evidence that the classic definition has lost its usefulness. Studies on 24 hour growth hormone profiles in short children have shown that the results of provocation tests are poor parameters of growth hormone secretory status and poor predictors of growth response to long term treatment.

In my opinion, growth hormone deficiency should be defined as the condition in which either the total 24 hours' production of growth hormone, or the frequency or amplitude of peaks, or both, is below normal. This does not imply that the classic criteria (growth velocity and biochemical tests) would lose their role in the diagnostic process. In case of low growth velocity and low responses to provocative stimuli, growth hormone deficiency can be diagnosed without 24 hour profiles. Such profiles, however, could be made in children with short stature or low growth velocity, or both, and growth hormone responses greater than 15 mU/l in order to confirm or exclude growth hormone deficiency. In case of normal growth hormone production a therapeutic trial might still be indicated, as children with abnormal growth hormone molecules or partial receptor defects seem to respond favourably to treatment.

In conclusion, in one issue of the Archives growth hormone deficiency is defined in the classic way2 3 as well as in a more updated way.1 4 Suggestions that growth
hormone response to provocative stimuli of more than 15 mU/l would exclude a positive response to long term treatment\(^2\) and could result in treatment being withheld from patients who might benefit from it.

References
\(^1\) Milner RDG. Who should get growth hormone? Arch Dis Child 1984;59:1115-7.

Dr Forsyth and co-workers comment:

Dr Wit in his letter makes several points requiring an answer.

(1) He wishes clarification of the investigation of growth hormone deficiency. The purpose of the two papers on exercise tests from Dundee and Newcastle was to emphasise the usefulness of exercise, a physiological stimulus, in the early investigation of growth hormone deficiency, provided the exercise is carried out in a scientific manner. The Dundee group mentioned only insulin stimulation for those later diagnosed as growth hormone deficient, as this was true for the nine children concerned. The most recent of these, however, was diagnosed in 1979 and thereafter opinion moved away from the use of insulin towards sleep, clonidine, L-dopa, arginine, and glucagon tests in the various United Kingdom growth centres.

(2) He challenges the classic definition of growth hormone deficiency, which, allowing for the different biochemical tests now in use, is at present the definition accepted by the Human Growth Hormone Health Services Committee. In addition, height prediction studies in relation to mid-parenatal height and assessment of the hypothalamo-pituitary axis are taken into consideration.

(3) He favours the use of 24 hour growth hormone profiles in children with short stature or low growth velocity, or both, and growth hormone responses greater than 15 mU/l, in order to confirm or exclude growth hormone deficiency and he suggests a definition based on this test.

With regard to confirmation of growth hormone deficiency, or at least of the benefit of treatment, the Human Growth Hormone Health Services Committee follows up all children on growth hormone in the United Kingdom through a coordinator, and these children have to show a satisfactory increase in height velocity during the first year of treatment in comparison with that during the previous year.

The use of a 24 hour sleep test as the final method of excluding growth hormone deficiency would create difficulties. Such a test is not easy to perform, especially during the night phase, when nervous children do not sleep deeply with an indwelling cannula in situ and, if used as a final definitive test, it would require routine electroencephalographic monitoring for the accurate assessment of the sleep pattern.

(4) He suggests that a therapeutic trial of growth hormone therapy for short, slowly growing children with normal peak growth hormone responses would be valuable. Such a trial is in progress in the United Kingdom as outlined by Professor Milner, Chairman of the Human Growth Hormone Health Services Committee, in his article.\(^1\)

Dr Brook comments:

I agree with Dr Wit that a 24 hour profile is likely to produce the most clinically relevant information on short children growing slowly. The performance of such a profile is unfortunately beyond the capacity of the majority of departments of paediatrics in this country. Since it is very difficult to justify the performance of profiles on normal patients, it may be quite difficult to assess the results from a single child.

Where there is the slightest doubt about the possible use of growth hormone, a centre specialising in the management of such cases should be consulted.

Complications of diazoxide in the treatment of nesidioblastosis

Sir,

McGraw and Price attribute the problem of cardiac failure in a patient with nesidioblastosis to a side effect of diazoxide.\(^1\) Like the author, this unit recently encountered a patient who developed cardiac failure while being treated for nesidioblastosis. A girl, birthweight 3.9 kg had a convulsion at 6 hours of age attributable to a blood sugar value of less than 1 mmol/l. Despite treatment with intravenous glucose and steroids it proved difficult to maintain normoglycaemia. Insulin concentrations were grossly raised at 90 mU/l. Medical treatment of the hyperinsulinism consisted of diazoxide, hydrocortisone, and glucagon. At the age of 2 weeks she had the first of many episodes of cardiac failure. Cardiac echo showed a structurally normal heart with poor myocardial contractility as seen in a cardiomyopathy. Treatment with digoxin and diuretics was begun but the hypoglycaemia and cardiac failure remained difficult to control and at age 5 weeks the child underwent subtotal pancreatectomy. Histology confirmed nesidioblastosis. Unfortunately, despite being able to maintain normoglycaemia relatively easily after the operation, the baby developed pseudomonas septicaemia and died.

The above case illustrates some of the problems that can arise when treating a patient with nesidioblastosis. Although the cardiac failure encountered in these patients may be partly attributable to diazoxide as McGraw and...