LETTERS TO THE EDITOR

Does growth hormone treatment improve final height attainment of children with intrauterine growth retardation?

SIR,—The potential indications for the therapeutic use of growth hormone have widened with the availability of more abundant supplies of growth hormone. For some of the new potential indications such as Turner's syndrome, intrauterine growth retardation (IUGR), etc, the growth-promoting benefits of growth hormone have usually been assessed in the short term by comparing the changes in height velocity SD score during the first treatment year and the pretreatment year, and, in some instances, by quantitating the psychological benefit gained by improved growth during the middle childhood years. In the long term the benefits of growth hormone can be assessed by comparing final height in a treated group with either that achieved in an untreated group or with the original pretreatment height prediction of the treated group.

In their recent article on the use of growth hormone in children with IUGR, Stanhope *et al* present three year growth data and suggest that the results are rather disappointing.¹ This conclusion is based on the fact that the height for bone age score did not change significantly over the three years of the study. With knowledge of the natural history of IUGR, Stanhope *et al* do, however, still believe that their growth hormone treated children may attain a greater final height than would have been the case if they had remained untreated. In their discussion Stanhope *et al* state that 'only the continuation of clinical trials such as this until final height will answer the question'. Others might feel that the current results are sufficiently disappointing for the study to be concluded now.

Certainly if the design of the study remains in its present form then, as the authors acknowledge, there is a real possibility that growth hormone treatment will reduce the duration of puberty and compromise final height prognosis. Thus, I would suggest that, if the study is to continue, one of their groups of IUGR children, who received growth hormone during prepubertal life, should not receive growth hormone during puberty. Furthermore, their results emphasise that individual children with IUGR seen by paediatricians around the UK should not be offered growth hormone on an *ad hoc* basis.

Finally, if the authors believe that possible growth hormone treatment induced gain in height for IUGR children can only be interpreted when the children attain final height, is much learnt by publishing the three year growth data?

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Dr Stanhope and Professor Preece comment:

We agree with Dr Shalet that there are many subgroups of children with short stature who may benefit from growth hormone treatment. However the only proved indication to final height is growth hormone deficiency.¹ The reason why we published our three year data of growth hormone treatment in children with intrauterine growth retardation (IUGR) was to emphasise that at the present time such treatment should remain part of a clinical trial and not be offered on an *ad hoc* basis. Height prediction depends on epiphyseal maturation, which is relatively inaccurate over short periods of time, especially in dysmorphic syndromes. However, we believe the natural history of the growth of children with IUGR is sufficiently disappointing to allow our trial to continue.²

Our study has been modified after one year,³ when the results from the lower dose growth hormone regimen were disappointing in terms of short term growth rate, and we may modify our trial again. Although growth hormone treatment may increase the rate of pubertal progress in a dose dependent fashion, this phenomenon has only been described in children with isolated growth hormone deficiency.⁴ Although growth hormone insufficiency is common among children with IUGR,⁵ our patients were carefully screened to avoid this ambiguity.

We believe that the continuation of this trial is justifiable and having done so, it is our duty to report the findings.

- 1 Brook CGD. Who is for growth hormone? *BMJ* 1992;304:131-2.
- 2 Davis PSW, Valley R, Preece MA. Adolescent growth and pubertal progress in the Silver-Russell syndrome. *Arch Dis Child* 1988;63:130-5.
- 3 Stanhope R, Ackland F, Hamill G, Clayton J, Jones J, Preece MA. Physiological growth hormone secretion in response to growth hormone treatment in children with short stature and intrauterine growth retardation. *Acta Paediatr Scand* 1989; suppl 349:47-52.
- 4 Stanhope R, Uruena M, Hindmarsh P, Leiper AD, Brook CGD. Management of growth hormone deficiency through puberty. *Acta Paediatr Scand* 1991; suppl 372:47-52.
- 5 Ackland FM, Stanhope R, Eyre C, Hamill G, Jones J, Preece MA. Physiological growth hormone secretion in children with short stature and intra-uterine growth retardation. *Horm Res* 1988;30:241-5.

Kawasaki disease

SIR,—I read with interest the annotation on Kawasaki disease by Levin *et al*.¹ I would like to draw attention to the fact that this disease, like any other vasculitis, can have a predominantly neurological presentation, with an encephalopathic/encephalitic illness. I have seen three such patients who all presented with high fever, diminished consciousness, a minimal increase in lymphocytes in the cerebrospinal fluid with normal protein and glucose, and a rash. In one child, a 7 year old, the most striking physical sign was bilateral papilloedema.

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Late intravenous gammaglobulin treatment in Kawasaki syndrome

SIR,—We wish to comment on the interesting article on intravenous gammaglobulin treatment for Kawasaki disease in which the Archivist mentioned it seems reasonable to treat if the disease is still active.¹ Indeed, the results published by Marasini *et al* suggest a favourable effect of gammaglobulins on established coronary abnormalities, at least in the midterm follow up.²

They studied two groups of children with a similar image of coronary abnormalities. The first group (nine children) was treated with aspirin (100 mg/kg/day) until the fever disappeared, followed by aspirin (5 mg/kg/day) and dipyridamole (5 mg/kg/day). The second group (seven children) received intravenous gammaglobulins (400 mg/kg/day) for five days after the 10th day from the onset of the disease, when coronary artery abnormalities had already developed.

In the first group four patients had a complete resolution of their abnormalities. Five had persistent abnormalities including three with myocardial infarction (one died from his myocardial infarction). In the second group, all coronary abnormalities had resolved during follow up.

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- 1 Archivist . . . and while on the subject. *Arch Dis Child* 1991;66:1407.
- 2 Marasini M, Pongiglione G, Gazzolo D, Campelli A, Ribaldone D, Caponnetto S. Late IV gammaglobulin treatment in infants and children with Kawasaki disease and coronary artery abnormalities. *Am J Cardiol* 1991;68:796-7.

Inherited metabolic diseases in the sudden infant death syndrome

SIR,—Holton and his coworkers set out to investigate among other causes the prevalence of medium chain acyl CoA dehydrogenase deficiency (MCAD) in cases of sudden infant death syndrome (SIDS).¹ They assert that the claim 'MCAD deficiency could cause 3% of cases of SIDS' is not supported by their findings.

Unfortunately their work, while exhaustive in its scope, demonstrates the difficulty in looking for rare events in small samples. Using binomial probability theorem

$$P(r) = \frac{n!}{r!(n-r)!} p^r q^{(n-r)}$$

the chance of finding 0 cases in a sample of 70 with a true population prevalence of 3% is 0.118. What the authors can say from their work is that with a 0.05 confidence, the true prevalence of MCAD in cases of SIDS is less than 4.2% and using a 0.01 confidence they can state the prevalence is less than 6.4%.

Support for their claim of a low prevalence rate of MCAD in SIDS is found in a recent report of carrier rate of the K 329E mutation for MCAD in population screening.^{2,3} These estimate the carrier rate to be between 1/40

1 Stanhope R, Preece MA, Hamill G. Does growth hormone treatment improve final height attainment of children with intrauterine growth retardation? *Arch Dis Child* 1991;66:1180-3.

1 Levin M, Tizard EJ, Dillon MJ. Kawasaki disease: recent advances. *Arch Dis Child* 1991;66:1369-72.