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Correspondence

Who should get growth hormone

Sir,

The prospect of a considerable increase in the availability of human growth homone due to biogenetic engineering will raise practical and ethical problems related to which children should receive treatment. It is most reassuring and appropriate that Professor Milner, Chairman of the Health Services Human Growth Hormone Committee, addresses the question in a recent annotation.[1]

Clinicians working in this field have been frustrated by their inability to help children whose growth velocity is poor, who are very short, and are predicted to achieve a final height which may be regarded as socially handicapping, but who have no identifiable pathogenesis for this poor growth and have normal growth hormone values in response to pharmacological testing. The distress caused to children and parents makes it an ethical priority to try to define the characteristics which identify the children (other than those with primary or secondary growth hormone deficiency) who would be helped by treatment, and equally the children who would not be helped.

Professor Milner mentions the United Kingdom trial for so called 'short normal' children and girls with Turner's syndrome. Unfortunately the design of this trial is unacceptable on ethical grounds to us in the North West Regional Growth Clinic. Since most patients treated in regional growth clinics have been referred by local paediatricians and children's surgeons it seems appropriate to raise the matter in these columns.

The UK multicentre trial has three parallel arms of treatment, namely a child may receive six months of growth hormone followed by six months of placebo, or six months of placebo followed by six months of growth hormone, or 12 months of growth hormone. Thereafter children can continue growth hormone treatment at the discretion of the clinician. The ethical problem is that two thirds of the children will receive six months' injections (three times a week) of 'placebo', that is, saline or an inactive vehicle without growth hormone. This did not seem acceptable to me or to our local ethical committee.

Would parents find the trial acceptable? Because every child would receive some growth hormone and would have the prospect of treatment after the trial, they might feel constrained to accept.

The justification for placebo injections is made on scientific grounds. Professor Milner states that 'Another defect in the clinical studies of 'normal' children has been the lack of an appropriate control: treatment with placebo, an omission that would not have occurred had the species studied not been man.' I would agree that any trial must have adequate controls. My own view is that to control for a placebo effect in this situation is unnecessary—do we really need to know whether six months' saline injections produce a minimal increase in velocity when we have no desire to use that as an alternative management? More important is observer bias which can be removed in other ways.

A valid alternative, already suggested to the Committee, would be to exclude the placebo components and to introduce the safeguard that the person measuring the child would not be told the phase of treatment. We, in the North West, are unable to pursue this alternative as there is only one source of growth hormone for treatment and trial in the UK! This must be equally frustrating in other regions, although to my surprise the present design has been approved by several local ethical committees.

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Professor Milner comments:

Dr Price is rightly concerned that children who will benefit from growth hormone treatment should be accurately identified, but he is unhappy that the methodology to be used should be uncompromisingly scientific. The UK multicentre trials of growth hormone treatment in Turner's syndrome and short slowly growing 'normal' children were carefully designed so that account could be taken of the very real possibility that a concentration of resources and interest in a patient might produce an unsuspected growth stimulating effect. Most clinicians dealing with growth disorders appreciate how sensitive a patient's growth is to psychosocial influences[2] and sometimes we have observed in the year immediately preceding growth hormone treatment, when many measurements and investigations are being performed, that there is a minor but clear increase in growth velocity. It is precisely this effect (sometimes referred to as the Hawthorn effect) that the trials will distinguish from what may well be only a minor true growth stimulating effect of growth hormone. This information is essential if soundly based advice is to be offered to the families of these patients.

It is noteworthy that Dr Price's clinic is one of only three clinics out of the 22 growth centres in the UK from which ethical consent for the trials was not forthcoming and that enquiry of the other trialists has not shown parental objection to the trial design.

References

[1] Milner RDG. Who should get growth hormone? *Arch Dis Child* 1984;**59**:115–7.
[2] MacCarthy D. The effects of emotional disturbance and deprivation on somatic growth. In: Davis JA, Dobbing J, eds. *Scientific foundations of paediatrics*. 2nd ed. London: William Heinemann Medical, 1981:54–73.