Correspondence

Birthweight between 14 and 42 weeks' gestation

Sir,

We were interested to read the recent paper by Keene and Pearse.¹ Unfortunately the emphasis placed on ultrasound assessment in respect of other methods of assessing gestational age was not disclosed. We believe it is important to stress the limitations of ultrasound.

Most departments of obstetrics use ultrasound routinely to assess gestational age. A fetal measurement (usually biparietal diameter) obtained by ultrasound is plotted on a chart to obtain gestational age. An assumption is made, however, that the fetus is on the 50th centile for that parameter. By definition most fetuses will not be on the 50th centile and hence this assumption may lead to considerable error. Serial ultrasound measurement to assess fetal growth velocity is a more appropriate use of ultrasound. This error in the method may account for some of the differences observed by Keene and Pearse from previous studies.²

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Drs Keene and Pearse comment:

While agreeing with Drs Stanhope and Brook on the limitations of fetal ultrasonography, we are unable to accept their suggestion that the differences between our data¹ and those of Gairdner and Pearson² are due to our reliance on this method of assessing gestational age.

Firstly, as our paper made clear, both ultrasonography and the Dubovitz method of gestational assessment were innovations used in this area and both were used alongside traditional methods calculated on the last menstrual period. Where there were gross discrepancies, paediatric assessment became the most important parameter, the baby himself being the most tangible of the three.

While it is indisputable that most fetuses will not be on the 50th centile, we would point out that equal numbers lie above and below that centile. Hence, it might be supposed that any errors in gestational assessment by ultrasound would also be equally distributed above and below that point, and so would not affect the mean. In our view, however, it is not the distribution of ultrasound data around the mean which is problematic, but the derivation of the mean itself. The problem with all methods of gestational assessment is that they are standardised on the last menstrual period, and given the variable relation between this and ovulation it is probably illusory to regard gestational assessment by any method as accurate to more than ± 1 week at the most optimistic.

Secondly, our paper referred to the problem of comparability between fetal growth charts as a consequence of the differential exclusion of data. We would suggest that this is much more likely to account for the difference observed between our data and those of Gairdner and Pearson.² The Gairdner and Pearson chart is based on data given by Thomson, Billewicz, and Hytten.³ The babies in this study are, in fact, among the largest reported in the world, and as Thomson and Tanner⁴ note, are certainly larger than those of the British Perinatal Mortality Study of 1958.⁵ It is interesting to note that the Thomson, Billewicz, and Hytten sample excluded illegitimate births (ranging from 5 to 6% of all births in Aberdeen during the study period) and a further 10% of data where it was not possible to date the last menstrual period accurately. Overall, in other words, some 14% of births were excluded.

If these exclusions had been random, the results of the study would not have been biased. There are, however, grounds for believing that they were not random. The mean weight of the excluded 10% was 0.08 kg lower than the rest of the sample and the authors believed there was an excess of mothers of low social class. Given the association of illegitimacy, low social class, and low birthweight, there is reason to suppose the Thomson, Billewicz, and Hytten study (and consequently the Gairdner and Pearson chart) to be biased towards higher birthweight.

References

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Oxandrolone in low dose for constitutional delay of growth and puberty in boys

Sir,

I read the paper by Drs Stanhope and Brook¹ with interest and strongly support them in their last paragraph where a plea is made for the ready availability of oxandrolone. I have, however, a number of anxieties about the data presented in their paper and am not convinced that they have shown all that they claim.

The most striking omission is the lack of any controls. It is well recognised that psychosocial factors can exert extreme effects on the growth of children, even at this relatively late age, and the increased attention plus a placebo effect could well have contributed substantially to the observed increase in growth. In particular, I note that all the children in this study were suffering from psychological disturbances of one type or another and I wonder how much active psychotherapy was provided at the same time as the endocrine treatment. This could only be interpreted if there were comparable control patients who were not given oxandrolone but whose management otherwise remained the same.

The second anxiety relates to the pubertal status. While I accept that one would not expect a substantial growth spurt due to puberty in boys with an average testicular volume of 9.3 ml, which was achieved at the end of their treatment period, one might certainly expect it in those boys near the extreme upper limit of their range (15 ml). I would suggest that in at least some boys all that was observed was the normal events of advancing puberty, and there is no evidence that oxandrolone influenced this.

Thirdly, only a mean and SEM are quoted for the change in growth velocity from pretreatment to treatment period (4.4 (0.37)) and unlike the other variables no range is given. As this implies a standard deviation of 1.8 cm/year there is an implication that in some boys the acceleration was extremely small unless the distribution was skewed. I think it would be helpful to know the minimum and maximum acceleration observed.

The observations that they make have important potential but, unfortunately, I think they are not really sustained by the present study. I would be interested to see further elaboration of their data to take in some of these points.

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Drs Stanhope, Noone, and Brook comment:

We are grateful to Dr Preece for giving us the opportunity to clarify some points about our paper.¹ He has raised three separate issues.

Adolescent boys who are small and delayed in puberty are anxious and unhappy and our treatment is aimed at alleviating this situation. Our Department of Child Psychiatry is actively involved in all the activities of our clinic and some of the boys in this study had diagnostic interviews; none entered a psychotherapeutic programme.

Although controls might be desirable, we are doubtful that a placebo treatment would now be justified in this clinical situation, since it has been known for at least 20 years that the growth inducing effects of anabolic steroids are not dose dependent.² We have recently published the results of another earlier study of a similar group of boys treated with low doses of the anabolic steroid fluoxymesterone (which is no longer available) with almost identical results,³ and we have now been able to confirm our hypothesis that oxandrolone acted by increasing growth

hormone secretion using 24 hour profiles of growth hormone concentrations.⁴

While this might have been secondary to psychological mechanisms, our profiles also showed a minor suppression of pulsatile luteinising hormone secretion and alterations in the concentrations of thyroxine binding globulin which one would expect after administering an anabolic steroid. These are not the hallmarks of a placebo effect.

The second point concerns growth velocity data and the raw data from our study are shown in the Figure. The changes between pretreatment and treatment growth velocities are obvious without statistical analysis. We have added growth velocity data from a further 17 boys with constitutional delay of growth and puberty treated with only 1.25 mg oxandrolone for three months. The results using either dose regimen are similar and we have still not defined the lowest effective dose.

With regard to pubertal status, mean testicular volume at the end of the treatment period using oxandrolone 2.5 mg daily was 9.3 ml with an upper range of 15 ml. Only two boys had testicular volumes greater than 12 ml and we accept that their growth acceleration may have been spontaneous. On the other hand the mean testicular volume at the end of treatment in the 17 boys shown in the Figure treated with oxandrolone in a dose of 1.25 mg daily was 6.9 ml and none was greater than 10 ml. It is certainly possible that as testicular volume increased during the post treatment periods a secondary effect on growth velocity became indistinguishable from spontaneous growth acceleration but this was after all the object of the exercise. Oxandrolone used for this indication was effective in

Figure Growth velocities of 24 boys treated with oxandrolone 2.5 mg daily (solid circles) and 17 boys treated with oxandrolone 1.25 mg daily (open circles). Before treatment, treatment, and after treatment periods were consecutive in each series.