Correspondence

Reversible inhibition of central precocious puberty with a long acting GnRH analogue

Sir,

We were interested to read the recent paper by Ward et al1 about the effect of the GnRH analogue (6-D-Ser) GnRH(Buserelin) on gonadotrophin pulsatility. This report raises the question of analysis of pulsatile hormone secretion, which has only recently come to the fore in paediatric practice. Because studies of this type will be increasingly performed, we wish to draw attention to what can and, perhaps more importantly, what cannot be learned from different methods of sampling.

It is apparent that the biological effect of both gonadotrophins2 and growth hormone are related to the pulsatile pattern of their secretion and not to mean blood concentrations. There is no consensus on the optimum method to identify gonadotrophin pulses in serum, although the method most commonly used is to withdraw blood during a 5–10 second period and repeat this procedure at intervals. The sampling interval needs to be chosen to reflect the approximate frequency of the natural hormone pulsatility and the biological half life of the hormone. For both gonadotrophins and growth hormone, the maximum time interval should not be greater than 15–20 minutes. The more frequent the sampling interval, the more pulses are detected.4 The method that Ward et al used was to withdraw blood continuously over 15 minutes and to measure the gonadotrophin concentration in the pooled sample. This method is not capable of revealing the frequency and amplitude of gonadotrophin pulses in serum unless very short (5 minutes or less) sampling intervals are employed.

Further ambiguity has been caused in Ward’s study by the use of sampling periods that varied between four and three quarters and five and three quarters hours. These are short compared with the known frequency of gonadotrophin pulses in puberty, which occur approximately every two hours.5 A more appropriate sampling period would be longer than eight hours.

The data presented by Ward et al provide information about mean serum gonadotrophin concentrations at night, but it is pulsatile gonadotrophin secretion that is the stimulus for gonadal maturation. As the authors have not assessed gonadotrophin pulsatility, their claims about reversibility of the effect of (6-D-Ser)GnRH could be premature.

References


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Rectal examination and acute appendicitis

Sir,

The short report on ‘Rectal examination and acute appendicitis’ 1 records the findings of two paediatric surgeons but fails to make a useful contribution for other clinicians managing children with acute abdominal pain. I am concerned that paediatricians, who are often reticent about performing rectal examinations, will quote this study as a reason for omitting this part of the clinical examination. The management of acute abdominal pain in children is not straightforward and ‘the man on the spot’ needs unequivocal guidelines rather than the contemplation of the fact that his colleagues can diagnose acute appendicitis in over 90% of cases without rectal examination. This report, which works back from the histology of the removed appendix to the clinical findings, is of no help to the surgeon at the bedside.

The third conclusion that ‘the rectal examination is sometimes useful when the diagnosis is uncertain’ is too vague for the trainee duty surgeon. The correct emphasis appears in the middle of the discussion where the rectal examination is described as ‘essential in those with acute abdominal symptoms, but with inconclusive or no abdominal signs’. This imperative should be given more prominence in the presentation and not omitted from the summary and conclusions.

A careful history and a thorough examination of the patient are essential,2 and the teaching of Hamilton Bailey is ignored at our patients’ peril. Perhaps your journal will publish a paper which makes a positive contribution to the management of the child with acute abdominal pain and thus encourages safe clinical standards for 100% of our patients rather than 90%.

References

Insufficient early weight gain in preterm babies and influence on weight at 12 months

Sir,

In an interesting though difficult paper Davies and Kennedy report that there was no influence of insufficient early weight gain in preterm babies on weight at 12 months.

I would like to comment on their introductory remarks that anxieties about poor early weight gain were ‘based largely and often uncritically on studies in laboratory animals’, citing a (wrongly dated) 19 year old paper by Winick and Noble that has now lost its currency, a classic paper of Widdowson and McCance, and an old one of our own.

It is true that paediatricians’ extrapolations from other animals to man are often uncritical, to the point that they may be rejected altogether except where they seem to bolster emotional belief, and this example is no exception. At the same time such comparisons can be very useful and should not be dismissed until they have been properly made. At the very least they must take account of the different time scales of growth between species, the different timing of birth in relation to developmental stages, and, especially, comparable stages of growth must be compared before the self evident conclusion is pronounced that animals are ‘of course’ not always like man.

In the present case growth restriction between birth and three weeks of age in the rat clearly results in a permanent resetting of the growth trajectory downwards, with ultimate stunting in adulthood, and in certain permanent alterations of brain anatomy and function. The comparable period in man is much longer, from about the beginning of the first trimester of gestation until about the second birthday. Whether or not man has a similar vulnerable period to that in rats awaits a demonstration of the long term consequences of growth restriction lasting for a major part of the entire period. Such restriction being to a comparable degree, so that by the age of 2 the child is not much more than half as large as it was, the outcome being assessed not earlier than the late teens. Of course, it is much easier to produce these conditions in experimental animals, but that is the whole point of using them. Children do exist, especially in underprivileged communities, whose early growth experience comes reasonably close to the model suggested by Widdowson and McCance in the rat, and there is reason to believe that in them a critical extrapolation bears fruit, the people in such communities being generally stunted. That the reason for their smallness is by no means wholly genetic is evident from their children’s response to the arrival of better environmental conditions, when they are seen to outstrip the growth attainments of their parents, often dramatically.

I hope that the strictures of Davies and Kennedy about extrapolating from animals to man will be heeded, not least by themselves!

References

Impact of neonatal care—South West Thames region (less than 1000 grams)

Sir,

Thompson and Kho have reported on the Brighton (South East Thames) experience on the reduction of mortality with the introduction of respiratory support. Not only does local mortality improve but so do expectations, and this is not just confined to the centres providing full neonatal intensive care with respiratory support. In the next door South West Thames region intensive care began probably with the opening of a new unit at St George’s in 1980. In the five years 1980-84 inclusive there has been a steady improvement in mortality figures both at St George’s and generally in the region. This has been accompanied by a regional increase in expectations. This is illustrated by the Table.

In 1980, 53 infants delivered with a birthweight less than 1000 g were resuscitated in the region, 13 (24%) at St George’s Hospital. Since then there has been a steady increase, so that in 1984 there were 72 infants of this weight resuscitated, 28 (39%) at St George’s. In 1980 only eight infants <1000 g in the region survived to go home, four (50%) from St George’s—that is, only 15% of those resuscitated. This had increased to 39 infants in 1984, of whom 18 (46%) were delivered at St George’s. Thus the overall regional survival for babies of this weight group has increased to 54%. Not only are more infants of this extremely low birthweight being resuscitated, but they are