Correspondence

Effect of treatment of malignant disease on growth in children

Sir,

We were pleased to find that the broad conclusions drawn by Griffin and Wadsworth reinforced our findings as well as those of other authors. Few children previously treated for acute lymphoblastic leukaemia (ALL) are clinically growth hormone (GH) deficient, and the loss in potential height caused by the treatment is moderate. Griffin and Wadsworth suggest that the poor growth velocity shown by such children during the first year of treatment is due to radiation-induced transient GH deficiency, and they support this view by quoting the work of Dacou-Voutetakis et al and by showing that the children they studied did not show a significantly reduced growth rate before radiotherapy. We disagree for the following reasons:

(1) Dacou-Voutetakis et al alone have found evidence of radiation-induced transient GH deficiency. Several years ago one of us (S M S) compared the GH responses with an insulin tolerance test and an arginine stimulation test before and after 20 ALL children received prophylactic cranial irradiation (DXT). There were no differences and no child had a subnormal GH response to these tests at the end of the radiation course.

(2) In a prospective study, with the measurements performed by a trained observer, we found that all the ALL children grew very slowly during the first year of treatment. The somatomedin activity was measured in these children at the time of diagnosis, at the time that they went into clinical remission, when they received their cranial DXT, and at the end of the first year of treatment. The mean somatomedin activity level was very low at presentation but when they were in clinical remission their somatomedin activity level was not greatly different from a group of normal age-matched controls. During the remainder of the first year of treatment there was no further significant change in somatomedin activity level, thus we found no evidence to support a diagnosis of transient GH deficiency.

(3) Finally, we think that Griffin and Wadsworth have misinterpreted some of their own data. They suggest that as the mean standard deviation (SD) score for height in their children at the time they received cranial DXT was not greatly different from the value at diagnosis, or from 0, their patients grew normally during the interval between diagnosis and cranial DXT; this is not true. The time interval between diagnosis and cranial DXT is so short—that is a few months—that a significant difference in the mean SD score between these two times would not be found even if the children grew at an exceptionally slow rate.

We still believe that the combination of cytotoxic drugs and steroids is the major cause of poor growth during the first year of treatment.

Dr Griffin and Miss Wadsworth comment:

We read with interest the observations by Shalet and Price. Our principal conclusion that children treated for ALL have only slight loss in potential height agrees with their findings although they prefer to attribute this to the effects of cytotoxic drugs and steroids rather than to transient GH deficiency. We believe that their hypothesis is not proved by their data, nor does it tally with our findings for the following reasons:

(1) Dacou-Voutetakis et al measured spontaneous nocturnal GH secretion in leukaemic children and found it was impaired. This is not necessarily incompatible with an ability to produce a rise in serum GH above an arbitrary level in response to hypoglycaemia. Shalet mentioned his own unpublished observations of GH response to hypoglycaemic and arginine stimulation in leukaemic children, but he did not say how long after cranial irradiation his observations were made. However, Shalet et al performed similar tests on patients who had received cranial irradiation for brain tumours and found a progressive impairment in response with time.
since treatment. This indicates that the timing of such tests is important, and sequential tests during the first year of treatment may be necessary to detect a transient GH deficiency.

(2) The comments of Shalet and Price about their prospective study are interesting but they are difficult to correlate with the data in the abstract where they reported that 29 children with ALL, who had been in complete remission for 4–8 years, had a normal mean height velocity SD score but that 17 of them had impaired GH responses to insulin, and one was clinically GH-deficient. No details are given about the number of children studied prospectively or the timing of the measurements. Fifteen children had somatomedin activity assayed in the first year of treatment but no anthropometric data are given on them.

(3) We feel that they have not understood the statistical methods we used. In an individual child growth rates over periods less than one year are unreliable, but by taking the mean of the SD scores of a large group of children, changes in growth rates over shorter periods can be demonstrated. The larger the group of children, the smaller is the change that is potentially detectable. A small change in growth rate in the time between presentation and the end of cranial irradiation might have been recognisable with a larger group of children, but our findings suggest that the principal effect on the growth rate occurs after cranial irradiation.

(4) It is known that both systemic disease and steroid therapy in children can affect growth rate, and it would be surprising if this were not so in children with malignant disease. However, children with solid tumours who also received cytotoxic drugs, usually including steroids, but did not receive cranial irradiation showed no significant alteration of growth during the first year of treatment.

While conceding that other factors are likely to affect the growth of children with leukaemia, we still believe that a transient interference with GH production is the major cause of the poor growth that we demonstrated in the first year of treatment.

We draw attention to the following error in our paper. On page 601 the formula for calculating the SD score should read: SD score = (x – x̄)/SD.

References


Bacteriuria in the neonate

Sir,

We read with interest the paper by Moncrieff et al. demonstrating a very low rate of incidence for asymptomatic bacteriuria in 151 healthy preterm babies. The incidence was zero in their series of 147 fully investigated babies; it would rise to 1.3% if 2 infants with pure growths of 100 000 organisms/ml on bag specimens, who could not be completely investigated, had significant bacteriuria. Two other infants with bacterial growths of 100 000 organisms/ml were considered 'most unlikely to have significant bacteriuria' because the cultures had grown two different organisms.

We make the following comments:

(1) A very low rate of incidence for asymptomatic bacteriuria, similar to that observed in healthy preterm babies, was also found in high-risk newborn infants. Only 9 out of 1762 high-risk neonates that we studied* presented with asymptomatic bacteriuria, giving a 0.5% incidence rate. From our study we, like Moncrieff et al., concluded that routine survey of bacteriuria was not essential in high-risk neonates, and that a thorough search for symptoms that suggested urinary tract infection appeared to be more effective.

(2) In our study a mixed infection was found in 4 out of 43 infants presenting with proved significant bacteriuria. This intriguing finding was confirmed in each case by a urine specimen obtained by suprapubic puncture. Escherichia coli and proteus were found in 2 cases, E. coli and enterococcus in one case, E. coli and klebsiella in one case. The fact that a mixed infection was confirmed by suprapubic aspiration excluded an artefact by external contamination but, as suggested by Fairley et al.,* it did not exclude contamination by retrograde aspiration of urethral organisms.

The significance of mixed infections in the neonate is still unclear. The phenomenon could be related to an unusual pattern of antibody synthesis and bacterial growth in the bladder of the neonate. However until this point can be elucidated, we do not think that the finding of a positive urine culture in the newborn infant can be ignored simply because it shows a mixed growth.

References