

LETTER TO THE EDITOR

Relationship between urinary and serum growth hormone and pubertal status

SIR,—We read with interest the paper by Crowne *et al* on the relationship between serum and urinary growth hormone concentrations during puberty.¹ As the authors pointed out we carried out very similar studies and came to very different conclusions. In our early studies of 24 normal children of both sexes over the full range of puberty stages we found very good correlation ($r=0.79$, $p<0.001$) between urinary growth hormone excretion and overnight mean plasma growth hormone concentration.² We have recently extended these studies comparing diabetic and normal adolescents and found the same correlation in both patient groups ($r=0.70$, $p<0.001$).³

Crowne *et al* suggest that the discrepancy between their study and ours could be explained by the fact that we studied mostly children in early puberty. In fact the predominance was in late (Tanner stages 3-5, $n=15$) rather than early puberty (stages 1-2, $n=9$). We have reanalysed our most recent results and still observe the same good correlation between urinary and plasma growth hormone in late ($r=0.69$, $n=17$) and early ($r=0.71$, $n=19$) puberty in both sexes.

The methodology for measurement of both urinary and plasma growth hormone concentrations was very similar in our studies and that of Crowne *et al*, and we believe that the important differences between the two studies are the collection methods and the way the urinary growth hormone data are presented. In the majority of their subjects Crowne *et al* used a 24 hour collection period with a 20 minute sampling interval for the serum profiles, whereas we used overnight collection with 15 minute blood sampling. The relationship between urinary growth hormone excretion and plasma growth hormone concentrations may not be constant throughout the 24 hours.

More importantly perhaps, Crowne *et al* reported urinary growth hormone excretion in relation to urinary creatinine excretion. Whereas this convention may be useful for checking the completeness of overnight urine collections, in this particular case it can be very misleading. We have examined overnight urine samples from 151 normal adolescents at different stages of puberty, and demonstrated that the urinary excretion of creatinine increases during puberty (see table). If urinary

growth hormone excretion rates are expressed as a ratio of creatinine excretion therefore, it will be difficult to discern any increase of excretion of growth hormone during puberty, and any correlation which exists with plasma growth hormone concentrations will be lost. If a small group were studied over a limited range of puberty stages, this change in creatinine excretion would not be so significant, and indeed Crowne *et al* did present some data to support this position. In the subgroups of prepubertal children and in the group of six boys in early puberty, significant correlations were seen between urinary growth hormone excretion related to creatinine and mean serum growth hormone concentrations ($r=0.82$ and $r=0.74$ respectively).¹

We believe that a note of caution should be added to the use of urinary creatinine ratios during puberty, and suggest that urinary growth hormone excretion should be expressed as a timed excretion rate without reference to creatinine. In our experience this does reflect overnight mean plasma growth hormone concentrations with some accuracy during normal puberty.

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- 1 Crowne, EC, Wallace WHB, Shalet SM, Addison GM, Price DA. Relationship between urinary and serum growth hormone and pubertal status. *Arch Dis Child* 1992;67:91-5.
- 2 Edge JA, Hourd P, Dunger DB, Edwards R. Urinary growth hormone during puberty in normal and diabetic children. *Clin Endocrinol (Oxf)* 1989;30:413-20.
- 3 Hourd P, Edge JA, Dunger DB, Dalton N, Edwards R. Urinary growth hormone excretion during puberty in type I (insulin-dependent) diabetes mellitus. *Diabetic Med* 1991;8:237-42.

Drs Crowne and Shalet comment:

We read the above letter with interest and thank the authors for their comments. In reply, although we reported our results as growth hormone: creatinine ratios, in line with other recent publications, we did also look at the correlation between total urinary growth hormone (uGH) excretion (pg/ml) and mean serum growth hormone. There was still no significant correlation between these parameters in the pubertal children, either in the total group ($n=22$) $r=-0.26$, $p=0.24$; group 1 (postcranial irradiation, $n=14$) $r=-0.02$, $p=1.0$; or group 2 (normals, $n=8$) $r=-0.4$, $p=0.22$.

Therefore the use of growth hormone: creatinine ratios cannot explain the different findings of the two studies. We feel that the inherent variability in uGH excretion in puberty as a result of changes in both growth hormone secretion and renal function must affect these correlations. The use of tightly defined subgroups of children in different pubertal stages may improve correlations between uGH and serum growth hormone but has implications for the establishment of normal ranges in pubertal children and therefore the use of uGH measurement in pubertal children with growth problems.

Neonatal BCG immunisation

SIR,—The annotation by Clarke and Rudd was a very helpful review of neonatal BCG immunisation.¹ However the technical difficulty of intradermal injections in newborn infants was not mentioned, although poor technique is likely to result in inadequate immunisation or avoidable local side effects.

The percutaneous multiple puncture technique, described over 30 years ago² appears to be both safe and effective.³ The multiple puncture technique requires a more concentrated vaccine, suspended in dextran, and an adapted Heaf gun with a 20 G needle head. Any risk of the transmission of infection can be eliminated by the use of disposable magnetic heads for the Heaf gun.

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- 1 Clarke A, Rudd P. Neonatal BCG immunisation. *Arch Dis Child* 1992;67:473-4.
- 2 Lorber J. Freeze dried BCG vaccination of newborn infants by the multiple puncture method. *Tubercle* 1959;40:21-5.
- 3 Cundall DB, Ashelford DJ, Pearson SB. BCG immunisation of infants by percutaneous multiple puncture. *BMJ* 1988;297:1173-4.

Malnutrition in children with cancer

SIR,—In their report of energy intake and basal metabolic rate in children with malignant disease receiving maintenance chemotherapy, Bond *et al*¹ refer to our work exploring the incidence of malnutrition in children with cancer.² They state that we found nutritional status to be generally adequate at diagnosis but to deteriorate as a result of treatment. In fact we found that nutritional status was frequently inadequate at diagnosis. This finding directly contrasts with nearly all other studies.^{3 4} Our study of 48 newly diagnosed children with malignant solid tumours showed a marked discrepancy in the incidence of malnutrition assessed by conventional means when compared with arm anthropometry. Using conventional indices of weight for height, and height for age (as used by Bond *et al* themselves) only 7% of our patients were assessed as being malnourished at diagnosis. However, using arm anthropometry (mid upper arm circumference and triceps skinfold thickness) 27% of our patients were identified as malnourished. These conclusions were confirmed in a larger series of 100 newly diagnosed patients from our own institution that included children with leukaemia.⁵ Attempts to assess energy intake at diagnosis suggested that a large number of patients (44%) were consuming considerably less energy both than the recommended daily allowance for their age, and estimates of their own previous 'normal' intakes. Children with intra-abdominal solid tumours were more likely to be malnourished at diagnosis (35%) than those with leukaemia (15%) or extra-abdominal solid tumours (7%). It is evident that the presence of a large tumour load in a young child (with or without ascites or pleural effusion) could have a significant influence on weight and weight for height, making this an unreliable index of nutritional status at diagnosis.

Mean (SEM) overnight urinary creatinine excretion (nmol/hour) in 151 normal adolescents. Figures in squared brackets indicate numbers of subjects at each puberty stage

Puberty stage	Boys	Girls	Combined
1	0.21 (0.02) [30]	0.22 (0.03) [7]	0.21 (0.02) [37]
2	0.28 (0.02) [25]	0.23 (0.03) [8]	0.27 (0.02) [33]
3	0.34 (0.03) [14]	0.42 (0.09) [23]	0.39 (0.05) [37]
4	0.37 (0.06) [8]	0.45 (0.05) [23]	0.39 (0.04) [31]
5	—	0.49 (0.04) [13]	0.49 (0.04) [13]