

## Correspondence

### Immediate effects of albumin infusion in ill premature neonates

Sir,

The paper on albumin infusion in neonates by Greenough *et al* gives us several reasons for concern.<sup>1</sup> One issue, the lack of non-treated comparison infants, has been dealt with in the commentary.<sup>2</sup> The weight loss in most preterm infants is, in our experience, independent of their degree of oedema and plasma albumin concentration, even in those sick with respiratory distress syndrome. We cannot agree, therefore, that it has been shown that albumin infusion caused the observed diuresis.

The authors have apparently measured urine passed in a number of discrete micturitions during a predetermined time interval, and have called this urine output. Bladder emptying is highly irregular, however, and variably incomplete in all sick preterm infants. We have observed micturition patterns in very low birthweight infants and have found the intermicturition interval to vary from less than one hour to more than 12 hours, and the volume passed from a few drops to 20 ml/kg. Measurement of urine passed in an interval of six hours is therefore an inaccurate estimate of renal water excretion rate, especially when this is at a maximum of about 10 ml/kg/6 hours as stated, and most certainly when only 0.7 or 1.3 ml is passed. In addition, parametric statistics have been used to compare these estimates of water excretion rates, which are highly unlikely to be normally distributed.

We are given urine output uncorrected for body size (water excretion rates in ml/kg/day would have been more helpful). Nevertheless prealbumin urine flow rates are low in all the infants studied (mean perhaps about 30 ml/kg/day). This is probably because water input in these infants was low; although this was not specified, it is implied that it remained around 40 ml/kg/day in the first few days. We give much larger volumes and only in exceptional cases is there an inability to excrete administered water, as has been found elsewhere in well babies.<sup>3</sup> We dispute therefore the contention that the prolonged oedema and oliguria are necessarily due to failure of renal water homeostatic mechanisms.

The study was designed to show whether albumin is effective in 'treating' hypoalbuminaemia. We find it hardly surprising that the rapid infusion of 20% albumin (200 g/l) into a vascular space where the albumin is mean 27 g/l raises the albumin concentration. The addition of 1 g/kg of albumin into what is probably a vascular space of about 50 ml/kg, however, raises the albumin concentration by only 5 g/l. This implies that an appreciable volume expansion has occurred, perhaps by as much as 50% if there really is no extravascular leak of the albumin. Such a volume expansion is likely to have caused an acute increase in glomerular filtration rate, which would have flooded the

immature renal tubules with an increased filtered load, when reabsorptive capacity is already compromised. This will have resulted not only in the observed diuresis, but also in an acute loss of other solutes, especially sodium, where renal sodium conservation is already poor.

In summary, the authors do not give any evidence that a rapid albumin infusion does cause a diuresis, let alone that the resulting acute disturbance in vascular and renal physiology is beneficial. We believe that such a disturbance is more likely to be harmful and that, in the absence of convincing scientific support, this practice should not be promoted.

#### References

- <sup>1</sup> Greenough A, Greenall F, Gamsu HR. Immediate effects of albumin infusion in ill premature neonates. *Arch Dis Child* 1988;**63**:307-8.
- <sup>2</sup> Rutter N. Commentary. *Arch Dis Child* 1988;**63**:309.
- <sup>3</sup> Coulthard MG, Hey EN. Effect of varying water intake on renal function in healthy premature babies. *Arch Dis Child* 1985;**60**:614-20.

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Dr Greenough comments:

We thank Dr Wilkins *et al* for their interest in our short report on albumin infusion in the neonate.<sup>1</sup> We have, however, already provided data within the report to answer their concerns. In summary: Dr Wilkins *et al* claim that, in their experience, weight loss and diuresis are independent of the degree of oedema and plasma albumin concentration, but unfortunately they do not present their data. In our study to document the effect of albumin infusion we measured both urine output and change in weight. Comparison of the control and treatment periods, during which no other changes were made, showed in eight of 10 infants urine output increased and all 10 infants lost weight after the infusion. As this response was seen in infants in varying stages of their respiratory illness the increase in urine output is likely to be associated with the albumin infusion.

We agree that the measurement of urine output in the preterm neonate is difficult. We therefore used the same method of urine collection during both periods, and in addition measured weight change. In the absence of change in fluid input and phototherapy status, changes in weight reflect changes in urine output. Using non-parametric statistics confirmed that both the increase in

urine output ( $p < 0.05$ ) and decrease in weight ( $p < 0.01$ ) after the infusion were significant.

Albumin was not given rapidly, but as part of the daily fluid requirements and at the same rate. This method of infusion seems unlikely to cause an appreciable volume expansion with an acute increase in glomerular filtration rate and loss of solutes. This hypothesis is supported by the lack of change in urea and electrolytes after the albumin infusion (results section). Albumin concentrations were only measured daily (methods section), the post infusion concentration thus reflects the amount remaining in the vascular space at that time, in infants in whom protein leaks are well recognised.<sup>2</sup>

The aim of our preliminary study was to investigate, using infants as their own controls, if albumin infusion was effective in treating hypoalbuminaemia in normotensive sick infants.<sup>1</sup> We were able to show that albumin infusions were effective and associated with a significant increase in urine output. Using these data we have now designed a randomised controlled trial to investigate the duration of effect of albumin infusions and if this treatment alters clinical status.

#### References

- Greenough A, Greenall F, Gamsu HR. Immediate effects of albumin infusion in ill premature infants. *Arch Dis Child* 1988;**63**:307-8.
- Jobe A, Jacobs M, Ikegami M, Berry D. Lung protein leaks in ventilated lambs: effect of gestational age. *J Appl Physiol* 1985;**58**:1246-51.

centration depended upon the therapeutic agent used in patients. On either low or high vitamin D supplementation,  $1,25(\text{OH})_2\text{D}_3$  was below the normal concentrations (25(20) and 5(20) compared with 108(30)pmol/l). Treatment with calcitriol and dihydrotachysterol significantly increased  $1,25(\text{OH})_2\text{D}_3$  above normal concentrations: 190(40) and 900(513) compared with 108(30)pmol/l.

The conclusion of our report<sup>2</sup> on cystinotic patients was in accord with that of Chesney *et al*<sup>3</sup> that circulating values of  $24,25(\text{OH})_2\text{D}_3$  were reduced in relation to the renal parenchymal damage. The low  $1,25(\text{OH})_2\text{D}_3$  concentrations could reflect (as also stated by Katzir *et al*) a renal phosphate leak with impairment of synthesis of  $1,25(\text{OH})_2\text{D}_3$  besides its correlation with renal insufficiency associated with intrarenal cystine accumulation.

#### References

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- Chesney RW, Hamstra J, Mazess RB, Rose P, DeLuca HF. Circulating vitamin D metabolites concentrations in childhood renal diseases. *Kidney Int* 1982;**21**:65-9.

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## Cystinosis and vitamin D

Sir,

Katzir *et al* reported a case of nephrogenic diabetes insipidus, cystinosis, and an abnormality of vitamin D metabolism.<sup>1</sup> The idea that nephrogenic diabetes insipidus might herald cystinosis is interesting. Their analysis of the serum vitamin D metabolite concentrations on the patient, however, should not be regarded as a feature of the described association but rather part of the natural course of cystinosis. In 1983 Steinherz *et al* reported on the circulating vitamin D metabolites in nephropathic cystinosis.<sup>2</sup> In this study, 10 cystinotic patients with various degrees of functional renal impairment were screened for their vitamin D metabolites. The mean (SD) concentrations of  $24,25$  dihydroxyvitamin  $\text{D}_3$  ( $24,25(\text{OH})_2\text{D}_3$ ) were reduced in those patients treated with low dose of ergocalciferol ( $< 25 \mu\text{g}$ ) but within the normal range in the patients who received above  $625 \mu\text{g}$  vitamin  $\text{D}_2$ :  $0.75$  ( $0.5$ ) and  $6.5$  ( $2.8$ ) nmol/l respectively, while normal concentrations were  $4.3$  ( $1.3$ ). These reduced  $24,25(\text{OH})_2\text{D}_3$  concentrations have previously been found in children with uraemia. (Among these patients there were three cases of cystinosis.<sup>3</sup>)

Serum  $1,25$  dihydroxy vitamin  $\text{D}_3$  ( $1,25(\text{OH})_2\text{D}_3$ ) con-

## Atopic eczema and preterm birth

Sir,

We noted with great interest the report stating that preterm infants are at decreased risk of suffering from atopic eczema,<sup>1</sup> and attempted to confirm this finding using data from a well known data source, the Collaborative Perinatal Project. This project was a prospective study of pregnancy and child development that from 1959 to 1966 enrolled approximately 55 000 pregnancies at 12 centres in the United States. The recruitment and follow up procedures have been described.<sup>2,3</sup> When the subjects were 1 year old, study physicians completed a diagnostic summary form that included a code for eczema. Infant gestational age was determined from the date of the mother's last menstrual period. Children whose birth weight was grossly incompatible with their gestational age were eliminated.

There were 44 793 children who survived the first year and for whom the presence or absence of eczema was known. Four thousand and eighty nine (9.1%) of these children were born after less than 37 completed weeks' gestation. Eczema was slightly less common among preterm infants: 1.5% of preterms had eczema compared with