Serum albumin concentrations and oedema in the newborn

Sir,

Cartlidge and Rutter have provided useful data relating serum albumin concentration to gestation and discuss its poor correlation with clinical oedema.¹ Their view, however, that 'hypoalbuminaemia of prematurity' is a 'normal not a pathological finding' is debatable. A biochemical or clinical finding that is consistently associated with prematurity is not necessarily 'normal' and may indeed be undesirable. In this study the authors have examined only one clinical aspect of hypoalbuminaemia, oedema; yet low serum albumin concentration may have diverse effects—for instance, on drug and bilirubin binding and toxicity.

Currently, we are analysing the relation between clinical outcome and plasma albumin concentration measured in over 4000 samples during a longitudinal study of 932 infants. Preliminary multiple regression analysis has reaffirmed the strong association between hypoalbuminaemia and respiratory disease, even after adjustment for gestation. Low plasma albumin concentration in this circumstance cannot be regarded as 'normal' and probably reflects excessive losses—for example, into alveoli—and the adverse effect of severe disease or suboptimal nutrition on protein synthesis by an immature liver. Yet sick infants must have comprised an appreciable proportion of the low gestation sample investigated by Cartlidge and Rutter.

These workers contend 'that measurement of serum albumin concentrations in preterm infants, either routinely or in the presence of oedema, is of little use in their management'. This conclusion might be misinterpreted. A low plasma albumin concentration may be used as a marker for the high risk neonate, may influence the interpretation of other biochemical findings, and may warrant intervention in its own right. Albumin estimation is cheap and, I believe, should not be abandoned as a routine investigation in very low birthweight infants in the neonatal period.

Reference

- ¹ Cartlidge P, Rutter N. Serum albumin concentrations and oedema in the newborn. *Arch Dis Child* 1986;**61**:661–5.

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Drs Rutter and Cartlidge comment:

We agree with Dr Lucas that a finding consistently associated with prematurity is not necessarily normal. We found though that serum albumin was a poor marker of illness in low gestation infants: concentrations were low in both sick and well infants. His unpublished study clearly contains many more infants and we look forward to seeing it. We still contend that routine measurement of serum albumin is of little use in the management of the preterm infant. Certainly, bilirubin and drug binding are affected

by low serum albumin concentrations, but routine measurements are not carried out with this in mind. Perhaps a case can be made for routinely measuring albumin whenever serum calcium concentrations are measured in the preterm infant. Hypocalcaemia is commonly diagnosed and treated on the basis of low uncorrected calcium concentrations, but it is largely an artefact caused by a low serum albumin concentration.

Minimal change nephrotic syndrome and cyclophosphamide

Sir,

The interesting annotation by Trompeter about minimal change nephrotic syndrome and cyclophosphamide rightly indicates that the use of alkylating agents is controversial in a 'non-malignant condition with an excellent long term prognosis'.¹

The point is well made that an increased risk of malignant disease after immunosuppressive drugs has been observed in both adults and children, but this is perhaps too broad a generalisation. It is possible to go further. Cyclophosphamide, chlorambucil, and nitrogen mustard all undoubtedly cause secondary leukaemias.^{2,3} Other immunosuppressive agents, such as methotrexate or azathioprine, apparently do not. In other words not all cytostatic immunosuppressants carry the same risk of inducing neoplasia. While I appreciate that they may not have an equivalent therapeutic effect either, nevertheless it is an important point that should be borne in mind by clinicians who may be tempted to prescribe one for any benign disorder.

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References

- ¹ Trompeter RS. Minimal change nephrotic syndrome and cyclophosphamide. *Arch Dis Child* 1986;**61**:727–9.
- ² International Agency for Research on Cancer. *Monographs on the carcinogenic risk of chemicals to humans*. Suppl 4. Lyon: IARC, 1982.
- ³ Rosner F, Grunwald H. Cytotoxic drugs and leukaemogenesis. *Clin Haematol* 1980;**9**:663–81.

High dose intravenous methylprednisolone in treatment of recessive osteopetrosis

Sir,

The paper of Dorantes *et al*¹ gives me an opportunity to report my results in treating recessive osteopetrosis with high dose intravenous methylprednisolone, which partially support their results.

Three infants, a 4 month old girl, a 5 month old boy, and, more recently, a 14 month old girl, with typical recessive osteopetrosis were treated with intravenous

methylprednisolone in doses of 30 mg/kg/day for three days, 20 mg/kg/day for four days, and subsequently 10, 5, and 2 mg/kg/day for one week each, respectively, followed by 1 mg/kg/day until their haemoglobin concentration reached 11 g/dl, as described previously in the treatment of childhood acquired aplastic anaemia.² Haemoglobin reached this concentration in 34, 62, and 194 days, respectively.

Liver and spleen became normal in size, with rises in leucocyte and platelet counts and haemoglobin concentrations to normal, a decrease in reticulocyte count, and disappearance of normoblastaemia in the first two cases and improvement in the third child. The patients' plasma haemoglobin concentration and alkaline phosphatase activity decreased to normal, with normalisation of haptoglobin concentrations. Their bone marrow became normocellular as studied by needle aspiration, but their bones have not been influenced by treatment yet according to findings on x ray film.

Although currently one child could only detect light and still had mild exophthalmus and all had macrocrania, their growth and development were appropriate for their ages. The two younger cases still required 2.5 mg prednisone daily and the third was currently on intravenous treatment. With the exception of Cushingoid appearance during high dose administration, they did not have any side effects of treatment with corticosteroid, such as hypertension, hyperglycaemia, or growth retardation.

I would also like to question the laboratory findings of the authors' second case, who had a normal (or raised) haptoglobin concentration (5 mg/dl), despite pronounced plasma free haemoglobin (125 mg/dl), which does not agree my findings or expectations.

References

- ¹ Dorantes LM, Mejia AM, Dorantes S. Juvenile osteopetrosis: effects on blood and bone of prednisone and a low calcium, high phosphate diet. *Arch Dis Child* 1986;**61**:666-70.
- ² Özsoylu Ş, Coşkun T, Minassazi Ş. High dose intravenous glucocorticoid in the treatment of childhood acquired aplastic anemia. *Scand J Haematol* 1984;**33**:309-16.

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Diamond Jubilee issue

Sir,

The Diamond Jubilee issue of the *Archives* provided fascinating accounts of those who over the years have guided it to its present state of eminence as a paediatric journal. Three citations were omitted—namely, those of the present editors Roy Meadow and Bernard Valman and the associate editor Malcolm Chiswick. While we recognise and respect their modesty, we should not let the occasion pass without acknowledging the very important part which they have played in maintaining and enhancing the position of the *Archives*. To Roy Meadow, who will shortly be giving up the senior editorship, we owe a particular debt of gratitude.

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Working party on cystic fibrosis

Sir,

In Dr Jackson's synopsis of the recent report of the British Paediatric Association working party on cystic fibrosis mention is made of the proposal 'that there should be one centre with from 50 to 100 patients in most regions'.¹ In some National Health Service regions it is clear that more than one cystic fibrosis centre will be needed so perhaps the proposal should be amended to 'at least one centre with from 50 to 100 patients in most regions'. The staffing levels suggested for a clinic with 50 patients should, of course, be increased pro rata for larger clinics.

Reference

- ¹ Jackson ADM. Working party on cystic fibrosis. *Arch Dis Child* 1986;**61**:724.

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