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Correspondence

Aetiology of Reye's syndrome

Sir,

Drs Bellman and Hall emphasise in their annotation[1] the importance of a precise diagnosis of Reye's syndrome. However, one of the criteria they propose is that no other cause for the encephalopathy should be identified. This criterion is inherently unsatisfactory because it depends on the thoroughness with which the physician investigates the patient. Many inborn errors of metabolism may simulate Reye's syndrome closely, but they are likely to remain undiagnosed unless the appropriate investigations are undertaken, or the child survives and has a further episode of encephalopathy. Reye's syndrome seems to be relatively uncommon in the United Kingdom and seems to affect a younger age group than in North America,[2] which suggests that inborn errors of metabolism may be important in the UK. If the study of the aetiology of Reye's syndrome is to provide satisfactory answers, then a protocol should be established for the investigation of these patients which would include screening for inborn errors of metabolism. As a minimum, plasma ammonia, plasma and urine amino acids, urine organic acids, and orotic acid should be measured in specimens collected during the acute phase of the illness. If a liver biopsy is taken, part of this should be deep frozen for enzyme analysis later, if necessary.

References

[1] Bellman MH, Hall SM. Aetiology of Reye's syndrome. *Arch Dis Child* 1983;**58**:670–2
[2] Hall SM, Bellman MH. Reye's syndrome in the British Isles. BPA/CDSC surveillance scheme. *Communicable Disease Report* 1983; CDR 83/39.

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Drs Bellman and Hall comment:

We are glad that Dr Leonard has commented on the importance of metabolic investigation in children presenting with symptoms of Reye's syndrome. A deliberate aim of the British Paediatric Association/Communicable Disease Surveillance Centre surveillance scheme was to identify, within notified cases, any children suffering from metabolic disorders, and for this reason notifying paediatricians were asked to collect specimens of blood and urine as early as possible in the illness. We now have a bank of deep frozen specimens at the Communicable Disease Surveillance Centre that will shortly be analysed appropriately. We hope that exclusion of positive cases will resolve the ambiguity of our criterion of ignorance to which Dr Leonard referred. Such cases will presumably have already been screened out before notification from centres where the relevant laboratory facilities exist and the further exclusions resulting from our investigations should leave a 'hard core' in whom the diagnosis can be regarded as precise. Thus, as long as the appropriate cases continue to be notified, the register should illustrate accurately the features of Reye's syndrome in this country.

Hypocalcaemia after calcium and phosphorus supplementation

I read with interest the experience of Kovar *et al*,[1] with hypocalcaemia after calcium and phosphorus supplementation. There are two issues concerning calcium and phosphorus supplementation that were not discussed in this paper. These issues centre on the physical nature of phosphorus and the compatibility of calcium and phosphorus in solution.

Firstly, from a practical point of view, phosphorus does not occur as a free element and is only available in nature and pharmaceutically in the form of phosphate. Since most labelling of phosphorus is expressed in terms of millimoles, milligrams, or grams of the phosphate salt, actually calculating the dose in terms of phosphorus can be a very laborious task.

The second issue centres on the bio-availability of calcium and phosphate in oral supplementation solutions. Unfortunately calcium and phosphate will precipitate after a critical concentration in solution is reached. This calcium phosphate precipitate may occur as the dibasic, monobasic, or tribasic form, which have the following water and alcohol solubilities: practically insoluble, moderately soluble, and practically insoluble. Whether these precipitates are bio-available when given orally has never been shown. Without this information no conclusion can be made on whether the hypocalcaemia was the result of some physiologic deleterious effect caused by an incorrect calcium to phosphorus ratio in the special formula replacement or simply a form of calcium and phosphorus mixture that was not bio-available. We have avoided this potential problem, as have others,[2] by giving oral calcium and phosphate separately, not in a special formula, and allowing at least two hours between these doses.

References

[1] Kovar IZ, Mayne PD, Robbe I. Hypophosphataemic rickets in the preterm infant; hypocalcaemia after calcium and phosphorus supplementation. *Arch Dis Child* 1983;**58**:629–31.
[2] Greer FR, Steichen JJ, Tsand RC. Calcium and phosphate supplements in breast milk-related rickets. *Am J Dis Child* 1982;**136**:581–3.

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