Correspondence

Aetiology of Reye’s syndrome

Sir,

Drs Bellman and Hall emphasise in their annotation 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, 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

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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 pharmacologically in the form of phosphates. The name phosphorus is derived from the Greek phoibein, meaning ‘to shine’, and it was originally obtained from animal and vegetable materials containing inorganic phosphates. These issues are important because the solubility of phosphates is crucial to their bioavailability. Phosphates are well absorbed orally, but are prone to precipitation. If the calcium and phosphorus are in the same solution, calcium will presumably precipitate as calcium phosphate. This is a weak acid, which may further increase its solubility. If the calcium is a monobasic form, the resulting solution will probably be alkaline. Calcium and phosphorus can be taken either as single supplements or in combination. It is probably wise to give these separately, although it is important to ensure that the dose of each is sufficient to prevent deficiencies. It is possible that giving both separately will allow a greater bioavailability of each, even though the possible interaction of the two elements may theoretically limit the bioavailability of one or the other. This is particularly true of the monobasic form of calcium, which is less bioavailable than the dibasic form. However, the monobasic form is generally better tolerated, and may be more suitable for long-term use.

Secondly, from a practical point of view, phosphorus is a component of many foods and is widely available in the diet. It is essential for several biological processes, including bone and tooth formation, and the maintenance of normal serum calcium levels. However, it is also a component of many medications, and can potentially cause hypocalcaemia if not taken in the correct form.

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, 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, Robbie I. Hypophosphataemic rickets in the preterm infant; hypocalcaemia after calcium and phosphorus supplementation. Arch Dis Child 1983;58:629–31

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