

## LETTERS TO THE EDITOR

### Crigler-Najjar syndrome type I: management with a phototherapy crib mattress

EDITOR,—Crigler-Najjar syndrome type I is a rare autosomal recessive disorder characterised by absence of uridine diphosphate glucuronic acid transferase activity. Affected newborns develop severe unconjugated hyperbilirubinaemia and are at risk of death or permanent neurological damage from kernicterus. Phototherapy is the basis of treatment until the child grows to a more favourable size for liver transplantation, the only cure presently available.<sup>1 2</sup>

A girl, born at term to non-consanguineous Italian parents, presented at 8 days of age with a total bilirubin concentration of 419  $\mu\text{mol/l}$  and no conjugated bilirubin. Investigations were normal including complete blood count, Coombs test, liver function tests, urine and blood cultures. Family history was negative for jaundice. After four days of phototherapy the baby was discharged and then readmitted two days later because of unconjugated hyperbilirubinaemia. Thyroid function tests, pyruvate kinase, and glucose-6-phosphate dehydrogenase activities were normal. A percutaneous liver biopsy specimen showed mild non-specific changes including steatosis of some hepatocytes and canalicular cholestasis. A diagnosis of Crigler-Najjar type I was based on the analysis of bile obtained by duodenal aspiration which contained unconjugated bilirubin only (Dr Roy Chowdhury, personal communication).

The baby was treated with phenobarbitone (5 mg daily) and with single and double banks of phototherapy lights (Sylvania F20T12/CW cool white and Philips TL20W/03T special blue) and discharged with a portable Ohmeda 'Bili Blanket' at 7 weeks of age. The bilirubin concentration increased by approximately 5  $\mu\text{mol/l}$  per day so additional phototherapy using two banks of billights was given twice a week for nine hours each time in a medical daycare unit. She was readmitted on three occasions for continuous double phototherapy when her bilirubin concentration rose above 250  $\mu\text{mol/l}$ , associated with viral illnesses or vaccination. The phenobarbitone did not induce bilirubin conjugation.

A fan cooled phototherapy lamp was designed to replace a standard crib mattress (130 cm $\times$ 70 cm) (figure). The 'treatment' surface consisted of a 9.5 mm thick trans-

parent acrylic lid. The lamp held ten 120 cm fluorescent tubes (Philips FT40T12/BB). The five ballasts (Philips Mark III, R2S40-TPC, sound rating A) to power the lamps were housed in a separate fan cooled enclosure, all necessary interconnections being made by a multicore cable and connector. Radiation levels at 450 nm, measured at the treatment surface, exceeded 25  $\mu\text{W/cm}^2$  (Bio-tek phototherapy radiometer, model 74345). A transparent layer of plastic air bubble sheeting (Astro Polyfoam, Toronto) was held in place on the treatment surface with a white crib sheet, lowering the light intensity to approximately 15  $\mu\text{W/cm}^2/\text{nm}$  and reducing the glare from the lamps to a more comfortable level. The baby slept with her head on a small pillow and was covered with a standard crib sheet and quilt.

The baby was treated initially with eight hours of phototherapy at night using standard 'daylight' fluorescent lamps but had significant skin tanning over a three week period. After the bed was refitted with the Philips F40T12/BB lamps the bilirubin concentration decreased and was maintained around 200–250  $\mu\text{mol/l}$  with eight hours of nightly phototherapy. No further admissions were required and the baby's development was appropriate at 16 months of age.

Side effects associated with phototherapy include headache, nausea, vertigo, painful sensations in the eyes and photophobia,<sup>3</sup> and retinal damage.<sup>4</sup> The eyes were covered during treatment with a black eye shield and later protected by her pillow. Ophthalmological examination was normal at 15 months of age.

There has been one other report of a phototherapy bed used to treat a 10 year old girl who remained well without neurological sequelae until lost to follow up at age 17 (J M Littlewood, personal communication).<sup>5</sup>

As the child gets older a new phototherapy mattress with more lights will be made to fit a standard twin bed frame. This way we hope to control the hyperbilirubinaemia for as long as possible while awaiting the development of new therapeutic techniques such as gene transfer<sup>6</sup> thus avoiding the need for liver transplantation.

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### Cystic fibrosis identified by neonatal screening: incidence, genotype, and early natural history

EDITOR,—The finding by Green *et al* of an apparent halving of the incidence of cystic fibrosis in East Anglia is a surprising one,<sup>1</sup> although with so few cases the confidence intervals are large. Averaging their first three and last three years shows a reduction from 5.5 per 10 000 to 3.4 per 10 000. Our own UK-wide survey covering two decades showed a relatively constant rate of 4.0 per 10 000, albeit with an apparent reduction in the last three years due to delayed ascertainment.<sup>2</sup>

The authors suggest a number of reasons why this apparent reduction in incidence might not be real. To these we would add two more. Firstly the screening test used does not always show a very high sensitivity, indeed only 68% of their cases were detected by screening alone. This then could lead to under ascertainment in the later years of the study of the same sort that we have observed. Secondly, the existence of the screening programme may have made clinicians less likely to diagnose cystic fibrosis in the mistaken belief that it would already have been diagnosed from the neonatal heel prick specimen. This also could lead to lower numbers in the later years.

We hope that the incidence of infants being born with cystic fibrosis will indeed decline as a result of early diagnosis, antenatal screening and genetic counselling, but we feel that it is premature to claim such a reduction in East Anglia on these data.

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### Transient hyperphosphatasemia of infancy and failure to thrive

EDITOR,—Transient hyperphosphatasemia of infancy (THI) is well described in biochemical journals but in spite of reported incidence figures of 1.1-3.5%<sup>1</sup> does not appear in standard paediatric texts. THI is an apparently benign condition characterised by a marked transient increase in serum alkaline phosphatase lasting several weeks in the absence of any clinical, radiological, or biochemical evidence of bone or liver pathology.<sup>2</sup> The rise in alkaline phosphatase is quite dramatic, often exceeding 10 times the upper limit for the laboratory.

We have seen 13 further cases of THI with an age range of 5-16 months, with peak values of alkaline phosphatase ranging from 1518-14 230 IU/l, all returning to normal within nine weeks. Three quarters of our cases (10/13) presented with failure to thrive or weight loss, and 60% (8/13) had diarrhoea, which was recurrent or persistent in five cases. Previous cases have been said to have no consistent clinical features with the raised alkaline



phosphatase being a chance finding. However when we reviewed the cases reported in the medical literature between 40–60% did actually have symptoms of failure to thrive or gastrointestinal disturbance.<sup>1–4</sup> This therefore appears to be a common clinical association.

In all our cases radiology and other liver function tests were normal. Isoenzymes were measured in six cases and all but one showed either a mixture of liver and bone activity or bands between the two, typical of THI.<sup>1</sup> There was a tendency for our cases to cluster during the autumn and winter months; this has been previously documented.<sup>4</sup> Although the aetiology of THI remains unclear it may be the end result of different insults (infective or otherwise) in different children<sup>3</sup>; rotavirus was found in one of our cases and adenovirus in another. The importance of the diagnosis currently is its recognition, and in the avoidance of extensive investigations. Other diseases associated with such raised alkaline phosphatase would have clinical correlates such as deranged liver function tests, or abnormal wrist or hand radiographs. A family history of familial study would detect the rare familial type of raised alkaline phosphatase.<sup>4</sup>

We suggest that the isolated finding of a massively raised alkaline phosphatase in an infant is assumed to be THI unless clinical circumstances suggest otherwise. Isoenzyme analysis and other investigations of bone and liver need only be undertaken after eight weeks if the alkaline phosphatase has not begun to fall. Finally as between a half and three quarters of cases present with the related symptoms of diarrhoea, malabsorption or failure to thrive, we suggest that THI should no longer be considered as a pure biochemical phenomenon but rather a condition that does appear to have definite clinical associations.

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### Dual marker one day pancreolauryl test

EDITOR,—Dr Green and colleagues present interesting data relating to a novel 'tubeless' test of pancreatic exocrine function.<sup>1</sup> However, their claim that this will greatly simplify the investigation of pancreatic exocrine dysfunction in childhood seems as difficult to swallow as 200 ml of mannitol solution and 500 ml of clear fluid! None of the controls were children and those patients with cystic fibrosis ranged up to 25 years of age. For various reasons some tests which perform well in adults turn out to be less useful in young children.<sup>2</sup> As paediatricians, it is likely to be

the infant with diarrhoea and failure to thrive whom we wish to investigate. As pancreatic insufficiency is relatively rare compared with other causes of this presentation, an investigation with high specificity is essential. As the authors have yet to produce any data on this crucial aspect of their test, may I recommend a simple, cheap, sensitive, specific, and repeatable alternative for which patients are generally only too happy to provide specimens – faecal chymotrypsin measurement.<sup>3</sup> The dual marker pancreolauryl test is promising but needs further evaluation; I hope it has not been patented prematurely.

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### Epilepsy in children and the risk of drowning

EDITOR,—Drs Kemp and Sibert raised the issue of death by drowning in children with epilepsy.<sup>1</sup>

We recently had a patient aged 10 years who had had epilepsy for four years and who was on treatment with sodium valproate. He had initially presented with frequent absences and these lasted only for a few seconds at a time. He had no other neurological problems. Before his death he had had no fits for the previous three weeks and had never had any generalised tonic-clonic seizures. He was found by his parents drowned in his bath having been in the bath for 5–10 minute period; he was resuscitated and was admitted to this hospital to the intensive care unit. On admission he was comatose, his pupils were fixed and dilated. He was treated by intermittent positive pressure ventilation, fluid restriction, and anticonvulsants. He developed further seizures the next morning, associated with hyperthermia and hypertension, and died 14 hours after the initial drowning episode. Postmortem examination showed presence of cerebral oedema and a few anoxic changes within his brain.

His history is a little similar to subject 1 in Kemp and Sibert's paper, that is, a child with normal intellect and no neurological signs who had had only a fairly minor form of epilepsy and no major motor problems. His death underlines the importance of supervision in the situation where drowning is a potential problem. All these cases support the view that all parents who have children, even if they have minor seizures, must either arrange for supervision of their children while they are in the bath or as suggested by Kemp and Sibert use a shower in an unlocked room.

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### Injury epidemiology: emerging statistics and strategy

EDITOR,—Recent articles in this journal are not only in tune with the World Health Organisation (WHO) message of the year 'handle life with care; prevent violence and negligence', but also have added significance to Third World readers.<sup>1–3</sup> International trends<sup>1</sup> in pedestrian injury mortality support the view that strategies directed towards upgrading the environment pay more dividends than educational awareness programmes.<sup>4</sup> However such conclusions may unwittingly convey to developing countries that these strategies are mutually exclusive. For instance, in a symposium on injury prevention and social responsibility organised in this institute on WHO day, the delegates were equivocal in their emphasis on the environment and education. We think that these approaches are interdependent and reflect the dynamics of socioeconomic and political processes of a particular society. Improvements in the environment cannot come about without society demanding it, and this later phenomenon of peoples' assertion is unlikely to come from populations who lack awareness and education.

In the epidemiology of injury the conventional classification of children's mortality statistics into an age group 5 to 14 years fails to differentiate and delineate the prevention of risks peculiar to distinct lifestyles of children who are aged less than 9 and those who are older. Instead, for the epidemiology of injury children should be subdivided into 5–9 and 10–14 year age groups. This would encourage a better epidemiological understanding of age related problems and facilitate effective interventions in the hazardous host-agent-environment relationship. For example, children under the age of about 9 years do not have the necessary perceptual abilities to assess all the sensory inputs of the accident scenario such as traffic signals, etc, and hence they are unable to make a quick decision to avoid the accident. For this particular age group education of the parents and environmental changes play a major part compared with education aimed at modifying the behaviour of children. This latter strategy impinges upon the normal development of children by suppressing their natural instincts and curiosity for exploring their environment. On the other hand children older than 9 may benefit from educational programmes to boost the effects of environmental measures.

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### Pressure reduction of intussusception

EDITOR,—In this January's issue of the journal you published a paper from this centre