Correspondence

Reye's syndrome: diagnosis by muscle biopsy?

Sir,

I read the paper by Shapira *et al.*¹ with great interest as it was, to my knowledge, the first report of this condition. Although recurrent Reye's syndrome has been reported,² Pichichero and McCabe did not obtain liver biopsies in any episode. Shapira *et al.*¹ noted the marked fat droplet infiltration in hepatocytes by electron microscopical examination but they did not mention any mitochondrial changes in their patients although they accepted the fact that primary generalised mitochondriopathy is the pathophysiological basis of Reye's syndrome. Were mitochondrial changes present in their case 3?

Shapira *et al.*¹ pointed out the potential danger of bleeding in percutaneous liver biopsy, but in our experience of liver biopsies on at least 947 children (311 of them below age 2 years), this danger should not be exaggerated, provided the necessary precautions are taken.³

High levels of plasma lactate, alanine, and glutamine were accepted as indicating intramitochondrial decreased oxidation of pyruvate as a result of primary generalised mitochondriopathy. Although mitochondrial structural alterations appear to be similar in brain, muscle, heart, lung, and kidney, the activities of mitochondrial enzymes—such as citrate synthase, glutamic dehydrogenase, succinic dehydrogenase, pyruvate carboxylase, and pyruvate dehydrogenase—are decreased in the liver but not in the brain or muscles.⁴ Therefore I think that morphological mitochondrial changes should be interpreted cautiously as evidence of primary generalised mitochondriopathy. Are these changes primary or secondary to carnitine depletion in cases of recurrent Reye's syndrome?⁵

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Dr Shapira and co-workers comment:

Cases 1 and 3 underwent both liver and muscle biopsies but Case 2 had only a muscle biopsy; morphological abnormalities in the mitochondria were identical in all 3 muscle biopsies and in both liver biopsies. It should be mentioned that liver biopsies were described in recurrent Reye's syndrome secondary to systemic carnitine deficiency.⁵

Dr Ozsoylu referred to his vast experience with 947 liver biopsies in children and said that the danger of bleeding should not be exaggerated provided the necessary precautions are taken.³ We agree with him, but in

Reye's syndrome the downhill course may often be very fast and not allow time for adequate correction of the bleeding diathesis; in such cases a muscle biopsy is useful.

The concept of a primary generalised mitochondriopathy in Reye's syndrome is based mainly on the mitochondrial morphological alterations seen simultaneously in the liver, muscle, brain, kidney, and heart. The fact that the activities of several mitochondrial enzymes (citrate synthase, glutamic dehydrogenase, pyruvate carboxylase, succinic dehydrogenase, and pyruvate dehydrogenase) were found to be abnormally low in the liver only, and were within the normal range in the muscle and brain tissues is disturbing.⁴ This may suggest that the liver is more affected in Reye's syndrome than the other tissues (brain, kidneys, and muscles). The cause of the morphological changes in the mitochondria in all those tissues remains unknown.

References

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Birthweight, child abuse, and infant death attributed to accidents, poisonings, or violence

Sir,

A recent analysis that links infant deaths that occurred in 1978 to birth records is very welcome.¹ One striking feature is the association of infant death attributed to accidents, poisonings, and violence (ICD code E800-999) with birthweight. The incidence of such death was 0.31 per 1000 live births. Rates within the birthweight bands <2000, 2001-3000, and ≥3001 g were 1.03, 0.47, and 0.25 per 1000 respectively, a highly significant trend ($\chi^2=35.1$, $df=2$, $P<0.001$). If these results are considered in the light of data from Cardiff² relating to the incidence of non-accidental injury (not necessarily fatal) in children aged 5 years and below, the incidence is 2.7 per 1000 live births in the entire series, and 13.0, 3.8, and

2.1 for the respective birthweights. The relative risks for the two outcomes by birthweight are similar.

Data for subsequent years will be of better quality than for 1978 as the birthweight is now recorded for a greater number of infant deaths. Such data will serve to confirm or refute the association pointed out here.

References

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Benign carotenaemia

Sir,

We read with interest the article by Congdon *et al.*¹ and should like to draw attention to a paper by Fishman and Joseph² which described 8 patients with this condition. Carotenaemia is common in this region but probably goes unrecognised because, except for the yellow tint of the skin, the children are asymptomatic. The condition is manifested by a generalised yellow pigmentation, particularly on the palms of the hands and soles of the feet, but is absent in the sclera and buccal mucosa. The icteric colour tends to give the patient an anaemic appearance.

Our patients were infants aged between 6 months and 1 year. Their source of carotene was mashed vegetables—such as squash and pumpkin—and an excessive amount of carrots and carrot juice. The infants were not fed homogenised foods. When these vegetables are excluded from the diet it takes about 6 to 8 weeks for the skin to regain a normal colour and the serum carotene level to return to normal.

It is important to consider carotenaemia in the differential diagnosis of jaundice in apparently well children.

References

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Hypertension and upper airways obstruction

Sir,

We were greatly interested in the paper by Serrato *et al.*¹ and the fact that they had found significant hypertension in 3 of 14 patients with upper airways obstruction associated with heart failure. We had a similar case recently.

A 30-month-old achondroplastic boy was admitted with congestive heart failure. He showed considerable respiratory distress and was cyanosed. Bilateral Harrison's sulci were noted, rhonchi and rales were audible in both lungs, and there was generalised oedema. Systolic blood pressure of 280 mmHg was recorded in the arm, and femoral pulses could easily be palpated. A chest x-ray film showed gross cardiomegaly and signs of pulmonary oedema. The frontal QRS axis of an electrocardiogram was +135° with evidence of right atrial and right ventricular enlargement.

His condition improved with administration of intramuscular penicillin, kanamycin, hydrallazine, and frusemide. Signs of cardiac failure had resolved 10 days later and his blood pressure was 120/60 mmHg. A chest x-ray film showed diminution of heart size and disappearance of congestive changes. An intravenous pyelogram was normal and so were levels of vanillyl-mandelic acid.

When last seen at age 3 years 2 months, our patient was clinically well but was noted still to be a mouth breather. No longer was he taking antihypertensive medication and the systolic blood pressure was 98 mmHg (Doppler) in the right arm. The repeat electrocardiogram now showed a QRS axis of +90° and was within normal limits for age.

There had been a history of recurrent upper respiratory tract infections which had started when he was aged 9 months. When 20 months old, enlarged adenoids had been removed and grommets inserted in the ears. Despite this he had two further episodes of infection culminating in the clinical picture of cor pulmonale as described above. Each episode seemed to be associated with upper airways obstruction, perhaps aggravated by his cranio-facial malformation.

We too were puzzled by the considerable systemic hypertension, and like Serrato *et al.*¹ postulated that the severe hypoxaemia, via central mechanisms, might have been responsible for the raised blood pressure. We agree that upper airways obstruction should be considered in the differential diagnosis of children presenting with heart failure, respiratory distress, and systemic arterial hypertension.

Reference

- ¹ Serrato M, Harris V J, Carr I. Upper airways obstruction. Presentation with systemic hypertension. *Arch Dis Child* 1981; **56**: 153-5.

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