There was, however, relative confidence with regard to immunisations, 6 week checks, heart murmurs, and other medical and surgical problems, which were perhaps well covered by vocational training.

Discussion

This study was done in a deprived inner city area where previous training and experience in paediatric surveillance has been low compared with other parts of the country.⁶ The high response rate suggests enthusiasm towards child health surveillance and an eagerness for appropriate training. General practitioners were fairly clear about the areas in which they wanted more training and opinion tended to be consistent.

As general practitioners perform more paediatric surveillance the health authority role may change, with training and advice for general practitioners becoming as important as providing clinical services. While theoretical courses can readily be tailored to address gaps in knowledge, the high demand for practical training has implications for community services. Speech therapy and audiology departments, district handicap teams, child guidance and social services could all provide training on an individual or small group basis.

The fact that so many doctors gain their

experience of child health surveillance within general practice suggests that the training role of these general practice clinics should be recognised and enhanced. This could be achieved through regular support from senior community paediatricians, perhaps visiting and contributing to after clinic meetings.

The key to a successful child health programme lies in the relationship between doctors, health visitors, and others in the community health services. Multidisciplinary refresher training is one way to strengthen these links at the grass roots but such courses must address specific needs. Although this survey provides information about the topics general practitioners would wish to cover, it would be helpful to have the same information from the other professionals.

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Haem arginate in acute hereditary coproporphyrria

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Abstract

An 11 year old boy presented with severe acute hereditary coproporphyrria. Despite supportive measures his condition deteriorated after admission. Haem arginate, started two days after presentation, produced appreciable inhibition of porphyrin precursor overproduction and clinical improvement.

Hereditary coproporphyrria is the least common of the hepatic porphyrias. About 35% of cases present acutely.¹ Recently haem arginate, a stable haem compound, has been shown to reduce porphyrin precursor overproduction during acute attacks.² We report its use during severe acute hereditary coproporphyrria.

Case report

An 11 year old boy was admitted after a generalised seizure. He was vomiting for nine days despite prochlorperazine and metoclopramide, and had lethargy, abdominal pain, and constipation for four days. He had eaten little in the week before admission. Apart from constipation he was previously well. His father, aged

44, had mild hypertension. Otherwise there was no significant family history.

On examination he was agitated and confused, but localising pain appropriately. Axillary temperature was 36.5 °C. The pupils were dilated but reactive, and there was no papilloedema. The ankle jerks were brisk, with clonus, and the plantar responses were equivocal. The pulse rate was 160/minute and blood pressure 150/110 mm Hg. The precordial impulse was hyperdynamic. The respiratory rate was 16/minute with shallow breaths. Abdominal examination was normal.

Investigations showed a normal peripheral white cell count and differential. Plasma urea concentration was 10 mmol/l, glucose 9.7 mmol/l, and electrolytes were normal. There was mixed respiratory and metabolic acidosis with arterial pH 7.083, carbon dioxide tension 8.27 kPa, oxygen tension 14.4 kPa, and base excess –12.9. Computed tomography of the brain was normal, and lumbar puncture showed normal cerebrospinal fluid.

Seizures persisted despite intravenous diazepam and he was given a single loading dose of intravenous phenytoin followed by a clonazepam infusion. Hypertension and tachycardia

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Urine porphyrin precursors before, during, and after treatment with haem arginate. Day 0 is the day of presentation

Day	DALA ($\mu\text{mol/l}$)†	Porphobilinogen ($\mu\text{mol/l}$)†
0	758.0	355.0
1		
2*		
3*		
4*	25.6	20.2
5*	24.7	ND
6	21.0	4.7
7	42.1	5.1
8	13.7	3.1

*Indicates days on which haem arginate (100 mg) was given.
†Reference ranges: DALA, 0.8–34.3 $\mu\text{mol/l}$; porphobilinogen, 0–8.8 $\mu\text{mol/l}$.

persisted, and there was progressive diminution in level of consciousness, accompanied by dystonic posturing and loss of the gag reflex. This deterioration continued despite stopping the clonazepam. Serum sodium concentration fell from 134 to 124 mmol/l with a urine sodium of 131 mmol/l. Urine osmolality was 940 mosm/kg compared with serum osmolality 245 mosm/kg, consistent with inappropriate antidiuretic hormone secretion. Urine studies showed massively raised porphyrin precursors (table). Supportive treatment consisted of intravenous dextrose, ventilation, fluid restriction, and demeclocycline. In order to inhibit porphyrin precursor overproduction, haem arginate was started two days after admission.

There was gradual clinical improvement during the next three days, and blood pressure and pulse returned to normal. Improvement began three days after the phenytoin and 1.5 days after clonazepam was stopped. No further seizures occurred and he was successfully weaned from ventilation on the fourth day of treatment with haem arginate. There was a dramatic fall in porphyrin precursor overproduction (table) and rise in serum sodium concentration to 136 mmol/l. This improvement continued after treatment with haem arginate was stopped and three weeks after admission he was clinically normal.

Faecal coproporphyrins were raised to 320 (normally up to 46) nmol/g dry weight. Epstein-Barr virus transformed lymphocytes showed reduced coproporphyrinogen oxidase activity: 4.7 nmol carbon dioxide/hour/mg protein compared with control values (range) of 8.8 (7.4–10.3), indicating hereditary coproporphyria. Similar activities were found in lymphocytes from his brother and mother indicating that he was affected and she was the carrier.

Discussion

This boy presented with classic features of acute porphyria: abdominal pain, constipation, hy-

pertension, encephalopathy, and inappropriate antidiuretic hormone production. Possibly phenytoin, given before the diagnosis was made, contributed to the deterioration after admission. Although hereditary coproporphyria is reputedly milder than acute intermittent porphyria, this episode was undoubtedly life threatening.

Haem production regulates, by feedback inhibition, δ -amino laevulinic acid (DALA) synthase. In acute porphyria defective haem biosynthesis results in overactivity of this enzyme. Clinical features are thought to be due to consequent overproduction of porphyrin precursors, though haem deficiency may also be relevant. For these reasons treatment with haem has been advocated. Haematin, produced by dissolving haemin in alkali, was first used. Solutions of haematin are unstable, which may have contributed to clinical ineffectiveness. In addition, haematin degradation products were implicated in side effects, including thrombophlebitis and coagulation disturbances.³

Recently, haem arginate has been shown to be much more stable than haematin with stability in stock solution of 96% in two years.³ In a double blind study in 12 patients with acute intermittent porphyria, haem arginate significantly inhibited porphyrin precursor overproduction.² Clinical benefits were less striking, the treated group showing non-significant reductions in analgesic requirement, pain score, and duration of admission. The only side effect noted was mild phlebitis at the injection site in five patients. The authors suggested that the lack of statistical significance was due to the small numbers studied. They recommended that haem arginate be given to patients with severe attacks or those with peripheral neuropathy.

Porphyria commonly presents around puberty and so may present to the paediatrician. Early diagnosis and appropriate management can lead to complete remission. The most important aspects of management are removal of aggravating factors, analgesia, careful fluid balance, and intensive monitoring. For severe cases rational treatment without appreciable side effects is now available.

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