4 others: a personal observation in 1977,[2] and papers by Sheffield *et al.* in 1976,[3] Oberholzer and Palmer in 1976,[4] and Mantagos *et al.* in 1978,[5] all of which were published in journals in the English language.

The presence of CPS 1 activity in duodenal mucosa has been documented[6] and in our case reduced CPS 1 activity in gut was found.[2] However, a duodenal biopsy during the neonatal period is technically difficult to perform without risk, and in the case related by Hoogenraad the biopsy was performed at 2 years of age. We agree that early diagnosis is important so a needle biopsy of the liver, taking the usual precautions, is probably the safest way to obtain tissue for enzymatic studies.

Our experience suggests that urinary orotic acid measurement is more helpful in diagnosis than was indicated by Hoogenraad. If the clinical presentation (normal delivery, short period without abnormal signs, neurological and digestive signs appearing when feeding is started) suggests an error of metabolism and if intense hyperammonaemia is noted without specifically abnormal amino-acid and organic acid patterns, ornithine transcarbamylase (OTC) or carbamyl-phosphate synthetase deficiencies should be considered. In such cases absence of orotic acidura rules out OTC deficiency. This method of reasoning permits one approach to diagnosis, while waiting for a clinical improvement which will allow biopsies.

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Dr Hoogenraad and Dr Mitchell comment:

In reply to the letter by Farriaux *et al.* we acknowledge that there are a number of documented cases of complete lack of CPS 1, and we thank them for drawing this omission to our attention.

We hope our report has drawn attention to the potential of duodenal biopsy tissue assay for confirming the diagnosis of a number of urea cycle enzyme defects. We made no claim that any of the enzymes had not previously been assayed in the duodenum. In view of the lack of information about the safety of percutaneous liver biopsy compared with duodenal biopsy for establishing an early diagnosis, the choice of method will depend largely on the experience with each technique within the unit.

We agree with, and do ourselves use, the presence of a raised urinary orotic acid level as a valuable indicator of OTC lesions. However, other defects beside OTC lesions may produce orotic aciduria, and orotic acidura may be absent in lesions other than CPS 1 defects—for example, defects in *N*-acetyl glutamate synthetase. Furthermore, there may be cases in which protein restriction began before full biochemical assessment. In such cases pyrimidine excretion patterns may be modified and no longer be typical of the underlying defect.

What to us appears to be of vital importance, both on clinical and genetic grounds, is the ability to identify carriers of urea cycle defects. In our experience, the measurement of orotic acid in urine after a protein load is a valuable and, perhaps, the best method for identifying carriers of OTC lesions.[1–2] However, this approach will not detect CPS 1 carriers and our report shows the value of duodenal biopsy assay for heterozygous CPS 1 detection. Haan *et al.*[2] identified previously undiagnosed female carriers with partial OTC deficiencies using duodenal biopsy samples. In their report, and our own, nonproband carriers of OTC and CPS were noted to be not entirely asymptomatic and in fact had self-selected low protein diets to avoid disturbing symptoms.

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