and has the potential risk of causing separation of solid fat (that is, butter). Finally, since fat is lighter its expulsion is aided by the use of an eccentric nozzle syringe, especially if the nozzle is tilted up as is done to expel air bubbles. Even in the horizontal position the eccentric nozzle syringe seems to be better. If the syringe and pump are tilted up care must always be taken to fix them well to ensure stability and to avoid accidental fall. Additional suggestions include the use of shorter feeding and connecting tubes, complete emptying of the syringe at the end of each feed, and the early initiation of intermittent bolus feeding. It would also be beneficial if manufacturers of infusion pumps and syringes ensured a basic uniformity of design to allow easy fitting.

It is important to make sure that all the nutrients in human milk are actually delivered to the infant.

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Received 27 January 1984

Severe ornithine transcarbamylase deficiency

Two and a half years' survival with normal development

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SUMMARY The clinical course and management of a boy with severe ornithine transcarbamylase deficiency are described. In addition to treatment with sodium benzoate and amino acid keto analogues, mannitol may be useful in hyperammonaemia and nocturnal gavage feeding aids maintenance treatment.

Untreated, severe ornithine transcarbamylase deficiency causes fatal neonatal hyperammonaemia. Treatment prolongs survival but only two boys living more than 18 months have been reported—one aged 22 months with normal development and one 5 year old with severe psychomotor retardation.^{1 2} We report a third.

Case report

A boy born in June 1981, the fourth child of unrelated French parents, was transferred to this hospital aged 3 days. His brothers had died as

neonates—two from congenital malformations with no hyperammonaemia and one from ornithine transcarbamylase deficiency. His mother is asymptomatic but her serum ammonia and urine orotic acid concentrations rose abnormally on protein challenge. Jejunal biopsies in both parents showed normal ornithine transcarbamylase activity.

On hospital admission the boy was unresponsive with a serum ammonia value of 714 $\mu\text{mol/l}$ (normal value less than 60 $\mu\text{mol/l}$) and he had *Escherichia coli* septicaemia. Intravenous antibiotics and a dietary mixture given by gavage stopped deterioration, but on day 7 osmotic diarrhoea led to dehydration and coma and his serum ammonia value was 819 $\mu\text{mol/l}$. He improved with exchange transfusion, diluted feeds, and sodium benzoate and was clinically normal on day 10. After milk feeding was started on day 18 he thrived and his height and growth centiles were -2 SD and -1 SD respectively.

He has had three febrile illnesses and three immunisations without problem. At age 3 months he had a needle liver biopsy. At age 19 months he had a

hyperammonaemic episode with coma but there was no specific evidence of raised intracranial pressure. He was alert 48 hours after treatment but did not walk or talk normally for three more days. Before discharge his development quotient was 110 by the Brunet-Lezine scales (based on Gesell). At 21 months he started to refuse his liquidised dietary mixture (which did taste horrible). Since then he has had a natural food diet and a formula milk by day and the remaining required elements by nocturnal gavage, which is well tolerated. At 30 months he is developing normally but is fussy about his daytime food.

The diagnosis of ornithine transcarbamylase deficiency was suggested by the family history and hyperammonaemia and was confirmed by a raised urine orotic acid excretion (750 $\mu\text{mol/l}$: normal value less than 10 $\mu\text{mol/l}$) and plasma amino acid chromatography which showed low citrulline and arginine values. Liver biopsy specimen (1 mg)³ showed no ornithine transcarbamylase activity in this child whereas a liver specimen (5 mg) from his affected brother had shown 0.5 to 1.0% activity (0.2 units/mg protein: normal mean (SD) 35.5 (9.5)) with normal kinetics and pH dependence.

Treatment. The neonatal mixture given to our patient contained (per kg/day) 3 g Ketoperlen (see Table), 0.3 g arginine, 125 kcal (given as Liprocol and Caloreen, Laboratories Sopharga), minerals, and vitamins. Sodium benzoate (300 mg) was added on day 8.

The hyperammonaemic episode at 19 months was treated with bolus intravenous sodium benzoate and arginine (0.25 g/kg each) followed by (per kg/day) 100 kcal intravenous lipid and dextrose with minerals and water and, by gavage, 2 g Ketoperlen, 0.25 g arginine and 0.25 g sodium benzoate. On this

regimen his serum ammonia value fell from 228 to 140 $\mu\text{mol/l}$ in 6 hours, plateaued for 24 hours, and then, coincident with four doses of intravenous mannitol (0.5 g/kg, 6 hourly), fell to normal over 12 hours.

Maintenance treatment changed with age. The neonatal mixture was continued and formula milk (Nursie 1° age, Societe Dietetique Gallia; cows' milk derived with 13.5 g protein/100 g) was added at 2 g powder/kg/day increasing to 10 g by age 2 months. This gave 1.8 g protein and amino acids and keto analogues equivalent to 0.7 g protein per kg/day. Over his first year fruit, vegetables, rice, butter, and sugar were added, with adjustments of the original ingredients to 2 g Ketoperlen, 3.5 g formula milk, and 40 kcal from Liprocol and Caloreen per kg/day. By age 1 year he had (per kg/day) 1.1 g protein, 0.3 g arginine, and keto analogues equivalent to 0.5 g protein. These totals have remained unchanged ever since. The diet is varied by alternating 0.5 g protein portions of fruit and vegetables to his taste. From age 21 months he has had the Ketoperlen, arginine, Liprocol, Caloreen, and sodium benzoate by nocturnal gavage (300 ml over 6 hours) via a nasogastric tube put in nightly by his mother.

Discussion

Ornithine transcarbamylase deficiency is a sex linked, dominant, urea cycle enzymopathy divided into severe and partial forms with biochemical and immunological subtypes.^{3,4} Our patient has the severe form and his favourable progress is due to early diagnosis and avoidance of hyperammonaemic crises. The management of hyperammonaemia was based on that of other authors^{1,2,5} but without using phenylacetate. To this we added mannitol, which was associated with clinical and biochemical improvement. Mannitol may increase nitrogen excretion secondary to a diuresis and it may reduce cerebral oedema, which is reported in four of 7 necropsies in which the brain was examined.^{4,5} As the neurological state is not related directly to ammonia concentrations, other factors must be important and cerebral oedema deserves further study.

Our maintenance treatment is a synthesis of those described,^{1,2,5} aiming to reduce the nitrogen load with a low protein diet and amino acid keto analogues, to give arginine, and to use alternative paths of nitrogen excretion (sodium benzoate). Success depends on the mother, who has a demanding regimen to follow, and acceptability to the child; we have solved this problem by using nocturnal gavage.

Table Composition of Ketoperlen* (per 100 g)

Histidine [†]	1.08 g
Lysine [†]	1.44 g
Threonine [†]	1.34 g
Tryptophan [†]	0.66 g
Keto-acid analogues of: [‡]	
Leucine	6.06 g
Isoleucine	4.86 g
Valine	6.32 g
Phenylalanine	3.38 g
Methionine	3.70 g
Calcium ion	84.8 mmol/3.4 g

*Pfimmer and Pfimmer Erlangen.

[†]These four amino acids were doubled in quantity during the neonatal period by external supplement.

[‡]Calcium salt: weights given as amino acid equivalents.

The prognosis depends on hyperammonaemic episodes—several children do well until a fatal crisis.¹ The intellectual prognosis may not only depend on the neonatal coma: a case report² and work on female carriers⁶ suggest that later episodes are important. In these, unless there is vomiting, the gavage pump should stop the rapid deterioration due to anorexia and so reduce severity.

We thank Dr Cathelineau, Laboratoire de Biochimie Genetique, Hôpital Necker-Enfants Malades, Paris and all those who have contributed to the care of our patients, especially Dr Divry and her team, Laboratoire de Biochimie, Hôpital Debrousse.

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Received 27 January 1984

Candida albicans skin abscesses

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SUMMARY Two neonates who developed *Candida albicans* skin abscesses are described. One developed disseminated infection. In the newborn abscesses cannot be assumed to be of bacterial origin.

Infection is a major cause of morbidity and mortality in the neonatal intensive care unit. *Candida albicans* is well recognised as a pathogen in the neonate, being responsible for infections ranging from superficial dermatitis to systemic candidiasis.¹ Increased use of broad spectrum antibiotics and prolonged periods of intravenous cannulation for parenteral nutrition in newborn infants have increased the incidence of the latter. Although candida skin abscesses have been described in an infant² and in adults,³ they have not been previously reported in a neonate. We describe the occurrence of multiple skin abscesses in two neonates undergoing intensive care.

Case reports

Patient 1. A boy weighing 1.53 kg at 30 weeks' gestation required ventilation from birth for severe

hyaline membrane disease. During his first 24 hours he had persistent fetal circulation treated by tolazoline infusion; he also had a patent ductus arteriosus which was successfully treated with indomethacin. His total period of ventilation was 47 days after which he was oxygen dependent due to bronchopulmonary dysplasia. He received total parenteral nutrition while being ventilated.

At age 5 weeks he had septicaemia due to *Staphylococcus epidermidis* which was treated with gentamicin and ampicillin. At age 6 weeks three abscesses developed on his forehead, left wrist, and upper right arm. Each was aspirated and immediate Gram stain and culture of the aspirate were carried out. The Gram stain showed polymorphs, amorphous debris, and numerous yeasts, many showing pseudohyphae (Figure). Culture showed a pure growth of *C albicans*. Swabs taken from the skin overlying the abscesses did not contain yeast nor was the baby colonised by yeasts at other sites. Blood and cerebrospinal fluid cultures taken at this time were negative. He was treated with oral ketoconazole (5 mg/kg/day). One week later he developed signs of systemic infection and cultures of both blood and cerebrospinal fluid grew *C albicans*. No ocular signs of infection were observed on direct ophthalmoscopy. His treatment was changed to