Thus the high incidence of low serum glucose concentrations in the babies studied by Sexson¹ may simply be because 72% of the babies studied had one or more of the recognised risk factors for hypoglycaemia.

The concern regarding the definition of hypoglycaemia arises from the established risk of neurological damage after repeated and prolonged episodes of low circulating glucose concentrations.⁵ This concern needs to be balanced by the need to avoid the unnecessary treatment and investigation of otherwise healthy babies. We suggest a more rational approach to the definition of hypoglycaemia would be to derive a functional definition based on a correlation between objective measurements of neurophysiological function and blood glucose concentrations. Indeed, such studies may show that the 'safe' blood glucose concentration may be different in varying clinical situations—for example, during hypoxia, polycythaemia, or convulsions—rather than being dependent upon the babies' gestational and postnatal age and birth weight. Further research is needed urgently to resolve the

dilemma over the definition of hypoglycaemia in the neonatal period.

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References

- 1 Sexson WR. Incidence of neonatal hypoglycaemia: a matter of definition. *J Pediatr* 1984;**105**:149–50.
- 2 *The directory of emergency and special care units* 1986. St Ives: CMA Medical Data, 1986.
- 3 Srinivasan G, Pildes RS, Cattamanchi G, Viora S, Lillien LD. Plasma glucose values in normal neonates: a new look. *J Pediatr* 1986;**109**:114–7.
- 4 Cornblath M, Schwartz P. *Disorders of carbohydrate metabolism in infancy*. Philadelphia: WB Saunders, 1976.
- 5 Aynsley-Green A, Soltesz G. *Hypoglycaemia in infancy and childhood*. London: Churchill Livingstone, 1985.
- 6 Heck LJ, Erenberg A. Serum glucose levels in term neonates during the first 48 hours of life. *J Pediatr* 1987;**110**:119–22.

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Transient neonatal galactosaemia

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SUMMARY A 4 week old infant who failed to thrive was found to have galactose in his urine. Plasma galactose concentration was grossly raised (4.48 mmol/l; reference range <0.24 mmol/l) but red cell transferase and epimerase activities were normal. He improved when dietary lactose was excluded. Clinical and biochemical tolerance to galactose was evident by 7 months of age.

Galactosaemia is a rare disorder (1/72 000 in the United Kingdom)¹ which presents classically with vomiting, diarrhoea, listlessness, and failure to thrive. Symptoms often start within the first week of life. Persistent jaundice may suggest the diagnosis and by two weeks hepatosplenomegaly and lenticular opacifications are easily detectable. Biochemical galactose intolerance may also occur secondarily to severe disease of the liver parenchyma.² We report an infant with galactose intolerance who failed to thrive yet had normal galactose-1-phosphate uridyl transferase (G₁PT) activity and evidence of only mild hepatic dysfunction.

Case report

A boy, the first child of unrelated parents, was born weighing 2380 g after an induced delivery at 36 weeks' gestation for maternal pre-eclampsia. There was no significant family history and the pregnancy was otherwise uneventful. The baby was initially breast fed but at 20 hours of age he was transferred to the special care baby unit because of poor feeding. He was found to be hypothermic (34.6°C) and hypoglycaemic (blood glucose concentration <1 mmol/l). At 4 days of age he became jaundiced (maximum serum bilirubin concentration 265 µmol/l on day 5) but this settled and he was discharged at 9 days. Over the next three weeks he became increasingly irritable, fed poorly with frequent possetting, and needed supplementation with formula milk. He had not regained his birth weight. Physical examination showed no abnormality except for mild generalised hypotonia.

A urine sample screened for metabolic abnormalities at 1 month of age contained reducing substances identified as galactose at a concentration of 11 mmol/l. Investigations that gave normal results at

this time were full blood count, electrolytes, calcium, random blood glucose, thyroid function tests, a screen for toxoplasma, other viruses, rubella, cytomegalovirus, and herpes virus, α_1 antitrypsin phenotype, and hepatitis B surface antigen. Liver function tests at 1 month of age were abnormal (reference ranges given in brackets): bilirubin 64 $\mu\text{mol/l}$ (<20), direct bilirubin 12 $\mu\text{mol/l}$ (<10), alkaline phosphatase 682 IU/l (135–550), total protein 38 g/l (55–75), and albumin 21 g/l (30–50); aminotransferase activities were normal. Blood and urine amino acid and urine organic acid concentrations were normal. The screening test for galactosaemia was normal as were the activities of G₁PT and uridine diphosphate galactose epimerase. The plasma galactose concentration at this time was 4.48 mmol/l (normal <0.24 mmol/l). Between 2 and 3 months of age there was a peak alkaline phosphatase activity of 1000 IU/l with a γ -glutamyltransferase of 203 IU/l (<45) and raised transaminases (aspartate aminotransferase 79 IU/l (<40), alanine aminotransferase 58 IU/l (<30)). Subsequently alkaline phosphatase and plasma protein concentrations became normal but the transaminase activities remained borderline raised. No cataracts were found on ophthalmological examination. At the age of 2 months the baby required a blood transfusion for anaemia (haemoglobin concentration 72 g/l, reticulocytes 5.9%).

It was felt that, in view of the symptoms and high plasma galactose concentrations, galactose should be excluded from the diet and a lactose free soy formula milk was prescribed (Formula S, Cow and Gate). Immediately his mother noticed a change in his behaviour, the infant becoming more placid and content. He gained weight rapidly and his muscle tone returned to normal. Plasma galactose concentrations fell to 0.03 mmol/l and galactose disappeared from the urine. The baby was challenged with galactose at an age of 3 months (6.5 g orally) resulting in a peak plasma galactose concentration of 2.56 mmol/l, which showed a continuing galactose intolerance. Erythrocyte galactose-1-phosphate concentrations, however, responded normally confirming that there was no impairment of the transferase pathway.

At 7 months of age his transaminase activities remained borderline raised but other liver function tests were normal and his galactose tolerance was investigated with an intravenous galactose load.³ Plasma galactose concentrations during the test decreased with a normal half life of 5 minutes (see figure). A supervised reintroduction of cows' milk was performed at 10 months without sequelae. One month later he was found to be thriving on a normal diet. His development is normal.

Figure Semilogarithmic plot of plasma galactose concentrations after a bolus injection of D(+) galactose 350 mg/kg body weight. Dashed lines indicate the limit of the normal range of half lives for this age (up to 10 minutes³).

Discussion

There have been many recorded variants of galactosaemia but this child did not appear to fall into any of these categories.⁴ Classical galactosaemia due to transferase deficiency was excluded by the normal activity of the enzyme. There was no negro blood in the family, a factor previously noted in children with transferase variants. All children with galactokinase deficiency have had cataracts, which this child did not, are asymptomatic at birth, and grow normally. The possibility of a deficiency of the epimerase type was considered but was excluded by enzyme assay. Kelly described suggestive symptoms or biochemical evidence of galactose intolerance in six of seven infants with the Duarte/classical galactosaemic genetic compound.⁵ Although at least two of these infants subsequently became galactose tolerant by 15 months, most were asymptomatic and blood galactose concentrations were substantially below those reported here. All seven had abnormal transferase activity.

It is possible that there had been transient liver damage in this child at or before delivery resulting in an inability to metabolise galactose. Galactose

intolerance in association with liver disease is well known and galactose challenge has been used as a dynamic test of liver function.³ Pronounced galactose intolerance, however, is usually associated with severe liver disease.² Hepatosplenomegaly was not noted in this infant and biochemical evidence was limited to moderate transient abnormalities of alkaline phosphatase, γ -glutamyltransferase, albumin, and a persisting borderline rise of transaminase activities. Early jaundice and anaemia are both features of galactosaemia; however, the jaundice was transient, and both prematurity and frequent blood sampling may have been contributory factors.

This child appears to be unusual in the degree of his intolerance to galactose in the absence of any detectable defect in galactose pathways and in the presence of only minimal biochemical evidence of liver disease. This intolerance appeared to be physiological as well as biochemical as the child's health improved promptly when he was given a galactose free diet. It appears unlikely that the biochemical and clinical improvements were unrelated. It is important that children with galactose

intolerance other than that due to inherited enzyme deficiencies be challenged with galactose at intervals so that they can return to normal feeds as soon as they are able to tolerate them.

Quantitative assays of erythrocyte enzymes and of galactose-1-phosphate were performed by the department of clinical chemistry, Southmead Hospital, Bristol.

References

- ¹ Schwarz V, Wells AR, Hotzel A, *et al.* A study of the genetics of galactosaemia. *Ann Hum Genet* 1961;25:179-88.
- ² Wharton BA, Scott PH. The newborn. In: Clayton BE, Round JM, eds. *Chemical pathology and the sick child*. Oxford and London: Blackwell, 1984:7-72.
- ³ Relander A. Intravenous galactose tolerance test. Normal series of children. *Scand J Clin Lab Invest* 1968;22:196-8.
- ⁴ Segal S. Disorders of galactose metabolism. In: Stanbury JB, Wyngaarden JB, Fredrickson DS, Golstein JL, Brown MS, eds. *The metabolic basis of inherited disease*. 5th ed. New York: McGraw-Hill, 1983:167-91.
- ⁵ Kelly S. Significance of the Duarte/classical galactosaemia genetic compound. *J Pediatr* 1979;96:937-40.

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Oral vancomycin in prevention of necrotising enterocolitis

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SUMMARY Eighty four very low birthweight babies (considered high risk for developing necrotising enterocolitis) were given vancomycin orally for 48 hours before introduction of oral feeds; one developed necrotising enterocolitis. One hundred and twenty very low birthweight babies (not considered such high risk) were fed without first receiving vancomycin; 17 developed necrotising enterocolitis. Although this was not a randomised control trial, results indicate a role for vancomycin in prophylaxis of necrotising enterocolitis.

The exact sequence of pathological events in necrotising enterocolitis has not been established, although there is general agreement that prematurity and neonatal illness predispose to it, and that invasion of the bowel wall by bacteria is the ultimate and most serious aspect of the pathological process. It is also widely accepted that necrotising enterocolitis rarely develops in babies who have not received enteral

feeds and indeed often manifests soon after feeds have been introduced. It could be that gut bacteria require food substrate in order to multiply sufficiently to invade the susceptible bowel wall. If this hypothesis is correct, then reducing the bacterial population in the bowel, particularly the gas producing anaerobes, before introducing milk feeds could reduce the incidence of necrotising enterocolitis.

According to this line of reasoning it has been our policy, during the past three years, to treat very low birthweight babies who have had prolonged intensive care, and are therefore at high risk of developing necrotising enterocolitis, with oral vancomycin for 48 hours before starting milk feeds. Vancomycin was chosen because of its activity against clostridial species and other anaerobes, and because it does not completely sterilise the bowel, which could promote colonisation by unwanted pathogens. Furthermore, vancomycin is poorly absorbed and so a high drug concentration can be achieved in the gut with minimal risk of systemic toxicity.

This paper presents our experience with necrotis-