

## Short reports

# Neonatal hypoglycaemia—the controversy regarding definition

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**SUMMARY** Major paediatric textbooks and the views of neonatologists in the United Kingdom were surveyed to establish a definition of neonatal hypoglycaemia. The definition ranged from a glucose concentration of <1 mmol/l to <4 mmol/l. Hypoglycaemia is recognised to cause neurological sequelae and yet there is no accepted definition of the lower limit of normality for circulating blood glucose concentrations.

There are few areas in neonatology that are as controversial as the definition of hypoglycaemia. Hypoglycaemia is recognised as a common problem in newborn babies but its incidence is difficult to ascertain due to the controversy over definition. Sexson highlighted the issue in his paper where he showed that the incidence of hypoglycaemia in the 232 babies he studied would be 8.1% if hypoglycaemia was defined as a blood glucose concentration of <1.7 mmol/l or 20.6% if it was defined as <2.2 mmol/l.<sup>1</sup>

The aim of our study was to establish the degree of variation in the definitions of hypoglycaemia among paediatric textbooks and paediatricians in charge of special care nurseries in the United Kingdom.

### Methods

The definition of hypoglycaemia, with reference to the glucose concentrations in whole blood in term babies who were born with a weight appropriate for gestational age and in babies who were preterm or small for gestational age, was ascertained (a) in 36 current paediatric textbooks and (b) from consultants in charge of special care nurseries with one or more intensive care cots. The names of the consultants were obtained from the Directory of Emergency and Special Care Units 1986,<sup>2</sup> and postal questionnaires were sent to them.

### Results

The definitions of hypoglycaemia obtained from the review of the 36 textbooks of paediatrics are shown in fig 1. There was a very wide variation in the definitions given ranging from a glucose concentration of <1 mmol/l to <2.5 mmol/l with a modal value of <1.7 mmol/l for term babies of appropriate weight, and <1.1 mmol/l for babies who were preterm or small for gestational age.

There were 242 paediatricians identified from the Directory of Emergency and Special Care Units.

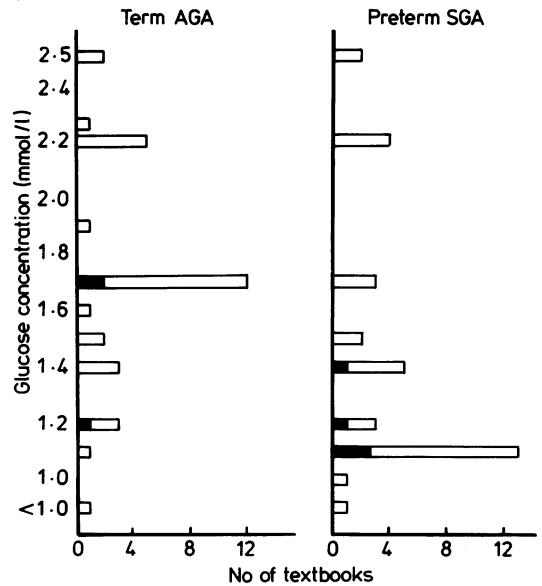


Fig 1 The definition of hypoglycaemia obtained from a review of 36 current textbooks of paediatrics. The shaded area of each histogram represents textbooks which define hypoglycaemia as two consecutive episodes of a blood glucose concentration below the given value. AGA=weight appropriate for gestational age, SGA=small for gestational age.

One hundred and seventy eight (73.5%) replied giving their definitions of hypoglycaemia and their responses are shown in fig 2.

There was an even greater controversy among the practising paediatricians whose definitions of hypoglycaemia ranged from a glucose concentration of  $<1$  mmol/l to  $<4$  mmol/l. The modal value for term babies of appropriate weight was  $<2.0$  mmol/l and  $<1.1$  mmol/l for babies who were preterm or small for gestational age. The response from paediatricians in charge of four or more intensive care cots was no more consistent than that from paediatricians in charge of less than four intensive care neonatal cots.

There were 41 special care nurseries from which two or more paediatricians replied. In these nurseries there were discrepancies in the definition of hypoglycaemia between paediatricians from the same unit in 25 (61%) cases. The discrepancy between their definitions ranged from 0.2 mmol/l to 1.8 mmol/l.

The site of sampling—that is, whether capillary, venous, or arterial blood was used for analysis of glucose concentration—was not included in the definition of hypoglycaemia by any of the textbooks reviewed nor by any of the paediatricians in our survey.

## Discussion

Our results show that the definition of hypogly-

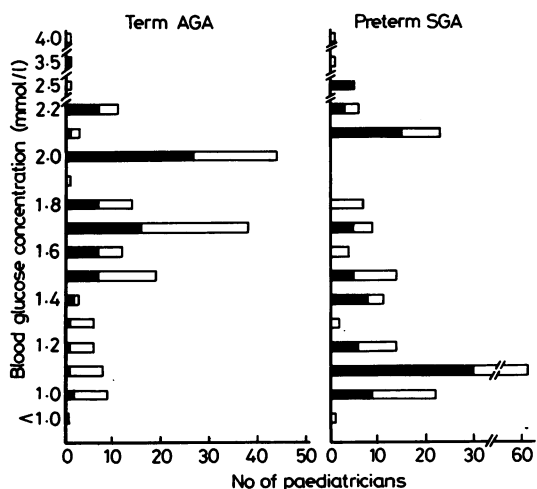


Fig 2 The definition of hypoglycaemia given by 178 paediatricians. The shaded area represents those paediatricians in charge of nurseries with four or more intensive care cots. AGA=weight appropriate for gestational age, SGA=small for gestational age.

caemia in the neonate continues to be a controversial and a confused issue. Not only is there no consistency in the definition between the paediatric textbooks, but of more importance there seems to be little agreement among neonatologists caring for the babies. Such discrepancy, which we have shown can occur even within the same nursery, must surely lead to confusion among junior medical and nursing staff and to inconsistency in the management of babies. There also appears to be a persistence of the belief that the brain of the infant who is premature or small for gestational age is more tolerant to low blood glucose concentrations than that of the full term normal baby.

The difficulty with the definition of hypoglycaemia is, however, understandable in view of the lack of reliable clinical signs in the neonate when the blood glucose concentrations fall, and in view of the continuing controversy over whether asymptomatic hypoglycaemia causes neurological damage.<sup>3</sup>

Previous definitions of hypoglycaemia have been based on the description of glucose concentrations in the blood, plasma, or serum in groups of newborn babies under various circumstances and the establishment of the range of values found.<sup>1-5</sup> Hypoglycaemia is then often defined as a glucose concentration less than one standard deviation below the mean value.<sup>4</sup> The limitations of this approach are most clearly shown by the discrepancy between various authors in the resulting definitions of hypoglycaemia. Srinivasan and colleagues for example, who measured plasma glucose concentrations in healthy term babies at varying ages, recommended that hypoglycaemia should be defined as a plasma glucose concentration of  $<2.2$  mmol/l in the first 24 hours after birth and  $<2.6$  mmol/l thereafter.<sup>3</sup> In contrast Heck and Erenberg, who similarly measured serum glucose concentration in healthy term babies at varying ages, recommended that hypoglycaemia be defined as  $<1.7$  mmol/l in the first day after birth and  $<2.2$  mmol/l thereafter.<sup>6</sup>

The range of concentrations of glucose obtained in a study of a population of babies is dependent upon many factors: (1) the presence of predisposing factors—for example, birth asphyxia, maternal diabetes, or being small for gestational age; (2) the physiological status of the baby at the time of sampling in relation to the method of feeding and the time from feeding to blood sampling; (3) whether venous, capillary, or arterial blood is obtained, and whether whole blood, serum, or plasma is used for the analysis; (4) the time between sampling and analysis and the technique of measurement used (whether Dextrostix, Reflolux, glucose oxidase technique, etc); and (5) the methods used to prevent glycolysis in the blood sample before assay.<sup>5</sup>

Thus the high incidence of low serum glucose concentrations in the babies studied by Sexson<sup>1</sup> 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.<sup>5</sup> 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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## 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)<sup>1</sup> 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.<sup>2</sup> We report an infant with galactose intolerance who failed to thrive yet had normal galactose-1-phosphate uridyl transferase (G<sub>1</sub>PT) 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