Commentary

AGA term newborn

The two papers agree that infants who fail to trigger a dual gluconeogenic and ketogenic response to the postnatal fall in plasma glucose concentration are at risk of neural impairment. The YSI glucose analyser is a useful tool in the management of such infants but should only be introduced if (i) access to its software is prohibited to avoid the generation of spurious results and (ii) training is provided to avoid technique related errors induced by blood clots, low sample volume, etc (Mr A Jarvis, Biochemical Medicine, Ninewells Hospital may be contacted for advice).

The paper by Hawdon *et al* does not advocate screening 'healthy' infants for hypoglycaemia but how is it then possible to distinguish the many normoglycaemic, sleepy babies from the few at risk of neural dysfunction? I agree that detection focused solely on an arbitrary glucose concentration makes it impossible to detect this minority without generating anxiety in the mothers of the remainder. Nevertheless, how is it possible to justify screening for phenylketonuria and hypothyroidism with all the anxiety their 'false positives' generate and yet shrink from the detection of hypoglycaemia when it coexists with hypoketonaemia? Nature may have provided a solution to the problem because insulin suppresses ketone formation at low concentrations, that is concentrations which do not augment peripheral glucose uptake. Thus the presence of ketones is reassuring and suggests that insulin has been unable to arrest the delivery of ketone precursors (fatty acids) to the liver and its activity is therefore unlikely to be detrimental to that infant. The major research study proposed in this paper must examine the sensitivity and specificity of current ketone detection systems (blood and urine) and go on to determine whether ketone positive, hypoglycaemic babies have a better outcome than a matched ketone negative group.

SGA infants

Both papers agree that hepatic glucose and ketones do not appear in the circulation of the fasting newborn infant spontaneously, that is they must be generated by a permissive hormonal environment. However, I cannot concur with the view that glycogenolysis and gluconeogenesis are temporally distinct. The hormonal milieu which permits glycogen breakdown simultaneously activates gluconeogenic enzymes and the urea cycle (the latter

to detoxify the amino nitrogen from incoming gluconeogenic amino acids). The corollary holds true – glycogen is often present during neonatal hypoglycaemia but cannot be released because portal insulin activity has not been adequately suppressed and in this environment, gluconeogenesis must also be deficient. A high intravenous dextrose requirement coupled to wide swings in plasma glucose concentration during milk feeding are key markers to distinguish such infants from those who are hypoglycaemic because they lack subcutaneous fat but are otherwise adapted to neonatal life. I disagree with the management of the former group. This paper advocates continuous feeding (oral and intravenous) but in my experience this method generates unpredictable swings in glucose concentration which are unresponsive to pharmacological glucagon concentrations (>1000 pg/ml). This glucagon 'resistance' is diminished when milk is withdrawn by nasogastric tube suggesting that the enteral acolytes of insulin were overactive in the fed state. A detailed study is needed.

Glucose boluses

I cannot find any justification for the use of glucose boluses. Compartmental glucose modelling in six preterm infants (A Mehta, R Wootton, D Halliday, unpublished data) shows that the non-steady state glucose disappearance rate after a bolus cannot match its rate of entry resulting in hyperglycaemia.

Finally, what is fasting hypoglycaemia?

In conclusion, to paraphrase J C Waterlow and A J W Sim¹: 'Biochemists draw the map of the roads, clinical investigators try to measure the traffic along them and the practising clinician decides on which road to go . . .'. Unfortunately, the neonatologist not only has a sketch for a map and many roads to choose from, but is also liable to end up carrying the petrol can, because, 70 years after its discovery, the essential role of glucagon is still not appreciated. On the journey to the definition of neonatal hypoglycaemia, we barely know how to count the cars. The next challenge must be to devise methods for the rapid measurement of ketone traffic in order to provide the neonatologist with a choice of route for safe arrival along the neurodevelopmental highway.

ANIL MEHTA

1 Sim AJW. Counteracting protein wasting in post-traumatic patients. In: Garrow JS, Halliday D, eds. *Substrate and energy metabolism in man*. London: John Libbey, 1985: 232–42.