Neonatal hypoglycaemia

Sir,

I feel that comment is called for on some of the points raised by Dr. R. D. G. Milner in his recent review of neonatal hypoglycaemia (*Archives*, 1972, **47**, 679).

Reference is made to the neuropathological consequences of untreated hypoglycaemia reported by Anderson, Milner, and Strich (1967). This paper, however, can be criticized: as only 3 untreated cases are described, there was no biochemical confirmation of hypoglycaemia during life in one of them, and the authors themselves admit that it is unlikely that all of the changes seen in the brain stem and cord occurred during life. The most recent experimental studies in primates (Brierley, Brown, and Meldrum, 1971a, b) have utilized perfusion fixation of the brain *in situ*, and showed that hypoxia and insulin-induced hypoglycaemia produce similar neuronal alterations, namely ischaemic cell change. Though the fact that the hypoglycaemia was insulin-induced may have had some protective effect, this is unlikely as I have observed similar changes in infants with neonatal hypoglycaemia. Brain sections from 17 infants who died after a limited period (under 24 hours with two exceptions) of hypoglycaemia in the newborn period were examined and compared with sections obtained from a control group of 17 normoglycaemic infants who had experienced a comparable degree of clinical perinatal hypoxia. Both groups were characterized by the presence of ischaemic nerve cell change of similar severity and distribution.

Meldrum, Horton, and Brierley (1971) found that 7 out of 15 adolescent monkeys subjected to insulin-induced hypoglycaemia had no histological evidence of brain damage at subsequent examination. The maximum period of exposure to blood glucose levels of less than 20 mg/100 ml in these 7 adolescents was 3 hours, while in a similar study Myers and Kahn (1971) found the longest period of exposure without subsequent brain damage to be 6 hours. It is likely that newborn monkeys could withstand longer periods as it is well-known that the newborn of many species are more resistant to hypoglycaemia than the adult, possibly owing to their higher energy reserves (Mayman and Tijerina, 1971).

It cannot be concluded, therefore, that exposure to a limited degree of hypoglycaemia in the newborn period invariably produces any excess CNS damage at a histological level over and above that produced by coincident hypoxia.

Dr. Milner attributes some of the confusion about the clinical significance of hypoglycaemia to my papers on this subject (Griffiths, 1968; Griffiths and Bryant, 1971). Perhaps, therefore, I may be allowed to clarify the problem.

Everyone would agree that 'true' symptomatic hypoglycaemia requires urgent treatment to avert permanent cerebral damage. This is an uncommon condition (1 to 3 per 1000 births) that usually presents after the first day of life, and in which symptoms are a direct consequence of the low blood glucose level, and are therefore alleviated partially or completely by i.v. glucose infusions.

What my papers have shown, on a statistical basis, is that in the large majority of hypoglycaemic infants during the first day of life symptoms are coincidental to the hypoglycaemia, that the hypoglycaemia has a strong tendency to spontaneous correction within this period, and that such infants at follow-up have no excess neurological or intellectual handicap over matched control infants. The prognosis for hypoglycaemic infants without symptoms of any sort during the first day of life is excellent, with no neurological impairment on later review.

If it is these findings which Dr. Milner finds confusing I can only admit my guilt, pleading in mitigation that by taking cognizance of them, treatment can be placed on a rational basis. I would suggest the following regimen.

If an infant is found to be hypoglycaemic during the first day of life and has symptoms, an i.v. diagnostic/therapeutic dose of glucose is given. If symptoms are relieved after this procedure, 'true' symptomatic hypoglycaemia is diagnosed, and is treated by continuing the i.v. infusion. If symptoms are not relieved, and in asymptomatic infants, the infant is monitored closely during the remainder of the first 24 hours of life and i.v. glucose is given only if spontaneous correction has not occurred within this period.

As my results apply to hypoglycaemia largely confined to the first day of life, it may be prudent, in the present state of knowledge, to treat all infants who are found to be hypoglycaemic after this period, regardless of the presence or absence of symptoms.

If this policy is combined with an adequate calorie intake and the avoidance of hypothermia, the number of infants requiring treatment for hypoglycaemia will be reduced with no corresponding increase in sequelae.

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