children, overt vitamin D deficiency rickets was diagnosed concomitantly with their coeliac disease. The ages at diagnosis of these three were 7, 10, and 11 months; their ages when first symptomatic were 4, 9, and 7 months. In the other six cases, where no overt rickets was recorded, the ages at diagnosis were 7, 18, 19, 21 months, 2 years 4 months, and 4 years 10 months, the ages when first symptomatic being 4, 16, 6, 8, 8, and 5 months. We are now analysing the time sequences of coeliac disease, rickets and, according to the teeth affected and the extent of hypoplasia, the possible concordance or discordance with the time of mineralisation of the affected areas in the diseased teeth. We feel that rickets, even when not clinically or biochemically evident, as is often the case in untreated coeliac disease, could be relevant to the development of enamel hypoplasia.

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Diagnosis and management of folate deficiency in low birthweight infants

Sirs,
I read with interest the paper by Strelling et al. (Archives, 1979, 54, 271). Although the erythrocyte folate levels suggested folate deficiency, the babies were too young to have megaloblastic anaemia. Herbert1 showed that serum folate levels decrease early (about 7 weeks) and it takes nearly 19 weeks for the real megaloblast to appear in the bone marrow.

The mean reticulocyte count for the babies was 2.64% (range 0 to 6, Table 1) which would not be expected in real megaloblastic anaemias. The rise of Hb and haemato-
crit values (such as 0.3 and 1%) in 2 to 4 weeks’ treat-
ment are well below a response to treatment.8

Because of the feeding history (including iron supple-
ment), the ages of the babies, and the slightly high reticulocyte count for age, I should like to see studies (such as hydrogen peroxide test and vitamin E levels) to exclude vitamin E deficiency. It is well known that megaloblastic changes of erythroid precursors occur in haemolytic anaemias regardless of the cause.

References

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Drs Strelling and Goodall comment:
Professor Ozsoyulu expresses doubts on theoretical grounds that our patients could have had megaloblastic anaemia related to folate deficiency when aged only 5 to
12 weeks. We should like to reassure him that the megaloblastic changes were unequivocal. The figure (Case 2) shows an undoubted megaloblast which was fully haemoglobinised. This was one of 82 such cells found in a buffy-coat smear made from a sample of blood. The time-scale at which a poor folate intake produces megaloblastosis is very different when a healthy adult physician is compared with rapidly growing tiny babies whose folate requirements may be relatively much greater. The megaloblastic preterm infants described by Gray and Butler were even younger (3 to 6 weeks) and other affected babies have been under 12 weeks.

We found, as have others, that a mild reticulocytosis was common in preterm infants in the first 3 months and was unrelated to megaloblastosis. Even so, the mean value (2.6%) in our groups of both normoblastic and megaloblastic infants was below that reported by Oski and Barness, and Ritchie et al. in infants with haemolytic anaemia due to vitamin E deficiency, namely 8.2 and 6.1% respectively.

The rate at which Hb rose after treatment with folic acid would be modified by physiological factors in infancy, such as growth and concomitant expansion of plasma volume, and should not be compared with that expected in an adult. Nevertheless, the falling Hb in each affected infant was invariably reversed after folic acid, even though in some the dose was probably suboptimal.

We are aware that lack of vitamin E has been suggested as a cause of megaloblastic anaemia in malnourished infants but even in the cases described by Majaj et al. folate deficiency was not completely excluded. Perhaps lack of vitamin E may affect the uptake of folate through cell membranes although in the vitamin E-deficient infants described by Oski and Barness, and Ritchie et al. the bone marrows examined were normoblastic.

In our infants treatment with folic acid but no other addition to diet was followed within a few days by complete normoblastic change associated with a reticulocyte response. As our facts do not fit with Professor Ozsoylu’s theories, we suggest the theories be changed to fit the facts.

References

Sodium nitroprusside and RDS—primum non nocere

Sir,

There have been two reports on the use of sodium nitroprusside (NaNP) to reduce pulmonary vascular resistance in severe respiratory distress syndrome (RDS).1-2 This new indication for an old drug represents an innovative pharmacological approach to the treatment of pulmonary hypertension in the newborn. However, several aspects of this drug must be evaluated before the apparent success reported leads to widespread use in nurseries. As most neonatal therapeutic tragedies have occurred due to altered drug metabolism and disposition in the newborn infant, this aspect needs to be investigated urgently.