FIG.—Persistence of haemagglutinating antibody (reciprocal titre, vertical axis) to group C meningococci in 3 cases of meningitis and in 10 carriers after treatment (school outbreak).

associated with immunity to disease, which may be more closely associated with bactericidal antibodies (Goldschneider, Gotschlich, and Artenstein, 1969). The haemagglutinating antibody titres observed in this family were lower than we have observed in patients who have recently carried or had clinical meningococcal infections, and this was associated with low levels of IgM and susceptibility to clinical disease. Familial predisposition to meningococcal septicaemia associated with IgM deficiency has been described (Hobbs, Milner, and Watt, 1967), though there is no constant association between the occurrence of meningococcal septicaemia and low levels of IgM (Kelly, Storm, and Juckett, 1970). Circulating antibody reduces the rate of acquisition of meningococci (Gold and Artenstein, 1971), and the re-establishment of the carrier state in the 3-year-old child who had had meningitis 3 months previously may also have been a manifestation of a deficiency of immunity.

Summary

During a 3-month period there were 3 cases of meningococcal meningitis in a family of 9 children. Sulphadiazine chemoprophylaxis failed, and carriage of the meningococcus continued in the family until finally eradicated by the use of rifampicin. 8 of the 9 children were found to have both a low IgM level and a low titre of meningococcal antibody.

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Plasma and erythrocyte folate concentrations in normal mature infants

Assessment of folate status in normal mature infants is a necessary preliminary to detailed investigation of abnormal conditions. There is evidence that maternal folate depletion is associated with intrauterine growth retardation (Hibbard and Hibbard, 1963) and also that infants of low birth-weight show a tendency to develop folate depletion (Strelling *et al.*, 1966).

Blood folate concentrations in the newborn infant are commonly higher than those in the mother (Grossowicz *et al.*, 1960; Landon and Oxley, 1971). Several factors may influence these values, in particular prenatal administration of folic acid (Landon and Oxley, 1971). In most previous studies of folate status in infants, only serum or whole blood folate concentrations were measured (e.g. Grossowicz *et al.*, 1960; Landon and Oxley, 1971).

Also, in series relating to predominantly normal infants, some of low birthweight were included and no distinction was drawn between pregnancies in which folic acid was taken prenatally by the mother and those in which no such therapy was taken (Roberts *et al.*, 1969).

The following survey was undertaken to estimate the normal range of plasma and erythrocyte folate levels in normal mature infants.

Material

577 infants were investigated during the period June to October 1970. All were born in Mill Road Maternity Hospital and satisfied the following criteria. (a) They were normal liveborn infants of singleton pregnancies. (b) Gestation period was known with reasonable certainty and was within the range 259 to 293 days. (c) Birthweight was above the 10th centile for the gestation period (Thomson, Billewicz, and Hytten, 1968). (d) Details concerning maternal haematinic therapy were available.

All the women studied had received iron therapy and 436 had taken at least 500 μg folic acid daily for a period of more than 4 weeks before delivery.

Methods

Blood samples were obtained from the umbilical cord by venepuncture immediately after delivery. Plasma and erythrocyte folate concentrations were assessed by the methods of Herbert (1961) and Hoffbrand, Newcombe, and Mollin (1966). Using these methods plasma and erythrocyte folate values in normal adults are 3 to 19.9 ng/ml (mean 7.8 ng/ml, SE 0.34) and 130 to 650 ng/ml (mean 257 ng/ml, SE 9.6) respectively. Hb concentration was estimated spectrophotometrically after conversion to cyanhaemoglobin. Packed cell volume (PCV) was measured by microhaematocrit and the mean corpuscular Hb concentration (MCHC) was calculated.

Results

Plasma and erythrocyte folate levels.

Plasma and erythrocyte folate levels were assayed on all specimens of umbilical cord blood. The values showed a skewed distribution and logarithmic values were found to be most satisfactory for statistical analysis. The differences in both plasma and erythrocyte folate in relation to maternal folic acid therapy were highly significant. (Plasma, $t = 6.5566$; $P < 0.001$; erythrocyte, $t = 3.5325$; $P < 0.001$).

Plasma and erythrocyte concentrations of folate in cord blood are shown in Table I.

Hb concentration, PCV, and MCHC were measured in 560 samples of cord blood; the other 17 samples of blood contained clots, and the results are detailed in Table II. Student's 't' test confirms

TABLE I
Plasma and erythrocyte concentrations of folate in cord blood

	No prenatal folic acid	Prenatal folic acid
No. infants investigated	141	436
Plasma folate concentration (ng/ml)		
Geometric mean	11.9	17.7
Mean $\pm$ 2SD	3.8-36.6	5.0-62.9
Erythrocyte folate concentration (ng/ml)		
Geometric mean	321	378
Mean $\pm$ 2SD	128-838	145-983

TABLE II
Hb concentration, packed cell volume, and mean corpuscular Hb concentration of cord blood

	No prenatal folic acid	Prenatal folic acid
No. cases investigated	131	429
Hb concentration (g/100 ml)		
Arithmetic mean	17.4 (SD 2.7)	17.5 (SD 2.7)
Packed cell volume (%)		
Arithmetic mean	56.7 (SD 6.9)	56.8 (SD 6.7)
Mean corpuscular Hb concentration (%)		
Arithmetic mean	30.8 (SD 3.7)	30.9 (SD 3.7)

that there is no significant difference between the two groups.

Discussion

Plasma and serum folate concentrations in normal newborn infants have been discussed previously by several authors including Landon and Oxley (1971). In these reports and in the present series a wide range of values is found. Grossowicz *et al.* (1960), Landon and Oxley (1971), and others measured whole blood folate concentrations in normal infants. However, such values are greatly influenced by PCV and do not provide precise assessment of folate status. Erythrocyte folate concentration provides a more significant assessment of folate status but this parameter has rarely been studied. Serum and erythrocyte folate levels in a group of 50 normal infants were studied by Roberts *et al.* (1969) who reported mean values which are higher than the results in the present series, but it is possible that most of the mothers received folic acid prenatally, and Landon and Oxley (1971) showed that such therapy resulted in relatively high infant folate levels.

In the present series prenatal administration of

folic acid resulted in significantly higher concentrations of both plasma and erythrocyte folate in newborn infants (Table I). However, high levels of blood folate do not necessarily imply clinical benefit and Hb concentration, PCV, and MCHC were similar in both groups (Table II), while none of the infants showed anaemia. The mothers who received no folic acid supplements prenatally were normal and showed no evidence of folate depletion, so that we conclude that folate levels in their infants (plasma folate—mean 11.9 ng/ml, range 3.8–36.6 ng/ml; erythrocyte folate—mean 321 ng/ml, range 128–838 ng/ml) can be regarded as normal for the mature newborn.

Summary

Plasma and erythrocyte folate levels in a group of normal mature newborn infants whose mothers had received a prenatal supplement of folic acid were compared with those from an untreated group. Infants in the treated group had significantly higher levels of both plasma and erythrocyte folate.

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