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.

We are grateful to Professor J. R. Hobbs for his advice and to Dr. Fraser Williams for specimens from the children admitted to hospital.

REFERENCES


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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) Birth-
weight was above the 10th centile for the gestation
period (Thomson, Billewicz, and Hytten, 1968). (d) Details concerning
maternal haematinicial 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 cyanmethaemoglobin. 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
erthrocyte folate in relation to maternal folic acid
treatment were highly significant. (Plasma,
t = 6.556; 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, packed cell volume, and mean
corpuscular Hb concentration of cord blood

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

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
erthrocyte 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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