Neonatal meningitis

M. J. Goldacre
M.A., B.M., B.Ch., M.F.C.M.

Department of Social and Community Medicine, University of Oxford, Oxford OX1 3QN

Summary

Some of the main features of neonatal meningitis, studied in a defined population of infants, are reviewed. The incidence rate was twenty-six cases per 100 000 live-births. The case fatality rate was 43%. Gram-negative intestinal bacilli were the commonest infecting organisms. Streptococci accounted for an important minority of cases. It is stressed that neonatal meningitis usually presents as a non-specific illness, without the clinical signs of meningitis which are familiar in older patients. Twenty-three of the seventy-six infants in this study (30%) weighed 2500 g or less at birth. Another eight infants were born to mothers whose membranes had been ruptured for 24 hr or more.

Introduction

A study of 800 consecutive, unselected neonatal post-mortems, published in 1930, reported thirty-three cases of meningitis (4% of all neonatal deaths) (Cruickshank, 1930). However, neonatal meningitis attracted surprisingly little study until about 25 years ago. A search of the world literature up to 1942 produced a total of only 131 published cases, including Cruickshank's thirty-three (Flensborg, 1943). The disease carries a poor prognosis. Case fatality rates from several recent series are shown in Table 1. Some of the main features of meningitis in the first 4 weeks of life are now reviewed. The data are from a population-based study in the North-West Thames region of England.

<table>
<thead>
<tr>
<th>Place</th>
<th>Years</th>
<th>Cases</th>
<th>Deaths</th>
<th>Case-fatality rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia (Yu and Graug, 1963)</td>
<td>1953–1962</td>
<td>47</td>
<td>28</td>
<td>60</td>
</tr>
</tbody>
</table>

Population and method

An attempt was made to identify all cases of bacterial or pyogenic meningitis in infancy which occurred in the region between 1969 and 1973. Cases were sought from several different sources: Hospital Activity Analysis, diagnostic indexes at individual hospitals, microbiology laboratory records, death certificates, and statutory notifications. The diagnostic criteria for inclusion in the study have been described in detail (Goldacre, 1976). The region has a population of 4 million people, and there were 295 000 live-births between 1969 and 1973. Infants with neural tube defects are excluded from this report.

Results

Seventy-six cases of meningitis, thirty-three of them fatal, were identified in infants under 4 weeks of age. This represents a case-fatality rate of 43%. Two-thirds of the cases developed while the infant was still in hospital after delivery (fifteen-one patients, twenty-two deaths). One-third developed outside hospital (twenty-five patients, eleven deaths). The case-fatality rate was similar in each group.

The main causative organisms are shown in Table 2. Gram-negative intestinal bacilli accounted for thirty-seven cases (Escherichia coli, 24; Klebsiella spp., 3; Salmonella spp., 3; Proteus spp., 1; coliform, 4; paracolon, 2). Streptococci accounted for ten cases (β-haemolytic Streptococcus 3, Enterococcus 3, Pneumococcus 2, other streptococci 2). Two cases were caused by Haemophilus influenzae and one by each of Staphylococcus aureus and Listeria monocytogenes. There were twenty-five cases of pyogenic meningitis where no organism was cultured: the

<table>
<thead>
<tr>
<th>Causative organism</th>
<th>No. of cases</th>
<th>No. of deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram-negative enteric bacilli</td>
<td>37</td>
<td>20</td>
</tr>
<tr>
<td>Streptococci</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Others</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Unknown</td>
<td>25</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>76</td>
<td>33</td>
</tr>
</tbody>
</table>
majority of these infants were already receiving antibacterial drugs at the time of lumbar puncture.

There was a tendency for the Gram-negative infections to develop in hospital within a few days of birth, and for the Gram-positive infections to develop later in the neonatal period (Fig. 1). This was, however, by no means invariable.

The typical clinical signs of meningitis, familiar in older patients, are usually absent in the newborn. Among the commonest signs recorded in the cases notes immediately before lumbar puncture were one or more of the following: The statement simply that the infant looked ill; was not feeding; was vomiting; was limp or floppy. A description of the infant’s colour as pale, grey, or cyanosed. A record of apnoeic attacks or cyanotic attacks; of grunting, twitching or convulsions.

The signs commonly found in older infants of a tense or bulging fontanelle, or of neck stiffness, should not necessarily be expected in neonates.

Some perinatal features of these infants are summarized in Table 3.

Table 3. Neonatal meningitis: associated features

<table>
<thead>
<tr>
<th>Features</th>
<th>Number</th>
<th>Percent of all cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight ≤ 2500 g</td>
<td>23</td>
<td>30</td>
</tr>
<tr>
<td>Membranes ruptured 24 h or more</td>
<td>8</td>
<td>11</td>
</tr>
<tr>
<td>Assisted delivery</td>
<td>12</td>
<td>16</td>
</tr>
<tr>
<td>Other procedures or problems</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>Normal history, delivery; normal infant</td>
<td>26</td>
<td>34</td>
</tr>
<tr>
<td>All cases</td>
<td>76</td>
<td>100</td>
</tr>
</tbody>
</table>

Discussion

As in other series, bacterial meningitis was commoner in the first year of life than in any subsequent year, and commoner in the first month of life than in any subsequent month (Goldacre, 1976). However, 4 weeks is a short time to be at high risk, and neonatal meningitis is an uncommon disease. The incidence rate in this population was twenty-six cases, and the mortality rate was eleven deaths, per 100 000 live-births. For comparison, an average of nine deaths in the neonatal age-group per 100 000 live-births is currently ascribed to meningitis in the Registrar General’s mortality statistics for England and Wales.

Gram-negative intestinal bacilli, notably *E. coli*, are responsible for the majority of cases of neonatal meningitis. *Streptococci* account for an important minority. These groups of organisms are uncommon in meningitis after the first 4 weeks of life. Conversely, the common causes of meningitis at older ages, the meningococcus, *haemophilus* and *pneumococcus*, are uncommon in the neonatal period.

Neonatal meningitis carries a particularly poor prognosis. At least 40% of affected infants die during the acute illness. A proportion of the survivors have serious neurological sequelae and some of these infants die later in infancy or childhood (Heckmatt, 1976).

Meningitis in the newborn is non-specific in its clinical presentation. An indication of the diagnostic difficulty which may be experienced can be seen by reviewing general practitioners’ referral letters. Of all children with meningitis, the referral letter suggested this diagnosis in 75% of children over 5 years of age, 55% of infants aged 4 weeks to 1 year, and 25% of infants under 4 weeks of age (Goldacre, 1977).

Most cases of neonatal meningitis are unrelated to others. Nursery outbreaks seem to be infrequent and none was identified in this study. When reported, they tend to involve the less common organisms, e.g. β-haemolytic streptococci, staphylococci,
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flavobacteria (Nicol, 1961; Shaffer et al., 1956; Cabrera and Davis, 1961).

With the exception of nursery outbreaks and the special case of infants with neural tube defects, the pathogenesis of neonatal meningitis is not well understood. It is known that the infecting organism may sometimes be recovered from the mother's genital tract (Benirschke, 1960). In most series there is an association with low birth-weight, prolonged rupture of the mother's membranes, and possibly with other obstetric or post-natal complications (Ziai and Haggerty, 1958; Overall, 1970). However, it is hard to show that these associations are causal. Twenty-three of the infants in this study (30% of the total) weighed 2500 g or less at birth. This is a significantly higher proportion (s.d., 5.26, \( P < 0.01 \)) than the 7% of low birth-weight infants in the general population (Baird, 1969). A further eight infants were born to mothers whose membranes had been ruptured for 24 hr or more. In five of the eight, meningitis was diagnosed within 48 hr of delivery and it seems likely that the organism was acquired from the mother's infected genital tract. An association with assisted delivery (forceps, artificial rupture of the membranes, Caesarian section) is less clear; and a causal association would be difficult to prove. The group 'other procedures or problems', in Table 3, includes a case of staphylococcal meningitis which developed after exchange transfusion; two mothers with gastroenteritis; one infant with congenital hydronephrosis and another with congenital heart disease; and one mother whose previous infant had died of coliform meningitis.

Although cause and effect are hard to demonstrate in these circumstances, one hope for reducing the incidence of neonatal meningitis may rest with the obstetric aim of uncomplicated full-term delivery. Because it is an uncommon disease, multicentre co-operative studies are needed to define more clearly its pathogenesis and possible means of prevention.

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References


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