Tuberculous meningitis in children in the Western Cape

Epidemiology and outcome

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Summary

The incidence of tuberculous meningitis in children was determined using hospital records as well as local authority notifications. One hundred and eighty-five cases occurred over a 3-year period. The age-specific incidence in the 0-14-year-old group was 7.5/100,000. In only 28 cases was the disease at an early stage when treatment was commenced. Young age and late-stage disease at presentation were associated with a poor outcome. The associated morbidity and mortality rates were high; the mortality rate was 24%, and nearly 50% of patients were left with a residual disability.

Tuberculous meningitis (TBM) usually develops within 6 months of acquiring primary tuberculosis and is commonest in infancy and early childhood. It is the most disastrous complication of this disease. Mortality is substantial, and even with early diagnosis and optimal treatment many children suffer neurological and intellectual impairment.

At the Red Cross War Memorial Children’s Hospital in Cape Town TBM is a not infrequent cause of disability in children referred to the Cerebral Palsy Clinic. Although the disorder is notifiable it is known that notification of tuberculosis, such as chest radiographic appearances, sputum or gastric washings positive on Mycobacterium tuberculosis culture, or a positive tuberculin skin test; (c) CSF culture positive, bromide partition ratio < 1.6 or CSF adenosine deaminase activity (ADA) > 5 U/l; and (d) clinical course consistent with TBM; or (ii) autopsy findings indicating TBM.

Staging of disease

The prognosis of TBM is known to correlate with the stage of the disease at the time of commencement of appropriate therapy. In staging the disease we used the system suggested by Kennedy and Fallon: (i) patient fully conscious and rational with signs of meningeal irritation, but with no focal neurological signs or evidence of hydrocephalus; (ii) patient mentally con-
A certain area was therefore used throughout (Table I).

**Outcome of the disease**

As in other similar studies we recognized four categories of outcome: (i) apparently good health or a minor physical abnormality which does not interfere with the child's lifestyle; (ii) minor sequelae such as mild mental retardation, epilepsy, deafness or behavioural problems; (iii) major sequelae — either severe mental retardation or mild mental retardation with physical abnormalities such as hemiparesis or athetoid movements; and (iv) death, within 1 year of onset of the disease (primary mortality), or after 1 year (secondary mortality).

**Results**

One hundred and eighty-five cases were identified over the 3-year period (49 in 1979, 61 in 1980 and 75 in 1981). For the remainder of the report the findings for the 3 years will be considered as a whole because of the relatively small numbers in each year.

Analysis of the age distribution showed the highest incidence in the younger age groups. The ages of the patients ranged from 3 months to 14 years; 102 (55%) were aged under 2 years at diagnosis, 52 (28%) 2 - 4 years, 23 (12%) 5 - 9 years, and 8 (5%) 10 - 14 years. There were 96 females (52%) and 89 males.

Of the 185 children, 125 were coloured, 59 were black and 1 white.

**Incidence**

The population denominator was derived from the 1980 census figures. The actual numbers of children aged under 15 were available for 24 of the 40 magisterial districts in the health region. For the remaining districts the relevant population was estimated from the total all-age figures.

The appropriate denominator for the region was 822,000 children aged under 15 years. The annual incidence was therefore 7,5/100,000.

The incidence by population group was as follows: white —0.2/100,000; coloured — 5,6/100,000; and black — 25.7/100,000. Of the 59 black children identified, 20 were either from Transkei or returned there after treatment. If these cases are excluded, the incidence for blacks becomes 18/100,000.

**Geography**

Of the total population of the Cape Western Health Region, 54% live in the area known as the 01 Economic Region, which comprises the magisterial districts of Simonstown, Wynberg, Cape Town, Goodwood and Bellville. Of our 185 cases 95 were from this area. The incidences for the metropolitan area and the rural area as a whole were therefore approximately equal. The rate was calculated for each magisterial district and varied between 0 and 28.4/100,000. Incidences were high in certain areas. Initially the rates were calculated on the basis of two population denominators: (i) the population aged under 14 years, all race groups; and (ii) the population aged under 14 years, black and coloured children only. Both sets of figures point to the areas of high incidence, but differ in magnitude. The denominator (i) was therefore used throughout (Table I).

**Stage of disease**

Table II shows the stage of disease at diagnosis in the 185 cases of TBM. Only 28 patients (15%) were known to have had stage I disease when treatment commenced; 42% had stage III disease, which is known to carry a grave prognosis even when appropriate therapy is vigorously applied.

**Outcome**

Approximately 25% of patients fell into each outcome category (49 are considered well, 43 have minor sequelae, 45 have major sequelae, and 44 died (primary and secondary mortality)). The outcome in 2 cases was unknown, and 2 children had cerebral palsy before developing TBM and the outcome was therefore not classified. Fig. 1 shows the outcome by age group (children who were well or had minor sequelae...
TBM is a problem in both urban and rural areas, but the higher individual rates were from the rural areas. Nevertheless there is a surprising variation between magisterial districts. Children from the rural areas were diagnosed at a later stage of the disease and more of them died. The level of ascertainment of the rural cases may be questioned. We have tried to achieve maximum detection by: (i) using a single health region (the Cape Western region) where all notifications came to a single centre; (ii) having access to the records of all the major hospitals in the Region and those of the hospitals catering for infectious diseases; and (iii) contacting the peripheral local authorities — we gave them details of cases from their districts already known to us and asked for records of any further cases.

It is known that in TBM a poor outcome correlates with young age and late-stage disease. These facts were amply confirmed by our findings. At first sight it is disquieting to note that in our study outcome in terms of both survival and absence of disability is no better than in earlier studies (Table III). However, these studies may not have been comparable as regards age, were based on referrals to single major hospitals, and did not reflect the situation for an area as a whole.

In summary, TBM remains a cause of significant neurological disability in children in the Western Cape. The overall finding that during 1979 - 1981 nearly 50% of patients either became severely handicapped or died as a result of the disease reflects continuing high morbidity and mortality, despite implementation of full antituberculosis therapeutic regimens. Efforts to reduce tuberculosis in the community and prevent its spread to paediatric contacts will therefore be doubly rewarded by a reduction in the incidence of this handicapping disease.

We wish to acknowledge the co-operation of local authorities and hospital superintendents in undertaking this study, and thank them for their help. We would also like to thank Dr J. G. L. Strauss, medical superintendent of the Red Cross War Memorial Children's Hospital, for permission to publish. This study was made possible by a generous donation from the Stella and Paul Loewenstein Charitable and Educational Trust.

REFERENCES

TABLE III. OUTCOME OF TBM IN VARIOUS SERIES

<table>
<thead>
<tr>
<th>Outcome (%)</th>
<th>Good</th>
<th>Minor sequelae</th>
<th>Major sequelae</th>
<th>Died</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Western Cape (1979 - 1981)</td>
<td>26</td>
<td>23</td>
<td>24</td>
<td>24*§</td>
<td>185</td>
</tr>
<tr>
<td>Smith, Australia (1961 - 1975)</td>
<td>44</td>
<td>14</td>
<td>26</td>
<td>16</td>
<td>43</td>
</tr>
<tr>
<td>Freiman and Geefhuysen, South Africa (1963 - 1967)</td>
<td>33</td>
<td>10</td>
<td>31</td>
<td>26</td>
<td>103*</td>
</tr>
<tr>
<td>Thomas et al, India (1971 - 1975)</td>
<td>25</td>
<td>49</td>
<td>-</td>
<td>26</td>
<td>232*</td>
</tr>
</tbody>
</table>

*The national case fatality rate for TBM for all ages in South Africa was 25.5% in 1980. This is equivalent to the 24% mortality in children in this series.
*Early deaths excluded.
§Adult age; excludes 4 cases not classified.
Is *Mycoplasma pneumoniae* a precipitating factor in acute severe asthma in children?

R. LEAVER, E. G. WEINBERG

**Summary**

A randomized prospective trial in 39 children with acute severe asthma admitted to the emergency ward of the Red Cross War Memorial Children's Hospital and a matched comparative group showed that *Mycoplasma pneumoniae* was not a precipitating factor.


It is well known that viral infections can precipitate severe attacks of asthma in susceptible children. *Mycoplasma pneumoniae* has been incriminated in many studies implicating infection as a precipitating factor. However, there have been few studies — and they were inadequately controlled — to determine the role of *Mycoplasma pneumoniae* in initiating asthma attacks. 1-5 We therefore carried out a controlled prospective study. The study was approved by the Red Cross War Memorial Children's Hospital and the University of Cape Town Ethics and Research Committees and informed parental consent was obtained in all cases.

**Patients and methods**

Acute severe asthma was diagnosed when a child needed to be admitted to the emergency ward with a severe wheezing episode not responding to two periods spent inhaling nebulized salbutamol. The salbutamol was diluted 1:1 with saline and given by a Hudson face mask nebulizer driven by oxygen at 6 l/min for 10 minutes, with a half-hour period between the inhalations. The patients were known asthmatics and had a positive family history of asthma and/or other atopic illnesses; they had all been fully investigated by the hospital's Allergy Clinic.

Every child admitted to the emergency ward with acute severe asthma between April 1983 and June 1983 was studied. There were 20 boys and 19 girls between 2 and 12 years old (mean age 6.07 years). The comparative group consisted of 21 boys and 10 girls (mean age 8.87 years) who were participating in a double-blind trial of an oral mast cell-stabilizing drug (ketotifen). These asthmatics were randomly selected and were well controlled on xanthines or β2-agonists. Sodium cromoglycate, antihistamines and, if possible, steroids were withheld during the trial. The two groups were matched for age and sex.

Blood samples for the routine work-up on any patient admitted with acute severe asthma were also used to measure *Mycoplasma* titres. A convalescent specimen was taken 14 - 28 days later. In the comparative group blood was taken each month during the trial. The timing of the trial coincided with the study period. Complement fixation tests for *Mycoplasma pneumoniae* were performed on an aliquot of each blood specimen. A fourfold rise in titre was taken as significant evidence of infection. A titre less than 1/16 was not regarded as significant evidence of past or recent infection.

Both groups of patients were instructed to contact one of us (R.L.: (i) if they developed any signs of infection — pyrexia, myalgia, sore throat with or without rhinorrhoea, cough; or (ii) if they showed any symptoms suggestive of asthma.

When this occurred, blood samples were taken for *Mycoplasma* titres.

**Results**

A total of 70 patients participated in the study; 39 had acute severe asthma and 31 were in the comparative group (Table 1). Only 1 patient showed a fourfold rise in titre. She presented with acute severe asthma. One other patient had a titre of 1/32, but did not show evidence of a rising titre.