

# Paediatric meningitis in the western Cape

## A 3-year hospital-based prospective survey

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### Summary

Between July 1981 and June 1984 1223 cases of meningitis were seen in the Department of Paediatrics, Tygerberg Hospital. The commonest form in each population group was aseptic meningitis. Positive viral cultures were obtained from the CSF in 108 cases. The median age of white children with aseptic meningitis, 64 months, was significantly greater than that of coloured children, 45 months ( $P > 0,0001$ ), and black children, 26 months ( $P > 0,014$ ). The commonest cause of confirmed bacterial meningitis was *Neisseria meningitidis* (140 cases; 11,5%), which continues to affect mainly young coloured children (median age 16,9 months). Resistance to sulphonamides was found among 21% of 114 *N. meningitidis* isolates. Among white children *Haemophilus influenzae* was responsible for 9 of the 18 cases of confirmed bacterial meningitis. Tuberculosis was responsible for 62 cases of meningitis (5%) and was a commoner cause of meningitis than either *H. influenzae* (47 cases) or *Streptococcus pneumoniae* (34 cases). Thirty-four confirmed cases of bacterial meningitis were seen in children less than 1 month old. *Klebsiella* species were responsible for 8 cases (24%), *Escherichia coli* for 6 cases (12%), group B  $\beta$ -haemolytic *Streptococcus* for 5 cases (15%) while 4 cases each were due to *N. meningitidis* and *Strept. pneumoniae*.

S Afr Med J 1986; 70: 391-395.

In the western Cape Province meningococcal meningitis has for some time been the dominant form of bacterial meningitis in childhood.<sup>1</sup> Tuberculous meningitis (TBM) must still be considered in the differential diagnosis of meningitis locally and the picture is further complicated by intermittent epidemic episodes of aseptic meningitis.

In July 1981 a prospective clinical and microbiological study of meningitis in childhood in the Cape Town area was undertaken covering all the teaching hospitals and the results of this 1-month survey have been reported.<sup>2</sup> This study was continued at Tygerberg Hospital and the findings for the 3-year period July 1981 - June 1984 are reported.

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### Patients and methods

For the purpose of this study meningitis was defined as the presence in the cerebrospinal fluid (CSF) of more than  $10 \times 10^6/1$  leucocytes in children older than 3 months and more than  $30 \times 10^6/1$  leucocytes in children younger than 3 months.<sup>3</sup> Irrespective of the CSF cell count, patients were also included in the survey if an organism — viral, bacterial or mycobacterial — was cultured from the CSF or if bacteria were visible on Gram staining of the CSF. Children whose CSF was bloodstained were not included in the survey unless an organism was cultured from the CSF or seen in the CSF on microscopy.

Children under 13 years of age with meningitis were identified at a daily meeting at which the results of all paediatric CSF specimens submitted to the Department of Medical Microbiology were evaluated. Children were classified according to the results of CSF examination and clinical course into several groups.

**1. Aseptic meningitis.** The diagnosis of aseptic meningitis was accepted if the patient had not received previous antibiotic therapy and had made a spontaneous recovery. When the CSF was not clearly that of a bacterial or tuberculous meningitis it was submitted for viral culture if there was sufficient available.

**2. Septic meningitis, cause unknown.** Children were placed in this 'unknown' meningitis group when they received antibiotic treatment as for a bacterial meningitis but no proof of the diagnosis was forthcoming. Many of these children had a purulent CSF, but in some cases treatment was initiated because of the child's clinical condition and doubt as to the precise diagnosis.

**3. Confirmed bacterial meningitis.** Cases were classified as confirmed bacterial meningitis: (i) if a bacterial organism was cultured from the CSF; (ii) if in the absence of a positive culture from the CSF bacterial organisms were visible following Gram staining of the CSF; and (iii) if bacteria were cultured from the blood in the presence of CSF containing more than  $10 \times 10^6/1$  leucocytes in a child older than 3 months or more than  $30 \times 10^6/1$  leucocytes in a child younger than 3 months.

**4. TBM.** TBM was confirmed by the culture of *Mycobacterium tuberculosis* from the CSF. A clinical diagnosis of TBM was accepted in the presence of supporting evidence such as a positive tuberculin test, a chest radiograph with changes indicative of pulmonary tuberculosis, or culture of *Myco. tuberculosis* from another source — usually gastric washings.

Antibiotic sensitivity was determined by the standardized single-disc method (Kirby-Bauer).<sup>4</sup>

Pairwise comparison of the median ages of children with meningococcal meningitis during the period 1978-1979 and 1981-1984 was by the Mann-Whitney *U*-test. The ages of children with different forms of meningitis in the different population groups were compared by the Kruskal-Wallis test.

### Results

During the period surveyed 1223 cases of meningitis were seen in the Department of Paediatrics at Tygerberg Hospital. The causes of meningitis and the distribution of cases between the sexes are summarized in Table I.

The commonest form of meningitis seen was aseptic meningitis in which a significant male predominance was evident, 61% of patients being male and 39% female ( $P > 0,0122$ ). In 108 cases a positive viral culture was obtained from the CSF and the viruses identified are summarized in Table II. Enteroviruses were respon-

TABLE I. CAUSES OF MENINGITIS, JULY 1981 — JUNE 1984

	Sex			Total
	Male	Female	unknown	
Aseptic meningitis	443	285	11	739 (60,4%)
'Septic unknown'	75	61	5	141 (11,5%)
<i>N. meningitidis</i>	70	68	2	140 (11,5%)
<i>H. influenzae</i>	23	24	—	47 (3,8%)
<i>S. pneumoniae</i>	18	14	2	34 (2,8%)
<i>Klebsiella</i>	4	8	2	14 (1,2%)
<i>E. coli</i>	4	2	1	7 (0,6%)
Other Gram-negative* organisms	5	5	1	11 (0,9%)
Group B $\beta$ -haemolytic <i>Streptococcus</i>	4	3	2	9 (0,7%)
<i>Staph. aureus</i>	10	6	—	16 (1,3%)
Other Gram-positive† organisms	2	1	—	3 (0,3%)
TBM	36	26	—	62 (5%)

\*Other Gram-negative organisms — *Proteus* species 5 cases, *Ps. aeruginosa* 3 cases, *Serr. marcescens* 2 cases, *Salmonella* group B 1 case.

†Other Gram-positive organisms — Group A  $\beta$ -haemolytic *Streptococcus* 1 case, diphtheroid organisms not further identified 1 case, Gram-positive cocci not clearly identifiable 1 case.

TABLE III. CAUSES OF MENINGITIS IN DIFFERENT POPULATION GROUPS

	Coloured	White	Black
	(median age (median age (median age (mo.)	mo.)	mo.)
Aseptic meningitis	562 (45,2)	150 (64,4)	27 (25,5)
Septic unknown	119 (7,4)	14 (18,0)	8 (9,0)
<i>N. meningitidis</i>	135 (16,9)	2 (13,7)	3 (7,2)
<i>H. influenzae</i>	37 (7,9)	9 (14,2)	1 (5,9)
<i>Strept. pneumoniae</i>	28 (7,9)	3 (69,7)	3 (2,5)
<i>Klebsiella</i>	8 (1,1)	—	6 (0,4)
<i>E. coli</i>	6 (0,4)	1 (0,3)	—
Other Gram-negative organisms	9 (1,1)	1 (1,2)	1 (23,9)
Group B $\beta$ -haemolytic streptococcus	7 (0,5)	1 (0,1)	1 (24,0)
<i>Staph. aureus</i>	14 (8,8)	2 (1,7)	—
Other Gram-positive organisms	3 (0,9)	—	—
TBM	57 (18,6)	—	5 (19,2)

sible for the largest number of cases and were particularly active during the summer of 1981 - 1982. Later in the survey period mumps became a more common cause of aseptic meningitis. In 4 cases the 'aseptic' picture in the CSF was associated with malignant involvement of the central nervous system (leukaemia in 3 cases, medulloblastoma in 1 case). In 1 case rabies was confirmed on autopsy examination of the brain. Kawasaki syndrome was suspected in 1 child, while another had a positive Paul-Bunnell test and clinical features of infectious mononucleosis.

*Neisseria meningitidis* was the commonest identified cause of bacterial meningitis and responsible for 11,5% of cases. The second commonest identifiable form of meningitis, other than confirmed viral meningitis, was TBM — 62 cases (5%). Among the Gram-negative organisms, other than *N. meningitidis* or *Haemophilus influenzae*, *Klebsiella* species (14 cases) were responsible for twice as many cases as *Escherichia coli* (7 cases).

In Table III the causes of meningitis among the three main population groups are set out, together with the median ages of the children in each of the groups. Similarly in Table IV the causes of meningitis in children less than 1 month old are tabulated. Very few Asian patients were seen and these were included with the coloured group.

In the coloured group *N. meningitidis* remains the commonest cause of bacterial meningitis in childhood and continues to affect mainly young children. The median age (16,9 months) of these children is not significantly different from the median age (13,2 months) of the children with meningococcal disease we saw during the epidemic period of 1978-1979.<sup>5</sup>

Among neonates *Klebsiella* species (8 cases) were, together with *E. coli* (6 cases), responsible for the majority of proven bacterial meningitis cases while *N. meningitidis* (4 cases) is again shown to

be not necessarily uncommon as a cause of bacterial meningitis in early infancy.<sup>6</sup>

In 16 children meningitis was associated with the presence of a ventriculoperitoneal shunt. In 7 cases no organism could be identified despite the presence of septic features such as a low CSF glucose and increased CSF protein value. In 6 children *Staphylococcus aureus* and in 1 each *Serratia marcescens*, a group B  $\beta$ -haemolytic *Streptococcus* and an unidentified diphtheroid organism were cultured from the CSF. In a further 5 children the growth of a Gram-negative organism from the CSF was associated with the presence of a myelomeningocele (*Proteus mirabilis* 2 cases and *Klebsiella* species, *E. coli* and *Pseudomonas aeruginosa* 1 case each).

*Staph. aureus* was a cause of meningitis in 16 patients. In 6 patients it was cultured from the CSF and was associated with a ventriculoperitoneal shunt as described above. In 9 cases it was grown from a blood culture and associated with a sterile CSF in which no organisms were seen. The CSF cell count in these patients varied from 25 to 402 x 10<sup>6</sup>/l leucocytes. In only 1 patient was a *Staph. aureus* isolated from both the CSF and blood.

The age distribution of children presenting with the six major causes of meningitis is illustrated in Fig. 1. Children who presented with aseptic meningitis (median age 48,9 months) were significantly older than children with any other form of meningitis ( $P < 0,001$ ) and this was true for each population group with the exception of the white group in whom the median age of the 3 patients with *Strept. pneumoniae* meningitis was 69,7 months and not significantly different from that of the white children with aseptic meningitis. The median age of white children for each of the different causes of meningitis was greater than that of each of the other two population groups but only in the case of aseptic meningitis was this statistically significant ( $P < 0,0001$ ).

The monthly incidence of the six major causes of meningitis is illustrated in Fig. 2. A marked increase in aseptic meningitis cases

TABLE II. POSITIVE VIRAL CULTURES FROM CSF

Period	1 July 1981 —	1 July 1982 —		1 July 1983 —		Total
	31 December 1981	1 January 1982 — 30 June 1982	31 December 1982	1 January 1983 — 30 June 1983	12 December 1983 — 1 January 1984 — 30 June 1984	
Enterovirus	48	9	—	—	10	68 (63%)
Coxsackie A	2	—	—	—	10	12 (11%)
Coxsackie B	—	—	—	1	—	1 (1%)
Mumps	2	1	5	1	10	27 (25%)

TABLE IV. CAUSES OF MENINGITIS IN CHILDREN LESS THAN 1 MONTH OLD IN DIFFERENT POPULATION GROUPS

	Aseptic meningitis	'Septic unknown'	<i>N. meningitidis</i>	<i>H. influenzae</i>	<i>Strept. pneumoniae</i>	<i>Klebsiella</i>	<i>E. coli</i>	<i>Staph. aureus</i>	Group B <i>Strep</i> *	Other organisms
Coloured	14	15	4	1	4	4	5	1	5	5
White	4	2	—	—	—	—	1	—	—	—
Black	1	1	—	—	—	4	—	—	—	—
Total	19 (27%)	18 (25%)	4 (6%)	1 (1%)	4 (6%)	8 (11%)	6 (9%)	1 (1%)	5 (7%)	5 (7%)

\*Group B *Strep* = Group B  $\beta$ -haemolytic *Streptococcus*.

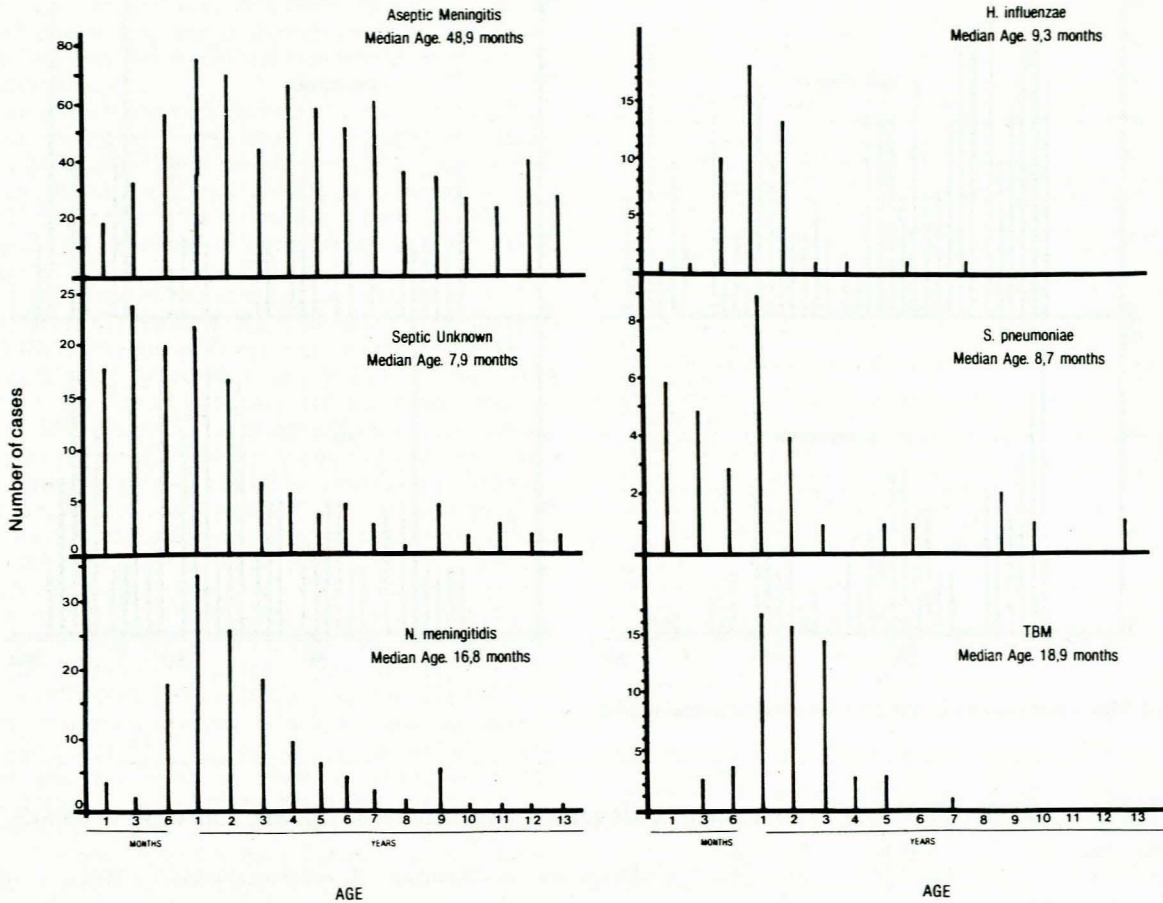


Fig. 1. Age distribution of children presenting with the six main causes of meningitis.

was evident during the summer of 1981-1982 and it is possible that a reflection of this increase is seen in the 'septic unknown' group as the greatest number of 'unknown' meningitis cases was seen in the same month as the peak in the aseptic meningitis group.

*N. meningitidis* infections followed the well-established pattern of exacerbation during the wet western Cape winter but it was not possible to identify any seasonal trend in *H. influenzae*, *Strept. pneumoniae* or TBM cases during the survey period.

Sulphonamide sensitivity was determined in 114 of the *N. meningitidis* cases and resistance found in 24 (21%). Ampicillin sensitivity was determined in 34 of the *H. influenzae* cases and resistance found in 2 (6%). None of the 28 pneumococci evaluated was resistant to penicillin.

### Discussion

The results of previous surveys of the incidence of meningitis in childhood in the Cape Town area are summarized in Table

V. The fact that children with meningococcal meningitis were frequently referred to the City Hospital for Infectious Diseases confuses the picture, but *N. meningitidis* appears to have been the dominant cause of bacterial meningitis in childhood for at least 15 years and remains so at present. The median age of paediatric *N. meningitidis* cases had remained unchanged since 1978-1979 during which period the serogroup B was the commonest type of meningococcus.<sup>5</sup> Meningococci were not typed during the period of this survey but experience in the latter part of 1984 indicates that the serogroup-B meningococcus is still the dominant form of the organism. It is important to note that 21% of *N. meningitidis* isolates were resistant to sulphonamides, in contrast to 4.9% in the period 1978-1979.

Among white children *H. influenzae* was the commonest cause of bacterial meningitis in this study. Previous studies from the Cape Town area did not always distinguish clearly between population groups, but between 1955 and 1957 *H. influenzae* was responsible for only 5 of 55 cases (9%) of

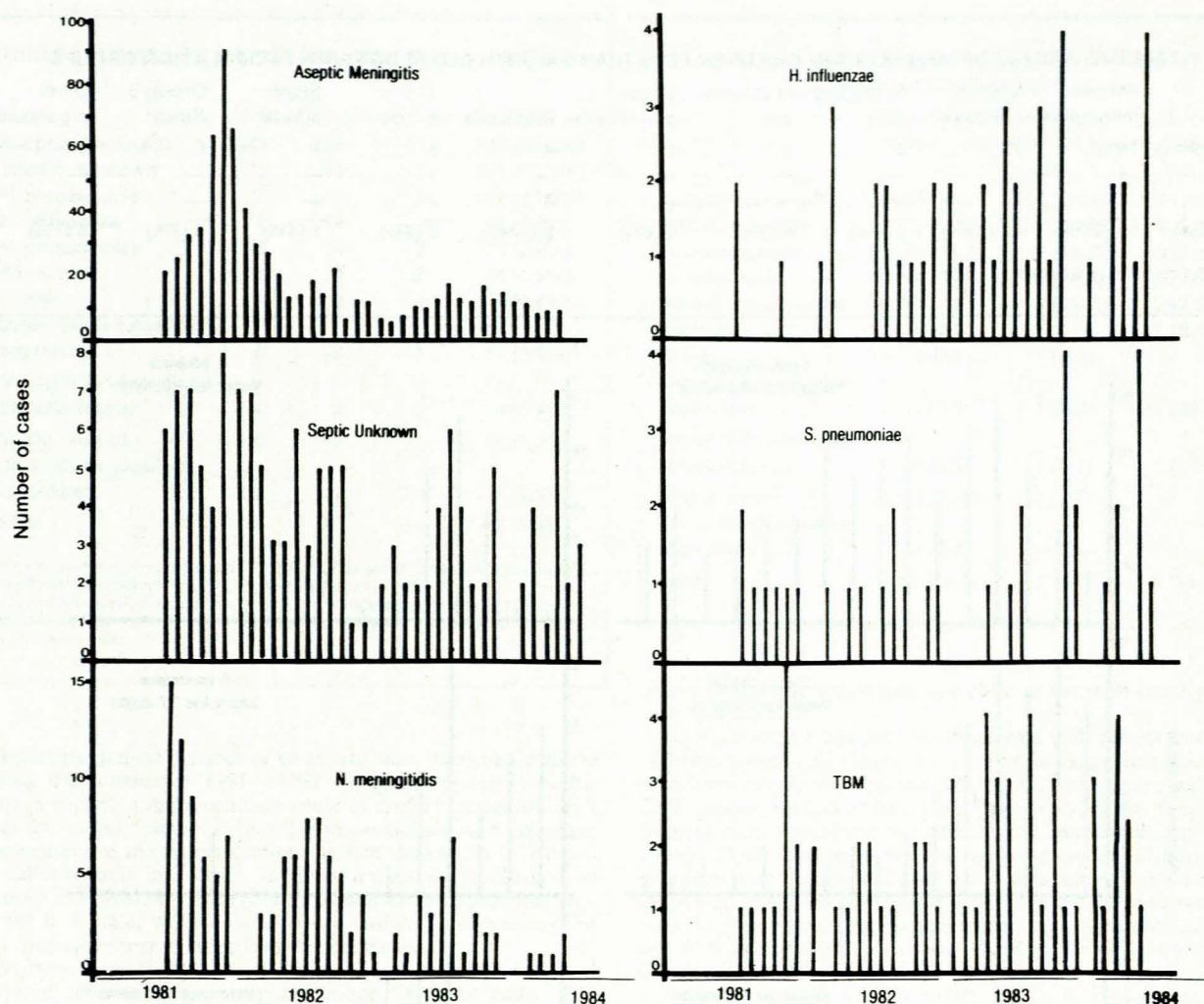


Fig. 2. Monthly incidence of the six main causes of meningitis.

TABLE V. PREVIOUS SURVEYS OF INCIDENCE OF MENINGITIS IN CHILDREN IN THE WESTERN CAPE PROVINCE

Reference, period surveyed	Aseptic meningitis	Unknown meningitis	<i>N. meningitidis</i>	<i>H. influenzae</i>	<i>Strept. pneumoniae</i>	TBM	Other
Zilberg, <sup>7</sup> 1955 - 1957 (meningococcal meningitis excluded) (GSH)	—	11 (21%)	—	19 (37%)*	22 (42%)	—	—
Esrachowitz, <sup>8</sup> 1955 - 1957 (CHID)	—	36 (17%)	139 (66%)	23 (11%)	12 (6%)	—	—
McDonald, <sup>9</sup> 1951 - 1964 (RCWMCH)	89 (16%)	65 (12%)	28 (5%)	72 (13%)	114 (21%)	144 (27%)	30 (6%)
Harris, <sup>1</sup> 1967 (RCWMCH)	114 (30%)	73 (20%)	126 (34%)	28 (7%)	23 (6%)	—	10 (3%)

\*10 cases due to *H. para-influenzae*.

GSH = Groote Schuur Hospital; CHID = City Hospital for Infectious Diseases; RCWMCH = Red Cross War Memorial Children's Hospital.

bacterial meningitis in white patients of all ages treated at the City Hospital for Infectious Diseases.<sup>7</sup> A recent report from the Johannesburg area for the period 1980-1982 recorded 21 cases of meningitis due to *H. influenzae* in white children compared with 20 due to *N. meningitidis* and 12 due to *Strept. pneumoniae*.<sup>10</sup> By contrast a review of pyogenic meningitis among black children in Durban during the period 1979-1980 found *H. influenzae* to be the commonest organism isolated

(30% of cases) and also reported that *H. influenzae* meningitis occurred more frequently in well-nourished than malnourished children.<sup>11</sup> The radical change in the epidemiology of *H. influenzae* infections in the USA between 1945 and 1970 which led to its becoming the commonest cause of bacterial meningitis is well known<sup>12</sup> and it will be important to watch the 'progress' of this organism among all population groups in the RSA.

The high prevalence of tuberculosis among the coloured population of the western Cape Province has been the subject of recent comment<sup>13</sup> and this prevalence is reflected in the fact that TBM is the second commonest identifiable cause of meningitis locally, excluding viral meningitis. TBM must be considered in the differential diagnosis in all cases of meningitis where another causative organism cannot be demonstrated. A similar relatively high incidence of TBM has been reported from large county hospitals in the USA within the last decade.<sup>14</sup>

Aseptic meningitis was the commonest form of meningitis in all three population groups. While not the cause of any great mortality or morbidity, aseptic meningitis may give rise to considerable anxiety at times and the confusion which may be caused by meningococcal meningitis presenting with a 'viral' CSF pattern has been documented previously.<sup>2</sup> It has also been suggested that enteroviral infections may not necessarily be innocuous.<sup>15</sup>

Other viral infections such as measles are known to affect children in 'developing' communities at a younger age than in developed communities, and it is interesting to note that the median age of white children with aseptic meningitis was considerably higher than that of coloured or black children.

Meningitis of 'unknown' aetiology made up the second largest group in this survey. This group appeared in the meningitis literature with the advent of antibiotics, and because the complications and sequelae seen in this group are frequently those of bacterial meningitis it has been remarked that this is an 'important group to include in any series of patients with meningitis'.<sup>16</sup> The size of this group varies in reported series from 5% to 32% of cases.<sup>16-21</sup> The majority of our patients in this group had a purulent CSF and undoubtedly suffered from bacterial meningitis when judged by normally accepted criteria. A proportion, however, were possibly cases of viral meningitis presenting with a CSF cell count of greater than  $500 \times 10^6/l$ , a lowered CSF glucose or a raised protein value; in several instances a virus was grown from CSF with such 'septic' features. Clinically it is probably wise to treat the majority of such patients initially as if suffering from a bacterial infection. It should also be borne in mind that a combination of bacterial and viral meningitis in the same patient has been reported.<sup>22</sup>

A winter peak in the incidence of meningococcal meningitis was again found in this study but no seasonal influence was evident in the case of *H. influenzae* meningitis or TBM. Previous studies in the northern hemisphere have found a spring and autumn peak in the incidence of *H. influenzae* infection<sup>23,24</sup> while TBM has been found to present more frequently in late winter and spring.<sup>25,26</sup>

In conclusion, during this inter-epidemic period *N. meningitidis* remains the commonest cause of bacterial meningitis in the western Cape Province and 21% of organisms are now resistant to sulphonamides. It continues to affect mainly young coloured children, reflecting the probable continued dominance of the serogroup-B meningococcus. Among white children *H. influenzae* is the commonest cause of bacterial meningitis and 6% of organisms tested were resistant to ampicillin. TBM must still be considered in the differential diagnosis of

meningitis while *Klebsiella* species (8 cases) and *E. coli* (6 cases) were the commonest causes of meningitis among neonates.

This study was supported by the Medical Research Council and undertaken by P.R.D. in partial fulfilment of the requirements of the University of Stellenbosch for the degree M.D.

The authors would like to thank the Institute for Biostatistics of the South African Medical Research Council for assistance with the analysis of the data, the Department of Didactics, University of Stellenbosch, for assistance with the figures and the Medical Superintendent of Tygerberg Hospital for permission to publish.

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