J. Hyg., Camb. (1983), **91**, 189–201
Printed in Great Britain

Bacterial meningitis in Nottingham

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(*Received* 10 *December* 1982; *accepted* 15 *April* 1983)

SUMMARY

Records of 171 cases of bacterial meningitis admitted to Nottingham hospitals from January 1974 to June 1980 were reviewed. The distribution of organisms producing meningitis and the factors influencing mortality in different age groups were assessed. *Neisseria meningitidis*, *Haemophilus influenzae* and *Streptococcus pneumoniae* accounted for 69% of all proven cases. The overall mortality was 26% being lowest in patients with meningococcal meningitis (0%) and highest in those with pneumococcal meningitis (53%). The following factors were associated with a poor prognosis: age more than 40 years, or less than 2 months; state of consciousness on admission; high CSF protein concentration; and a positive blood culture. There was no evidence that antibiotic therapy prior to admission affected prognosis. Although many laboratory findings were altered by prior treatment with antibiotics, this did not prevent the establishment of a diagnosis in the individual patient.

INTRODUCTION

In recent years there have been several reviews of selected types of meningitis (Farries *et al.* 1975; Ware & McLauchlan, 1978; Kennedy & Fallon, 1979; Heckmatt, 1976) from individual hospitals or areas, and a report on mortality from meningitis in a district general hospital (Chattopadhyay, 1980). The Public Health Laboratory Service through its weekly Communicable Disease Report also gives information on the incidence and mortality of all culture positive cases, based on the information supplied by laboratories in England and Wales.

However, since the comprehensive account by Goldacre of the incidence and mortality of acute bacterial meningitis in childhood in the North West Metropolitan region (Goldacre, 1976) there had been no wide ranging review of pyogenic meningitis in this country. It was therefore decided to review all cases of bacterial meningitis in Nottingham hospitals served by this laboratory over the last six and a half years, and to analyse factors that appeared to affect the outcome. Despite the fact that 30–50% of patients with acute meningitis receive antimicrobial therapy before lumbar puncture, the role of prior therapy in obscuring the diagnosis is still controversial (Converse *et al.* 1973; Jarvis & Saxena, 1972; Editorial, 1977; Mandal, 1976; Goldacre, 1977; Pickens *et al.* 1978; Geiseler *et al.* 1980). An attempt was therefore made in this study to assess whether pretreatment modified cerebrospinal fluid (CSF) findings, altered culture results, or affected prognosis in pyogenic meningitis.

Since the present review was prepared another survey, from Birmingham, has appeared (Davey *et al.* 1982).

METHODS

Case notes were reviewed of all patients admitted to hospital in whom a diagnosis of bacterial meningitis was established. The survey covered admissions to the City and Sherwood Hospitals between January 1974 and the end of June 1980, and to University Hospital from the time that it opened in 1978 to the end of June 1980.

All cases were included in which, in addition to a compatible clinical diagnosis of meningitis, one or more of the following criteria were satisfied:

(*a*) The causative agent was identified in CSF.

(*b*) CSF pleocytosis was present and the patient was treated as bacterial meningitis; a proportion of these cases had positive blood cultures.

(*c*) Blood cultures were positive and post-mortem evidence of meningitis was obtained.

Results were analysed for significance using the χ^2 test with Yates' correction where necessary.

RESULTS

During the six and a half years covered by this review more than 250 case notes were scrutinized, and 191 episodes of acute bacterial meningitis were identified in 188 patients. Six patients had two attacks of meningitis, but only three of these had both episodes in the period under study. For the purpose of this study, recurrence was considered as a separate case. Eight cases in which the diagnosis was unsuspected in life but made at autopsy, and 12 patients with tuberculous meningitis are excluded from the analysis.

The causative organism was established in life in 154 (90%) of the 171 cases of acute pyogenic meningitis. *Neisseria meningitidis* (27%), *Streptococcus pneumoniae* (23%) and *Haemophilus influenzae* (type b) (19%) together accounted for 107 of all proven cases. Six of the 36 patients with pneumococcal meningitis were less than 1 year old and 14 were over 60 years.

Apart from the three principal pathogens, twelve other bacterial species were isolated from 47 cases of pyogenic meningitis. These included gram-negative bacilli in 24 cases (15 *Escherichia coli*); streptococci in seven cases (four Group B); Staphylococci in nine cases (five *Staphylococcus aureus*); and *Listeria monocytogenes* in seven cases. In a further 17 cases a bacteriological diagnosis could not be established – culture negative pyogenic meningitis (CNPM).

Treatment regimens

Meningococcal and pneumococcal meningitis. The standard treatment during the period of the survey was with a penicillin. Thirty-eight patients received benzylpenicillin administered parenterally in a dose of 0·25–2 mega units (depending upon body weight) every 2–4 h; a proportion of them also received ampicillin for a period not exceeding 24 h; the remainder were treated in various ways: some received a combination of penicillin and ampicillin until CSF culture confirmed the absence of *H. influenzae*, when ampicillin was discontinued; others received

ampicillin alone. A small minority were treated with a variety of other antibacterial regimens.

H. influenzae meningitis. Twenty-eight patients were treated with ampicillin. The majority received 400 mg/kg/day in six divided doses. Three patients were treated with chloramphenicol, one received chloramphenicol alone; another received the drug in combination with ampicillin; the third was given chloramphenicol following bacteriological and clinical failure of ampicillin. This strain was shown to be sensitive to ampicillin.

Enterobacterial and pseudomonal meningitis. Most patients received a combination of ampicillin or chloramphenicol with an aminoglycoside (gentamicin in all but one case). Seven neonates and one adult also received intrathecal gentamicin and another neonate was given intrathecal cephaloridine.

Meningitis due to other organisms. Appropriate therapy was given according to laboratory findings.

Culture-negative pyogenic meningitis. High dose ampicillin was the mainstay of therapy. Of 17 patients with CNPM, ten received ampicillin alone and five were given the antibiotic in combination with either benzylpenicillin, chloramphenicol, or (in the case of a child with cystic fibrosis) cloxacillin.

Mortality

Forty-four of the 171 patients with acute pyogenic meningitis died, giving a case fatality of 26 %. However, three of the deaths were not directly attributable to the meningitis or its treatment, and if these are omitted, the mortality figure becomes 24 %. Outcome was assessed in terms of mortality alone, no systematic attempt has been made to assess complications or sequelae.

Aetiological agent and age

The single death from *H. influenzae* meningitis occurred in a 3-year-old boy admitted in a semicomatose state. In pneumococcal meningitis the mortality was high, especially in the elderly: all but one of 14 patients over the age of 60 died.

Mortality in meningitis associated with organisms other than the three main pathogens was high both in the neonatal period (15 deaths in 27 cases) and in the older age groups (eight deaths in 20 cases). However, three of the latter patients died after the episode of meningitis had been adequately treated.

In 17 cases of CNPM, the outcome was excellent; with the exception of one child with cystic fibrosis who died shortly after admission, all made an uneventful recovery.

The relationship of age to aetiology and mortality is shown in Table 1. For comparison, Table 2 shows the distribution of the aetiological agent in pyogenic meningitis and its associated mortalities in some recent reports from America, Denmark and England.

Duration of illness prior to admission and state of consciousness on admission

Only patients who had meningitis due to the three common pathogens and CNPM cases are considered under this heading, since many of the others were neonates, or other patients in whom it was difficult to pinpoint the onset of symptoms and define the state of consciousness. The 3-day old neonate with

Table 1. *Relationship of age to aetiology and mortality*

Organism	Number of cases (deaths)				Total		
	< 2 months	2 months–14 years	15–40 years	> 40 years	Cases	Deaths	Mortality %
N. meningitidis	1	33	7	—	41	—	—
H. influenzae (type b)	1	29 (1)	—	—	30	1	3
S. pneumoniae	1 (1)	8 (1)	8 (1)	19 (16)	36	19	53
Others*	27 (15)	5 (1)	4 (1)	11 (6)	47	23	49
CNPM	—	5 (1)	6	6	17	1	6
Total	30 (16)	80 (4)	25 (2)	36 (22)	171	44	26
Mortality (%)	53	5	8	61			

* Others = *Escherichia coli* (15); *Proteus mirabilis* (3); *Klebsiella aerogenes* (1); *Citrobacter koseri* (1); *Salmonella typhimurium* (1); *Pseudomonas aeruginosa* (3); Group B streptococci (4); *Streptococcus faecalis* (2); *Str. mitior* (1); *Staphylococcus aureus* (5); *Staph. epidermidis* (4); *Listeria monocytogenes* (7).

† CNPM = Culture-negative pyogenic meningitis.

Table 2. *Bacterial meningitis–aetiology and mortality in the present study and in five recent series*

Aetiological agent	Swartz & Dodge, 1965 1956–62		Hodges & Perkins, 1975 1949–73		Rømer, 1977*a* 1960–74		Geiseler *et al.* 1980 1954–76		Davey *et al.* 1982 1968–77		Present series 1974–80	
	No. of cases (%)	Percent mortality	No. of cases (%)	Percent mortality	No. of cases (%)	Percent mortality	No. of cases (%)	Percent mortality	No. of cases (%)	Percent mortality	No. of cases (%)	Percent mortality
N. meningitidis	39 (19)	13	42 (12)	17	30 (33)	—	396 (32)	6	113 (42)	4	41 (24)	—
H. influenzae	52 (25)	8	15 (4)	7	22 (24)	—	458 (38)	3	52 (19)	8	30 (18)	3
S. pneumoniae	56 (27)	21	88 (25)	31	18 (20)	17	178 (15)	18	40 (15)	30	36 (21)	53
Others	41 (20)	46	57 (17)	61	4 (4)	—	40 (3)	30	17 (6)	41	47 (27)	49
CNPM	19 (9)	10	147 (42)	14	18 (19)	—	148 (12)	5	48 (18)	6	17 (10)	6
Total no. of cases	207 (100)		349 (100)		92 (100)		1220 (100)		270 (100)		171 (100)	
Total no. of deaths	42		90		3		92		30		44	
Overall mortality (%)	20		26		3·2		7·5		11·0		26	

Table 3. *Relationship of duration of illness and state of consciousness to mortality (meningitis due to the three common organisms and CNPM only)*

Duration of illness prior to admission	State of consciousness on admission				Total	
	Alert	Drowsy	Semi-conscious	Unconscious	Cases	Deaths
	No. of patients (deaths)					
< 24 h	12	19 (5)	6 (1)	11 (6)	48	12
2 days	12	9	2 (1)	2 (1)	25	2
3–5 days	14	24 (2)	6 (3)	1 (1)	45	6
> 5 days	3	2	—	—	5	0
Total	41	54 (7)	14 (5)	14 (8)	123	20
Mortality %	—	13	36	57		

pneumococcal meningitis is excluded from analysis. The state of consciousness of 123 patients were classified into the following groups (*a*) fully conscious/alert; (*b*) drowsy/confused; (*c*) semi-conscious; (*d*) unconscious. Forty-eight patients were admitted into hospital within 24 h of the onset of illness and in this group the mortality was highest (Table 3), accounting for 12 (60%) of the total of 20 deaths. However, the difference was not statistically significant ($P = > 0{\cdot}05$). Eighteen of the 20 deaths occurred in patients with pneumococcal meningitis. All 41 patients who were alert on admission survived including eight patients with pneumococcal meningitis. In contrast, over a third of the patients who were semicomatose and more than half who were unconscious on admission, died. The relationship of state of consciousness on admission to mortality was highly significant ($P = < 0{\cdot}001$).

Eleven patients died within 48 h of admission; seven of these had been admitted within 24 h of the onset of symptoms.

Laboratory findings

CSF was not available in five cases; three died shortly after admission or birth, before lumbar puncture could be performed; in one patient repeated attempts to obtain CSF failed; the fifth patient was transferred to another hospital for a brain scan before lumbar puncture was performed. Blood cultures were obtained in all five of these patients and were positive in all cases.

Gram stain and culture of CSF were carried out in 166 cases; the organism was detected in the Gram film in 66% of cases and was isolated by culture in 87% of cases. Blood culture was performed in 151 patients and 64% were positive (Table 4). Blood culture was positive in 93% of cases of pneumococcal meningitis, but in only 40% of cases of meningococcal meningitis.

Mortality was significantly higher in those patients in whom blood culture was positive or who had an increased level of CSF protein ($P = < 0{\cdot}001$ in both cases). Prognosis also appeared worse in patients with a low CSF cell count ($\leqslant 500$ cells/μl) or very low CSF glucose level ($\leqslant 1{\cdot}0$ mmol/l). However, these differences were not significant ($P = > 0{\cdot}05$).

Three patients with pneumococcal meningitis, whose CSF contained less than 100 leucocytes/μl, all died; in two of these cases, the CSF Gram film showed numerous bacteria.

Table 4. *Relationship of result of laboratory investigations to outcome*

Laboratory investigation	Results	No. of cases	Deaths	Mortality %	Statistical significance
(a) *CSF*					
Gram stain	Positive	110	30	27	NS
(n = 166)	Negative	56	9	16	
Culture (n = 166)	Positive	144	35	24	NS
	Negative	22	4	18	
Leucocyte count/μl	⩽ 500	48	14	29	NS
(n = 153)	> 500	105	21	20	
Protein g/l	< 1·0	31	1	3	P = < 0·001
(n = 146)	1·0–2·9	41	6	15	
	3·0–5·0	34	9	26	
	> 5·0	40	16	40	
Glucose mmols/l	⩽ 1·0	75	19	25	NS
(n = 119)	> 1·0	44	8	18	
(*b*) Blood					
Blood culture	Positive	96	35	36	P = < 0·001
(n = 151)	Negative	55	3	5	

NS = Not significant.

Table 5. *Response to therapy of meningitis due to the three common organisms and CNPM (survivors)*

Organism	No. of cases	Mean duration (days) of: Pyrexia	Intravenous antibiotics	Stay in hospital
N. meningitidis	34	3·0	5·4	9·5
H. influenzae	24	5·9	8·1	12·2
Str. pneumoniae	13	3·3	7·6	11·7
CNPM	14	2·6	6·9	10·8

Outcome of antibiotic treatment

(i) *Survivors.* The effectiveness of treatment was judged by the period to defervescence, the duration of intravenous therapy and the length of stay in hospital. The numbers of patients with individual types of meningitis receiving different antibacterial regimens were too small to assess the merits of any particular type of therapy. However, a difference did emerge when uncomplicated cases of meningitis due to the three major pathogens, and the culture negative cases, were analysed (Table 5). All these patients received 'standard' therapy, as described above. The response to therapy of meningococcal and culture-negative pyogenic meningitis was particularly dramatic, the temperature usually returning to normal within 3 days; the duration of stay in hospital was also shorter for these patients. In contrast, 62% of patients with *H. influenzae* meningitis remained febrile for 5 days or more, and the mean duration of intravenous therapy and stay in hospital were longest in this group. However, these differences were not statistically significant.

(ii) *Deaths.* An attempt was made to analyse mortality in meningitis due to *S. pneumoniae* and enteric gram-negative bacilli, the groups in which 34 of the 44

https://doi.org/10.1017/S0022172400060198 Published online by Cambridge University Press

Table 6. *Effect of pretreatment on mortality in meningitis due to the three common pathogens and CNPM*

Duration of illness prior to admission	No pretreatment		Pretreatment	
	Cases	Deaths	Cases	Deaths
< 24 h	34	11	14	1
2 days	14	1	11	1
3–5 days	21	4	24	2
> 5 days	—	—	5	—
Total	69*	16	54	4
Mortality %		23		7

* Four of these received antibiotics in hospitals prior to lumbar puncture.

deaths occurred. The numbers were again too small to allow conclusions to be drawn about the effect of any particular treatment. Nine patients with pneumococcal meningitis died before antibiotics had time to act. However, a further ten patients died despite more than 24 h of high-dose antibiotic therapy.

Among 24 patients with meningitis due to enteric gram-negative bacilli, 15 of whom died, it was striking that six of nine patients who received intrathecal therapy survived.

Effect of pre-treatment

Full information about the dosage and duration of preadmission treatment was not available in many cases, but 69 (40 %) patients in this series had received one or more antibiotics prior to the diagnostic lumbar puncture. Twelve patients had received antibiotics while in hospital; five were neonates, and all of these had positive CSF cultures despite having received parenteral therapy in the preceding 48 h. In seven patients, meningitis was not suspected on admission to hospital (*S. pneumoniae* 3; *H. influenzae* 1; *L. monocytogenes* 1; Group B streptococci 1; *S. faecalis* 1) in three cases the organism was subsequently isolated from CSF despite parenteral therapy; in three others blood culture, taken before antimicrobial therapy commenced, was positive; in the seventh case, diagnosis was made only by Gram film and by counterimmunoelectrophoresis of CSF.

Fifty-seven patients had received oral antibiotic therapy prior to admission. Most had been given penicillin V (17 patients) or ampicillin/amoxycillin (14 patients). The remainder had received a variety of other antibiotics: erythromycin (5), cephalexin (5), co-trimoxazole (3), tetracycline (6), cloxacillin (2). In five cases the antibiotic given was not specified.

Effect of pretreatment on mortality. Since duration of illness prior to admission was an important factor in assessing the effect of pretreatment, neonates and other patients in whom it was difficult to ascertain the precise onset of symptoms were omitted from analysis. Table 6, therefore, only considers meningitis due to the three common pathogens and CNPM. Of these cases, 7 % of patients who had received antibiotic prior to lumbar puncture died compared to 23 % in the untreated group.

Effect of pretreatment on laboratory findings. The overall frequency of positive bacteriological findings was significantly lower ($P = < 0{\cdot}01$) in those patients who had received prior antibiotic therapy than in those who had not (Table 7), but the

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Table 7. *Effect of pretreatment on the results of bacteriological findings in bacterial meningitis*

Laboratory investigation /organism	No pretreatment			Pretreated			Statistical significance
	Number of cases	Number positive	Percent positive	Number of cases	Number positive	Percent positive	
CSF Gram film							
Total ($n = 166$)	99	74	75	67	36	54	$P = < 0{\cdot}01$
N. meningitidis ($n = 41$)	25	21	84	16	9	56	NS
H. influenzae ($n = 30$)	11	8	73	19	13	68	NS
Str. pneumoniae ($n = 34$)	23	20	87	11	8	73	NS
CSF culture							
Total ($n = 166$)	99	92	93	67	52	78	$P = < 0{\cdot}01$
N. meningitidis ($n = 41$)	25	25	100	16	15	94	NS
H. influenzae ($n = 30$)	11	11	100	19	19	100	NS
Str. pneumoniae ($n = 34$)	23	23	100	11	9	82	NS
Blood culture							
Total ($n = 151$)	96	69	72	55	27	49	$P = < 0{\cdot}01$
N. meningitidis ($n = 35$)	22	11	50	13	3	23	NS
H. influenzae ($n = 28$)	11	9	82	17	13	82	NS
Str. pneumoniae ($n = 29$)	19	19	100	10	8	80	NS

NS = Not significant.

Table 8. *Effect of pretreatment on the results of laboratory tests of CSF in bacterial meningitis*

Laboratory investigation	Result	No pretreatment: No. of cases	No pretreatment: %	Pretreatment: No. of cases	Pretreatment: %	Statistical significance
Leucocytes (number/l)	⩽ 500	27	30	21	34	NS
	501–5000	50	55	32	52	
	> 5000	14	15	9	14	
Total		91		62		
Polymorphonuclear leucocytes (percentage of total leucocytes)	⩽ 50	5	7	10	17	NS
	51–80	7	9	8	14	
	> 80	65	84	41	69	
Total		77		59		
Protein (g/l)	< 1·0	10	12	21	34	$P = < 0{\cdot}001$
	1–2·9	18	21	23	38	
	⩾ 3·0	57	67	17	28	
Total		85		61		
Glucose (mmols/l)	⩽ 1·0	46	67	29	58	NS
	> 1·0	23	33	21	42	
Total		69		50		

NS = Not significant.

causative organism could still be isolated from CSF in 78% of cases who had received treatment prior to lumbar puncture. Of the 17 patients in whom a causative agent was not established (CNPM), 10 (59%) had received antibiotic before admission.

The effect of pretreatment was most marked in CSF Gram stain and blood culture results in patients with meningococcal meningitis: four out of seven of those patients whose CSF Gram film was negative, and five of the ten whose blood culture was negative had received penicillin V. CSF cultures were negative in only three laboratory confirmed cases of meningitis due to the three common organisms; two of these patients had pneumococcal meningitis and both had received parenteral penicillins prior to lumbar puncture.

The effect of pretreatment on the results of CSF leucocyte counts and protein and glucose estimations are analysed in Table 8. Although the total number of leucocytes did not differ in the treated and untreated groups, the former tended to exhibit a lower proportion of polymorphonuclear leucocytes. CSF protein was significantly lower ($P = < 0{\cdot}001$) in those who had received antibiotic treatment prior to lumbar puncture. CSF glucose concentrations were not so markedly affected.

DISCUSSION

Aetiology and mortality

During the six and a half years of this survey, 171 cases of pyogenic meningitis were detected. As expected, *N. meningitidis*, *S. pneumoniae* and *H. influenzae* accounted for over two thirds of bacteriologically proven cases. *H. influenzae* was

https://doi.org/10.1017/S0022172400060198 Published online by Cambridge University Press

isolated less frequently than the other two organisms, but the figures are distorted by the fact that laboratory services for the Nottingham Children's Hospital were provided elsewhere until November 1978, when it moved to University Hospital.

Pneumococcal meningitis appeared to cluster at the extremes of life and mortality was high in the elderly. Mortality is known to increase progressively with age (Weiss *et al.* 1967; Hodges & Perkins, 1975) except in tropical Africa, where mortality is high among young adults (Baird, Whittle & Greenwood, 1976).

Organisms other than the three main pathogens accounted for 27% of cases in this study, a figure higher than that quoted by Davey *et al.* (1982). However, more than half the cases in the present series were in neonates, a group not clearly identified by those authors; furthermore, our figures include meningitis secondary to cerebral abscess or shunt infection, groups excluded from the series of Davey *et al.* (1982). The overall mortality of 49%, though unacceptably high, was not surprising.

In 10% of the total number of cases a bacteriological diagnosis could not be established. The low mortality, the dramatic response to therapy and, in two cases, the presence of rash, suggests that some of these patients may have been suffering from meningococcal meningitis.

Factors influencing prognosis

Patients with pneumococcal meningitis admitted in an unconscious state had the worst prognosis. Many of these patients had a short fulminating illness and died in coma within a short period after admission to hospital. This contrasts with the recent experience of Davey *et al.* (1982) who found the mean duration of illness in patients dying of pneumococcal meningitis was 3·75 days.

Among laboratory findings, a raised CSF protein and isolation of the organism by blood culture offered the clearest evidence of a poor prognosis (Table 4). The observed mortality of 36% with bacteraemia and 5% without, is consistent with other reports (Weiss *et al.* 1967; Hodges & Perkins, 1975; Laxey & Marks, 1977). A low CSF white cell count and a low glucose concentration were associated with a trend towards higher mortality, supporting the findings of several other groups (Quaade & Kristensen, 1962; Hodges & Perkins, 1975; Baird, Whittle & Greenwood, 1976). Quaade & Kristensen (1962) found the combination of a low CSF leucocyte count with a large number of organisms to be a serious prognostic sign in pneumococcal meningitis. Two such cases were encountered in the present study, both of whom died.

Response to treatment

There were no deaths from meningococcal meningitis in this series and most patients made a rapid and uneventful recovery. Mortality was also low in *H. influenzae* meningitis although patients did not respond to therapy so promptly.

Pneumococcal meningitis

In the present study, and in others (Carpenter & Petersdorf, 1962; Baird, Whittle & Greenwood, 1976) the highest mortality was found in patients who had been ill for 24 h or less. Almost half our patients who died did not live long enough to have been influenced by antimicrobial treatment; the remainder died despite appropriate high dose therapy. Thus, although failure of therapy can be partly explained by

the fact that many patients have a fulminating illness and die before adequate therapy can be instituted, this is clearly not the only reason for therapeutic failure. Alternative approaches to the prevention and management of pneumococcal meningitis have been discussed by Baird, Whittle & Greenwood (1976) and Davey *et al.* (1982).

Enterobacterial and pseudomonal meningitis

In meningitis due to enteric gram-negative bacilli, it is well recognized that the combination of agents usually recommended, an aminoglycoside plus chloramphenicol, leaves much room for improvement. Aminoglycosides do not achieve bactericidal levels in CSF unless given intraventricularly (Kaiser & McGhee, 1975), a procedure that is not without risks (McCracken, Mize & Threkeld, 1980), and about which conflicting views have been expressed (Swartz, 1981). Chloramphenicol levels achieved in CSF are inadequate to kill gram-negative bacilli (Rahal & Simberkoff, 1979).

The newer β-lactam antibiotics, such as cefotaxime and latamoxef (Moxalactam) merit serious consideration in the therapy of meningitis, including that due to enterobacteria, since they are very active and appear to achieve satisfactory concentrations in CSF (Landesman *et al.* 1981).

Effect of pretreatment on diagnosis and prognosis

A high proportion of patients in this series had received antibiotics before admission to hospital. Treatment ranged from a single dose to a week's course of therapy. Some workers (Jarvis & Saxena, 1972; Goldacre, 1977), have noted a lower mortality in patients treated before admission and superficially the present findings support this (Table 6). However, these figures are weighted by the fact that 34 of the 69 patients who had received no treatment were admitted within 24 h of the onset of symptoms, and were thus less likely to have received antibiotics. Nevertheless, 11 of these 34 patients died, whereas only one of 14 patients died among the group whose illness developed during the 24 h prior to admission and who received antibiotics during this period. However, by chance, only two of this latter group of 14 proved to have pneumococcal meningitis, the condition responsible for most deaths.

It is possible that the improved prognosis seen in the pretreated group is due not to the antibiotic received, but to the fact that the onset of illness was less severe, enabling such patients to seek the advice of their general practitioner (Rømer, 1977*b*). This is not to say that antibacterial therapy should be withheld before admission to hospital in suspected cases. Indeed, the importance of prompt parenteral therapy in children suspected of meningococcal infection has been stressed (Editorial, 1979).

Although 69 patients had received antibiotics prior to lumbar puncture, a bacteriological diagnosis was still possible in 59 of them. It is customary to attribute negative bacteriological findings to preadmission antimicrobial therapy but this does not explain culture–negative cases that were observed in the pre-antibiotic era (Neal, 1935), nor the failure to demonstrate organisms in some untreated patients (Editorial, 1977; Geiseler, Nelson & Levin, 1981). In the present

series 41 % of patients with culture-negative pyogenic meningitis had received no antibiotics prior to lumbar puncture.

Preadmission antibiotic therapy can also produce changes in total CSF cell count, the type of cellular response, and in protein and glucose levels (Converse *et al.* 1973; Geiseler *et al.* 1980). However, therapy does not usually alter all of these parameters and the low glucose level characteristic of pyogenic meningitis is often retained (Editorial, 1977). In the present series, five patients were identified whose CSF findings were consistent with viral meningitis except for low glucose levels. Four of these patients were known to have received antibiotic treatment of 2–5 days prior to admission. Despite the abnormal results, all five were culture-positive so that there was no risk of confusion with viral meningitis in these cases.

This study was possible because of the close liaison that exists betwen the physicians and microbiologists in Nottingham. I therefore wish to thank all consultant and other medical staff for their co-operation and for permission to study patients under their care. I also wish to thank the Medical Records Officers and their staff in the Nottingham District for their help in tracing case notes.

The manuscript was prepared with the generous assistance of Dr David Greenwood, Senior Lecturer in the Department of Microbiology in Nottingham. Finally, I am indebted to Mrs Susan Brailsford for typing the many drafts of this report.

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