J. Hyg., Camb. (1986), 97, 219–228
Printed in Great Britain

Non-neonatal meningitis due to less common bacterial pathogens, the Netherlands, 1975–83

By L. SPANJAARD, P. BOL and H. C. ZANEN

University of Amsterdam, Department of Medical Microbiology (Netherlands Reference Laboratory for Bacterial Meningitis of the National Institute of Public Health and Environmental Hygiene), Meibergdreef 15, 1105 AZ Amsterdam, The Netherlands

(*Received 3 March 1986; accepted 22 May 1986*)

SUMMARY

In the Netherlands, case histories of 160 patients aged more than 1 month with meningitis due to bacteria other than *Neisseria meningitidis*, *Haemophilus influenzae* and *Streptococcus pneumoniae* were reviewed in order to look for associations between the bacteriological data and the course of disease.

The incidence of such cases was about 0·8/100000/year. *Escherichia coli* and *Listeria monocytogenes* each accounted for about 15% of the cases. The case-fatality rate was 18·8% (Gram-negative bacteria, 25%; Gram-positives, 15%) and sequelae occurred in 13·3% of the surviving patients (14 and 13% Gram-negative and Gram-positive, respectively). Hearing loss was the most prevalent sequela (5·0%). Predisposing factors were present in 70% of patients (69 and 71% respectively), especially in meningitis due to enteric Gram-negative bacteria (except for salmonella) and due to staphylococci.

Surveillance is important because the incidence of meningitis due to these micro-organisms is likely to increase and because the problems in antibiotic treatment have not yet been solved.

INTRODUCTION

Although *Neisseria meningitidis*, *Haemophilus influenzae* and *Streptococcus pneumoniae* account for the majority of cases of bacterial meningitis (BM), in about 15% of patients BM is caused by less common pathogens such as enteric Gram-negative bacteria, streptococci (other than *Str. pneumoniae*), staphylococci and *Listeria monocytogenes* (Jonsson & Alvin, 1971; Finland & Barnes, 1977; Bohr *et al.* 1983; Netherlands Reference Laboratory, 1985). Although these less common bacteria are rare in BM in the general population, they are frequently isolated from the cerebrospinal fluid (CSF) of neonates, the elderly and immunocompromised patients (Cherubin *et al.* 1981; Gorse *et al.* 1984; Mulder & Zanen, 1984). The case-fatality rate (CFR) is high in these patient groups, varying from 25 to more than 60% (Lavetter *et al.* 1971; Jonsson & Alvin, 1971; Finland & Barnes, 1977; Cherubin *et al.* 1981; Bohr *et al.* 1983; Gorse *et al.* 1984; Mulder & Zanen, 1984).

Within the framework of an extensive study of the epidemiology of BM in the Netherlands (Netherlands Reference Laboratory, 1985) we investigated 160 records of patients aged more than 1 month with BM due to less common pathogens. (Information about neonatal meningitis has already been published (Mulder & Zanen, 1984)). The main purpose of our study was to associate bacteriological data with the outcome and complications of the disease and with predisposing factors.

POPULATION AND METHODS

Strains of bacteria isolated from patients with BM were submitted to the Netherlands Reference Laboratory for Bacterial Meningitis of the National Institute of Public Health and Environmental Health by bacteriological laboratories throughout the country (Netherlands Reference Laboratory, 1985). The strains were identified and typed as described previously (Mulder & Zanen, 1984). By *Staphylococcus epidermidis* we mean coagulase negative staphylococci.

The present study is part of a study of BM due to all pathogens. Information on patients from whom a strain had been isolated and submitted was collected in three ways:

(1) we reviewed hospital records of 98 patients as follows:

(*a*) 86 patients admitted to 24 hospitals throughout the country (period mid-1975 to 1981; all causes of non-neonatal meningitis: 835 patients in 45 hospitals)

(*b*) 12 children younger than 16 years admitted to nine paediatric wards throughout the country (period April 1982–March 1983; all causes of BM: 234 patients in 73 paediatric wards)

(2) we requested discharge letters concerning 62 patients in the whole country in 1983 (all causes of BM: 580 patients).

These records and letters were analysed for predisposing factors, complications and outcome. We considered the following factors as predisposing to BM: malignancy, immunosuppression, diabetes mellitus, alcohol abuse, absence of the spleen, factors facilitating direct invasion of the subarachnoidal space (severe head injury, ventricular shunt *in situ*, neurosurgical procedure, CSF leak through a fistula), and (if the patient was in the first half year of life) a history of abnormalities during pregnancy or delivery.

The following signs were included as central nervous system (CNS) complications: convulsions, hydrocephalus and focal neurological signs (abnormality of a cranial nerve, forced deviation of head and/or eyes, dysphasia, ataxia, nystagmus, limb paralysis or reflex abnormality). Sequelae included: hearing loss, developmental motor disturbance, paralysis, epilepsy and hydrocephalus. For the computation of the percentage of patients with sequelae the denominator included only patients discharged alive from hospital; so, the numbers both of patients dying from BM and of patients dying from other diseases were subtracted from the total.

For computerized data processing, the 'Statistical Package for the Social Sciences' was used; significance testing was done with the chi-square test (with Yates's correction for 2×2 tables).

RESULTS AND DISCUSSION

(1) *Incidence and CFR*

We reviewed 160 case histories of patients with BM due to less common pathogens. These represented about 10% of all patients with BM studied during the period mid-1975 to 1983 (cf. Population and methods section). The overall incidence of BM being 8·0 per 100000 per year in the Netherlands (Spanjaard *et al.* 1985), the incidence of BM due to less common pathogens in patients more than 1 month of age amounted to about 0·8.

The most frequently isolated pathogens were *Escherichia coli* (15·6%), *L. monocytogenes* (14·4%), *Staph. aureus* (9·4%), *Staph. epidermidis* (8·1%) and *Str. agalactiae* (7·5%) (Table 1).

The overall CFR was 18·8%, varying from 0% in BM due to *Staph. epidermidis* to 50% in pseudomonas or enterobacter meningitis. In addition to these 30 deaths, 10 patients died from a concurrent illness (or from both this illness and the BM), resulting in a total CFR of 25·0%.

A minor part (12 cases) of our sample concerned patients from a study of records from paediatric wards only (Spanjaard *et al.* 1986). The CFR and the age distribution were slightly different when these patients were omitted: the CFR decreased from 18·8% in the whole sample to 18·2% (27 of 148) without these 12 children, whereas the mean ages were 30·3 years and 32·6 years respectively.

In New York, enteric Gram-negative bacteria cause about 6% of all cases of BM and *L. monocytogenes* about 2% (Cherubin *et al.* 1981). We found 3·2 and 1·4% respectively in patients aged more than 1 month. Because about 50% of enteric Gram-negative BM and about 20% of listeria meningitis occur in neonates (Netherlands Reference Laboratory, 1981), our figures appear to be similar to those from New York.

In other series, the CFR ranged from 30% to over 60% (Jonsson & Alvin, 1971; Finland & Barnes, 1977; Cherubin *et al.* 1981; Bohr *et al.* 1983). Most other studies described patients from academic or other referral hospitals, where the CFR is likely to be high (Mulder & Zanen, 1984), whereas our study included a representative sample of all hospitals in the Netherlands, both academic and general. On the other hand, we certainly missed cases, because we were dependent on the collaboration of bacteriologists in submitting strains and of hospitals in providing us the clinical data. It cannot be excluded that a fatal outcome was more frequent among these missing cases.

(2) *Gram-negative pathogens* (Table 2)

BM due to *E. coli* or salmonella occurred most frequently in the age group 1–11 months, whereas the other bacteria were isolated most frequently from older children or from patients aged 20–59 years. Among the aged (more than 60 years), *E. coli* caused 62% of cases (8 of 13).

E. coli K1 was isolated from 7 patients, all children 1–11 months of age, whereas only 17% (3 of 18) of other K-types occurred in this age group (Fisher's exact test: $P < 0{\cdot}002$). The overall CFR in Gram-negative BM was 25% (16 of 65). Among patients more than 60 years the CFR was 46% (n. s.). The three patients in this age group with BM due to 'other Gram-negative rods' all died.

Table 1. *Non-neonatal BM due to less common bacterial pathogens, the Netherlands, 1975–1983; pathogens and CFR*

Pathogen	No. (% of total)	Died from: Bacterial meningitis (CFR)*	Died from: all causes (CFR)
Escherichia coli	25 (15·6)	7 (28)	10 (40)
Other Gram-negative rods	27 (16·9)	8 (30)	9 (33)
Klebsiella	8	3	4
Salmonella	8	1	1
Pseudomonas	4	2	2
Enterobacter	4	2	2
Proteus	2	0	0
Pasteurella	1	0	0
Staphylococcus aureus	15 (9·4)	3 (20)	4 (27)
Staphylococcus epidermidis	13 (8·1)	0 (0)	1 (8)
Streptococcus agalactiae (group B)	12 (7·5)	2 (17)	2 (17)
Other streptococci	30 (18·8)	2 (7)	3 (10)
Str. suis (group R)	8	0	0
Str. salivarius	7	2	2
Str. pyogenes (group A)	3	0	1
Str. faecalis (group D)	3	0	0
Others	9	0	0
Listeria monocytogenes	23 (14·4)	7 (30)	9 (39)
Others	15 (9·4)	1 (7)	2 (13)
Acinetobacter	5	0	0
Other Neisseriaceae	3	0	0
Mixed infections†	4	1	2
Miscellaneous‡	3	0	0
Total	160 (100·0)	30 (18·8)	40 (25·0)

* CFR in %.

† *E. coli*+*Staph. epidermidis* (2×), *E. coli*+klebsiella+*H. influenzae* (1×), *E. coli*+*Str. sanguis* (1×).

‡ Bacteroides, microbacterium, corynebacterium (one patient each).

Six (14%) of the 44 surviving patients had one or more sequelae. Hearing loss, hydrocephalus and developmental motor disturbance were each reported in two patients, paralysis and epilepsy each in one patient.

Thirty-two per cent of the patients suffered from a CNS complication. BM due to klebsiella or enterobacter was complicated in 58% of the patients; on the contrary, none of the patients with BM due to 'miscellaneous Gram-negative pathogens' had complications ($P < 0{\cdot}05$). Death or sequelae occurred in 43% of the patients with a complicated course of disease and in 30% of the patients without a complication (n. s.). A brain abscess occurred in one patient with an intestinal carcinoma, which was complicated by fatal septicaemia and meningitis due to *Klebsiella pneumoniae*.

Two patients had recurrent BM. One had an operation at the age of 1 month because of a spina bifida. Afterwards *Morganella morganii* was isolated from the

Table 2. *Gram-negative meningitis: distributions according to age, sequelae, complications, predisposing factors and hospital-acquired infection*

	E. coli	Other Gram-negative rods: Klebs/Enter	Other Gram-negative rods: Salmonella	Other Gram-negative rods: Other	Miscellaneous*	Total (CFR due to BM)
Age						
1–11 months	10	4	7	0	3	24 (21)
1–19 years	5	1	1	2	7	16 (19)
20–59 years	2	6	0	3	1	12 (17)
⩾ 60 years	8	1	0	2	2	13 (46)
Total	25	12	8	7	13	65 (25)†
	Percentages per pathogen					
Age						
1–11 months	40	33	88	0	23	37
1–19 years	20	8	13	29	54	25
20–59 years	8	50	0	43	8	18
⩾ 60 years	32	8	0	29	15	20
Sequelae‡	13	17	14	20	9	14
CNS complications	36	58	38	29	0	32§
Predisposing factors						
Access to CSF	24	33	0	71	38	31
Immunocompromised	12	0	0	14	8	8
Other/combinations	36	50	25	14	15	31
No predisposing factors	28	17	75	0	38	31
Hospital acquired infection	52	58	0	43	15	39

* Including mixed infections.

† Comparison of CFR in the various age groups: $X^2 = 4{\cdot}1$; D.F. $= 3$; $P > 0{\cdot}2$.

‡ Percentage of surviving patients (cf. Table 1; the denominator is: [No. of patients] minus [patients dead from all causes]).

§ $X^2 = 10{\cdot}2$; D.F. $= 4$; $P < 0{\cdot}05$.

CSF and a hydrocephalus developed. BM due to *M. morganii* occurred on two further occasions. The other patient (61 years) suffered from chronic lymphocytic leukaemia and had an aortic valve prosthesis which appeared to be the source of two episodes of *Pseudomonas aeruginosa* meningitis.

Predisposing factors were present in 69% of the patients. Factors facilitating direct invasion of the subarachnoid space were common in BM due to 'other Gram-negative rods' and in patients from whom more than one pathogen had been isolated. Salmonella meningitis often occurred without a recognized risk factor. The CFR was low in patients without predisposing factors (5%) and among those with a skull fracture (11%), whereas the CFR was 36% in other patients with 'access to CSF', 60% among the immunocompromised and 35% in the other patients with predisposing factors.

In 25 patients (39%), BM was hospital-acquired. This was common in BM due to *E. coli*, klebsiella or enterobacter. Skull fractures and neurosurgical procedures were associated with 28 and 20% respectively of the cases of hospital-acquired BM.

Although neonates were not included in this series, BM due to *E. coli* appeared to be most frequent in the youngest age group (40% of isolates). The percentage of patients more than 60 years (32%) was lower than that described by others (76%; Cherubin *et al.* 1981). The heterogeneity of *E. coli* strains is well known (Levine, 1985): in our series K1 was isolated only from the youngest group, whereas other K-types were most prevalent among the aged. The CFR was highest in the oldest age group, mainly due to the high CFR in enteric Gram-negative BM among these patients.

In older patients Gram-negative bacteria are often associated with skull fractures and neurosurgical procedures (Mombelli *et al.* 1983). The CFR is reported to be more than 50%. This is partly due to the inadequacy of the current antibiotic therapy: several agents do not achieve bactericidal levels in the CSF and resistance to β-lactam antibiotics is increasing (Landesman *et al.* 1981). It remains to be proven whether the newer cephalosporins are an improvement in therapy (McCabe, 1982; Sanders & Sanders, 1985).

(3) *Gram-positive pathogens* (Table 3)

Str. agalactiae (group B streptococcus) was isolated most frequently from patients 1–11 months of age. *Staph. epidermidis* meningitis occurred most frequently among the older children. The prevalence of BM due to *L. monocytogenes* rose with the age. The overall CFR in Gram-positive BM was 15% (14 of 95). The CFR was significantly higher among the aged (35%; $P < 0{\cdot}025$).

Ten (13%) of the 76 surviving patients had one or more sequelae. This percentage varied from 0% in BM due to *Staph. epidermidis* to 40% in BM due to *Str. agalactiae* (n.s.). Hearing loss was recorded in four patients who all had suffered from streptococcal meningitis (two group R, one group A, one group B). Developmental motor disturbance and epilepsy occurred each in three patients and paralysis and hydrocephalus each in one patient.

CNS complications occurred in 38% of these were significantly associated with sequelae or a fatal outcome (12% of patients without a complication *v.* 47% of patients with; $P < 0{\cdot}001$). Seizures, one of the CNS complications, occurred in 15% of patients. This complication did not occur in *Staph. epidermidis* meningitis, only

Table 3. *Gram-positive meningitis: distributions according to age, sequelae, complications, predisposing factors and hospital-acquired infection*

	Staphylococcus		*Streptococcus*		*L. mono-cytogenes*	Miscel-laneous	Total (CFR due to BM)
	aureus	*epiderm*	Group B	Other			
Age							
1–11 months	5	1	8	1	0	1	16 (13)
1–19 years	2	9	0	10	2	1	24 (4)
20–59 years	5	2	2	13	10	0	32 (9)
⩾ 60 years	3	1	2	6	11	0	23 (35)
Total	15	13	12	30	23	2	95 (15)*
	Percentages per pathogen						
Age							
1–11 months	33	8	67	3	0	50	17
1–19 years	13	69	0	33	9	50	25
20–59 years	33	15	17	43	44	0	34
⩾ 60 years	20	8	17	20	48	0	24
Sequelae†	9	0	40	11	14	0	13
CNS complications	47	8	58	33	48	0	38
Predisposing factors							
Access to CSF	33	62	8	33	9	100	30
Immunocompromised	13	0	0	7	30	0	12
Other/combinations	40	38	42	30	13	0	29
No predisposing factors	13	0	50	30	48	0	29
Hospital acquired infection	33	62	17	30	13	100	31‡

* Comparison of CFR in the various age groups: $X^2 = 10{\cdot}3$; D.F. = 3; $P < 0{\cdot}025$.
† Percentage of surviving patients (see footnote of Table 2).
‡ $X^2 = 14{\cdot}9$; D.F. = 5; $P = 0{\cdot}01$.

once in *Staph. aureus* meningitis (combined: 4%), whereas it was found in 21% of the patients with streptococcal meningitis (42% group B; 13% other groups). A brain abscess occurred in one patient with an intestinal carcinoma, which was complicated by fatal septicaemia and meningitis due to *Staph. aureus*.

Four patients had recurrent BM. Isolated micro-organisms and predisposing factors were: *Staph. aureus* (1×; CSF leackage after hypophysectomy; isolate of the first episode not known); *Staph. epidermidis* (2×; both patients had a shunt after a neurosurgical procedure; all causal organisms were *Staph. epidermidis*; one patient had already had four episodes of BM); *Str. agalactiae* (1×; CSF fistula after head injury; isolate of the first episode not known).

Predisposing factors were present in 71% of the patients. Factors facilitating direct invasion of the subarachnoid space were common in staphylococcal meningitis. Meningitis due to *Staph. epidermidis* never occurred in the absence of such a factor. *L. monocytogenes* was often isolated from immunocompromised patients. Alcohol abuse was recorded in five patients, four of whom suffered from listeria meningitis. All patients with meningitis due to *Str. suis* (group R) had had contact with contaminated pigs or pork (Arends *et al.* submitted). In 14%, *Staph. aureus* meningitis was a complication of vertebral osteomyelitis (3 of 21); this predisposing factor was associated exclusively with *Staph. aureus*. The CFR was 27% in immunocompromised patients, 20% after a skull fracture and 18% among those without predisposing factors, but it was only 9% in other patients with 'access to CSF' and 11% in the other patients with predisposing factors.

Hospital-acquired infections were seen significantly more often in BM due to staphylococci (46%), especially *Staph. epidermidis*, than in BM due to the other Gram-positive organisms (24%; $P = 0{\cdot}01$).

As was found in *E. coli* meningitis, the highest prevalence of *Str. agalactiae* was in the youngest age group. This bacterium was seldom isolated from older patients. *Staph. epidermidis* caused nine cases in the age group of 1–19 years. This organism acts as a meningitis pathogen only in the presence of a predisposing factor such as a shunt and causes a mild disease (Finland & Barnes, 1977); in our series no patient died or acquired any sequela from meningitis due to *Staph. epidermidis*.

Hearing loss was a common sequela after non-group B streptococcal meningitis (11%); this has been reported for *Str. suis* (Chau, Huang & Kay, 1983; Arends *et al.* submitted).

About 50% of patients with listeria meningitis have been reported to have predisposing factors (Lavetter *et al.* 1971; Bouvet *et al.* 1982; Tim *et al.* 1984). In our series this percentage was 52%, including two factors previously reported to be important: malignancies (Chernik, Armstrong & Posner, 1973) and alcohol abuse (Lavetter *et al.* 1971; Cherubin *et al.* 1981; Bouvet *et al.* 1982; Tim *et al.* 1984).

Streptococci caused convulsions more often than staphylococci. To our knowledge, this has not been reported previously.

Staph. aureus meningitis is known to complicate vertebral osteomyelitis sometimes (Waldvogel & Vasey, 1980), when the bacterium directly invades the CSF from an infected vertebra; our results confirm this.

In summary, the less common meningitis pathogens cause a considerable mortality and post-meningitic morbidity. The incidence is likely to increase

because predisposing factors such as neurosurgical procedures, malignancies and immunosuppression will be more and more common. This feature and the increasing resistance of the Gram-negative bacteria to many antibiotics urge the need for careful surveillance.

This study was supported by a grant from the Praeventiefonds, research no. 28–644. We are indebted to all bacteriologists and clinicians who provided us with strains and information on patients. We thank Pamela Wright for reviewing the English manuscript and Mieke van Doorn for secretarial assistance.

REFERENCES

ARENDS, J., BOL, P., SPANJAARD, L. & ZANEN, H. C., (1986). Meningitis caused by *Streptococcus suis* in man. Thirty cases, a review of the literature and a comparison with *Streptococcus pneumoniae* meningitis. Submitted for publication.

BOHR, V., HANSEN, B., JESSEN, O., JOHNSEN, N., KJERSEM, H., KRISTENSEN, H. S., NYBOE, J. & RASMUSSEN, N. (1983). Eight hundred and seventy-five cases of bacterial meningitis. Part I of a three-part series. Clinical data, prognosis and the role of specialised hospital departments. *Journal of Infection* **7**, 21–30.

BOUVET, E., SUTER, F., GIBERT, C., WITCHITZ, J. L., BAZIN, C. & VACHON, F. (1982). Severe meningitis due to *Listeria monocytogenes*. A review of 40 cases in adults. *Scandinavian Journal of Infectious Diseases* **14**; 267–270.

CHAU, P. Y., HUANG, C. Y. & KAY, R. (1983). *Streptococcus suis* meningitis. An important underdiagnosed disease in Hong Kong. *Medical Journal of Australia* **1**, 414–417.

CHERNIK, N. L., ARMSTRONG, D. & POSNER, J. B. (1973). Central nervous system infections in patients with cancer. *Medicine* **52**, 563–581.

CHERUBIN, C. E., MARR, J. S., SIERRA, M. F. & BECKER, S. (1981). *Listeria* and Gram-negative bacillary meningitis in New York City, 1972–1979; frequent causes of meningitis in adults. *American Journal of Medicine* **71**, 199–209.

FINLAND, M. & BARNES, M. W. (1977). Acute bacterial meningitis at Boston City Hospital during 12 selected years, 1935–1972. *Journal of Infectious Diseases* **136**, 400–415.

GORSE, G. J., THRUPP, L. D., NUDLEMAN, K. L., WYLE, F. A., HAWKINS, B. & CESARIO, T. C. (1984). Bacterial meningitis in the elderly. *Archives of Internal Medicine* **144**, 1603–1607.

JONSSON, M. & ALVIN, A. (1971). A 12-year review of acute bacterial meningitis in Stockholm. *Scandinavian Journal of Infectious Diseases* **3**, 141–150.

LANDESMAN, S. H., CORRADO, M. L., SHAH, P. M., ARMENGAUD, M., BARZA, M. & CHERUBIN, C. E. (1981). Past and current roles for cephalosporin antibiotics in treatment of meningitis; emphasis on use in Gram-negative bacillary meningitis. *American Journal of Medicine* **71**, 693–703.

LAVETTER, A., LEEDOM, J. M., MATHIES, A. W. JR., IVLER, D. & WEHRLE, P. F. (1971). Meningitis due to *Listeria monocytogenes*, a review of 25 cases. *New England Journal of Medicine* **285**, 598–603.

LEVINE, M. M. (1985). *Escherichia coli* infections. *New England Journal of Medicine* **313**, 445–447.

MCCABE, W. R. (1982). Empiric therapy for bacterial meningitis. *Reviews of Infectious Diseases* **5** supplement, S74–83.

MOMBELLI, G., KLASTERSKY, J., COPPENS, L., DANEAU, D. & NUBOURGH, Y. (1983). Gram-negative bacillary meningitis in neurosurgical patients. *Journal of Neurosurgery* **58**, 634–641.

MULDER, C. J. J. & ZANEN, H. C. (1984). A study of 280 cases of neonatal meningitis in The Netherlands. *Journal of Infection* **9**, 177–184.

NETHERLANDS REFERENCE LABORATORY FOR BACTERIAL MENINGITIS (1981, 1985). Bacterial meningitis in the Netherlands; annual reports, 1980, 1984. University of Amsterdam.

SANDERS, C. C. & SANDERS, W. E. JR. (1985). Microbial resistance to newer generation β-lactam antibiotics: clinical and laboratory implications. *Journal of Infectious Diseases* **151**, 399–406.

SPANJAARD, L., BOL, P., EKKER, W. & ZANEN, H. C. (1985). The incidence of bacterial meningitis in the Netherlands; comparison of three registration systems, 1977–1982. *Journal of Infection* **11**, 259–268.

SPANJAARD, L., BOL, P., DE JONG, M. C. J. W. & ZANEN, H. C. (1986). Bacterial meningitis in 366 children in the Netherlands, 1982–1983. Epidemiology and antibiotic therapy. *Tijdschrift voor Kindergeneeskunde* **54**, 1–8.

TIM, M. W., JACKSON, M. A., SHANNON, K., COHEN, B. & MCCRACKEN, G. H. JR. (1984). Non-neonatal infection due to *Listeria monocytogenes*. *Pediatric Infectious Disease* **3**, 213–217.

WALDVOGEL, F. A. & VASEY, H. (1980). Osteomyelitis: the past decade. *New England Journal of Medicine* **303**, 360–370.