CONTEMPORARY ISSUES IN INFECTIOUS DISEASES

BACTERIAL MENINGITIS

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Preface

The purpose of this book is to incorporate within one volume the relevant new aspects of pathogenesis, pathophysiology, therapy, and prevention of bacterial meningitis. To accomplish this we have taken a similar approach to that used in our two preceding volumes in this series and have invited the leading experts in specific investigative fields to present their individual contributions and ideas. The resulting product is an authoritative text representative of the most up-to-date published and unpublished information available concerning meningitis.

Considerable emphasis is placed on the pathogenesis of the disease. By publishing this information for the first time under one cover we provide the reader with the opportunity to compare the work and theories from three exceptionally active and productive scientists (Drs. Smith, Moxon, and Scheld) regarding the mysteries surrounding the development of bacterial meningitis. These observations have been put in perspective by Dr. Broome's discussion of the importance of this disease in the United States and her review of the epidemiology of the various pathogens and also by Dr. Kaplan's review of his experience with the clinical presentation and diagnostic aspects.

The final chapters deal with the treatment and prevention of the various forms of bacterial and fungal meningitis. A discussion of the various critical principles derived from the use of animal models of the disease is followed by a specific discussion of the individual patient populations at risk. Dr. Glode's chapter reviews the recent studies dealing with antibiotic prophylaxis; Dr. Gold's, immunoprophylaxis.

This volume represents, as do the two preceding volumes in this series, the editors' attempt to bring exciting scientific observations into clinical focus while updating the physician on current aspects of practical patient management. We feel that this volume effectively accomplishes that goal.

We would like to thank Rebecca Brooks-Fournier and Betsy Zickler for their hard work, long hours, and superb organizational talents while working on this book.

We would also like to thank Hoechst-Roussel Pharmaceutical Company for funding a symposium that was the stimulus for production of this volume.

Merle A. Sande, M.D. Arnold L. Smith, M.D. Richard K. Root, M.D.

BACTERIAL MENINGITIS

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Recent Developments in the Epidemiology of Bacterial Meningitis

Claire V. Broome Walter F. Schlech III

Information on the epidemiology of bacterial meningitis is important to the clinician, both for assessing the probable etiologic agents in an individual case, and for applying appropriate measures of treatment and prevention of the disease. This review summarizes some of the basic epidemiologic characteristics of the disease and focuses on selected aspects in epidemiology which may be useful for decisions about antibiotic therapy, vaccine usage, and chemoprophylaxis for prevention of secondary cases.

METHODOLOGY

Information regarding attack rates can be derived from several published population-based studies. In these studies, active case finding has been performed for a defined population. ^{1–5} All cases of meningitis observed during a defined period have been identified by review of hospital, clinical and laboratory records, and death certificate data. Because most patients with bacterial meningitis are hospitalized, a relatively complete case ascertainment has been possible. Furthermore, because a specific diagnosis can be made based on a characteristic clinical picture, a cerebrospinal fluid profile, and an identification of a causative organism in the blood or cerebrospinal fluid by isolation or antigen detection, the basic epidemiology of bacterial meningitis can be defined with considerable precision. Although each of these pop-

ulation based studies includes a small number of cases, the consistency of attack rates among the studies suggests that the data are representative.

The second source of data on the epidemiology of bacterial meningitis is the passive surveillance system maintained by the Centers for Disease Control (CDC). CDC receives reports on cases of bacterial meningitis from 27 states that voluntarily participate in the system. Data from this system have been analyzed for the period 1978–1981.⁶ Because the system is based on passive surveillance, there is undoubtedly underreporting. In spite of the known and unknown biases introduced by this underreporting, the surveillance data are frequently useful for identification of temporal trends. Furthermore, information is obtained on such a large number of cases that patterns can be identified that would not be obvious in the smaller hospital-based or population-based studies.

The third source of bacterial meningitis data are the clinical isolates of *Strepto-coccus pneumoniae* and *Neisseria meningitidis* submitted to the CDC for serotyping and serogrouping, respectively.^{7,8}

DESCRIPTIVE EPIDEMIOLOGY

Etiologic Agents. A number of population-based studies have identified the agents that most commonly cause bacterial meningitis in this country. *Haemophilus influenzae* has been the leading cause, followed by *S. pneumoniae* and *N. meningitidis*. ^{1–5} There are, however, major differences in the relative importance of these and other pathogens for different age groups. Table 1-1 shows the data for one population-based study, with the familiar predominance of organisms such as group B streptococci and *Escherichia coli* in the group less than 1 month of age, the predominance of *H. influenzae* in the age group 1 month to 4 years of age, and the more prominent role of pneumococcus and meningococus in older age groups. ¹

Host Characteristics. Patient age appears to be one of the most important factors affecting both absolute attack rate for bacterial meningitis, and host susceptibility to illness when infected with specific organisms. For *H. influenzae*, population-

	Age of Cases						
Bacteria	<1 month	1 month– 4 years	5-59 years	60+ years			
H. influenzae	0	39	0.1	0.9			
S. pneumoniae	0	9	0.6	0.4			
N. meningitidis	0	5	0.4	0.0			
Other	290†	2	0.4	3.4			
Unknown	30	0	0.0	.4			
Total	310	55	1.7	5.1			

Table 1-1. Incidence rate* of bacterial meningitis by age and organism, Bernalillo County, New Mexico, 1964–1971

^{*}Cases per 100,000 population per year; 184 cases total.

[†] Streptococci; E. coli, Proteus spp.

⁽Fraser DW, Geil CC, Feldman RA: Bacterial meningitis in Bernalillo County, New Mexico: a comparison with three other American populations. Am J Epidemiol, 100:29, 1974)

based studies show the highest attack rates for children under 1 year of age; a peak incidence of 180 cases per 100,000 population occurs for children 6–7 months of age. Children under 1 year of age also have the highest attack rates for meningococcal and pneumococcal meningitis; however, the peak attack rates of approximately 50 per 100,000 population per year are several-fold lower than those for *H. influenzae*.¹

In addition to the differences in attack rates by age, several reports have noted a higher attack rate among blacks, especially for disease due to *H. influenzae* and to *S. pneumoniae*.^{3,5,9} Likewise higher attack rates of *H. influenzae* disease have been noted among native American populations, especially in Alaska and among the Navajo.^{5,10} The age distribution of cases of *H. influenzae* meningitis is also different in native American populations. Whereas only 50 percent of cases in the white and black populations occur in children less than 1 year of age, 75 percent of cases in Alaskan natives and American Indians occur in this age group.^{4,6,10} The reason for these variations in attack rate by race are not understood; some investigators have suggested that socioeconomic differences may explain some of the contrasting rates¹, but the question of susceptibility by race has not been resolved.

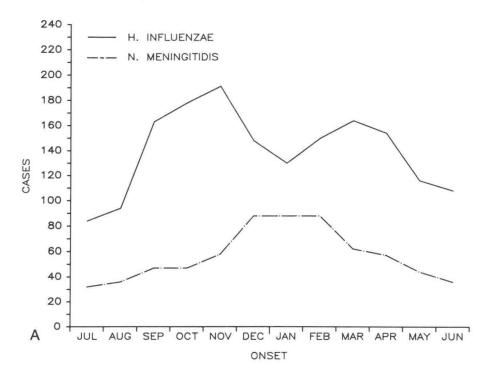
Some studies have also shown a slightly increased attack rate for males compared with females. 1.5.6 The basis for this difference, if it is real, is not understood.

Geographic characteristics in the attack rate of meningitis by geographic location, beyond those attributable to differences in racial composition of the population, have not been well documented. Fraser et al. showed very similar attack rates for *H. influenzae* among four widely differing geographic locations. Regional differences in incidence have been suggested for meningococcal disease, but potential differences in reporting to the surveillance system cannot be excluded as a cause.⁸

Seasonal trends in occurrence of bacterial meningitis have been noted previously. Meningococcal disease incidence peaks between January and March, and pneumococcal meningitis occurs most frequently in the winter months. A striking seasonal pattern of *H. influenzae* meningitis has emerged from the CDC surveillance data, with peaks in the early winter and early spring, and a decrease in cases in January and February (Fig. 1-1A). This pattern has been observed before, and the second peak had been attributed to seasonally related factors in birth cohorts. However, the same pattern of seasonal peaks can be seen for children 1 year of age and older (Fig. 1-1B), suggesting that the season of birth is not the determining factor. Of further interest is the different seasonal trends for states above and below the forty-first parallel; the second peak is pronounced in the northern states and is essentially absent in the southern states (Fig. 1-1C). The reason for this unusual pattern is unknown.

Case fatality rates for disease due to each bacterial pathogen can be derived from the CDC bacterial meningitis surveillance system. For the three most common etiologic agents, case-fatality rates were consistently higher for pneumococcal meningitis, compared with meningococcal meningitis and *H. influenzae* meningitis, for all age groups studied (Table 1-2).⁶ The overall case-fatality rate for pneumococcal meningitis was 26 percent, as compared with 6 percent for *H. influenzae* and 10 percent for *N. meningitidis*. For the organisms producing meningitis in neonates, the case-fatality rate for group B streptococcal meningitis was 22 percent, whereas the case-fatality rate for *Listeria* was 28 percent.⁶

4 Bacterial Meningitis



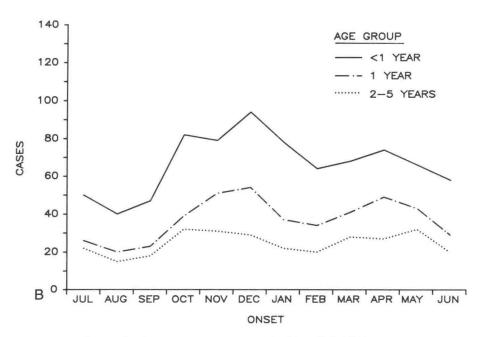


Fig. 1-1 (A) Seasonal occurrence of bacterial meningitis, 1978–1981. (B) Seasonal occurrence of *H. influenzae* meningitis, by patient age, 1978–81. (Figure continues).

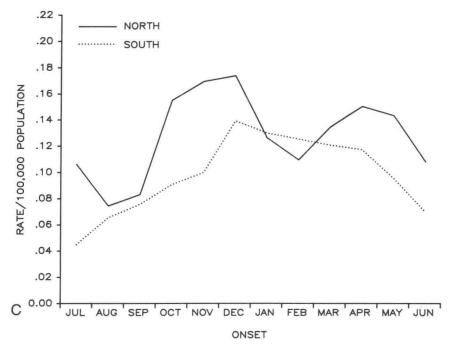


Fig. 1-1 (Continued). (C) Seasonal occurrence of *H. influenzae* meningitis by region, 1978–1981.

EPIDEMIOLOGY OF ANTIBIOTIC RESISTANCE

Since the initial reports of isolates of *H. influenzae* resistant to ampicillin appeared in 1974, multiple studies have appeared in the literature on the increasing prevalence of ampicillin resistance strains among clinicial isolates. ^{12–17} The meningitis surveillance system has obtained national information on the portion of isolates of *H. influenzae* from meningitis cases that were reported to be ampicillin resistant in 1978–81. This information is based on hospital reporting of resistance, and the

Table 1-2. Fatality in bacterial meningitis by agent and age of patient

	< 1 month		1 mo4 yrs.		5-45 yrs.		>45 yrs.	
	% fatal	# (cases)	% fatal	# (cases)	% fatal	# (cases)	% fatal	# (cases)
H. influenzae	23	(70)	5	(5466)	9	(342)	20	(114)
N. meningitidis	23	(39)	8	(1208)	10	(947)	20	(260)
S. pneumoniae	28	(32)	13	(665)	19	(421)	47	(566)
L. monocytogenes	6	(47)	*				38	(151)
E. coli	21	(38)			_		===	
Group B Streptococcus	22	(287)	-				_	

^{*}Too few cases for analysis.

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