Alcohol abuse and its sequelae of both trauma and chronic disease were most closely associated with the highest rates of utilization of ambulatory care services. This relationship might be expected to hold true for hospitalizations. In fact, in addition to more frequent clinic visits, the high-utilizer group had many more hospitalizations in the followup period. Men in the high utilization group had three times as many hospitalizations in the followup period as the controls. The corresponding group of women had twice as many hospitalizations as the controls. This finding is consistent with other studies in the literature. For example, Putnam investigated alcohol, morbidity, and care-seeking behavior and found hospitalization rates for alcoholics almost two and one-half times the rate of controls (*5*).

Can we modify our intervention and make a difference for the patient? Jones and Vischi reviewed the research literature on medical care utilization behavior and the impact of alcohol, drug abuse, and mental health treatment (*6*). Twenty-five studies were examined and, in general, reductions in utilization in the range of 20–40 percent occurred after treatment. However, causality was not established. Also, time spans were short, making it unclear whether these differences lasted or not.

In my experience, there are several useful approaches to those who are high-utilizers. A well-organized medical record is imperative. At the minimum, it is necessary to have a complete problem list on the record and some type of indexing that makes the various types of subjective and objective data easy to find. Just as helpful is only having one or several health care providers consistently see the patient at each encounter. The patients are more satisfied, and it is much easier for the physician who no longer has to review a complicated problem list and complex chart of an unknown patient. The goal is to not miss diagnosing and treating what is amenable to treatment.

However, many of the issues that cause the high utilizers to seek medical care cannot be solved by health care providers. Nor is it fair or realistic to say that these problems can only be solved by the patient. These issues are more complex than that. High utilization is a result of patterns of behavior from the patient's distant past and interactions with his environment and other people. Our responsibility as clinicians is to treat him for what we know how to treat and support him to the extent possible as he seeks to deal with all other issues that bring him to our offices.

Is this approach successful? There are few objective data to answer this question. One could hope for studies that demonstrate intervention strategies make a difference in both morbidity and mortality. At the Alaska Native Medical Center, we do see high-utilizer patients whose health improves. When they are asked how it happened, they say that they had to do it by themselves and in their own way. Does this group of patients have some common characteristics? This question needs to be answered.

In the meantime, we must all first recognize and then remind ourselves that patients who are high utilizers of ambulatory care services represent a subgroup of patients at high risk for hospitalization and early death.

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Epidemiology of *Haemophilus Influenzae* Type B Disease Among Navajo Indians

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Synopsis

During a 7-year period ending June 30, 1980, the annual incidence of all Haemophilus influenzae *type b disease among Navajo children less than 5 years old was 214 per 100,000, and that of* H. influenzae *meningitis was 152 per 100,000. Eighty-one percent of* H. influenzae *meningitis occurred in children 12 months of age or younger, and 64 percent clustered in children ages 4 through 8 months. Meningitis accounted for 70 percent of all invasive disease. No epiglottitis was observed. The epidemiology is similar to that in Yupik Eskimos, who have an even higher rate of* H. influenzae *type b disease than Navajos but are a much smaller population. Mortality from* H. influenzae *meningitis was low (4 percent) among Navajo children, but neurological sequelae were observed in at least 16 percent of the survivors. This high rate of sequelae may be due in part to clustering of cases in infancy.*

Among normal Navajo neonates, 79 percent had maternal capsular type b antibody titers greater than or equal to 0.15 micrograms per deciliter (μg per dl), and the whole group had a geometric mean titer of 0.51 μg per dl. By age 4 months, when meningitis cases became frequent, only 14 percent of Navajo infants had antibody titers ≥0.15 μg per dl. Twelve of 67 asymptomatic infants (18 percent), each monitored every 2 months, had H. influenzae *type b or a cross-reacting organism isolated from the pharynx on at least one occasion before they were 9 months old. Active immunization would be theoretically indicated in this population with high* H. influenzae *type b exposure and disease, but a vaccine would have to confer substantial immunity in very young infants.*

We previously reported that the incidence of *Haemophilus influenzae* type b meningitis in Navajo Indians was four to six times greater than reported in other populations in the United States and that a larger proportion of cases in Navajo children occurred under 1 year of age (*1,2*). Recently, a *H. influenzae* type b capsular polysaccharide vaccine, polyribosyl-phosphate (PRP), was reported to be immunogenic in infants (*3,4*). It appeared to us that Navajo infants and young children might be suitable candidates for artificial immunization against *H. influenzae* b. This report describes our confirmation of a current high incidence in Navajo infants and children of *H. influenzae* type b disease with serious sequelae, identification of protective levels of *H. influenzae* type b antibody in Navajo newborns with subsequent antibody titer reduction in the early months of life, and pharyngeal colonization of *H. influenzae* type b in Navajo infants.

Methods

Clinical description. We used the same methods to study the incidence of bacterial meningitis in Navajos from July 1, 1973, through June 30, 1980, that we reported previously for 1968–73 (*1*). We reviewed hospital records of all Navajo patients, discharged from hospitals serving the 25,000-square-mile Navajo Indian Reservation, who had any type of bacterial meningitis during the entire 7-year period. We also reviewed laboratory records of *H. influenzae* type b isolations from cerebrospinal fluid (CSF), blood, or other specimens during 2 years, July 1978 through June 1980. A case of *H. influenzae* or other bacterial meningitis was considered "confirmed" only if the organism was cultured from CSF. Episodes of tuberculous meningitis, which were also reviewed to ensure completeness, required (*a*) clinical evidence of meningitis, (*b*) CSF pleocytosis, and (*c*) documentation of infection with *Mycobacterium tuberculosis* either through positive acid fast stain or subsequent positive culture of CSF or other material. A case of bacterial meningitis was "probable" if there were both polymorphonuclear leukocytosis ≥ 1,000 cells per ml in the CSF and bacteria observed on CSF Gram stain but not grown in culture. "Neurological sequelae" refer to dysfunctions diagnosed as secondary to infectious disease of the central nervous system and still present at least 6 months after the acute illness. Neurological sequelae included (*a*) a seizure disorder requiring medication, (*b*) paresis or paralysis, (*c*) hydrocephalus, (*d*) cortical blindness, and (*e*) deafness.

Population estimates. Three widely different estimates of Navajo population have been used in recent years: the 1970 U.S. census, Navajo Area Bureau of Indian Affairs (BIA) Population Register, and estimates by the U.S. Office of Revenue Sharing. In 1976 the BIA accepted the last as most accurate (*5*), and we used this estimate to calculate a midpoint denominator for this study. As of July 1, 1975, the Navajo population was estimated to be 134,340 persons. With an annual growth factor of 2.9 percent, the size of the Navajo population at the study's 7-year midpoint of January 1977 was esti-

'Overall, H. influenzae *caused 60 percent of bacterial meningitis, with a mean annual incidence of 152.5 cases per 100,000 children under age 5 years.'*

mated to be 142,245 persons. Percentages of the population in various age groups were ascertained from BIA data.

In our earlier report on bacterial meningitis (*1*), the higher estimate of the BIA was used to calculate annual incidence of disease. The BIA estimates resulted in a different age distribution than the Office of Revenue Sharing estimates used in this study. For example, 11.9 percent of the Navajos were 0–4 years old in the earlier study, compared with 13.5 percent in 1977. Rates for the 1968–73 series were recalculated, using the new population estimates to allow comparison between the two intervals.

***H. influenzae* type b antibody in newborns.** Samples of umbilical cord blood were obtained from 100 consecutive Navajo infants born at Gallup (N. Mex.) Indian Medical Center in December 1980 and January 1981. Samples of sera were extracted within 4 hours of birth, stored at −20° centigrade, and shipped to Lederle Laboratories in Pearl River, N.Y. Samples were analyzed there for antibodies to *H. influenzae* type b capsular antibody using the radioimmunoassay technique with tritium-labeled antigen PRP described by Kuo and his associates (*6*).

***H. influenzae* type b antibody in infants.** *H. influenzae* type b antibody titers also were determined for 37 Navajo infants who served as a placebo control group in a *H. influenzae* type b vaccine immunogenicity trial. Blood samples were drawn at 1–2, 3–4, 5–6, and 7–8 months of age. *H. influenzae* capsular antibody levels were determined as described previously. In all cases group results were expressed as a geometric mean titer. Undetectable antibody levels (<0.04 μg per dl) were considered to have the specific value of 0.02 μg per dl in order to assign a logarithm and calculate the geometric mean titer.

Prevalence of *H. influenzae* type b infection in infants. Pharyngeal and rectal swab samples were obtained at 1–2, 3–4, 5–6, and 7–8 months of age from 37 control and 30 immunized participants in a *H. influenzae* type b vaccine trial reported elsewhere (*4*). These swabs were inoculated directly on *H. influenzae* type b antiserum agar, and colonies of *H. influenzae* or organisms with cross-reacting antigens, such as *Escherichia coli* K 100, were identified by halos of antigen-antibody precipitate (*7,8*).

Results

***H. influenzae* type b disease.** Table 1 summarizes the annual incidence by infectious agent of 341 confirmed cases of bacterial meningitis among the Navajo during 1974–80. Overall, *H. influenzae* caused 60 percent of bacterial meningitis, with a mean annual incidence of 152.5 cases per 100,000 children under age 5 years. All but one of the *H. influenzae* cases occurred in children of this age group, with 81 percent in the first year of life and 64 percent clustered in children ages 4–8 months. There were no cases in the first month of life, one during the second month, and seven (3 percent) during the third month. This age distribution, in comparison with those of other types of bacterial meningitis, is shown in the chart.

Two patients had recurrent episodes of *H. influenzae* meningitis, one at 5 and 8 months and one at 11 and 13 months. Thirty-four deaths were recorded, including 9 of the 206 persons with *H. influenzae* (4 percent) and 12 of the 77 persons with *Streptococcus pneumoniae* (16 percent). These case fatality rates were approximately one-half as high as those we reported among the Navajo for 1968–73—9 percent and 33 percent (*1*). Thirteen percent, or 26 children, with bacterial meningitis had *H. influenzae* type b isolates from CSF that were reported to be resistant to ampicillin when standard Kirby-Bauer disc sensitivities were used, but there was no evident trend toward increasing antibiotic resistance observed over the 7-year period.

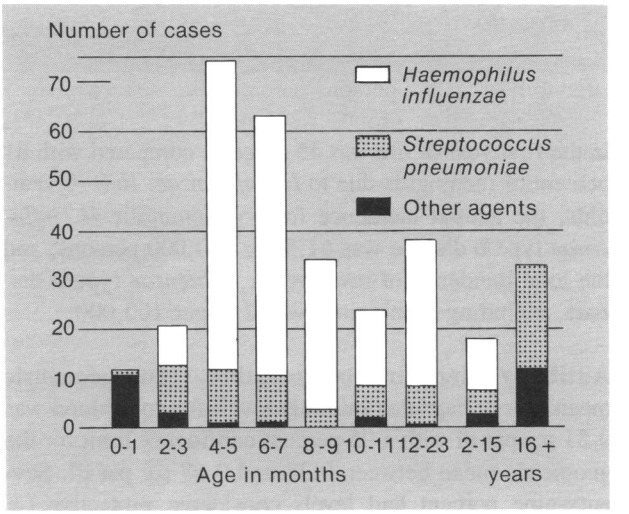
Forty-three additional patients had probable bacterial meningitis on the basis of CSF pleocytosis and presumptive identification of an organism on CSF Gram stain. Among 10 patients with probable *H. influenzae*, 2 died and 3 were subsequently noted to have neurological sequelae. It is likely that these cases were, in fact, caused by the organisms specified, and failure to culture was secondary to earlier treatment with antibiotics.

Forty-one meningitis patients (13 percent of 307 who survived) had no recorded subsequent hospital or clinic visits or had inadequate chart information for determination of whether neurological sequelae were present. The charts of the remaining 266 survivors who had at least one recorded observation 6 months or more after hospital discharge were reviewed for documented seizure disorder, paralysis or paresis, hydrocephalus, or other se-

quelae present more than 6 months after the acute episode. Table 2 shows the prevalence of serious sequelae, assuming that children who had not returned to any hospital or clinic were all well. Thus, these are minimum prevalence estimates. Of the cases of bacterial meningitis caused by *M. tuberculosis*, 44 percent resulted in significant neurological defects. Of those caused by *S. pneumoniae* and *H. influenzae*, 20 percent and 16 percent, respectively, resulted in significant neurological sequelae. In addition, seven patients (4 percent) with *H. influenzae* became at least partially deaf, and four (2 percent) developed cortical blindness thought secondary to meningitis. Twenty-nine *H. influenzae* survivors (18 percent) developed neurological sequelae during the first year of life; only two older children with meningitis (5 percent) had such sequelae.

Twenty-nine cases of other invasive *H. influenzae* disease were documented among the Navajo during 2 years in which there were also 67 confirmed cases of *H. influenzae* meningitis. Thus, meningitis accounted for 70 percent of all invasive *H. influenzae* disease. Syndromes identified with nonmeningitic, invasive *H. influenzae* type b disease included septicemia without focal disease (7 cases), pneumonia (11), septic arthritis or osteomyelitis (5), periorbital cellulitis (3), and other lesions (3). All isolates were *H. influenzae* type b. No epiglottitis was observed, and pediatricians from several hospitals reported they had never seen a case of epiglottitis in a Navajo child. A separate search revealed no hospital discharges of Navajos with a diagnosis of epiglottitis during the entire 7 years. One patient with septicemia died. Most cases of nonmeningitic *H. influenzae* occurred in young children, but the proportion of disease

Meningitis cases by age and etiology among Navajo Indians, 1974-80[1]



[1] 317 cases, excluding 7 of meningococcal and 17 of tubercular meningitis.

Table 1. Bacterial meningitis among the Navajo, etiology and incidence, 1974–80 and 1968–73

Etiologic agent	Number of cases		Percent of all bacterial meningitis, 1974–80	Annual incidence per 100,000, ages 0–4[1]	
	Confirmed	Probable		1974–80	1968–73[2]
Haemophilus influenzae	206	10	60.4	152.5	152.3
Streptococcus pneumoniae	77	10	22.6	45.5	50.4
Neisseria meningitis	7	1	2.0	0.5	12.6
Mycobacterium tuberculosis	17	0	5.0	2.2	8.8
Other organisms	34	22	10.0	15.6	15.1
Total	341	43	100.0	216.3	239.2

[1] Only confirmed cases considered.

[2] Rates recalculated from data presented in reference *1* using revised population estimate.

Table 2. Percentage of 307 bacterial meningitis survivors with neurological sequelae, by etiological agent[1]

Etiologic agent	*Number*[2]	*Overall significant defects*[3]	*Seizure disorder*	*Paralysis or paresis*	*Hydrocephalus*
Haemophilus influenzae	197	16	14	9	2
Streptococcus pneumoniae	65	20	18	12	8
Mycobacterium tuberculosis	16	44	12	44	12
Other agents	29	13	13	10	7

[1] Inadequate information for determination of sequelae in 13 percent.
[2] Deaths excluded.

[3] Seizures, motor defects (paresis of paralysis), or hydrocephalus, (columns 3–5). Many patients had multiple sequelae.

'Of the cases of bacterial meningitis caused by M. tuberculosis, *44 percent resulted in significant neurological defects. Of those caused by* S. pneumoniae *and* H. influenzae, *20 percent and 16 percent, respectively, resulted in significant neurological sequelae.'*

in the first year of life was 45 percent, compared with 81 percent of meningitis due to *H. influenzae*. In 0–4-year-olds, the annual incidence for nonmeningitic *H. influenzae* type b disease was 61.5 per 100,000 persons, and the total incidence of invasive *H. influenzae* type b disease, including meningitis, was 214 per 100,000.

Antibody titers and colonization. The geometric mean titer of capsular antibody levels for cord blood was 0.51 μg per dl with a 95 percent confidence limit for the geometric mean between 0.38 and 0.68 μg per dl. Seventy-nine percent had levels considered protective (≥ 0.15 μg per dl). Table 3 indicates *H. influenzae* type b capsular antibody levels through 8 months of age in the 37 infants participating as controls in a *H. influenzae* vaccine immunogenicity trial. The dropoff of maternally acquired antibody protection by 3 months coincides with the peak occurrence of *H. influenzae* meningitis among infants 4–8 months old.

Twelve of 67 asymptomatic infants (18 percent) followed as part of a vaccine trial had pharyngeal *H. influenzae* type b or an antigenically similar organism identified by antiserum agar before they were 9 months old. Five were noted at 1–2 months; six at 5–6 months; and one at 7–8 months only, with a second isolate from a baby also positive at 5–6 months. Six of these had positive pharyngeal cultures only, and six had rectal cultures positive as well. No subculturing was performed and the latter group may have included cross-reacting enteric organisms.

Discussion

This study reconfirms the high frequency of invasive *H. influenzae* type b disease among Navajo children and extends our earlier observations in several ways. First, the hospital chart survey showed a 16 percent prevalence of neurological sequelae in *H. influenzae* meningitis survivors. This estimate is conservative because the 13 percent who were lost to followup or had inadequate chart documentation were treated in the calculation as if they were normal. Sequelae were substantially more frequent than those reported in recent surveys (*9,10*), but less frequent than the 30–50 percent reported in another survey (*11*). Levy found that the prevalence of epilepsy was higher in Navajo children and adolescents than in a Rochester, Minn., reference group, and that 19 percent of the cases were considered secondary to meningitis, compared with 3 percent in Rochester (*12*). Among Navajos under 10 years old, the prevalence of seizures was 0.4 percent in Levy's study, compared with 14 percent in our series of *H. influenzae* meningitis survivors. Children who develop *H. influenzae* meningitis relatively early in infancy may have a greater risk of seizures or other sequelae due to the immaturity of the central nervous system during this period.

Second, we found that 79 percent of Navajo newborns had transplacentally acquired antibody protection against *H. influenzae* type b. The pattern of high antibody geometric mean titer at birth followed by peak frequency of clinical disease corresponding to loss of maternal immunoglobulin G by 4 months of age is similar to that reported by Ward and coworkers in Yupik Eskimos (*13*). It suggests that excess cases in these communities occur secondary to frequent exposure in this vulnerable 4-month-old age group.

Third, we surveyed a group of 67 asymptomatic children every 2 months for a total of four times and found that 12 children (18 percent) carried *H. influenzae* or a cross-reacting organism on at least one occasion. In a

Table 3. *Haemophilus influenzae* type b capsular antibody levels and occurrence of meningitis, by month of age for 37 Navajo infants

Age group (months)	Antibody levels: Geometric mean titer (μg per dl)	Antibody levels: 95 percent confidence limits for mean (μg per dl)	Percent with protective antibody titers (≥0.15 μg per dl)	H. influenzae meningitis, 1974–80 (number of cases)
1–2	0.167	0.113–0.249	57	1
3–4	0.037	0.026–0.051	14	31
5–6	0.034	0.024–0.049	14	63
7–8	0.038	0.026–0.054	16	44
9–11	. . .	. . .	. . .	28

cross-sectional study Ward and coworkers reported no pharyngeal carriage of *H. influenzae* type b among 17 Eskimo infants surveyed between 2 and 9 months of age, but one case in children over 10 months (5 percent) (*13*). The prevalence of pharyngeal carriage in each of our surveys ranged from 0 to 9 percent, with the most frequent occurrence (six cases) being at 5–6 months of age.

Previously we used PRP vaccine with pertussis in diphtheria-pertussis-tetanus (DPT) vaccine adjuvant to immunize 30 Navajo infants and found that 50 percent developed antibody titers considered protective against *H. influenzae* type b infection (*4*). However, these titers were achieved generally after three immunizations at 7–8 months of age, toward the end of peak meningitis incidence. Additionally, 5 of 37 infants (14 percent) who received only DPT vaccine developed protective antibody titers, and three of them were found to have positive pharyngeal cultures at least once. The limiting factors in achieving earlier immunity may include interference from passively acquired maternal antibody, for which we found no evidence in the vaccine trial (*4*), and relative immunologic incompetence of the younger infants. It is possible that future developments of *H. influenzae* type b PRP vaccine will have greater antigenicity.

The 46 percent of *H. influenzae* meningitis in infants less than 7 months of age presumably could not be prevented with current vaccine schedules, unless one or two doses led to a more prompt and greater antibody response to natural infection. Moreover, although more than 90 percent of Navajo babies would be expected to have completed their initial DPT immunizations by 13 months of age (R. Baylis, Immunization Status Report, Navajo Area Indian Health Service, Window Rock, Ariz., 1981), only 69 percent of the children with meningitis in our series were up-to-date on immunizations at the time of their illnesses. At those rates, even a vaccine 90 percent effective after three doses might only prevent 34 percent of meningitis cases (54 percent × .9 × .69) and 50 percent of other invasive *H. influenzae* infections in that population. These concerns are less paramount in lower risk populations; for example, in Pittsburgh only 41 percent of *H. influenzae* meningitis occurs in persons less than 1 year of age (*2*). Our observations do, however, illustrate that a useful *H. influenzae* vaccine would have to confer substantial immunity in very young infants, particularly in those populations among whom the disease is most frequent.

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