

Prevalence of Ampicillin-Resistant Strains of *Haemophilus influenzae* Causing Systemic Infection

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Surveillance of *Haemophilus influenzae* bacteremia and meningitis in Omaha during the 6-year period 1974 to 1979 revealed no upward trend in ampicillin resistance. The overall proportion was 5%, and the annual prevalence ranged from 0 to 9%.

An increase in the prevalence of ampicillin resistance among nontypable *Haemophilus influenzae* causing otitis media has been noted in Washington, D.C. (6) and Huntsville, Ala. (7). Reports from Boston (7), Los Angeles (W. Mason and H. Wright, Clin. Res. 26:187A, 1978), Denver (4), Canada (5), and Dallas (4a) suggest that a similar increase in ampicillin resistance has occurred among the predominantly type b strains of *H. influenzae* causing systemic disease. Our surveillance of blood and cerebrospinal fluid isolates of *H. influenzae* in Omaha (2) over a 6-year period indicates that the increase in resistance is not universal.

We reviewed the antibiotic susceptibility of all *H. influenzae* strains causing bacteremia and meningitis at the University of Nebraska Medical Center, Childrens Memorial Hospital, and St. Joseph Hospital from 1 January 1974 through 31 December 1979. These three hospitals care for almost all of the patients with systemic *H. influenzae* infection in Omaha.

Ampicillin resistance was defined as a minimum inhibitory concentration of $\geq 3.12 \mu\text{g/ml}$ as determined by tube-dilution testing, using an inoculum size of 10^4 colony-forming units per ml. All ampicillin-resistant strains were beta-lactamase positive.

During 1974 to 1979, there were 240 patients with 244 episodes of *H. influenzae* bacteremia or meningitis; two patients each had two separate episodes of bacteremia, and one patient had three separate episodes of meningitis. Two-thirds of the patients lived in the metropolitan Omaha area. The remaining patients came from elsewhere in Nebraska and other states. Of those isolates typed, 91% were type b, 3% were types a, c, or d, and 6% were nontypable.

The proportion of strains that were resistant to ampicillin during the 6-year period was 5%, and the annual prevalence showed no upward

trend (Table 1). Disease caused by ampicillin-resistant strains occurred sporadically, with an interval between cases as long as 24 months, from December 1974 to December 1976. The frequency of ampicillin-resistant strains among patients who lived in the metropolitan Omaha area (4%) and among those from elsewhere in Nebraska and from other states (7%) was not significantly different. Patients with ampicillin-resistant infection had no contact with each other. There was no relationship between prior use of beta-lactam antibiotics and infection with an ampicillin-resistant strain. All 13 ampicillin-resistant *H. influenzae* isolates were type b.

There has been no systemic infection with chloramphenicol-resistant *H. influenzae* in Omaha to date.

Two of the children with ampicillin-resistant *H. influenzae* meningitis were initially treated only with ampicillin, one for 5 days and one for 6 days, and both had persistently positive cultures and sustained major neurological damage.

A child hospitalized in Omaha in May 1974 was one of the earliest reported cases of ampicillin-resistant *H. influenzae* meningitis (1). Cases of ampicillin-resistant *H. influenzae* infection have continued to occur in Omaha since that time, but at a low frequency that has shown no tendency to increase.

There are several possible explanations for the discrepancy between our continuing low annual prevalence of ampicillin-resistant bacteremia and meningitis and the increasing frequency reported from other areas. First, short-term fluctuations may be misleading. For example, the increase reported from Los Angeles (Mason and Wright, Clin. Res. 26:187A, 1978) was based on figures of 8.8 and 10.2% for blood and cerebrospinal fluid isolates, respectively, during the first nine months of 1977; that from Denver (4) was based on a figure of 13% for septicemia and meningitis patients for the 9 months from November 1977 through July 1978; and that from Canada (5) was based on a figure of 13% for

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TABLE 1. Annual prevalence of ampicillin-resistant *H. influenzae* strains causing bacteremia and meningitis in Omaha from 1 January 1974 through 31 December 1979

Year	Bacteremia		Meningitis		Total		
	No.	Resistant	No.	Resistant	No.	Resistant	%
1974	4	0	32	2	36	2	6
1975	10	0	26	0	36	0	0
1976	19	0	26	1	45	1	2
1977	16	0	24	3	40	3	8
1978	14	1	27	2	41	3	7
1979	16	3	30	1	46	4	9

isolates from patients with systemic infection during the first 6 months of 1978. This source of variation is illustrated by our 24-month hiatus between ampicillin-resistant cases and by the experience in Atlanta (3), where the proportion of systemic infection caused by ampicillin-resistant strains was 17.6% in January and February 1974, 0% for the next 11 months, and then 13.3% in February and March 1975.

Second, conclusions need to be based on a consistent surveillance system. Inclusion of isolates from sites other than blood and cerebrospinal fluid, for example, makes the data from Boston (7) difficult to interpret.

And third, there may be real differences in the prevalence of resistance in different geographic locations. In Dallas (4a) there has been a gradual increase from 5% in 1975 to 22% in 1979 among patients with *H. influenzae* type b septic arthritis and meningitis. However, factors which foster the spread of ampicillin-resistant *H. influenzae* in Dallas may not be operative in Omaha. A nationwide survey of ampicillin-resistant *H. influenzae* causing meningitis and bacteremia from 1 October 1975 through 30 September 1976, conducted by the Center for Disease Control (8), found an overall prevalence of 4.5%, with variation ranging from 3.0% in the Pacific region to 8.9% in the Western region (which includes both Nebraska and Texas). A similar survey should be repeated to determine the current extent of geographic differences in the United States.

There is continuing need for long-term and consistent local surveillance of ampicillin resist-

ance. However, even if the frequency in a particular geographic location remains low, because of the dire consequences for the individual patient who might have ampicillin-resistant infection, initial therapy of *H. influenzae* meningitis must include chloramphenicol.

It should be emphasized that data on ampicillin-resistant *H. influenzae* systemic infection cannot be applied to *H. influenzae* otitis media. There may be significant disparity between the frequency of resistant type b strains causing bacteremia and meningitis and nontypable strains causing ear infection in a particular geographic location, just as there may be variation in different places.

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