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Penicillin Susceptibility of *Streptococcus pneumoniae* in a Private Pediatric Hospital in Houston, Texas

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Of 493 isolates of *Streptococcus pneumoniae*, 14 were found to have decreased penicillin susceptibility as determined by the oxacillin disk test. Of these 14 isolates, 4 were relatively resistant by quantitative susceptibility studies and 1 was penicillin resistant (MIC, 2 μg/ml). This is the first confirmed penicillin-resistant isolate in the Houston, Tex., area.

Streptococcus pneumoniae, a major cause of morbidity and mortality in children, has until recently been considered universally susceptible to penicillin. In the last decade, however, reports of *S. pneumoniae* isolates with decreased susceptibility to penicillin have appeared (1, 3–7, 9, 12–14, 16, 17). These isolates can be detected presumptively by a zone of inhibition (ZI) of <20 mm surrounding a 1-μg oxacillin disk. The reported prevalence of *S. pneumoniae* relatively resistant to penicillin in pediatric hospitals in the United States ranges from 2.1% (17 of 828 isolates) in Alabama (17) to 16.6% (6 of 36 isolates) in Oklahoma (16). Higher frequencies have been reported elsewhere. The Children's Hospital in Barcelona, Spain, reported decreased penicillin susceptibility in 51% of *S. pneumoniae* isolates; 31 of 100 were relatively resistant, and 20 of 100 were frankly resistant (9). In South Africa, *S. pneumoniae* isolates resistant to multiple antibiotics have been reported (7). The purpose of the present study was to determine the prevalence of penicillin-resistant and relatively resistant *S. pneumoniae* causing infection at the Texas Children's Hospital in Houston, Tex., during a 4.5-year period (1984 to 1988) and to describe the clinical conditions associated with these organisms.

All clinical isolates of *S. pneumoniae* identified between January 1984 and July 1988 which exhibited a ZI of <20 mm around a 1-μg oxacillin disk were studied. The oxacillin screening procedure employed has been described previously (15). An inoculum corresponding to the turbidity of a 0.5 McFarland standard was streaked onto a Mueller-Hinton agar plate containing 5% sheep blood, and a 1-μg oxacillin disk was applied to the plate. ZIs were measured following overnight incubation at 35°C. Organisms with ZIs of >20 mm were reported as susceptible to penicillin; ZIs of <20 mm were presumed to indicate decreased penicillin susceptibility.

Oxacillin disk diffusion results were confirmed by determination of the MIC by using a broth macrodilution procedure recommended by the National Committee for Clinical Laboratory Standards (11). As outlined by this procedure, organisms were grown overnight in Trypticase soy broth at 35°C. The inoculum was adjusted with Mueller-Hinton broth to a final concentration of approximately 10^5 CFU/ml. Penicillin G concentrations ranged from 128 to 0.004 μg/ml. The tubes were incubated at 35°C for 18 to 20 h. The MIC was defined as the lowest concentration of antibiotic in which no turbidity was seen. The MBC was the lowest concentration of penicillin G in which 99.9% of the organisms were killed, as determined following plating to antibiotic-free TSA II sheep blood agar (BBL Microbiology Systems) and overnight incubation. The organism was adjudged susceptible (MIC, ≤0.06 μg/ml), relatively resistant (MIC, 0.1 but ≤1 μg/ml), or resistant (MIC, >1 μg/ml) (15).

During the 4.5-year study period, 14 of 493 isolates of *S. pneumoniae* were determined by the screening test to have increased resistance to penicillin (Table 1). When the penicillin susceptibilities of these 14 strains were measured by broth dilution, 9 isolates had MICs of <0.06 μg/ml, 4 (2 of serotype 19 and 2 of unknown serotypes) had MICs of ≥0.1 but ≤1 μg/ml, and 1 recent isolate (serotype 6) produced no ZI around the oxacillin disk and was resistant to penicillin (MIC, 2 μg/ml; MBC, 4 μg/ml). These findings were confirmed by the Centers for Disease Control. MIC determinations for multiple antibiotics showed that this recent isolate was also relatively resistant to cephalothin and cefaclor.

Penicillin-resistant *S. pneumoniae* was isolated from the middle ear of an 11-month-old girl who had been treated for 5 months with various antibiotics (ampicillin, trimethoprim-sulfamethoxazole, erythromycin-sulfisoxazole, cefaclor, and amoxicillin-clavulanate) for chronic otitis media. Pressure equalization tubes were placed when the child was 11 months old, and the exudate obtained at surgery was cultured. Penicillin-resistant *S. pneumoniae* was isolated in pure culture from this specimen. The otitis media resolved postoperatively in response to cefaclor.

The four relatively resistant strains in this study were isolated from the blood (n = 2), cerebrospinal fluid (n = 1), and pleural fluid (n = 1) of children less than 2 years of age. Three of the four patients had received beta-lactam antibiotic therapy at least 3 weeks prior to admission. All infections apparently were community acquired. In the hospital, the patients were treated with a broad-spectrum cephalosporin (cefuroxime or cefotaxime) and penicillin or ampicillin. Three of the patients responded rapidly to therapy. The fourth had a prolonged hospital course due to pneumonia complicated by an empyema.

Because of the emergence of penicillin-resistant *S. pneumoniae*, the National Committee for Clinical Laboratory Standards now recommends screening for resistance with a 1-μg oxacillin disk, since this disk has greater sensitivity than the 10-U penicillin disk or the 5-μg methicillin disk (10). The ZI obtained with the 1-μg oxacillin disk is not reliable in differentiating between a relatively resistant and a resistant

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TABLE 1. Penicillin susceptibility of *S. pneumoniae* determined to be penicillin resistant by screening test

Yr	Age	Sex[a]	Diagnosis	Site of origin[b]	MIC (μg/ml)	MBC (μg/ml)	Penicillin susceptibility[c]
1984	11 mo	M	Meningitis	CSF	<0.006	<0.006	S
1984	21 mo	F	Pneumonia	Pleural fluid, blood	<0.006	<0.006	S
1984	9 mo	M	Ethmoiditis	Nasal fluid		<0.006	S
1985	15 yr	F	Meningitis	CSF	<0.006	<0.006	S
1985	11 mo	F	Meningitis	CSF	<0.006	<0.125	S
1987	12 mo	M	Meningitis	CSF, blood	<0.004	<0.004	S
1987	9 mo	F	Meningitis	CSF, blood	0.004	0.125	S
1988	2 mo	M	Sepsis	Blood	0.06	0.06	S
1988	12 mo	F	Otitis media	Middle ear	0.03	0.06	S
1985	21 mo	M	Pneumonia	Pleural fluid	0.25	0.25	I
1986	22 mo	M	Bacteremia	Blood	0.125	0.50	I
1987	24 mo	M	Bacteremia	Blood	0.25	0.50	I
1988	2 mo	F	Meningitis	CSF	0.25	0.25	I
1988	11 mo	F	Otitis media	Middle ear	2.0	4.0	R

[a] M, Male; F, female.
[b] CSF, Cerebrospinal fluid.
[c] S, Susceptible; I, relatively resistant; R, resistant.

isolate (15), and there are some false-positives. Therefore, quantitative susceptibility studies should be performed on strains showing decreased penicillin susceptibility by the screening test. *S. pneumoniae* showing true decreased susceptibility should also be tested for multiple-antibiotic resistance.

To provide adequate antibiotic coverage until penicillin susceptibility can be determined by MICs, we recommend treating bacteremic patients empirically with a broad-spectrum cephalosporin. Bosley et al. have shown that MICs of these antibiotics demonstrate sufficiently high activity to provide effective therapy for strains relatively resistant to penicillin even in cases of meningitis (2).

The penicillin-resistant *S. pneumoniae* discussed in this report caused the first confirmed infection with such an organism in the Houston area. However, the prevalence of *S. pneumoniae* with decreased susceptibility to penicillin at our hospital was only 1% (5 of 493 isolates), a rate lower than that previously reported by pediatric hospitals (1, 6, 16, 17) or than the national average of 3.7% (4). It is also lower than that previously reported in the Houston area (8). The explanation for this difference is not clear but may be related to different patient populations. However, identification of penicillin-resistant *S. pneumoniae* suggests that the incidence of pneumococci with decreased penicillin susceptibility may be increasing in the Houston area.

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