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Pneumococcal Resistance in Southwest Virginia

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Resistance patterns of *Streptococcus pneumoniae* in southwest Virginia were determined for 100 consecutive, hospital-based isolates, mostly from adults. Oxacillin disk screening identified all resistant isolates. Sixteen percent of the isolates were penicillin resistant (10% were highly resistant). E-strip testing revealed the following MICs (in micrograms per milliliter, with percentages of isolates in parentheses): cefotaxime, ≤0.5 (92%); ceftriaxone, ≤0.5 (95%); ceftizoxime, ≤0.5 (85%); erythromycin, ≤1 (87%); ofloxacin, ≤2 (80%); vancomycin, ≤1 (98%).

The relatively rapid rise in the isolation of pneumococci designated relatively resistant or highly resistant to penicillin throughout the United States and the rest of the world is well documented in the recent medical literature (1–3, 5–7, 9, 10). However, the number of reports of isolates from adults in community hospitals and clinic settings is relatively small. In addition, the resistance of these strains of pneumococcus to other antibiotics has varied between studies, leading to the recent recommendations that each community establish its own surveillance system to determine the local epidemiology of this emerging problem.

(Results were presented at the 1994 Infectious Diseases Society of America Annual Meeting, Orlando, Fla., 1994.)

A 32-year-old female was admitted to a local hospital after suffering a severe motor vehicle accident. On day 5 she developed pneumonia, with sputum examination revealing gram-positive diplococci. She was treated with penicillin G, 10^6 U every 4 h, but did not defervesce, and on day 3 pneumococcus was still growing from her sputum. The MIC for the isolate was found by E-strip testing to be 1.5 μg/ml; treatment was changed to cefotaxime, 1 g intravenously every 8 h, and she recovered without complication. Spurred on by this event, and two other clinical failures, we undertook a study of 100 consecutive pneumococcal isolates from four clinical microbiology laboratories in southwest Virginia.

All isolates from any body site obtained between April 1994 and July 1994 identified as *Streptococcus pneumoniae* were sent to one central laboratory for further study. The clinical microbiology laboratories serve three large community hospitals (>300 beds) and one Veterans Affairs Hospital. All but a few of the isolates (<5%) were from adult, hospitalized patients. Strains were identified as pneumococci by colony morphology and optochin disk testing. All strains were screened for potential penicillin resistance by oxacillin disk zone size (and were judged susceptible if the zone was >20 mm). The strains were frozen on plastic beads in Trypticase soy agar with 10% glycerol (Key Scientific Products, Pound Rock, Tex.) and later thawed in Mueller-Hinton broth, grown to a 0.5 McFarland standard, and streaked onto a Mueller-Hinton plate supplemented with 5% sheep blood, onto which E strips (AB Biodisk, Piscastaway, N.J.) were placed. This methodology has been shown to be similar to Mueller-Hinton dilution MICs (4, 8). E-strip MICs were read 18 to 24 h later according to the manufacturer's recommendation.

Of the 100 strains of pneumococcus, 32 were shown to be possibly resistant by oxacillin disk testing. No strain for which the MIC was ≥0.1 μg/ml was missed by the oxacillin disk (100% sensitivity), although 16 were shown to be susceptible to penicillin (50% specificity). When 9 mm was used as the cutoff for defining resistance, the specificity increased to 100% with no loss in sensitivity. Of the 16 strains with zone sizes from 10 to 15 mm, MICs were found to be ≥0.06 μg/ml for 4 strains, and the MICs for the remaining 12 strains were 0.016 to 0.032 μg/ml.

Of the 100 strains, the MICs of penicillin for 16% of the strains were ≥0.125. (Table 1). Only one strain was highly resistant if the ≥2-μg/ml cutoff was used. However, the MICs for nine isolates were 1.5 μg/ml, a finding which means that, if the cutoff is placed at >1 μg/ml, 10% of the strains were highly resistant. The MICs for a further four strains (all judged penicillin resistant by the oxacillin disk test) were either 0.064 μg/ml or 0.094 μg/ml. This would lead to 20% total resistance

TABLE 1. Relative susceptibilities of the 16 penicillin-resistant strains to the antibiotics utilized in this study

Penicillin MIC	MIC (μg/ml)					
	Vancomycin	Erythromycin	Ofloxacin	Ceftriaxone	Ceftizoxime	Cefotaxime
0.125[a]	0.75	0.19	1.5	0.125	0.38	0.125
0.25	0.5	0.094	1	0.125	1.5	0.25
0.5	0.75	0.25	0.5	0.125	0.25	0.38
0.5	0.75	0.25	3	0.38	4	0.5
1	0.75	4	1.5	0.38	1	0.38
1	0.75	24	1.5	0.25	1	0.38
1.5	0.5	6	0.75	0.38	3	0.75
1.5	0.75	4	2	0.38	8	1
1.5	0.75	6	3	0.75	12	1
1.5	0.75	12	1	0.25	0.75	0.38
1.5	0.75	3	2	0.75	12	1.5
1.5	0.75	0.25	2	0.5	8	0.75
1.5	0.75	12	1.5	0.25	1	0.38
1.5	0.75	3	2	1	12	1
1.5	0.75	6	2	1.5	16	1.5
4	0.75	3	1	1	64	2

[a] Oxacillin disk zone, 9 mm. All other strains were 0 mm by oxacillin disk testing.

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TABLE 2. Overall susceptibilities of the 100 strains

Drug	% Strains for which the MIC (μg/ml) was:								
	≤0.03	0.06	0.12	0.25	0.5	1	2	4	8
Penicillin	73	80	84	86	88	90	99	100	
Cefotaxime	66	74	83	86	92	97	100		
Ceftizoxime[a]	2	26	67	81	85	90	91	93	95
Erythromycin[a]	1	2	15	85	87	87	88	94	97
Ceftriaxone	74	78	84	90	95	99	100		
Vancomycin				0	14	98	99	100	
Ofloxacin				0	1	15	80	97	100

[a] 99 and 100% of the strains were susceptible at 16 and 32 μg/ml, respectively.

if the susceptibility criterion is set at the standard of an MIC of ≤0.06 μg/ml.

Eleven of these 16 strains were resistant to erythromycin (MIC ≥ 1 μg/ml). Of note, although cefotaxime and ceftriaxone susceptibilities followed closely those of penicillin, the ceftizoxime MICs tended to be 4- to 32-fold higher. Most strains were susceptible to vancomycin (MIC for 98% of the strains, ≤1 μg/ml), and the majority were at or near the ofloxacin breakpoint (MIC for 97% of the strains, ≤4 μg/ml), whether penicillin resistant or not (Table 2).

It should be realized that the E-strip system often reads 1 tube dilution below standard diffusion techniques and would thus have a tendency to underrepresent resistant strains (4, 7, 8). The problem with interpretation of MICs between those determined by standard twofold dilutions may lead to a need to define new susceptibility standards for E strips. Although the 16% resistance seen in this study is similar to those in other recent surveys in the United States, the 10% high-level resistance is greater than that of most areas in which E strips were not used to determine susceptibilities (2).

These data have led to a change in the recommendation for the treatment of pneumococcal disease, including pneumonia, in our area. With the additional high level of resistance to trimethoprim-sulfamethoxazole (1, 3, 7), the number of potentially adequate outpatient regimens for the treatment of penicillin-resistant pneumococcus appears quite limited. The extent of pneumococcal resistance which has emerged in the adult population in southwest Virginia is alarming. The rates are likely to be much higher in the pediatric and day care communities, as has been shown in other studies. However, the situation is clearly in a state of constant flux and will require ongoing surveillance and reevaluation.

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