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Drug-resistant *Streptococcus pneumoniae* . . . 5

Drug-Resistant *Streptococcus pneumoniae*

As part of the Connecticut Emerging Infections Program (EIP), the Connecticut Department of Public Health (DPH) is conducting active, population-based laboratory surveillance for invasive *Streptococcus pneumoniae* infections. The purpose of this surveillance system is to provide an assessment of geographic and temporal trends in drug-resistant *S. pneumoniae* (DRSP) (1).

All isolates of pneumococci from normally sterile sites are reported to the Epidemiology Program by 34 acute-care hospital microbiology laboratories. Additional antimicrobial susceptibility testing is performed at a Centers for Disease Control and Prevention (CDC) reference laboratory using the National Committee for Clinical Laboratory Standards (NCCLS) approved broth microdilution methods (2). The NCCLS minimum inhibitory concentration (MIC) breakpoints are used to define isolates as susceptible or non-susceptible for each antimicrobial tested (see insert). The MIC data are linked to patient medical information collected by EIP staff.

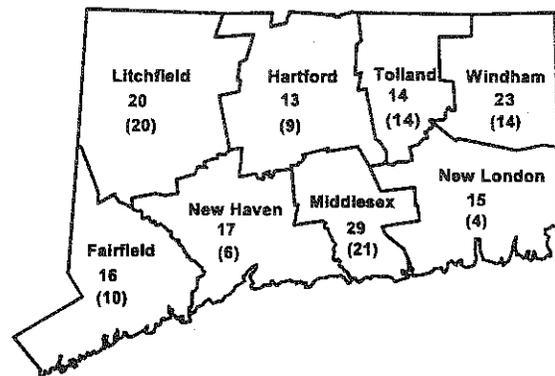
NCCLS MIC Interpretative Standards for *Streptococcus pneumoniae*

Penicillin	MIC(μ g/ml)
Susceptible	≤ 0.06
Non-Susceptible	≥ 0.1
Intermediate	≥ 0.1 & ≤ 1.0
(Highly) Resistant	≥ 2.0

The following summarizes results from the first 12 months of active surveillance, March 1, 1995 through February 29, 1996. A total of 801 cases of invasive pneumococcal disease were identified. Penicillin MICs were determined on 733 isolates from 705 (88%) cases: 119 (16%) were penicillin non-susceptible and 67 (9%) were penicillin (highly) resistant. Of the 733 isolates, 676 (92%) were obtained from blood, 30 (4%) were from cerebrospinal fluid, 12 (2%) from pleural fluid, and 15 (2%) from other sterile sites. There were no significant differences in the percentage of penicillin non-susceptibility by source of isolate.

Penicillin non-susceptible *S. pneumoniae* cases were reported from all counties in Connecticut, ranging from 13% in Hartford County to 29% in Middlesex County. The percentage of penicillin (highly) resistant *S. pneumoniae* ranged from 6% in New Haven County to 21% in Middlesex County (Figure 1).

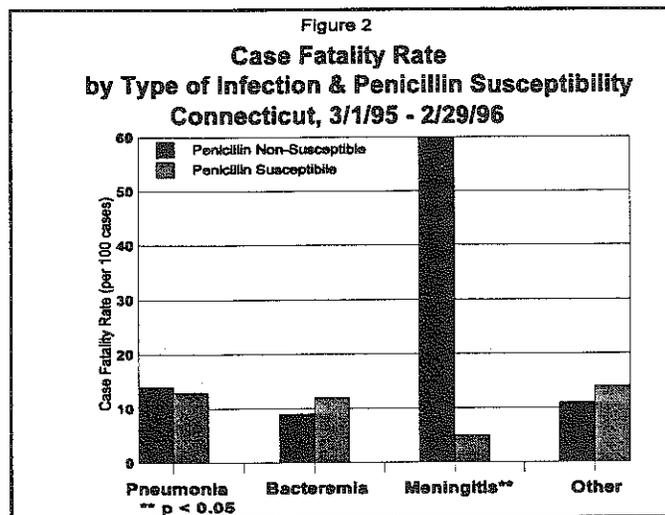
Figure 1
Percentage of Penicillin Non-Susceptible and
(Highly Resistant) *Streptococcus pneumoniae*
by County, Connecticut, 3/1/95 - 2/29/96



The rate of invasive pneumococcal disease was highest among those aged 0-4 years, those 65

years and older, and among blacks (Table 1). Although the rate of invasive pneumococcal disease was lowest among whites, levels of penicillin non-susceptible and penicillin (highly) resistant *S. pneumoniae* were much higher in whites than other groups. No cases of penicillin non-susceptible or penicillin (highly) resistant *S. pneumoniae* were reported among Hispanics.

The 705 patients with known MICs were further characterized clinically. Overall, 467 (66%) had pneumonia, 151 (21%) had bacteremia without focus, 47 (7%) had meningitis, and 63 (9%) had other types of infection. Case fatality rates were significantly higher among penicillin non-susceptible cases with meningitis than in cases with other types of infection (Figure 2).



The percentage of penicillin susceptible *S. pneumoniae* isolates that were resistant to other antimicrobials was low. However, at least 50% of penicillin non-susceptible *S. pneumoniae* isolates were resistant to one or more other antimicrobials and ranged from <1% (rifampin) to 70% (trimethoprim-sulfamethoxazole). The percentage of penicillin (highly) resistant isolates resistant to other antimicrobials ranged from 2% (rifampin) to 97% (trimethoprim-sulfamethoxazole) (Table 2).

Editorial Note

Streptococcus pneumoniae is a leading cause of morbidity and mortality in the United States, resulting each year in an estimated 3000 cases of meningitis, 50 000 cases of bacteremia, 500 000 cases of pneumonia, and 7 million cases of otitis

media (3-5). Case-fatality rates vary by age and underlying illnesses of patients: 40% of elderly persons with pneumococcal bacteremia, 6% of meningitis cases among children, and 30% of adult meningitis cases are fatal despite appropriate antimicrobial therapy (6). The emergence of DRSP further complicates management and treatment of these common infections.

In the United States, high-level resistance to penicillin has increased substantially in the last decade (3). In 1992, a Connecticut laboratory survey for resistant *S. pneumoniae* identified five (1.25%) of 400 sterile isolates that were penicillin non-susceptible and 1 (0.25%) that was penicillin (highly) resistant (7). Current surveillance has found a 12 fold increase in penicillin non-susceptible *S. pneumoniae*, and a 36 fold increase in penicillin (highly) resistant *S. pneumoniae*. The emergence of DRSP in Connecticut presents a challenge to both the medical and public health communities.

Data from the Connecticut EIP show that penicillin non-susceptible *S. pneumoniae* is widespread in the state and occurs more frequently in very young children and older adults. In addition, although the rate of pneumococcal disease was higher in blacks, the rate of penicillin non-susceptible *S. pneumoniae* disease was highest in whites. This result is consistent with at least one other recent study (8) and may reflect recently identified risk factors for DRSP. These risk factors include prior antibiotic exposure, extremes in age, and daycare attendance especially in children under 2 years of age (9). The reason for the significantly higher case fatality rates in penicillin non-susceptible *S. pneumoniae* cases with meningitis has not yet been determined. Of additional concern is the high degree of resistance to other commonly used antimicrobials among penicillin non-susceptible *S. pneumoniae* cases.

Controlling the increase of resistant pneumococci will require more judicious use of antimicrobial agents and wider use of the existing pneumococcal vaccine. Although appropriate antimicrobial-drug use has unquestioned benefit, often these agents are used inappropriately by physicians and patients, creating additional selective pressure from antibiotic resistance (10). The vaccine for the 23 most common serotypes of *S. pneumoniae* has been available since the early 1980s (11), but remains underutilized (12).

States that conduct surveillance for invasive *S. pneumoniae* infections include those participating in CDC's Emerging Infections Program (California, Connecticut, Georgia, Maryland, Minnesota, New York and Oregon). Health-care providers can use information generated by this surveillance system to select appropriate antimicrobial agents when initiating empiric treatment for persons with presumptive pneumococcal infections. Public health officials can use such information to develop interventions for their communities (1).

For more information about surveillance for invasive *S. pneumoniae* infections, contact Nancy L. Barrett or Craig Morin at the DPH, Epidemiology Program, (860)-509-7994.

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Table 1
**Incidence of Invasive Pneumococcal Disease and
 Percentage of Isolates Resistant to Penicillin by Age and by Race
 Connecticut, 3/1/95 - 2/29/96**

Characteristic	Total (n=705)	Rate* of Disease	% of Isolates	
			Penicillin Non-Susceptible	Penicillin (Highly) Resistant
<i>Age, years</i>				
0 - 4	126	55**	16%	12%
5 - 64	308	12	16%	8%
65+	271	61**	16%	8%
<i>Race/Ethnicity</i>				
White	454	17**	19%**	12%**
Black	154	59**	15%	6%
Hispanic	51	24	0%**	0%**
Other/Unk.	46	81	13%	7%

* Group specific rate per 100,000 population (1990 census).

** p < 0.05

Table 2

**Percentage of Penicillin Susceptible, Non-susceptible, and (Highly) Resistant
Pneumococcal Isolates Resistant to Selected Antimicrobials
Connecticut, 3/1/95 - 2/29/96**

Antimicrobial	Penicillin Susceptible	Penicillin Non-susceptible	Penicillin (Highly) Resistant
Amoxicillin	0	52*	92*
Cefotaxime	<1	55*	94*
Chloramphenicol	<1	13*	20*
Clindamycin	<1	6*	8*
Erythromycin	2	18*	19*
Ofloxacin	<1	2	3
Rifampin	<1	<1	2
Tetracycline	2	17*	22*
TMP-S	8	70*	97*
Vancomycin	0	0	0

*p < 0.05

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