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Penicillin-Resistant *Streptococcus pneumoniae* in Virginia

Background

Although *Streptococcus pneumoniae* was once considered to be universally susceptible to penicillin and other antibiotics, the incidence of penicillin-resistance as well as multi-drug resistant strains has increased to the point of being of public health concern. Penicillin-resistant (PEN-resistant) strains of *S. pneumoniae* have been identified with increasing frequency since the first clinical isolate in 1965.[1] Initial reports identified intermediate or high-level resistance in isolates from South Africa, Australia, Spain, Eastern Europe and limited regions of the United States.[2] In the majority of the United States, isolation of PEN-resistant strains was considered uncommon prior to 1988 but recent reports from Texas[3], New York[4], Missouri[5], Kentucky and Tennessee[6,7] indicate that identification of PEN-resistant pneumococci, particularly in children, is becoming more universal. The Centers for Disease Control and Prevention (CDC) reported that "during 1979-1987, only one (0.02%) of 4585 pneumococcal sterile-site isolates submitted to CDC's sentinel hospital surveillance system was highly resistant to penicillin; in comparison, during 1992, seven (1.3%) of 544 such isolates were highly resistant."[6]

In addition to the increase in PEN-resistance, multi-drug resistant strains of *S. pneumoniae* (DRSP) are being identified with unexpected frequency. One Tennessee children's hospital determined that a high rate of cephalosporin-resistance accompanied PEN-resistance in pneumococci isolated from normally sterile sites, such as blood and cerebrospinal fluid (CSF).[7] The results of this study led the authors to recommend an alternative treatment strategy for all children admitted to the hospital with suspected pneumococcal infections.

A recent article in the CDC publication "Morbidity and Mortality Weekly Report" (MMWR) described investigations in Kentucky and Tennessee into the increasing incidence of DRSP associated with otitis media in children.[6] In one Kentucky community, pediatricians reported that 28% of all pneumococcal isolates from middle ear fluid were found to be PEN-resistant. In a subsequent study, nasopharyngeal (NP) cultures were performed on children attending a large day care center and children attending a non-acute county public health clinic. PEN-resistance was found in 61% of the pneumococcal isolates from children attending the day care center and 33% of those from children using the public health clinic. In addition, 43% of all the PEN-resistant strains were found to be resistant to erythromycin (ERY) and trimethoprim-sulfamethoxazole (TMP/SMZ) and 27% were resistant to cefotaxime. In the Tennessee study, the authors examined NP cultures from children with otitis media over a five month period. They found that 29% (32/110) of all pneumococci isolated were resistant to pencillin, with 25% of these also resistant to cefotaxime, ERY and TMP/SMZ.

The noted increase in incidence of DRSP since 1992 has led CDC to list it as an important example of emerging infectious diseases and to recommend four approaches to help deal with this problem.[6]

- First, CDC is working with the Association of State and Territorial Public Health Laboratory Directors and the Council of State and Territorial Epidemiologists to develop strategies for better, more comprehensive, surveillance for DRSP, including the screening of invasive pneumococcal isolates for resistance to penicillin and other drugs.
- Second, CDC suggests modification of the recommended treatment for cases of meningitis potentially caused by pneumococci in areas determined to have high rates of pneumococcal resistance to extended spectrum cephalosporins.
- Third, they recommend and promote strategies for "rational antimicrobial use." For example, they suggest that the emergence of DRSP associated with otitis media indicates a need to re-examine the effectiveness of prophylactic antimicrobial regimens for children with recurrent ear infections.
- Fourth, the Advisory Committee on Immunization Practices recommends that any person two years of age or younger who is at increased risk for serious pneumococcal infection and all persons 65 years of age and older should receive the 23-valent pneumococcal capsular polysaccharide vaccine.[8]

A second MMWR article, published in April 1994, describes a study done in Connecticut by the Department of Public Health and Addiction Services.[9] This study was designed to identify how many laboratories in that state were routinely determining antimicrobial susceptibility patterns in pneumococcal isolates and to determine the incidence of DRSP in Connecticut. The study was done in cooperation with CDC and emphasized the importance of characterizing local DRSP activity so that appropriate recommendations could be made for the treatment of possible pneumococcal infections.

In This Issue:

What's Happening in Virginia

Pneumococcal infections are not a reportable disease in Virginia unless they are the cause of a bacterial meningitis, so no up to date information is available as to how many PEN-resistant *S. pneumoniae* or DRSP isolates, if any, are being identified in the state. In order to gather that data, a questionnaire, similar to the one used in Connecticut, was designed and mailed to hospital microbiology laboratories, commercial laboratories and health department laboratories that offer services in Virginia. These laboratories were requested to supply information about procedures and any *S. pneumoniae* identified between June 1, 1993 - May 31, 1994, and found to be resistant to penicillin or the extended-spectrum cephalosporins.

Results of the Study

Sixty-five of 112 laboratories (58%) returned the questionnaire. A total of 53 laboratories of the 65 responding (81.5%) reported that they perform some sort of screening or susceptibility testing for antibiotic resistance of *S. pneumoniae* isolates. Of the 12 laboratories that do not do so, three refer isolates to a reference laboratory for further testing, eight send all of their bacteriology work to reference facilities, and one laboratory offers no testing of any *S. pneumoniae* organisms. Ten of the respondents indicated that their procedures had been changed within the last two months or would change this fall, to include more testing of isolates.

Nine of the 53 (17%) laboratories that provide some form of susceptibility testing indicated that they only perform qualitative screening of pneumococcal isolates with a 1-ug oxacillin disk and report out penicillin-resistance based on the size of the zone of no growth surrounding the oxacillin disk, using National Committee for Clinical Laboratory Standards (NCCLS) recommendations.[10] The other 44 (83%) perform more complete antibiotic testing including additional antibiotics in their test. The various methods employed by these laboratories included the E-test, used by three labs for penicillin testing with the Kirby-Bauer disk diffusion for other antibiotics, the Kirby-Bauer test exclusively (18 laboratories), and quantitative minimum inhibitory concentration (MIC) procedures used by 22 labs. The MIC methods included commercially available MicroScan or Micro Media systems as well as the NCCLS tube dilution method.

Different laboratories used different criteria to determine whether or not to screen or test isolates for penicillin resistance. Seven of the nine laboratories that limit their testing to screening with the oxacillin disk, indicated that they screen all pneumococcal isolates, while the other two labs screen isolates from normally sterile sites only. Forty-one percent of the laboratories that perform quantitative testing and determine susceptibility patterns against a panel of antibiotics (44) reported testing all pneumococcal isolates, 38.6% examine isolates from sterile sites only, 6.8% test isolates found resistant during a screening procedure and 13.6% perform complete antibiotic testing on both isolates found to be resistant by screening and those from normally sterile sites. The additional antibiotics most commonly included were vancomycin (41/44 labs), erythromycin (39/44), tetracycline (34/44), clindamycin (31/44) and TMP/SMZ (27/44).

The respondents were asked if they had identified any penicillin-resistant pneumo cocci over the specified time period. The number of positive responses was surprising. Of the 51 laboratories that had the information available, 26 reported identifying one or more penicillin-resistant strains of *S. pneumoniae*. The number of isolates varied from one to 45 for the year's time with a mean number of seven isolates per year. The degree of resistance, whether intermediate or high-level, can be determined only if quantitative MIC procedures are used. Data concerning this issue were incomplete, but intermediate level penicillin resistance appeared to be more prevalent than high-level resistance. It was interesting to learn that hospitals in localities all across the state are looking for PEN-resistant pneumococci and detection is widespread. (Figure 1)

The most commonly reported sites for PEN-resistant pneumococcal isolates were blood (38 isolates), sputum / NP (31 isolates), middle ear (7 isolates) and other respiratory sites (6 isolates). The percentage of blood isolates that were found to be resistant ranged from 2.6% to 50% with a mean of 17.2%. The percentage of identified sputum/NP cultures that were found to be resistant ranged from 2% to 40% with a mean of 17%.

The respondents were asked if they had seen any isolates that were also resistant to extended-spectrum cephalosporin antibiotics. Five of 38 laboratories that answered that question indicated that they had seen multi-drug resistant pneumococci. Again, the most common sites for these isolates were blood, sputum and other respiratory sites; two laboratories reported DRSP from the eye. These five laboratories were in hospitals located in localities as diverse as Wythe, Patrick, Smyth, Henrico counties and Hampton city.

Conclusion

The results of this study indicate that PEN-resistant and multi-drug resistant strains of *S. pneumoniae* are present in all regions of Virginia. An indication of the significance being attached to these organisms is the fact that so many facilities have already begun to examine susceptibility patterns of pneumococcal isolates. The high percentage of sterile-site and respiratory culture isolates found to be PEN-resistant, as well as the reported incidence of multi-drug resistant isolates, emphasizes the need for careful assessment as to the

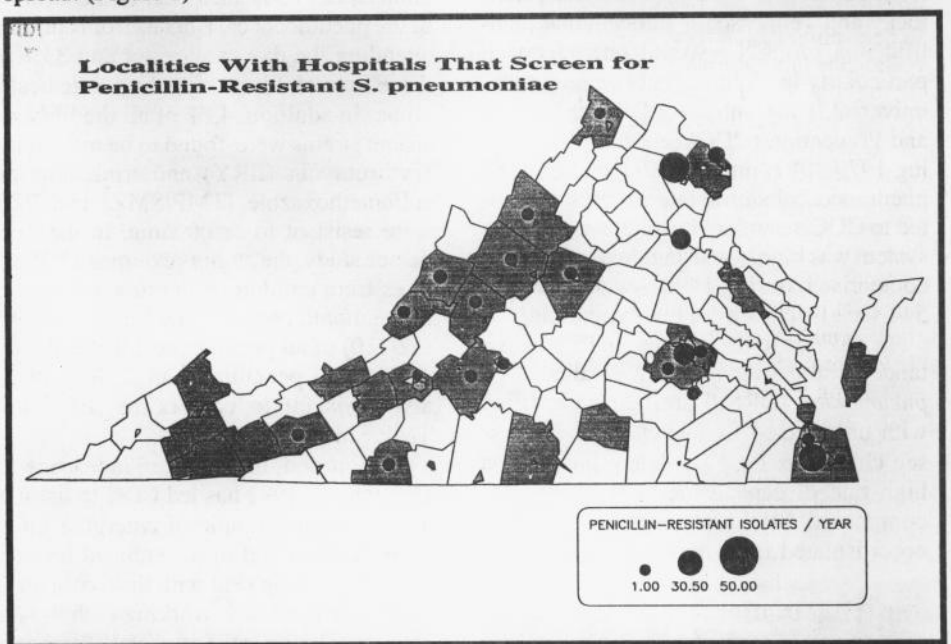

Figure 1. Localities with Hospitals that Screen/Test for Penicillin-Resistant *S. pneumoniae*. The shaded areas represent counties and cities with hospitals that examine pneumococcal isolates for penicillin resistance. The symbols located within some of the localities indicate where penicillin-resistant isolates have been found.

best initial treatment for individuals with suspected pneumococcal infections.

The Virginia Department of Health, Office of Epidemiology is closely following the progress made by CDC in developing effective ways to deal with this emerging infectious agent. Any new recommendations will be included in future issues of the Virginia Epidemiology Bulletin as they become available.

References:

1. Kislak JW, Razaui LMB, Daly AK, Finland M. Susceptibility of pneumococci to nine antibiotics. Am J Med Sci, 1965;250:261-8.

2. Appelbaum PC. Antimicrobial resistance in *Streptococcus pneumoniae*: An overview. Clinical Infectious Diseases, 1992;15:77-83.

3. Nelson CT, Mason EO, Kaplan SL. Activity of oral antibiotics in middle ear and sinus infections caused by penicillin-resistant *Streptococcus pneumoniae*: implications for treatment. Pediatr Infect Dis J, 1994;13:585-9.

4. Faden H, Doern G, Wolf J, Blocker M. Antimicrobial susceptibility of nasopharyngeal isolates of potential pathogens recovered from infants before antibiotic therapy: implications for the management of otitis media. Pediatr Infect Dis J, 1994;13:609-12.

5. Welby PL, Keller DS, Cromien JL, Tebas P, Storch GA. Resistance to penicillin and non-beta-lactam antibiotics of *Streptococcus pneumoniae* at a children's hospital. Pediatr Infect Dis J, 1994; 13:281-7.

6. CDC. Drug-resistant *Streptococcus pneumoniae*--Kentucky and Tennessee, 1993. MMWR, 1994;43:23-5,31.

7. Leggiadro RJ. Penicillin- and cephalosporin-resistant *Streptococcus pneumoniae*: An emerging microbial threat. Pediatrics, 1994;93:500-3.

8. ACIP. Update on adult immunization: recommendations of the Immunization Practices Advisory Committee (ACIP). MMWR 1991; 40(no. RR-12):42-4.

9. CDC. Prevalence of penicillin-resistant *Streptococcus pneumoniae*--Connecticut, 1992-1993. MMWR 1994;43:216-18,223.

10. National Committee for Clinical Laboratory Standards. Performance standards for antimicrobial disk susceptibility tests. 4th ed. Villanova, Pa: National Committee for Clinical Laboratory Standards; 1990. M2-A4.

What Do "Routine" Stool Cultures Look For?

As reported in the June 1994 Virginia Epidemiology Bulletin, *E. coli O157:H7* has emerged as an important pathogen since it was first associated with hemorrhagic colitis in 1982. A number of confirmed cases of *E. coli O157:H7* that occurred sporadically or in relation to outbreaks were investigated by the Virginia Department of Health (VDH) this past summer. It is probable that there were many more cases in Virginia that were never identified because of specific microbiological stool culturing requirements.

Because of the multitude of organisms normally present in the stool, stool culture techniques utilize special media to screen for specific pathogenic species. Different laboratories include different types of media and therefore screen for different organisms. In order to determine which fecal pathogens laboratories throughout Virginia screen for, a telephone survey was conducted.

A total of 106 hospital laboratories, representing all licensed general hospitals and nine specialty hospitals, as well as five commercial laboratories were contacted. Seven of the hospital laboratories reported that they do not offer stool cultures. Of the remaining 99 hospital labs, 78 (78.8%) perform stool cultures in-house and 21 (21.2%) send specimens to a reference facility for culture. All commercial labs offer stool culturing.

How each laboratory defined "routine testing" for fecal bacterial pathogens was evaluated. It was determined that stool samples submitted for "routine culture" to the 78 hospital-based labs that do stool cultures in-house or the five commercial labs were always examined for the presence of *Salmonella* and *Shigella* (83/83 = 100%). Only 73 of 83 labs (88%), including all five commercial labs, routinely cultured specimens for *Campylobacter sp.*. Hospital lab supervisors were also asked about the less frequently seen pathogens, *Yersinia* and *Vibrio sp.*. Twenty-nine percent of the labs indicated screening for *Yersinia* in a routine culture, 18% routinely looked for *Vibrio*. The remaining labs indicated that a request or certain additional requirements were needed to look for those agents.

Microbiology supervisors were also asked about their laboratory's policy regarding *E. coli O157:H7*. Of the 78 hospital laboratories that culture in-house, 14 (17.9%) screen all stools for *E. coli O157:H7* as part of their "routine" procedure; 14 (17.9%) screen if requested, if the stool is grossly bloody, or if patients are of certain ages; and 50 (64.1%) reported screening for *E. coli O157:H7* only when it is requested by the clinician.

The policy for *E. coli O157:H7* screening could be determined for 16 of the additional 21 facilities that send stool specimens to other hospital or reference labs. Two utilized labs that screen for the organism routinely, two more screened if the stool was grossly bloody or from a pediatric patient, and 12 reported screening only if specifically requested.

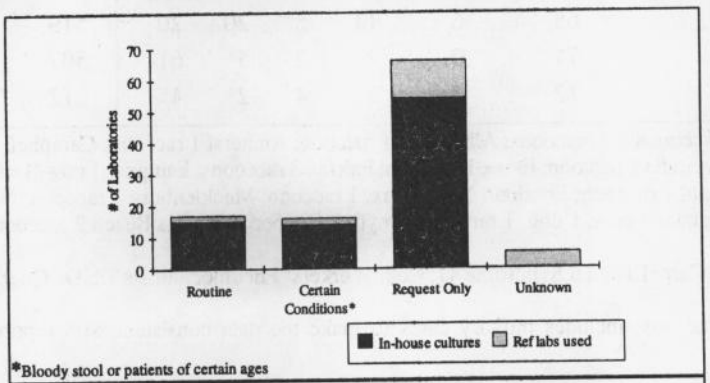

Figure 1. Laboratory Policies for Culturing *E. coli O157:H7*

Four of five commercial labs indicated they require a specific request to look for *E. coli O157:H7*. This is significant because these laboratories are often utilized by individual medical practices and identification of an infection with *E. coli O157:H7* should be possible in an outpatient setting. Cumulative data are shown in Figure 1.

Although this *E. coli* organism can be easily identified by screening with specific culture media, it was clear that many labs either do not yet have this capability or have just recently initiated the procedure. All but one laboratory capable of in-house screening reported that this was a recent change, instituted within the last 1.5 years or less. It should also be noted that several laboratories in this survey reported upcoming changes regarding screening for *E. coli O157:H7*. As more information is disseminated concerning the importance of this organism and the relative ease of identifying it, the percentage of labs routinely looking for it will hopefully increase.

The results of this survey emphasize the fact that there are differences in how each microbiology lab defines "routine stool culture." The VDH, Office of Epidemiology recommends that all clinicians check with the laboratory they utilize for current "routine" or "by request" policies when they next consider stool culture for bacterial pathogens.

The Office of Epidemiology would like to thank Barbara J. Frost, M.D., for conducting this survey and for providing this report of the results.

Cases of Selected Notifiable Diseases, Virginia, August 1 through August 31, 1994.*

Disease	Total Cases Reported This Month						Total Cases Reported to Date in Virginia		
		Regions							
	State	NW	N	SW	C	E	This Yr	Last Yr	5 Yr Avg
AIDS	40	4	7	9	10	10	733	1237	571
Campylobacteriosis	87	22	9	19	15	22	501	467	422
Gonorrhea†	1225	-	-	-	-	-	8820	7985	10594
Hepatitis A	18	1	9	0	0	8	109	94	136
Hepatitis B	13	1	3	2	4	3	84	93	150
Hepatitis NANB	0	0	0	0	0	0	18	22	31
Influenza	0	0	0	0	0	0	823	1020	895
Kawasaki Syndrome	3	0	1	1	0	1	19	15	17
Legionellosis	0	0	0	0	0	0	5	4	8
Lyme Disease	59	5	15	10	6	23	105	46	66
Measles	0	0	0	0	0	0	2	1	28
Meningitis, Aseptic	35	4	13	1	1	16	152	171	177
Meningitis, Bacterial‡	9	4	0	0	2	3	55	62	93
Meningococcal Infections	2	1	0	0	0	1	51	31	38
Mumps	3	2	0	1	0	0	32	19	58
Pertussis	10	3	3	2	0	2	27	38	21
Rabies in Animals	38	10	6	10	4	8	262	250	192
Reye Syndrome	0	0	0	0	0	0	1	1	1
Rocky Mountain Spotted Fever	5	1	2	1	1	0	12	8	10
Rubella	0	0	0	0	0	0	0	0	0
Salmonellosis	166	28	40	23	32	43	690	607	757
Shigellosis	65	6	14	5	20	20	519	446	261
Syphilis (1° & 2°)†	71	0	2	3	5	61	507	431	519
Tuberculosis	12	0	2	4	2	4	212	299	244

Localities Reporting Animal Rabies: Accomack 2 raccoons; Albemarle 1 raccoon; Amherst 1 raccoon; Campbell 1 groundhog; Caroline 1 skunk; Craig 1 raccoon; Cumberland 1 raccoon; Dinwiddie 1 raccoon; Essex 1 raccoon; Fairfax 3 raccoons; Fauquier 1 cow, 1 raccoon; Floyd 1 cat,1 raccoon; Franklin 1 raccoon; Halifax 1 skunk; Isle of Wight 1 raccoon; Loudoun 1 cat, 1 fox, 1 raccoon; Mecklenburg 1 raccoon; Northumberland 1 cat; Rappahannock 1 raccoon; Rockbridge 1 skunk; Rockingham 1 cow, 1 dog, 1 raccoon; Smyth 1 raccoon; Virginia Beach 2 raccoons; Warren 1 raccoon; Williamsburg 1 cat; Wythe 2 cats, 1 raccoon.

Occupational Illnesses: Asbestosis 8; Carpal Tunnel Syndrome 41; Coal Workers' Pneumoconiosis 18; De Quervain's Syndrome 1, Lead Poisoning 1, Loss of Hearing 11.

*Data for 1994 are provisional. †Total now includes military cases to make the data consistent with reports of the other diseases. ‡Other than meningococcal.

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