Section 4

Summary of Antimicrobial Resistance Surveillance

Antibiotics are one of the single most impressive medical achievements of the twentieth century. However, the continuing emergence and spread of antimicrobial resistance jeopardizes the utility of antibiotics and threatens public health globally. Additionally, resistant pathogens are often associated with increased morbidity and mortality, prolonged hospital stays, and increased intensity and duration of treatment.

The Florida Department of Health (FDOH) conducts surveillance for antibiotic resistance in five microorganisms. Practitioners, hospitals, and laboratories are required to report people infected with *Streptococcus pneumoniae* at a normally sterile site, including antibiotic susceptibility testing results. Practitioners, hospitals, and laboratories are required to report people infected with vancomycin non-susceptible *Staphylococcus aureus*. Laboratories participating in electronic laboratory reporting are required to report all *S. aureus* isolates from a normally sterile site with antibiotic susceptibility testing results. Isolates of *Neisseria meningitidis* from cases of meningococcal disease are sent to the Centers for Disease Control and Prevention (CDC) for additional laboratory testing as part of MeningNet. *Neisseria gonorrhoeae* isolates from the first 25 men with urethral gonorrhea seen each month in one sexually transmitted disease (STD) clinic in Miami are forwarded to CDC for susceptibility testing as part of the Gonococcal Isolate Surveillance Project (GISP).

Ideally, each patient presenting with an infection suspected to be caused by any of these organisms would be treated based on antimicrobial resistance testing of their own isolate conducted prior to the determination of an antimicrobial regimen. As that is not always possible, a cumulative or community aggregate antibiogram can provide useful operational information for the selection of an empiric therapy for a presumptive diagnosis. The selection of an antibiotic for empiric treatment should not be based solely on the community antibiogram. The community antibiogram should be considered in conjunction with factors such as the pharmacology of the antibiotic, its toxicity, the patient's hypersensitivity, the potential for interaction of the drug with other drugs the patient may be taking, the effectiveness of the patient's defense mechanisms, and the cost of the drug. Community antibiograms are also useful for tracking the antibiotic resistance patterns of clinically important microorganisms and for detecting trends towards antimicrobial resistance.

Streptococcus pneumoniae

Background

Streptococcus pneumoniae causes many clinical syndromes, depending on the site of infection (e.g., otitis media, pneumonia, bacteremia, meningitis, sinusitis, peritonitis, and arthritis). Invasive disease, for reporting purposes, includes cultures obtained from a normally sterile site, such as blood or cerebrospinal fluid. Drug-resistant *S. pneumoniae* invasive disease (DRSP) was added to Florida's list of notifiable diseases in mid-1996. Drug-susceptible *S. pneumoniae* invasive disease (DSSP) was added to Florida's list of notifiable diseases in mid-1999 to permit the assessment of the proportion of pneumococcal isolates that are drug-resistant; however, electronic data capture of resistance testing results was not fully implemented until 2005. When analyzing susceptibility testing results for *S. pneumoniae*, only one susceptibility result per case was included, in accordance with Clinical Laboratory Standards Institute (CLSI) guidelines. If there was more than one susceptibility result per case, results were then ranked on date of specimen collection (earliest to latest), date of report (latest to earliest), and the number of antibiotics tested (most to least), with the top ranking result selected for inclusion. The decision to include the first result was based on the goal of this report, which is to guide clinicians in the selection of empirical antimicrobial therapy for initial infections.

Not every specimen was tested for resistance to every antibiotic included in this report. When calculating percent susceptibility to an antibiotic, the denominator is the number of cases with an isolate tested for that particular antibiotic. Susceptibility results are presented for only those antibiotics which are recommended for routine testing and reporting, per 2008 CLSI guidelines. The CLSI guidelines split antibiotics into three groups for the purposes of reporting susceptibility testing results. Groups are based on clinical efficacy, prevalence of resistance, minimizing emergence of resistance, cost, FDA clinical indications for usage, and current consensus recommendations for first-choice and alternative drugs. Group A includes antibiotics that

CLSI considers appropriate for inclusion in routine, primary testing; Group B includes agents that may warrant primary testing but which CLSI recommends only selective reporting; Group C includes agents considered to be alternative or supplemental. Please note that cumulative aggregate susceptibility results for antimicrobials in Group B and C may underestimate the actual susceptibility rates in the community if only those isolates resistant to Group A antimicrobials are tested against Group B or C agents.

Data Summary

There were a total of 679 DSSP cases and 645 DRSP cases in 2011. Of the 679 DSSP cases, seven (1.0%) did not have antibiotic susceptibility data, most often because the patient died and further testing was not done.

The aggregate percent susceptibility for Group A agents were between 56% and 69% (Table 1). Aggregate percent susceptibility among Group B agents were more variable, ranging from 77% susceptibility to tetracycline to greater than 99% susceptibility to the fluoroquinolones (levofloxacin, moxifloxacin, and ofloxacin). Aggregate percent susceptibility for Group C agents ranged from 71% to 100%, although susceptibility percentages for Group C agents should be interpreted carefully, as often only isolates with specific susceptibility profiles against Group A or B agents are tested for susceptibility to Group C agents.

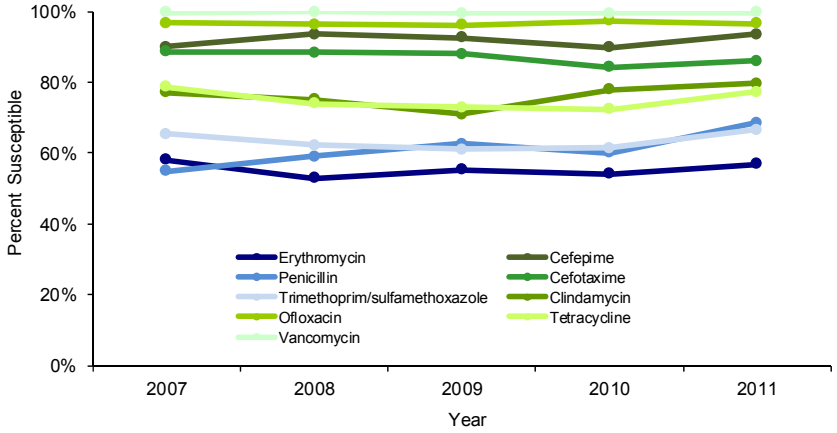
Table 1. Reported *Streptococcus pneumoniae*, Invasive Disease, Cumulative Antibiogram by CLSI Antibiotic Groups*, Florida, 2011

CLSI group	Antibiotic name	Number of cases tested	Percent of cases tested		
			Susceptible	Intermediate	Resistant
Group A*	Erythromycin	1,019	57	1	42
	Penicillin	1,166	69	14	17
	Trimethoprim/sulfamethoxazole	843	67	7	27
Group B*	Cefepime	157	94	5	2
	Cefotaxime	608	86	8	6
	Clindamycin	439	80	2	19
	Levofloxacin	901	99	1	0
	Moxifloxacin	298	100	0	0
	Ofloxacin	87	97	3	0
	Meropenem	317	82	11	7
	Tetracycline	703	77	1	21
	Vancomycin	1,180	100	0	0
Group C*	Amoxicillin/clavulanic acid	214	88	6	6
	Amoxicillin	222	91	6	4
	Chloramphenicol	335	99	0	1
	Imipenem	45	71	27	2
	Linezolid	255	100	0	0
	Rifampin	78	100	0	0

*Group A includes antibiotics that CLSI considers appropriate for inclusion in routine, primary testing; Group B includes agents that may warrant primary testing but which CLSI recommends only selective reporting; Group C includes agents considered to be alternative or supplemental.

S. pneumoniae susceptibility to most Group A and Group B antibiotics stayed relatively stable from 2007 to 2011 (Figure 1). There was a slight increase in susceptibility to penicillin.

Figure 1. Reported *Streptococcus pneumoniae*, Invasive Disease, Cumulative Percent Susceptibility to Select CLSI Group A* and Group B* Antibiotics, Florida 2007-2011



*Group A includes antibiotics that CLSI considers appropriate for inclusion in routine, primary testing; Group B includes agents that may warrant primary testing but which CLSI recommends only selective reporting. Group A antimicrobial agents are depicted on this graph with solid lines while Group B agents are depicted with dashed lines. Note: In 2010, FDOH revised the antimicrobial agents for which susceptibility testing results were collected. Prior to 2010, cumulative susceptibility results are not available for these antimicrobials (levofloxacin, moxifloxacin, and meropenem) and they are not included on this graph.

In general, the lowest cumulative susceptibility was seen among young children and youth (Table 2). For example, only 40% of cases in infants and young children (less than 4 years old) and 39% of cases in youth (15 to 24-year-olds) tested for resistance to erythromycin were susceptible, versus over 55% in all other age groups. Fewer than 63% of cases in young children (1 to 4-year-olds) and youth (15 to 24-year-olds) were susceptible to penicillin, versus more than 69% in all other age groups. Likewise, less than 56% of cases in young children and youth were susceptible to trimethoprim/sulfamethoxazole, versus more than 62% in other age groups.

Table 2. Reported *Streptococcus pneumoniae*, Invasive Disease, Cumulative Percent Susceptibility to CLSI Group A* and Group B* Antibiotics by Age Group, Florida, 2011

Age Group	Number of cases	Cumulative Percent of Cases Susceptible to Antibiotic											
		Group A*			Group B*								
		Erythromycin	Penicillin	Trimethoprim/ sulfamethoxazole	Cefepime	Cefotaxime	Clindamycin	Levofloxacin	Moxifloxacin	Ofloxacin	Meropenem	Tetracycline	Vancomycin
<1 (infant)	33	40**	55**	56**	**	83**	80**	100**	**	**	62**	91**	100
1-4 (young child)	105	40	57	46	**	75	58	100	100**	**	60	51	98
5-14 (child)	52	56	74	62	**	69**	81**	100	100**	**	70**	77	100
15-24 (youth)	40	39**	63	42**	**	76**	54**	100**	**	**	83**	44**	100
25-64 (adult)	636	62	71	71	93	89	80	98	99	93	86	78	100
65+ (senior)	458	55	69	68	97	89	88	99	100	100**	87	82	100

*Group A includes antibiotics that CLSI considers appropriate for inclusion in routine, primary testing; Group B includes agents that may warrant primary testing but which CLSI recommends only selective reporting.

**Too few cases (<30) were tested to produce reliable estimates of resistance. Results of age group/drug combinations where there were less than 10 cases tested were suppressed.

Resistance patterns were also summarized by Florida Regional Domestic Security Task Force Regions (map available at http://dohiws.doh.ad.state.fl.us/Divisions/DEMO/BPR/PDFs/rdstf-map.pdf). The southwest region tended to have the lowest cumulative susceptibility for the majority of the antimicrobials, while the northern regions (northeast, north central, and northwest) tended to have the highest cumulative susceptibility (Table 3).

Table 3. Reported *Streptococcus pneumoniae*, Invasive Disease, Cumulative Percent Susceptibility to CLSI Group A* and Group B* by Regional Domestic Security Task Force Region, Florida, 2011

Region	Number of cases	Cumulative Percent of Cases Susceptible to Antibiotic											
		Group A*			Group B*								
		Erythromycin	Penicillin	Trimethoprim/ sulfamethoxazole	Cefepime	Cefotaxime	Clindamycin	Levofloxacin	Moxifloxacin	Ofloxacin	Meropenem	Tetracycline	Vancomycin
East Central	247	49	59	63	**	77	78	98	100	98	77	74	100
North Central	44	77	88	64**	**	92**	90	100	**	**	**	83**	100
North East	160	69	71	75	96	89	81	100	100**	**	88	85	99
North West	107	49	74	71	95	96	91	100	100	**	90	86	100
South East	362	59	76	67	96**	88	74	98	100	100**	73	72	100
South West	133	50	72	67	**	91	76**	98	100	100**	84	72	100
West Central	271	57	59	63	87**	83	77	99	99	83**	78	78	100

*Group A includes antibiotics that CLSI considers appropriate for inclusion in routine, primary testing; Group B includes agents that may warrant primary testing but which CLSI recommends only selective reporting.

**Too few cases (<30) were tested to produce reliable estimates of resistance. Results of age group/drug combinations where there were less than 10 cases tested were suppressed.

Neisseria meningitidis

Background

N. meningitidis is a bacterium that is a leading cause of bacterial meningitis in the U.S. and may also cause overwhelming sepsis, purpura fulminans, or (rarely) benign meningococcemia. The emergence of quinolone-resistant *N. meningitidis* in the U.S. has raised important questions regarding current chemoprophylaxis guidelines and highlights the expanding threat of antimicrobial resistance in bacterial pathogens. The CDC responded to this concern by forming MeningNet, an enhanced meningococcal surveillance system to monitor antimicrobial susceptibility. As part of MeningNet, the Bureau of Public Health Laboratories (BPHL) began forwarding all *N. meningitidis* isolates to the CDC for antibiotic susceptibility testing in late 2008. All isolates are tested for susceptibility to penicillin, ceftriaxone, ciprofloxacin, rifampin, and azithromycin. Results are interpreted as susceptible, intermediate, or non-susceptible for penicillin, ciprofloxacin, rifampin, and susceptible or non-susceptible for ceftriaxone and azithromycin.

Data Summary

Of the 51 cases of meningococcal disease reported in Florida in 2011, 42 had isolates submitted to CDC for testing as part of MeningNet. One isolate was contaminated upon arrival at CDC, so a total of 41 isolates were tested for antibiotic susceptibility.

Statewide, there were 17 serogroup W-135, 12 serogroup B (one was contaminated and susceptibility was not tested), eight serogroup C, and five serogroup Y isolated from Florida cases (Table 4). All 41 isolates

were susceptible to ceftriaxone, ciprofloxacin, and rifampin. One isolate was non-susceptible to azithromycin, six isolates exhibited intermediate susceptibility to penicillin, and one isolate was non-susceptible to azithromycin and showed intermediate susceptibility to penicillin.

Table 4. 2011 *Neisseria meningitidis* susceptibility to select antibiotics

Serogroup	Total cases tested	Antibiotic name	Cases tested		
			Susceptible	Intermediate	Non-susceptible
B	11*	Penicillin	7	4	0
		Ceftriaxone	11	NA	0
		Ciprofloxacin	11	0	0
		Rifampin	11	0	0
		Azithromycin	11	NA	0
C	8	Penicillin	6	2	0
		Ceftriaxone	8	NA	0
		Ciprofloxacin	8	0	0
		Rifampin	8	0	0
		Azithromycin	7	NA	1
W-135	17	Penicillin	16	1†	0
		Ceftriaxone	17	NA	0
		Ciprofloxacin	17	0	0
		Rifampin	17	0	0
		Azithromycin	16	NA	1†
Y	5	Penicillin	5	0	0
		Ceftriaxone	5	NA	0
		Ciprofloxacin	5	0	0
		Rifampin	5	0	0
		Azithromycin	5	NA	0

*12 serogroup B cases; one was contaminated and susceptibility was not tested.
†Same case.

Two cases were epidemiologically linked and their isolates demonstrated intermediate susceptibility to penicillin. Five cases had a history of travel: Cuba (two cases); Sweden (one case); Tampa, FL (one case); and Orlando, FL (one case). All five cases with travel history had isolates that were susceptible to all five antibiotics screened. Seven cases were linked by pulsed-field gel electrophoresis patterns; all were part of an ongoing Miami-Dade outbreak of the W-135 strain and were susceptible to all five antibiotics screened.

Neisseria gonorrhoeae

Background

N. gonorrhoeae is a bacterium that can grow easily in the warm, moist areas of the reproductive tract, urethra, mouth, throat, eyes, and anus and causes the STD gonorrhea. Resistance to several antibiotics over time has challenged the treatment and control of gonorrhea. In the 1970's, the standard treatments, penicillin and tetracycline, were abandoned due to increased resistance to these agents. As recently as 2007, an increase in fluoroquinolone-resistant isolates prompted recommendations for new treatment guidelines supporting the use of cephalosporins, including ceftriaxone and cefixime, for gonococcal infections. In some parts of the world, *N. gonorrhoeae* is now showing potential resistance to cephalosporins, which are the only recommended class of antibiotics left to treat this common infection.

The Gonococcal Isolate Surveillance Project (GISP) was established in 1986 to continuously monitor trends

in antimicrobial resistance of *N. gonorrhoeae* across 30 cities in the U.S. The Miami-Dade STD clinic in Florida has served as one of 29 GISP sites since 1998. The Miami GISP site collects specimens each month from symptomatic males. If the Gram stain indicates the presence of diplococci, the specimen is forwarded to BPHL for culture, and the isolate is shipped to the CDC until 25 viable isolates are reached for the month. At the CDC, all isolates are tested for susceptibility to cefixime, cefpodoxime, ceftriaxone, tetracycline, spectinomycin, ciprofloxacin, penicillin, and azithromycin.

Data Summary

In the past five years, 1,119 viable isolates were collected from the Miami GISP site. In 2011, 166 specimens were submitted in which resistance to penicillin and tetracycline remained high and resistance to ciprofloxacin increased (Table 5). There were no isolates resistant to azithromycin observed in 2011. Recommendations to only use cephalosporins in 2007 have been credited with the steady decline of gonorrhea in Florida. Currently, ceftriaxone and cefixime (the cephalosporin antibiotics) have not shown any signs of resistance in isolates submitted by Florida.

Table 5. Cumulative Percent Susceptibility of *Neisseria gonorrhoeae* Isolates, Miami-Dade Gonococcal Isolate Surveillance Project Site, 2007-2011

Year	Number of isolates tested	Cumulative Percent of Isolates Susceptible to Antibiotic						
		Penicillin	Tetracycline	Spectinomycin	Ciprofloxacin	Ceftriaxone	Cefixime	Azithromycin
2007	266	79	62	100	81	100	N/A*	100
2008	259	87	61	100	84	100	N/A*	100
2009	219	88	65	100	88	100	100	100
2010	209	79	67	100	85	100	100	99
2011	166	81	63	100	77	100	100	100

*Isolates were not tested for cefixime susceptibility in 2007 and 2008.

For treatment of uncomplicated urogenital, anorectal, and pharyngeal gonorrhea, CDC recommends combination therapy with a single intramuscular dose of ceftriaxone 250 mg plus either a single dose of azithromycin 1 g orally or doxycycline 100 mg orally twice daily for seven days.

References

Centers for Disease Control and Prevention. Gonorrhea - CDC Fact Sheet. Available at http://www.cdc.gov/std/Gonorrhea/STDFact-gonorrhea.htm.

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