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Resistance Surveillance of Bacterial Pathogens from North American Patients Hospitalized with Pneumonia: A 10-Year Report from the SENTRY Program (1997-2006)

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SENTRY ANTIMICROBIAL SURVEILLANCE

AMENDED ABSTRACT

Objectives: The emergence of resistance (R) among pneumonia pathogens has resulted in increasing reliance upon fluoroquinolones and advanced-generation beta-lactams, including carbapenems. We summarize the prevalence and susceptibility (S) profiles of bacterial pneumonia pathogens collected during ten years of the SENTRY Antimicrobial Surveillance Program (1997-2006).

Methods: Participating North American medical centers (≥24/year) referred 50 consecutive, non-duplicate pathogens (19,406 isolates) from lower respiratory tract sites determined to be the probable cause of pneumonia in hospitalized patients (community and nosocomial in origin). Isolate identifications were confirmed and susceptibility testing was performed using CLSI reference methods at a central laboratory (JMI Laboratories, North Liberty, IA).

Results: Selected pathogens with unique or emerging R characteristics are in the Table. The 10 ranked pathogens comprised 90.4% of all isolates and included: *S. aureus* (SA; 28.1%) > *P. aeruginosa* (PSA; 19.4%) > *Klebsiella* spp. (KSP; 7.9%) > *H. influenzae* (7.7%) > *S. pneumoniae* (SPN; 6.6%) > *Enterobacter* spp. (6.3%) > *E. coli* (EC; 4.1%) > *Serratia* spp. (3.8%) > *S. maltophilia* (3.6%) > *Acinetobacter* spp. (ASP; 2.8%). Among Gram-positive species, R emergence was notable for SA (oxacillin [OXA] -R currently 61.4%; ERY-non-susceptibility [NS], 69.2%) and SPN (ERY-R, 29.4%; PEN-R, 11.8%). Among enterics, CIP-R (30.8% for EC in 2006) and ESBL-phenotype rates (KSP and EC; ranges 6.7-23.9% and 3.8-11.7%, respectively) have increased considerably. An increase in IMP-R in KSP primarily results from a continued east coast epidemic of clonal strains expressing serine carbapenemase (primarily KPC-2) enzymes. While CAZ- and IMP-R among PSA has increased, R to CAZ and fluoroquinolones have become predominant among ASP; only polymyxins remain largely S (>97%).

Species (no. tested)	Antimicrobial agent	% R 1997	% R 2002	% R 2006
SA (5,447)	OXA	39.4	45.9	61.4
PSA (3,764)	CAZ	19.0	12.6	17.4
	IMP	8.0	7.3	13.6
	CIP	15.3	23.8	23.0
KSP (1541)	CRO	1.2 (9.3)	6.9 (21.7)	5.3 (12.6)
	IMP	0.0	0.4	3.2
	CIP	3.2	5.8	9.5
SPN (1282)	PEN	9.2	16.4	11.8
	ERY	14.5	23.7	29.4
EBS (1222)	CRO	13.2	7.8	17.9
	CIP	3.4	3.9	7.7
EC (798)	CRO	1.6 (7.0)	1.0 (7.2)	7.7 (7.7)
	CIP	1.6	9.3	30.8
ASP (540)	CAZ	29.5	39.0	58.8
	IMP	3.3	5.1	14.7
	CIP	34.4	54.2	73.5

* Numbers in parentheses are ESBL-phenotype rates (% ≥2 mg/L).

Conclusions: Although temporary resistance declines were detected among some North American pneumonia pathogens, all showed increasing resistance to most class agents during the monitored period. Continued longitudinal comparisons of emerging pathogens and changing susceptibility profiles are critical elements in guiding empiric therapies and epidemiologic interventions.

INTRODUCTION

Patients hospitalized with lower respiratory tract infections (pneumonia) can acquire their infections from the community, hospital, or other health care facility. Community-acquired pneumonia (CAP) is often treated empirically with oral antimicrobial agents unless the patient is admitted to the hospital. Patients with hospital-acquired pneumonia can benefit from properly collected lower respiratory tract diagnostic specimens and the resulting identification and antimicrobial susceptibility testing. In more recent years, the health care system has shifted traditional hospital care to the community setting. Increasing numbers of patients are in nursing homes, receive outpatient parenteral therapy, attend dialysis clinics and receive domiciliary care. Those patients with healthcare-associated pneumonia when compared to CA will often be older, have more co-morbid conditions, and have pneumonia caused by antimicrobial-resistant pathogens.

In all three of the settings noted above, resistance to commonly used antimicrobials is increasing. This has resulted in increased reliance on fluoroquinolones and advanced-generation beta-lactams, including carbapenems. Rapid isolation, identification and susceptibility test result reporting of pathogens causing pneumonia will minimize empiric therapy, lead to more rapid use of directed therapy, decrease use of multiple agents, reduce spread of resistant pathogens and minimize infection control complications.

This report summarizes the frequency of occurrence and key antimicrobial susceptibility patterns for pathogens (community- or hospital-acquired, or healthcare-associated) causing pneumonia in hospitalized patients in North America (1997-2006).

MATERIALS AND METHODS

Organism collection: The SENTRY Antimicrobial Surveillance Program has collected pathogens from medical centers globally since 1997. The program directed medical centers to send 50 consecutive, non-duplicate pathogens from lower respiratory tract infection determined to be the probable cause of pneumonia in hospitalized patients. In North America, 19,406 isolates were collected from 25 or more medical centers per year (1997-2006). All isolates were shipped on charcoal swabs to a central laboratory (JMI Laboratories, North Liberty, Iowa, USA). Isolate identifications were verified upon receipt (when indicated, biochemical tests and or VITEK [Biomerieux, USA] were used to confirm pathogen identifications).

Antimicrobial susceptibility testing: Susceptibility testing was performed using validated broth microdilution panels (TREK Diagnostic Systems, Inc., Ohio, USA) according to CLSI methods (M7-A7, 2006). Quality control isolates utilized included *Escherichia coli* ATCC 25922 and 35218, *Pseudomonas aeruginosa* ATCC 27853, *Staphylococcus aureus* ATCC 29213, *S. pneumoniae* ATCC 49619 and *Enterococcus faecalis* ATCC 29212; interpretive criteria used were those recommended by the CLSI (M100-S18; 2008). Confirmation methods utilized include disk diffusion and Etest (AB BIODISK, Sweden) also utilizing CLSI methods and interpretive criteria.

RESULTS

- There were few changes in the rank order of the 10 most common pathogens (>90%) causing lower respiratory infections (pneumonia) in hospitalized patients. Increases noted for *S. aureus* (approximately 16%) and decreases for *H. influenzae* and *S. pneumoniae* (-8.4 and -6.0%, respectively; Table 1) indicate greater resistance burden of MRSA and decreased hospitalizations for CAP.
- Among *S. aureus*, significant decreases (10-20%) in susceptibility were noted for oxacillin, erythromycin, clindamycin and ciprofloxacin. Gentamicin became more active (susceptible rate) and linezolid and vancomycin remained very active agents (Table 2).
- Decreases in the susceptibility rates for broad-spectrum ß-lactams against *P. aeruginosa* (4-8%) were noted.
- A significant decrease in susceptibility (22.5%) occurred in ciprofloxacin for *E. coli*. ESBL rates for *E. coli* and *Klebsiella* spp. increased 5.9 and 13.0%, respectively (Table 2).
- Increases in imipenem resistance among *Klebsiella* spp. are primarily the result of a continued epidemic of clonal strains expressing serine carbapenemases (primarily KPC-2 and -3) enzymes in the New York City area (data not shown).
- Erythromycin and clindamycin susceptibilities decreased for *S. pneumoniae.* Levofloxacin and ceftriaxone remain highly active. Penicillin was 92.8 – 96.9% susceptible under 2008 CLSI breakpoint for parenteral usage (non-meningitis; ≤2 mg/L; Table 2).

Table 1. Rank order by year of 19,406 pathogens collected from hospitalized patients with pneumonia in the SENTRY Program (North America 1997 to 2006).

Organism/rank	10 year total (%)	Occurrence (%) by year: 1997	1998	1999	2000	2001	2002	2004	2005	2006
1. *S. aureus*	5447(28.1)	602(22.2)	709(25.4)	777(27.1)	760(28.0)	653(29.4)	748(27.2)	397(32.5)	387(36.4)	414(38.3)
2. *P. aeruginosa*	3764(19.4)	490(18.1)	520(18.7)	577(20.1)	543(20.0)	408(18.4)	571(20.8)	269(22.0)	173(16.3)	213(19.7)
3. *Klebsiella* spp.	1541(7.9)	247(9.1)	193(6.9)	195(6.8)	203(7.5)	149(6.7)	276(10.1)	95(7.8)	88(8.3)	95(8.8)
4. *H. influenzae*	1501(7.7)	282(10.4)	260(10.1)	260(9.1)	199(7.3)	183(8.2)	200(7.3)	34(2.8)	61(5.7)	22(2.0)
5. *S. pneumoniae*	1282(6.6)	207(7.6)	225(8.1)	204(7.1)	246(9.1)	166(7.5)	101(3.7)	33(2.7)	32(3.0)	17(1.6)
6. *Enterobacter* spp.	1222(6.3)	204(7.5)	186(6.7)	184(6.4)	156(5.8)	122(5.5)	153(5.6)	96(7.9)	56(5.3)	65(6.0)
7. *E. coli*	798(4.1)	128(4.7)	119(4.3)	124(4.3)	105(3.9)	79(3.6)	97(3.5)	46(3.8)	48(4.5)	52(4.8)
8. *Serratia spp.*	742(3.8)	72(2.7)	96(3.4)	117(4.1)	96(3.5)	87(3.9)	126(4.6)	62(5.1)	44(4.1)	42(3.9)
9. *S. maltophilia*	702(3.6)	102(3.8)	114(4.1)	87(3.0)	94(3.5)	99(4.5)	101(3.7)	37(3.0)	34(3.2)	34(3.1)
10. *Acinetobacter spp.*	540(2.8)	61(2.3)	84(3.0)	59(2.1)	72(2.7)	65(2.9)	59(2.1)	66(5.4)	40(3.8)	34(3.1)
Total (% of top 10)	17539(90.4)	2395(88.4)	2506(89.9)	2584(90.2)	2474(91.2)	2011(90.5)	2432(88.6)	1135(92.9)	963(90.5)	988(91.5)

Table 2. Susceptibility[a] profiles among key pathogens causing pneumonia from patients hospitalized in North America (1998, 2001, 2005).

Organism (no. tested)/ antimicrobial agent	1998 MIC$_{50}$	1998 % S	2001 MIC$_{50}$	2001 % S	2005 MIC$_{50}$	2005 % S
S. aureus (1,749)	(709)		(653)		(387)	
Oxacillin	1	65.3	>2	49.3	>2	42.6
Erythromycin	1	43.8	>2	38.2	>2	29.6
Clindamycin	0.25	69.5	0.12	58.4	≤0.25	60.2
Gentamicin	0.5	84.8	≤2	88.2	≤2	96.7
Ciprofloxacin	0.5	64.9	>2	46.1	>2	44.0
Linezolid	4[b]	100.0	2	100.0	2	100.0
Vancomycin	1	100.0	1	100.0	1	100.0
P. aeruginosa (1,101)	(520)		(408)		(173)	
Ceftazidime	4	77.7	≤2	83.6	2	73.4
Cefepime	4	81.4	4	84.8	4	76.9
Piperacillin/tazobactam	8	87.5	8	88.0	8	79.8
Imipenem	2	78.5	1	89.0	1	78.6
Gentamicin	2	81.9	2	85.8	≤2	82.7
Amikacin	4	91.8	4	96.3	4	94.3
Ciprofloxacin	0.25	72.3	0.25	73.8	0.25	72.7
Klebsiella spp. (430)	(193)		(149)		(88)	
Ceftriaxone	≤0.25	99.0 (5.1)[c]	≤0.25	99.3 (5.4)[c]	≤0.25	84.1 (18.1)[c]
Ceftazidime	0.25	96.4 (5.1)[c]	≤2	97.3 (4.7)[c]	≤1	84.1 (17.0)[c]
Cefepime	≤0.12	99.0	≤0.12	100.0	≤0.12	92.1
Piperacillin/tazobactam	4	91.1	2	93.9	4	86.4
Imipenem	0.25	99.5	0.12	99.3	≤0.12	92.0
Gentamicin	0.5	94.2	≤2	96.6	≤2	88.6
Ciprofloxacin	0.03	96.4	0.03	95.3	≤0.03	87.5
H. influenzae (504)	(260)		(183)		(61)	
Ampicillin	-	-	≤2	78.1[d]	≤1	78.3
Amoxicillin/clavulanic acid	0.5	98.1	≤2	99.5	≤1	100.0
Ceftriaxone	-	-	≤0.25	100.0	≤0.25	100.0
Azithromycin	1.0	100.0	-	-	-	-
Levofloxacin	≤0.5	100.0	≤0.03	100.0	≤0.5	100.0
S. pneumoniae (423)	(225)		(166)		(32)	
Penicillin[e]	≤0.03	96.4	≤0.015	92.8	≤0.015	96.9
Penicillin[f]	≤0.03	78.2	≤0.015	67.5	≤0.015	65.6
Ceftriaxone	-	-	≤0.25	92.2	≤0.25	100.0
Erythromycin	≤0.25	86.7	≤0.06	67.5	≤0.25	65.7
Clindamycin	≤0.06	96.5	≤0.06	86.8	≤0.25	87.5
Levofloxacin	1	100.0	1	99.4	1	100.0
Enterobacter spp. (364)	(186)		(122)		(56)	
Ceftriaxone	≤0.25	75.8	≤0.25	88.5	≤0.25	80.3
Ceftazidime	0.5	79.0	≤2	83.6	≤1	78.5
Cefepime	≤0.12	100.0	≤0.12	100.0	≤0.12	96.4
Piperacillin/tazobactam	4	80.1	2	88.5	4	82.2
Imipenem	0.5	100.0	0.5	100.0	0.5	100.0
Gentamicin	0.5	92.9	≤2	93.5	≤2	91.1
Ciprofloxacin	0.03	95.1	≤0.03	95.9	≤0.03	94.6

Organism (no. tested)/ antimicrobial agent	1998 MIC$_{50}$	1998 % S	2001 MIC$_{50}$	2001 % S	2005 MIC$_{50}$	2005 % S
E. coli (246)	(119)		(79)		(48)	
Ampicillin	4	57.2	4	63.3	>16	37.5
Ceftriaxone	≤0.25	97.5 (2.5)[b]	≤0.25	100.0 (3.8)[b]	≤0.25	95.8 (6.3)[b]
Ceftazidime	0.25	97.5 (3.3)[b]	≤2	97.4 (2.6)[b]	≤1	95.8 (8.4)[b]
Cefepime	≤0.12	98.4	≤0.12	100.0	≤0.12	97.9
Piperacillin/tazobactam	2	91.6	1	100.0	1	97.9
Imipenem	0.12	100.0	0.12	100.0	≤0.12	100.0
Gentamicin	1	96.6	≤2	94.9	≤2	85.4
Ciprofloxacin	≤0.015	97.5	≤0.03	93.7	≤0.03	75.0
Serratia spp. (227)	(96)		(87)		(44)	
Ceftriaxone	≤0.25	93.8	≤0.25	95.5	≤0.25	100.0
Ceftazidime	0.25	95.9	≤2	98.9	≤1	97.7
Cefepime	≤0.12	98.0	≤0.12	100.0	≤0.12	100.0
Piperacillin/tazobactam	2	92.8	2	93.1	2	95.5
Imipenem	1	100.0	0.5	98.9	0.5	100.0
Gentamicin	1	98.0	≤2	92.0	≤2	97.7
Ciprofloxacin	0.12	87.5	0.06	92.0	0.06	93.2
S. maltophilia (247)	(114)		(99)		(34)	
Trimethoprim/sulfamethoxazole	≤0.5	97.4	≤0.5	99.0	≤0.5	100.0
Piperacillin/tazobactam	32	-	>64	-	>64	-
Tetracycline	8	-	>8	-	>8	-
Amikacin	>32	-	>32	-	>32	-
Levofloxacin	2	69.3	1	84.8	1	91.2
Acinetobacter spp. (189)	(84)		(65)		(40)	
Ampicillin/sulbactam	-	-	-	-	8	57.5
Ceftazidime	8	60.7	8	50.8	>16	32.5
Piperacillin/tazobactam	16	54.8	32	44.7	32	40.0
Imipenem	0.25	91.7	0.5	89.3	0.5	92.5
Amikacin	4	76.2	2	89.2	8	80.0
Ciprofloxacin	0.5	53.6	>2	44.6	>4	25.0
Tigecycline	-	-	-	-	1	-
Polymyxin B	-	-	≤1	98.5	≤0.5	100.0

a. Percent susceptible was based upon CLSI recommended breakpoints (M100-S18); - = not tested.
b. Linezolid elevated in 1998 due to inappropriate interpretations of trailing end points at 80% inhibition level.
c. ESBL rates based upon CLSI recommendations (M100-S18) with MIC values ≥2 mg/L.
d. Includes susceptible and intermediate.
e. Penicillin CLSI breakpoint for parenteral (non-meningitis).
f. Penicillin CLSI breakpoint for parenteral (meningitis) or (oral penicillin V).

- While resistances among *Enterobacter* spp., *H. influenzae*, *Serratia* spp. and *S. maltophilia* were generally unchanged. *Acinetobacters* isolated from respiratory tract cultures were consistently more resistant in 2006-2007 for most ß-lactams and fluoroquinolones (25% susceptible to ciprofloxacin).

CONCLUSIONS

- The rank order of pathogens causing lower respiratory tract infections (pneumonia) in North American hospitalized patients has not changed significantly in 10 years.
- Temporary increases in susceptibility were detected for some North American pathogens. However, all monitored pathogens showed decreases to one or more class agents during the monitored decade.
- CAP (especially considering the increase of virulent MRSA clones in the community) and the increasing rates of healthcare-associated pneumonia require continued monitoring to guide empiric treatment.
- Rapid pathogen isolation, identification, and susceptibility testing are critical to treating and monitoring hospitalized pneumonia patients. Global, longitudinal comparisons of these emerging pathogens originating in the community and hospital and their changing resistance profiles are a necessity to guide effective therapies and epidemiological interventions.

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