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Trends in Prevalence and Antimicrobial Susceptibilities Among Skin and Skin Structure Infection Pathogens in North America: Report from the SENTRY Program (1997-2005)

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SENTRY ANTIMICROBIAL SURVEILLANCE

ABSTRACT

Objectives: Rising resistance (R) rates being observed globally in skin and skin structure infection (SSSI) pathogens are challenging accepted approaches to empiric management. We present a nine year summary of the prevalence and susceptibility (S) trends of bacterial pathogens producing SSSI collected from USA and Canadian medical centers participating in the SENTRY Antimicrobial Surveillance Program.

Methods: Participating North American (NA) medical centers were directed to send 50 consecutive, non-duplicate SSSI pathogens/year. USA (>=21) and Canadian (5) medical centers submitted isolates for the years 1997-2002 and 2004-2005 (USA sites only). Isolate identifications were confirmed and susceptibility testing was performed using CLSI reference methods at a central laboratory (JMI Laboratories, North Liberty, IA).

Results: The top 7 ranked pathogens comprised 85.2% of the total (8,520 isolates; see Table) with *S. aureus* (SA) being predominant, ranging from 40.4-53.1% between years. Other ranking pathogens included *P. aeruginosa* (PSA), *Enterococcus* spp. (ENT), and *E. coli* (EC) which were second to fourth each year except in 2004, when ENT and PSA reversed rank. Prevalence of beta-haemolytic streptococci (BHS) varied from fifth in 1998, ninth in 2000, then fifth again in 2004/2005. The all-years NA MRSA rate was 35.9% (9% in Canada) and ranged from 31.3 to 56.2% among USA census zones. Highest ENT vancomycin R (VAN-R; 16.5%) was found in 2005 and highest erythromycin R rate (25.8%) in BHS was found in 2004. Trending increases in fluoroquinolone (FQ) R rates among EC and *Klebsiella* spp. (KSP) reached 24.4 and 12.8%, respectively. ESBL phenotype rates for EC (12.8%) peaked in 2004 and for KSP (20.5%) in 2005. In contrast to these changes, ceftazidime-, imipenem- and levofloxacin-R rates for PSA (higher in earlier years) have trended downwards.

Organism (no.)	R pattern	% R All Years	% R (Range)
SA (3,862)	MRSA	35.9	24.0-49.4
PSA (908)	Imipenem (IMP)-R	6.1	1.1-9.8
	Ceftazidime (CAZ)-R	10.0	7.8-13.1
	Levofloxacin (LEV)-R	18.9	15.7-22.5
ENT (748)	Vancomycin (VAN)-R	12.4	7.6-16.5
EC (610)	CAZ-R	2.8	0.0-7.0
	LEV-R	9.3	2.4-24.4
EBS (409)	CAZ-R	17.8	7.6-25.5
BHS (379)	Erythromycin (ERY)-R	19.8	8.8-25.8
KSP (344)	CAZ-R	5.2	0.0-17.9
	LEV-R	3.2	1.4-12.8

Conclusions: SSSI pathogen prevalence has changed minimally since 1997 (exception, BHS). MRSA rate differences are notable between countries and between USA census zones. R rates for ENT (VAN-R), and EC and KSP (FQ and ESBLs) are increasingly of concern whereas R among key agents targeting PSA have improved from earlier SENTRY surveillance periods. Continued surveillance monitoring of these trends, both locally and globally, provides useful information for empiric management of SSSI and in assessing needed changes to antimicrobial therapy guidelines.

INTRODUCTION

Management of community-acquired and nosocomial skin and skin structure infections (SSSI) continues to be a serious health-care problem with an estimated 700,000 patients being hospitalized annually in the United States (USA) alone. The microbiologic diversity of prevalent pathogens complicates treatment options, as does the widely-recognized emergence of resistance to leading oral and parenteral antimicrobial agents. Empiric therapy decisions are usually made based upon professional consensus guidelines using existing knowledge of expected pathogens, local/regional susceptibility profiles, risk factors, and rapid diagnostic laboratory results such as the Gram's stained smear.

While the continued high prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) is a widely recognized problem among healthcare-associated SSSI, the emergence of community-associated MRSA (CA-MRSA) clones in otherwise healthy individuals is also of great concern. Likewise, the recent documented spread of these CA-MRSA clones into the hospital environment is producing new challenges to established infection control practices. Among Gram-negative pathogens, resistance to commonly utilized ß-lactam and fluoroquinolone agents, among others, similarly is limiting treatment options.

The SENTRY Antimicrobial Surveillance Program has performed longitudinal antimicrobial resistance surveillance globally for more than 10 years. This report describes the trending of SSSI pathogen prevalence and key resistance profiles, as well as overall susceptibilities to commonly utilized antimicrobials among isolates collected from North American patients between the years of 1997 to 2005.

MATERIALS AND METHODS

Organism Collection: Medical center sites participating in the SENTRY Program protocol submited 50 consecutive, nonduplicate community-acquired or nosocomial SSSI pathogens per year to the central laboratory monitor (JMI Laboratories, Iowa, USA). Pathogens were submitted for identification confirmation and susceptibility testing against 30 or more antimicrobial agents. For the years 1997 to 2005, a total of 8,520 SSSI pathogens were collected from North American medical centers including 21-25 sites in the USA and 5-8 in Canada (1997-2002 only). The nine most frequently encountered pathogens comprised >90% of isolates (Table 1).

Antimicrobial susceptibility testing: Susceptibility testing was performed using validated broth microdilution panels (TREK Diagnostic Systems, Inc., Ohio, USA) with testing performed according to CLSI methods (M7-A7, 2006). Quality control (QC) isolates utilized included *Escherichia coli* ATCC 25922 and 35218, *Pseudomonas aeruginosa* ATCC 27853, *S. aureus* ATCC 29213, *Streptococcus pneumoniae* ATCC 49619 and *Enterococcus faecalis* ATCC 29212; QC ranges and interpretive criteria were those recommended by the CLSI (M100-S18). Enterobacteriaceae with elevated MIC values (≥2 mg/L) for ceftazidime and/or ceftriaxone and/or aztreonam were considered as extended-spectrum ß-lactamase-producing phenotypes using CLSI (M100-S18) criteria.

RESULTS

- *S. aureus* remains as the predominant SSSI pathogen in North America (53% in the USA in 2005), followed by *P. aeruginosa, Enterococcus spp.*, and *E. coli*. Ranking of these top four pathogens (72% of SSSI) has remained unchanged.
- MRSA rates have been significantly different between USA and Canada (Table 2), with Canadian rates remaining stable during the survey period, but USA rates increasing 20.4%. Among USA census zones, the MRSA rate varied from 31.3 to 56.2% (data not shown).
- Linezolid, daptomycin and vancomycin continued to remain effective against all staphylococci; only rare quinupristin/dalfopristin resistance (0.4%) was found among coagulase-negative strains (Table 3).
- Vancomycin resistance was detected in 20.3% of *Enterococcus* spp. in 2005, 6.5% higher than the total for all years (Table 2). Linezolid and daptomycin retained near-complete coverage of enterococci (Table 3).
- Among ß-haemolytic streptococci, resistance was most noted for erythromycin (19.7%) and tetracycline (50.9%); linezolid, quinupristin/dalfopristin and vancomycin remained highly effective (100% susceptible). Rare fluoroquinolone-resistant strains were detected.
- *E. coli* and *Klebsiella* spp. were >99% susceptible to carbapenems but less so to 'third and fourth' generation cephalosporins, due to continued presence of ESBL enzymes (Table 4); the ESBL phenotype rate for *E. coli* increased 2-fold (6.3 to 12.8%) and *Klebsiella spp*. 4-fold (5.3 to 20.3%) during the course of the study (Table 2).
- No increase was seen in multidrug-resistant *P. aeruginosa*, with an overall rate of 3.3% (Table 2). Fluoroquinolone (levofloxacin) resistance rates were 18.9% using CLSI breakpoints and 24.6% by EUCAST criteria. Polymyxin B was the only agent active against all *P. aeruginosa* (Table 4).

Table 1. Rank order by year of pathogens causing SSTI collected as part of the SENTRY Program (North America 1997 to 2005).

			Occurrence (%) by year:						
Organism/rank		Total (%)	1997	1998	1999	2000	2002	2004	2005
1.	*S. aureus*	3862(45.3)	667(42.6)	535(42.5)	178(40.4)	644(45.9)	606(40.5)	639(51.6)	593(53.1)
2.	*P. aeruginosa*	908(10.7)	176(11.2)	160(12.7)	48(10.9)	152(10.8)	186(12.4)	102(8.2)	85(7.6)
3.	*Enterococcus* spp.	748(8.8)	127(8.1)	105(8.3)	47(10.7)	115(8.2)	153(10.2)	122(9.8)	79(7.1)
4.	*E. coli*	610(7.2)	112(7.2)	85(6.8)	42(9.5)	98(7.0)	111(7.4)	86(6.9)	76(6.8)
5.	*Enterobacter* spp.	409(4.8)	82(5.2)	49(3.9)	22(5.0)	81(5.8)	79(5.3)	51(4.1)	45(4.0)
6.	ß-Streptococcus	379(4.4)	79(5.0)	57(4.5)	15(3.4)	32(2.3)	67(4.5)	66(5.3)	63(5.6)
7.	*Klebsiella* spp.	344(4.0)	57(3.6)	41(3.3)	18(4.1)	71(5.1)	69(4.6)	49(4.0)	39(3.5)
8.	*P. mirabilis*	242(2.8)	42(2.7)	45(3.6)	5(1.1)	42(3.0)	42(2.8)	32(2.6)	34(3.0)
9.	CoNS	235(2.8)	58(3.7)	30(2.4)	16(3.6)	48(3.4)	44(2.9)	23(1.9)	16(1.4)
Total isolates tested (% of top 9)		7737(90.8)	1400(89.4)	1107(88.0)	391(88.7)	1283(91.4)	1357(90.7)	1170(94.4)	1030(92.2)

Table 2. Key antimicrobial resistance trends by year occurring in North America (SENTRY Program, 1997-2005).

		Year/no. isolates (% resistant)[a]						
Organism/region	Total	1997	1998	1999	2000	2002	2004	2005
S. aureus (oxacillin-resistant)								
North America	3862(35.9)	667(24.0)	535(26.2)	178(36.0)	644(29.5)	606(39.1)	639(47.4)	593(49.4)
USA	3396(39.6)	483(29.0)	441(30.6)	157(39.5)	560(32.7)	523(43.8)	639(47.4)	593(49.4)
Canada	466(9.0)	184(10.9)	94(5.3)	21(9.5)	84(8.3)	83(9.6)	-	-
Enterococcus spp. (vancomycin-resistant)[b]								
North America	748(13.8)	127(16.5)	105(8.6)	47(12.8)	115(9.6)	153(14.4)	122(14.8)	79(20.3)
P. aeruginosa (multidrug-resistant)[c]								
North America	908(3.3)	176(4.5)	160(1.3)	48(2.1)	152(4.6)	186(3.8)	102(3.9)	85(1.2)
E.coli (ESBL-phenotype)[d]								
North America	610(6.1)	112(6.3)	85(3.5)	42(7.1)	98(6.1)	111(4.5)	86(12.8)	76(12.8)
Klebsiella spp. (ESBL-phenotype)[d]								
North America	344(10.8)	57(5.3)	41(4.9)	18(0.0)	71(11.3)	69(7.2)	49(16.3)	39(20.5)

a. Resistance criteria based upon CLSI breakpoints [2008].
b. Vancomycin MIC, ≥8 mg/L.
c. Non-susceptible to representatives from four drug classes (ceftazidime, piperacillin, gentamicin, and ciprofloxacin).
d. Rates based upon MIC values ≥2 mg/L for ceftazidime or ceftriaxone or aztreonam [CLSI, 2008].

Table 3. Antimicrobial activity of selected agents tested against the top four ranked Gram-positive pathogens causing SSTI in the North American SENTRY Program (1997 - 2005).

	MIC (mg/L)		CLSI % by category[a]		EUCAST % by category[a]	
Organism (no. tested)	50%	90%	Susceptible	Resistant	Susceptible	Resistant
S. aureus (3862)						
Oxacillin	0.5	>2	64.1	35.9	-	-
Erythromycin	1	>2	48.7	47.8	27.1	51.3
Clindamycin	≤0.25	>2	78.3	21.4	77.2	21.7
Levofloxacin	≤0.5	>4	67.6	31.6	67.6	31.6
Gentamicin	≤2	≤2	93.8	2.7	92.2	7.8
Daptomycin	0.25	0.5	100.0	0.0	100.0	0.0
Linezolid	2	2	100.0	0.0	100.0	0.0
Quinupristin/dalfopristin	0.5	0.5	99.8	0.0	99.8	0.0
Tetracycline	≤4	≤4	92.1	6.9	92.1	7.8
Trimethoprim/ sulfamethoxazole	≤0.5	≤0.5	96.3	3.7	96.3	3.7
Vancomycin	1	1	99.9	0.0	100.0	0.0
Enterococcus spp. (748)						
Ampicillin	≤2	>16	16.0	15.2	-	-
Erythromycin	>2	>2	11.8	58.4	-	-
Levofloxacin	2	>4	52.4	46.3	-	-
Gentamicin HL	≤500	>1000	70.6	29.4	-	-
Daptomycin	1	2	100.0	0.0	-	-
Linezolid	2	2	99.0	0.0	99.0	0.0
Quinupristin/dalfopristin	>2	>2	15.9	76.6	15.9	76.6
Tetracycline	>8	>8	36.0	63.2	-	-
Vancomycin	1	>16	86.2	12.4	86.2	13.8
Coagulase-negative staphylococci (235)						
Oxacillin	>2	>2	25.6	65.9	-	-
Erythromycin	>2	>2	36.9	61.3	37.8	61.3
Clindamycin	≤0.25	>2	67.7	31.9	66.8	32.3
Levofloxacin	0.5	>4	51.8	43.6	51.8	43.6
Gentamicin	≤2	>8	74.8	19.2	68.9	31.1
Daptomycin	0.5	0.5	100.0	0.0	100.0	0.0
Linezolid	1	2	100.0	0.0	100.0	0.0
Quinupristin/dalfopristin	0.25	0.5	99.6	0.4	99.6	0.4
Tetracycline	≤4	>8	83.5	15.7	82.9	16.6
Trimethoprim/ sulfamethoxazole	≤0.5	>1	88.1	11.9	88.1	11.9
Vancomycin	1	2	100.0	0.0	100.0	0.0
ß-haemolytic streptococci (379)						
Penicillin	0.03	0.12	100.0	-	-	-
Erythromycin	≤0.25	>2	80.0	19.7	80.0	19.7
Clindamycin	≤0.25	≤0.25	91.8	7.1	92.9	7.1
Levofloxacin	0.5	1	99.5	0.5	97.6	0.5
Linezolid	1	1	100.0	0.0	100.0	0.0
Quinupristin/dalfopristin	≤0.5	≤0.5	100.0	0.0	-	-
Tetracycline	8	>8	48.0	50.9	47.7	51.7
Vancomycin	0.5	0.5	100.0	0.0	100.0	0.0

a. Criteria as published by the CLSI [2008] or EUCAST [2008]; - = agent not tested, or criteria not available.

Table 4. Antimicrobial activity of selected antimicrobial agents tested against Gram-negative pathogens causing SSTI in the North American SENTRY Program (1997 - 2005).

	MIC (mg/L)		CLSI[a] % by category		EUCAST[a] % by category	
Organism (no. tested)	50%	90%	Susceptible	Resistant	Susceptible	Resistant
P. aeruginosa (908)						
Cefepime	2	16	88.6	5.0	88.6	11.4
Ceftazidime	2	16	86.5	10.0	86.5	13.5
Levofloxacin	0.5	>4	75.4	18.9	66.5	24.6
Gentamicin	≤0.5	8	89.0	6.5	89.0	11.0
Imipenem	1	8	88.3	6.1	88.3	6.1
Polymyxin B	≤1	2	99.7	0.0	-	-
Piperacillin/tazobactam	4	64	90.9	9.1	-	-
E. coli (610)						
Ampicillin	4	265	55.8	43.4	-	-
Amoxacillin/clavulanate	4	16	78.3	8.4	-	-
Cefepime	≤0.12	0.25	96.2	2.0	96.2	2.8
Ceftazidime	≤1	≤1	95.9	2.8	94.6	4.1
Ceftriaxone	≤0.25	≤0.25	96.2	2.0	94.5	5.0
Levofloxacin	≤0.5	4	89.6	9.3	89.4	10.4
Gentamicin	≤2	4	91.0	8.0	88.7	9.0
Imipenem	≤0.5	≤0.5	100.0	0.0	100.0	0.0
Piperacillin/tazobactam	2	8	95.7	1.5	-	-
Tetracycline	≤4	>8	71.0	27.5	-	-
Trimethoprim/ sulfamethoxazole	≤0.5	>2	78.7	21.3	78.7	21.3
Enterobacter spp. (409)						
Cefepime	≤0.12	1	98.5	1.0	90.1	2.5
Ceftazidime	≤1	>16	79.0	17.8	73.8	22.5
Ceftriaxone	≤0.25	32	81.3	9.5	78.4	24.3
Levofloxacin	≤0.5	0.5	95.6	3.2	93.9	4.4
Gentamicin	≤2	2	93.7	5.6	93.2	6.3
Imipenem	0.5	1	99.3	0.2	99.3	0.2
Piperacillin/tazobactam	2	64	82.6	6.1	-	-
Tetracycline	≤0.5	8	86.8	9.0	-	-
Trimethoprim/ sulfamethoxazole	≤0.5	≤0.5	90.9[b]	9.1[b]	90.9	9.1
K. pneumoniae (344)						
Amoxacillin/clavulanate	2	16	89.1	6.7	-	-
Cefepime	≤0.12	0.25	99.2	0.4	96.3	0.8
Ceftazidime	≤1	1	92.4	5.9	90.8	7.6
Ceftriaxone	≤0.25	0.5	95.7	1.3	92.3	7.7
Levofloxacin	≤0.5	1	92.4	3.4	91.6	7.6
Gentamicin	≤2	≤2	93.7	2.9	91.6	6.3
Imipenem	≤0.5	≤0.5	99.2	0.4	99.2	0.4
Piperacillin/tazobactam	2	16	93.7	3.8	-	-
Tetracycline	≤0.5	>8	81.5	14.3	-	-
Trimethoprim/ sulfamethoxazole	≤0.5	>2	88.0	12.0	88.0	12.0
P. mirabilis (242)						
Ampicillin	≤2	>16	87.6	12.4	-	-
Cefepime	≤0.12	≤0.12	99.6	0.4	99.2	0.8
Ceftazidime	≤1	≤1	100.0	0.0	98.8	1.2
Ceftriaxone	≤0.25	≤0.25	99.6	0.4	99.6	0.4
Levofloxacin	≤0.5	2	92.1	5.0	89.2	7.9
Gentamicin	≤2	4	93.8	0.8	90.0	6.2
Imipenem	1	2	93.4	0.0	93.4	0.0
Piperacillin/tazobactam	≤0.5	≤0.5	99.6	0.4	-	-
Trimethoprim/ sulfamethoxazole	≤0.5	>2	84.3	15.7	84.3	15.7

a. Criteria as published by the CLSI [2008] or EUCAST [2008]; - = agent not tested, or interpretive criteria not available.
b. Based on 2004 and 2005 data only.

CONCLUSIONS

- SSSI pathogen prevalence has changed minimally in North America since 1997 (exception, ß-haemolytic streptococci), with *S. aureus, P. aeruginosa, Enterococcus* spp., and *E. coli* predominating.
- Overall, *S. aureus* (and MRSA) continues to increase in prevalence, with concomitant proportional decreases being seen in several other ranking pathogens.
- Resistance rates for *Enterococcus* spp. (vancomycin), and *E. coli* and *Klebsiella* spp. (fluoroquinolones and ESBLs) are increasingly of concern, whereas key antimicrobial susceptibilities for *P. aeruginosa* have actually improved from earlier monitored periods.
- Continued surveillance monitoring of these trends, both locally and globally, provides useful information for empiric management of SSSI and in assessing needed changes to antimicrobial therapy guidelines.

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