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Occurrence of Blood Stream Infection Pathogens and Key Resistances From SENTRY Antimicrobial Surveillance Program, A 5-Year Report

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ABSTRACT

Background: The occurrence of blood stream infections (BSI) pathogens in North America (NA; 1997-2001) was determined from > 35,000 SENTRY Program isolates tested. Rates of MRSA, VRE, PEN-resistant (R) *S. pneumoniae* (SPN; PRSP), ESBL production among enteric bacilli, as well as the susceptibility (S) profiles of key anti-pseudomonal agents were assessed.
Methods: Centers sent the first 20 BSI isolates monthly. The monitor confirmed identification when necessary by appropriate methods or screening tests. Isolates were S tested and ESBL rates determined using NCCLS methods. Among 35,384 (6,337 to 7,853/year) BSI tested, only the top 9 were analyzed (≥ 90.9%/all years). *P. aeruginosa* (PSA) isolates are reported against aminoglycosides (AG), fluoroquinolones (FQ), and ß-lactams (BL). SPN analysis included PRSP, erythromycin (ER), ceftriaxone (CTX) and cefepime (CPM).
Results: The overall rank order of the BSI isolates was: *S. aureus* (SA) 25.7% > *E. coli* (EC) 17.6% > CoNS 12.0% > *Enterococcus* spp. 10.2% > *Klebsiella* spp. (KSP) 7.6% > viridans gr./ß -haemolytic strept. 5.2% > SPN 4.6% > PSA 4.4% > *Enterobacter* spp. 3.8%. The rank order of the top 5 BSI pathogens did not change over 5 years. SPN ranked 6th in 1997, 7th in 1998-99, 8th in 2000 and 9th in 2001. MRSA increased from 22.4% in 1997 to 38.7% in 2001. Mupirocin-R in SA was 5.5 - 5.8%. The VRE frequency remained stable for *E. faecalis* (2.3%), but was higher in 1999 - 2001 for *E. faecium* (50%), up from 40% in 1997. PRSP continues to increase (highest in 2001, 13.8%). ER-S among SPN has declined and no significant change in S to CTX or CPM was noted. The ESBL rates remained stable for EC (3.1%) and KSP (6.9%) in NA. PSA S rates are also stable among BL, FQ and AG with meropenem (93.5%), ciprofloxacin (84.4%) and tobramycin (94.7%) the most active among their respective classes.
Conclusions: The rank order of the top 5 BSI pathogens was unchanged over 5 years. MRSA, VRE, PRSP or ER-R SPN continue to increase. ESBL in EC and KSP remained stable and key anti-pseudomonal agents continue to be effective in NA BSI.

INTRODUCTION

The morbidity and mortality caused by blood stream infections (BSI) is a significant problem worldwide. The SENTRY Antimicrobial Surveillance Program was designed to determine antimicrobial resistance trends through a global network of sentinel hospitals in the Americas, Europe and the Asia-Pacific regions. Previous SENTRY Program data has demonstrated significant inter-regional differences in the antimicrobial susceptibility patterns among bacterial pathogens which commonly cause sepsis.

Oxacillin-resistant *Staphylococcus* spp. and penicillin-resistant *Streptococcus* spp. strains have continued to increase in most hospital settings and outpatient populations, respectively, over the last decade. Vancomycin-resistant *Enterococcus* spp. have become endemic in many institutions in North America, although the rate of resistance has stabilized due to more diligent infection control practices. The rate of extended spectrum ß-lactamase producing strains (ESBL) among enteric bacilli, particularly *E. coli* and *K. pneumoniae* in the United States and Canada is also stable, but high endemic rates have been noted in some institutions. Non-enteric Gram-negative bacilli isolates resistant to multiple antimicrobial classes have remained a problem in North America.

In this report, we document both the frequency of occurrence and the antimicrobial susceptibility profiles of BSI isolates from North American hospitals participanting in the SENTRY Program during 1997 through 2001. Previous reports from this study have not documented a significant difference in pathogen occurrence. Resistance profiles, however, have been dynamic and the maintenance of surveillance systems to monitor resistance trends remains important to their understanding or epidemiology of resistant pathogens.

MATERIALS AND METHODS

The SENTRY Program has monitored blood stream infections including bacteremia and fungemia since the inception of the program (1997). Initiated as a longitudinal comprehensive study, participating institutions have ranged from 23 (2001) - 29 (1997) medical centers in the USA. Eight participants in Canada in 1997 and five thereafter (same centers) also contributed strains to the North American surveillance network (1997 - 2001).

Each medical center contributed 20 consecutive, clinically significant blood culture isolates from individual patients during each month of the year. The organism identification, date of culture and other patient demographic information were provided by the originating site. The isolates were forwarded to the regional monitor (JMI Laboratories, Iowa) for reference susceptibility testing using a wide range of antimicrobials. ESBL rates were based on the ceftazidime or ceftriaxone or aztreonam MIC breakpoints recommended by NCCLS guidelines (≥ 2 µg/ml). All isolates were scrutinized for identification accuracy and confirmed using Vitek identification cards when needed.

All antimicrobial susceptibility testing was performed and interpreted using NCCLS broth microdilution methods and interpretive guidelines. Quality control was performed by testing *Escherichia coli* ATCC 29522 and 35218, *S. aureus* ATCC 29213, *P. aeruginosa* ATCC 27853, *S. pneumoniae* ATCC 49619, *Enterococcus faecalis* ATCC 29212 and *Haemophilus influenzae* ATCC 49247 and 49766.

RESULTS

Table 1. Frequencies of occurrence of bacterial pathogens associated with BSI in participating medical centers in the SENTRY Antimicrobial Surveillance Program (North America 1997-2001).

1997			1998			1999			2000			2001		
Rank	Pathogen (n=7854)	No (%)	Rank	Pathogen (n=6878)	No (%)	Rank	Pathogen (n=7635)	No (%)	Rank	Pathogen (n=6682)	No (%)	Rank	Pathogen (n=6337)	No (%)
1	*S. aureus*	1802(22.9)	1	*S. aureus*	1683(24.5)	1	*S. aureus*	1945(25.5)	1	*S. aureus*	1917(28.7)	1	*S. aureus*	1742(27.5)
2	*E. coli*	1461(18.6)	2	*E. coli*	1183(17.2)	2	*E. coli*	1315(17.2)	2	*E. coli*	1118(16.7)	2	*E. coli*	1133(17.9)
3	CoNS	1008(12.8)	3	CoNS	879(12.8)	3	CoNS	935(12.2)	3	CoNS	739(11.1)	3	CoNS	674(10.6)
4	*Enterococcus* spp.	745(9.5)	4	*Enterococcus* spp.	724(10.5)	4	*Enterococcus* spp.	775(10.2)	4	*Enterococcus* spp.	709(10.6)	4	*Enterococcus* spp.	660(10.4)
5	*Klebsiella* spp.	592(7.5)	5	*Klebsiella* spp.	518(7.5)	5	*Klebsiella* spp.	597(7.8)	5	*Klebsiella* spp.	494(7.4)	5	*Klebsiella* spp.	488(7.7)
6	*S. pneumoniae*	441(5.6)	6	ß / viridans *Streptococcus*	385(5.6)	6	ß / viridans *Streptococcus*	424(5.6)	6	ß / viridans *Streptococcus*	334(5.0)	6	ß / viridans *Streptococcus*	288(4.6)
7	ß / viridans Streptococcus	413(5.2)	7	*S. pneumoniae*	345(5.0)	7	*S. pneumoniae*	349(4.6)	7	*P. aeruginosa*	306(4.6)	7	*Enterobacter* spp.	259(4.1)
8	*P. aeruginosa*	359(4.6)	8	*P. aeruginosa*	306(4.4)	8	*P. aeruginosa*	335(4.4)	8	*S. pneumoniae*	261(3.9)	8	*P. aeruginosa*	244(3.9)
9	*Enterobacter* spp.	312(4.0)	9	*Enterobacter* spp.	230(3.3)	9	*Enterobacter* spp.	287(3.8)	9	*Enterobacter* spp.	239(3.6)	9	*S. pneumoniae*	218(3.4)
10	Acinetobacter spp.	117(1.5)	10	P. mirabilis	112(1.6)	10	Serratia spp.	136(1.8)	10	P. mirabilis	98(1.5)	10	P. mirabilis	105(1.7)
	Percentage of Total [a]	92.2			92.4			93.1			93.1			91.8

a. Proportion of strains in the top 10 pathogens.

Table 2. Antimicrobial susceptibility among blood stream isolates from SENTRY North America 1997 through 2001 for selected antimicrobial agents.

		% susceptible (no. tested)				
Organism	Antimicrobial agent	1997	1998	1999	2000	2001
S. aureus	Oxacillin	77.6(1802)	72.2(1683)	69.3(1945)	65.6(1917)	61.3(1742)
	Mupirocin	NT[a]	NT	NT	94.2(1917)	94.5(1742)
E. faecium	Vancomycin	59.9(167)	56.6(173)	49.9(165)	51.9(160)	50.0(184)
E. faecalis	Vancomycin	96.2(469)	97.5(442)	99.4(470)	96.6(408)	98.8(414)
S. pneumoniae	Penicillin susc.	65.8(441)	81.2(345)	78.2(349)	78.2(261)	76.6(218)
	Penicillin resist.	9.4(441)	8.4(345)	10.3(349)	7.6(261)	13.8(218)
	Erythromycin	89.3(441)	89.6(345)	88.5(349)	84.7(261)	83.5(218)
	Ceftriaxone	NT	NT	96.6(349)	97.3(261)	95.0(218)
	Cefepime	94.6(441)	98.6(345)	98.0(349)	98.1(261)	98.2(218)
E. coli	Ceftazidime	99.2(1461)	98.6(1183)	99.4(1315)	99.0(1118)	98.9(1133)
	Cefepime	99.9(1461)	99.7(1183)	99.8(1315)	100.0(1118)	99.3(1133)
	Ciprofloxacin	97.5(1461)	97.4(1183)	95.4(1315)	95.2(1118)	92.6(1133)
	Gentamicin	95.6(1461)	96.4(1183)	96.9(1315)	97.8(1118)	96.6(1133)
Klebsiella spp.	Ceftazidime	96.3(592)	95.4(518)	96.3(597)	96.0(494)	95.2(488)
	Cefepime	98.8(592)	99.4(518)	98.8(597)	98.7(494)	99.7(488)
	Ciprofloxacin	96.1(592)	95.6(518)	96.5(597)	96.0(494)	95.0(488)
	Gentamicin	95.6(592)	95.0(518)	96.6(597)	97.2(494)	94.0(488)
P. aeruginosa	Tobramycin	95.0(359)	96.4(306)	97.0(335)	91.5(306)	93.4(244)
	Ciprofloxacin	88.9(359)	85.9(306)	85.4(335)	78.8(306)	83.2(244)
	Gatifloxacin	79.9(359)	81.4(306)	79.7(335)	76.8(306)	80.7(244)
	Ceftazidime	86.9(359)	83.0(306)	85.1(335)	88.2(306)	87.7(244)
	Cefepime	88.3(359)	87.9(306)	88.1(335)	89.5(306)	88.5(244)
	Piperacillin/Tazobactam	92.8(359)	91.1(306)	89.9(335)	92.4(306)	91.0(244)
	Imipenem	87.5(359)	91.8(306)	90.7(335)	92.2(306)	91.0(244)
	Meropenem	95.0(359)	95.4(306)	93.1(335)	92.2(306)	91.8(244)
Enterobacter spp.	Ceftazidime	77.9(312)	75.2(230)	77.7(287)	81.2(239)	79.9(259)
	Cefepime	100.0(319)	99.1(230)	99.0(287)	99.2(239)	98.5(259)

a. Antimicrobial agent not tested.

- During the five year study period (1997 - 2001), a total of 35,384 blood stream infection isolates were collected by North American SENTRY Program participants. The frequency of the 10 most common pathogens accounted for 92-93% of all BSI (Table 1). The rank order of the top five pathogens did not change during this study interval.
- Between 1997 and 2000, the percentage of BSI caused by *S. aureus* increased (22.9 to 28.7%).
- Table 2 shows that oxacillin-resistant *S. aureus* isolates have markedly increased from 22.4% (1997) to 38.7% (2001). The isolation of mupirocin-resistant *S. aureus* was stable (5.5 - 5.8%) during the two monitored years (2000 and 2001).
- Vancomycin resistance among *E. faecalis* isolates has remained stable over the past five years. Vancomycin resistance among *E. faecium* isolates have also remained stable during the last two years after increasing from 40% in 1997 to 50% in 1999.
- Invasive pneumococcal disease has gradually decreased each study year. However, *S. pneumoniae* isolates from BSI have shown an increase in high-level resistance to penicillin (MIC, ≥ 2 µg/ml) from 9.4% in 1997 to 13.8% in 2001. Relative to this decline in penicillin susceptibility is the diminished activity of macrolides which has also steadily decreased from 89.3% (1997) to 83.5% (2001).

Table 3. Bloodstream infection isolates of *E. coli* and *Klebsiella* spp. isolated from the SENTRY Program (1997 – 2001) which met ESBL screening criteria (NCCLS).

	Percent of ESBL positive (no. tested)					
Organism	1997	1998	1999	2000	2001	Average
E. coli	2.7(1461)	3.8(1183)	2.4(1315)	2.7(1118)	3.7(1133)	3.1(1242)
Klebsiella spp.	6.9(592)	9.7(518)	5.7(597)	6.3(494)	6.1(488)	6.9(538)

- The activity of "third- and fourth-generation" cephalosporins has been maintained over the five-year period (> 95%) for enteric bacilli. ESBL rates for *E. coli* (3.1%) and *Klebsiella* spp. (6.9%) have remained stable in North America over the past five years using ceftazidime as a phenotypic marker (Table 3).
- The susceptibility rates for anti-pseudomonal agents show continued activity among ß-lactams, fluoroquinolones, and aminoglycosides with meropenem (93.5%), ciprofloxacin (84.4%) and tobramycin (94.7%) being the most active compounds in their respective drug classes.
- Susceptibility rates for *Enterobacter* spp. show ceftazidime (75.2 - 81.2%) was stable and cefepime has remained highly active (≥ 99%) during the last five years.

CONCLUSIONS

- The rank order of the top five blood stream isolates remained unchanged during the past five years. In contrast, the isolation of *S. pneumoniae* has gradually decreased.
- Increasing resistance was observed among *S. aureus* and *S. pneumoniae*. ESBL rates in *E. coli* and *Klebsiella* spp. remains stable overall. The activity of several anti-pseudomonal agents continue to be effective in North America.
- On-going surveillance remains essential and should be used to limit the extent of resistance worldwide by making appropriate, guided, empiric therapy choices.

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