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Assessment of Pathogens and Resistance Patterns Among Infected Patients in Intensive Care Units in North America (NA): Initial Focused Report from the SENTRY Antimicrobial Surveillance Program (2001)

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ABSTRACT

Background: The SENTRY Program initiated a focused objective to assess the Intensive Care Unit (ICU) pathogens and determine antimicrobial resistance (R) patterns indexed by site and patient demographics.
Methods: From 28 ICUs 1,321 strains from blood, respiratory tract, urine and wound sites were tested by NCCLS susceptibility (S) methods against 43 antimicrobials at a central laboratory.
Results: *S. aureus* (SA n=319;24%), *P. aeruginosa* (PSA 161;12%), *E. coli* (EC 134;10%), *Klebsiella* spp (KSP 117;9%), Enterococcus spp. (ECS 95;7%), *Coagulase negative staphylococci* (CoNS 93;7%), and *Enterobacter* spp (EB 92;7%) were the top pathogens. The incidence was similar to ICARE reports; exception CoNS (14% or 2x greater) which was the most prevalent pathogen (1989 - 98). MRSA rate was 51% and vancomycin (VAN; MIC_{90}: 1 - 2 µg/ml/R = 0.0%), teicoplanin (TEI; 1-8/0.0 - 1.1%), linezolid (LZD; 2/0.0) and quin/dalfo (QD; 0.5/0.0) were the most active against staphylococci. Amikacin (R = 3.1%), cefepime (CPM; 8.1), and pip/tazo (P/T; 130), tobramycin (TOB; 12.4), meropenem (MER; 12) and the lowest R rates in PSA. Among agents tested against EC, KSP and EB, imipenem (MIC_{90}; 0.12 - 2 µg/ml), MER (≤ 0.06 - 0.12), amikacin (2 - 4) and CPM (≤ 0.12 - 2) showed the lowest R rates of 0.0 - 3.4%. Agents with high S vs these species were: GENT (90 - 96%), TOB (86 - 96), CIPRO (85 - 89), and GATI (86 - 92). ESBL phenotypes were 11.2 and 17.1% in EC and KSP, respectively (12% in ICARE 1997). Finally, VAN (R = 28.4%/MIC_{90} > 16 µg/ml) and TEI (22.1/> 16) were less effective against ECS, however, LZD (R = 1.1%/MIC_{90}, 2 µg/ml) had the best activity, and the specific resistance (G2576U) was identified.
Conclusions: CPM and carbapenems for Gram-negatives, and LZD for Gram-positives provide the widest empiric clinical utility via cited S patterns against contemporary ICU pathogens. Accurate surveillance for antimicrobial R requires use of longitudinal, complimentary programs (SENTRY, ICARE) to guide effective interventions.

INTRODUCTION

Patients in the Intensive Care Unit (ICU) are often at higher risk for nosocomial infections such as pneumonia, urinary tract infections, and bloodstream infection. The seriousness of illness associated with being in the intensive care unit lengthens the time that patients are exposed to potentially harmful bacteria in the hospital environment. Bacteria from colonized patients can transfer and infect an entire ICU via carriage on the unwashed hands of healthcare workers. Patients transferred from other facilities can also bring in bacteria that they were exposed to, and thus introduce new bacteria to the ICU. ICU patients are also more susceptible to nosocomial infections because most membrane and skin barriers are compromised by the use of invasive devices such as indwelling catheters, central lines, and mechanical ventilation apparatus.

The ICARE Program has provided 10 years of data describing pathogens associated with nosocomial infections within the ICU setting, and has effectively documented the importance of the ICU setting in determining prevalence rates of antimicrobial resistance. In 2001, the SENTRY Antimicrobial Surveillance Program initiated an objective focusing on antimicrobial resistance patterns in ICU infections.

MATERIALS AND METHODS

A total of 1,321 strains from 28 ICUs in North America isolated from bloodstream, respiratory, urinary, tissue, body fluids, and cutaneous sites were collected. The organisms were identified by the participant sites and sent to the SENTRY Program monitor (North Liberty, Iowa) for susceptibility testing.

MICs were performed for up to 43 antimicrobials using reference panels prepared by TREK Diagnostics (Westlake OH) using National Committee for Clinical Laboratory Standards (NCCLS) methods. The production of extended-spectrum ß-lactamases (ESBLs) was confirmed using the ESBL E-test strip (AB BIODISK, Solna, Sweden).

RESULTS

- *S. aureus* (n=319, 24%), *P. aeruginosa* (161, 12%), *E. coli* (134, 10%), *Klebsiella* spp. (117, 9%), Enterococcus spp. (95, 7%), *Coagulase negative staphylococci* (93, 7%), and *Enterobacter* spp (92, 7%), were the top pathogens and these isolates represented nearly 80% of bacteria obtained during the initial year (**Table 1**).

Table 1. Frequency of occurrence of 1,321 bacterial pathogens from ICU's in North American medical centers participating in the 2001 SENTRY Program

Organism	Number of isolates/% of total
Staphylococcus aureus	319 (24.1)
Pseudomonas aeruginosa	161 (12.2)
Escherichia coli	134 (10.1)
Klebsiella spp.	117 (8.9)
Enterococcus spp.	95 (7.2)
Coagulase negative staphylococci	93 (7.0)
Enterobacter spp.	92 (7.0)
Acinetobacter spp.	53 (4.0)
Serratia spp.	40 (3.0)
Stenotrophomonas maltophilia	40 (3.0)
Haemophilus influenzae	37 (2.8)
Streptococcus pneumoniae	31 (2.3)
Other streptococci	23 (1.7)
Other species	86 (6.7)

RESULTS

Table 2. Activities and spectrum for activity of 20 antimicrobial agents tested against the four most prevalent causes of Gram-negative infection in the SENTRY Program from Participating ICU's in North America (45% of total isolates).

	Pseudomonas aeruginosa (161)		*Escherichia coli* (134)		*Klebsiella* spp. (117)		*Enterobacter* spp. (92)		*Serratia* spp. (40)		*Acinetobacter* spp. (53)	
	Activity[a] by organism (no. tested):											
Antimicrobial class/ agent tested	MIC50/90	% S/R	$MIC_{50/90}$	% S/R	$MIC_{50/90}$	% S/R	$MIC_{50/90}$	% S/R	$MIC_{50/90}$	% S/R	$MIC_{50/90}$	% S/R
Penicillins												
Ampicillin	>16/>16	0.0/97.5	>16/>16	46.3/52.2	>16/>16	0.9/82.9	>16/>16	1.1/85.9	>16/>16	5.0/80.0	>16/>16	5.7/75.5
Amoxicillin/Clavulanate	>16/>16	0.6/97.5	8/>16	74.6/13.4	4/16	86.3/6.0	>16/>16	1.1/96.7	>16/>16	0.0/100.0	>16/>16	22.6/58.5
Piperacillin	8/>128	83.2/16.8	8/>128	56.7/33.6	8/>128	70.9/24.8	2/>128	70.7/19.5	2/8	97.5/2.5	32/>128	35.8/37.8
Piperacillin/Tazobactam	8/>64	87.0/13.0	2/8	95.5/3.0	2/32	89.7/6.0	2/64	73.9/8.7	2/4	97.5/2.5	16/>64	58.5/30.2
Ticarcillin	32/>128	68.9/31.1	32/>128	49.3/46.3	128/>128	2.6/79.5	4/>128	64.8/33.0	4/>128	85.0/12.5	32/>128	49.1/35.9
Ticarcillin/Clavulanate	32/>128	68.3/31.6	8/64	69.4/8.2	4/128	77.8/12.0	4/>128	65.2/29.3	4/16	95.0/5.0	32/>128	49.1/35.8
Cephalosporins												
Cefoxitin	>32/>32	c	4/16	80.6/9.7	4/32	80.3/11.1	>32/>32	3.3/96.8	16/>32	10.0/45.0	>32/>32	c
Cefuroxime	>16/>16	c	4/16	84.3/7.5	4/>16	74.4/17.1	8/>16	50.0/37.0	>16/>16	2.5/92.5	>16/>16	c
Ceftazidime	≤2/>16	77.0/19.3	≤2/≤2	97.0/3.0(8.2)[b]	≤2/>16	85.5/13.7(16.2)[b]	≤2/>16	71.7/26.1	≤2/4	97.5/0.0	8/>16	56.6/37.7
Ceftriaxone	>32/>32	10.6/65.5	≤0.25/≤0.25	97.0/1.5(4.4)[b]	≤0.25/16	89.7/2.6(15.4)[b]	≤0.25/32	77.2/9.8	≤0.25/2	92.5/0.0	16/>32	24.5/35.8
Cefepime	4/16	80.1/8.1	≤0.12/≤0.12	100.0/0.0	≤0.12/1	98.3/1.7(15.4)[b]	≤0.12/2	98.9/0.0	≤0.12/0.5	97.4/0.0	8/>16	50.9/35.8
Other ß-lactams												
Aztreonam	8/>16	60.2/26.7	≤0.12/2	96.3/2.2(11.1)[b]	≤0.12/>16	86.3/12.8	≤0.12/>16	70.7/17.4	≤0.12/0.5	95.0/5.0	>16/>16	5.7/69.8
Imipenem	1/>8	78.3/16.1	0.12/0.12	100.0/0.0	0.12/0.25	100.0/0.0	0.5/2	97.8/2.2	0.5/1	97.5/2.5	0.25/>8	81.1/11.3
Meropenem	1/>8	79.5/12.4	≤0.06/≤0.06	100.0/0.0	≤0.06/≤0.06	100.0/0.0	≤0.06/0.12	97.8/1.1	≤0.06/0.12	100.0/0.0	1/>8	79.2/20.8
Fluoroquinolones												
Ciprofloxacin	0.25/>2	69.6/24.8	≤0.015/>2	87.3/12.7	0.03/>2	84.6/12.8	≤0.015/2	89.1/9.8	0.06/2	85.0/7.5	1/>2	52.8/1.9
Gatifloxacin	1/>4	62.7/25.5	≤0.03/>4	87.3/11.9	0.06/4	86.3/5.1	≤0.03/2	92.4/3.3	0.25/4	87.5/7.5	0.5/>4	54.7/37.7
Garenoxacin	2/>4	c	≤0.03/>4	c	0.12/4	c	0.12/4	c	c	c	c	c
Aminoglycosides												
Amikacin	4/8	96.9/3.1	2/4	99.3/0.0	1/2	95.7/3.4	2/4	97.8/1.1	2/4	100.0/0.0	4/>32	81.1/11.3
Gentamicin	2/>8	80.7/13.7	≤1/2	92.5/5.3	≤1/8	89.7/6.8	≤1/≤2	95.7/4.3	≤1/≤2	90.0/2.5	2/>8	52.8/34.0
Tobramycin	0.5/>16	87.6/12.4	1/2	96.3/2.9	0.5/8	86.3/7.7	0.5/1	94.6/5.4	2/4	90.0/7.5	1/>16	75.5/20.8

a. MIC_{50} and MIC_{90} in µg/ml at which 50 and 90% of the isolates, respectively, were inhibited. % S, percent of isolates susceptible per NCCLS [2002] criteria, % R percent of isolates resistant using NCCLS [2002] criteria.
b. Percentage in parenthesis indicates the ESBL phenotype rates using MIC concentrations of ≥ 2 µg/ml for aztreonam or ceftazidime or ceftriaxone.
c. No interpretive criteria have been established.

- The most active antimicrobials against *P. aeruginosa* were amikacin (Susceptible/Resistant- 97/3%), tobramycin (88/12%), piperacillin/tazobactam (87/13%), cefepime (80/8%), and meropenem (80/12%) (**Table 2**).

- Imipenem and meropenem demonstrated complete activity against *E. coli* and *Klebsiella* spp., but meropenem was ≥ two-fold more potent. Other agents demonstrating acceptable susceptibilities included: cefepime (100, 98%, respectively), amikacin (99, 96%), ceftriaxone (97, 90%), piperacillin/tazobactam (96, 90%), and gentamicin- (93, 90%) (**Table 2**).

- Rank order of susceptibilities against the *Enterobacter* spp. was: cefepime (99%) > imipenem = meropenem = amikacin (98%) > gentamicin (96%) > tobramycin (95%) > gatifloxacin (92%) > ciprofloxacin (89%) (**Table 2**).

- The incidence of ESBL phenotypes ranged from 4.4 to 16.2% of *E. coli* and *Klebsiella* spp. strains, respectively. However, upon further confirmation only 33% of *E. coli* strains and 83% of *Klebsiella* spp. were positive for the presence of an ESBL (**Table 2**).

- The incidence of methicillin-resistant *S. aureus* was 51%. Vancomycin and teicoplanin (MIC_{90},1µg/ml), linezolid (MIC_{90}, 2µg/ml), and quinupristin/dalfopristin (MIC_{90}, 0.5µg/ml) demonstrated complete activity. Linezolid (MIC_{90}, 2 µg/ml), vancomycin (2 µg/ml), and quinupristin/dalfopristin (0.5 µg/ml) demonstrated 100% susceptibilities to CoNS (**Table 3**).

- The incidence of resistance among enterococcal isolates to vancomycin and teicoplanin was 28 and 22%, respectively (**Table 3**). *E. faecium* represented 93% of all glycopeptide-resistant enterococci (25/27).

- Gatifloxacin (Susceptible/Resistant-90/5%), levofloxacin (90/7.5%), and trimethoprim/sulfamethoxazole (90/10%) were the most active antimicrobials against *Stenotrophomonas maltophilia* isolates (**Table 4**).

Table 3. Activities and spectrum for activity of 18 antimicrobial agents tested against the three most prevalent causes of Gram-positive infection in the SENTRY Program from Participating ICU's in North America (38% of total isolates).

	Staphylococcus aureus (319)		*Enterococcus* spp. (95)		Coagulase-negative staphylococci (93)	
	Activity[a] by organism (no. tested):					
Antimicrobial class/ agent tested	$MIC_{50/90}$	% S/R	$MIC_{50/90}$	% S/R	$MIC_{50/90}$	% S/R
Penicillins						
Oxacillin	>8/>8	48.6/51.4	>8/>8	[b]	8/>8	16.1/83.9
Penicillin	16/>32	4.4/95.6	4/>32	64.2/35.8	8/32	65/93.5
Cephalosporins						
Cefazolin	>16/>16	0.0/99.4	NT[b]	[b]	NT[b]	[b]
Ceftazidime	16/>16	46.1/44.5	>16/>16	[b]	>16/>16	19.4/55.9
Ceftriaxone	16/>32	49.8/29.5	>32/>32	[b]	16/>32	40.9/20.4
Cefepime	4/>16	65.5/28.2	>16/>16	[b]	4/>16	68.8/17.2
Other ß-lactams						
Imipenem	0.12/>8	79.6/18.2	2/>8	[b]	1/>8	75.3/22.6
Fluoroquinolones						
Ciprofloxacin	>2/>2	47.0/52.4	>2/>2	37.9/55.8	>2/>2	33.3/65.6
Gatifloxacin	2/>4	55.8/25.7	>4/>4	46.3/51.6[c]	2/>4	79.6/18.3
Macrolides-Lincosidamines-Streptogramins						
Clindamycin	0.12/>8	56.1/43.9	>8/>8	[b]	>8/>8	48.4/51.6
Erythromycin	>8/>8	36.7/63.3	>8/>8	13.7/56.9	>8/>8	25.9/73.1
Quinupristin/Dalfopristin	0.5/0.5	100.0/0.0	4/8	37.9/57.9	0.25/0.5	100.0/0.0
Glycopeptides						
Vancomycin	1/1	100.0/0.0	2/>16	70.5/28.4[c]	2/2	100.0/0.0
Teicoplanin	0.5/1	100.0/0.0	0.25/>16	74.7/22.1[c]	2/8	94.6/1.1
Other classes						
Chloramphenicol	8/8	90.9/1.6	8/16	86.3/8.4	4/8	95.7/4.3
Linezolid	2/2	100.0/0.0	2/2	95.8/1.1	1/2	100.0/0.0
Tetracycline	≤4/>4	95.6/3.4	>8/>8	38.9/60.0	≤4/>8	84.9/14.0
Trimethoprim/sulfamethoxazole	≤0.5/≥0.5	96.2/3.8	≤0.5/>2	[b]	2/>2	51.6/48.4

a. MIC_{50} and MIC_{90} in µg/ml at which 50 and 90% of the isolates, respectively, were inhibited. % S, percent of isolates susceptible per NCCLS [2002] criteria, % R percent of isolates resistant using NCCLS [2002] criteria.
b. No interpretive criteria have been published. NT = Not tested
c. 78% of vancomycin-resistant strains (21/27) were characterized as Van A patterns of resistance.

Table 4. Activities and spectrum for activity of seven antimicrobial agents tested against *Stenotrophomonas maltophilia* in SENTRY Program for participating ICU's in North America.

	S. maltophilia (40)	
	Activity[a] by organism (no. tested)	
Antimicrobial class/agent tested	$MIC_{50/90}$	% S/R
Penicillins		
Ticarcillin/Clavulanate	32/128	42.5/17.5
Other ß-lactams		
Meropenem	>8/>8	2.5/97.5
Fluoroquinolones		
Ciprofloxacin	2/>2	35.0/37.5
Gatifloxacin	1/2	90.0/5.0
Levofloxacin	1/2	90.0/7.5
Other Classes		
Tetracycline	>8/>8	5.0/82.5
Doxycycline[b]	>8/>8	5.0/82.5
Trimethoprim/Sulfamethoxazole	≤0.5/1	90.0/10.0

a. MIC_{50} and MIC_{90} in µg/ml at which 50 and 90% of the isolates, respectively, were inhibited. % S, percent of isolates susceptible per NCCLS [2002] criteria, % R percent of isolates resistant using NCCLS [2002] criteria.
b. Results based on those obtained for tetracycline testing.

CONCLUSIONS

- Cefipime, the carbapenems, and linezolid demonstrated excellent susceptibility and low resistance patterns against the most prevalent bacterial pathogens in SENTRY Program ICUs during the first year of this objective.
- ICU bacterial isolate frequencies are similar to those reported from the ICARE project with the exception of CoNS (14%), which was identified as the most prevalent pathogen during the 10-year surveillance period.
- As ESBL phenotypes increase in North America, epidemic clusters have been routinely identified. Three *K. pneumoniae* isolates from New York were ribotyped as the same strain and two additional *K. pneumoniae* isolates from Boston were also detected as an epidemic.
- The percentage of enterococcal isolates resistant to vancomycin was significantly higher than that reported in the ICARE program (22% in 1997). However, the prevalence of Van A patterns of resistance (78%) was similar to the three-year report (73%) from the SENTRY Program, which included both ICU and non-ICU patients in North America.
- Continued evaluation for antimicrobial resistance requires complimentary longitudinal surveillance programs such as SENTRY and ICARE in order to allow the development of therapeutic strategies to avoid resistance-related adverse outcomes.

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