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Geographic Occurrence and Resistance Patterns Among Pathogens Isolated from Skin and Soft Tissue Infections (SSTI): A Report from the SENTRY Antimicrobial Surveillance Program (2004)

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SENTRY ANTIMICROBIAL SURVEILLANCE

AMENDED ABSTRACT

Background: SSTI and wound infections in hospitalized patients were assessed by the SENTRY Program in 2004 to detect pathogen prevalence and resistance (R) variation within three geographic regions: North America (NA), Latin America (LA) and Europe (EU).
Methods: 50 pathogens/site were collected from medical centers (22 NA, 10 LA and 23 EU) and susceptibility (S) tested by CLSI broth microdilution methods; ESBL rates were determined using the disk approximation test. Possible epidemic clones were subjected to automated ribotyping and PFGE analysis.
Results: SSTI pathogens by region and key resistance markers:

Pathogen	Pathogen rate in % (no. strains) NA (1,239)/LA (553)/EU (1,167)	R marker	% R NA/LA/EU
S. aureus (SA)	51.6/31.6/40.5	MRSA	47.6/38.3/22.4
Enterococci (ENC)	9.8/6.3/5.6	VRE	14.8/2.9/7.7
P. aeruginosa (PSA)	8.2/9.9/9.4	Ceftazidime (CTZ)	7.8/23.6/14.5
E. coli (EC)	6.9/16.3/11.4	Ciprofloxacin (CIPRO)	26.7/44.5/28.6
ß-haemolytic streptococci	5.3/1.3/5.3	Erythromycin (ERY)	25.8/14.3/17.7
Enterobacter spp. (ENT)	4.1/5.6/5.3	CTZ	25.5/38.7/22.6
Klebsiella spp. (KSP)	4.0/8.1/4.3	CIPRO	4.1/28.9/10.0
P. mirabilis (PM)	2.6/4.5/3.8	CIPRO	12.5/20.0/11.4

Pathogen prevalence and rank order varied considerably between regions with EC being 2nd in LA and EU, but 4th in NA. Among key R markers, MRSA and VRE were highest in NA, whereas LA had the highest R among PSA and ENT to CTZ; and among EC, KSP and PM to CIPRO. Three ESBL-positive EC clones and two *E. cloacae* (ECL) clones were detected in one Turkish medical center. In a second Turkish site, an ECL clone with an IMP-1 metallo-ß-lactamase was observed. ESBLs (%) in EC, KSP and PM were NA, 12.8/16.3/0.0; LA, 24.4/62.2/24.0; and EU, 19.5/24.0/11.4, respectively.
Conclusions: Globally, SA remains the predominant SSTI pathogen. ENC is 2nd only in NA; EC and PSA are 2nd and 3rd in both LA and EU. The continued emergence of R among Gram-negative pathogens, including ESBL-positive strains, expanded most dramatically in LA; clonal spread of ESBL- and carbapenemase-producing strains as documented by the SENTRY Program is a worrisome development that continues to be increasingly detected globally.

INTRODUCTION

Skin and soft tissue infections (SSTIs) are often mild and may be treated with oral drugs. However, moderate or severe cases of SSTI may require hospitalization and parenteral therapy. In 1995 only, an estimated 330,000 patients required hospital treatment for SSTI in the United States (USA). In addition, surgical site infections (SSI) are the second most common nosocomial infection in the USA with annual estimates of 500,000 cases causing 3.7 million excess hospital days and > $1.6 billion in additional hospital charges.

Antimicrobial treatment options for SSTI continue to be problematic. Such infections are typically managed with antimicrobial therapy based on the results of cultures and susceptibility testing. However, several factors may cause clinical failure, including inadequate antimicrobial concentrations at the site of infection, the presence of more than one pathogen and an inadequate coverage. Nonetheless, initial antimicrobial therapy usually remains empiric, it is therefore, important to follow longitudinal patterns of antimicrobial resistance in programs that address SSTI.

This report from the SENTRY Antimicrobial Surveillance Program presents pathogen prevalence, resistance rates variation from geographic regions in North America, Latin America and Europe associated with SSTI and SSI in hospitalized patients.

MATERIALS AND METHODS

Bacterial isolates. The SENTRY Program tested 2,959 pathogens causing SSTI or SSI in hospitalized patients from 55 medical centers over three continents in 2004. The distribution of medical centers included: North America (22 sites; all from the USA); Latin America (10 sites including Argentina, Brazil, Chile, Mexico and Venezuela); and Europe (23 sites including France, Germany, Ireland, Israel, Italy, Spain, Sweden, Switzerland, Turkey and the United Kingdom). Each medical center forwarded 50 consecutive pathogens determined to be clinically significant by local criteria to the regional monitor (JMI Laboratories, North Liberty, IA, USA) along with clinical/patient demographics. The isolates were subcultured, reviewed for identification accuracy and then stored at -80°C. Questionable species identification was confirmed by biochemical tests and/or the Vitek System (bioMerieux, Hazelwood, MO, USA).

Susceptibility testing. Susceptibility testing was performed using reference broth microdilution methods according to Clinical and Laboratory Standards Institute (CLSI) procedures. Quality control (QC) was performed weekly using *Escherichia coli* ATCC 25922 and 35218, *Staphylococcus aureus* ATCC 29213, *Pseudomonas aeruginosa* ATCC 27853, *Streptococcus pneumoniae* ATCC 49619 and *Enterococcus faecalis* ATCC 29212.

E. coli, *Klebsiella* spp. and *Proteus mirabilis* isolates with ceftazidime or ceftriaxone or aztreonam MIC values of ≥ 2 μg/ml were screened for ESBL production by the disk approximation method. *Pseudomonas* spp., *Acinetobacter* spp. and *Enterobacter* spp. resistant to carbapenems and ceftazidime were screened for metallo-ß-lactamase (MßL) enzymes also by a disk approximation method.

Molecular typing. Isolates with similar susceptibility profiles from the same medical center and temporally related in time and location were typed by automated ribotyping and pulsed-field gel electrophoresis (PFGE).

RESULTS

- The rank order of pathogens from North America for 2004 was: *S. aureus* (51.6%) > enterococci (9.8%) > *P. aeruginosa* (8.2%) > *E. coli* (6.9%) > ß-haemolytic streptococci (5.3%) > *Enterobacter* spp. (4.1%) > *Klebsiella* spp. (4.0%) > *P. mirabilis* (2.6%) > CoNS (1.9%) > *Serratia* spp. (1.4%) > *Acinetobacter* spp. (0.8%) > Indole-positive *Proteus* (0.6%; Table 1).
- *S. aureus* was the predominant pathogen representing 43.5% of all pathogens collected over all continents. Enterococci was the second most frequently isolated pathogen in North America (9.8%), fourth in Europe (5.6%) and fifth in Latin America (6.3%). ß-haemolytic streptococci was the fifth most frequent pathogen in North America (5.3%) and Europe (5.3%), but fell to 12th in Latin America (1.3%). The top four Gram-positive pathogens account for 68.6% of the isolates in North America, 56.3% in Europe, but only 44.5% in Latin America (Table 1).
- *E. coli* and *P. aeruginosa* were the second and third most frequent pathogens in Latin America and Europe. In addition, *Klebsiella* spp. ranked fourth in Latin America (8.1%), pushing the Gram-negatives to 55.2% of total strains, compared to 30.4% in North America and 42.9% in Europe (Table 1).
- Oxacillin resistance rate among *S. aureus* was highest in North America (47.6%), followed by Latin America (38.3%) and Europe (22.4%; Table 2).
- Vancomycin resistance in enterococci was highest in North America (14.8%) over Europe (7.7%) and Latin America (2.9%; Table 2).
- ß-haemolytic streptococci resistance rates for erythromycin and clindamycin were 25.8 and 10.6% in North America, 17.7 and 3.2% in Europe and 14.3 and 14.3% in Latin America, respectively. The percentages of strains exhibiting mef(A) phenotype (erythromycin-resistant, clindamycin-susceptible) were 58.9, 81.9 and 0.0%, respectively.

Table 1. Rank order of skin and soft tissue infections (SSTI) from medical centers in North America, Latin America and Europe (SENTRY Program, 2004).

Rank	Organism	All regions (2,959)	No. of organisms tested (%) by region: North America (1,239)	Latin America (553)	Europe (1,167)
1	*S. aureus*	1,287 (43.5)	639 (51.6)	175 (31.6)	473 (40.5)
2	*E. coli*	309 (10.4)	86 (6.9)	90 (16.3)	133 (11.4)
3	*P. aeruginosa*	267 (9.0)	102 (8.2)	55 (9.9)	110 (9.4)
4	Enterococci	222 (7.5)	122 (9.8)	35 (6.3)	65 (5.6)
5	*Klebsiella* spp.	144 (4.9)	49 (4.0)	45 (8.1)	50 (4.3)
6	*Enterobacter* spp.	144 (4.9)	51 (4.1)	31 (5.6)	62 (5.3)
7	ß-haemolytic streptococci	135 (4.6)	66 (5.3)	7 (1.3)	62 (5.3)
8	CoNS	109 (3.7)	23 (1.9)	29 (5.2)	57 (4.9)
9	*P. mirabilis*	101 (3.4)	32 (2.6)	25 (4.5)	44 (3.8)
10	Indole-positive *Proteae*	50 (1.7)	8 (0.6)	11 (2.0)	31 (2.7)
Total		2,768 (93.5)	1,178 (95.1)	503 (91.0)	1,087 (93.1)

Table 2. Antimicrobial activity of selected antimicrobial agents tested against eight pathogens causing SSTIs in North America, Latin America and Europe (SENTRY Program, 2004).

Organism /antimicrobial agent	North America (rank; no. by region) MIC 50%	90%	%S/R[a]	Latin America (rank; no. by region) MIC 50%	90%	%S/R[a]	Europe (rank; no. by region) MIC 50%	90%	%S/R[a]
S. aureus		(1; 639)			(1; 175)			(1; 473)	
Oxacillin	1	>2	52.4/47.6	0.5	>2	61.7/38.3	0.5	>2	77.6/22.4
Penicillin	16	>32	8.9/91.1	32	>32	2.9/97.1	8	>32	17.8/82.2
Clindamycin	0.12	>8	76.7/23.2	0.12	>8	64.0/36.0	0.12	0.25	90.9/8.9
Q/D	≤0.25	0.5	100.0/0.0	0.5	0.5	100.0/0.0	0.5	0.5	98.9/1.1
Ciprofloxacin	0.5	>4	63.2/36.0	0.5	>4	62.3/37.7	0.25	>4	75.5/23.3
Levofloxacin	0.25	>4	64.3/34.3	0.25	>4	62.3/36.0	0.12	>4	76.7/21.6
Gentamicin	≤2	≤2	97.2/2.7	≤2	>8	68.0/31.4	≤2	≤2	92.4/6.8
Rifampin	≤0.5	≤0.5	98.1/1.3	≤0.5	2	84.6/1.1	≤0.5	≤0.5	97.3/2.1
Tetracycline	≤2	≤2	93.9/5.6	0.5	>8	76.6/22.9	≤2	≤2	92.0/7.6
Trim/Sulfa	≤0.5	≤0.5	98.3/1.7	≤0.5	>2	84.0/16.0	≤0.5	≤0.5	97.0/3.0
Vancomycin	1	1	100.0/0.0	1	1	100.0/0.0	1	1	100.0/0.0
Teicoplanin	0.5	1	100.0/0.0	1	2	100.0/0.0	0.5	1	100.0/0.0
Linezolid	2	2	100.0/-[a]	2	2	100.0/-	2	2	100.0/-
E. coli		(4; 86)			(2; 90)			(2; 133)	
Ceftriaxone	≤0.25	32	88.4/9.3	≤0.25	>32	81.1/17.8	≤0.25	32	86.5/9.8
Cefepime	≤0.12	4	91.9/7.0	≤0.12	>16	85.6/12.2	≤0.12	4	93.2/5.3
Ceftazidime	≤1	8	90.7/7.0	≤1	16	82.2/8.9	≤1	>16	87.2/10.5
Ampicillin	>16	>16	40.7/59.3	>16	>16	31.1/68.9	>16	>16	35.3/63.9
Amox/Clav	8	16	67.4/8.1	8	>16	64.4/13.3	8	>16	70.7/11.3
Pip/Taz	2	32	88.4/2.3	2	64	86.7/8.9	2	32	88.0/3.8
Imipenem	≤0.12	0.25	100.0/0.0	≤0.12	0.25	100.0/0.0	≤0.12	≤0.12	100.0/0.0
Gentamicin	≤2	>8	79.1/18.6	≤2	>8	78.9/21.1	≤2	8	89.5/8.3
Levofloxacin	≤0.03	>4	73.3/24.4	0.06	>4	55.6/32.2	≤0.03	>4	71.4/21.8
Ciprofloxacin	≤0.03	>4	73.3/26.7	≤0.03	>4	55.5/44.4	≤0.03	>4	71.4/28.6
Tetracycline	2	>8	62.8/36.0	4	>8	50.0/48.9	2	>8	55.6/43.6
Trim/Sulfa	≤0.5	>2	67.4/32.6	>2	>2	48.9/51.1	≤0.5	>2	65.2/34.8
P. aeruginosa		(8; 102)			(3; 55)			(3; 110)	
Ceftriaxone	>32	>32	3.9/81.4	>32	>32	5.5/87.3	>32	>32	2.7/77.3
Cefepime	2	16	87.3/5.9	4	16	74.5/9.1	4	16	80.0/6.4
Ceftazidime	4	16	86.3/7.8	4	>16	72.7/23.6	4	>16	81.8/14.5
Aztreonam	4	>16	70.6/11.8	8	>16	61.8/29.1	8	>16	73.6/16.4
Pip/Taz	8	>64	89.2/10.8	8	>64	78.2/21.8	8	>64	89.1/10.9
Imipenem	1	8	83.3/4.9	1	>8	67.3/16.4	1	8	81.8/9.1
Gentamicin	≤2	8	88.2/5.9	≤2	>8	70.9/23.6	≤2	>8	76.4/21.8
Tobramycin	0.5	1	94.1/5.9	0.5	>16	74.5/25.5	0.5	>16	80.0/19.1
Levofloxacin	0.5	>4	72.5/22.5	1	>4	67.3/29.1	0.5	>4	69.1/29.1
Ciprofloxacin	0.12	>4	73.5/22.5	0.25	>4	67.3/29.1	0.12	>4	70.0/27.3
Enterococcus spp.[a]		(2; 122)			(5; 35)			(4; 65)	
Ampicillin	2	>16	81.1/18.9	2	8	91.4/8.6	2	>16	83.1/16.9
Erythromycin	>8	>8	7.4/61.5	4	>8	17.1/48.6	>8	>8	4.6/58.5
Q/D	>2	>2	18.0/73.0	>2	>2	5.7/85.7	>2	>2	15.4/75.4
Ciprofloxacin	4	>4	45.9/50.8	1	>4	62.9/28.6	1	>4	56.9/40.0
Levofloxacin	2	>4	50.0/47.5	1	>4	74.3/17.1	1	>4	63.1/36.9
Gentamicin HL	≤500	>1000	68.0/32.0	≤500	>1000	80.0/20.0	≤500	>1000	72.3/27.7
Streptomycin HL	≤1000	>2000	66.4/33.6	≤1000	>2000	62.9/37.1	≤1000	>2000	63.1/36.9
Chloramphenicol	8	8	91.0/8.2	8	>16	74.3/25.7	8	>16	73.8/23.1
Tetracycline	>8	>8	32.8/67.2	>8	>8	31.4/68.6	>8	>8	35.4/64.6
Vancomycin	1	>16	85.2/14.8	2	2	97.1/2.9	1	2	92.3/7.7
Teicoplanin	0.25	>16	86.1/12.3	0.25	0.5	97.1/2.9	0.25	0.5	92.3/6.2
Linezolid	2	2	100.0/0.0	2	2	100.0/0.0	2	2	100.0/0.0

Organism /antimicrobial agent	North America (rank; no. by region) MIC 50%	90%	%S/R[a]	Latin America (rank; no. by region) MIC 50%	90%	%S/R[a]	Europe (rank; no. by region) MIC 50%	90%	%S/R[a]
Klebsiella spp.		(7; 49)			(4; 45)			(8; 50)	
Ceftriaxone	≤0.25	4	91.8/2.0	16	>32	48.9/37.8	≤0.25	32	86.0/6.0
Cefepime	≤0.12	2	100.0/0.0	2	>16	64.4/31.1	≤0.12	2	94.0/6.0
Ceftazidime	≤1	16	87.8/8.2	4	>16	57.8/37.8	≤1	>16	88.0/12.0
Amox/Clav	2	8	91.8/4.1	16	>16	35.6/22.2	4	16	74.0/6.0
Pip/Taz	2	16	93.9/4.1	16	>64	53.3/35.6	4	>64	80.0/16.0
Imipenem	≤0.12	0.25	100.0/0.0	≤0.12	0.25	100.0/0.0	≤0.12	0.25	100.0/0.0
Gentamicin	≤2	4	93.9/4.1	4	>8	51.2/44.2	≤2	8	88.0/10.0
Levofloxacin	0.06	1	93.9/2.0	0.06	>4	71.1/28.9	0.06	0.5	92.0/8.0
Ciprofloxacin	≤0.03	0.25	93.9/4.1	≤0.03	>4	68.9/28.9	≤0.03	0.25	90.0/10.0
Tetracycline	≤2	>8	79.6/18.4	8	>8	46.7/44.4	≤2	8	88.0/10.0
Trim/Sulfa	≤0.5	1	91.8/8.2	≤0.5	>2	62.2/37.8	≤0.5	>2	86.0/14.0
Enterobacter spp.		(6; 51)			(6; 31)			(6; 62)	
Ceftriaxone	≤0.25	>32	76.5/13.7	0.5	>32	58.1/38.7	≤0.25	>32	72.6/14.5
Cefepime	≤0.12	2	94.1/5.9	0.25	>16	87.1/12.9	≤0.12	4	95.2/3.2
Ceftazidime	≤1	>16	72.5/25.5	≤1	>16	58.1/38.7	≤1	>16	75.8/22.6
Pip/Taz	4	64	74.5/7.8	4	>64	54.8/35.5	4	64	77.4/8.1
Amox/Clav	>16	>16	3.9/94.1	>16	>16	0.0/93.5	>16	>16	3.2/93.5
Imipenem	0.5	1	96.1/0.0	0.25	0.5	100.0/0.0	0.25	1	95.2/0.0
Gentamicin	≤2	≤2	92.2/7.8	≤2	>8	77.4/22.6	≤2	8	87.1/6.5
Levofloxacin	0.06	2	90.2/2.0	0.06	>4	77.4/22.6	≤0.03	2	91.9/4.8
Ciprofloxacin	≤0.03	2	88.2/7.8	≤0.03	>4	77.4/22.6	≤0.03	2	88.7/9.7
Tetracycline	≤2	>8	82.4/13.7	2	>8	67.7/25.8	2	8	88.7/9.7
Trim/Sulfa	≤0.5	>2	84.3/15.7	≤0.5	>2	67.7/32.3	≤0.5	>2	83.9/16.1
ß-haemolytic streptococci		(5; 66)			(12; 7)			(5; 62)	
Cefepime	≤0.12	≤0.12	100.0/-	≤0.06	-	100.0/-	≤0.12	≤0.12	100.0/-
Ceftriaxone	≤0.25	≤0.25	100.0/-	0.06	-	100.0/-	≤0.25	≤0.25	100.0/-
Penicillin	≤0.016	0.06	100.0/-	≤0.03	-	100.0/-	≤0.016	0.06	100.0/-
Erythromycin	≤0.06	8	74.2/25.8	≤0.25	-	85.7/14.3	≤0.06	2	82.3/17.7
Clindamycin	≤0.06	4	89.4/10.6	≤0.25	-	85.7/14.3	≤0.06	≤0.06	96.8/3.2
Q/D	≤0.25	0.5	100.0/0.0	≤0.5	-	100.0/0.0	≤0.25	0.5	100.0/0.0
Levofloxacin	0.5	1	98.5/1.5	0.5	-	100.0/0.0	0.5	1	100.0/0.0
Tetracycline	1	>8	53.1/45.3	-	-	0.0/0.0	≤2	>8	50.0/48.4
Vancomycin	0.5	0.5	100.0/-	0.5	-	100.0/-	0.25	0.5	100.0/-
Linezolid	1	1	100.0/-	1	-	100.0/-	1	1	100.0/-
Coagulase-negative staphylococci		(9; 23)			(7; 29)			(7; 57)	
Oxacillin	>2	>2	21.7/78.3	2	>2	24.1/75.9	2	>2	19.3/80.7
Penicillin	8	32	8.7/91.3	8	>32	10.3/89.7	4	32	17.5/82.5
Clindamycin	≤0.06	>8	73.9/26.1	0.12	>8	72.4/27.6	≤0.06	>8	73.7/26.3
Q/D	≤0.25	≤0.25	100.0/0.0	≤0.25	0.5	100.0/0.0	≤0.25	0.5	100.0/0.0
Ciprofloxacin	4	>4	43.5/52.2	0.25	>4	58.6/34.5	4	>4	43.9/52.6
Levofloxacin	4	>4	43.5/52.2	0.25	>4	58.6/31.0	2	>4	45.6/45.6
Gentamicin	≤2	>8	73.9/17.4	≤2	>8	65.5/27.6	≤2	>8	68.4/24.6
Rifampin	≤0.5	≤0.5	100.0/0.0	≤0.5	>2	82.8/17.2	≤0.5	>2	86.0/12.3
Tetracycline	0.5	2	95.7/4.3	0.5	2	93.1/6.9	1	>8	80.7/17.5
Trim/Sulfa	≤0.5	>2	73.9/26.1	≤0.5	>2	64.3/35.7	≤0.5	>2	71.9/28.1
Vancomycin	1	2	100.0/0.0	1	2	100.0/0.0	1	2	100.0/0.0
Teicoplanin	2	4	100.0/0.0	2	8	93.1/0.0	1	8	98.2/0.0
Linezolid	1	1	100.0/-	1	1	100.0/-	1	1	100.0/-

a. Susceptibility criteria are those of CLSI (2005); - = no interpretive criteria have been published.
Trim/Sulfa = Trimethoprim/Sulfamethoxazole; Q/D = Quinupristin/Dalfopristin; Amox/Clav = Amoxicillin/Clavulanic acid; Pip/Taz = Piperacillin/Tazobactam

- Ciprofloxacin resistance among *E. coli* and *Klebsiella* spp. was highest in Latin America (44.4 and 28.9% respectively) followed by Europe (28.6 and 10.0%) and North America (26.7 and 4.1%; Table 2).
- Ceftazidime resistance among *Enterobacter* spp. and *P. aeruginosa* was highest in Latin America (38.7 and 23.6% respectively), followed by Europe (22.6 and 14.5%) and North America (25.5 and 7.8%; Table 2).
- ESBL production among *Klebsiella* spp., *E. coli* and *P. mirabilis* remains an important problem in Latin America and Europe. The percent of isolates with ESBL phenotypes and confirmed ESBL producers was highest in Latin America for all three organisms (Table 3).
- Clonal dissemination of Gram-negative bacteria was detected in Turkey. The dissemination of three ESBL-positive *E. coli* clones and two *E. cloacae* clones was documented in a Turkish medical center. In addition, the dissemination of two metallo-ß-lactamase (IMP-1)-producing *E. cloacae* clones was observed in a second Turkish medical center.

Table 3. ESBL resistance rates among *E. coli*, *Klebsiella* spp. and *P. mirabilis* isolated from SSTI in North America, Latin America and Europe (SENTRY Program, 2004).

Organism/region (no.)	% ESBL phenotype[a]	% confirmed ESBL-positive phenotype[b]	% total ESBL confirmed
E. coli			
North America (86)	12.8	81.8	10.5
Latin America (90)	24.4	81.8	20.0
Europe (133)	19.5	76.9	15.0
Klebsiella spp.			
North America (49)	16.3	87.5	14.3
Latin America (45)	62.2	96.5	60.0
Europe (50)	24.0	91.7	22.0
P. mirabilis			
North America (32)	0.0	0.0	0.0
Latin America (25)	24.0	100.0	24.0
Europe (44)	11.4	60.0	6.8

a. Percentages based on ceftazidime or ceftriaxone or aztreonam MIC at ≥ 2 μg/ml (CLSI, 2005).
b. Disk approximation method was utilized.

CONCLUSIONS

- *S. aureus* was the most frequent pathogen isolated from SSTI in all regions of the world evaluated.
- Gram-positive bacteria were the predominant cause of SSTI in North America with MRSA and VRE occurrence rates well above other regions.
- Gram-negative bacteria were the predominant cause of SSTI in Latin America and the most frequent Gram-negative pathogens showed elevated rates of antimicrobial resistance when compared to other regions monitored.
- In order to determine regional antimicrobial resistances and to guide empiric choices of antimicrobial agents, continuing surveillance of cutaneous or wound infections at regular intervals will be a necessary and prudent practice.

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