Bloodstream Infections in the United States and Europe: Etiology and Antimicrobial Susceptibility Results from the SENTRY Antimicrobial Surveillance Program (2016-2019)

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Background

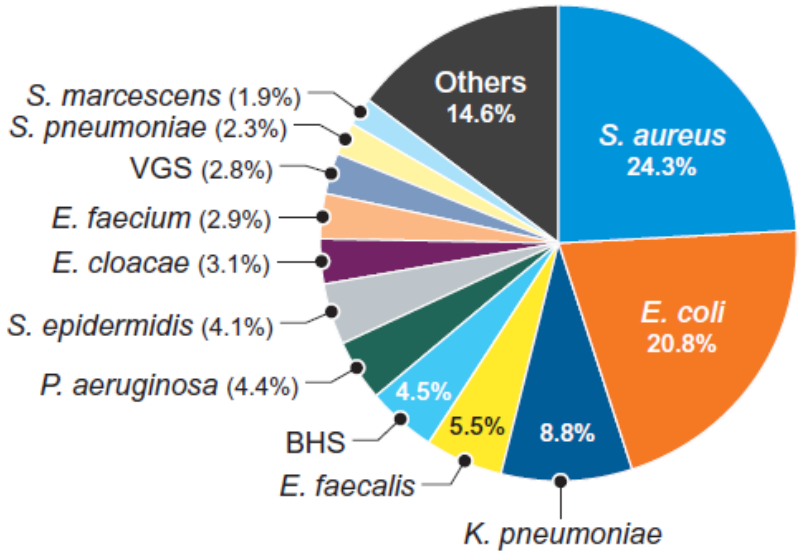
- The SENTRY Antimicrobial Surveillance Program monitors the etiology of bloodstream infections (BSI) and other infections worldwide since 1997.
- The etiology of BSI has changed substantially in the last 2 decades due to an increase of gram-negative pathogens outnumbering gram-positive pathogens.
- Recently, the most significant changes have been in the antimicrobial resistance patterns, especially among gram-negative organisms recovered from BSIs.
- We evaluated the results for BSI in the United States (US) and Europe (EU).

Methods

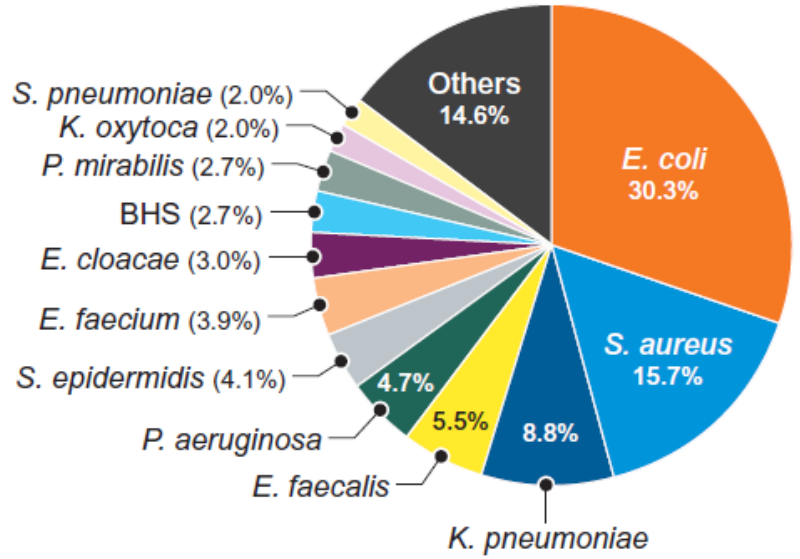
- Organisms were collected consecutively (1/patient):
  - United States (US): 12,748 isolates from 35 medical centers
  - Western Europe (W-EU): 12,198 isolates from 29 medical centers from 10 nations (Belgium, France, Germany, Ireland, Italy, Portugal, Spain, Sweden, Switzerland, and the UK)
  - Eastern Europe (E-EU): 3,297 isolates from 15 medical centers from 12 nations (Belarus, Croatia, Czech Republic, Greece, Hungary, Israel, Poland, Romania, Russia, Slovakia, Slovenia, and Turkey)
- Only isolates determined to be significant by local criteria as the reported probable cause of BSI were included in the program.
- Organisms were susceptibility tested by reference broth microdilution methods in a central laboratory (JMI Laboratories, Iowa, USA).

Results:
Frequency of occurrence

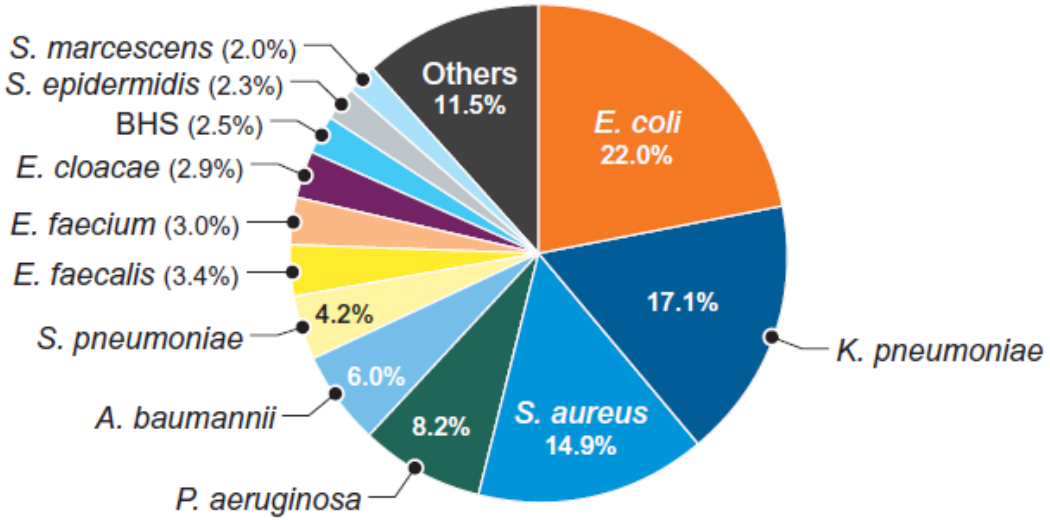
A. United States (n=12,748)



B. Western Europe (n=12,198)

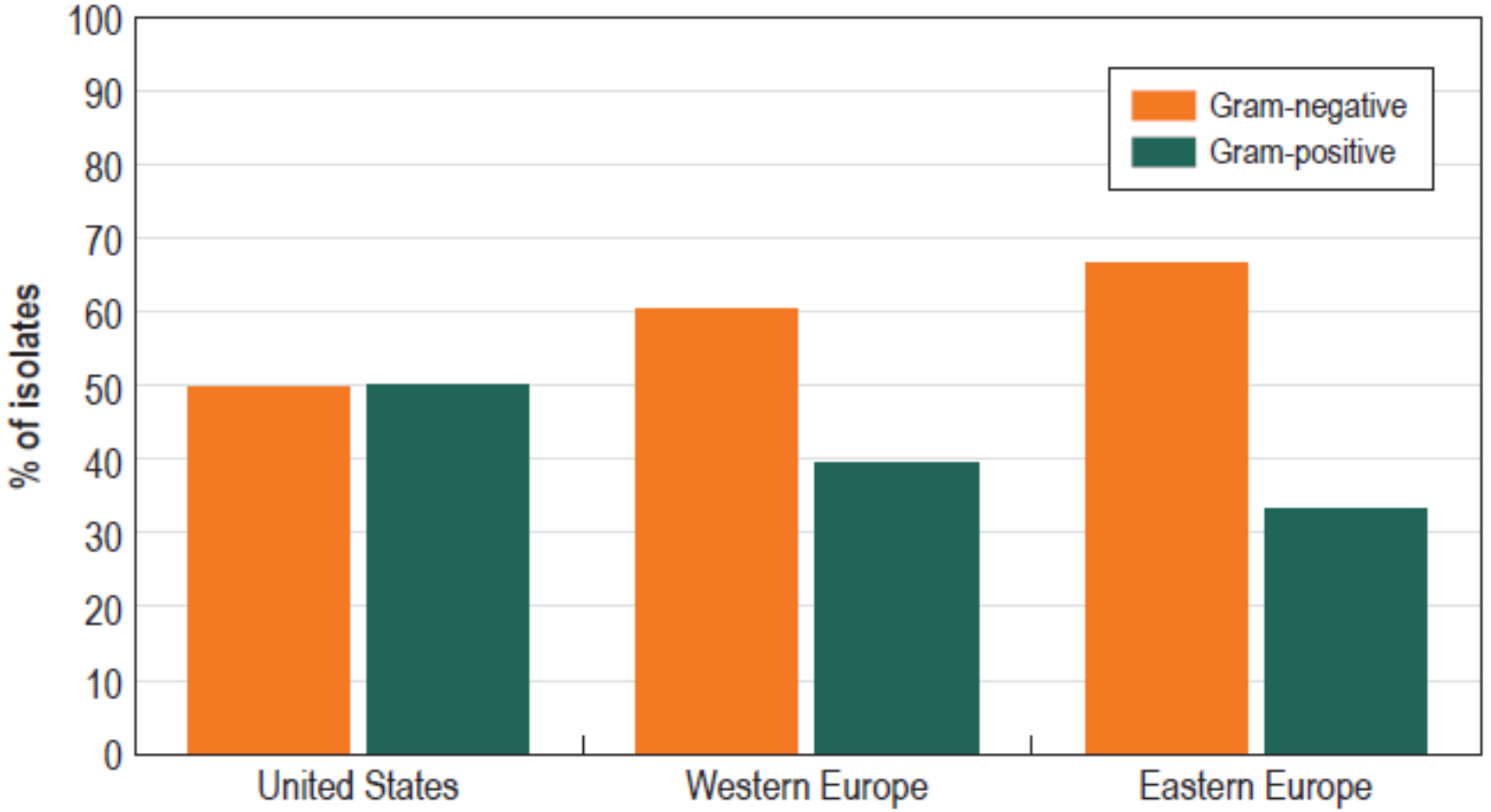


C. Eastern Europe (n=3,297)



Results:

Percentages of Gram-negative and Gram-positive organisms isolated from patients hospitalized with BSI stratified by geographic region (2016-2019)



Results:

Frequency of occurrence

- The most common organism found was *S. aureus* in the US and *E. coli* in W-EU and E-EU.
- *E. coli, S. aureus,* and *K. pneumoniae* represented the top 3 organisms in all 3 regions and accounted for 53.9-54.8% of the collection.
- Gram-negative bacilli (GNB) represented 48.8% of organisms in the US, 59.8% in W-EU, and 65.6% in E-EU.

Results:

Antimicrobial susceptibility – Gram-positives

Antimicrobial agent	% Susceptible by geographic region (no. of isolates)[a]		
	USA	W-EU	E-EU
S. aureus	(3,103)	(1,912)	(491)
Oxacillin	58.4	75.6	75.4
Ceftaroline	97.4	95.5	96.7
Daptomycin	99.9	100.0	100.0
Levofloxacin	64.6	76.8	87.4
Minocycline	98.7	99.5	99.4
TMP-SMX[b]	97.6	99.2	99.8
Teicoplanin	100.0	100.0	100.0
Vancomycin	100.0	100.0	100.0
S. epidermidis	(517)	(500)	(76)
Oxacillin	24.0	29.2	9.2
Ceftaroline	[99.8][c]	[99.6][c]	[97.4][c]
Daptomycin	100.0	99.8	100.0
Levofloxacin	39.8	41.0	31.6
Minocycline	96.7	100.0	100.0
TMP-SMX[b]	53.0	59.2	69.7
Teicoplanin	99.2	99.0	98.7
Vancomycin	100.0	100.0	100.0

[a] Criteria as published by CLSI (2020).

[b] TMP-SMX, trimethoprim-sulfamethoxazole.

[c]. Percentage inhibited at ≤1 mg/L, which is the susceptible breakpoint for *S. aureus*, for comparison purpose.

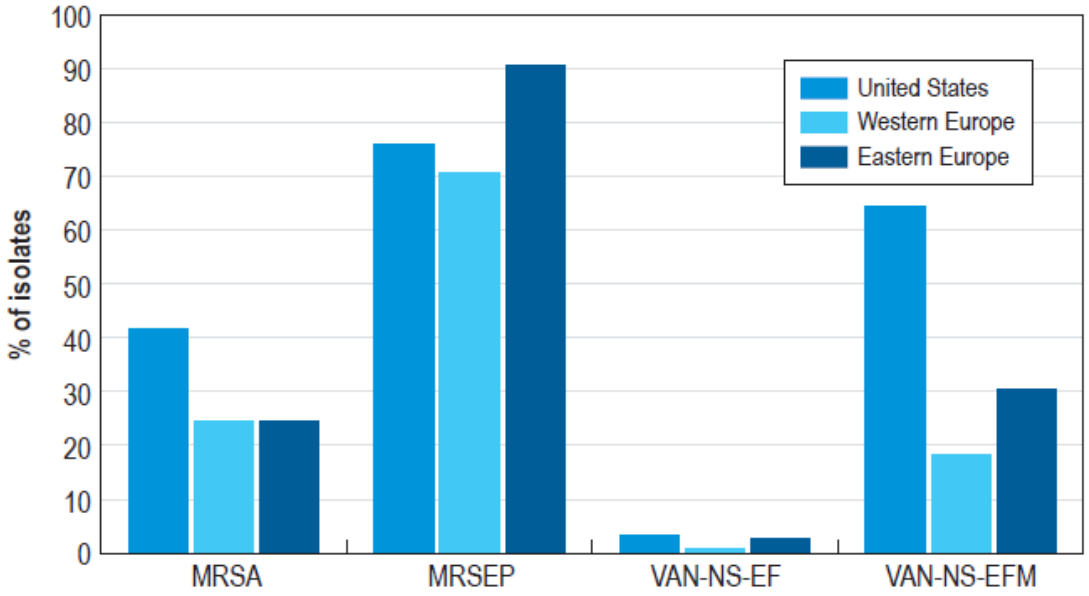
Antimicrobial agent	% Susceptible by geographic region (no. of isolates)[a]		
	USA	W-EU	E-EU
E. faecalis	(695)	(668)	(112)
Ampicillin	100.0	100.0	100.0
Daptomycin	99.9	99.6	100.0
Levofloxacin	76.9	71.6	62.5
Minocycline	34.5	33.5	30.4
Teicoplanin	96.8	99.1	98.2
Vancomycin	96.8	99.1	97.3
E. faecium	(370)	(478)	(98)
Ampicillin	20.0	11.5	5.1
Daptomycin	[95.9][b]	[98.1][b]	[98.0][b]
Levofloxacin	13.2	8.4	1.0
Minocycline	52.7	70.1	63.3
Teicoplanin	38.4	86.6	75.5
Vancomycin	35.4	81.8	69.4

[a] Criteria as published by CLSI (2020).

[b] Percentage inhibited at ≤2 mg/L, which is the susceptible breakpoint for *E. faecalis*, for comparison purpose.

Results:

Frequency of key resistance phenotypes – Gram-positives



- MRSA rates were higher in US (41.6%) compared to W-EU (24.4%) and E-EU (24.6%).
- Vancomycin-nonsusceptibility (VRE):

Organism	VRE Rates		
	US	W-EU	E-EU
E. faecalis	3.2%	0.9%	2.7%
E. faecium	64.6%	18.2%	30.6%

Results:

Antimicrobial susceptibility – Gram-negatives

Antimicrobial agent	% Susceptible by geographic region (no. of isolates)[a]		
	USA	W-EU	E-EU
E. coli	(2,653)	(3,697)	(724)
Ceftriaxone	83.0	83.3	66.4
Ceftazidime-avibactam	100.0	>99.9	99.9
Ceftolozane-tazobactam	98.7	98.9	96.5
Piperacillin-tazobactam	95.3	93.5	87.6
Meropenem	99.8	99.8	99.9
Levofloxacin	65.8	73.5	55.8
Gentamicin	86.2	88.2	81.2
K. pneumoniae	(1,127)	(1,076)	(563)
Ceftriaxone	86.6	64.3	30.2
Ceftazidime-avibactam	99.8	99.3	95.4
Ceftolozane-tazobactam	96.6	81.0	57.0
Piperacillin-tazobactam	92.5	72.3	46.5
Meropenem	98.7	84.8	72.5
Levofloxacin	86.6	66.9	38.4
Gentamicin	91.3	80.8	56.0

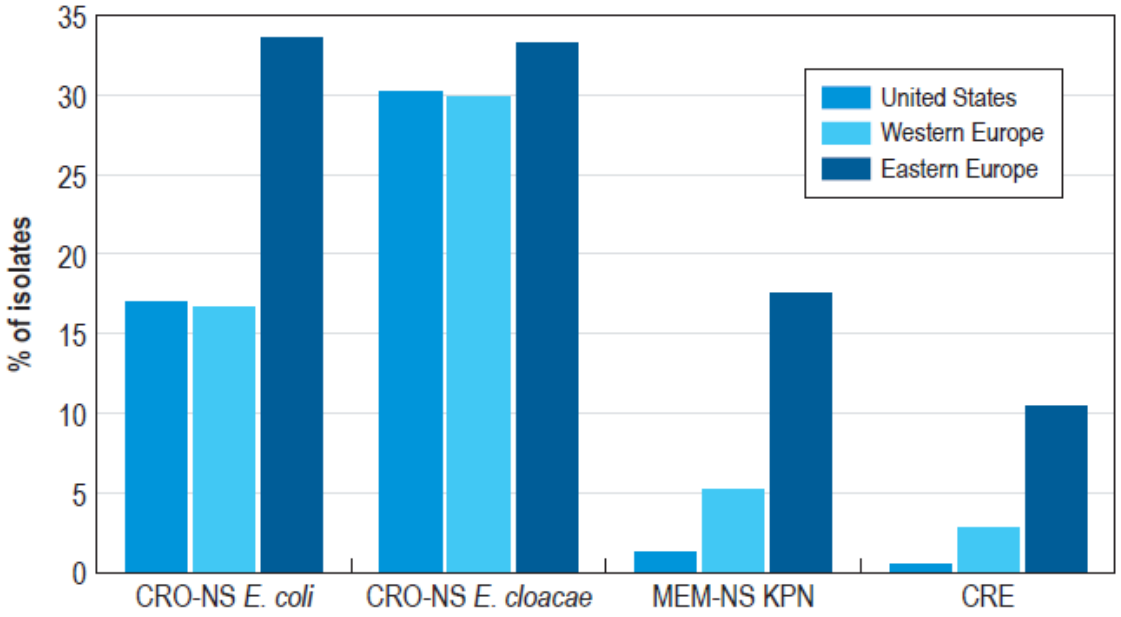
[a] Criteria as published by CLSI (2020).

Antimicrobial agent	% Susceptible by geographic region (no. of isolates)[a]		
	USA	W-EU	E-EU
E. cloacae	(401)	(358)	(93)
Ceftriaxone	69.8	70.1	66.7
Ceftazidime-avibactam	99.8	99.7	95.7
Ceftolozane-tazobactam	83.7	85.7	82.4
Piperacillin-tazobactam	81.8	82.1	75.3
Meropenem	98.8	99.2	92.5
Levofloxacin	91.5	91.6	89.2
Gentamicin	95.3	94.7	88.2
P. aeruginosa	(565)	(576)	(271)
Ceftazidime	88.3	84.5	65.7
Ceftazidime-avibactam	97.9	95.8	80.4
Ceftolozane-tazobactam	98.2	96.3	80.7
Piperacillin-tazobactam	84.8	81.4	64.6
Meropenem	83.7	82.4	57.6
Levofloxacin	71.7	74.8	55.7
Tobramycin	96.6	93.1	69.7

[a] Criteria as published by CLSI (2020).

Results:

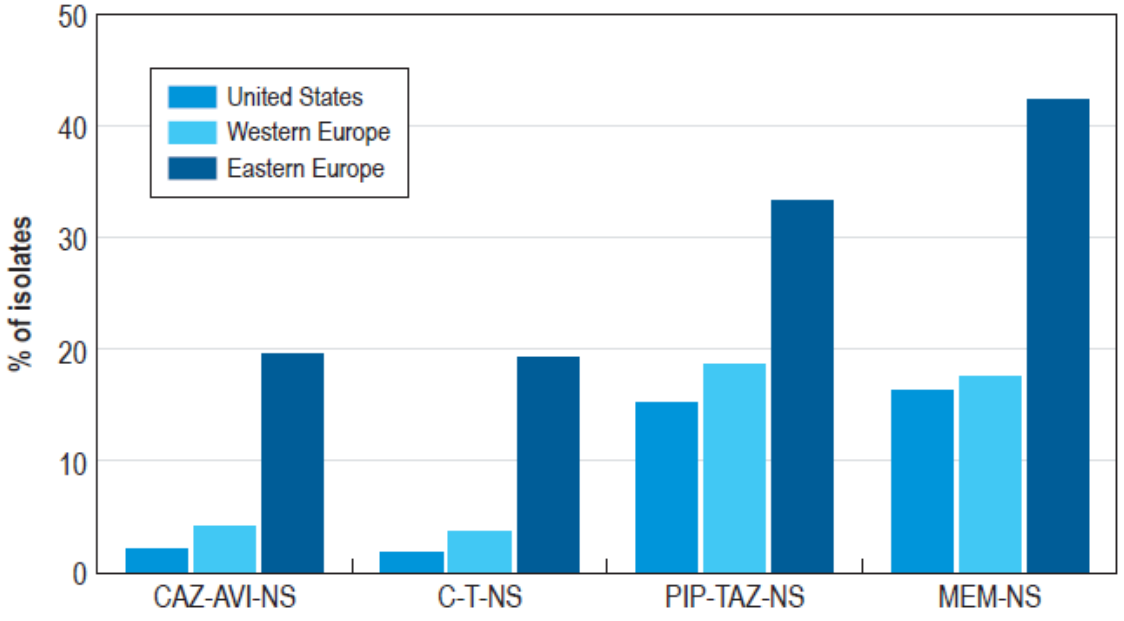
Frequency of key resistance phenotypes - *Enterobacterales*



- *E. coli*:
  - Resistance to ceftriaxone were higher in E-EU (33.6%) compared to W-EU (16.7%) and the US (17.0%)
  - Resistance to levofloxacin were also higher in E-EU (44.2%) compared to W-EU (26.5%) and the US (34.2%).
- *E. cloacae*:
  - Resistance to ceftriaxone were 30.2% in US, 29.9% in W-EU, 33.3% in E-EU
- *K. pneumoniae*:
  - Resistance to ceftriaxone were 13.4% in US, 35.7% in W-EU, 69.8% in E-EU
  - Resistance to meropenem were 1.3% in US, 15.3% in W-EU, and 27.5% in E-EU
- CRE rates were lower in US (0.5%) compared to W-EU (2.8%) and very high in E-EU (10.4%).

Results:

Frequency of key resistance phenotypes – *P. aeruginosa*



Abbreviations: CAZ-AVI, ceftazidime-avibactam; C-T, ceftolozane-tazobactam; PIP-TAZ, piperacillin-tazobactam; MEM, meropenem.

- CAZ-AVI and C-T showed similar activity against *P. aeruginosa* in all 3 regions, and were highly active in the US and W-EU.
- Resistance to CAZ-AVI and C-T were lower in the US (1.8-2.1%) and W-EU (3.7-4.2%) than in E-EU (19.3-19.6%).
- Resistance to levofloxacin were also higher in E-EU (44.2%) compared to W-EU (26.5%) and the US (34.2%).
- Resistance to PIP-TAZ were 15.2% in US, 18.6% in W-EU, 35.4% in E-EU.
- Resistance to meropenem were 16.3% in US, 17.6% in W-EU, and 42.4% in E-EU.

Conclusions

- The frequency of organisms and their antimicrobial susceptibility varied markedly by geographic region.
- The frequency of Gram-negative bacilli was lower in the US compared to W-EU and E-EU.
- Antimicrobial resistance rates among Gram-positive cocci were higher in the US compared to W-EU and E-EU.
- Among Gram-negatives, resistance rates generally were higher in E-EU compared to W-EU and the US.

Conclusions

- The SENTRY Program provides very useful data on the occurrence of key antimicrobial resistance phenotypes worldwide, such as:
  - Insight on the emergence and spread of resistant organisms and
  - Information on important resistance mechanisms to target for new drugs.
- The epidemiology of antimicrobial resistance varies widely by geography and drug-bug combination, requiring continued surveillance.

Acknowledgements

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