Abstract: P908

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Epidemiology of antibiotic resistance of bacterial pathogens from intensive care units: the SENTRY surveillance program in Europe 2000

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On behalf of the Euro SENTRY Program

Objectives:
To describe the frequency and resistance rates of bacterial pathogens from patients admitted to intensive care units (ICU) from a network of European hospitals.
Methods:
During the year 2000, 18 hospitals from 12 European countries referred a total of 8062 bacterial pathogens. In vitro susceptibility of 32 antimicrobial agents isolated from hospitalized patients (pts), was tested by broth microdilution method as described by the NCCLS.
Results:
Among all pathogens, 30% were from pts admitted to ICU. In these patients, the most frequent pathogens were *S. aureus* (20%), *P. aeruginosa* (15%), *E. coli* (11%), *K. pneumoniae* (8%), coagulase-negative staphylococci (7%), *A. baumannii* (7%), *E. cloacae* (5%) and *E. faecalis* (4%). Isolates from ICU pts were recovered from bloodstream (49%), lower respiratory tract (39%), skin (7%) and urinary tract infection (6%). The mean (intercenter range) proportion of *P. aeruginosa* isolates nonsusceptible to ceftazidime and cefepime was 31% (0-82) and 35% (0-82), respectively, in ICU pts, versus 25 and 23% in non-ICU pts ($P = 0.07$ and $P < 0.01$, respectively). Ciprofloxacin resistance rates in ICU was 33% (0-88). Rates of nonsusceptibility to imipenem and meropenem were 32 and 31%, respectively, versus 20 and 17% in non-ICU pts ($P < 0.001$). In *K. pneumoniae*, the proportion of decreased susceptibility to ceftazidime (MIC 32 µg/mL) was 43% versus 29 in non-ICU ($P < 0.01$); cefepime 15% versus 7% in non-ICU pts ($P < 0.01$). Resistance of *A. baumannii* to meropenem was seen in 43% isolates from ICU pts versus 16 in non-ICU pts ($P < 0.01$). The proportion of oxacillin resistance in *S. aureus* from ICU pts was 47% (0-100) versus 25% in non-ICU pts ($P < 0.0001$). Resistance to vancomycin was similarly low in ICU versus non-ICU pts in *E. faecalis* (1% vs. 3%). High level of gentamicin resistance was expressed by 36% of *E. faecalis* isolates from ICU pts versus 32% in non-ICU pts.
Conclusions:
These data confirm that the prevalence of antimicrobial resistance in several Gram-negative pathogens and *S. aureus* isolates is higher from patients admitted to ICU than to other wards in these hospitals. Large intercenter variation underline the need to adapt the therapeutic approach to local resistance data.

Epidemiology of antibiotic resistance of bacterial pathogens in Intensive Care Units from the SENTRY surveillance program in Europe 2000

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ABSTRACT

Objectives: To describe the frequency and resistance rates of bacterial pathogens from patients admitted to intensive care units (ICU) from a network of European hospitals.

Methods: During the year 2000, 18 hospitals from 12 European countries referred a total of 8062 bacterial pathogens. In vitro susceptibility of 32 antimicrobial agents isolated from hospitalized patients (pts), was tested by broth microdilution method as described by the NCCLS.

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Objectives

The SENTRY program is a longitudinal surveillance program designed to monitor the predominant pathogens and antimicrobial resistance patterns of nosocomial and community acquired infections via an international network of sentinel hospitals. We analyzed the SENTRY data from the year 2000, to update the antimicrobial resistance rates in ICU isolates from a network of European hospitals.

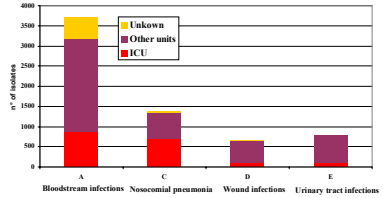
Materials and Methods

During the year 2000, 18 hospitals from 12 European countries: 6 Mediterranean countries and 6 other countries participed (Table 1). Of these centers, 11 (61%) had participated in the SENTRY program during 1997-98. As part of the SENTRY program, the monitored infections include the first 20 clinically significant consecutive blood isolates of any species per month (objective A), pneumonia in hospitalized patients (objective C), wound or skin and soft tissue infections (objective D) and urinary tract infections (objective E). Only 1 isolate per patient was submitted. All strains were sent to the regional monitor (RN Jones, University of Iowa, Iowa. USA) for susceptibility testing to >20 antimicrobials and confirmation of organism identification. Antimicrobial susceptibility testing of isolates was performed using a broth microdilution method according to the National Committee for Clinical Laboratory Standards (NCCLS) guidelines. Among a total of 8061 pathogens recovered from objectives A, C, D, E, only those with complete data concerning ICU admision (a total of 5966 pathogens) were included in this analysis.

Table 1: List of participating centers

Center	Country
CHRU de Lille, Lille	France
National University of Athens Med Sch., Athens	Greece
The Chaim Sheba Medical Center, Tel-Hashomer	Israel
University Hospital Virgen de la Macarena, Sevilla	Spain
Hospital de Bellvitge, Barcelona	Spain
Hospital Ramon y Cajal, Madrid	Spain
Hacettepe Universitesi Tip Fakultesi, Sihhiye Ankara	Turkey
Maramara Universitesi Tip Fakultesi, Altuizade Istanbul	Turkey
Universita degli studi di Genova	Italy
Azienda Policlinico Univ. Catania	Italy
Policlinico Agostino Gemelli, Roma	Italy
Hôpital Erasme-Université Libre de Bruxelles	Belgium
Unité de Bacteriologie CHU Lausanne	Switzerland
Inst for Micobiology and virology Heinrich-Heine	Germany
Zentrum der Inneren Medizin, Frankfurt	Germany
University Hospital, Linkoping	Sweden
Sera & Vaccines Central Research Lab, Warsaw	Poland
St. Thomas Hospital, London	UK

Figure 1: Distribution of pathogens collected from SENTRY objectives by type of patient care unit of admission



Results

•Most isolates from both ICU and non- ICU patient groups were recovered from bloodstream infections followed by lower respiratory tract infection in ICU group.

•*S.aureus* was the most frequent etiologic agent of bloodstream and skin infection in ICU patients. *P.aeruginosa* was the most common cause of respiratory tract infection and *E.coli* was the most common cause of urinary tract infection (Table 2).

• Several leading ICU pathogens showed a significantly larger proportion of strains resistant to one or more classes of antimicrobial agents in isolates from ICU versus non-ICU patients:

- •Resistance to oxacillin, fluoroquinolones, macrolides, lincosamides in *S.aureus* and CNS (Table 3).
- •Suspicion of ESBL-producing *K.pneumoniae* (Ceftazidime MICs >=2µg/mL, 43% vs 29%, p<0.01).
- • Resistance to ß-lactam antimicrobials agents in *P.aeruginosa* (Table 4).
- • Resistance to carbapenems in *A.baumannii* (Table 4).

•There was a large inter-center variation in the proportion of these resistant ICU strains (Fig 2-5). No obvious regional trend was noted with ß-lactam resistant *P.aeruginosa* and *S.aureus*. In contrast carbapenem-resistant *A. baumannii* and ESBL-producing *K.pneumoniae* were more frequently seen in ICU in Mediterranean countries.

•The most active antimicrobials against these problem pathogens from ICU patients were:

- •*S. aureus* and CNS: glycopeptides, linezolid.
- •*K. pneumoniae*: carbapenems and amikacin.
- •*P.aeruginosa:* amikacin and piperacillin-tazobactam.
- •*A.baumannii:carbapenems and amikacin.*
- •*Enterobacter spp:*carbapenems, amikacin and cefepime.

References:
(1) Hanberger, H, Diekema D, Fluit A, Jones R, Struelens M, Spencer R, Wolff M.Surveillance of antibiotic resistance in European ICUs. Journal of Hospital Infection 2002; 48:161-176;

Table 2: Frequency of occurrence of top 10 pathogens in ICU patients by objective category. Euro SENTRY 2000.

	Objective A Bloodstream		Objective C Nosocomial pneumonia		Objective D Wounds		Objective E Urinary tract infection		total
Microorganism	ICU	(%)	ICU	(%)	ICU	(%)	ICU	(%)	ICU (%)
Staphylococcus aureus	177	20	155	22	28	24	1	1	361 (20)
Pseudomonas aeruginosa	70	8	176	25	15	13	16	16	277(15)
Escherichia coli	93	11	53	8	13	11	39	39	198 (11)
Klebsiella pneumoniae	83	9	45	6	10	8	10	10	148(8)
CNS	109	12	5	1	9	8	0	0	123(21)
Acinetobacter baumannii	46	5	66	9	2	2	4	4	118(7)
Enterobacter cloacae	34	4	37	5	11	9	2	2	84(5)
Enterococcus faecalis	51	6	5	1	4	3	11	11	71(4)
Serratia marcescens	20	2	29	4	3	3	1	1	53(3)
Enterobacter aerogenes	17	2	13	2	0	0	2	2	32(2)
Other	177	20	120	17	24	20	15	15	1465(81)
Total	877	100	704	100	119	100	101	100	1801(100)

Figures 2 to 5: Variation in the proportion of major ICU pathogens by center and geographyc region

Figure 2: Ceftazidime resistance among *Pseudomonas aeruginosa*

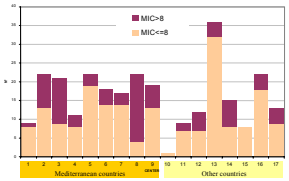


Figure 3: oxacillin resistance among *Staphylococcus aureus*

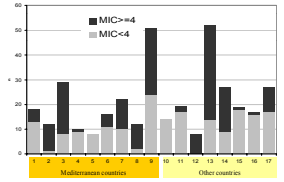


Figure 4: Meropenem resistance among *A. baumannii*

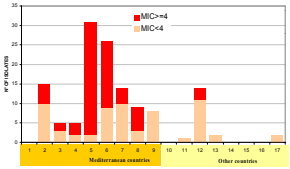


Figure 5: Decrease susceptibility among to ceftazidime *K.pneumoniae*
(suspect ESBL production)

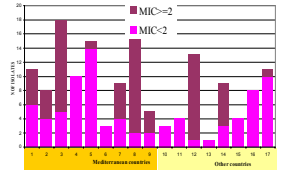


Table 3: Susceptibility profile of top 3 gram-positive pathogens from ICU versus non-ICU patients.

	S.aureus		*CNS*		*E.faecalis*	
	ICU n=361	No ICU n=701	ICU n=128	No ICU n=330	ICU n=75	No ICU n=207
Compound	% S	% S	% S	% S	% S	% S
Amox-clav	56	78***	63	78***	NA	NA
Ampicillin	0	0	9		100	98
Bmsq	NA	NA	NA	NA	NA	NA
Cefazolin	56	79***	71	85***	NA	NA
Chloramphenicol	88	89	64	81***	69	69
Ciprofloxacin	51	73***	36	55	52	61
Clindamycin	71	81***	52	70***	NA	NA
Doxycycline	80	91***	89	83	39	32
Erythromycin	49	70***	26	42**	18,7	20,3
Genta-High	NA	NA	NA	NA	64	68
Genta-Low	64	82***	35,2	53***	NA	NA
Imipenem	62	84***	68	80**	NA	NA
Linezolid	100	100	100	100	99	100
Mupirocin	NA	NA	NA	NA	NA	NA
Nitrofurantoin	99	100	98	99	97,3	97,6
Oxacillin	53	75***	12	26**	NA	NA
Penicillin	10	16	6	13*	99	96
Quinu-dalfopristin	99	97	97	98	4	1
Rifampin	79	93***	72	46***	28	29
Streptomycin	NA	NA	NA	NA	51	63
Teicoplanin	100	100	92	95	100	100
Tetracyclin	77	85***	84	75*	35	29
Vancomycin	100	100	100	100	99	97

* P<0.05; **P<0.01 *** P<0.001

Table 4: Susceptibility profile of top 4 gram-negative pathogens from ICU versus non-ICU patients.

	P.aeruginosa		*E.coli*		*K.pneumoniae*		*A.baumannii*	
	ICU (n=277)	No ICU (n=424)	ICU (n=198)	No ICU (n=1030)	ICU (n=177)	No ICU (n=317)	ICU (n=132)	No ICU (n=73)
Compound	% S	% S	% S	% S	% S	% S	% S	% S
Amikacin	84	85	100	99	86	93*	35	29
Amox-clav	NA	NA	74	81	59	74***	NA	NA
Ampicillin	NA	NA	53	48*	5	5,7	NA	NA
Aztreonam	35	45**	98	96	63	79***	4	1
Cefazolin	NA	NA	87	87	51	66**	NA	NA
Cefepime	65	77**	99	99	85	93**	29	30
Cefoxitin	NA	NA	97	96	93	92,4	NA	NA
Ceftazidime	69	76	98	98	67	84***	18	21
Ceftriaxone	9	12	98	96	66	82***	10	8
Cefuroxime	NA	NA	89	92	59	72**	NA	NA
Ciprofloxacin	65	69	93	86	86	91,4	21	24
Gentamicin	69	69	94	92	68	82***	12	15
Imipenem	66	80***	100	100	100	100	67	85**
Isepamicin	NA	NA	NA	NA	NA	NA	NA	NA
Meropenem	69	83***	100	100	100	100	57	84***
Nalidixic acid	NA	NA	86	78*	72	83**	NA	NA
Nitrofurantoin	NA	NA	92	94	66	73,5	NA	NA
Pip-tazobactam	77	87**	93	96*	70	82**	15	23
Piperacillin	71	82***	59	54,1	49	62**	8	8
Ticarcillin-clavulanic	59	71**	73	75	53	69***	15	11
Ticarcillin	59	70***	55	49	5	6	11	8
Tobramycin	73	75	94	93	60	77***	34	56**

* P<0.05; **P<0.01 *** P<0.001

Conclusions

• The prevalence of antimicrobial resistant *P.aeruginosa*, *K.pneumoniae*, *A. baumannii* and staphylococci was 1.5 to 3 fold higher in clinical isolates from ICU patients compared to those admitted to other wards in this survey.

• Presumptive ESBL-producing *K.pneumoniae* and carbapenem resistant *A. baumannii* were especially common in ICU isolates from hospitals in Mediterranean countries as noted in previous surveys [1], whereas MRSA and ß-lactam resistant *P.aeruginosa* were geographically more widespread.

• Large inter-center variation in the proportion of these resistant pathogens points to possible infection control problems and underlines the need for adapting therapeutic strategies to local epidemiology.