

ESKAPE bacteremia in immunocompromised hosts

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BSI in immunocompromised hosts

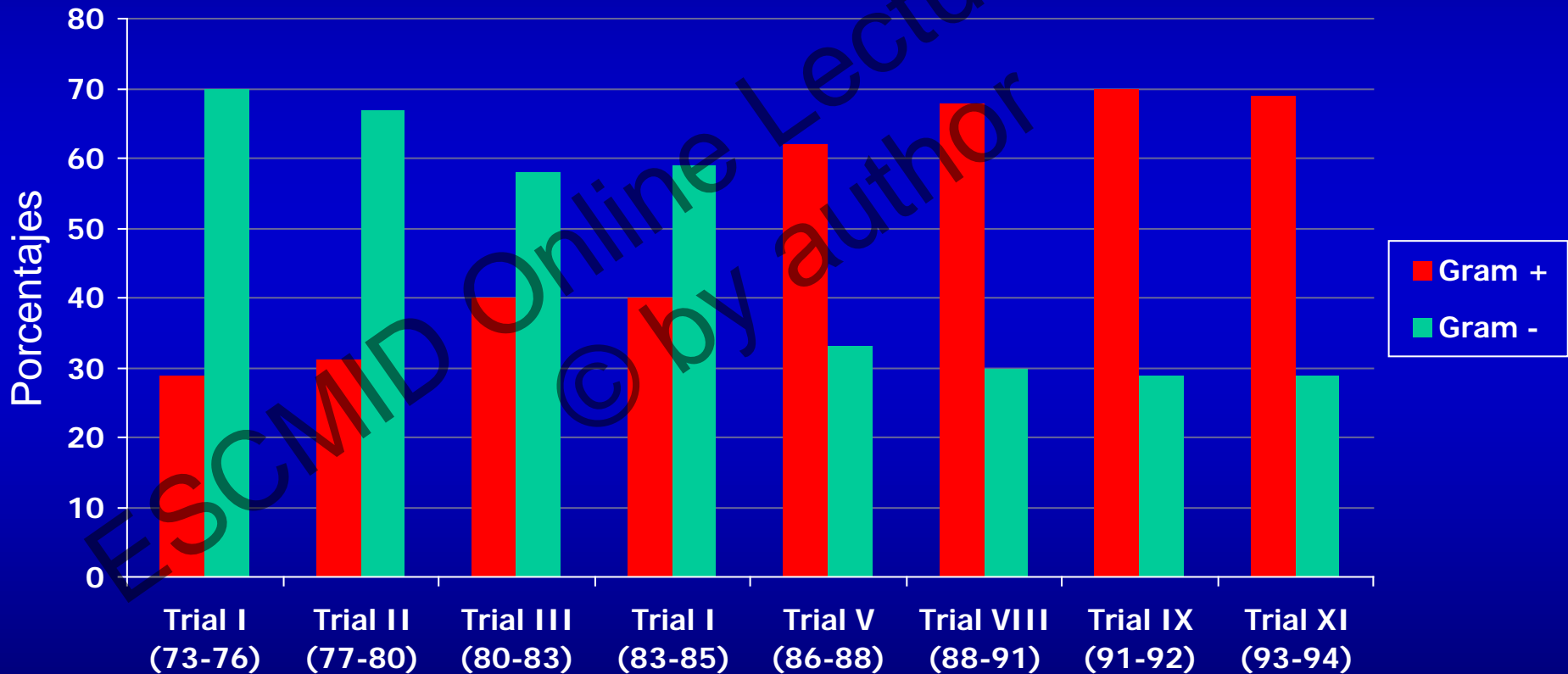
- BSI remains a serious complication in cancer patients and SOT recipients
- BSI accounts for 25-30% of febrile episodes in patients with cancer and neutropenia
- The incidence of BSI in SOT recipients ranges from 8% to 20% depending on the type of SOT
- The in-hospital mortality rate of BSI in these immunocompromised hosts ranges from 8% to 42%

Trends in the incidence of hospital-acquired infections in patients with hematological malignancies

A surveillance-based study



Single agent bacteremia in neutropenic patients with cancer: EORTC – IATG Trials



Distribution of etiologic agent isolated from BSI in patients with cancer in published studies since 2008

Characteristic/ agent	Irfan et al., 2008 [6]	Cattaneo et al., 2012 [14]	Kjellander et al., 2012 [15]	Chong et al., 2011 [16]	Kang et al., 2012 [18]
Study period	2001–2006	2004–2010	2002–2008	2006–2009	2006–2007, 2008
Country	Pakistan	Italy	Sweden	Japan	South Korea
Prophylaxis	Not reported	Not reported	No prophylaxis	No prophylaxis	No prophylaxis
Gram negative	41 %	57.3 %	46.9 %	48.1 %	55.6 %
<i>Pseudomonas aeruginosa</i>	9.7 %	15 %	5.3 %	14.7 %	7.1 %
<i>E. Coli</i>	36.6 %	NS	17.8 %	18.6 %	25 %
<i>Stenotrophomonas maltophilia</i>	2 %	NS	0.8 %	NS	NS
<i>Acinetobacter</i> spp.	14.8 %	NS	0.1 %	NS	2.6 %
<i>Klebsiella</i> spp.	11.6 %	NS	9.8 %	9 %	16.2 %
<i>Enterobacter</i> spp.	8.5 %	NS	5.4 %	3.5 %	4.7 %
<i>Citrobacter</i> spp.	1.7 %	NS	1.3 %	NS	NS
Gram positive	54 %	33.6 %	53.1 %	45.5 %	32.7 %
<i>Staphylococcus</i> spp.	55.2 %	NS	NS	33 %	NS
<i>Staphylococcus aureus</i>	9.5 %	NS	6.9 %	1.3 %	9.8 %
Coagulase-negative <i>staphylococcus</i>	NS	NS	14.7 %	23.1 %	8.3 %
<i>Enterococcus</i> spp.	5.1 %	NS	9.5 %	5.8 %	9.2 %
<i>Streptococcus</i> spp.	5.5 %	NS	NS	6.4 %	3.4 %
<i>Streptococcus pneumoniae</i>	3.5 %	NS	2.3 %	NS	2 %
<i>Streptococcus viridans</i>	NS	NS	14 %	5.8 %	NS

FIRST PERIOD

SECOND PERIOD

Observational
prospective cohort study
Neutropenic adult patients
with hematological
malignancies and HSCT

Jan 1991 – Dec 1996 (n= 272)

Jan 2006 – Mar 2010 (n= 283)

Norfloxacin 400 mg daily

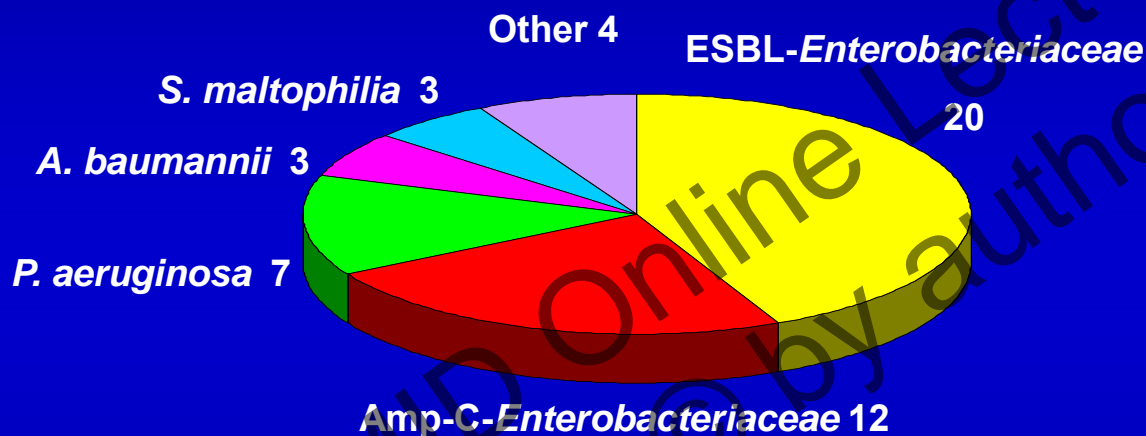
No antibacterial prophylaxis

Causative agents of bacteremia in neutropenic patients

Causative organism	First period %	Second period %	<i>p</i>
Gram-positive bacteria	64	41	<0.001
CNS	46	43	
Viridans group streptococci	42	23	
<i>Enterococcus</i> spp.	6	23	
Gram-negative bacteria	28	49	<0.001
<i>Escherichia coli</i>	67	9	
<i>Pseudomonas aeruginosa</i>	27	68	
<i>Klebsiella pneumoniae</i>	7	22	
Multidrug-resistant GNB	3	11	0.04

Bacteremia due to multidrug-resistant gram-negative bacilli in cancer patients: risk factors, antibiotic therapy and outcomes

- Of 747 bacteremias (2006-2009), 372 were due to GNB
- 51 of 372 (13.7%) were caused by MDRGNB



MDRGNB risk factor for 30-day mortality
(OR 3.5, 95% CI 1.4-9.1)

Characteristic	MDRGNB, N= 51, n (%)	Non-MDRGNB, N= 312, n (%)	P
Inadequate initial empirical antibiotic therapy	35 (69)	29 (9)	<0.001
Time to adequate antibiotic therapy >48 h	21 (41)	13 (4)	<0.001
ICU admission	7 (14)	14 (4)	0.023
Invasive mechanical ventilation	7 (14)	10 (3)	0.005
Early case-fatality rate (7 days)	9 (18)	33 (11)	0.15
Overall case-fatality rate (30 days)	20 (39)	62 (20)	0.003

Drug-resistant ESKAPE (rESKAPE)

- Vancomycin-resistant *E. faecium*
- Methicillin-resistant *S. aureus* (MRSA)
- ESBL-producing *K. pneumoniae*
- Carbapenem-resistant *A. baumannii*
- Carbapenem and quinolone-resistant *P. aeruginosa*
- Derepression chromosomal β -lactam and ESBL producing *Enterobacter spp.*

Epidemiology, antibiotic therapy, and outcomes of bacteremia caused by rESKAPE in cancer patients

1148 cases of bacteremia (2006-2011)

382 (33%) ESKAPE bacteremia

Non-rESKAPE

328 cases

rESKAPE

54 cases (14.4%)

Bodro M. (Submitted)

ESKAPE pathogens isolated in 1148 bacteremias in cancer patients (2006-2011)

Organism	ESKAPE total (n= 382)	R-ESKAPE (n= 54) n (%)
<i>Enterococcus faecium</i>	44	0 (0)
<i>Staphylococcus aureus</i>	93	13 (24)
<i>Klebsiella pneumoniae</i>	95	7 (13)
<i>Acinetobacter baumannii</i>	7	4 (7)
<i>Pseudomonas aeruginosa</i>	106	18 (33)
<i>Enterobacter spp.</i>	47	12 (22)

Risk factors for rESKAPE bacteremia by multivariate analysis

Variable	rESKAPE	Other	OR (95% CI)
Medical comorbidities	53%	37%	1.8 (1.1 - 3.3)
Prior antibiotic therapy	76%	48%	1.5 (1.1 - 2.2)
Urinary catheter	28%	8%	3.7 (1.9 - 7.1)

Antibiotic therapy and outcomes of cancer patients with rESKAPE bacteremia

Variable	rESKAPE n=54 (%)	Other n=1094 (%)	P
Inadequate ATB therapy	30 (57)	238 (21)	<0.001
ICU admission	4 (8)	39 (4)	0.40
Persistence of sepsis	13 (25)	104 (10)	<0.001
Early case-fatality rate (7d)	12 (22)	120 (11)	0.026
Overall case-fatality rate (30d)	18 (34)	235 (22)	0.062

Vancomycin-resistant *Enterococcus* bacteremia in hematopoietic stem cell transplant recipients

- Screening at admission and weekly for VRE in allo-HSCT (2004)
- 247 adults with HSCT (2008-2009)
- 27% colonized pre-HSCT
 - 11% developed BSI, 85% within first 10 days
- Risk factors for VRE BSI: VRE colonization and T cell depletion
- Leading cause of BSI (53.5%)
- Attributable mortality was 9%

Pseudomonas aeruginosa bacteremia among hematological patients

Of 441 cases of BSI (2004-2010),
66 were caused by *P. aeruginosa*,
and 33% were due to MDR strains
30-day mortality

- Risk factors:
 - Active disease
 - *P. aeruginosa* BSI
- Higher in **MDR strains:**
(37% vs 23%, p=0.26)
- Higher if inadequate initial
ATB therapy:
(83% vs 19%, p=.01)

Risk factors for infections with **MDR**
P. aeruginosa in patients with cancer
(June 2001 – July 2002)
Cases (n= 18) / Controls (n= 36)

Variable	Univariate P value	Multivariate		
		P value	OR	95% CI
Carbapenem use \geq 7 defined daily dose	< 0.001	0.001	23.8	3.5-166.67
History of previous <i>P. aeruginosa</i> infection	< 0.001	0.12	13.7	1.79-111.1
Steroid use during prior 30 days	0.007			
Chronic obstructive pulmonary disease	0.04	0.033	25.0	1.30-480.90
Leukemia	0.05			

Bloodstream Infections Among Transplant Recipients

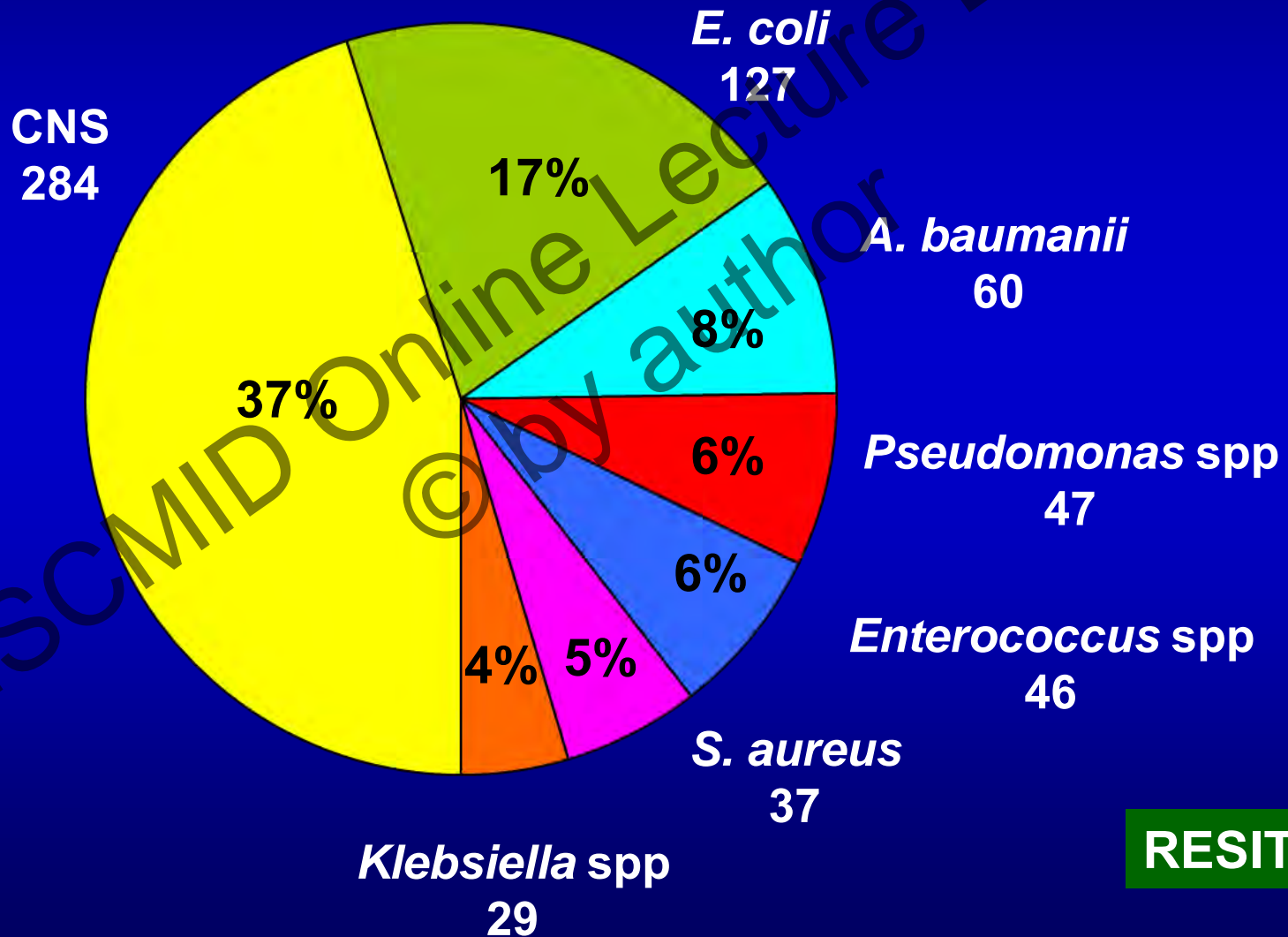
Results of a Nationwide Surveillance in Spain

	Kidney	Liver	Heart	Lung	Pancreas
Transplants (n)	1400	1012	291	167	65
Episodes (n)	121	134	32	17	17
Patients (n)	102	105	24	14	13
Incidence (%)	8.6	13.2	11	10.2	26.1

Crude mortality: 8%

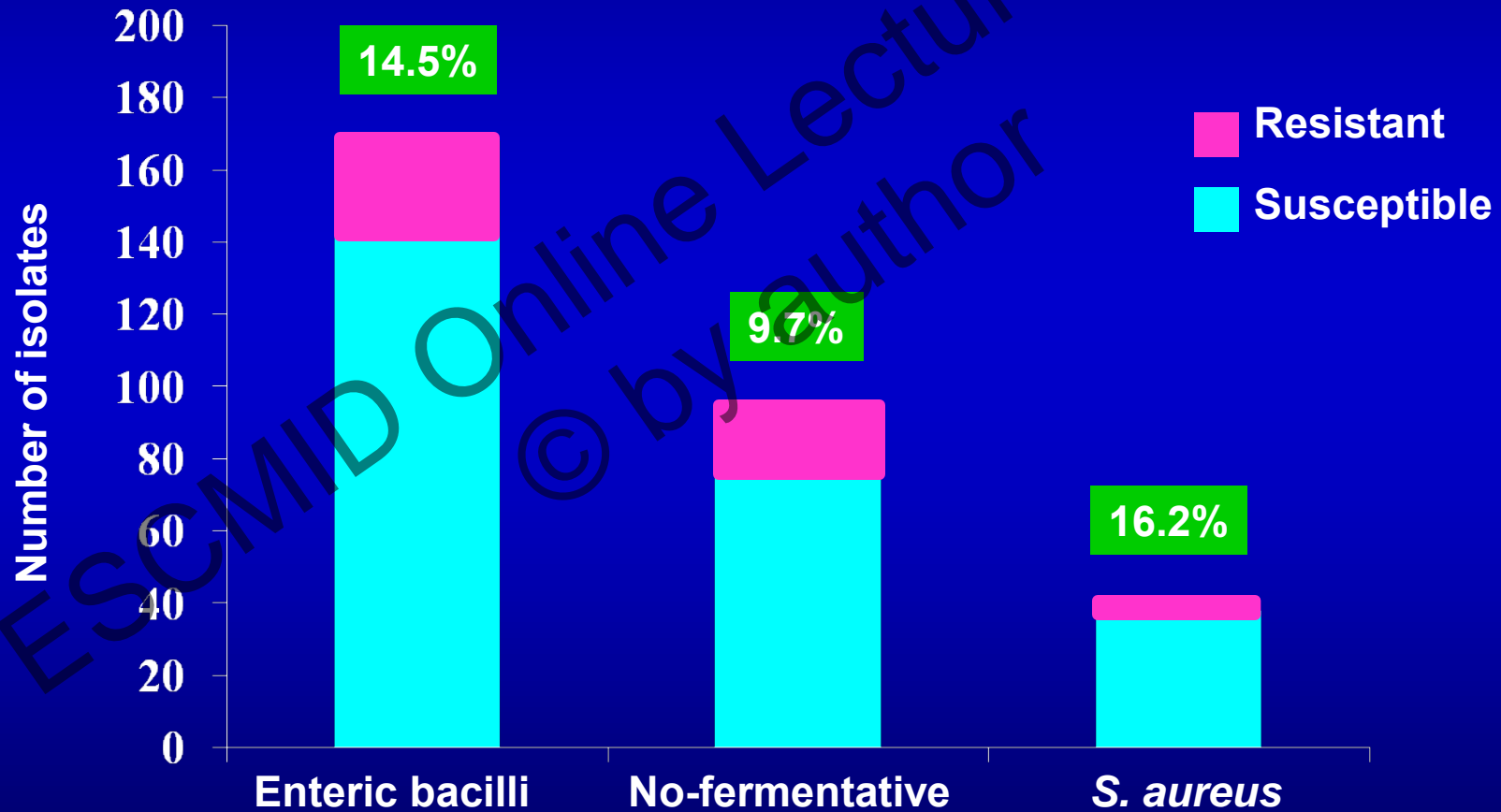
Moreno A. Am J Transpl 2007

Etiology of 321 episodes of bacteremia in SOT recipients



Bloodstream infections among SOT recipients

Proportion of resistant organisms (2003-2005)



Overall, 12% of isolates were MDR

Epidemiology, antibiotic therapy, and outcomes of bacteremia caused by rESKAPE in SOT recipients

276 cases of bacteremia

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graph TD; A[276 cases of bacteremia] --> B[130 (47%) ESKAPE bacteremia]; B --> C[Non-rESKAPE 76 cases]; B --> D[rESKAPE 54 cases (19.6%)];
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130 (47%) ESKAPE bacteremia

Non-rESKAPE

76 cases

rESKAPE

54 cases (19.6%)

ESKAPE pathogens isolated in 276 bacteremias in SOT recipients

Organism	ESKAPE total (n= 130)	R-ESKAPE (n= 54)
<i>Enterococcus faecium</i>	16	0
<i>Staphylococcus aureus</i>	18	5
<i>Klebsiella pneumoniae</i>	39	10
<i>Acinetobacter baumannii</i>	11	8
<i>Pseudomonas aeruginosa</i>	35	26
<i>Enterobacter spp.</i>	11	5

Risk factors for rESKAPE bacteremia in SOT recipients by multivariate analysis

Variable	OR	95% CI
Prior transplantation	3.1	1.1 – 9.4
Prior antibiotic therapy	4.0	1.5 – 10.6
Septic shock	2.8	1.4 – 5.7

Antibiotic therapy and outcomes of SOT recipients with rESKAPE bacteremia

Variable	rESKAPE n=54	Other n=222	P
Inadequate ATB therapy	41%	22%	0.01
ICU admission	52%	25%	<0.001
Mechanical ventilation	39%	17%	0.001
Overall case-fatality rate (30d)	35%	14%	0.001

MRSA bacteremia in liver transplant recipients

Rochester, USA: 6.5%

Lee SO. Liver Transpl 2011

Kyoto, Japan: 7.7%

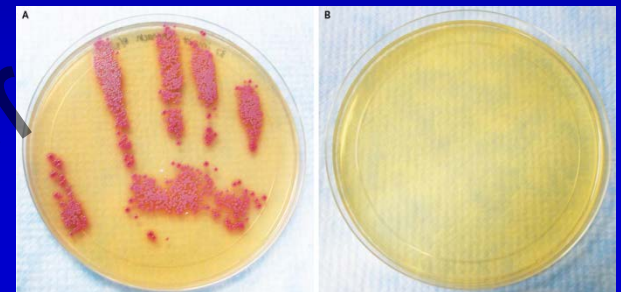
Lida T. Liver Transpl 2010

Clichy, France: 14%

Bert F. Liver Transpl 2010

MRSA infection in SOT recipients has been associated with **increased mortality** (OR 9.0)

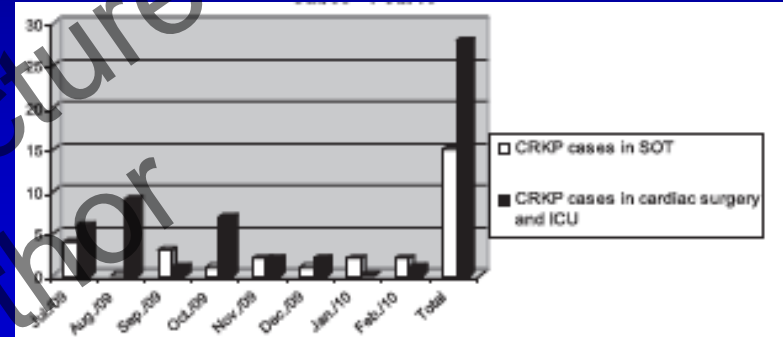
Yamada K. Tohoku J Exp Med 2011



Donskey CJ. NEJM 2009

Infection with KPC-producing *Klebsiella pneumoniae* in SOT recipients

- Outbreak of 12 cases of **KPC-2** producing KP in Sao Paulo.
- Incidence: **26% KT** (6); 17% HT (2); 13% LT (4). Median time to infection: **20 days**.
- Site of infection: urinary tract (4), bacteremia (4), pneumonia (2), SSI (2).
- All but 1 patient had received prior antibiotic therapy (30 days).
- Treatment: Tige + PB (3); PB + carbapenem (3); PB (3); Tige + Imip (1)
- Overall 30-day mortality: **42%**.



Empirical treatment of suspected bacteremia in immunocompromised hosts

Escalation strategy

- An uncomplicated presentation
- Without specific risk for resistant pathogens
- In centres where infections due to resistant pathogens are rare

De-escalation strategy

- Pts with complicated presentations
- Individual risk factors for resistant pathogens
- Centres where resistant pathogens are frequent

Where are we going?

- **Increasing prevalence of ESKAPE and other MDR organisms**
- **Updated knowledge of local epidemiology and resistance patterns**
- **No new antibacterials to treat infections due to MDR organisms will be available**
- **Selective effect of the increasing use of last resort antibiotics of great concern**
- **Need to improve preventive strategies and to optimize antibiotic therapy**



Thank you for your attention!

