5. Symposium der Bayerischen Landesarbeitsgemeinschaft multiresistente Erreger (LARE), Oberschleißheim, 04.12.2013

Acinetobacter baumannii:
Epidemiologie, Klinik und Therapie

Harald Seifert

Institut für Medizinische Mikrobiologie, Immunologie und Hygiene der Universität zu Köln

Multidrug-Resistant *Acinetobacter* Extremity Infections in Soldiers

Kepler A. Davis,* Kimberly A. Moran,† C. Kenneth McAllister,* and Paula J. Gray*

Twenty-three soldiers wounded in Iraq and subsequently admitted to Brooke Army Medical Center, San Antonio, Texas from March 2003 to May 2004 had wound cultures positive for *Acinetobacter calcoaceticus-baumannii* complex. Eighteen had osteomyelitis, 2 burn infection, and 3 deep wound infection. All isolates were MDR, 4 were resistant to imipenem.

Davis KA et al. Emerg Infect Dis. 2005; 11:1218-24

High Priority Pathogens Listed by the Antimicrobial Availability Task Force of the IDSA

- ***Enterococcus faecium* (VRE)**
- ***Staphylococcus aureus* (MRSA)**
- ***Klebsiella pneumoniae* (ESBL)**
- ***Acinetobacter baumannii***
- ***Pseudomonas aeruginosa***
- ***Enterobacter* spp.**

Boucher HW et al. **Bad Bugs, No Drugs: No ESKAPE**! An Update from the Infectious Diseases Society of America. Clin Infect Dis. 2009; 48:1–12 .

Genus *Acinetobacter* - Current Taxonomy

~30 named and 9 unnamed species

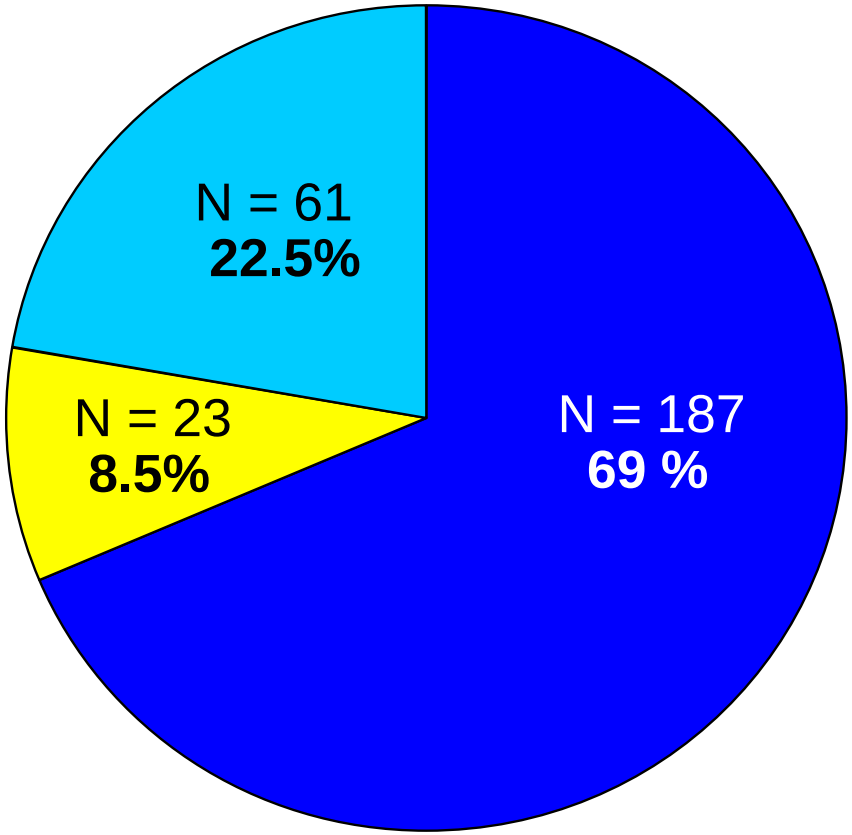
Named species	Unnamed species
A. baumannii	***A. pittii* (DNA group 3)**
A. calcoaceticus	DNA group 6

A. calcoaceticus - A. baumannii complex

A. junii	***A. nosocomialis* (DNA group 13 TU)**
A. lwoffii	DNA group 13 BJ/14 TU
A. parvus	DNA group 14 BJ
A. radioresistens	DNA group 15 BJ

***Acinetobacter** puyangensis* - Int J Syst Evol Microbiol. 2013 Feb 8.
***Acinetobacter** nectaris* - Int J Syst Evol Microbiol. 2013;63:1532-9
***Acinetobacter** boissieri* - Int J Syst Evol Microbiol. 2013;63:1532-9.

What's behind an "*A. baumannii*" ?



- *A. baumannii*
- *A. pittii* (gen. sp. 3)
- *A. nosocomialis* (gen. sp.13TU)

271 *A. baumannii* group isolates from bloodstream infection

Wisplinghoff H et al. Nosocomial bloodstream infections due to *A. baumannii*, *A. pittii* and *A. nosocomialis* in the United States. J Infect. 2012; 64: 282-290.

Phenotypic Identification of *Acinetobacter* spp.

- Scheme of ~28 physiological and biochemical tests

  Bouvet & Grimont (1986), Gerner-Smidt et al. (1990)

→ Not suitable for routine microbiological diagnostics

- Manual commercial ID systems (Api 20NE etc.….)

→ Completely unreliable

- Automated commercial identification systems (VITEK..)

→ Improving

Rapid and accurate identification of genomic species from the *Acinetobacter baumannii* (Ab) group by MALDI-TOF MS

P. Espinal[1], H. Seifert[2], L. Dijkshoorn[3], J. Vila[1] and I. Roca[1]

1) *Department of Clinical Microbiology, Hospital Clinic of Barcelona, School of Medicine, University of Barcelona, IDIBAPS, and Barcelona Centre for International Health Research (CRESIB), Barcelona, Spain,* 2) *Institute for Medical Microbiology, Immunology and Hygiene, University of Cologne, Cologne, Germany and* 3) *Department of Infectious Diseases, Leiden University Medical Center, Leiden, the Netherlands*

Clin Microbiol Infect 2012; **18:** 1097–1103

TABLE 1. MALDI-TOF MS identification of *Acinetobacter* spp. relative to log score values

Log score	*A. baumannii* (%)	*A. pittii* (%)	*A. nosocomialis* (%)	Other Acinetobacter species (%)	Total (%)
2.3–3.0	18 (100)	13 (76.5)	18 (100)	3 (42.9)	52 (86.7)
2.0–2.3	0	4 (23.5)	0	3 (42.9)	7 (11.6)
1.7–2.0	0	0	0	1 (14.2)	1 (1.7)
<1.7	0	0	0	0	0
Total	18	17	18	7	60/60

Acinetobacter baumannii

- Identification in the routine diagnostic laboratory -

- No fully reliable test system available for routine use
- No rapid test available
- Basic criteria (Gram's stain, oxidase, motility, smell)
- Use automated system or MALDI for presumptive identification of *A. baumannii* - sufficient for day-to-day clinical work
- For definite identification of *A. baumannii*
  - ➢ *bla*$_{\text{OXA-51-like}}$-PCR; *gyrB*-PCR

Acinetobacter – Common Misconceptions

Misjudgement:

„Ubiquitous organism“,

„Harmless commensal“

- *A. baumannii* is an aerobic, gram-negative coccobacillus that is highly prevalent in nature. These organisms are usually commensal, but they are emerging as important op 1998)
- A. *baumann* ous in fresh water and s al. (Chen et al., Chest, 2005
- *A. baumann* teria commonly found in wat ntibiotics in the 1970s. (Fou
- *A. baumann* m soil, water, animals, an ants of human skin. For this reason, it has been suggested that human skin could be the source of severe infections. (Fournier and Richet, Clin Infect Dis, 2006)
- Its natural habitats are water and soil, and it has been isolated from foods, arthropods, and the environment. (Munoz-Price and Weinstein, N Engl J Med 2008)

Acinetobacter baumannii Infektionen
- Krankheitsspektrum -

Nosokomiale Infektionen

- Harnwegsinfektionen
- Meningitis (Shunt-related)
- (Verbrennungs)Wundinfektionen
- Pneumonie (VAP)
- Bakteriämie (BSI)
  - ➢ Katheter-assoziierte BSI

Ambulant-erworbene Infektionen

- Harnwegsinfektionen
- Wundinfektionen
- Meningitis
- Endokarditis
- Pneumonie (in den Tropen)

A. baumannii infection requires

1. a susceptible patient

2. presence of the organism (endemic or epidemic)

Risk factors for *A. baumannii* nosocomial bacteremia in critically ill patients

Risk factors	OR (95% CI)	*p*
Immunosuppression	2.99 (1.26-7.13)	0.019
Unscheduled admission	3.29 (1.27-8.53)	0.008
Respiratory failure at admission	2.90 (1.45-5.82)	0.003
Previous antimicrobial therapy	2.35 (1.10-5.03)	0.025
Previous sepsis in ICU	4.36 (1.82-10.3)	<0.001
Invasive procedures index	1.82 (1.38-2.39)	<0.001

Garcia-Garmendia et al. (2001) CID 33: 939-46

Severe community-acquired pneumonia (CAP) due to *A. baumannii*

Design: Retrospective chart review.

Setting: Patients with severe CAP admitted to Taiwan University hospital between 1993 and 1999 and *A. baumannii* isolated from blood or pleural fluid at admission

Results: 13 patients met entry criteria. Predisposing factors were male gender, old age, alcoholism, malignancy, diabetes, and liver cirrhosis. 12 patients presented with septic shock and respiratory failure, 11 needed mechanical ventilation, 8 patients (62%) died.

Chen et al. (2001) Chest 120: 1072-1077

MAJOR ARTICLE

Acinetobacter baumannii Skin and Soft-Tissue Infection Associated with War Trauma

8 cases of *A. baumannii* SSTI were associated with combat trauma wounds. Median age of the patients was 26 y. Patients presented with cellulitis with a “peau d’orange” appearance with overlying vesicles and, when untreated, progressed to necrotizing infection with bullae (hemorrhagic and nonhemorrhagic). All isolates were multidrug resistant, and clinical success was achieved for 7 of 8 patients with débridement and carbapenem therapy.

Sebeny PJ et al. Clin Infect Dis. 2008;47:444-9

Natural habitat of *Acinetobacter*

- *A*. non*baumannii*: Water, soil, plants, vegetables, human skin
  - Baumann et al., J Bact 1968; Seifert et al. JCM, 1997; Berlau et al. JHI, 1999; Berlau et al. EJCMID, 1999; Houang et al., JCM, 2001
- ***A. baumannii* is <u>not</u> an „ubiquitous organism“**
  - A hospital-adapted pathogen
  - The colonized patient is the reservoir
  - Hospital - respiratory tubing, computer keyboards, cellphones… (Cefai et al., JHI 1900; Neely et al., CID 1999; Borer et al., EID 2005)
  - Natural habitat remains to be defined

Acinetobacter baumannii infections

- Burden of disease –

CoNS	15.8	31.3 (1)	35.9 (1)	26.6 (1)	20.7	25.7	13.8
S. aureus	10.3	20.2 (2)	16.8 (2)	23.7 (2)	25.4	34.4	18.9
Enterococcus spp.	4.8	9.4 (3)	9.8 (4)	9.0 (3)	33.9	43.0	24.0
Candida spp.	4.6	9.0 (4)	10.1 (3)	7.9 (4)	39.2	47.1	29.0
Escherichia coli	2.8	5.6 (5)	3.7 (8)	7.6 (5)	22.4	33.9	16.9
Klebsiella spp.	2.4	4.8 (6)	4.0 (7)	5.5 (6)	27.6	37.4	20.3
P. aeruginosa	2.1	4.3 (7)	4.7 (5)	3.8 (7)	38.7	47.9	27.6
Enterobacter spp.	1.9	3.9 (8)	4.7 (6)	3.1 (8)	26.7	32.5	18.0
Serratia spp.	0.9	1.7 (9)	2.1 (9)	1.3 (10)	27.4	33.9	17.1
A. baumannii	**0.6**	**1.3 (10)**	**1.6 (10)**	**0.9 (11)**	**34.0**	**43.4**	**16.3**

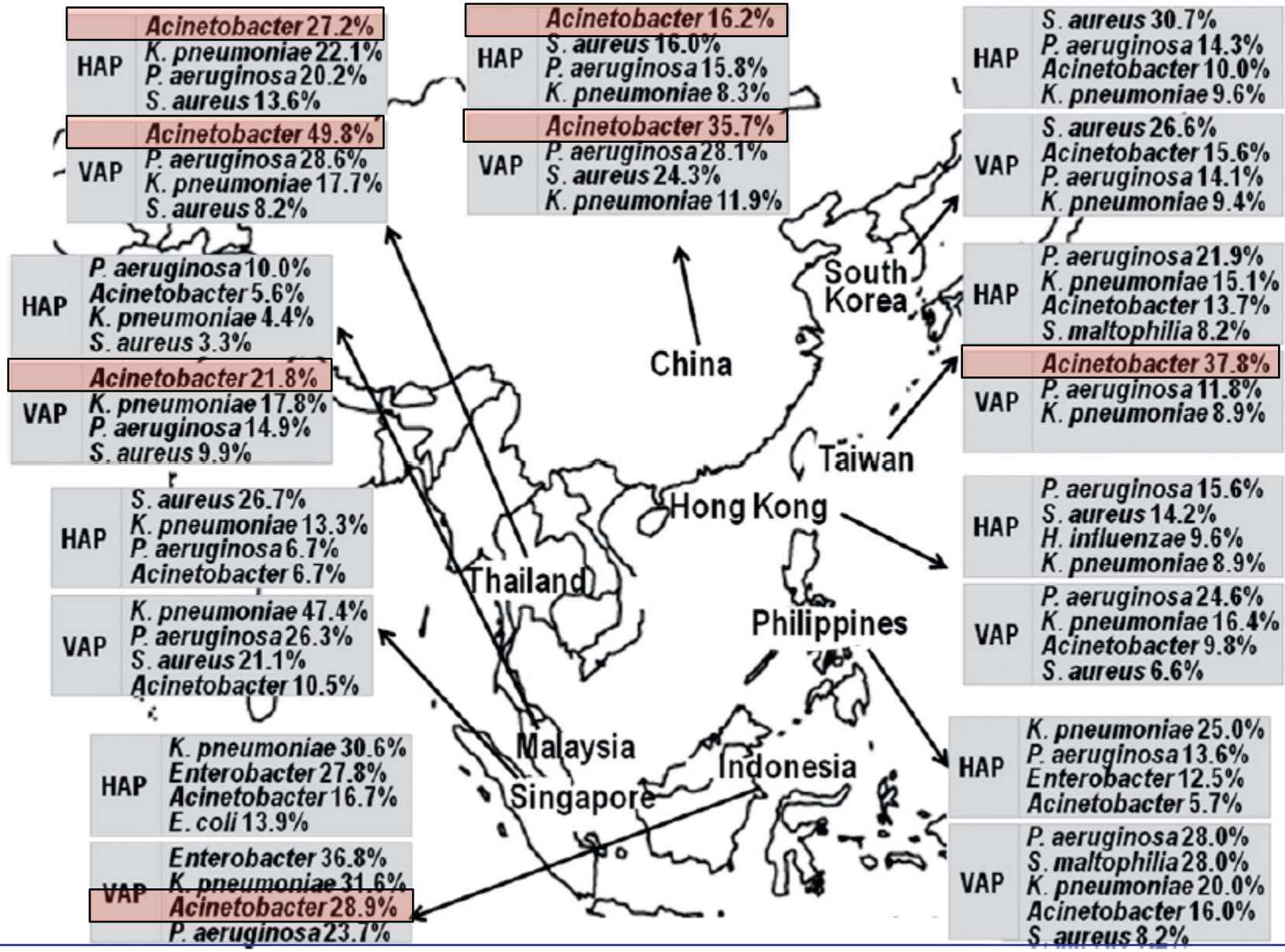
Wisplinghoff H et al. **Nosocomial bloodstream infections** in US hospitals: analysis of 24,179 cases from a prospective nationwide surveillance study. Clin Infect Dis. 2004;39:309-17.

Major bloodstream pathogens in Brazil

Pathogen	% BSI (rank)		
	Total (n = 2,447)	ICU (n = 1,196)	Non-ICU (n = 1,251)
S. aureus	15.4 (1)	12.8 (3)[a]	17.9 (1)
CoNS	13.8 (2)	16.6 (1)[a]	11.2 (3)
Klebsiella spp.	13.2 (3)	11.8 (4)[b]	14.5 (2)
Acinetobacter spp.	12.5 (4)	15.2 (2)[a]	10.0 (4)
P. aeruginosa	8.9 (5)	10.0 (5)	7.9 (5)
Enterobacter spp.	6.1 (6)	5.8 (7)	6.4 (6)
Candida spp.	5.6 (7)	7.4 (6)[a]	3.9 (7)
Enterococcus spp.	4.5 (8)	5.5 (8)[b]	3.6 (9)
Serratia spp.	3.5 (9)	3.2 (9)	3.8 (8)
Proteus spp.	1.6 (10)	1.8 (10)	1.6 (10)

Marra AR et al. Nosocomial Bloodstream Infections in Brazilian Hospitals: Analysis of 2,563 Cases from a Prospective Nationwide Surveillance Study. JCM 2011;49:1866–1871

Major organisms isolated from HAP and VAP in Asia



Chung DR et al. Am J Respir Crit Med 2011;184:1409-1417

Epidemiology *of A. baumannii*

- Transmission from a common source
- Airborne transmission (Bernards et al., AJIC 1998)
- **Patient-to-patient transmission**
  - Hands of hospital personnel
  - Contamination of environmental surfaces
  - Contamination of medical equipment

➔ **Colonized patient is the primary reservoir**

Epidemiology *of A. baumannii*

- Multiple hospital outbreak within a city
  - New York (Landman et al., ArchIM 2002)
  - London (Turton et al., JHI 2004)
  - Johannesburg (Marais et al., AJIC 2004)
- Multiple city outbreaks within a country
  - Czech Republic (Nemec et al., JMM 2004)
  - Southeast England (Coelho et al., JCM 2004)
  - France (Naas et al., EID 2006)
- Outbreaks from hospitals in several countries in Europe
  - van Dessel et al., Res Microbiol 2004
  - Towner et al., CMI 2008
  - Higgins et al., JAC 2010

Worldwide increase of resistance in *Acinetobacter* spp.

Prospective worldwide surveillance study (2005-2008)

Antibiotic	Susceptibility (%); n=4204			
	2005	2006	2007	2008
Imipenem	**77.0**	**65.9**	**63.9**	**50.2**
Meropenem	**70.8**	**63.8**	**63.0**	**48.9**
Ceftazidime	34.5	35.8	39.3	26.9
Levofloxacin	36.6	37.6	41.7	29.0
Amikacin	49.3	46.4	53.2	39.0
Tobramycin	58.6	52.5	58.0	45.9
Tigecycline	**97.5**	**98.8**	**96.0**	**96.5**
Colistin	**99.7**	**99.2**	**99.3**	**99.2**

➲ Mendes RE. C2-621, ICAAC, San Francisco, 2009

First report of „panresistant“ *A. baumannii*

- Outbreak of ESBL producing *K. pneumoniae* (TEM-26) in a New York City hospital
- Control of ceftazidime use and infection control measures
- Use of imipenem for resistant organisms

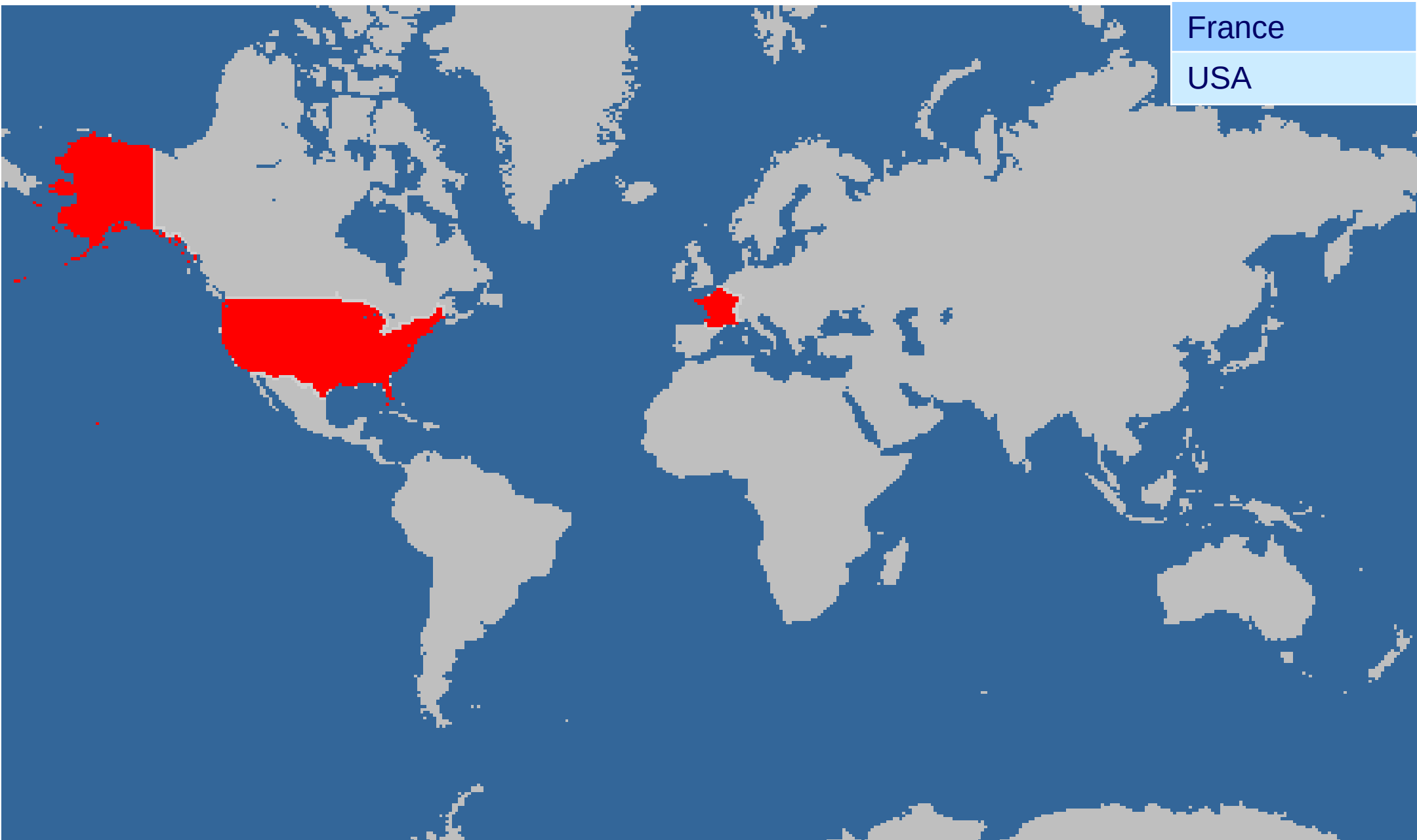
→ Decrease of ESBL *K. pneumoniae*

→ ICU outbreak of multi-resistant *A. baumannii*, sensitive to

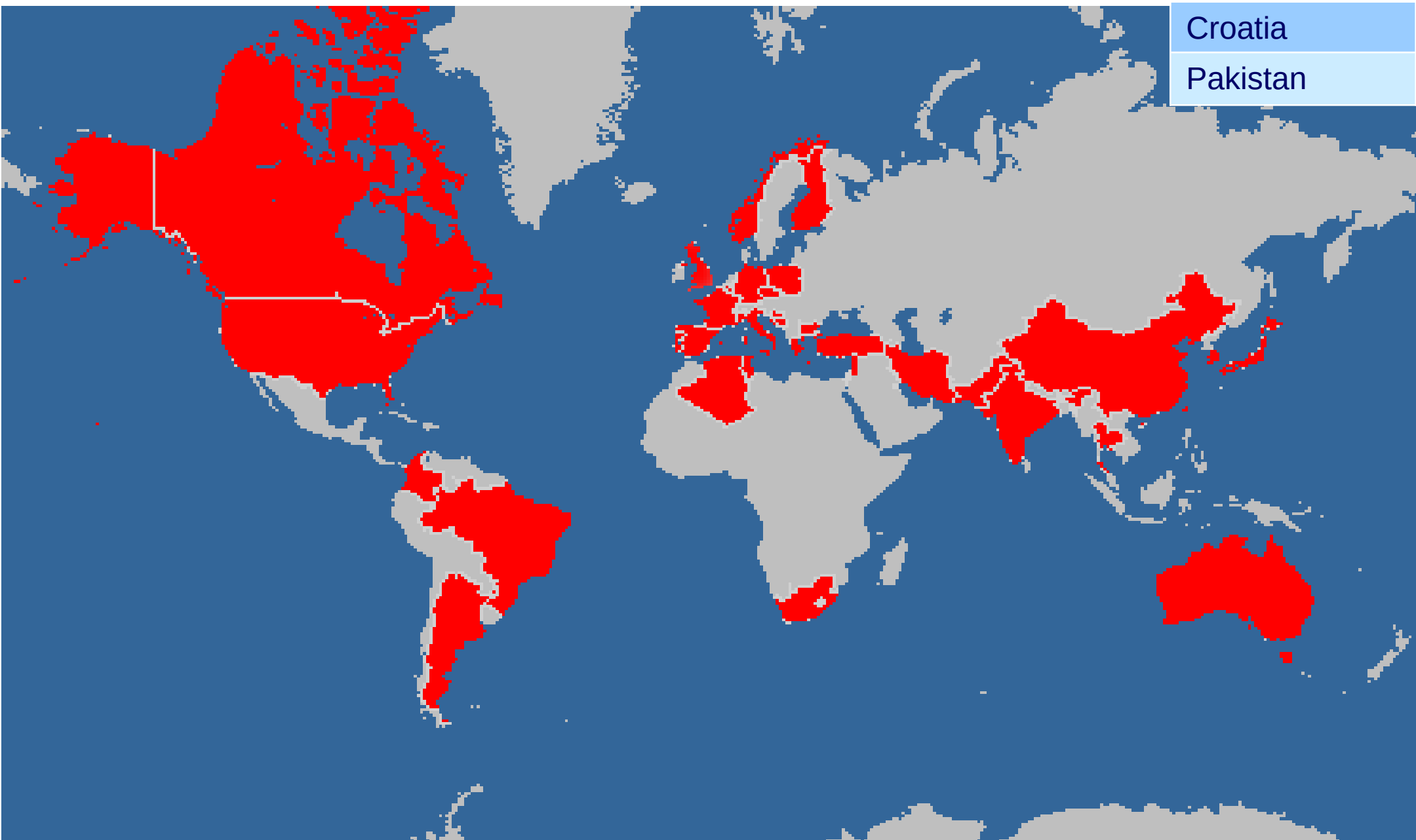
→ colistin and sulbactam only

Go et al. (1994) Lancet 344: 1329-32

1994



2011



Acinetobacter baumannii infections
– The „European (EU) Clones“–

- There was published evidence that three pan-European *A. baumannii* clones (lineages) are spreading in Europe
- (Dijkshoorn et al., JCM 1996; Nemec et al., JMM 2004; Turton et al., CMI 2007)

ORIGINAL ARTICLE

Clin Microbiol Infect 2007; **13**: 190–195

Identification of widespread, closely related *Acinetobacter baumannii* isolates in Portugal as a subgroup of European clone II

G. Da Silva[1], L. Dijkshoorn[2], T. van der Reijden[2], B. van Strijen[2] and A. Duarte[3]

International Journal of Antimicrobial Agents 38 (2011) 257–260

Contents lists available at ScienceDirect

International Journal of Antimicrobial Agents

journal homepage: http://www.elsevier.com/locate/ijantimicag

Short communication

Spread of imipenem-resistant *Acinetobacter baumannii* of European clone II in Western China

Chao He[a,1], Yi Xie[a,1], Hong Fan[a], Mei Kang[a], Chuanmin Tao[a], Rong Zhang[b], Yunjian Hu[c], Zhixing Chen[a], Lanlan Wang[a,*]

Journal of Antimicrobial Chemotherapy (2008) **62**, 484–489
doi:10.1093/jac/dkn205
Advance Access publication 13 May 2008

Emergence of carbapenem resistance in *Acinetobacter baumannii* in the Czech Republic is associated with the spread of multidrug-resistant strains of European clone II

Alexandr Nemec[1,2]*, Lenka Křížová[1], Martina Maixnerová[1], Laure Diancourt[3], Tanny J. K. van der Reijden[4], Sylvain Brisse[3], Peterhans van den Broek[4] and Lenie Dijkshoorn[4]

JAC

Antimicrobial Agents and Chemotherapy, July 2011, p. 3201–3206
0066-4804/11/$12.00 doi:10.1128/AAC.00221-11

Vol. 55, No. 7

Diversity and Evolution of AbaR Genomic Resistance Islands in *Acinetobacter baumannii* Strains of European Clone I[▽]†

Lenka Krizova,[1,2] Lenie Dijkshoorn,[3] and Alexandr Nemec[1]*

Laboratory of Bacterial Genetics, National Institute of Public Health, Šrobárova 48, 100 42 Prague, Czech Republic[1]; Department of Genetics and Microbiology, Faculty of Science, Charles University in Prague, Viničná 5, 128 44 Prague, Czech Republic[2]; and Department of Infectious Diseases, Leiden University Medical Center, P.O. Box 9600, 2300 RC Leiden, Netherlands[3]

ORIGINAL ARTICLE

Clin Microbiol Infect 2009; **15**: 347–357

Epidemic multidrug-resistant *Acinetobacter baumannii* related to European clonal types I and II in Rome (Italy)

S. D'Arezzo[1], A. Capone[1], N. Petrosillo[1] and P. Visca[1,2], on behalf of GRAB[3]

1) National Institute for Infectious Diseases "Lazzaro Spallanzani", I.R.C.C.S., Rome, 2) Department of Biology, University "Roma Tre", Rome, Italy and 3) GRAB (Gruppo Romano Acinetobacter baumannii) members are: M. Ballardini, S. Bartolini, E. Bordi, A. Di Stefano, M. Galiè, R. Minniti, M. Meledandri, L. Pacciani, G. Parisi, G. Prignano, C. Santini, M. Valmarin, M. Venditti, S. Ziantoni

Journal of Medical Microbiology (2005), **54**, 851–856

DOI 10.1099/jmm.0.45986-0

Short Communication

Repetitive-DNA-element PCR fingerprinting and antibiotic resistance of pan-European multi-resistant *Acinetobacter baumannii* clone III strains

Geert Huys,[1] Margo Cnockaert,[1] Alexandr Nemec,[2] Lenie Dijkshoorn,[3] Sylvain Brisse,[4] Mario Vaneechoutte[5] and Jean Swings[1,6]

[1,6]Laboratory of Microbiology[1] and BCCM/LMG Bacteria Collection[6], Ghent University, K. L. Ledeganckstraat 35, B-9000 Ghent, Belgium

Correspondence
Geert Huys

Acinetobacter baumannii infections
– The „European (EU) Clones“–

- There is evidence that three pan-European *A. baumannii* clones (lineages) are spreading in Europe
- (Dijkshoorn et al., JCM 1996; Nemec et al., JMM 2004; Turton et al., CMI 2007)
- Unlike MRSA, there was no estimate of the true contribution of the various EU clones to the global epidemiology of *A. baumannii*

Global Spread of Carbapenem-Resistant *Acinetobacter baumannii* (CRAb)

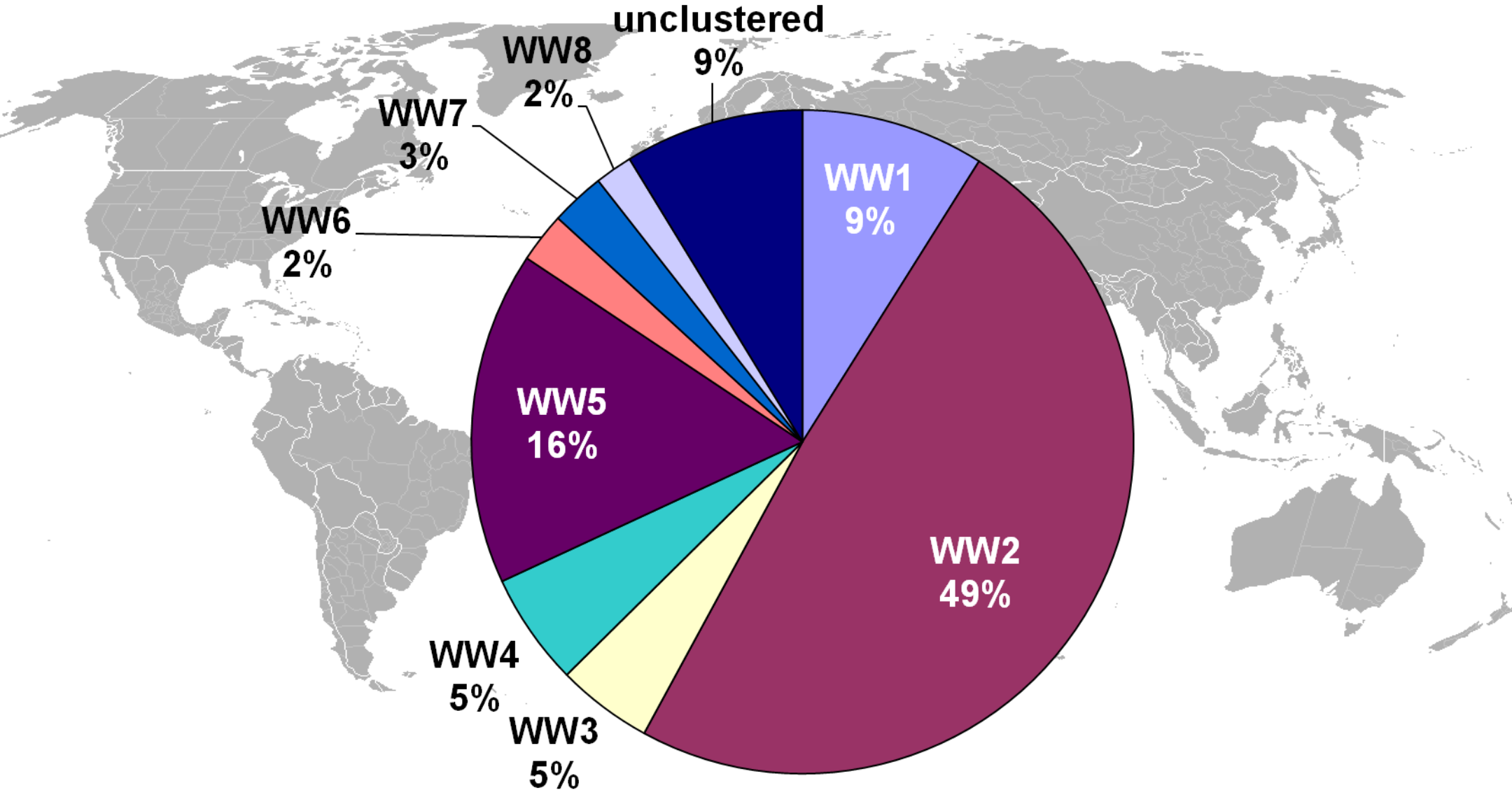
Methods 492 carbapenem-resistent (MIC ≥ 8mg/L) *A. baumannii* isolates from a world-wide surveillance study (Tigecycline Evaluation and Surveillance Trial (T.E.S.T.), 2004-2006) were typed by rep-PCR (DiversiLab) to assess clonal relatedness.

Results

The vast majority of isolates (91%) were grouped into 8 distinct clusters (WW1–WW8) including European clones EU I, II and III.

Higgins P et al. JAC 2010; 65:233-238

Proportion of carbapenem resistant *A. baumannii* clustering with the Worldwide clonal lineages (N = 492)



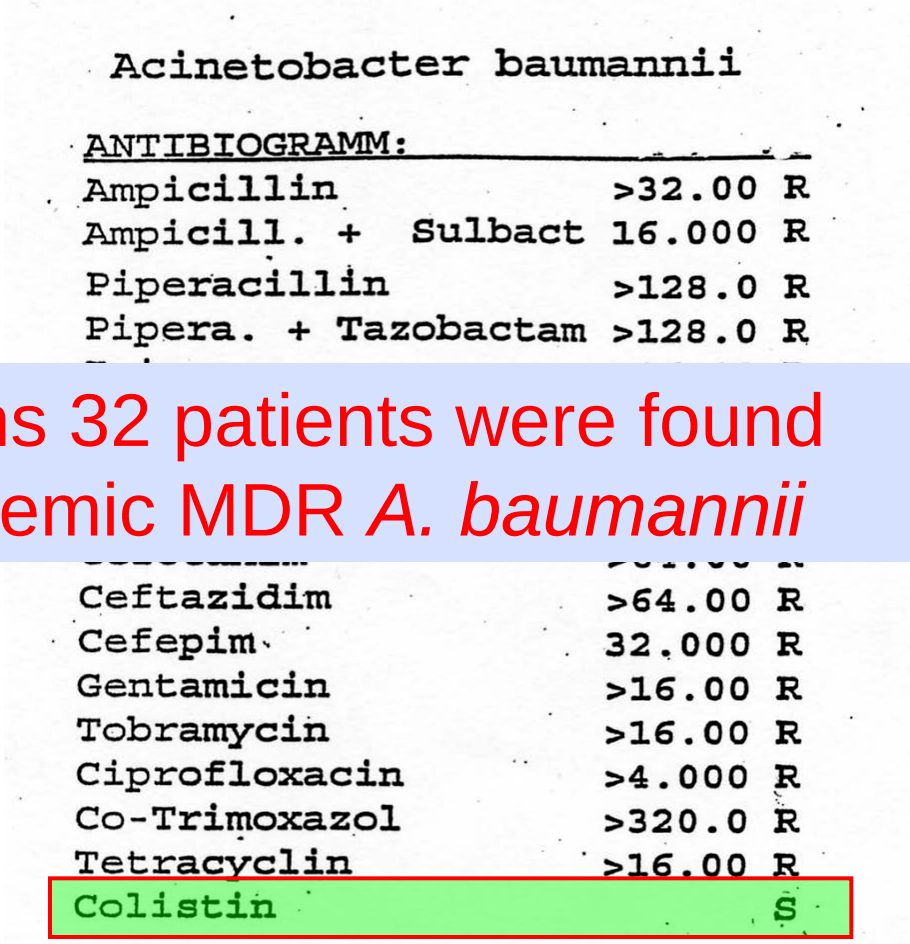
Outbreak of carbapenem-resistant *A. baumannii* carrying OXA-23 in a German university medical centre

- 61-year-old patient transferred from Thailand
- motor vehicle accident

During the following 9 months 32 patients were found colonized/infected with epidemic MDR *A. baumannii*

infection and osteomyelitis to a surgical ward

- perforated diverticulitis
- wound culture (02’06):



Acinetobacter baumannii

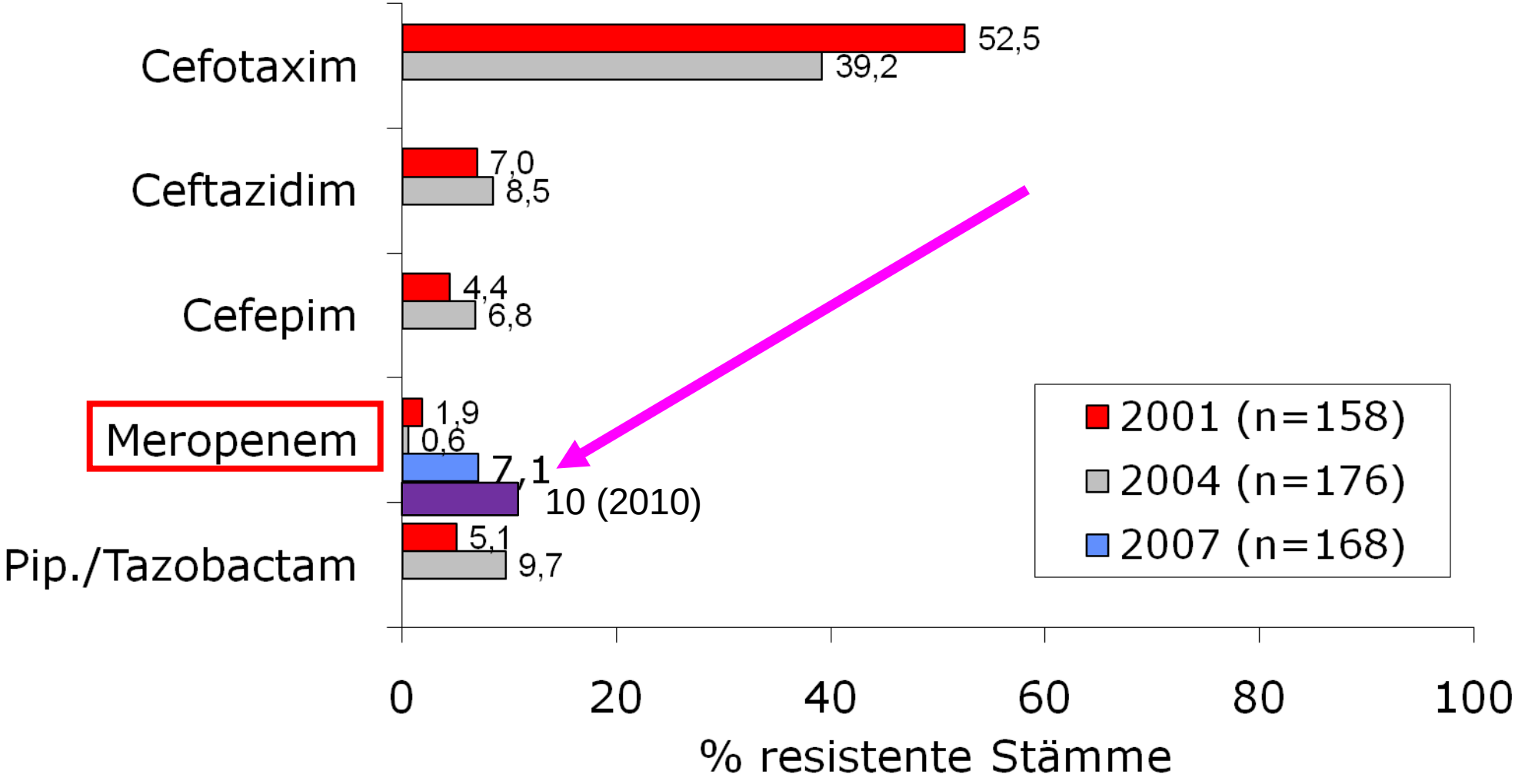
ANTIBIOGRAMM:

Ampicillin	>32.00	R
Ampicill. + Sulbact	16.000	R
Piperacillin	>128.0	R
Pipera. + Tazobactam	>128.0	R
Ceftazidim	>64.00	R
Cefepim	32.000	R
Gentamicin	>16.00	R
Tobramycin	>16.00	R
Ciprofloxacin	>4.000	R
Co-Trimoxazol	>320.0	R
Tetracyclin	>16.00	R
Colistin		S

Kohlenberg et al. J Med Microbiol. 2009; 58:1499-507.

Acinetobacter baumannii

Entwicklung der Resistenzlage 2001 - 2010



Quelle: PEG Resistenzstudie, M. Kresken

ORIGINAL ARTICLE 10.1111/1469-0691.12026

Molecular epidemiology of *Acinetobacter baumannii* and *Acinetobacter nosocomialis* in Germany over a 5-year period (2005–2009)

X. Schleicher[1], P. G. Higgins[1], H. Wisplinghoff[1], B. Körber-Irrgang[2], M. Kresken[2,3] and H. Seifert[1]

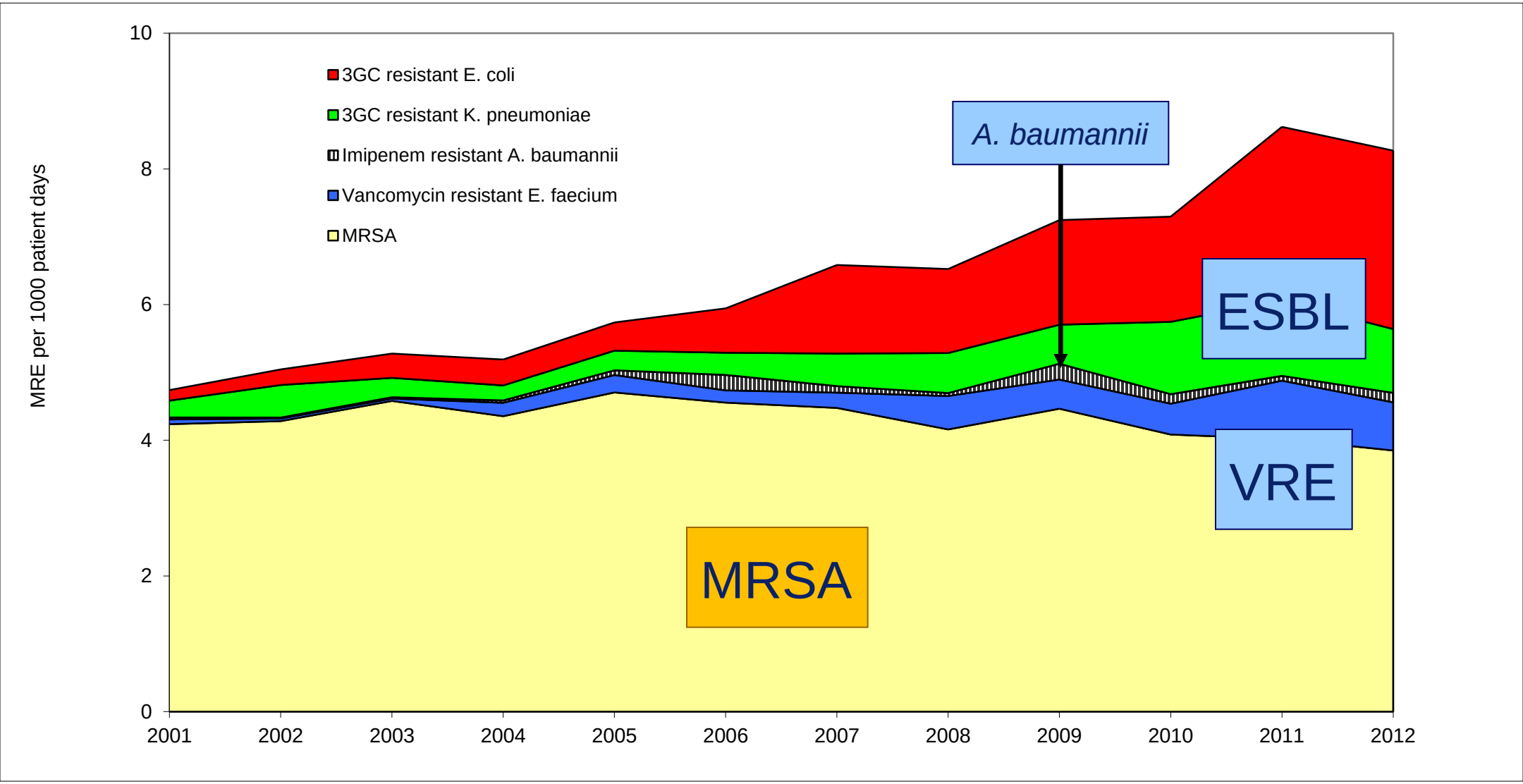
1) *Institute for Medical Microbiology, Immunology and Hygiene, University of Cologne, Cologne, Germany,* 2) *Anti-infectives Intelligence GmbH, Campus of the University of Applied Sciences, Rheinbach, Germany and* 3) *Rhine University of Applied Sciences, gGmbH, Cologne, Germany*

Carbapenem-Resistenz bei *A. baumannii* (n=140):

2005: 4%; 2009: 24%

Clin Microbiol Infect. 2012 Sep 7. [Epub ahead of print]

MDRO-Trend in Germany: SARI Intensive care units



P. Gastmeier, E. Meyer

KRINKO: Definition der Multiresistenz

Antibiotikagruppe	Leitsubstanz	*Enterobacteriaceae*		*Pseudomonas aeruginosa*		*Acinetobacter* spp.	
		3MRGN[1]	4MRGN[2]	3MRGN[1]	4MRGN[2]	3MRGN[1]	4MRGN[2]
Acylureidopenicilline	Piperacillin/ Tazobactam	R	R	Nur eine der vier Antibiotika-gruppen wirksam (sensibel)	R	R	R
Cephalosporine der 3./4. Generation	Cefotaxim und/ oder Ceftazidim	R	R		R	R	R
Carbapeneme	Imipenem und/ oder Meropenem	S	R		R	S	R
Fluorchinolone	Ciprofloxacin	R	R		R	R	R

Tab. 1: Klassifizierung multiresistenter gramnegativer Stäbchen auf Basis ihrer phänotypischen Resistenzeigenschaften (R = resistent oder intermediär sensibel, S = sensibel)

[1] 3MRGN (**M**ultiresistente **gram**negative Stäbchen mit Resistenz gegen **3** der 4 Antibiotikagruppen)

[2] 4MRGN (**M**ultiresistente **gram**negative Stäbchen mit Resistenz gegen **4** der 4 Antibiotikagruppen)

Epidemiologisches **Bulletin,**12. September 2011 / Nr. 36

Acinetobacter baumannii

- Therapieoptionen -

Therapie der Wahl

- Imipenem (zunehmende Resistenz!)
- (Chinolone)
- Aminoglykoside (als Kombinationspartner)

Alternativen

- Sulbactam
- Tigecyclin
- Doxycyclin / Minocyclin ??
- Polymyxin B / Colistin

Acinetobacter. Is it the Gram-ve MRSA?

6th International Conference of the Hospital Infection Society
Amsterdam, NL, 15-18 October 2006

If one wants to match *Acinetobacter* with gram-positive pathogens in terms of clinical impact, its most appropriate peer would appear coagulase-negative staphylococci rather than MRSA

Rello & Diaz, Int Care Med (2003), 29:350-351. *Acinetobacter baumannii*: a threat for the ICU?

Mortality from *A. baumannii* bloodstream infection in a military hospital

Methods Retrospective cohort study of patients with *A. baumannii* BSI in Walter Reed Army Medical Center. Comparison of patients with age < 60 and > 60 years.

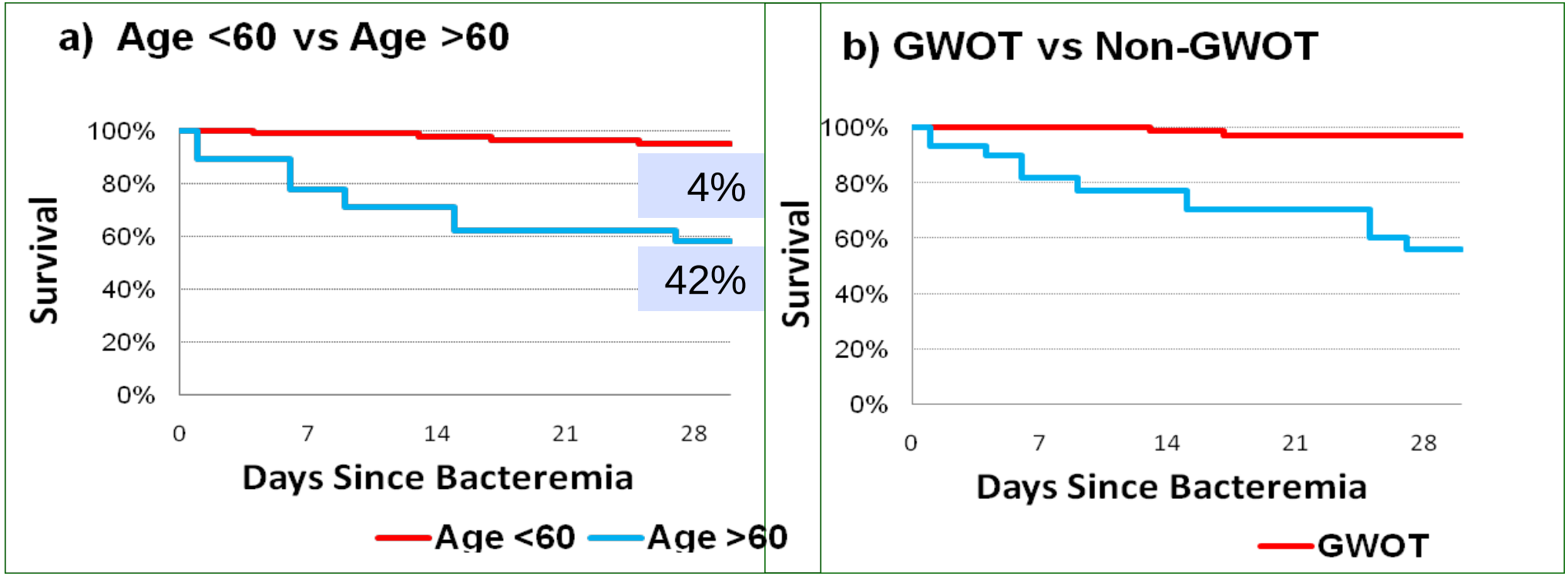
Results 122 patients were included. 60% of patients were <30 years of age, 76% were war trauma patients. 82% of *A. baumannii* isolates were MDR.

The overall 30-day mortality was 9.8%. Mortality in patients < 60 years was 4% versus 42% in patients > 60 years ($p<0.005$). Risk factors for an adverse outcome were age, higher APACHE II and Charlson (comorbidity) Score.

➲ Kang G et al. K-3352, ICAAC 2008

Mortality from *A. baumannii* bloodstream infection in a military hospital

30-day survival via Kaplan-Meier following *A. baumannii* bacteremia



GWOT, Global War on Terrorism

➲ Kang G et al. K-3352, ICAAC 2008

Commentary

Attributable mortality of *Acinetobacter baumannii*: no longer a controversial issue

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Comparison of patients with *Acinetobacter baumannii* (AB) infections with matched controls

Reference	Site of infection, patients and setting	Cases	Controls	Matching of controls to cases	Infection Mortality Cases	Infection Mortality Controls	Attributable mortality	*P* value/ odds ratio (95% CI)
Sunenshine and colleagues, 2007 [6]	MDR *Acinetobacter* spp. infections in two tertiary care hospitals in Baltimore, USA	96 patients with MDR *Acinetobacter* infection	91 patients with susceptible *Acinetobacter* infection (control group 1) or 89 uninfected patients (control group 2)	For control group 1: (1) similar exposure time (preinfection length of stay within 5% of matched reference), (2) similar institution	26%	17.6%	8.4%	0.21*/2.6** (0.3–26.1)
				For control group 2: (1) length of stay, (2) same ward (within 30 days)	26%	11.2%	14.8%	<0.01*/6.6** (0.4–108.3)
Grupper and colleagues, 2007 [7]	Nosocomial AB bacteremia in patients in ICU, medical and surgical wards in Israel	52 patients with *Acinetobacter* spp. bacteremia	52 matched controlled patients	(1) Age (±10 years), (2) sex (±3 years), (3) primary and secondary diagnosis of ICU admission, (4) operative procedures, (5) date of admission	29/52 (55.7%)	10/52 (19.2%)	36.5%	<0.001*/4.41 (1.98–9.87)** <0.001**
Playford and colleagues, 2007 [8]	Nosocomial acquisition of carbapenem-resistant AB in general ICU in Australia	66 patients (34 infected and 32 colonized) with AB	131 patients without any AB isolation	(1) Sex, (2) age (±3 years), (3) APACHE II score, (4) period at risk (date of admission to carbapenem-resistant AB acquisition (for cases) or to discharge (controls))	Inhospital: 15/34 (44%)	Inhospital 16/68 (24%)	20.0%	0.03/ adjusted† odds ratio: 3.9 (1.4–10.7)
Kwon and colleagues, 2007 [9]	Nosocomial AB bacteremia in three tertiary care hospitals in Korea (ICU and wards)	40 patients with imipenem nonsusceptible AB bacteremia	40 patients with imipenem-susceptible AB bacteremia	1) Age (± 5 years)	(Cumulative: 5 days, 37.5%	Cumulative: 5 days, 12.5%	25.0%	<0.05
				(2) Pitt bacteremia score (±1 point)	10 days, 50%	10 days 17.5%	32.5%	<0.05
				(3) Date of admission	30 days, 57.5%	30 days 27.5%	30%	<0.05
Robenshtok and colleagues, 2006 [10]	Nosocomial AB bacteremia and nosocomial *K. pneumoniae* bacteremia in a single centre in Israel	112 patients with AB bacteremia	90 patients with *K. pneumoniae* bacteremia	Patients with underlying conditions (comparative cohort study)	61.6%	38.9%	22.7%	0.001*/3.6 (1.5–8.39)**