The *Acinetobacter* Nightmare: Mechanisms and Clinical Implications

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Disclosures

- Advisory Board
  - Meiji
  - Roche
  - The Medicines Company
- Research Grant
  - Accelerate Diagnostics
- Clinical trials
  - Shionogi

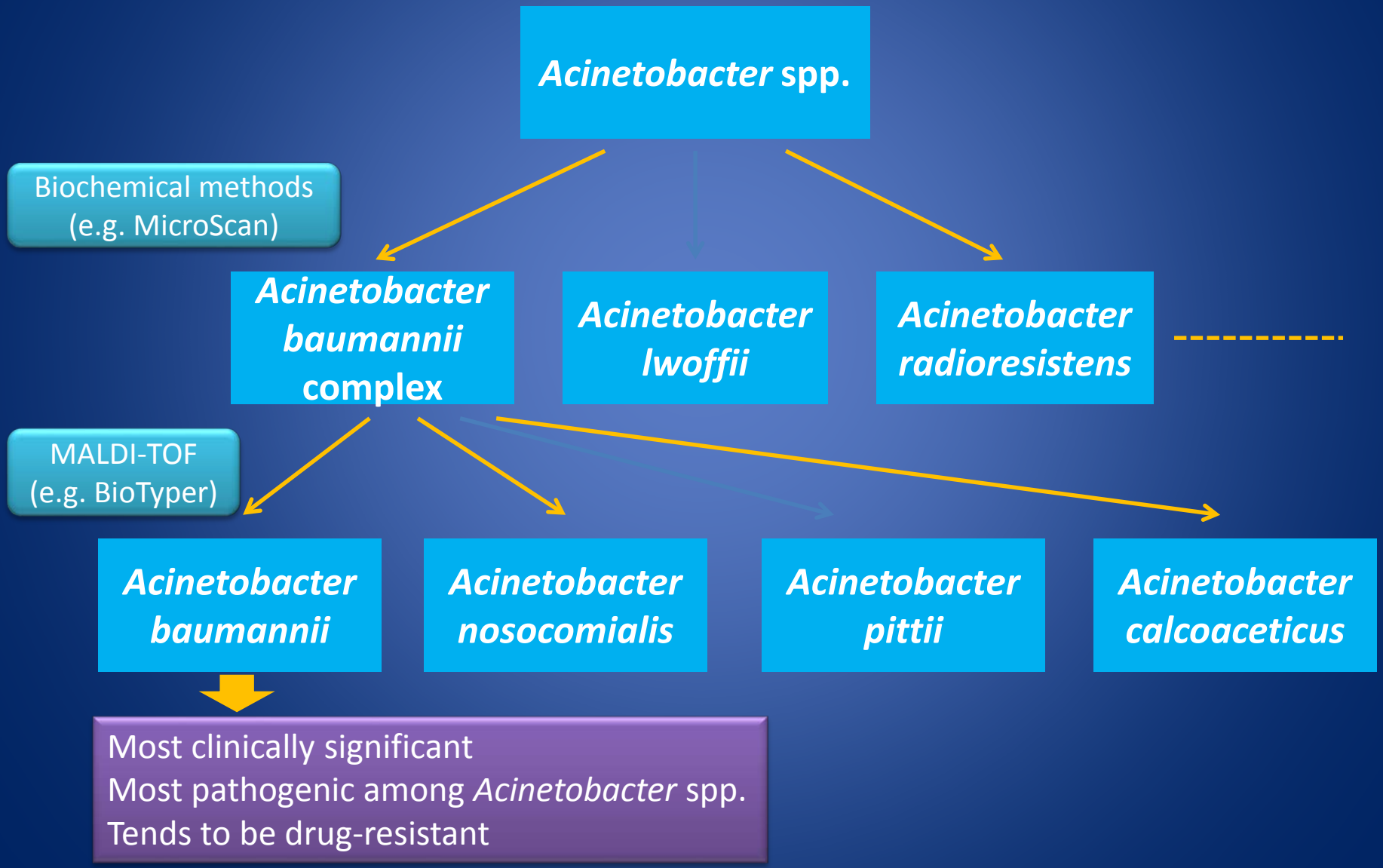
Objectives

- Understand trends in antimicrobial susceptibility of *Acinetobacter baumannii*
- Review the key resistance mechanisms
- Review new treatment modalities in the pipeline

Introduction

- *Acinetobacter* spp.
  - A group of genetically related non-lactose-fermenting, oxidase-negative, gram-negative coccobacilli
  - Most species are environmental and non-pathogenic
- *Acinetobacter baumannii* complex
  - The clinically significant group of species that includes four "genomospecies"

Species identification



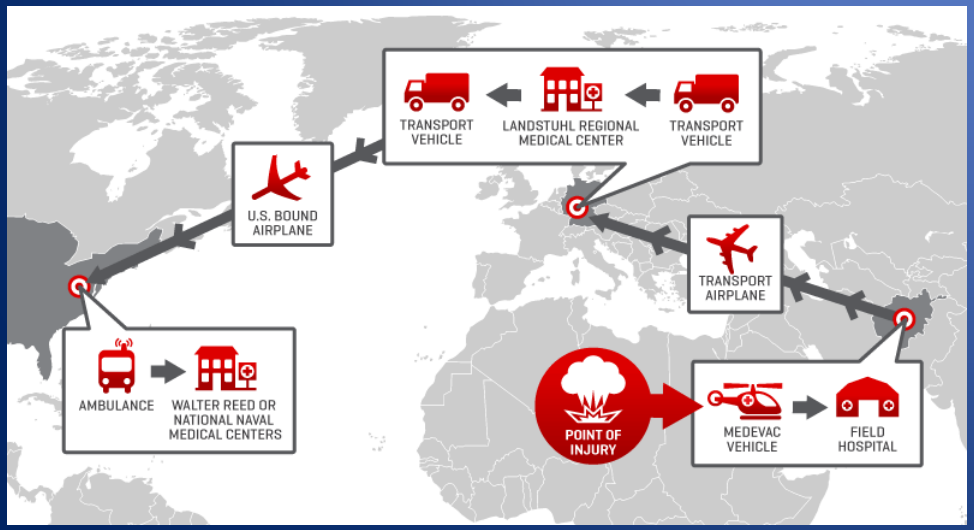
Clinical relevance

- *A. baumannii* causes
  - Ventilator-associated pneumonia
  - Bacteremia
  - Wound infection
- Risk factors
  - Antibiotic use (especially carbapenems)
  - Catheters (intravenous, urinary)
  - Severity of illness
  - Duration of hospital stay
  - ICU stay

Doi Y, et al. Semin Respir Crit Care Med 2015;36:85

Clinical relevance

- Outbreaks are difficult to control
  - Resistance to desiccation
  - Aerosolization
  - Antimicrobial resistance



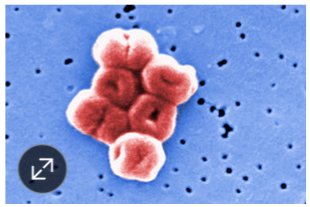
THE WALL STREET JOURNAL. ≡

'Superbugs' That Strike the Sickest Patients

By LAURA LANDRO
Updated Oct. 1, 2008 12:01 a.m. ET

In hospitals' war against drug-resistant superbugs, a class of bacteria once thought to be fairly benign is emerging as a deadly threat to the sickest and most vulnerable patients. The scourge -- known as gram-negative bacteria -- is throwing a new wrench into efforts to contain the spread of deadly infections.

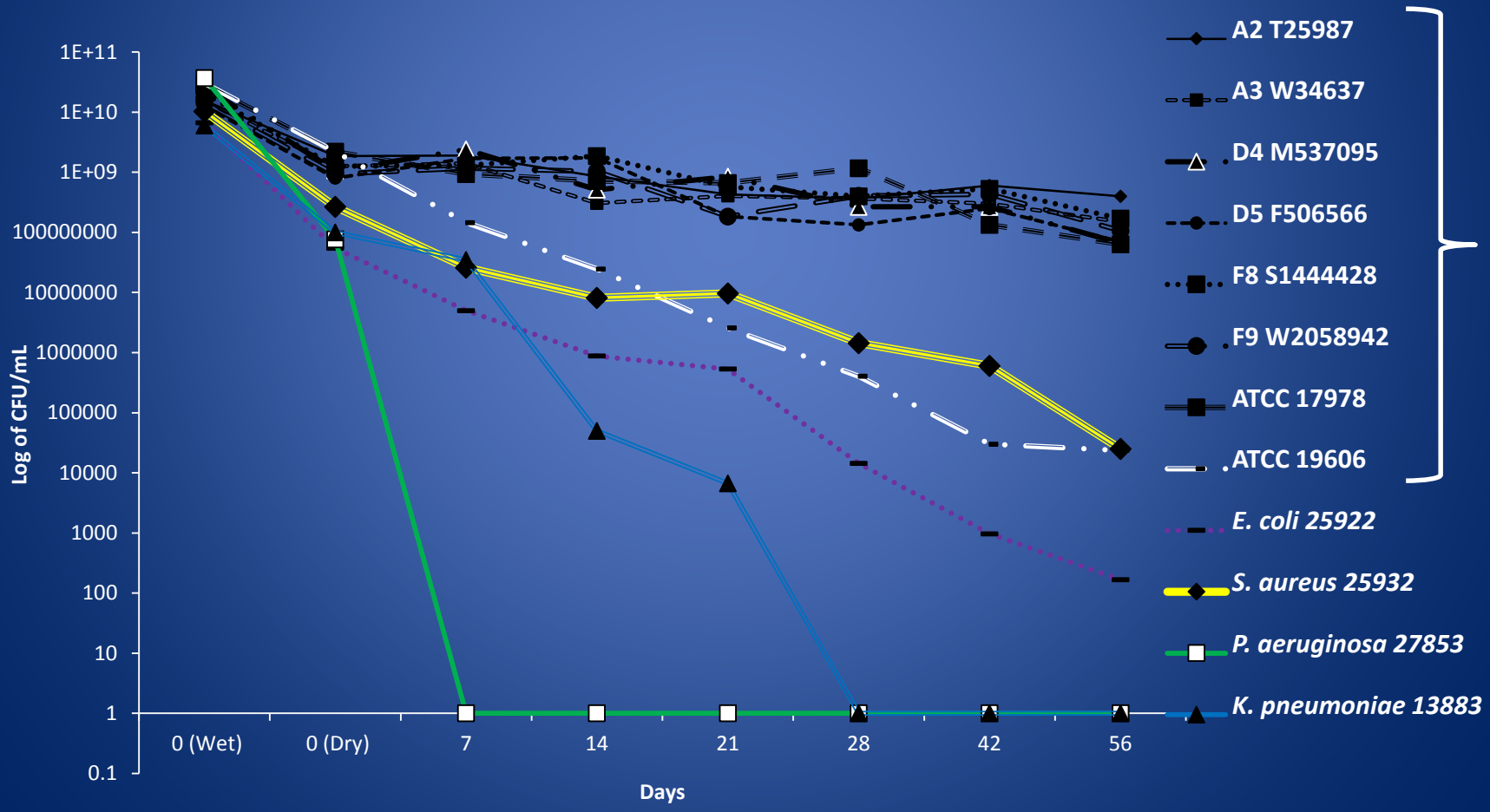
Amid more than 1.7 million infections annually in hospitals, prevention efforts have been aimed at the most widespread organisms, like the staph infection MRSA and others in the so-called gram-positive category. These can still be thwarted by antibiotics such as vancomycin.



But some of these bugs' wily cousins -- which don't pick up the purplish dye used in the test to distinguish them from gram-positive bacteria -- are becoming ultra-resistant. The extra outer membrane that rejects the stain also gives them additional armor against antibiotics. Some also produce an enzyme, known as ESBL, that enables them to break

Clinical relevance

- *A. baumannii* is extremely desiccation-resistant



Bethany Townsend, unpublished data

Clinical relevance

- *A. baumannii* can aerosolize
  - Trauma ICU in a Florida hospital with a longitudinal outbreak
  - 11/21 (52.4%) of air cultures grew *A. baumannii* in rooms occupied by *A. baumannii*-positive patients
  - 0/25 for *A. baumannii*-negative patients ($p < 0.0001$)

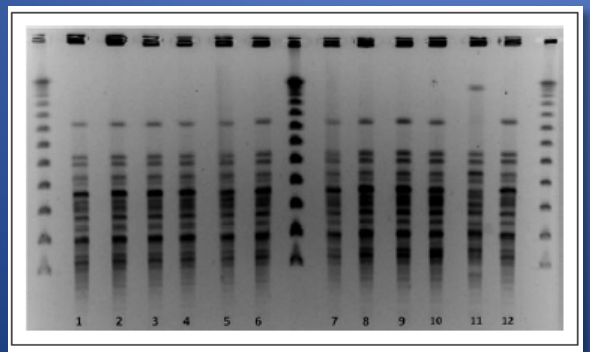


Figure 3. Pulse field gel electrophoresis on air and clinical isolates. (1–9) Environmental *Acinetobacter baumannii* isolates; all from air samples except for line 3 that corresponds to the isolate obtained after swabbing an intake air duct. (10–12) Carbapenem-resistant *A. baumannii* clinical isolates from patients present in the unit on the day air cultures were performed. Isolates 7, 8, and 9 corresponded to the air of the patients with clinical isolates 10, 11, and 12, respectively.

Munoz-Price LS, et al. Crit Care Med 2013;41:1915

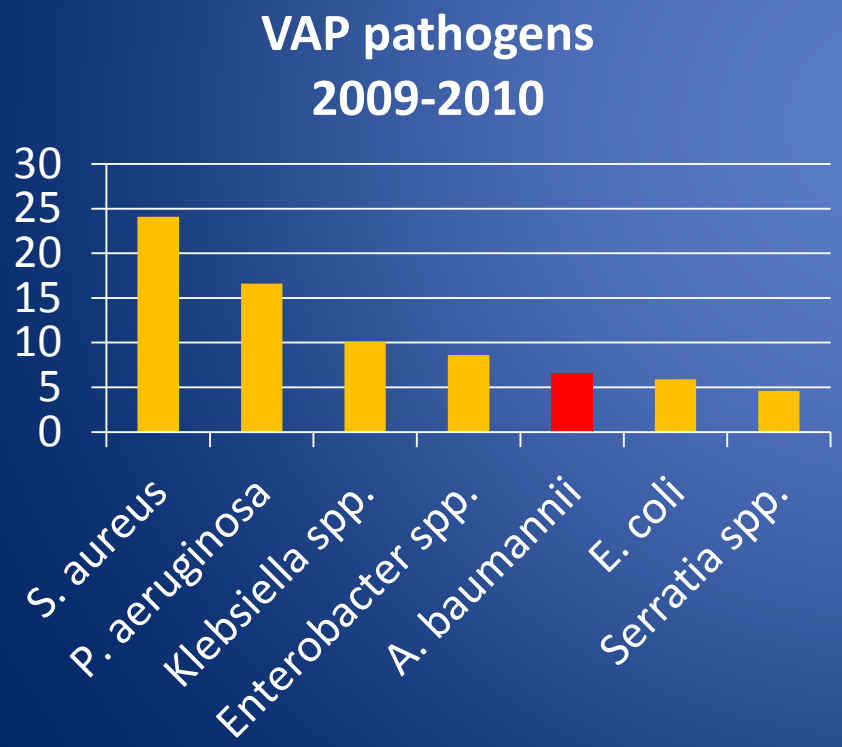
Aerosolization of *Acinetobacter baumannii* in a Trauma ICU*

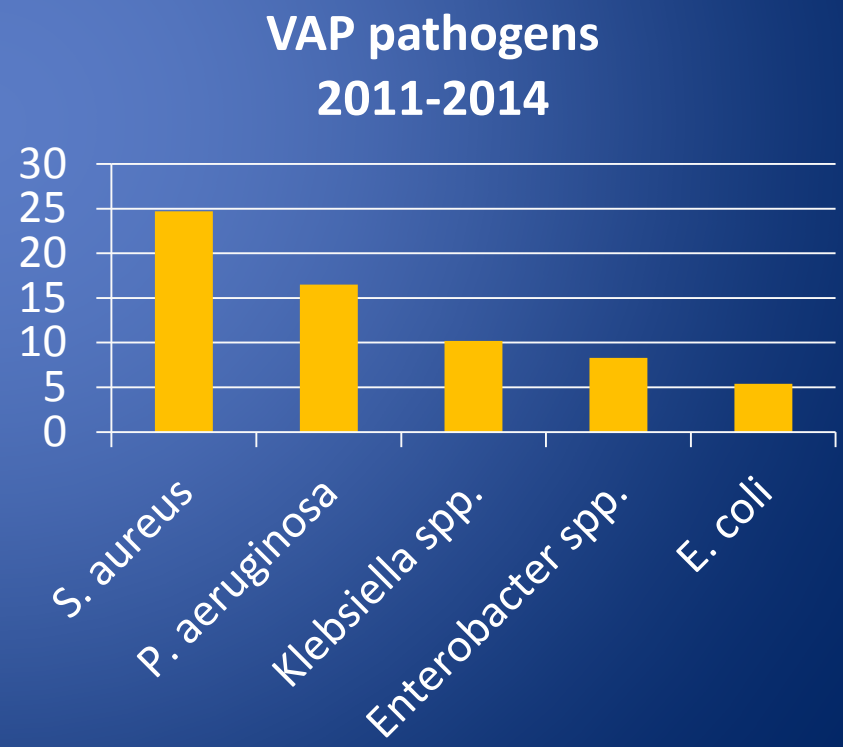
L. Silvia Munoz-Price, MD[1,2,4]; Yovanit Fajardo-Aquino, MD[4]; Kristopher L. Arheart, EdD[2,5]; Timothy Cleary, PhD[6]; Dennise DePascale, MT[4]; Louis Pizano, MD[3]; Nicholas Namias, MD[3]; Jesabel I. Rivera, BS[7]; Jessica A. O'Hara, MPH[7]; Yohei Doi, MD, PhD[7]

Objective: To establish the presence of air contamination with *Acinetobacter baumannii* in the trauma ICU.
Design: Point prevalence microbiological surveillances.
Settings: A 1,500-bed public teaching hospital in the Miami metro area.
Patients: Trauma ICU patients.
Conclusions: Aerosolization *of A. baumannii* in the ICUs is a concern, and its role in the transmission of this organism among patients should be further clarified. (*Crit Care Med* 2013; 41:1915–1918)
Key Words: *Acinetobacter* species; air contamination; ICU

Clinical relevance

- *A. baumannii* ranked 5th as the causative organism of ventilator-associated pneumonia (6.6%) in 2009-2010; its rank dropped to below 15th in 2011-2014





Sievert DM, et al. Infect Control Hosp Epidemiol 2013;34:1
Weiner LM, et al. Infect Control Hosp Epidemiol 2016;37:1288

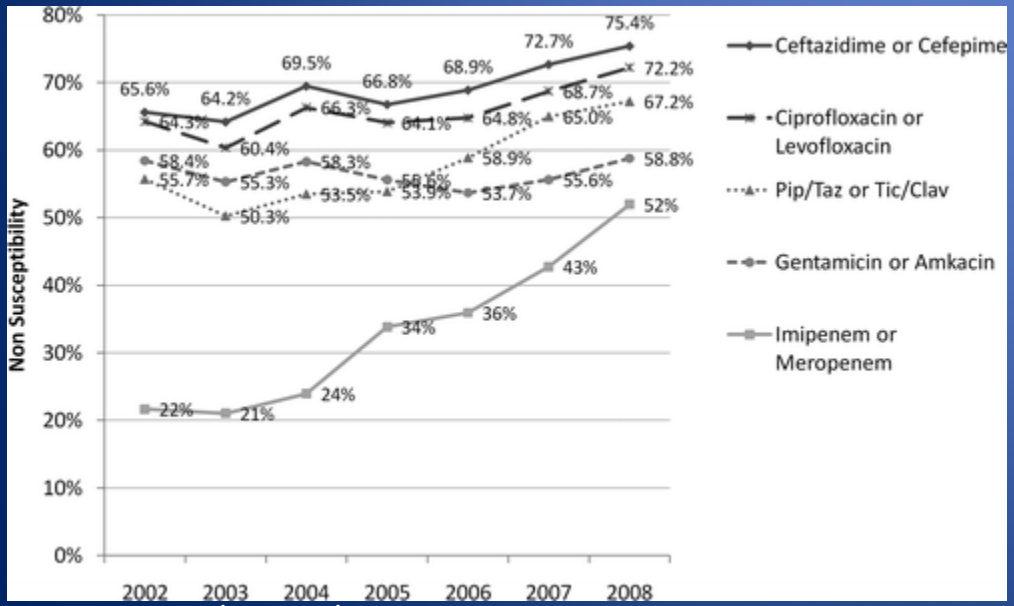
Evolution of resistance in *A. baumannii*

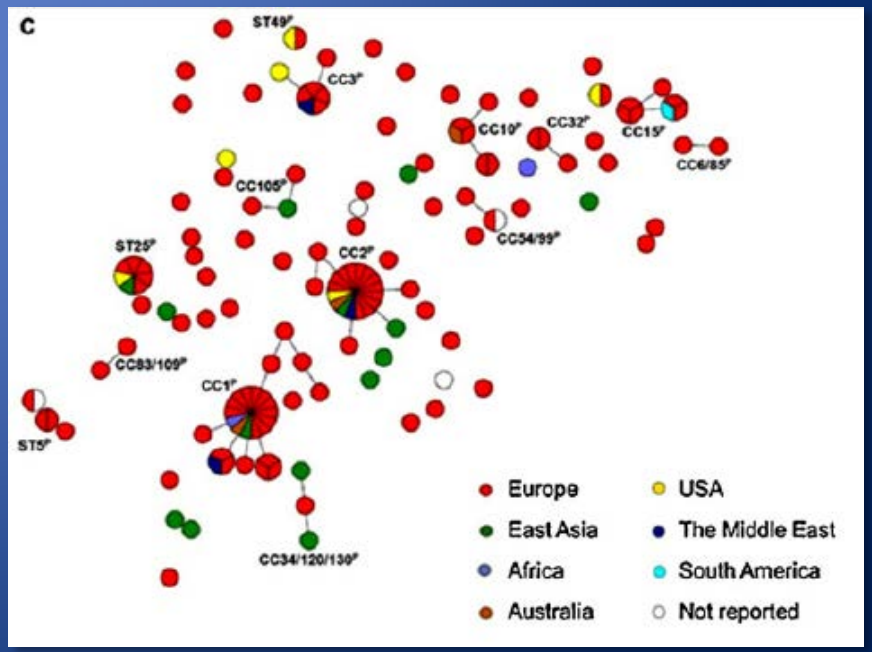
- *A. baumannii* was not always MDR/XDR
  - *Herellea vaginicola*
- Early 1970s
  - "treated successfully with gentamicin, minocycline, nalidixic acid, ampicillin, or carbenicillin"
- By early 1990s
  - "many … are resistant to … aminopenicillins, ureidopenicillins, … cephalosporins, most aminoglycosides…"
  - "Imipenem remains the most active drug"
- 1991-1992
  - Outbreak of imipenem-resistant *A. baumannii* in Queens, NY

Bergogne-Bérézin E, Towner KJ. Clin Microbiol Rev 1996;9:148
Go ES, et al. Lancet 1994;344:1329

“International Clones” predominate

- MDR is accounted for by International clones (ICs) 1, 2 and 3
- Propagation of MDR in the 2000s likely represented replacement of indigenous strains by epidemic strains rather than evolution of existing strains





Mera RM, et al. Microb Drug Resist. 2010;16:209
Karah N, et al. Drug Resist Updat. 2012;15:237-47

Bipolar susceptibilities

Indigenous *A. baumannii* strain

Last Update: 1/28/15 12:53 PM
Collected: 1/23/15 5:15 PM
Specimen Desc: Bronch wash

BRONCHIAL WASHING CULTURE

Accession Num: F6715105
Special Request: None
Status: Modified

Gram Stain: Rare WBCs present; Few Gram Positive Cocci; Many Gram Positive Rods
Culture: Moderate Acinetobacter baumanii/haemolyticus (anitratus)
Moderate Serratia marcescens
Moderate Normal Respiratory Flora

ACINETOBACTER ANITRATUS (BAUM./HAEMOLY.)

	MIC (mcg/mL)	MIC Interpretation
Amikacin	<=16	Sensitive
Amp/Sulbactam	<=8/4	Sensitive
Cefepime	<=4	Sensitive
Ceftazidime	4	Sensitive
Ceftriaxone	8	Sensitive
Ciprofloxacin	<=1	Sensitive
Gentamicin	<=4	Sensitive
Levofloxacin	<=2	Sensitive
Meropenem	<=1	Sensitive
Sulfa/Trimethoprim	<=2/38	Sensitive
Tobramycin	<=4	Sensitive

Epidemic *A. baumannii* strain

Last Update: 2/01/15 10:48 AM
Collected: 1/28/15 9:34 AM
Specimen Desc: Tissue SACRAL CORAPOSITION

TISSUE/SURGICAL CULTURE

Accession Num: W7027329
Special Request: None
Status: Final

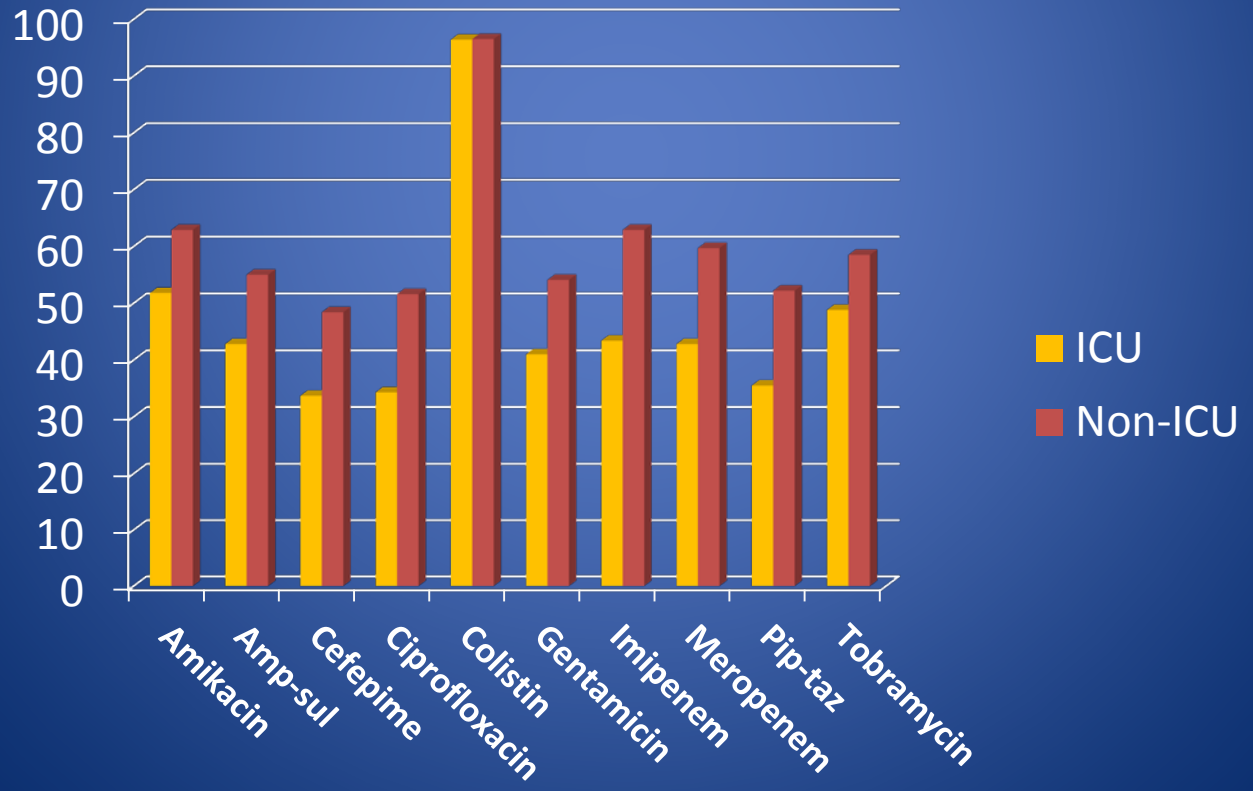
Gram Stain: Moderate WBCs present; No organisms present
Culture: Moderate Pseudomonas aeruginosa
Moderate Acinetobacter baumanii/haemolyticus (anitratus)
Rare Enterococcus faecalis Vancomycin Resistant

ACINETOBACTER ANITRATUS (BAUM./HAEMOLY.)

	MIC (mcg/mL)	MIC Interpretation
Amikacin	>32	Resistant
Amp/Sulbactam	16/8	Intermediate
Cefepime	>16	Resistant
Ceftazidime	>16	Resistant
Ceftriaxone	>32	Resistant
Ciprofloxacin	>2	Resistant
Gentamicin	>8	Resistant
Levofloxacin	4	Intermediate
Meropenem	>8	Resistant
Sulfa/Trimethoprim	>2/38	Resistant
Tobramycin	>8	Resistant

Antimicrobial susceptibility

- Antimicrobial susceptibility of ICU and non-ICU clinical isolates in the U.S. (2009-2011)



Sader HS, et al. Diagn Microbiol Infect Dis 2014;78:443

IC2 (CC2/CC92)

- 65 carbapenem-nonsusceptible *A. baumannii* isolates
  - Collected from 6 hospitals across the U.S. in 2008-2009 (NY, PA, MO, FL, NV, CA)
  - 24 PFGE clusters for 65 isolates
  - By MLST, STs belonging to Clonal Complex (CC) 92/CC2 accounted for 55/65 isolates

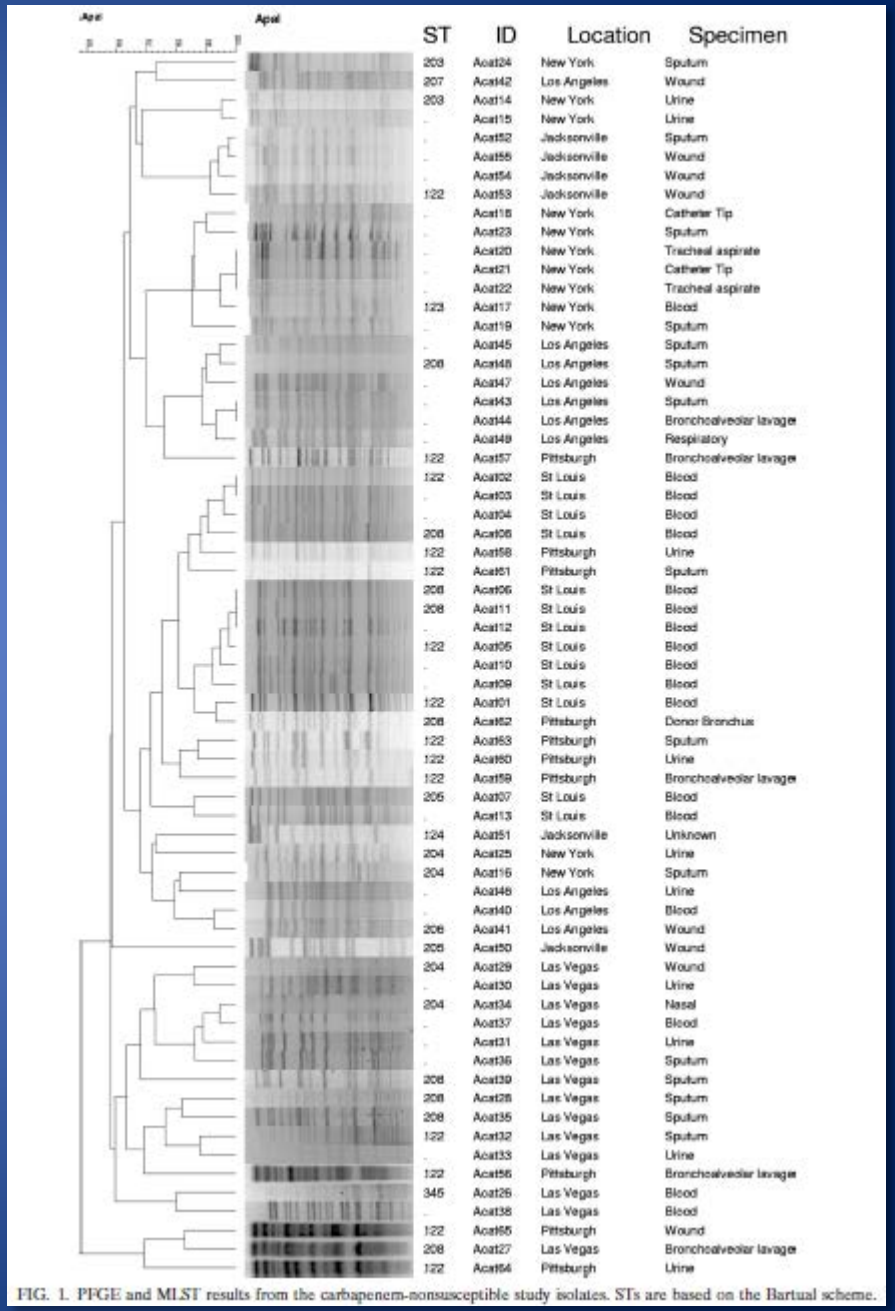


FIG. 1. PFGE and MLST results from the carbapenem-nonsusceptible study isolates. STs are based on the Bartual scheme.

Adams-Haduch JM, et al. J Clin Microbiol 2011;49:3849

Resistance mechanisms

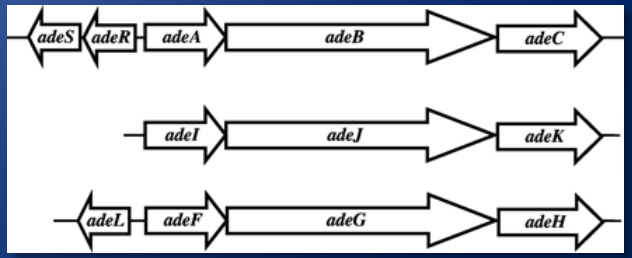
- *A. baumannii* is intrinsically resistant to antimicrobials
- Highly impermeable outer membranes
    - 2-7-fold less permeable to cephalosporins than *P. aeruginosa*
- Efflux pumps
    - MFS (major facilitator superfamily) and RND (resistance-nodulation-division) family

Efflux by Ade transporters

- RND family transporters of *A. baumannii*
  - AdeABC
    - Regulator = AdeRS (activator)
    - Substrates = cephalosporins, carbapenem, aminoglycosides, fluoroquinolones, tigecycline
  - AdeFGH
    - Regulator = AdeL (activator-repressor)
    - Substrates = fluoroquinolones, trimethoprim
  - AdeIJK
    - Regulator = AdeN (repressor)
    - Substrates = cephalosporins, meropenem, fluoroquinolones, tigecycline

Acquired resistance

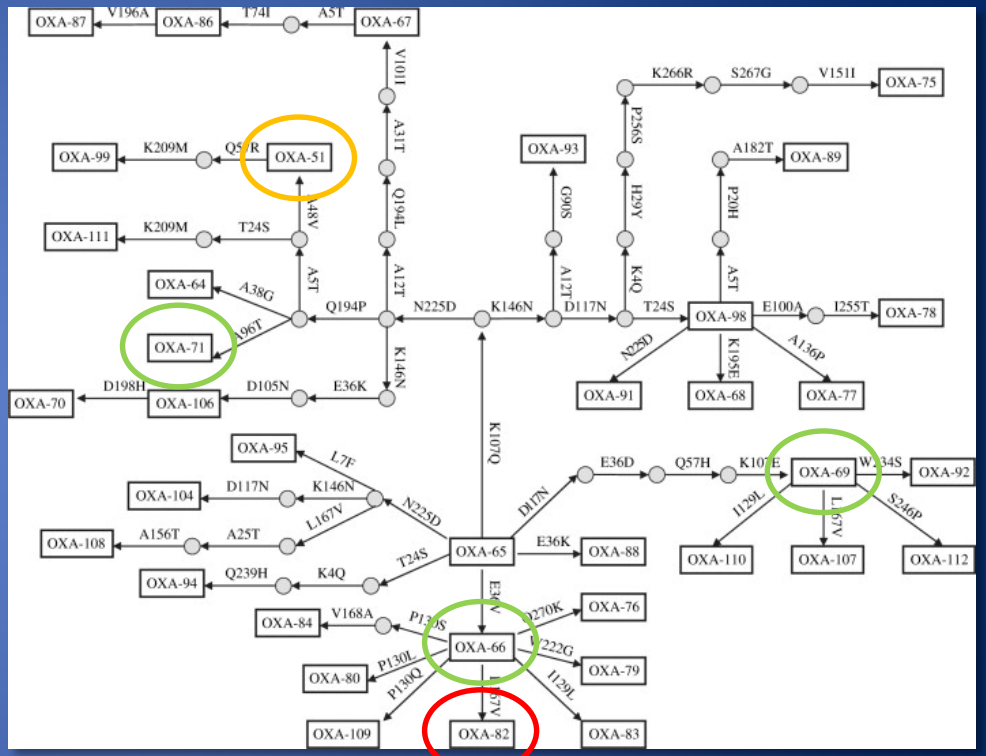
Intrinsic resistance

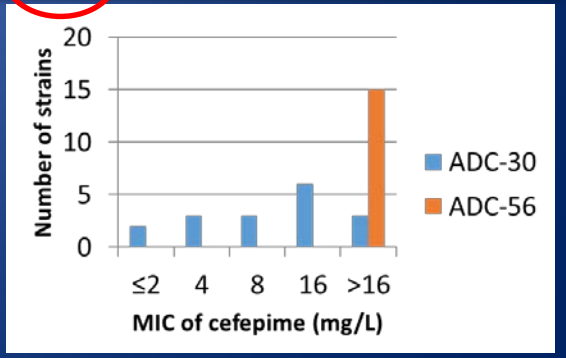


Coyne S, et al. Antimicrob Agents Chemother 2011;55:947
Yoon EJ, et al. mBio 2015;6:e00309-15

β-lactamases of *A. baumannii*

- Intrinsic β-lactamases
  - OXA-51 group
    - Weak carbapenemases
    - IC1 → OXA-69
    - IC2 → OXA-66
    - IC3 → OXA-71
  - ADC (AmpC)
    - Cephalosporinase
    - ADC-56 confers cefepime resistance

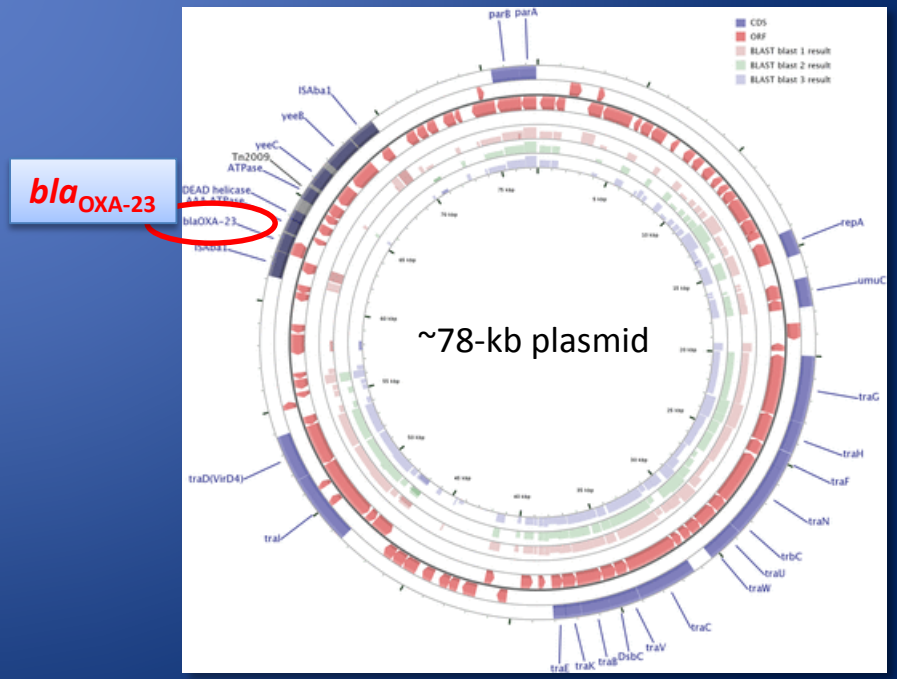




Evans BA, et al. Clin Microbiol Infect 2008;14:268
Tian GB, et al. Antimicrob Agents Chemother 2011;55:4922

β-lactam resistance

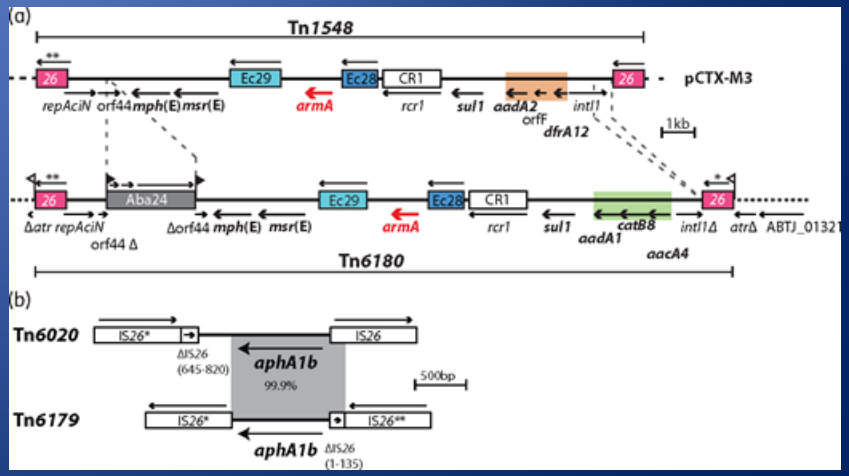
- Acquired β-lactamases
  - ESBLs (CTX-M, PER, GES)
  - Acquired OXA carbapenemases
- Carbapenem resistance is largely mediated by production of acquired OXA carbapenemases
  - **OXA-23**
  - OXA-40
  - OXA-58
  - OXA-143/253
  - OXA-235



Huang H, et al. J Antimicrob Chemother 2012;67:2825

Aminoglycoside resistance

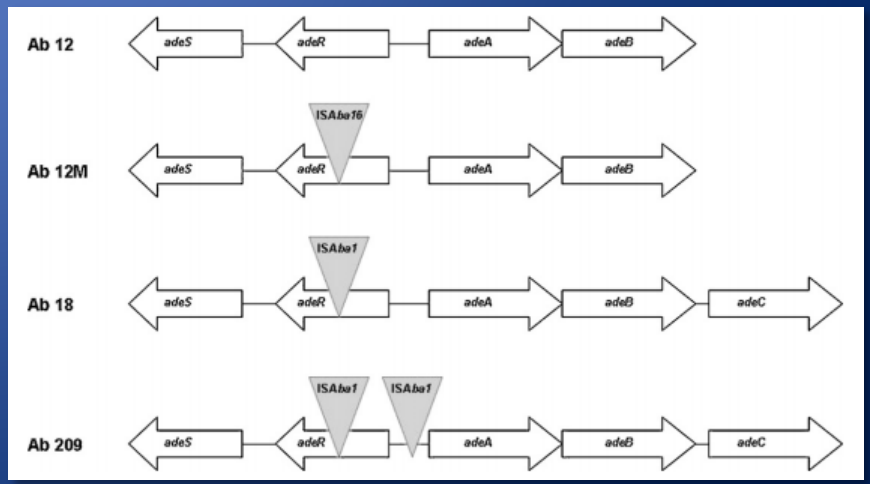
- Efflux
  - AdeABC
- Aminoglycoside-modifying enzymes
  - AAC(6')-Ib
  - AAC(3)-Ia
  - APH(3')-IIb
  - APH(3')-VIa etc.
- 16S rRNA methyltransferase
  - ArmA
  - Located on Tn*6180*
  - High-level GEN/TOB/AMK resistance



Blackwell GA, et al. J Antimicrob Chemother 2017;72:1031

Fluoroquinolone resistance

- Efflux
  - AdeABC
  - AdeIJK
- QRDR mutations
  - Quinolone Resistance Determining Regions
  - GyrA: Ser83→Leu
  - ParC: Ser80 →Leu
- Likely working synergistically for high-level resistance



Lopes BS, Amyes SG. Int J Antimicrob Agents 2013;41:117

How do we treat this?

- The standard approach at UPMC Presbyterian Hospital has been to treat infections with doripenem + colistin
- The combination is bactericidal *in vitro*
- 4/5 transplant patients survived infection with this this combination (as opposed to 1/11 with others)

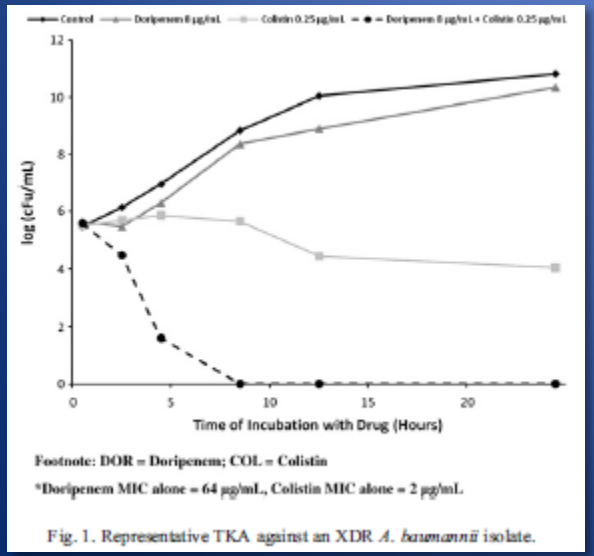


Fig. 1. Representative TKA against an XDR *A. baumannii* isolate.

Shields RK, et al. Diagn Microbiol Infect Dis 2011;70:246

Available online at www.sciencedirect.com
ScienceDirect
ELSEVIER
Diagnostic Microbiology and Infectious Disease 70 (2011) 246–252
DIAGNOSTIC MICROBIOLOGY AND INFECTIOUS DISEASE
www.elsevier.com/locate/diagmicrobio

Antimicrobial Susceptibility Studies

High mortality rates among solid organ transplant recipients infected with extensively drug-resistant *Acinetobacter baumannii*: using in vitro antibiotic combination testing to identify the combination of a carbapenem and colistin as an effective treatment regimen ☆,☆☆,★

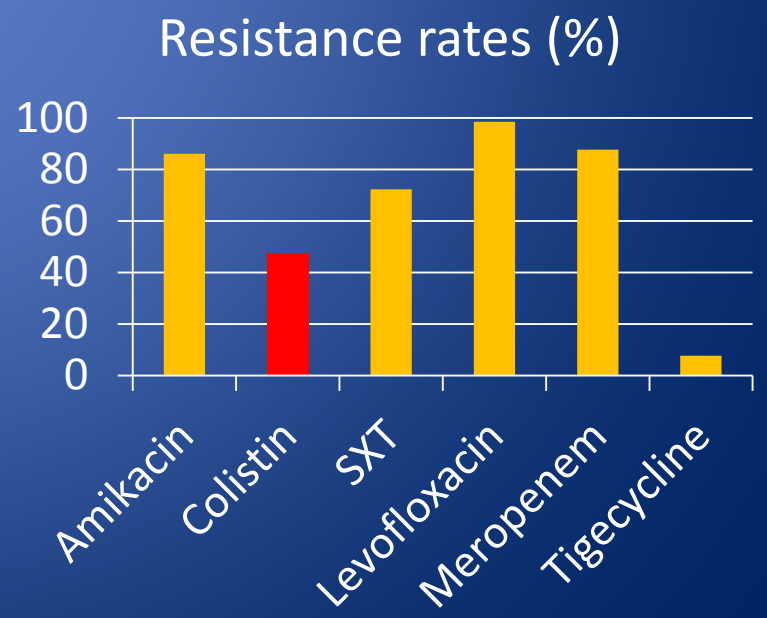
Ryan K. Shields[a,1], Eun J. Kwak[a,1], Brian A. Potoski[a], Yohei Doi[a], Jennifer M. Adams-Haduch[a], Fernanda P. Silviera[a], Yoshiya Toyoda[a], Joseph M. Pilewski[a], Maria Crespo[a], A. William Pasculle[a], Cornelius J. Clancy[a,b,*], M. Hong Nguyen[a]

[a]*University of Pittsburgh, Pittsburgh, Pennsylvania, USA*
[b]*V.A. Pittsburgh Healthcare System, Pittsburgh, Pennsylvania, USA*

Received 18 June 2010; accepted 27 December 2010

Colistin resistance

- Carbapenem-resistant infections are treated with colistin (typically in combinations)
  - Cationic peptide which binds lipid A
- Colistin resistance is an emerging issue
  - Global surveillance suggests1.8-7.5% colistin resistance among XDR *A. baumannii*
  - 65 *A. baumannii* VAP isolates from Greece, Spain, Italy
  - 48% resistance to colistin



Flamm RK, et al. Diagn Microbiol Infect Dis 2016;85:352
Nowak J, et al. J Antimicrob Chemother 2017;72:3277

Colistin resistance

- Carbapnem/colistin-resistant infection cases

Pt	Underlying condition	Type of infection	Colistin therapy	Survival	Paired strains	PFGE†	Colistin MIC
1	Lung transplant	VAP	Yes	No	Yes	0	2/>256
2	Heart transplant	Mediastinitis	Yes	No	Yes	0	1/>256
3	Lung transplant	VAP	Yes	No	Yes	0	1/>256
4	Respiratory failure	VAP	Yes	Yes	No	-	128
5	Kidney transplant	VAP	Yes	Yes	Yes	0	2/4*
6	Respiratory failure	VAP	Yes	Yes	Yes	0	2/>256
7	Intracranial hemorrhage	VAP	Yes	No	Yes	0	2/>256
8	Cirrhosis	VAP	Yes	No	Yes	0	2/>256
9	Lung transplant	VAP	Yes	Yes	Yes	0	2/>256
10	Heart/lung transplant	VAP	Yes	Yes	Yes	1	2/>256
11	Liver transplant	VAP	Yes	Yes	Yes	0	2/>256
12	Lung transplant	VAP	Yes	Yes	Yes	6	2/>256
13	Cirrhosis	colonization	No	No	No	-	16
14	Liver transplant	bacteremia	Yes	Yes	No	-	>256
15	Lung transplant	VAP	Yes	Yes	Yes	0	2/>256
16	Cerebral palsy	VAP	Yes	No	Yes	0	2/>256
17	Toxic epidermal necrolysis	VAP	Yes	No	No	-	16
18	Intracranial hemorrhage	VAP	Yes	Yes	Yes	5	2/8
19	Stroke	VAP	Yes	Yes	Yes	1	2/256
20	Lung transplant	VAP	Yes	Yes	Yes	1	2/16
21	Lung transplant	VAP	Yes	Yes	Yes	2	0.25/16

Seventeen of the Col^R strains are accompanied with Col^S strains. Pt, patient; VAP, ventilator-associated pneumonia. MICs shown in

Colistin resistance

- Most were in ICU and had VAP; 28-day mortality = 30%

Table 1. Characteristics and Outcomes of Patients With Colistin-Resistant *Acinetobacter baumannii*

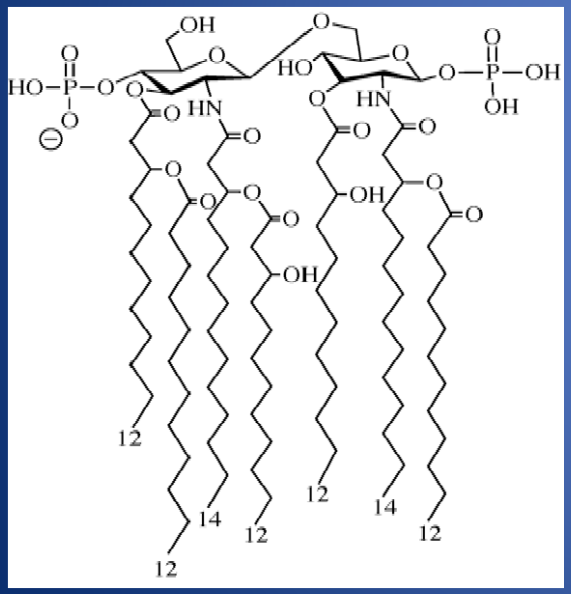
Patient	Age	Sex	Underlying Diseases	Culture Site	Type of Infection	ICU	APACHE II Score	Prior Intravenous CMS, d[a]	Prior Inhaled CMS, d[a]	Treatment of Colistin-Resistant Infection	Clinical Response	30-d Mortality	Death Attributable to Infection	90 d Recurrence
1	55	F	Lung transplant	Sputum	VAP	Yes	21	16	16	CMS, TIG, AMS	Failure	Yes	Yes	. . .
2	63	M	Heart transplant	Mediastinal fluid	Mediastinitis	Yes	25	8	None	CMS, TIG	Failure	Yes	Yes	. . .
3	43	M	Lung transplant	BAL	VAP	Yes	19	76	84	AMS, TIG, RIF	Failure	Yes	No[b]	. . .
4	53	M	Renal transplant	Sputum	VAP	Yes	20	5	None	CMS, DOR, AMS	Success	No	. . .	No
5	84	F	Dementia, recurrent pneumonia	Tracheal aspirate	VAP	Yes	20	14	14	CMS, DOR	Success	No	. . .	Yes
6	76	F	CVA	BAL	VAP	Yes	28	15	9	AMS	Failure	Yes	No[b]	. . .
7	36	M	Morbid obesity, liver cirrhosis	BAL	VAP	Yes	25	10	11	CMS, DOR	Failure	No	. . .	. . .
8	68	M	Lung transplant	Sputum	Colonization	Yes	22	4	7	None	. . .	No	. . .	No
9	61	M	Heart and lung transplant	Sputum	HAP	No	15	5	9	CMS, DOR, AMS	Success	No	. . .	Yes
10	52	F	Liver transplant	BAL	VAP	Yes	20	11	10	CMS, DOR, AMS	Success	No	. . .	No
11	62	M	Lung transplant	Bronchial wash	VAP	~~No~~	12	14	14	CMS, DOR, AMS	Success	No	. . .	No
12	71	M	Lung transplant	Bronchial wash	VAP	Yes	17	None	9	CMS (inhaled only), DOR	Success	No	. . .	No
13	62	F	Mental retardation, Parkinson's disease	BAL	VAP	Yes	13	28	28	CMS, DOR	Failure	Yes	Yes	. . .
14	66	F	CVA	BAL	VAP	Yes	20	32	15	CMS, DOR	Failure	Yes	Yes	. . .
15	63	M	CVA	BAL	Colonization	Yes	15	2	None	None	. . .	No	. . .	No
16	77	M	Lung transplant	Sputum	Colonization	Yes	17	7	7	None	. . .	No	. . .	No
17	63	F	Lung transplant	BAL	VAP	Yes	10	30	6	CMS, DOR, AMS	Success	No	. . .	No
18	25	F	Toxic epidermal necrolysis	Pleural fluid	VAP	Yes	19	21	21	CMS, MEM	Success	No	. . .	No
19	73	M	Lung transplant	Blood	Bacteremia	Yes	19	None[c]	None[c]	CMS, DOR, AMS	Success	No	. . .	No
20	57	M	COPD, tonsillar carcinoma	Blood	Bacteremia	Yes	27	7	5	CMS, DOR, AMS	Success	No	. . .	No

Qureshi ZA, et al. Clin Infect Dis 2015;60:1295

- Most isolates were carbapenem-resistant and belonged to IC2 (CC2/CC92)

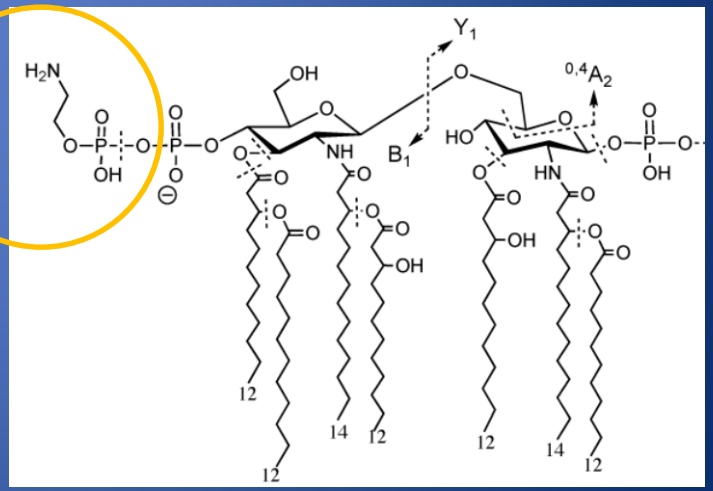
Colistin resistance

- Colistin resistance is due to modification of hepta-acylated lipid A



Colistin-susceptible

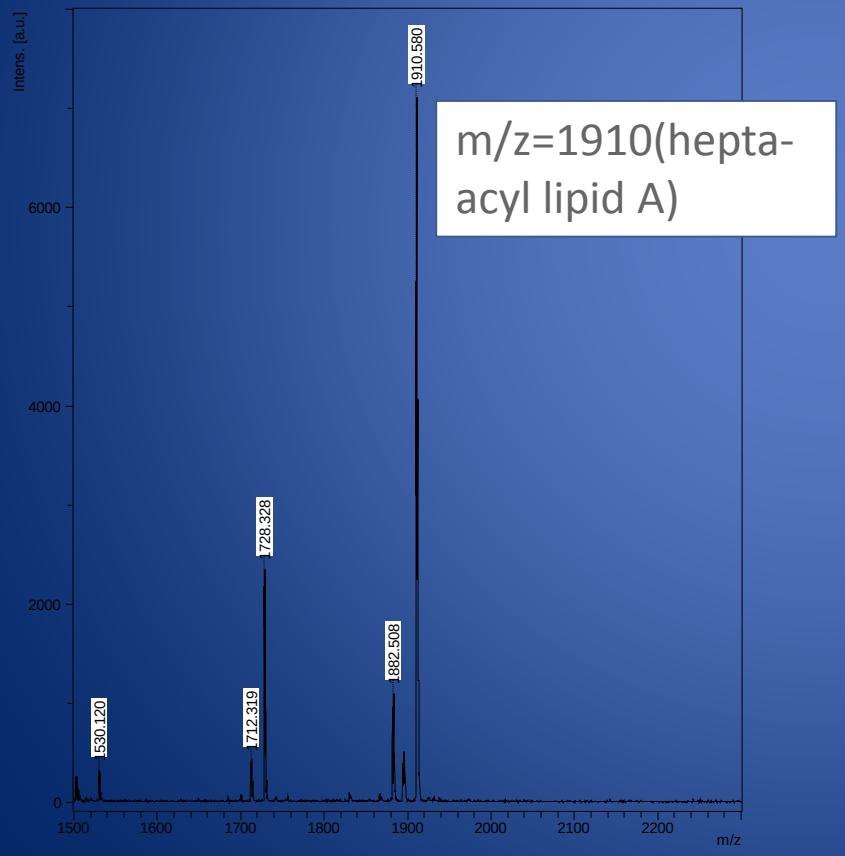
Phosphoethanolamine



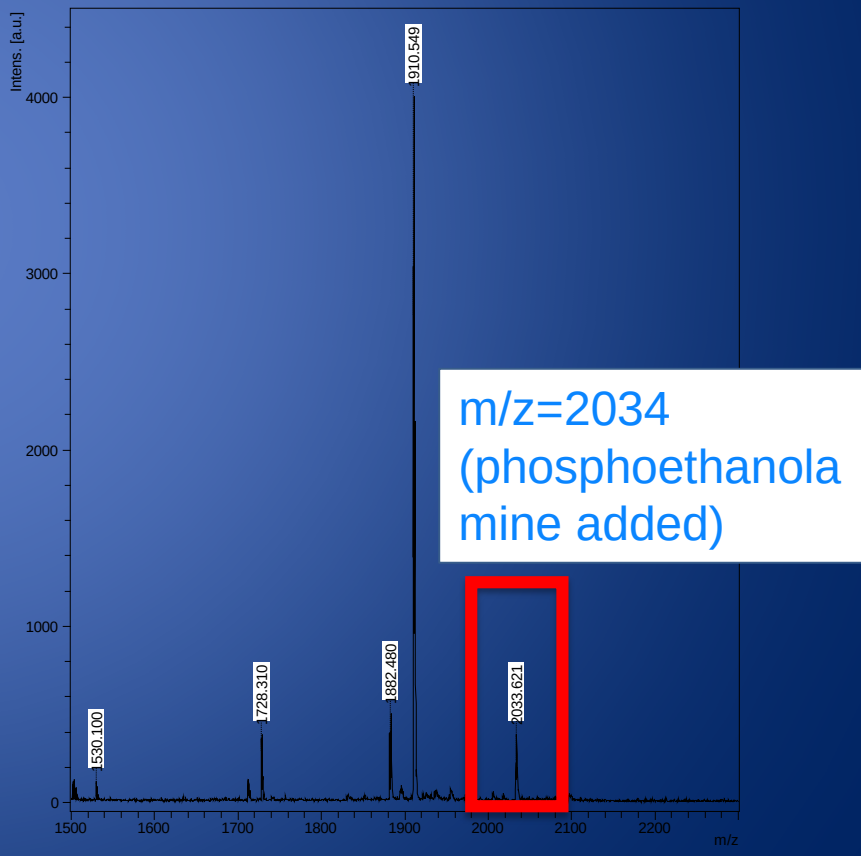
Colistin-resistant

Colistin resistance

- Phosphoethanolamine modification is detected by mass spectrometry



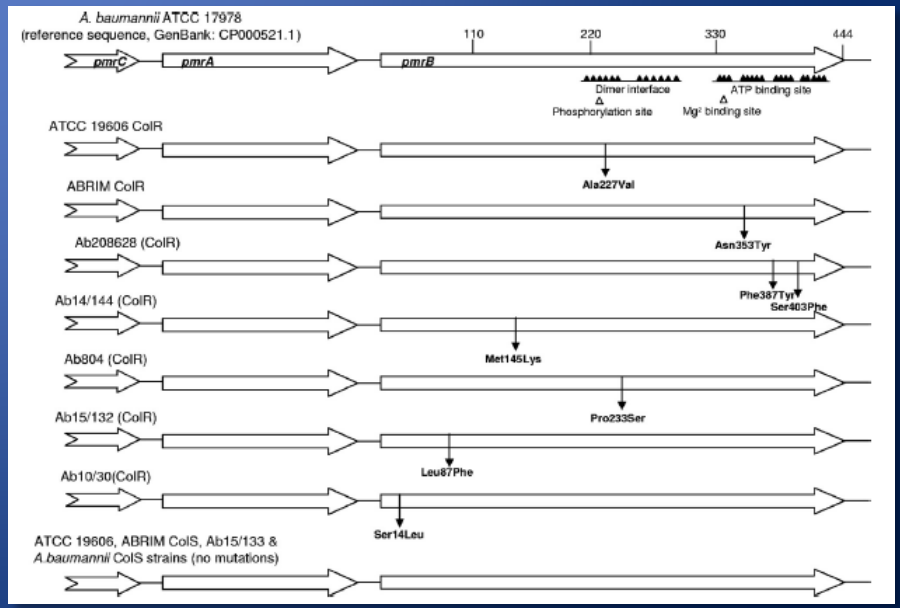
Colistin-susceptible



Colistin-resistant

Colistin resistance

- Addition of phosphoethanolamine is modulated by the *pmrCAB* operon
  - *pmrA* = response regulator
  - *pmrB* = sensor kinase
  - *pmrC* = phosphoethanolamine transferase
- Associations have been made between specific mutations and resistance



Beceiro A, et al. Antimicrob Agents Chemother 2011;55:3370
Arroyo LA, et al. Antimicrob Agents Chemother 2011;55:3743

Colistin resistance

- Complementation of each mutation indicates only some of reported mutations confer resistance
- The end result is lipid A modification by phosphoethanolamine

		Amino acid mutations					
		pmrA (224 aa)		pmrB (444 aa)			
Strain	Colistin MIC µg/ml	Rec (aa 5-116)	aa 117-161	aa 1-215	HisK (aa 216-276)	aa 277-330	HATPaseC (aa 331-419)
3A4	>256			P190S			
1E4	>256			A183T			
1G2	>256			E186D			
1A3	>256				Q227P		
1H7	>256			P76L, R91S, T192I			
2C9	32			P190T	L249H		
1A7	>256	L20F					
1D5	128	M12I					

Red = confers resistance

Blue = does not confer resistance

Colistin resistance

- MALDI-TOF as a diagnostic tool?
  - All *A. baumannii* complex isolates were prospectively collected at UPMC clinical microbiology laboratory for 3 years
  - 451 isolates were identified as *Acinetobacter* spp. and subjected to:
    - Genospecies identification (MALDI-TOF MS)
    - Colistin susceptibility (microbroth MIC)
    - Lipid A profile (MALDI-TOF MS)

Colistin resistance

451 "*A. baumannii* complex" isolates from 284 patients

362	*A. baumannii*
61	*A. pittii*
14	*A. nosocomialis*
6	*A. calcoaceticus*
3	non reliable ID
2	*A. radioresistens*
1	*A. baylyi*
1	*A. guillouiae*
1	*A. junii*

380 isolates from 245 patients

-Susceptible by MIC
-No PEtN peak

38 isolates from 17 patients
-Non-susceptible by MIC
-PEtN peak present

36	*A. baumannii*
1.	*A. pittii*
1	*A. nosocomialis*

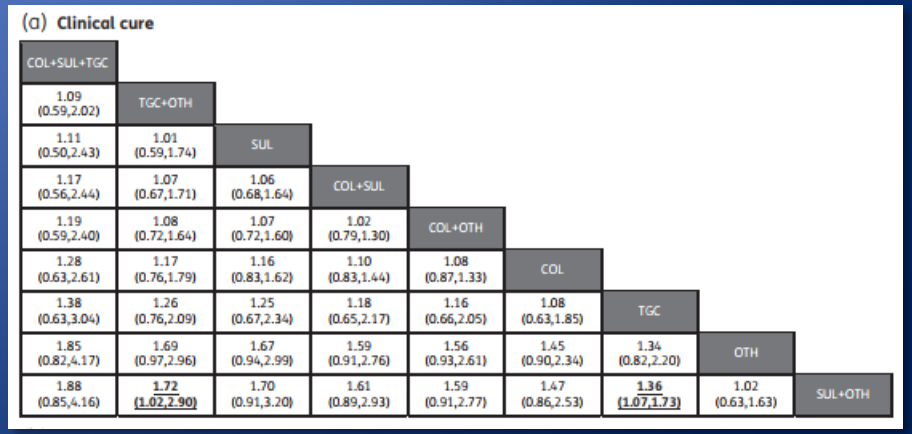
33 isolates from 21 patients
-Unstable MICs
-Unstable PEtN peak

29	*A. baumannii*
3	*A. pittii*
1	*A. junii*

- ~8% colistin resistance
- 100% sensitivity & specificity of MALDI-TOF in ID'ing col-R

Treatment of *A. baumannii* infection

- We still know little
- Key agents
  - Colistin
  - Sulbactam
  - Tigecycline
  - Carbapenem
- Colistin + sulbactam + tigecycline?
  - Network meta-analysis of MDR/XDR infections suggests so
  - Colistin should be in the mix
  - Tigecycline monotherapy to be avoided



Kengkla K, et al. J Antimicrob Chemother 2018;73:22

Treatment of *A. baumannii* infection

- Outstanding questions regarding therapy:

1. Colistimethate (CMS) or polymyxin B?
2. Does nebulized CMS help for VAP?
3. How much sulbactam should one give?
4. Is there a role for double-dose tigecycline?
5. How about intravenous minocycline?

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COMBACTE-NET Status: N/A

WP8: Study into the safety and efficacy of minocycline in treating infections due to Acinetobacter species.

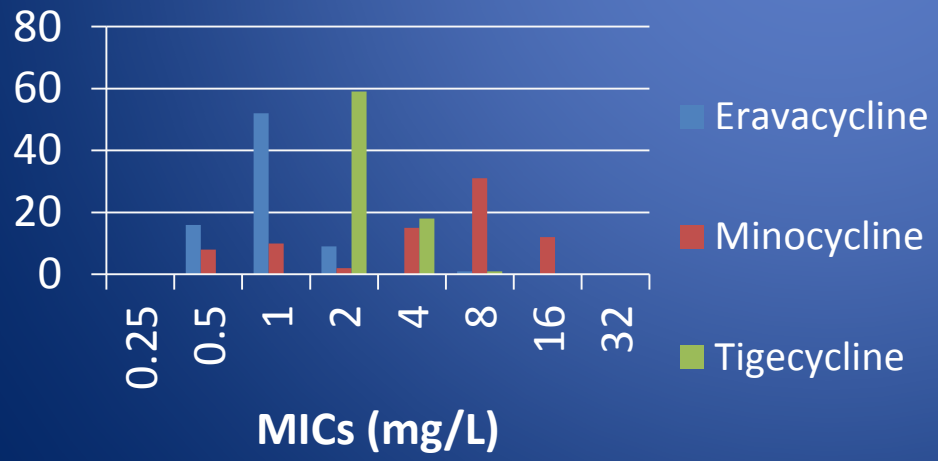
WP8 studies the intravenous formulation of minocycline against *Acinetobacter* infections, of which isolates often prove to be multiple resistant. The Medicines Company's MINOCIN® for Injection has been registered in the United States, but in Europe it is not yet available. WP8 aims for European authorization of this agent.

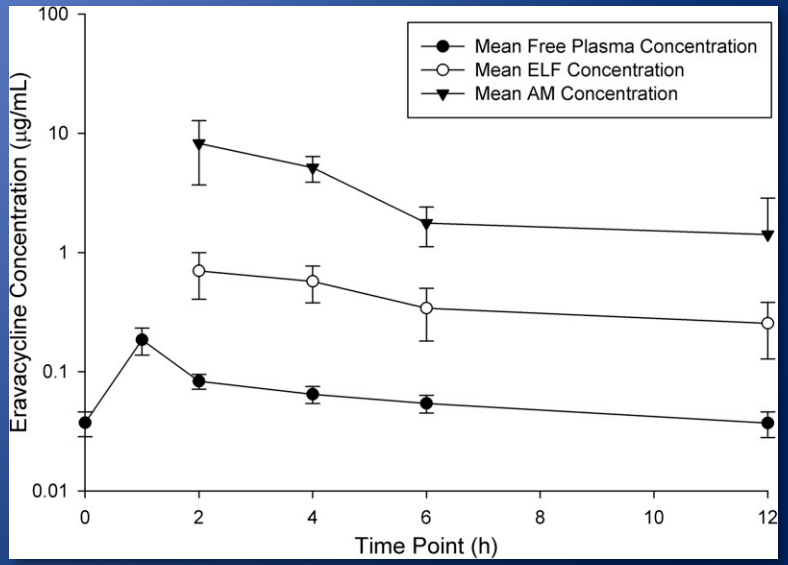
Treatment options in the pipeline

- Many of the new agents are not active against *A. baumannii*
  - Ceftolozane-tazobactam
  - Ceftazidime-avibactam
  - Meropenem-vaborbactam
  - Plazomicin
- Ones with anti-*A. baumannii* activity
  - Eravacycline
  - Cefiderocol

Eravacycline

- Synthetic fluorocycline
- Highly active *in vitro* to *A. baumannii*
- Unique pharmacokinetics

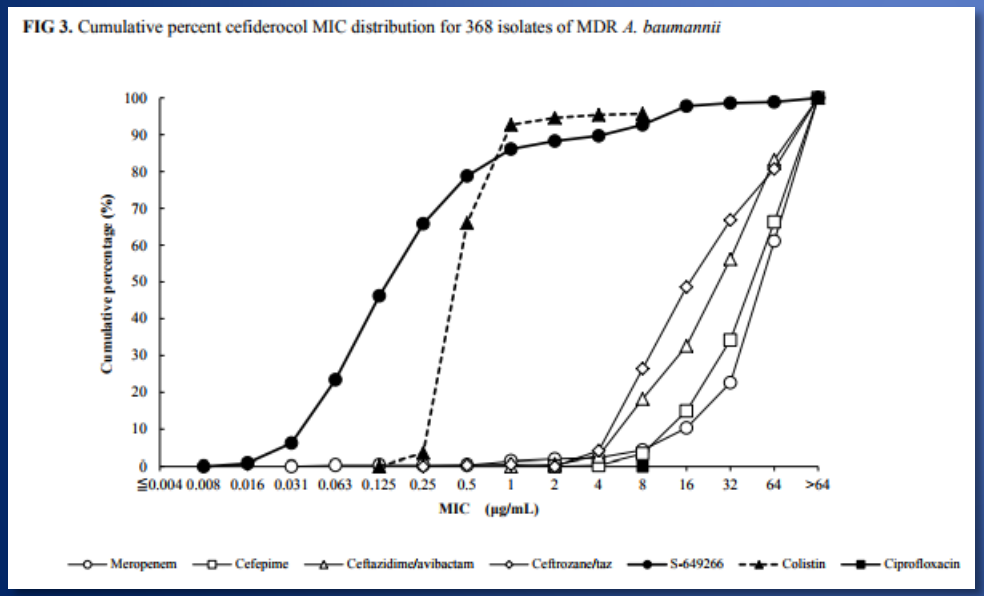


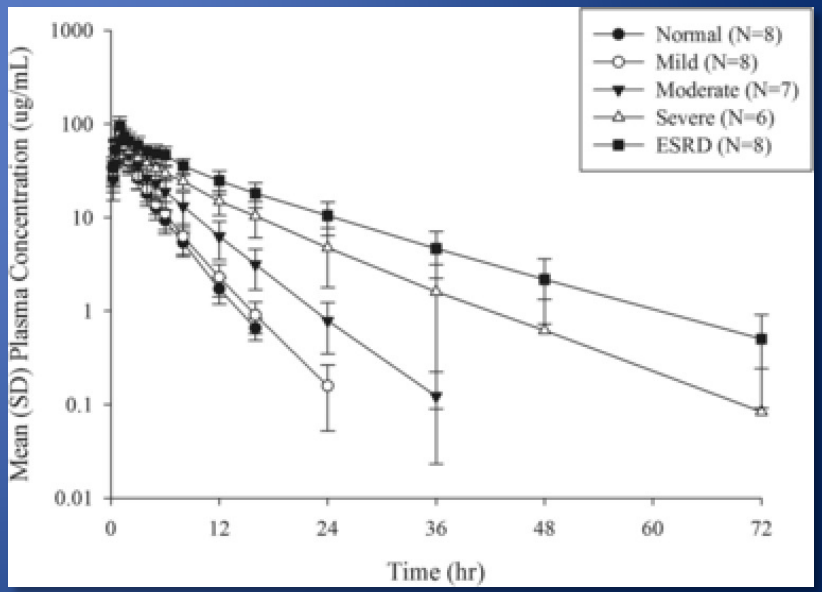


Connors KP, et al. Antimicrob Agents Chemother 2014;58:2113
Seifert H, et al. Int J Antimicrob Agents 2018;51:62

Cefiderocol

- Siderophore cephalosporin
- Highly active *in vitro* to *A. baumannii*
- Pharmacokinetically behaves as a β-lactam

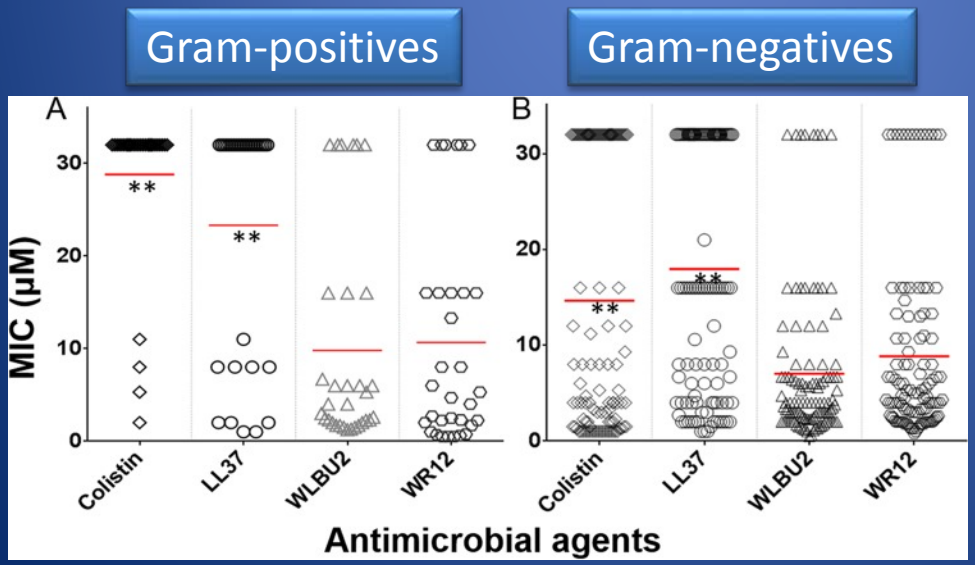


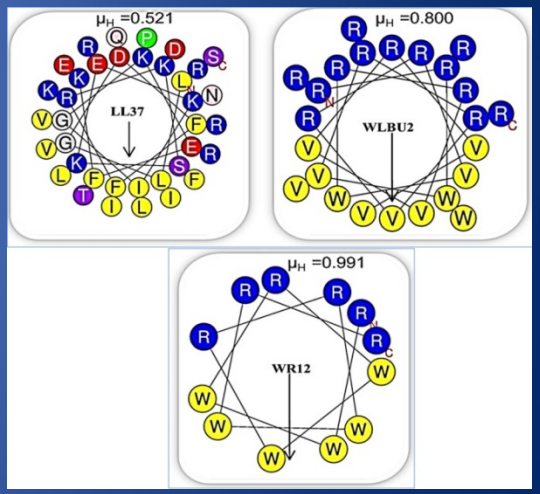


Katsube T, et al. J Clin Pharmacol 2017;57:584
Hackel MA, et al. Antimicrob Agents Chemother 2017;24:61:e01968-17

Engineered peptides

- Synthetic cationic antibiotic peptides
- Lead (WLBU2 = 24-mer) is more active than colistin against carbapenem-resistant bacteria including *A. baumannii*
- Also active against Gram-positives

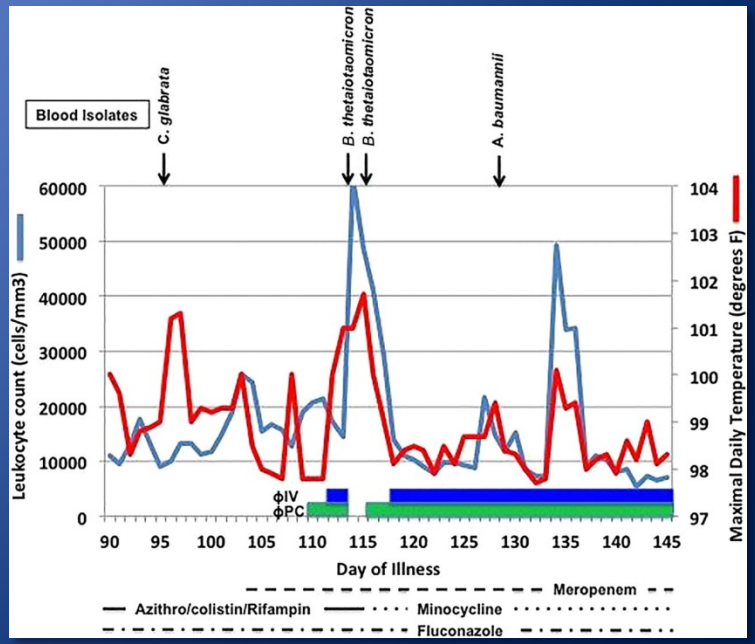




Deslouches B, et al. Antimicrob Agents Chemother 2015;59:1329

Bacteriophage therapy

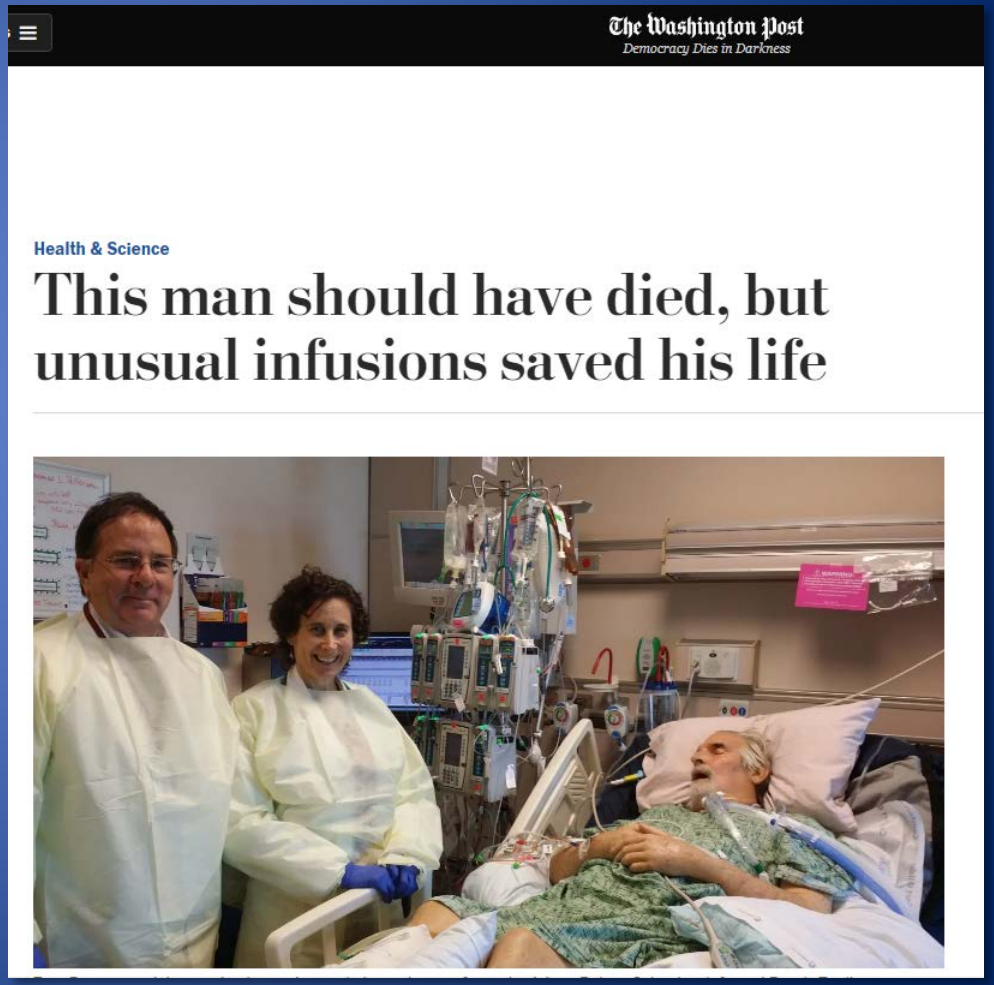
- Phage cocktail given to a patient on an eIND basis
  - Developed necrotizing pancreatitis while in Egypt and repatriated
  - Treated with vancomycin, meroepenem, colistin, tigecycline
  - Pseudocyst fluid grew MDR *A. baumannii*
  - Treated with colistin, azithromycin
  - Developed septic shock
  - A cocktail of 4 anti-*A. baumannii* phages were given to the cavities, then intravenously for 59 days



Schooley RT, et al. Antimicrob Agents Chemother 2017;61:e00954-17

Bacteriophage therapy

- He was discharged home 5 months later
- Caveats
  - Minocycline was added while on bacteriophage therapy
  - Resistance developed, necessitating change of the cocktail twice



In conclusion

- *Acinetobacter baumannii* continues to be a major cause of “untreatable” healthcare-associated infections
- Efflux and other class-specific resistance mechanisms contribute to multidrug resistance
- Specific epidemic clones predominate and should be the focus of research
- High-quality clinical data and trials are still scarce compared with other resistant pathogens of interest
- New treatment options are emerging, both close to clinic and early stage

Acknowledgments

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  - Christi McElheny
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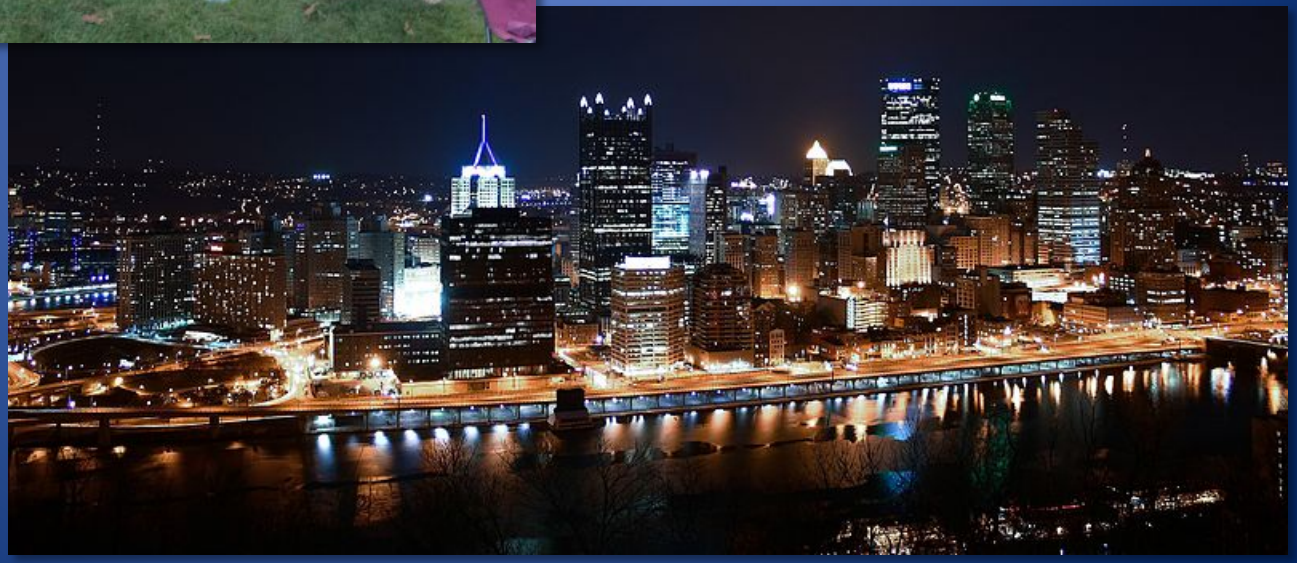

Number of publications

- PubMed search - “carbapenem AND resistance AND (acinetobacter OR klebsiella[title])”