

# SUPER BUGS AND SUPER DRUGS, PART 2!

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NO RELEVANT DISCLOSURES

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July 8, 2021, 9:22 p.m. ET  
Maggie Astor

**An antibiotic with a schwa**



Dhroov Bharatia misspells "cloxacillin." Scott McIntyre for The New York Times

Dhroov Bharatia was just eliminated on the word *cloxacillin*, meaning "a semisynthetic oral nontoxic antibiotic effective especially against staphylococci which secrete beta-lactamase." It comes from Greek- and Latin-derived elements of international scientific vocabulary.

It was that pesky schwa again: He spelled it C-L-O-X-O-C-I-L-L-I-N.

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## OBJECTIVES

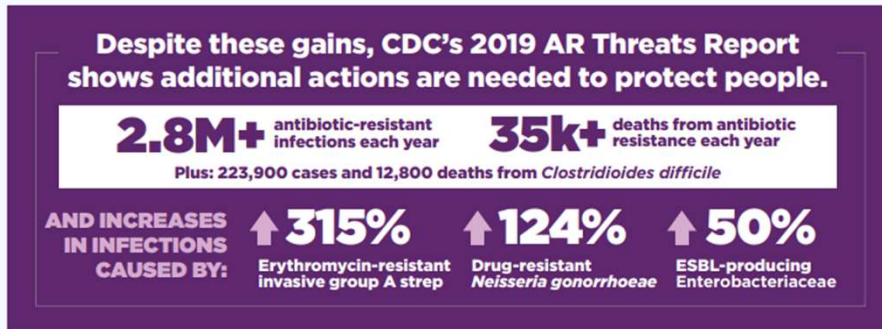
1. Classify gram-negative resistance mechanisms
2. Recognize incidence of gram-negative resistant infections
3. Categorize antibiotic activity based on resistance mechanism
4. List optimal antibiotic according to resistance mechanism
5. Recall IDSA guidance for treatment of resistant infections
6. Recognize preferred antibiotic regimens for resistant infections

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super bugs!

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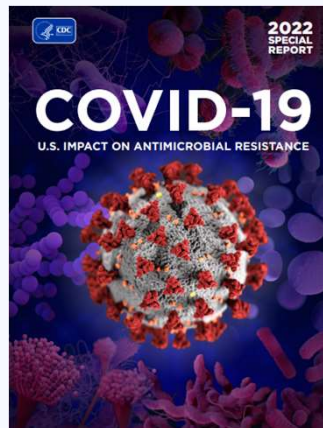
## 2019 CDC ANTIBIOTIC RESISTANCE THREATS REPORT



Centers for Disease Control and Prevention. Antibiotic Resistance Threats in the United States, 2019.

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## EVEN MORE PROMINENT THREAT




Centers for Disease Control and Prevention. 2022 Special Report COVID-19 U.S. Impact on Antimicrobial Resistance, 2022.

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## URGENT AND SERIOUS THREATS

REQUIRE URGENT AND AGGRESSIVE ACTION

Carbapenem-resistant  
*Acinetobacter species*



+ 78%

CAUSE A RANGE OF SERIOUS INFECTIONS

**AmpC  $\beta$ -lactamase-producing Enterobacterales (AmpC-E)**

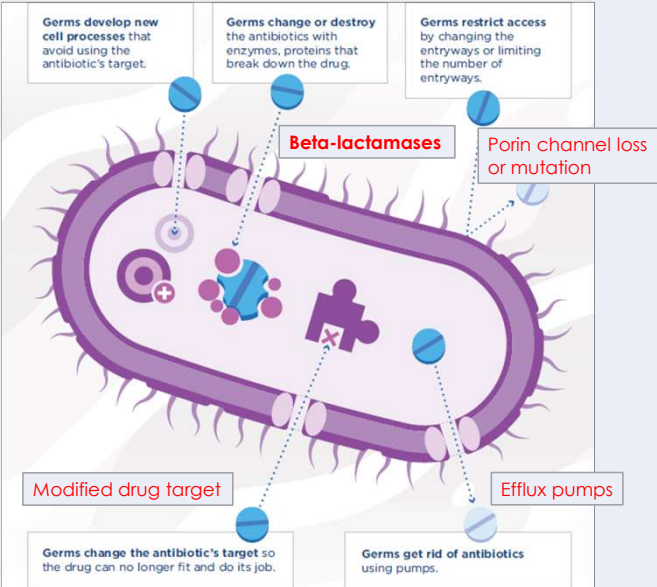
***Stenotrophomonas maltophilia***

Centers for Disease Control and Prevention. Antibiotic Resistance Threats in the United States, 2019.  
Centers for Disease Control and Prevention. 2022 Special Report COVID-19 U.S. Impact on Antimicrobial Resistance, 2022.

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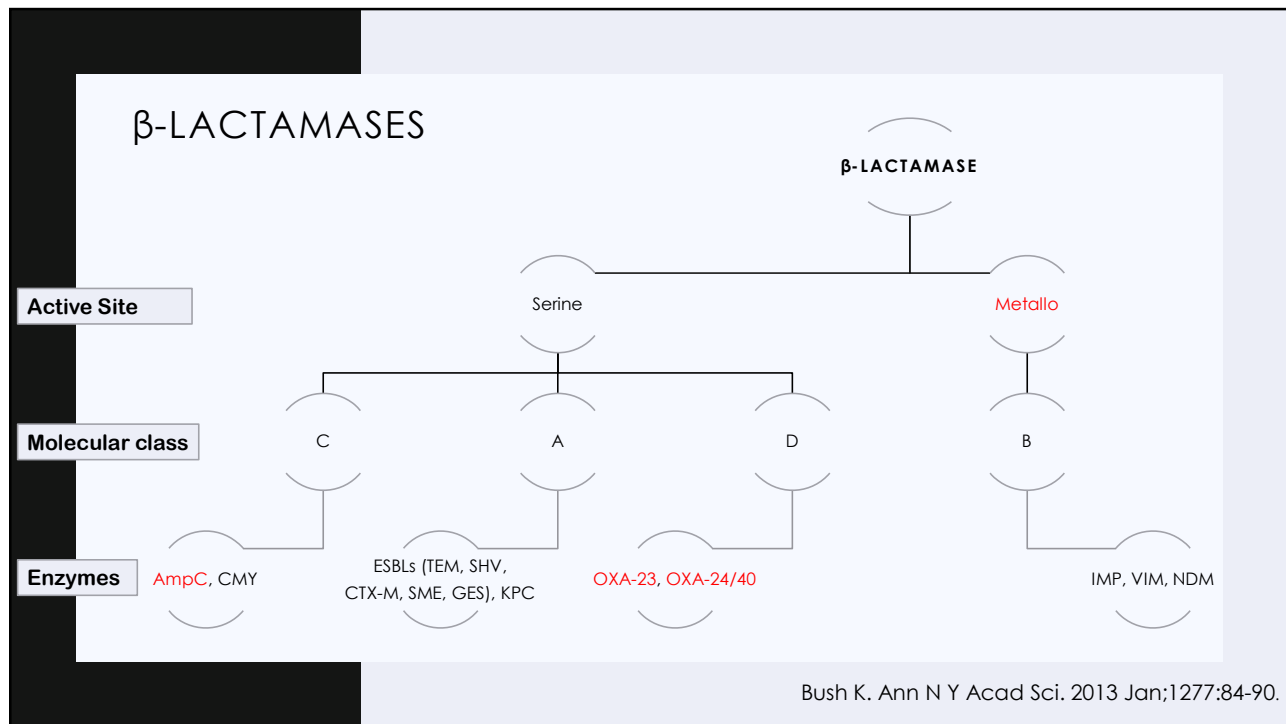
## RESISTANCE MECHANISMS

- Beta-lactamases
  - AmpC, ESBL, Carbapenemases
- Modified drug target
- Ribosomal modifications
- Porin channel loss or mutation
- Efflux pumps

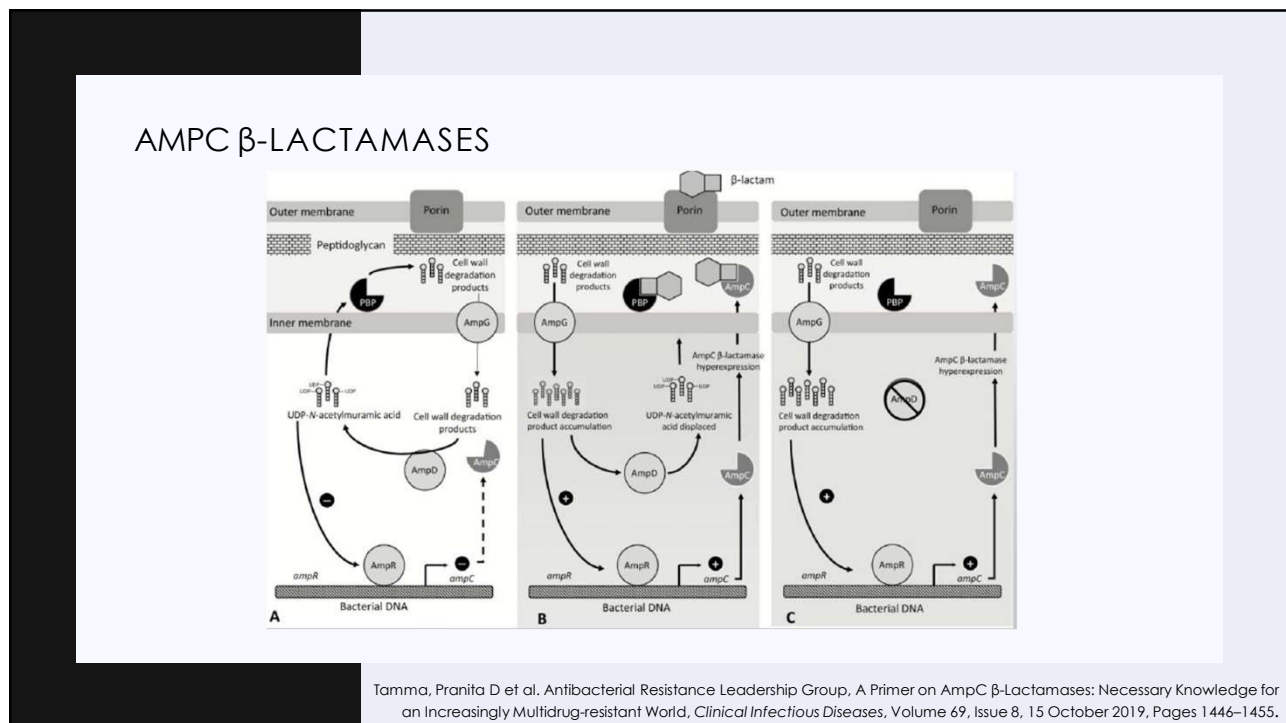


Centers for Disease Control and Prevention. Antibiotic Resistance Threats in the United States, 2019.

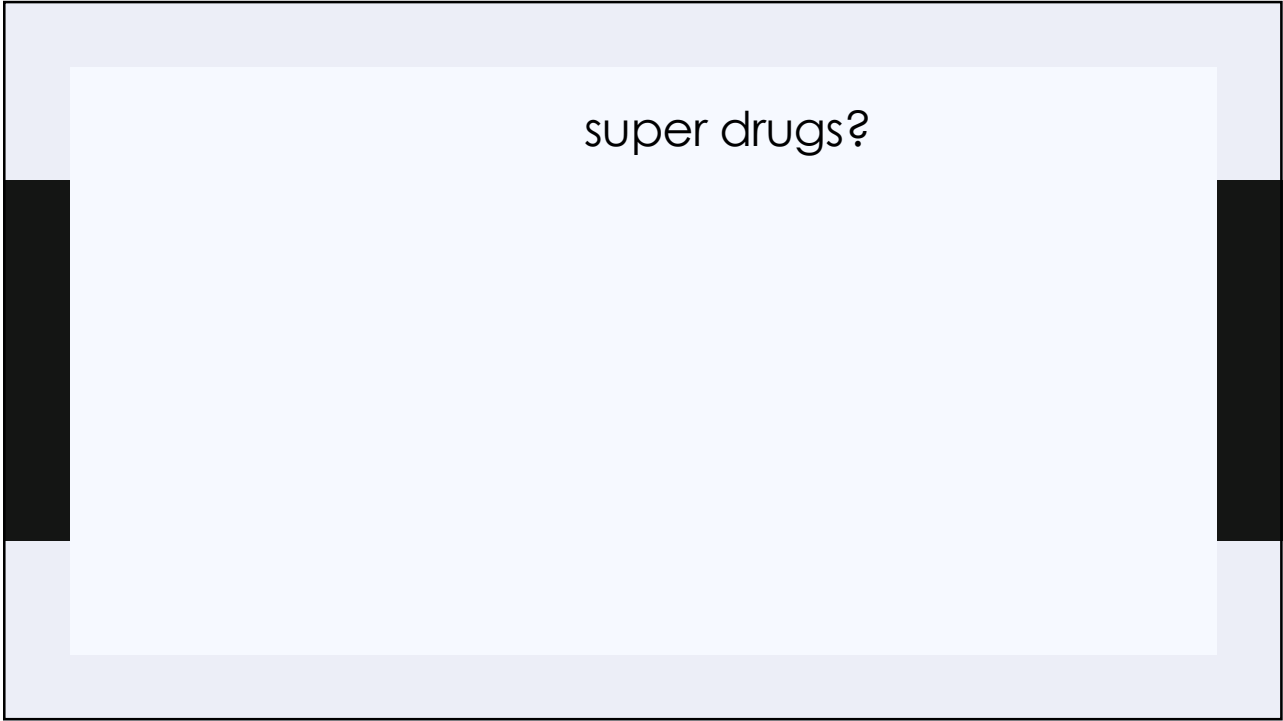
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## CEFTAZIDIME/AVIBACTAM

### MOA: CEPHALOSPORIN + NOVEL $\beta$ -LACTAMASE INHIBITOR

#### FDA indications:

- HAP/VAP
- Complicated UTIs, including pyelonephritis
- Complicated intra-abdominal infections (with metronidazole)

#### IDSA dosing recommendations:

- 2.5 g IV q8h, infused over 3 hours

Tamma, Pranita D et al. Clin Infect Dis. Oct. 2020 Oct 27;ciaa1478.

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## MEROPENEM/VABORBACTAM

### MOA: CARBAPENEM + NOVEL, CYCLIC BORONIC ACID $\beta$ -LACTAMASE INHIBITOR

#### FDA indications:

- Complicated UTIs, including pyelonephritis

#### IDSA dosing recommendations:

- 4 g (2g meropenem) IV q8h, infused over 3 hours

Tamma, Pranita D et al. Clin Infect Dis. Oct. 2020 Oct 27;ciaa1478.

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## IMIPENEM/RELEBACTAM

**MOA: CARBAPENEM (+ DEHYDROPEPTIDASE INHIBITOR) + NOVEL  $\beta$ -LACTAMASE INHIBITOR**

FDA indications:

- HAP/VAP
- Complicated UTIs, including pyelonephritis
- Complicated intra-abdominal infections

IDSA dosing recommendations:

- 1.25 g (500 mg imipenem) IV q6h, infused over 30 minutes

Tamma, Pranita D et al. Clin Infect Dis. Oct. 2020 Oct 27;ciaa1478.

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## SPECTRUM OF ACTIVITY COMPARISON

BETA LACTAM + BETA LACTAMASE INHIBITORS

Agent	AMPC-E	KPC	<i>S. maltophilia</i>	OXA-48-like	DTR- <i>P. aeruginosa</i>	CRAB
Ceftazidime/ avibactam	+	+	S	+	+/-	-
Meropenem/ vaborbactam	+	+	-	-	-	-
Imipenem/ relebactam	+	+	-	-	+	-

S = synergy

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**CEFIDEROCOL**

**MOA: NOVEL SIDEROPHORE CEPHALOSPORIN  
(SAME R1 SIDE CHAIN AS CEFTAZIDIME)**

FDA indications:

- Complicated UTIs, including pyelonephritis
- HAP/VAP\*

\*Warning for **higher all-cause mortality** compared to BAT in patients with pneumonia, bloodstream infections/sepsis, or cUTI caused by CRE and CR-*Acinetobacter*\*

IDSA dosing recommendations:

- 2 g IV q8h, infused over 3 hours

BAT = best-available therapy

Tamma, Pranita D et al. Clin Infect Dis. Oct. 2020 Oct 27;ciaa1478.

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## CEFIDEROCOL Spectrum



- Activity against:
  - AmpC-E
  - ESBL-E
  - KPC
  - Mettalo- $\beta$ -lactamases(i.e. NDM)
  - Some oxacillinases (i.e. OXA-48-like)
  - DTR-*P. aeruginosa*
  - **CRAB**

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## ERAVACYCLINE

**MOA: FLUOROCYCLINE MOSTLY UNAFFECTED BY EFFLUX PUMPS AND RIBOSOMAL PROTECTION PROTEINS**

FDA indications:

- Complicated intra-abdominal infections
- **NOT** indicated for Complicated UTIs

IDSA dosing recommendations:

- 1 mg/kg IV q12h, infused over 1 hour

Tamma, Pranita D et al. Clin Infect Dis. Oct. 2020 Oct 27;ciaa1478.

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## SPECTRUM OF ACTIVITY COMPARISON

### OTHER NEW AGENTS

Agent	AMPC-E	KPC	<i>S. maltophilia</i>	OXA-48-like	DTR- <i>P. aeruginosa</i>	CRAB
Eravacycline	+	+/-	+/-	+/-	-	+/-
Cefiderocol	+	+	+	+	+	+

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Agent	AMPC-E	KPC	<i>S. maltophilia</i>	OXA-48-like	DTR- <i>P. aeruginosa</i>	CRAB
Ceftazidime/ avibactam	+	+	S	+	+/-	-
Meropenem/ vaborbactam	+	+	-	-	-	-
Imipenem/ relebactam	+	+	-	-	+	-
Eravacycline	+	+/-	+/-	+/-	-	+/-
Cefiderocol	+	+	+	+	+	+

S = synergy

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IDSA Guidance

**IDSA Guidance on the Treatment of Antimicrobial-Resistant Gram-Negative Infections: Version 2.0**

Published by IDSA, 3/31/2022

A focus on AmpC  $\beta$ -lactamase-Producing Enterobacterales, Carbapenem-Resistant *Acinetobacter baumannii*, and *Stenotrophomonas maltophilia* Infections

Pranita D. Tamma\*, Samuel L. Aitken, Robert A. Bonomo, Amy J. Mathers, David van Duin, Cornelius J. Clancy

\*Corresponding Author

Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America Guidance on the Treatment of AmpC  $\beta$ -lactamase-Producing Enterobacterales, Carbapenem-Resistant *Acinetobacter baumannii*, and *Stenotrophomonas maltophilia* Infections. Infectious Diseases Society of America 2022; Version 2.0

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AmpC  $\beta$ -lactamase-producing Enterobacterales (AmpC-E)

**CHALLENGE: WHICH BUGS ARE AT GREATEST RISK?**

Moderate to high risk for clinically significant AmpC production:

- *Enterobacter cloacae*, *Klebsiella aerogenes*, *Citrobacter freundii*

Emergence of resistance after treatment

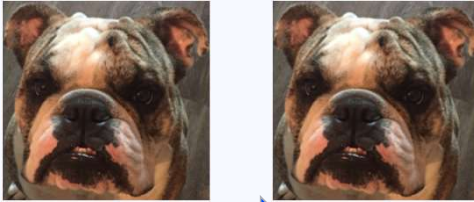
- Can be observed after even a few doses of ceftriaxone or ceftazidime
- Resistance after exposure can occur ~8-40% of infections

Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America Guidance on the Treatment of AmpC  $\beta$ -lactamase-Producing Enterobacterales, Carbapenem-Resistant *Acinetobacter baumannii*, and *Stenotrophomonas maltophilia* Infections. Infectious Diseases Society of America 2022; Version 2.0

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~~SPACE~~

SPACE BUGS ARE CANCELLED



**E** *Enterobacter cloacae*

**C** *Citrobacter freundii*

**K** *Klebsiella aerogenes*

*Enterobacter aerogenes* → *Klebsiella aerogenes*

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## PREFERRED ANTIBIOTICS FOR AMPC-E INFECTIONS

Source of infection	Preferred Treatment	Alternative Treatment
Cystitis	Nitrofurantoin Trimethoprim-sulfamethoxazole Single-dose IV aminoglycoside	Ceftriaxone (if susceptible) Ceftazidime (if susceptible)

\*moderate to high risk of significant AmpC production (i.e., *E. cloacae*, *K. aerogenes*, and *C. freundii*)

Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America Guidance on the Treatment of AmpC  $\beta$ -lactamase-Producing Enterobacterales, Carbapenem-Resistant *Acinetobacter baumannii*, and *Stenotrophomonas maltophilia* Infections. Infectious Diseases Society of America 2022; Version 2.0

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## PREFERRED ANTIBIOTICS FOR AMPC-E INFECTIONS

Source of infection	Preferred Treatment	Alternative Treatment
All other infections	Cefepime 2 g IV q8h, infused over 3 hours <ul style="list-style-type: none"> <li>• if MIC <math>\leq</math> 2 mcg/mL</li> </ul> Ertapenem 1 g IV q24h, infused over 30 min Meropenem 1-2 g IV q8h, infused over 30 min <ul style="list-style-type: none"> <li>• if cefepime MIC <math>\geq</math> 4 mcg/mL</li> </ul>	Ceftazidime-avibactam Meropenem-vaborbactam Imipenem-cilastatin-relebactam Cefiderocol

\*moderate to high risk of significant AmpC production (i.e., *E. cloacae*, *K. aerogenes*, and *C. freundii*)

Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America Guidance on the Treatment of AmpC  $\beta$ -lactamase-Producing Enterobacterales, Carbapenem-Resistant *Acinetobacter baumannii*, and *Stenotrophomonas maltophilia* Infections. Infectious Diseases Society of America 2022; Version 2.0

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## MERINO-2 TRIAL

Open Forum Infectious Diseases  
MAJOR ARTICLE

### Meropenem Versus Piperacillin-Tazobactam for Definitive Treatment of Bloodstream Infections Caused by AmpC β-Lactamase-Producing *Enterobacter* spp, *Citrobacter freundii*, *Morganella morganii*, *Providencia* spp, or *Serratia marcescens*: A Pilot Multicenter Randomized Controlled Trial (MERINO-2)

Analysis	Primary Outcome, No./Total No. (%)		Risk Difference, % (2-Sided 95% CI)	P Value
	PTZ	Meropenem		
Primary analysis	11/38 (29)	7/34 (21)	8.4 (-11 to 28)	.41
Per-protocol analysis	8/32 (25)	6/32 (19)	6.2 (-14 to 26)	.55
<b>Subcomponents of the primary outcome</b>				
Death	0/38 (0)	2/34 (6%)	5.9 (-13 to 2)	.13
Clinical failure	8/38 (21)	4/34 (12)	9.3 (-8 to 28)	.29
Microbiological failure	8/38 (21)	0/34 (0)	13.2 (2 to 24)	.03
Microbiological relapse	0/38 (0)	3/34 (9)	8.8 (-18 to 1)	.06
<b>Subgroup analyses</b>				
<b>Infecting species</b>				
Enterobacter spp	5/18 (28)	1/14 (7)	20.7 (-4 to 45)	.14
Other	6/14 (43)	6/14 (43)	0.0 (-28 to 28)	1.0
<b>Urinary tract vs non-urinary tract source</b>				
Urinary tract	1/8 (12)	1/6 (17)	-4.2 (-42 to 33)	.83
Non-urinary tract	10/30 (33)	6/28 (21)	11.9 (-11 to 35)	.31
<b>Infection</b>				
Healthcare-associated	11/35 (31)	5/24 (21)	10.6 (-12 to 33)	.37
Non-health care associated	0/3 (0)	0/3 (0)	...	...
<b>Appropriate empirical antibiotic therapy</b>				
Appropriate	10/35 (29)	7/33 (21)	7.4 (-13 to 28)	.48
Inappropriate	1/3 (33)	0/1 (0)	33.3 (-20 to 87)	.50
<b>Immunocompromise</b>				
Present	1/6 (17)	1/5 (20)	-3.3 (-49 to 43)	.89
Absent	10/32 (31)	6/29 (21)	-10.5 (-11 to 32)	.35
<b>qSOFA ≥2</b>				
Yes	2/9 (22)	2/9 (22)	0.0 (-38 to 38)	1.0
No	9/29 (31)	5/25 (20)	11.0 (-12.0 to 34)	.36
<b>Total duration of study drug</b>				
<5 d	6/20 (30)	2/17 (12)	18 (-7 to 43)	.18
≥5 d	5/18 (28)	5/17 (30)	-16 (-32 to 28)	.91

Stewart AG et al. Meropenem Versus Piperacillin-Tazobactam for Definitive Treatment of Bloodstream Infections Caused by AmpC β-Lactamase-Producing *Enterobacter* spp, *Citrobacter freundii*, *Morganella morganii*, *Providencia* spp, or *Serratia marcescens*: A Pilot Multicenter Randomized Controlled Trial (MERINO-2). *Open Forum Infect Dis* 2021;8(8):ofab387.

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## PUTTING IT ALTOGETHER : AMPC-E

Preferred
Cefepime

- Unless cefepime MIC ≥ 4, use carbapenems
- Non β-lactam / oral step down: TMP-SMX or fluoroquinolones

Caution
Piperacillin/tazobactam

- Use caution for serious infections
- May be reasonable for mild infections

Avoid
Ceftriaxone, ceftazidime

- Unless uncomplicated cystitis

Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America Guidance on the Treatment of AmpC β-lactamase-Producing Enterobacteriales, Carbapenem-Resistant *Acinetobacter baumannii*, and *Stenotrophomonas maltophilia* Infections. Infectious Diseases Society of America 2022; Version 2.0

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WHAT IS WRONG WITH THIS PICTURE?

Klebsiella (Enterobacter) aerogenes		
Drug	MIC Interp	MIC Dilutn
Amikacin	S	<=2
Ampicillin (3)		
Cefazolin (1)	R	>=64
Ceftriaxone	S	<=1
Ciprofloxacin	S	<=0.25
Gentamicin	S	<=1
Gentamicin synergy (2)		
Levofloxacin	S	<=0.12
Linezolid		
Nitrofurantoin	I	64
Piperacillin/Tazobactam	S	<=4
Tobramycin	S	<=1
Trimethoprim/Sulfamethoxazole	S	<=20
Vancomycin		

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super doses!

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## Carbapenem-Resistant *Acinetobacter baumannii* (CRAB)

### CHALLENGE: COLONIZER VS PATHOGEN; FEW THERAPEUTIC OPTIONS

2020: overall increase 35% & hospital onset increased 78%!

Micro/molecular:

- Resistant to at least one carbapenem or producing a carbapenemase
- Phenotypic and molecular testing can identify carbapenemase families
- PBPs, aminoglycoside modifying enzymes, efflux pumps

Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America Guidance on the Treatment of AmpC  $\beta$ -lactamase-Producing Enterobacterales, Carbapenem-Resistant *Acinetobacter baumannii*, and *Stenotrophomonas maltophilia* Infections. Infectious Diseases Society of America 2022; Version 2.0

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## PREFERRED ANTIBIOTICS FOR CRAB INFECTIONS

Source of infection	Preferred Treatment	Alternative Treatment
Mild infections <ul style="list-style-type: none"> <li>• UTI</li> <li>• SSTI</li> <li>• Tracheitis</li> </ul>	High dose ampicillin-sulbactam <ul style="list-style-type: none"> <li>• if susceptible</li> </ul> High dose ampicillin-sulbactam + 2 <sup>nd</sup> agent* <ul style="list-style-type: none"> <li>• if non-susceptible to ampicillin/sulbactam</li> </ul>	Standard dose ampicillin-sulbactam High dose minocycline High dose tigecycline Polymyxin B Colistin (cystitis only) Cefiderocol

\*second agents include **minocycline**, tigecycline, polymyxin B

Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America Guidance on the Treatment of AmpC  $\beta$ -lactamase-Producing Enterobacterales, Carbapenem-Resistant *Acinetobacter baumannii*, and *Stenotrophomonas maltophilia* Infections. Infectious Diseases Society of America 2022; Version 2.0

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## SUPER DOSES FOR CRAB INFECTIONS

Ampicillin-sulbactam Dosing	
Standard dose	3 g IV q4h
High dose	9 g IV q8h over 4 hours <b>OR</b> 27 g IV q24h as a continuous infusion

Tetracycline Derivative Dosing	
Minocycline	200 mg IV/PO q12h
Tigecycline	200 mg IV x 1, then 100 mg IV q12h

Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America Guidance on the Treatment of AmpC  $\beta$ -lactamase-Producing Enterobacterales, Carbapenem-Resistant *Acinetobacter baumannii*, and *Stenotrophomonas maltophilia* Infections. Infectious Diseases Society of America 2022; Version 2.0

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## PREFERRED ANTIBIOTICS FOR CRAB INFECTIONS

Source of infection	Preferred Treatment	Alternative Treatment
Moderate to severe infections	High dose ampicillin-sulbactam + preferred 2 <sup>nd</sup> agent* • Even if non-susceptible to ampicillin/sulbactam	High dose ampicillin-sulbactam + extended infusion meropenem + polymyxin B

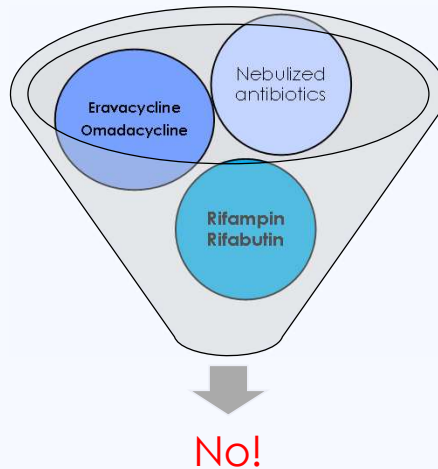
\*preferred second agents include **minocycline**, tigecycline, polymyxin B, extended infusion meropenem, or cefiderocol

Combination therapy is suggested even if a single agent is susceptible!

Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America Guidance on the Treatment of AmpC  $\beta$ -lactamase-Producing Enterobacterales, Carbapenem-Resistant *Acinetobacter baumannii*, and *Stenotrophomonas maltophilia* Infections. Infectious Diseases Society of America 2022; Version 2.0

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## ANTIBIOTICS NOT RECOMMENDED FOR CRAB INFECTIONS



Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America Guidance on the Treatment of AmpC  $\beta$ -lactamase-Producing Enterobacterales, Carbapenem-Resistant *Acinetobacter baumannii*, and *Stenotrophomonas maltophilia* Infections. Infectious Diseases Society of America 2022; Version 2.0

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## PUTTING IT ALTOGETHER: CRAB

### Preferred

### High dose ampicillin-sulbactam + second agent

- Second agent: **minocycline**, tigecycline, or polymyxin B
- Alternative second agents: extended infusion meropenem, cefiderocol

### Caution

### Monotherapy

- May be reasonable for mild infections
- Ampicillin-sulbactam is preferred

### Avoid

### Neb antibiotics, rifamycins, eravacycline

Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America Guidance on the Treatment of AmpC  $\beta$ -lactamase-Producing Enterobacterales, Carbapenem-Resistant *Acinetobacter baumannii*, and *Stenotrophomonas maltophilia* Infections. Infectious Diseases Society of America 2022; Version 2.0

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*Stenotrophomonas maltophilia***CHALLENGE: COLONIZER VS PATHOGEN; BIOFILM**

Standard of care?

Micro/molecular:

- $\beta$ -lactamase-producing or producing a carbapenemase
- Aminoglycoside acetyl transferase enzymes, efflux pumps

Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America Guidance on the Treatment of AmpC  $\beta$ -lactamase-Producing Enterobacterales, Carbapenem-Resistant *Acinetobacter baumannii*, and *Stenotrophomonas maltophilia* Infections. Infectious Diseases Society of America 2022; Version 2.0

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PREFERRED ANTIBIOTICS FOR *S. maltophilia* INFECTIONS

Source of infection	Preferred Treatment	Alternative Treatment
Mild infections	Trimethoprim-sulfamethoxazole Minocycline	Tigecycline Levofloxacin Cefiderocol

Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America Guidance on the Treatment of AmpC  $\beta$ -lactamase-Producing Enterobacterales, Carbapenem-Resistant *Acinetobacter baumannii*, and *Stenotrophomonas maltophilia* Infections. Infectious Diseases Society of America 2022; Version 2.0

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## PREFERRED ANTIBIOTICS FOR *S. maltophilia* INFECTIONS

Source of infection	Preferred Treatment	Watch & wait
Moderate to severe infections	Trimethoprim-sulfamethoxazole + watch & wait Trimethoprim-sulfamethoxazole + minocycline Ceftazidime-avibactam + aztreonam	Trimethoprim-sulfamethoxazole... • If delay in clinical improvement, add 2 <sup>nd</sup> agent: Minocycline Tigecycline Levofloxacin Cefiderocol

Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America Guidance on the Treatment of AmpC  $\beta$ -lactamase-Producing Enterobacterales, Carbapenem-Resistant *Acinetobacter baumannii*, and *Stenotrophomonas maltophilia* Infections. Infectious Diseases Society of America 2022; Version 2.0

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## SUPER DOSES FOR *S. maltophilia* INFECTIONS

### Trimethoprim-sulfamethoxazole Dosing

Cystitis	160 mg (trimethoprim component) IV/PO q12h
Other infections	8-12 mg/kg/day (trimethoprim component) IV/PO divided q8-12h*

\*consider max dose of 960 mg trimethoprim component per day

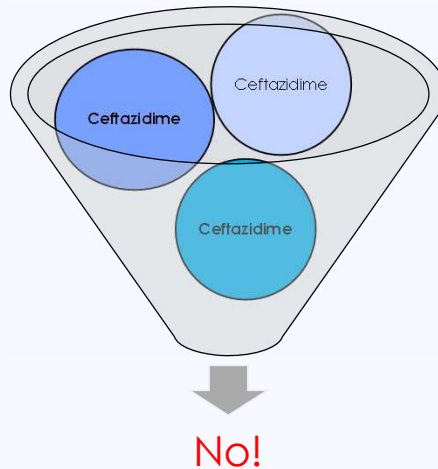
### This is weird! Dosing

Ceftazidime-avibactam + aztreonam	Ceftazidime-avibactam 2.5 g IV q8h, infused over 3 hours PLUS Aztreonam 2 g IV q8h, infused over 3 hours ADMINISTERED AT THE SAME TIME!
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Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America Guidance on the Treatment of AmpC  $\beta$ -lactamase-Producing Enterobacterales, Carbapenem-Resistant *Acinetobacter baumannii*, and *Stenotrophomonas maltophilia* Infections. Infectious Diseases Society of America 2022; Version 2.0

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## ANTIBIOTICS NOT RECOMMENDED FOR *S. maltophilia* INFECTIONS



Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America Guidance on the Treatment of AmpC  $\beta$ -lactamase-Producing Enterobacterales, Carbapenem-Resistant *Acinetobacter baumannii*, and *Stenotrophomonas maltophilia* Infections. Infectious Diseases Society of America 2022; Version 2.0

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## PUTTING IT ALTOGETHER: *S. maltophilia*

### Preferred

### TMP-SMX +/- second agent

- Second agent: **minocycline**, tigecycline, levofloxacin, cefiderocol
- Alternative regimen: ceftazidime/avibactam + aztreonam

### Caution

### Monotherapy

- May be reasonable for mild infections
- TMP-SMX or minocycline is preferred

### Avoid

### Ceftazidime

- Regardless of severity of infection
- Regardless of susceptibility

Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America Guidance on the Treatment of AmpC  $\beta$ -lactamase-Producing Enterobacterales, Carbapenem-Resistant *Acinetobacter baumannii*, and *Stenotrophomonas maltophilia* Infections. Infectious Diseases Society of America 2022; Version 2.0

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## IDSA GUIDANCE CLINICAL PEARLS

### Empiric therapy patient risk factors

- Previous organisms and associated susceptibility data in past **6 months**
- Antibiotic exposure in the past **30 days**
- Severity of illness
- Source of infection

### Duration of therapy

- Prolonged treatment courses are **not** necessary against infections by resistant pathogens

### Oral step-down therapy

- Susceptible to oral agent
- Hemodynamically stable
- Source control
- Sufficient intestinal absorption

Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America Guidance on the Treatment of AmpC  $\beta$ -lactamase-Producing Enterobacterales, Carbapenem-Resistant *Acinetobacter baumannii*, and *Stenotrophomonas maltophilia* Infections. Infectious Diseases Society of America 2022; Version 2.0.

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## CONCLUSIONS

Lots of super bugs

Some super drugs

Super doses

Pharmacists can play a vital role

- Be aware and cautious of agents that have failed in clinical trials
  - Higher mortality, specific infection types
- Make IDSA guidance supported recommendations

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# SUPER BUGS AND SUPER DRUGS, PART 2!

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