

Klebsiella pneumoniae

Antibiotic	MIC (R)
Ampicillin	≥32
Ampicillin/sulbactam	≥32/16
Piperacillin/tazobactam	≥128/4
Aztreonam	≤4
Cefazoline	≥32
Cefoxitin	≥32
Ceftazidime	≥16
Ceftriaxone	≥4
Cefepime	≥32
Imipenem	≤1
Meropenem	≤1
Gentamicin	≤4
Colistin	≤2
Tigecycline	≤2

What is the mechanism of resistance?

- ESBL
- VIM
- KPC
- ESBL+VIM

- 30 yo man with AML, day 15 of neutropenia, S/P induction chemotherapy developed fever.
- Blood cultures grew *K. pneumoniae*

Klebsiella pneumoniae

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Ampicillin	≥32
Ampicillin/sulbactam	≥32/16
Piperacillin/tazobactam	≥128/4
Aztreonam	≥16
Cefazoline	≥32
Cefoxitin	≥32
Ceftazidime	≥16
Ceftriaxone	≥4
Cefepime	≥32
Imipenem	4
Meropenem	2
Gentamicin	<4
Colistin	1
Tigecycline	1

What is the mechanism of resistance?

- ESBL
- VIM
- KPC
- ESBL+VIM

What would you recommend for treatment?

1. Colistin
2. Gentamicin
3. Colistin plus gentamicin
4. Meropenem plus gentamicin

Pseudomonas aeruginosa

Antibiotic	MIC
Ampicillin	R
Ampicillin/sulbactam	R
Piperacillin/tazobactam	R
Aztreonam	S
Cefazoline	R
Cefoxitin	R
Ceftazidime	R
Ceftriaxone	R
Cefepime	R
Imipenem	R
Meropenem	R
Gentamicin	≥16
Colistin	≤2

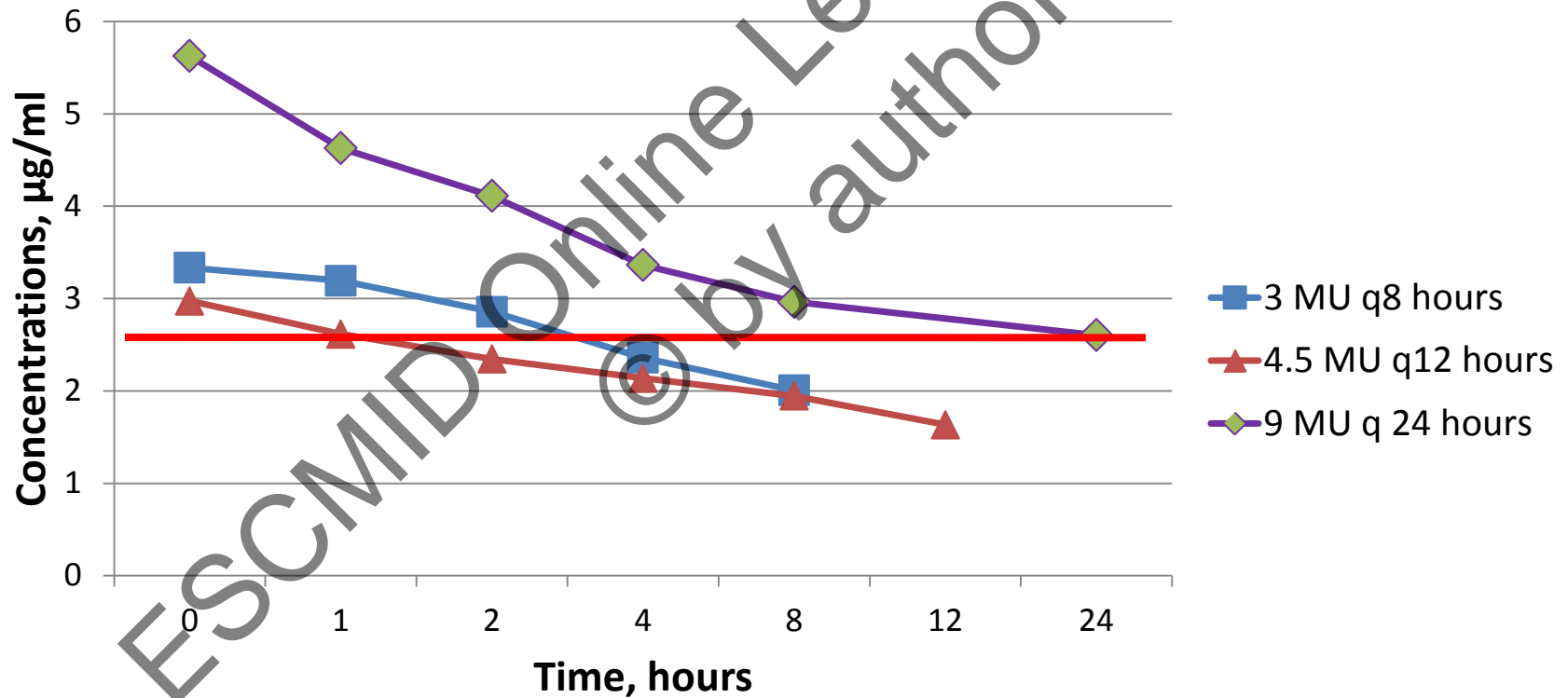
What is the mechanism of resistance?

- ESBL
- VIM
- KPC
- ESBL+VIM

What treatment would you recommend

- Aztreonam
- Colistin
- Colistin plus aztreonam

Mean serum concentrations of colistin with three different dosing regimens



Pseudomonas aeruginosa

Antibiotic	MIC
Piperacillin/tazobactam	S
Aztreonam	S
Cefazoline	R
Cefoxitin	R
Ceftazidime	S
Cefotaxime	R
Cefepime	S
Imipenem	R
Meropenem	R
Gentamicin	S
Colistin	S

What is the mechanism of resistance?

- ESBL
- VIM
- KPC
- Other

Case

- A 52 year-old woman, who had been hospitalized for more than 2 months due to acute leukemia, developed new-onset of fever. The patient was profoundly neutropenic (absolute neutrophil count $< 100/\mu\text{L}$) after salvage therapy with mitoxantrone, fludarabine, and cytarabine.
- During her hospitalization, she had received multiple courses of antimicrobial therapy for prior episodes of febrile neutropenia.

Case

- There were no localizing symptoms or signs of the infection. She had a femoral venous catheter in place.
- In active surveillance cultures (rectal swabs) she had been found to be a KPC carrier

What treatment would you recommend?

- 1. Colistin plus gentamicin
- 2. Colistin plus tigecycline
- 3. Meropenem plus gentamicin plus colistin
- 4. Meropenem plus gentamicin
- 4. Meropenem
- 5. Colistin

Case (continued)

- The patient was started on empirical therapy with meropenem plus gentamicin.
- Two days later the initial blood cultures (peripheral plus femoral catheter) grew KPC-producing *Klebsiella pneumoniae* that was resistant to all antimicrobials tested, except for colistin (MIC: 0.125 mg/L), gentamicin (MIC \leq 4 mg/L), tigecycline (MIC: 0.75 mg/L), and fosfomycin (MIC: 32 mg/L).

What is the Infection/colonization ratio

- 1. 10%
- 2. 20%
- 3. 30%
- 4. 50%

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- Data regarding the infection/colonization ratio are very limited, it is estimated that a portion of colonized patients ranging from 10 to 30 % will develop a CPE infection.
- This ratio may, nevertheless, vary by disease severity and co-morbid conditions of the host

Borer AL et al. Am J Infect Control, ahead of print

How would you modify the treatment

- 1. Colistin plus gentamicin
- 2. Colistin plus gentamicin plus fosfomycin
- 3. Colistin plus tigecycline
- 4. Fosfomycin
- 5. Fosfomycin plus tigecycline

Case 1 cont/ed

- The patient's condition deteriorated, she was on severe sepsis.
- The femoral catheter was removed and the antimicrobial regimen was modified to colistin (9 million units as a loading dose and then 4.5 million units twice daily), gentamicin (5 mg/kg once daily), and fosfomycin (6 g four times daily).

Case (continued)

- The patient's clinical condition partially improved, but low-grade fever persisted.
- Blood cultures were persistently positive for KPC-Kp.
- The KPC blood isolate recovered 11 days after the institution of fosfomicin-based regimen exhibited resistance to fosfomicin (MIC > 1024 mg/L).

Mutant Frequency

Isolate	B-lactamase	Fosfomycin selecting concentration	
		50 mg/L	100 mg/L
Kpn LA-20	KPC-2	1.7×10^{-6}	1.4×10^{-7}
Kpn LA-22	KPC-2	4.6×10^{-6}	4.0×10^{-6}
Kpn LA-24	KPC-2	9.4×10^{-6}	1.9×10^{-6}
Kpn 6/100	VIM-1	2.6×10^{-6}	7.8×10^{-7}
Kpn SOT-25	SHV-5	$< 8.4 \times 10^{-7}$	$< 8.4 \times 10^{-7}$

What would you do

- 1. Tigecycline plus gentamicin plus colistin
- 2. Colistin plus gentamicin
- 3. Continue the same treatment

- The patient continued treatment with colistin plus gentamicin plus tigecycline without response and died 8 days later in septic shock.
- A KPC-producing *K. pneumoniae* isolate cultured 5 days following discontinuation of fosfomycin remained fosfomycin-resistant (MIC: >1024 mg/L).

K. pneumoniae BSIs in Patients with Hematologic Malignancies

Host	CPKP	No CPKP	P
With disease	17	6	<0.001
Without disease	2	12	

Mortality of Neutropenic Patients with *K. pneumoniae* BSIs

