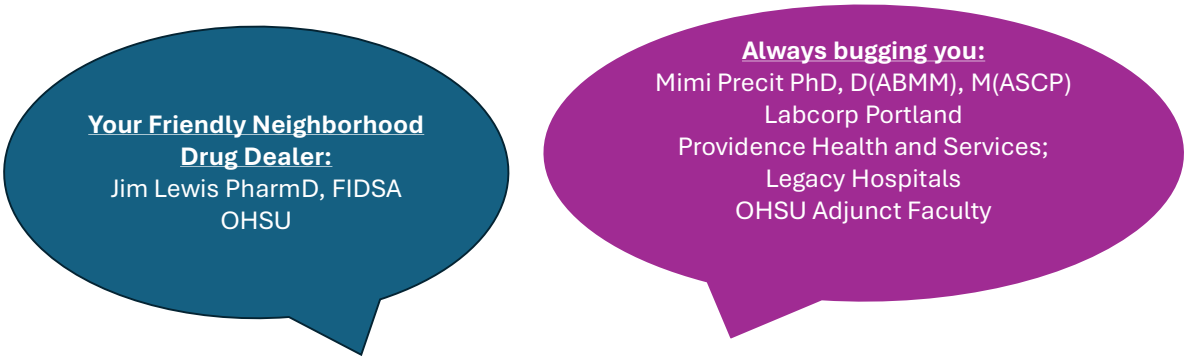
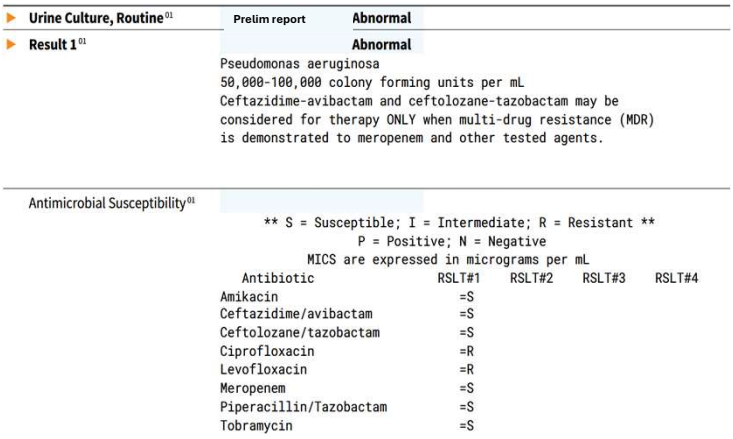
A pharmacist and a microbiologist walk into a bar, they were (unsurprisingly) met with resistance



Case 1: Something's missing

- 78 y/o male with history of bladder cancer on BCG therapy.
- Recent *Pseudomonas aeruginosa* UTI previously treated with Ceftazidime / Tobramycin.
- Recurrence of symptoms within 3 days of discharge - Frequency, urgency, burning with urination.
- Urine was collected and sent for culture.

What was reported:



Urine Culture, Routine [01] — Prelim report — **Abnormal**

Result 1 [01] — **Abnormal**

Pseudomonas aeruginosa
50,000-100,000 colony forming units per mL
Ceftazidime-avibactam and ceftolozane-tazobactam may be considered for therapy ONLY when multi-drug resistance (MDR) is demonstrated to meropenem and other tested agents.

Antimicrobial Susceptibility [01]

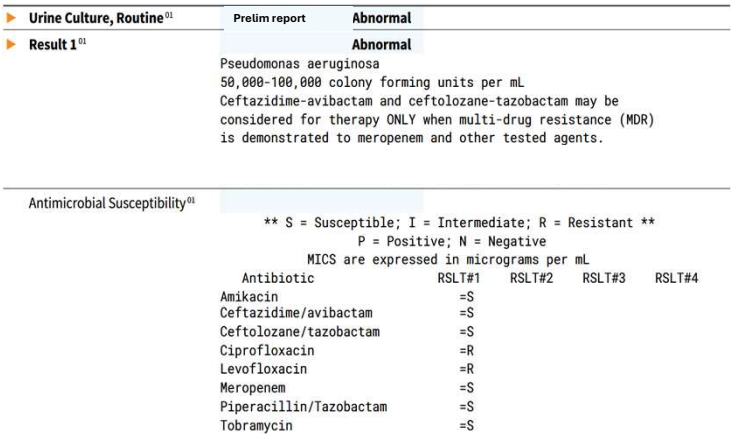
** S = Susceptible; I = Intermediate; R = Resistant **
P = Positive; N = Negative
MICS are expressed in micrograms per mL

Antibiotic	RSLT#1	RSLT#2	RSLT#3	RSLT#4
Amikacin	=S			
Ceftazidime/avibactam	=S			
Ceftolozane/tazobactam	=S			
Ciprofloxacin	=R			
Levofloxacin	=R			
Meropenem	=S			
Piperacillin/Tazobactam	=S			
Tobramycin	=S			

- Repeat (outpatient) urine culture with PSA with FQ-resistance.
- No oral options to treat suspected bacterial prostatitis.
- Patient scheduled for direct admit tomorrow afternoon.

J

Polling question



Urine Culture, Routine [01] — Prelim report — **Abnormal**

Result 1 [01] — **Abnormal**

Pseudomonas aeruginosa
50,000-100,000 colony forming units per mL
Ceftazidime-avibactam and ceftolozane-tazobactam may be considered for therapy ONLY when multi-drug resistance (MDR) is demonstrated to meropenem and other tested agents.

Antimicrobial Susceptibility [01]

** S = Susceptible; I = Intermediate; R = Resistant **
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Antibiotic	RSLT#1	RSLT#2	RSLT#3	RSLT#4
Amikacin	=S			
Ceftazidime/avibactam	=S			
Ceftolozane/tazobactam	=S			
Ciprofloxacin	=R			
Levofloxacin	=R			
Meropenem	=S			
Piperacillin/Tazobactam	=S			
Tobramycin	=S			

So what do you do?

A. Treat with ceftaz/avi

B. Treat with meropenem

C. Cancel the admit and send him home he's probably fine

D. Call the microbiology lab

J

Pharmacist:

Dr. Precit – Where the heck are the cefepime and ceftaz for this *Pseudomonas aeruginosa* UTI patient?!

Microbiologist:

There could be a few reasons. It's policy to report cefepime and ceftazidime on *P. Aeruginosa* (CLSI Tier 1 drugs). Report is in prelim status so that tells me we're not quite done here

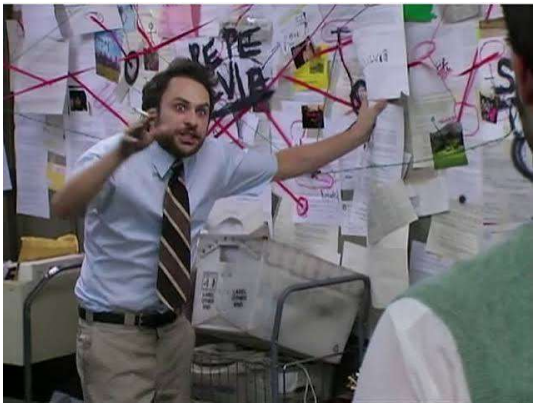
Send me the patient information and let me double check ASAP and get back to you

Tier 1: Antimicrobial agents that are appropriate for routine, primary testing and reporting
Ceftazidime
Cefepime
Piperacillin-tazobactam
Tobramycin
Ciprofloxacin Levofloxacin



J to M

INTERLUDE: CUE JEOPARDY MUSIC



If you walked into the lab how you'd actually find me

M

Micro Reports Back…

Ceftazidime and Cefepime are in progress, you should have results by tomorrow

There were manufacturer limitations preventing release from our automated method



M

What's happening in the lab: Automated susceptibility









Bug goes in



MIC comes out



Reporting preliminary and/or final results

Results reviewed and steps taken by laboratory technologists: nothing, reflex testing, repeat testing, additional testing

M

The *"fine print"* - certain drug/bug results are not reliable on automated methods and reflex testing is required

Card Limitations

Suppress from reporting and, if requested, instead perform an alternative method of testing for these combinations.

1. **Amikacin**: *Acinetobacter baumanii* complex, *Proteus vulgaris*, *Providencia* spp., *Pseudomonas* spp (R only), *E coli* (R only), *Proteus* spp (R only), *Klebsiella* spp (R only), *Enterobacter* spp (R only), *Klebsiella aerogenes* (R only), *Serratia* spp (R only), *Citrobacter freundii* (R only)
2. **Ampicillin/sulbactam**: *Citrobacter* spp, *Enterobacter* spp, *Klebsiella aerogenes*, *Pantoea* spp, *Serratia* spp, *Cronobacter sakazakii*
3. **Cefepime**: *Hafnia alvei*, *Morganella* spp, *Aeromonas* spp (R only), *Vibrio* spp (R only), *Pseudomonas aeruginosa* (MIC is 8 or 16)
4. **Ceftazidime**: *Morganella morganii*, *Citrobacter koseri* (R only), *Yersinia enterocolitica* (R only), *Pseudomonas aeruginosa* (MIC is 8), *Aeromonas* spp (R only), *Vibrio* spp (R only)
5. **Ceftazidime/Avibactam**: *Providencia rettgeri, Pseudomonas aeruginosa* (MIC ≥16)
6. **Ceftolozane/Tazobactam**: *Morganella morganii*, *Providencia rettgeri, Serratia marcescens*, *Citrobacter koseri* (R only), *Proteus mirabilis* (R only), *Proteus vulgaris* (R only), *Serratia liquefacians* (R only)
7. **Ciprofloxacin**: *Providencia rettgeri* (MIC is 0.25 or 0.5), *Serratia marcescens* (MIC is 0.5), *Klebsiella pneumoniae* (MIC is 0.5), *Salmonella enteritidis* (R only), *S. typhi* (R only), *Shigella sonnei* (R only)
8. **Imipenem/Relebactam**: *Proteus* spp, *Providencia* spp, *Morganella* spp, *Serratia* spp, *Citrobacter freundii* (R only), *C koseri* (R only), *Enterobacter asburiae* (R only)
9. **Meropenem**: *Enterobacter cloacae* (MIC ≥ 16), *Proteus vulgaris*, *Klebsiella oxytoca* (R only), *Proteus mirabilis* (R only), *Citrobacter koseri* (R only), *Hafnia alvei* (R only), *Aeromonas* spp. (R only), *Vibrio* spp (R only)
10. **Minocycline**: *Shigella* spp
11. **Piperacillin/Tazobactam**: *Serratia marcescens*,
12. **Tobramycin**: *Providencia stuartii*, *Klebsiella aerogenes* (R only), *Enterobacter cloacae* (R only), *Proteus mirabilis* (R only), *Proteus vulgaris* (R only), *Citrobacter koseri* (R only), *Morganella morganii* (R only)

Card limitations

Suppress from reporting and, if requested, instead perform an alternative method of testing for these combinations.

1. **Amikacin**: *Acinetobacter baumanii* complex, *Proteus vulgaris*, *Providencia* spp., *Pseudomonas* spp (R only), *E coli* (R only), *Proteus* spp (R only), *Klebsiella* spp (R only), *Enterobacter* spp (R only), *Klebsiella aerogens* (R only), *Serratia* spp (R only), *Citrobacter freundii* (R only)
2. **Ampicillin/sulbactam**: *Citrobacter* spp, *Enterobacter* spp, *Klebsiella aerogenes*, *Pantoea* spp, *Serratia* spp, *Cronobacter sakazakii*
3. **Aztreonam**: *Pseudomonas* spp, *Aeromonas* spp (R only)
4. **Cefotaxime**: *Pseudomonas fluorescens*, *Alcaligenes faecalis*, *Achromobacter denitrificans*, *Hafnia alvei*, *Shigella* spp, *Proteus vulgaris* (MIC is 1-4)
5. **Ceftazidime**: *Morganella morganii*, *Citrobacter koseri* (R only), *Yersinia enterocolitica* (R only), *Pseudomonas aeruginosa* (MIC is 8), *Aeromonas* spp (R only), *Vibrio* spp (R only)
6. **Ceftazidime/Avibactam**: *Providencia rettgeri, Pseudomonas aeruginosa* (MIC ≥16)
7. **Ceftolozane/Tazobactam**: *Morganella morganii*, *Providencia rettgeri, Serratia marcescens*, *Citrobacter koseri* (R only), *Proteus mirabilis* (R only), *Proteus vulgaris* (R only), *Serratia liquefacians* (R only)
8. **Delafloxacin**: *Serratia* spp
9. **Eravacycline**: *Proteus* spp, *Providencia* spp, *Morganella* spp, *Serratia* sp, *Citrobacter freundii* (R only), *C koseri* (R only), *E coli* (R only), *Klebsiella oxytoca* (R only), *Klebsiella pneumoniae* (MIC is 0.5)
10. **Imipenem**: *Klebsiella aerogenes*, *Proteus* spp, *Providencia* spp, *Morganella* spp, *Serratia* spp
11. **Imipenem/Relebactam**: *Proteus* spp, *Providencia* spp, *Morganella* spp, *Serratia* spp, *Citrobacter freundii* (R only), *C koseri* (R only), *Enterobacter asburiae* (R only)
12. **Meropenem/Vaborbactam**: *Enterobacter cloacae* complex (R only), *Citrobacter freundii* (R only), *C koseri* (R only), *Klebsiella aerogenes* (R only), *K oxytoca* (R only), *Morganella morganii* (R only), *Proteus mirabilis* (R only), *Providencia* spp (R only), *Serratia marcescens* (R only)

Card Limitations

1. **Amox/Clav limitations:** *Providencia* spp, *Proteus* spp (I or R only)**; Vitek Performs Amox/Clav on** all Enterobacterales
2. **Ampicillin limitations**: *Citrobacter* spp, *Cronobacter sakazakii*, *Enterobacter* spp, *Klebsiella aerogenes*, *Pantoeae* spp, *Serratia* spp; **Vitek Performs Ampicillin on** all Enterobacterales
3. **Cefazolin limitations:** Suppressed for All Enterobacterales **EXCEPT** *Kleb pneumo*, *E.coli*, and *Proteus mirabilis*
4. **Cefepime limitations:** *Hafnia alvei*, *Morganella* spp, *Aeromonas* spp (R only), *Vibrio* spp (R only), *Pseudomonas aeruginosa* (MIC is 8 or 16)**; Vitek Performs Cefepime on** *Enterobacter, E. coli, K. aerogenes, pneumo & oxytoca, P. mirabilis & vulgaris, C. koseri & freundii, P. agglomerans, P. rettgeri, & stuartii, S. marcescens*
5. **Cefpodoxime limitations**: *Morganella morganii*, *Serratia* spp**; Vitek performs Cefpodoxime on** all Enterobacterales
6. **Ceftriaxone limitations**: *Enterobacter cloacae*, *E. cloacae* complex, *Morganella* spp, *Proteus vulgaris*, *Proteus penneri, Providencia rettgeri* (R only), *Salmonella* spp (R only), *Shigella* sppp (R only)**; Vitek Performs Ceftriaxone on** *E. coli, K. aerogenes, pneumo & oxytoca, P. mirabilis, C. koseri & freundii, Providencia spp, S. marcescens*
7. **Ciprofloxacin limitations**: *P. rettgeri* (MIC is 0.25 or 0.5), *S. marcescens* (MIC is 0.5), *Kleb pneumo* (MIC is 0.5) **; Vitek Performs Cipro on** C. freundii & koseri, E. cloacae, E. coli, Kleb pneumo, oxytoca, & aerogenes, M. morganii, P. mirabilis & vulgaris, P. rettgeri & stuartii, S. marcescens.
8. **Ertapenem limitations**: *Hafnia alvei, Aeromonas* spp (R only), Gram negative isolates with MIC's in the range of 0.25 to 0.5 ug/mL. **; Vitek Performs Erta on** *E.coli, Kleb pneumo oxytoca & aerogenes, C. freundii & koseri, E. cloacae, M. morganii, P. mirabilis & vulgaris, P. rettgeri and stuartii, S. marcescens*
9. **Gentamicin limitations**: *Citrobacter koseri* (R only), *Klebsiella aerogenes* (R only), *Enterobacter cloacae* (R only), *Serratia marcescens* (R only), *Proteus vulgaris* (R only) ; **Vitek Performs Gent on** *Citrobacter, Enterobacter, Klebsiella, Proteus, Serratia*
10. **Levofloxacin :** *Aeromonas spp (R only) Citrobacter freundii* (R only), *K. aerogenes* (R only), *E. cloacae* (R only), *K. oxytoca* (R only), *Morganellla morganii* (R only), *Pantoea agglomerans* (R only), *Proteus mirabilis* (R only), *Proteus vulgaris* (R only), *Providencia rettgeri* (R only), *Providencia stuartii* (R only), *Salmonella spp* (R only) **.; Vitek Performs Levo on** *E. cloacae, Ecoli, K. pneumo, oxytoca, & aerogenes, P. mirabilis & vulgaris, S. marcescens, C. freundii & koseri, E and C. sakazakii, M. morganii, P. agglomerans, P. rettgeri & startii*
11. **Meropenem limitations**: *Enterobacter cloacae* (MIC ≥ 16), *Proteus vulgaris*, *Klebsiella oxytoca* (R only), *Proteus mirabilis* (R only), *Citrobacter koseri* (R only), *Hafnia alvei* (R only), *Aeromonas* spp. (R only), *Vibrio* spp (R only) **; Vitek Performs Mero on** *Ecoli, Kleb pneumo & oxytoca, P. mirabilis & vulgaris, C. freundii & koseri, E. cloacae, M. morganii, S. marcescens, H. alvei,*
12. **Pip/Tazo limitations**: *Serratia marcescens* **; Vitek Performs Pip/Tazo on** *E. coli, Kleb pneumo, C. koseri, M. morganii, P. vulgaris, P. rettgeri, P. stuartii,*
13. **Tobramycin limitations**: *Providencia stuartii*, *Klebsiella aerogenes* (R only), *Enterobacter cloacae* (R only), *Proteus mirabilis* (R only), *Proteus vulgaris* (R only), *Citrobacter koseri* (R only), *Morganella morganii* (R only) **; Vitek Performs Tobra on** *Citrobacter, Enterobacter, Ecoli, Klebsiella, M. morganii, P mirabilis & vulgaris, Providencia, Serratia*
14. **SXT performed on** *Klebsiella, Enterobacter, M. morganii, P. mirabilis & vulgaris, C. sakazakii*
15. **Cefoxitin, Nitro, Tetracycline, Performed** on all Enterobacterales

M

The *"fine print"* - certain drug/bug results are not reliable on automated methods and reflex testing is required

Card Limitations

Suppress from reporting and, if requested, instead perform an alternative method of testing for these combinations.

1. **Amikacin**: *Acinetobacter baumanii* complex, *Proteus vulgaris*, *Providencia* spp., *Pseudomonas* spp (R only), *E coli* (R only), *Proteus* spp (R only), *Klebsiella* spp (R only), *Enterobacter* spp (R only), *Klebsiella aerogenes* (R only), *Serratia* spp (R only), *Citrobacter freundii* (R only)
2. **Ampicillin/sulbactam**: *Citrobacter* spp, *Enterobacter* spp, *Klebsiella aerogenes*, *Pantoea* spp, *Serratia* spp, *Cronobacter sakazakii*
3. **Cefepime**: *Hafnia alvei*, *Morganella* spp, *Aeromonas* spp (R only), *Vibrio* spp (R only), *Pseudomonas aeruginosa* (MIC is 8 or 16)
4. **Ceftazidime**: *Morganella morganii*, *Citrobacter koseri* (R only), *Yersinia enterocolitica* (R only), *Pseudomonas aeruginosa* (MIC is 8), *Aeromonas* spp (R only), *Vibrio* spp (R only)
5. **Ceftazidime/Avibactam**: *Providencia rettgeri, Pseudomonas aeruginosa* (MIC ≥16)
6. **Ceftolozane/Tazobactam**: *Morganella morganii*, *Providencia rettgeri, Serratia marcescens*, *Citrobacter koseri* (R only), *Proteus mirabilis* (R only), *Proteus vulgaris* (R only), *Serratia liquefacians* (R only)
7. **Ciprofloxacin**: *Providencia rettgeri* (MIC is 0.25 or 0.5), *Serratia marcescens* (MIC is 0.5), *Klebsiella pneumoniae* (MIC is 0.5), *Salmonella enteritidis* (R only), *S. typhi* (R only), *Shigella sonnei* (R only)
8. **Imipenem/Relebactam**: *Proteus* spp, *Providencia* spp, *Morganella* spp, *Serratia* spp, *Citrobacter freundii* (R only), *C koseri* (R only), *Enterobacter asburiae* (R only)
9. **Meropenem**: *Enterobacter cloacae* (MIC ≥ 16), *Proteus vulgaris*, *Klebsiella oxytoca* (R only), *Proteus mirabilis* (R only), *Citrobacter koseri* (R only), *Hafnia alvei* (R only), *Aeromonas* spp. (R only), *Vibrio* spp (R only)
10. **Minocycline**: *Shigella* spp
11. **Piperacillin/Tazobactam**: *Serratia marcescens*,
12. **Tobramycin**: *Providencia stuartii*, *Klebsiella aerogenes* (R only), *Enterobacter cloacae* (R only), *Proteus mirabilis* (R only), *Proteus vulgaris* (R only), *Citrobacter koseri* (R only), *Morganella morganii* (R only)

Card limitations

Suppress from reporting and, if requested, instead perform an alternative method of testing for these combinations.

1. **Amikacin**: *Acinetobacter baumanii* complex, *Proteus vulgaris*, *Providencia* spp., *Pseudomonas* spp (R only), *E coli* (R only), *Proteus* spp (R only), *Klebsiella* spp (R only), *Enterobacter* spp (R only), *Klebsiella aerogens* (R only), *Serratia* spp (R only), *Citrobacter freundii* (R only)
2. **Ampicillin/sulbactam**: *Citrobacter* spp, *Enterobacter* spp, *Klebsiella aerogenes*, *Pantoea* spp, *Serratia* spp, *Cronobacter sakazakii*
3. **Aztreonam**: *Pseudomonas* spp, *Aeromonas* spp (R only)
4. **Cefotaxime**: *Pseudomonas fluorescens*, *Alcaligenes faecalis*, *Achromobacter denitrificans*, *Hafnia alvei*, *Shigella* spp, *Proteus vulgaris* (MIC is 1-4)
5. **Ceftazidime**: *Morganella morganii*, *Citrobacter koseri* (R only), *Yersinia enterocolitica* (R only), *Pseudomonas aeruginosa* (MIC is 8), *Aeromonas* spp (R only), *Vibrio* spp (R only)
6. **Ceftazidime/Avibactam**: *Providencia rettgeri, Pseudomonas aeruginosa* (MIC ≥16)
7. **Ceftolozane/Tazobactam**: *Morganella morganii*, *Providencia rettgeri, Serratia marcescens*, *Citrobacter koseri* (R only), *Proteus mirabilis* (R only), *Proteus vulgaris* (R only), *Serratia liquefacians* (R only)
8. **Delafloxacin**: *Serratia* spp
9. **Eravacycline**: *Proteus* spp, *Providencia* spp, *Morganella* spp, *Serratia* sp, *Citrobacter freundii* (R only), *C koseri* (R only), *E coli* (R only), *Klebsiella oxytoca* (R only), *Klebsiella pneumoniae* (MIC is 0.5)
10. **Imipenem**: *Klebsiella aerogenes*, *Proteus* spp, *Providencia* spp, *Morganella* spp, *Serratia* spp
11. **Imipenem/Relebactam**: *Proteus* spp, *Providencia* spp, *Morganella* spp, *Serratia* spp, *Citrobacter freundii* (R only), *C koseri* (R only), *Enterobacter asburiae* (R only)
12. **Meropenem/Vaborbactam**: *Enterobacter cloacae* complex (R only), *Citrobacter freundii* (R only), *C koseri* (R only), *Klebsiella aerogenes* (R only), *K oxytoca* (R only), *Morganella morganii* (R only), *Proteus mirabilis* (R only), *Providencia* spp (R only), *Serratia marcescens* (R only)

Card Limitations

1. **Amox/Clav limitations:** *Providencia* spp, *Proteus* spp (I or R only)**; Vitek Performs Amox/Clav on** all Enterobacterales
2. **Ampicillin limitations**: *Citrobacter* spp, *Cronobacter sakazakii*, *Enterobacter* spp, *Klebsiella aerogenes*, *Pantoeae* spp, *Serratia* spp; **Vitek Performs Ampicillin on** all Enterobacterales
3. **Cefazolin limitations:** Suppressed for All Enterobacterales **EXCEPT** *Kleb pneumo*, *E.coli*, and *Proteus mirabilis*
4. **Cefepime limitations:** *Hafnia alvei*, *Morganella* spp, *Aeromonas* spp (R only), *Vibrio* spp (R only), *Pseudomonas aeruginosa* (MIC is 8 or 16)**; Vitek Performs Cefepime on** *Enterobacter, E. coli, K. aerogenes, pneumo & oxytoca, P. mirabilis & vulgaris, C. koseri & freundii, P. agglomerans, P. rettgeri, & stuartii, S. marcescens*
5. **Cefpodoxime limitations**: *Morganella morganii*, *Serratia* spp**; Vitek performs Cefpodoxime on** all Enterobacterales
6. **Ceftriaxone limitations**: *Enterobacter cloacae*, *E. cloacae* complex, *Morganella* spp, *Proteus vulgaris*, *Proteus penneri, Providencia rettgeri* (R only), *Salmonella* spp (R only), *Shigella* sppp (R only)**; Vitek Performs Ceftriaxone on** *E. coli, K. aerogenes, pneumo & oxytoca, P. mirabilis, C. koseri & freundii, Providencia spp, S. marcescens*
7. **Ciprofloxacin limitations**: *P. rettgeri* (MIC is 0.25 or 0.5), *S. marcescens* (MIC is 0.5), *Kleb pneumo* (MIC is 0.5) **; Vitek Performs Cipro on** C. freundii & koseri, E. cloacae, E. coli, Kleb pneumo, oxytoca, & aerogenes, M. morganii, P. mirabilis & vulgaris, P. rettgeri & stuartii, S. marcescens.
8. **Ertapenem limitations**: *Hafnia alvei, Aeromonas* spp (R only), Gram negative isolates with MIC's in the range of 0.25 to 0.5 ug/mL. **; Vitek Performs Erta on** *E.coli, Kleb pneumo oxytoca & aerogenes, C. freundii & koseri, E. cloacae, M. morganii, P. mirabilis & vulgaris, P. rettgeri and stuartii, S. marcescens*
9. **Gentamicin limitations**: *Citrobacter koseri* (R only), *Klebsiella aerogenes* (R only), *Enterobacter cloacae* (R only), *Serratia marcescens* (R only), *Proteus vulgaris* (R only) ; **Vitek Performs Gent on** *Citrobacter, Enterobacter, Klebsiella, Proteus, Serratia*
10. **Levofloxacin :** *Aeromonas spp (R only) Citrobacter freundii* (R only), *K. aerogenes* (R only), *E. cloacae* (R only), *K. oxytoca* (R only), *Morganellla morganii* (R only), *Pantoea agglomerans* (R only), *Proteus mirabilis* (R only), *Proteus vulgaris* (R only), *Providencia rettgeri* (R only), *Providencia stuartii* (R only), *Salmonella spp* (R only) **.; Vitek Performs Levo on** *E. cloacae, Ecoli, K. pneumo, oxytoca, & aerogenes, P. mirabilis & vulgaris, S. marcescens, C. freundii & koseri, E and C. sakazakii, M. morganii, P. agglomerans, P. rettgeri & startii*
11. **Meropenem limitations**: *Enterobacter cloacae* (MIC ≥ 16), *Proteus vulgaris*, *Klebsiella oxytoca* (R only), *Proteus mirabilis* (R only), *Citrobacter koseri* (R only), *Hafnia alvei* (R only), *Aeromonas* spp. (R only), *Vibrio* spp (R only) **; Vitek Performs Mero on** *Ecoli, Kleb pneumo & oxytoca, P. mirabilis & vulgaris, C. freundii & koseri, E. cloacae, M. morganii, S. marcescens, H. alvei,*
12. **Pip/Tazo limitations**: *Serratia marcescens* **; Vitek Performs Pip/Tazo on** *E. coli, Kleb pneumo, C. koseri, M. morganii, P. vulgaris, P. rettgeri, P. stuartii,*
13. **Tobramycin limitations**: *Providencia stuartii*, *Klebsiella aerogenes* (R only), *Enterobacter cloacae* (R only), *Proteus mirabilis* (R only), *Proteus vulgaris* (R only), *Citrobacter koseri* (R only), *Morganella morganii* (R only) **; Vitek Performs Tobra on** *Citrobacter, Enterobacter, Ecoli, Klebsiella, M. morganii, P mirabilis & vulgaris, Providencia, Serratia*
14. **SXT performed on** *Klebsiella, Enterobacter, M. morganii, P. mirabilis & vulgaris, C. sakazakii*
15. **Cefoxitin, Nitro, Tetracycline, Performed** on all Enterobacterales

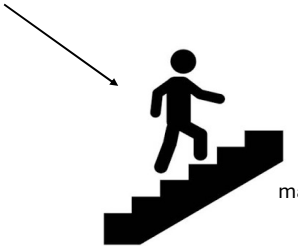
M

The results from the automated instrumentation were not reliable i.e. “limitation”



For *Pseudomonas aeruginosa:*

- If Ceftazidime MIC is 8 instrument will not report
- If Cefepime MIC is 8 or 16 instrument will not report



This alerts the lab and we set up manual method for these drugs, which adds a day.

In the meantime, we release the susceptibility results we DO have. Report can look incomplete and the clinical teams may have questions…. Such as…

M

The real time back and forth discussion in real time Q/A

Pharmacist:

Question1: Can you set up ceftaz and cefepime via manual method ahead of time in case the results fall into this “limitation” category?

Question2: Can you put a comment in that additional MICs are in progress so we know other drugs are coming?

Answer 3: Obviously No!

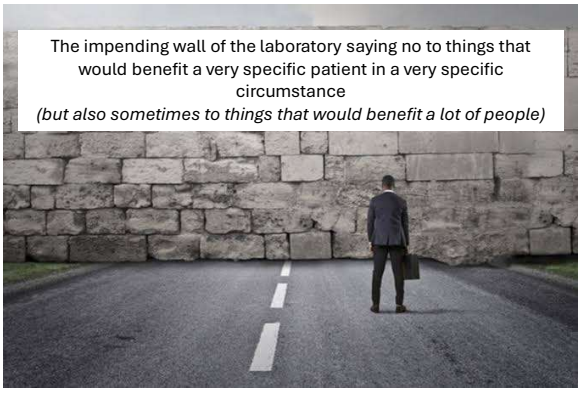
Microbiologist:

Answser1: Most isolates test with MICs below the limitation values - would be a lot of work for occasional outlier. Manual methods are laborious (it’s why automates was implemented)

Question2: We try our best to do this for our inpatients but outpatient results do not file the same and comments don’t cross. Additionally, it’s an extra step for the tech and you may see variability in compliance. But the report does say prelim NOT final

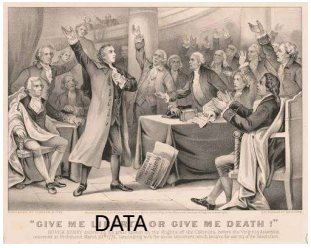
Question3: Would you rather I hold off reporting the full susceptibility report until I have all results back?

M&J



Options:

- Always welcome to contact the laboratory through the appropriate channels if you are missing something.
- If we start to see certain trends with regularity, then manual set up preemptively may be the best course of action.
- In the case of this patient… while you wait where do you stand?



M

Is there a crystal ball for this?

▶ **Urine Culture, Routine** [01]	Prelim report	**Abnormal**
▶ **Result 1** [01]		**Abnormal**

Pseudomonas aeruginosa
50,000-100,000 colony forming units per mL
Ceftazidime-avibactam and ceftolozane-tazobactam may be considered for therapy ONLY when multi-drug resistance (MDR) is demonstrated to meropenem and other tested agents.

Antimicrobial Susceptibility [01]

** S = Susceptible; I = Intermediate; R = Resistant **
P = Positive; N = Negative
MICS are expressed in micrograms per mL

Antibiotic	RSLT#1	RSLT#2	RSLT#3	RSLT#4
Amikacin	=S			
Ceftazidime/avibactam	=S			
Ceftolozane/tazobactam	=S			
Ciprofloxacin	=R			
Levofloxacin	=R			
Meropenem	=S			
Piperacillin/Tazobactam	=S			
Tobramycin	=S			



Livermore DM. *Clin Infect Dis* 2002;34:634
Murata M, et al. *Microbiol Spectr* 2025;13(5):e0279024

J

The next day:

Urine Culture, Routine [01]	Final report	Abnormal
Result 1 [01]		Abnormal

Pseudomonas aeruginosa
50,000-100,000 colony forming units per mL
Ceftazidime-avibactam and ceftolozane-tazobactam may be considered for therapy ONLY when multi-drug resistance (MDR) is demonstrated to meropenem and other tested agents.

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Ceftazidime/avibactam	=S			
Ceftolozane/tazobactam	=S			
Ciprofloxacin	=R			
Levofloxacin	=R			
Meropenem	=S			
Piperacillin/Tazobactam	=S			
Tobramycin	=S			



J

Take home points – Case 1

What the microbiologist wants you to remember

- Susceptibility testing is complex with multiple methods all with various limitations being employed at once
- The lab balances workload and workflow with clinician requests and desired patient driven procedural changes
- If you see something unexpected say something
- While the laboratory is essential to patient care, we don't interface close to the patient; can sometimes forget our IMPACT

What the pharmacist wants you to remember

- Limitations are the bane of our existence
- A problem with newer systems and revised cards
- You're going to lose 1 day, **if** you catch it immediately
- Can you predict from the rest of the susceptibility result? - It depends

M, J

Case 2: What in the Antibiogram is going on?

- You are a pharmacist reviewing the latest antibiogram
- You notice the following for cefazolin and *Proteus mirabilis*

Organism	Cefazolin % Susceptibility 2024	Cefazolin % Susceptibility 2025
Proteus mirabilis	72%	15%

J

Pharmacist:

So, who broke Cefazolin/*P. mirabilis* on the latest antibiogram?

Microbiologist:

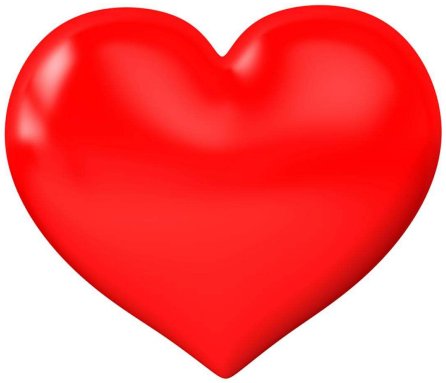
We (FINALLY) adopted the new lower cefazolin breakpoints within the past year



J to M

It's cefazolin, why do I care?

YOU should



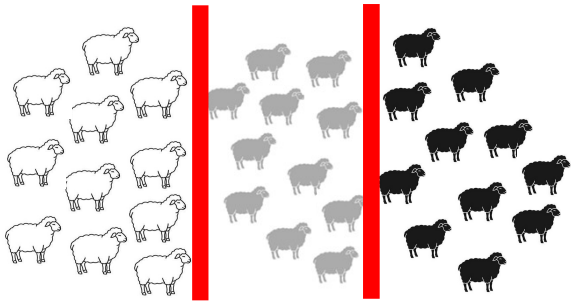
Cefazolin

J

How will breakpoint changes impact your antibiogram?

Organism	Cefazolin % Susceptibility 2024	Cefazolin % Susceptibility 2025
Proteus mirabilis	72%	15%

- As with all things… It depends…
  - Where is the wild type distribution
  - How much resistance do you see
  - How much does the resistance mechanism increase the MIC?



Susceptible 8 ug/mL | Intermediate 16 ug/mL | Resistant 32 ug/mL

J

So why did the % susceptibility change with a breakpoint change

Organism	Cefazolin % Susceptibility 2024	Cefazolin % Susceptibility 2025
Proteus mirabilis	72%	15%

- When a breakpoint is lowered FEWER isolates within a population will be susceptible
- Most of our *P. mirabilis* test around an MIC of 4 which historically was susceptible but now 4 is intermediate. Shifted the cumulative % data DOWN



Susceptible 2 ug/mL | Intermediate 4 ug/mL | Resistant 16 ug/mL

J

Proteus is a PROBLEM: Why you don't cut into the wild type

Table 1. Cefazolin Minimum Inhibitory Concentration (MIC) Distributions of the Common Enterobacteriaceae that Do Not Possess Chromosomal Cephalosporinases [7]

Species (cumulative %)	MIC, µg/mL 0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	512	ECV[a] (µg/ml)
Escherichia coli			37	131[b]	37	27	12	5	4	1	1			4
			14.5%	65.9%	80.4%	91.0%	95.7%	97.6%	99.2%	99.6%	100%			
Klebsiella pneumoniae			5	71	82[b]	17	8	6	12	1	5	1		4
			2.4%	36.5%	76.0%	84.1%	88.0%	90.9%	96.6%	97.1%	99.5%	100%		
Klebsiella oxytoca			1	11	41[b]	16	17	11	4	3	12	1	4	4
			0.8%	9.9%	43.8%	57.0%	71.1%	80.2%	83.5%	86.0%	95.9%	96.7%	100%	
Proteus mirabilis					60	156[b]	43	16	4	1	5	1	1	8
					20.9%	75.3%	90.2%	95.8%	97.2%	97.6%	99.3%	99.7%	100%	
Salmonella species		8	842	537	1116[b]	41	8	5	1	4				8
		0.3%	33.2%	54.1%	97.7%	99.3%	99.6%	99.8%	99.8%	100%				

[a] Epidemiological (wild-type) cutoff value, estimated by the statistical method of Turnidge et al 2006 [8].
[b] Wild-type mode.

Turnidge JD, et al. *Clin Infect Dis* 2011;52:917

J

Let's take a step back - What is a breakpoint

- MIC distributions and mechanisms of resistance (the bug) 
- PK-PD (the drug and the body) 
- Clinical data (the population) 

Pierce VM, et al. J Peds Infect Dis Soc 2022;11:73
CLSI Document M23 5th ed

J

Next step - Who develops Breakpoints (the cliff notes version)

- FDA
- CLSI
- EUCAST (and USCAST – long story there)
- The laboratory has their work cut out for them…

J

Next step - Who develops Breakpoints (the cliff notes version)

- FDA
- CLSI

Lab perspective: Not all CLSI breakpoints are FDA approved… which means from a laboratory perspective sometimes best practice guidelines are totally OFF label… Some labs do off label validations/implementations. Others DON'T. Inhibits standardization.

- EUCAST (and USCAST – long story there and the microbiologist is just going to ignore this)
- The laboratory has their work cut out for them… WE DO

M

Breakpoint Audit (instrumentation based)

Bug	Drug	Year adopted by CLSI	CLSI breakpoints (µg/ml)			FDA vs CLSI	Year FDA cleared	Reportable range	Comments
			S	I	R				
E. coli, P. mirabilis	Cefazolin	2011	≤ 2	4	≥ 8	Partial overlap, see comment	2023	1 - 32	Current FDA/CLSI systemic breakpoints. NOTE: FDA recognizes CLSI breakpoints for systemic sources only. If using CLSI breakpoints for uncomplicated urinary tract infections, a validation study is required.

We do this for every drug/bug/breakpoint across all automated systems…

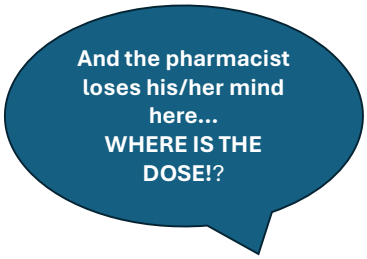


M

History of Cefazolin CLSI Breakpoints

CLSI Breakpoints	Pre - 1987			Year Revised	2010 and 2016 revisions		
Cefazolin	S	I	R		S	I	R
Systemic	≤ 8	16	≥32	2011	≤ 2	4	≥8
Urine	≤ 8	16	≥32	2016	≤ 16		≥32

Criterion	Example of recent revisions
Recognition that the antimicrobial dosage regimens used in widespread clinical practice differ substantially from the dosage regimens that were used to establish previous breakpoints	Cefazolin for Enterobacterales



M & j

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Local Lab (blood only systemic cases of urosepsis)				2011	≤ 4		≥8

Criterion	Example of recent revisions
Recognition that the antimicrobial dosage regimens used in widespread clinical practice differ substantially from the dosage regimens that were used to establish previous breakpoints	Cefazolin for Enterobacterales

WHY would we go completely off label with these breakpoints for so long?

Why did it take (OVER) a decade to adopt the new cefazolin breakpoints?

M







Automated susceptibility instrumentation is "fixed"

CLSI Breakpoints	Pre - 1987			Year Revised	2010 and 2016 revisions		
Cefazolin	S	I	R		S	I	R
Systemic	≤ 8	16	≥32	2010	≤ 2	4	≥8
Urine	≤ 8	16	≥32	2016	≤ 16		≥32
Local Lab (blood only systemic – in cases of urosepsis)				2011	≤ 4		≥8
Cefazolin dilution range on commercial AST system in use (not all manufacturers impacted)	4ug/ml to 32ug/ml The dilution range **did NOT go low** enough to capture the susceptible breakpoint						



M

Breakpoint Audit (instrumentation based)

Bug	Drug	Year adopted by CLSI	CLSI breakpoints (µg/ml)			FDA vs CLSI	Year FDA cleared	Reportable range	Comments
			S	I	R				
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Back to this table quickly FDA didn't clear the 2011 breakpoints until 2023

M

Polling Question

You're the microbiologist - What do you do?

A) Set up cefazolin by manual method for at least *Proteus mirabilis* or probably all Enterobacterales.

B) Change vendors for commercial susceptibility testing ASAP

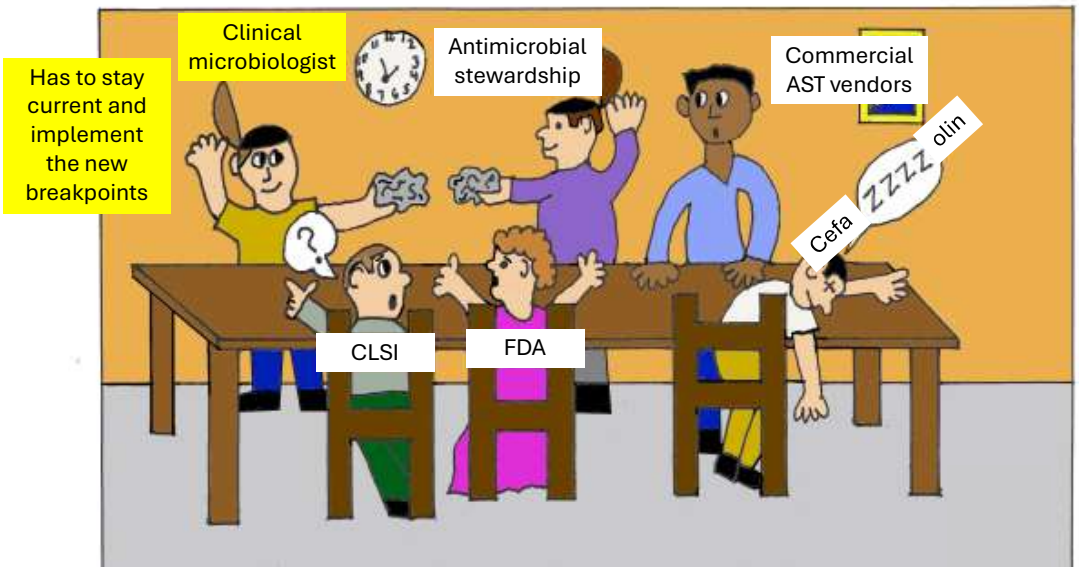
C) Discuss with vendor timeline for dilution range modification and future adoption of new breakpoints.

D) Operate on old/modified breakpoints since it serves your patient population, no need to fix what isn't broken for your hospital.

E) Quit and start a bakery.

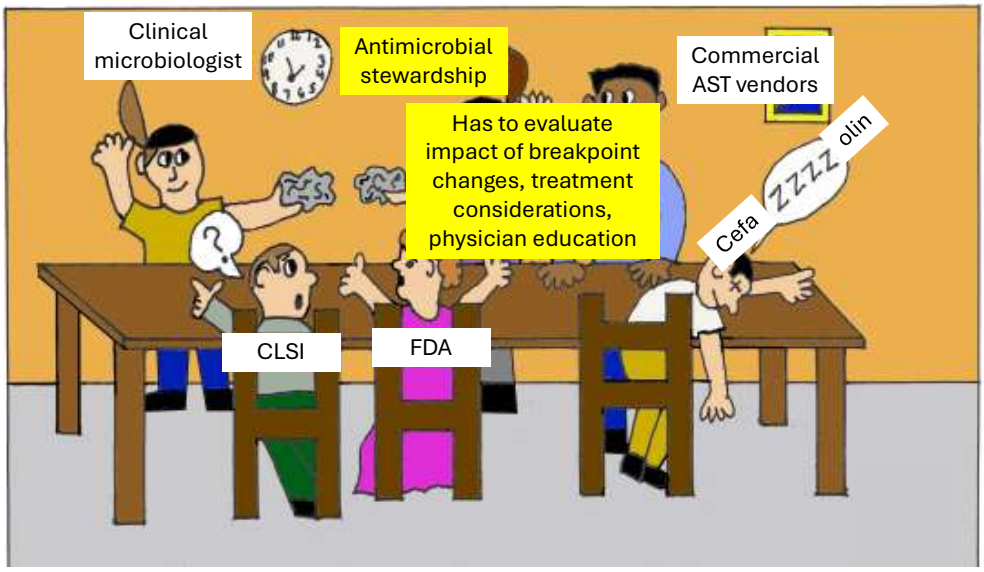
M

The organized chaos of a breakpoint change is a multidisciplinary/group effort



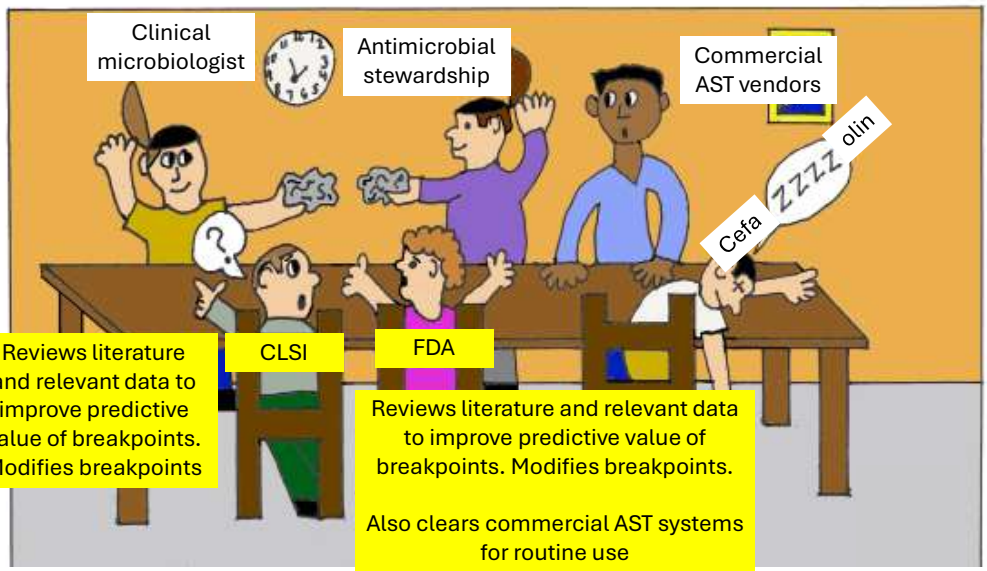
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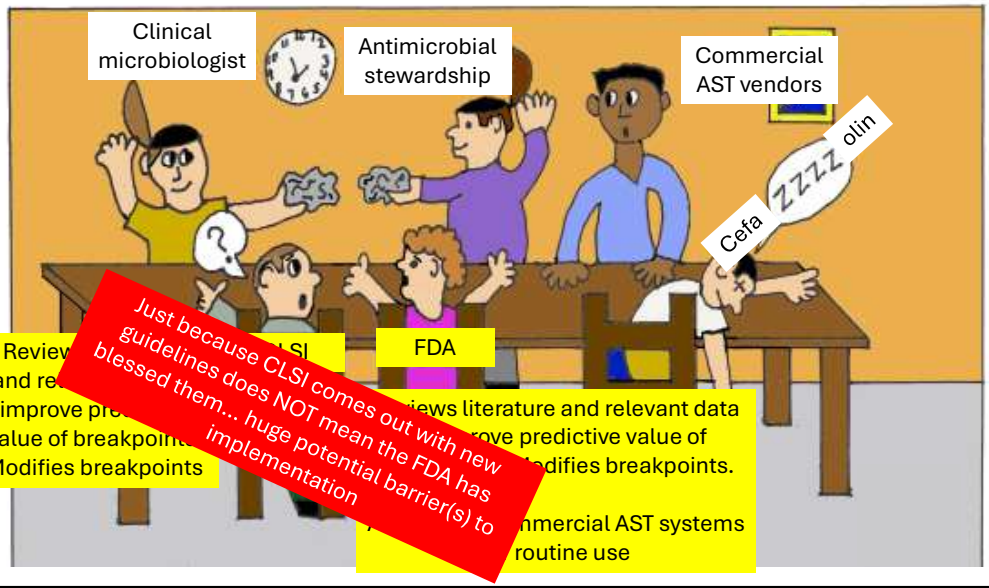
M

The organized chaos of a breakpoint change is a multidisciplinary/group effort



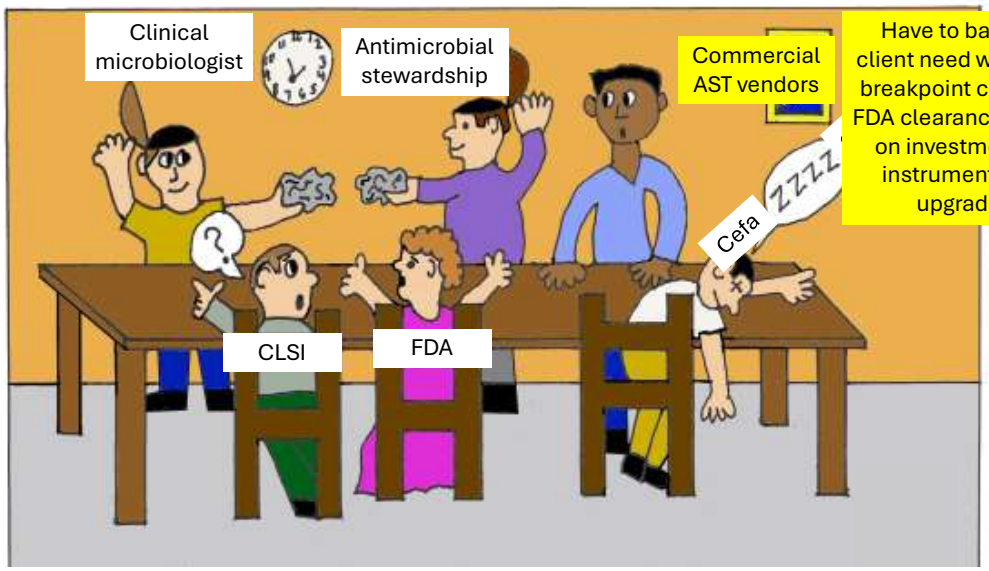
M

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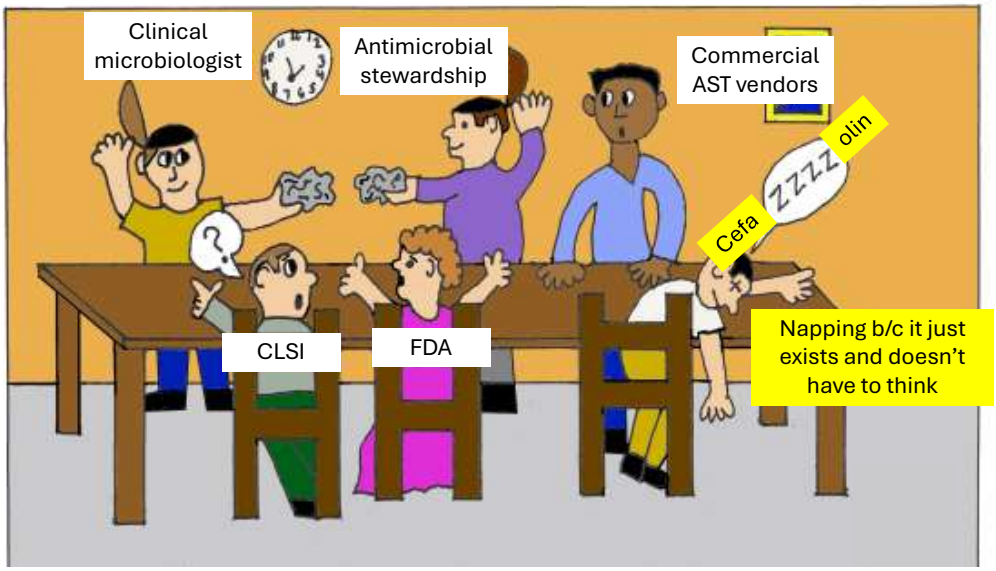
M

The organized chaos of a breakpoint change is a multidisciplinary/group effort



M

The organized chaos of a breakpoint change is a multidisciplinary/group effort



M

Take home points – Case 2

What the microbiologist wants you to remember

- Adopting new breakpoints is often not trivial and can take a long time
- We are regulatory bound now to adopt new breakpoints within 3 years of publish
- The CLSI publishes a new breakpoint guidance document annually (not everything changes annually but often hard to keep up)
- Antibiogram data can be impacted by resistance mechanisms, breakpoint changes, testing method changes

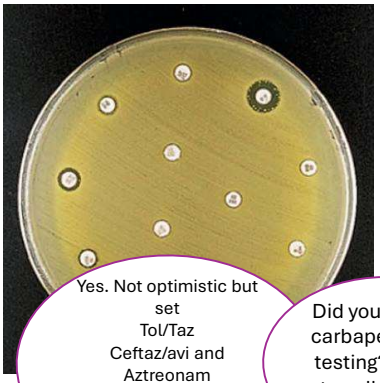
What the pharmacist wants you to remember

- The cefazolin breakpoint is… challenging
- The breakpoint is built around 2g Q8h
- Don't be afraid of 2g Q6h
- Systemic breakpoint vs urine breakpoint
- What cefazolin urine predicts and what it doesn't

M & J

Case 3: The metal(los) are making me mental

You are the microbiologist and your supervisor asks you to look at something



Pseudomonas aeruginosa

Drug	Interpretation
Ceftazidime	R
Cefepime	R
Cipro	R
Levo	R
Piperacillin/Tazobactam	R
amycin	R
enem	

Yes. Not optimistic but set Tol/Taz Ceftaz/avi and Aztreonam And sub for send out. I'm going to call ID pharm

Did you reflex to carbapenemase testing? I'll wait to call until we have that result

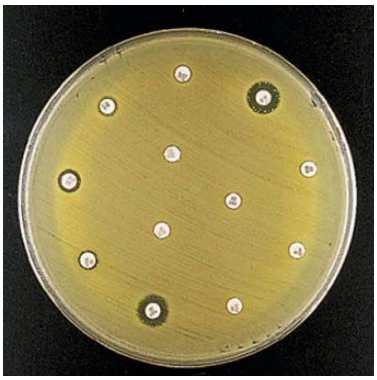
Yes. Setting that up today

Supervisor asks: Do you want me to set up anything else?

M

Case 3: The metal(los) are making me mental

You are the microbiologist and your supervisor asks you to look at something



Pseudomonas aeruginosa

Drug	Interpretation
Ceftazidime	R
Cefepime	R
Cipro	R
Levo	R
Piperacillin/Tazobactam	R
Tobramycin	R
Meropenem	R
Aztreonam	R
Ceftolozane/Tazobactam	R
Ceftazidime/Avibactam	R
Carbapenemase	IMP Detected



M

Microbiologist:

We recovered and just reported results for an IMP producing MDR-*Psuedomonas aeruginosa*. It's pan resistant, we've exhausted our testing options here. Wanted to discuss potential options…

Pharmacist:

Well that's a bad day at the office… can we send out for:

Poll the audience

M & J

Microbiologist:

We recovered and just reported results for an IMP producing MDR-*Psuedomonas aeruginosa*. It's pan resistant, we've exhausted our testing options here. Wanted to discuss potential options…

Pharmacist:

Cefiderocol

Aztreonam/avibactam

and/or-

Ceftaztidime/avibactam + Aztreonam testing

Cefiderocol – yes!

Aztreonam/avibactam there is an Etest but no breakpoints for PA… maybe I can beg someone to do it and report MIC?

Ceftaz/avi + Aztreonam is basically (very advanced) witchcraft, so no one does it

M & J

First the good news…

- Carbapenem resistant *P. aeruginosa* is **not** rare in the U.S.
- But carbapenemase producing *P. aeruginosa* **is** (+/-2% of CRPA)
- The combination of mero R, pip-tazo R, cefepime R, **PLUS** ceftolozane-tazo R is a really good predictor
- Can be confirmed with FDA cleared carbapenemase tests
- However…

Gottesdiener LS, Satlin MJ. *JAC Antimicrob Resist* 2026: https://doi.org/10.1093/jacamr/dlag208 J

First up – aztreonam-avibactam for *P. aeruginosa*

Agent	ICU isolates (n=1304)
Aztreonam-avibactam	78% (**note** using breakpoint of 8/4)
Ceftazidime-avibactam	96.3%
Ceftolozane-tazobactam	97.2%
Imipenem-relebactam	97.1%
Meropenem	77.8%
Cefepime	84.7%
Piperacillin-tazobactam	76.9%

Sader HS, et al. *Antibiotics* 2024;13:564 J

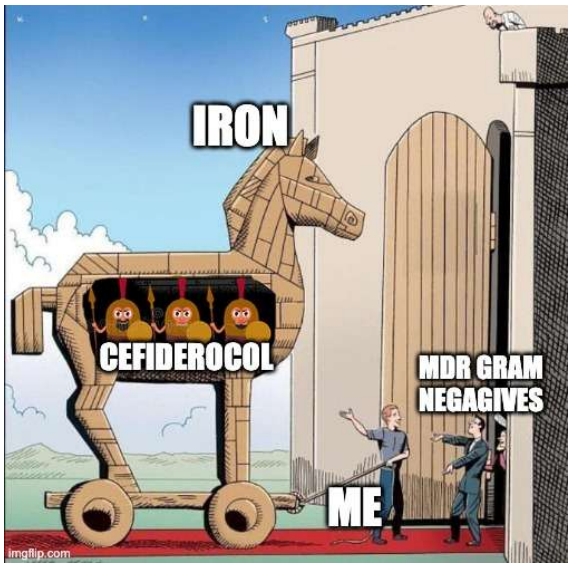
Aztreonam-Avibactam for MBL producing *P. aeruginosa*

- Minimal MIC improvement compared to aztreonam alone
- 1-2 dilutions at best
- Most MICs remain above the 4/4 breakpoint for Enterobacterales
- Likely not a viable option
- No CLSI Breakpoints
- Not recommended in the 2026 IDSA Gram negative guidance for these organisms

Collar GDS, et al. *Eur J Clin Micro Infect Dis* 2026. https://doi.org/10.1007/s10096-026-05647-6
Tamma PD, et al. *Clin Infect Dis* 2026. https://doi.org/10.1093/cid/ciag481

J

Cefiderocol it is then…

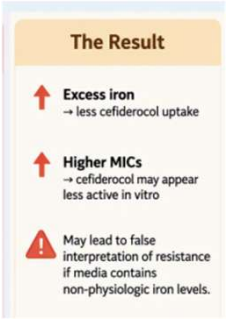


- First-in-class siderophore cephalosporin antibiotic that operates via a **"Trojan horse"** mechanism.
- Binds iron which the organism needs and sneaks into the periplasmic space, once there binds penicillin binding proteins (transpeptidase enzymes), arresting cell wall synthesis
- PK-PD targets appeared higher than standard cephalosporins in
- Potential challenges with NDM-1 and 5 (nature & lancet ID), maybe NDM-7 (AAC this week)
- Not impacted as much by IMP and VIM
- Xeruborbactam unlikely to save the day for *P. aeruginosa*
- BUT there are some caveats that we need to consider…

J

The Achilles heal of the Trojan Horse? Actually doing the testing (reliably)…

- Reference method is broth microdilution – requires use of iron depleted media
- Iron depletion impacts the reproducibility of the method
  - CLSI and EUCAST have disclaimers about variability in testing methods
- Difficulty in interpretation/reading (trailing growth in test wells)
- All breakpoint generating bodies disagree … FDA/CLSI/EUCAST all have different breakpoints
- Due to these challenges and infrequent use most labs don't bother



Simner PJ, Patel R 2020. J Clin Microbiol 59:10.1128/jcm.00951-20.

M

Back to our IMP producing PA case: what to do clinically with these folks?

Pseudomonas aeruginosa

Drug	Interpretation
Ceftazidime	R
Cefepime	R
Cipro	R
Levo	R
Piperacillin/Tazobactam	R
Tobramycin	R
Meropenem	R
Aztreonam	R
Ceftolozane/Tazobactam	R
Ceftazidime/Avibactam	R
Carbapenemase	IMP Detected



- Request send out susceptibility results
- Accept the limitations and timelines
- Start Cefiderocol
- Remember the dosing goes up to **2g Q6h** for CrCl >120ml/min
- Be aggressive with your dosing

J

Take home points – Case

What the microbiologist wants you to remember

- PAN resistant isolates make us squirrely too. We want to make sure you get the testing you need.
- The PNW has pretty friendly GNRs we don't see carbapenemase producers often. Since they are unusual we often trip up with how to handle them (easier methods help with this like CARBA5)
- Call us when you've got a weird bug like this if we don't call you first.
- Some drugs will be available in house some will be send outs

What the pharmacist wants you to remember

- Aztreonam-avi isn't the answer for these
- Cefiderocol is first line
- However, Cefiderocol is not foolproof here
- Many MBL producers also have ARM genes
- Disturbingly close to a return to the dark days

M & J

THANK YOU!

