

Choose your own adventure antibiotics

CLINID conference

Hunter Ratliff

10/29/2026

*Ages, dates, and other identifying
information may have been changed
I have no conflict of interest in relation to this presentation*



Shortcuts



Case 1: Start | Day 0 | Overview

Discussion: Start | Objectives

Polls: Q-D.1 | Q-D.2

Takeaways

Key discussion slides

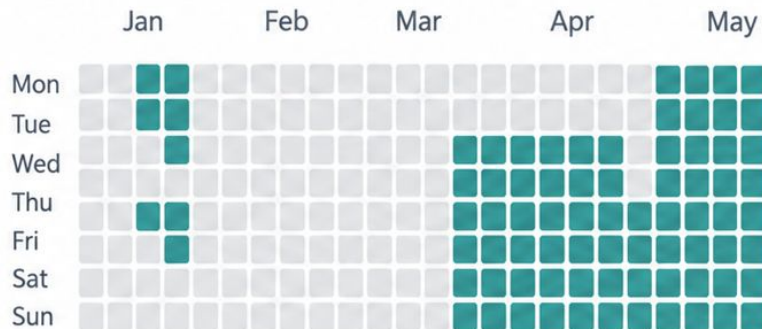
- **Clonal isn't uniform** | Selection | One specimen
- **His micro** | Antibigram | Day 11–105 | Weird case
- **Cefiderocol** | Hard to test | CREDIBLE-CR | MERINO
- **Back to the patient** | Cure | Was he a 60?

Can we do it? Yes we can (maybe)



Today we are going to cover **200 days worth of data** (~75% of the year so far)

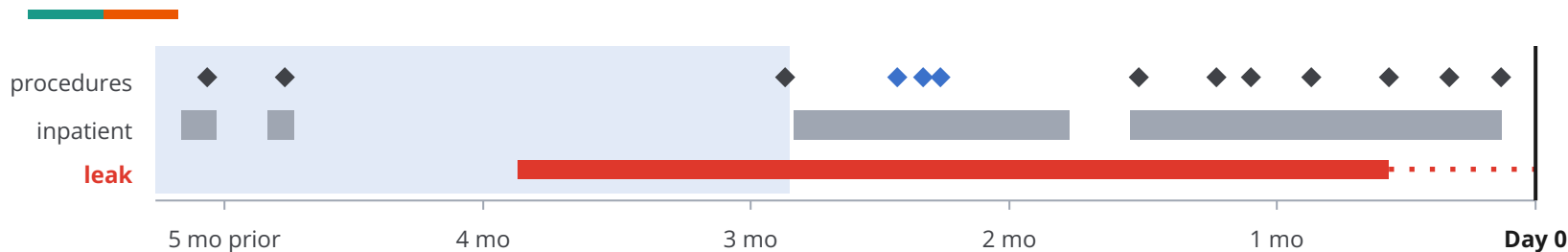
Buckle up!



Responsible use of AI

- **Claude** Opus 5.5 (Anthropic) drafted the slide design, first-draft text, and created timeline graphics
- ChatGPT 6 (Open AI) and **Nano Bannana 2** (Google) created some graphics, but Anthropic is a more ethical choice
- I chose the content and cases, educational points, and verified the literature search. **Hunter is responsible** for content and accuracy of this presentation
- No patient identifiers were shared with the AI (aside from **Abridge**, which was clutch)
- Dates are presented as hospital days relative to date of admission

Case 1: Never achieved source control

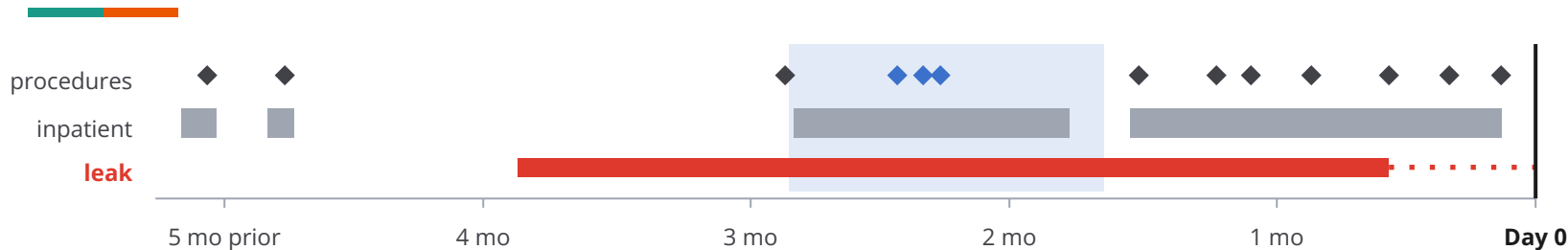


A 57 y/o M with no major PMH presents **5 months** after partial cholecystectomy

- **5 months prior:** RUQ pain; lap chole found a gangrenous, perforated gallbladder → subtotal cholecystectomy + drain; no antibiotics at discharge
- **1 week later:** drain removed, pus expressed → retained stone in the gallbladder fossa → perc chole tube; 4 days of Augmentin
- **4 months prior:** failed cap trial; fluoro showed a **stump leak** and a patent cystic duct draining into the CBD
- **3 months prior:** ERCP with CBD stent

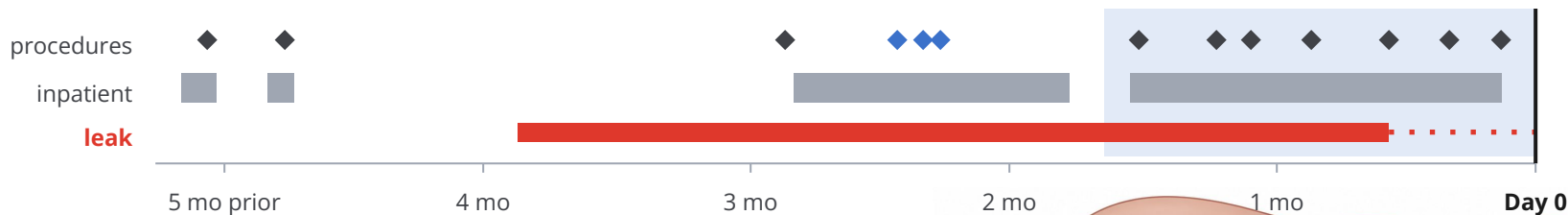
Developed **ERCP pancreatitis** into ongoing biliary leak :(

Case 1: Post-ERCP pancreatitis and the ICU



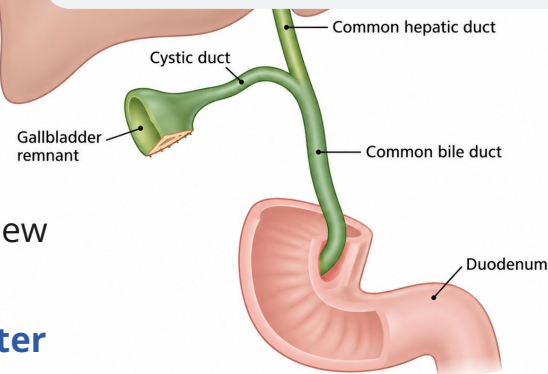
- **3 months prior:** post-ERCP pancreatitis, the day after the ERCP
- *Serratia marcescens* bacteremia
- Multiorgan failure requiring CRRT; abdominal compartment syndrome
- **3 laparotomies in 5 days:** 2 decompressive, then closure with bridging mesh
- Treated with Merrem and Zosyn; discharged after **1 month**

Case 1: Infected necrosis, ongoing leak



- **7 weeks prior:** admitted here with lobulated free fluid c/w peritonitis and pancreatitis
- IR drain grew mixed flora; bilateral ureteral stents for compression
- EUS with LAMS: *Pseudomonas* + *Serratia* → Merrem + micafungin; 2 necrosectomies
- **2.5 weeks prior:** ERCP confirmed the **cystic duct leak** → new cystic duct + CBD stents
- Discharged on Merrem + micafungin; readmitted **4 days later (Day 0)**

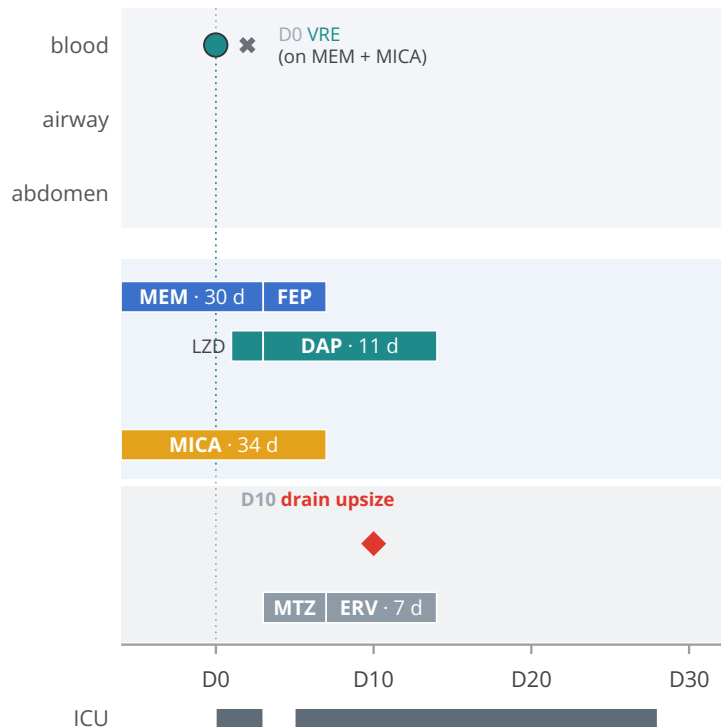
Before Day 0:
13 procedures
leak documented for 100+ days



Day 0

- Don't worry, details are not (that) important
- Well, some are, but we'll touch on them again

1: Admitted for VRE bacteremia



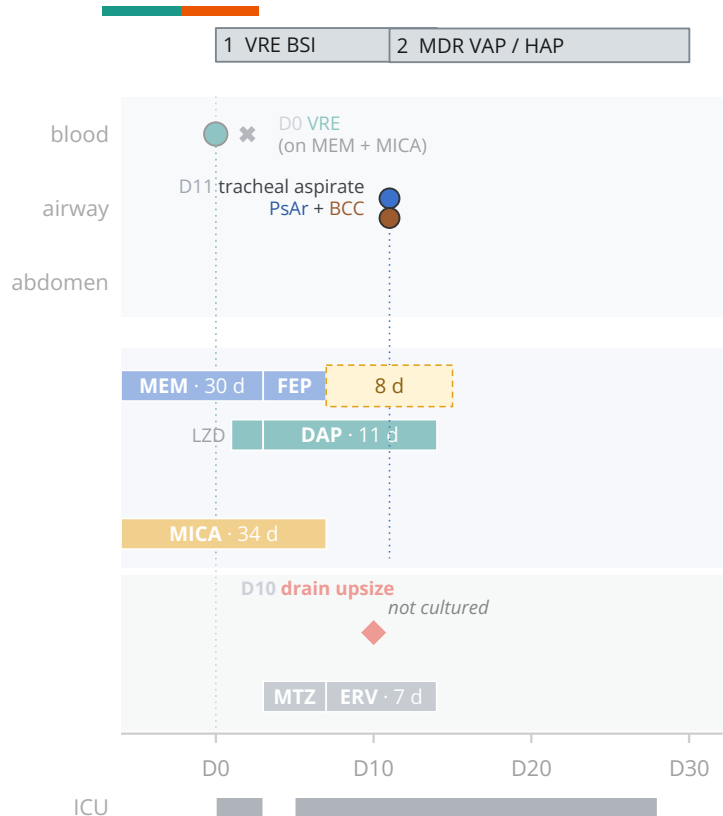
Admitted with sepsis

- Found to have **VRE bacteremia**
- Was on **Merrem** & **micafungin** OPAT

Started on **linezolid** / **daptomycin** (& eravacycline)

- BCx cleared quickly
- Had IR drain upsize (day 10)
 - No micro sent :(

2: MDRO gram negative pneumonia



Admitted with sepsis 2/2 **VRE bacteremia**

- Was on Merrem & micafungin OPAT
- Started on linezolid & daptomycin
- Got IR drain upsize, no micro

Developed **pneumonia** while on daptomycin & eravacycline

- 3+ & 2+ MDR *Pseudomonas aeruginosa* (2 strains)
- 3+ Muroid *Pseudomonas aeruginosa*
- 3+ *Burkholderia cepacia* complex

Pseudomonas testing

Resistant: Cefepime, Zosyn, Merrem

Sensitive: ceftolaz/tazo (Zerbaxa), cefiderocol (Fetroja)

***Burkholderia cepacia* complex**

Don't you wish we could

2: MDRO gram negative pneumonia



Developed **pneumonia** while on **daptomycin** & **eravacycline**

- 3+ & 2+ MDR **Pseudomonas aeruginosa** (2 strains)
- 3+ Muroid **Pseudomonas aeruginosa**
- 3+ **Burkholderia cepacia complex**

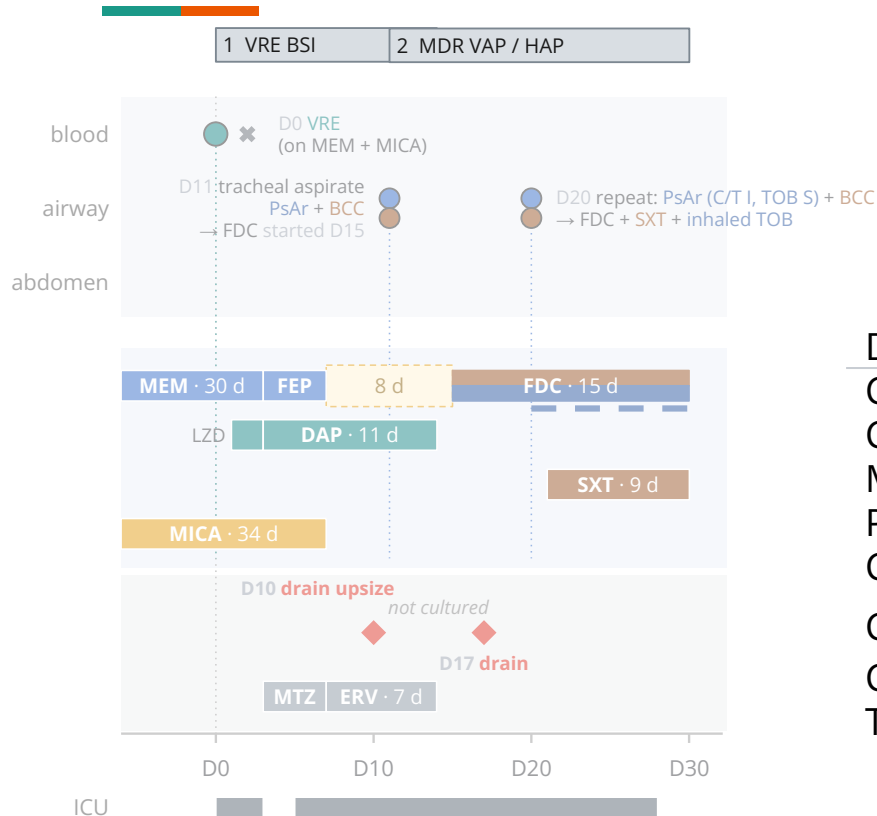
Started on **cefiderocol** (Fetroja), which should treat both the **PsAr** and **Burkholderia cepacia complex** (BCC)

Repeat trach Cx flora shifting:

- 3+ **Burkholderia cepacia complex**
- 1+ **Pseudomonas aeruginosa**
- This is only after a few days of therapy

Bactrim is added, but the **pseudomonas** looks different

2: MDRO gram negative pneumonia

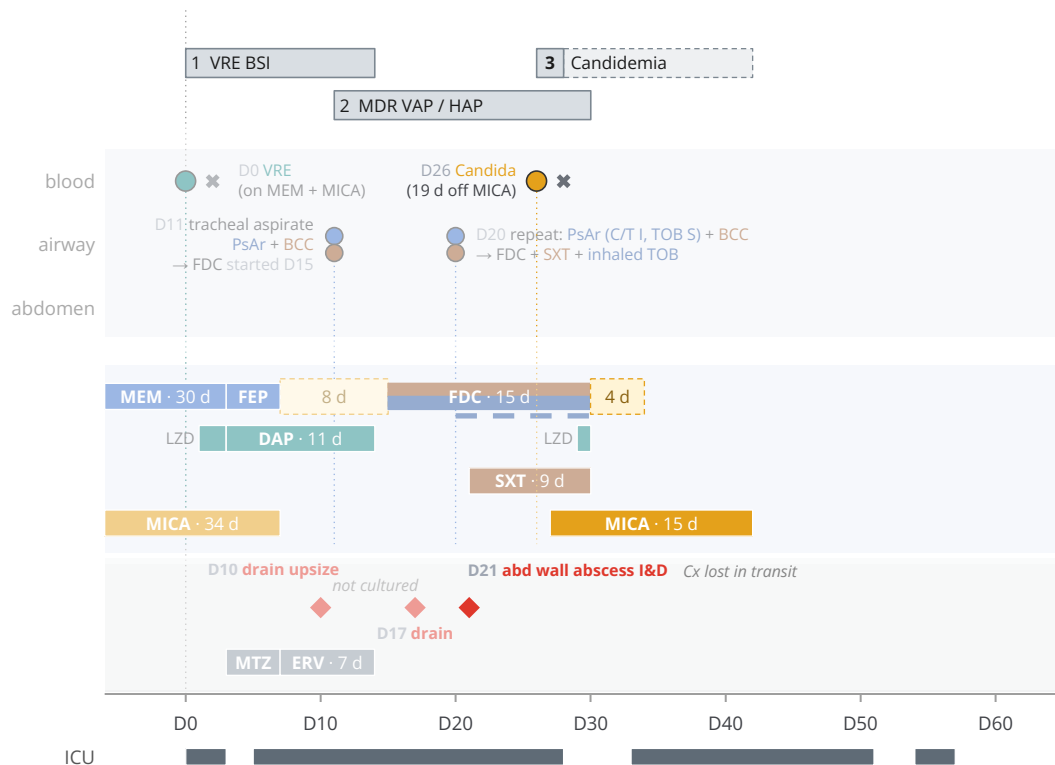


Day	D11		D20
Cefepime	R	R	R
Ceftazidime	I	R	R
Meropenem	R	R	R
Pip-tazo (TZP)	R	R	R
Ceftaz-avibactam (CZA)	S	R	S
Ceftolozane-tazo (C/T)	S	S	I
Cefiderocol (FDC)	S	S	S
Tobramycin	S	S	S

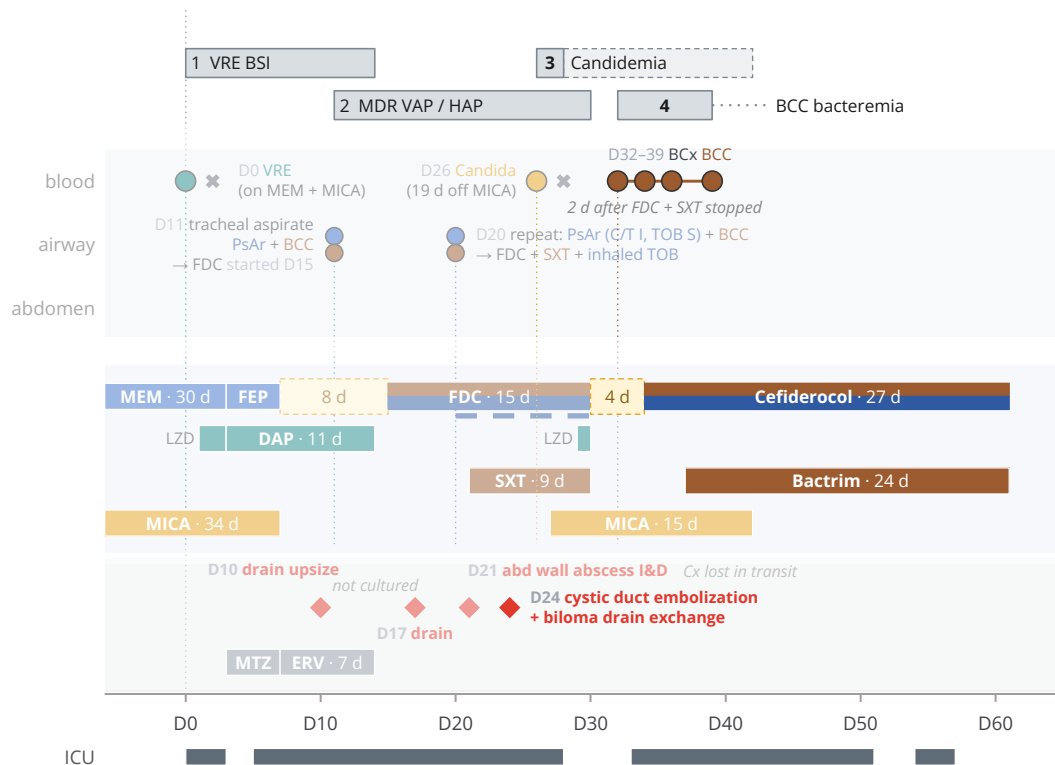
3-5: Series of bacteremias

Low grade **Candida lusitanae** fungemia

- **Micafungin** & cleared BCx



3-5: Series of bacteremias



Low grade **Candida lusitanae** fungemia

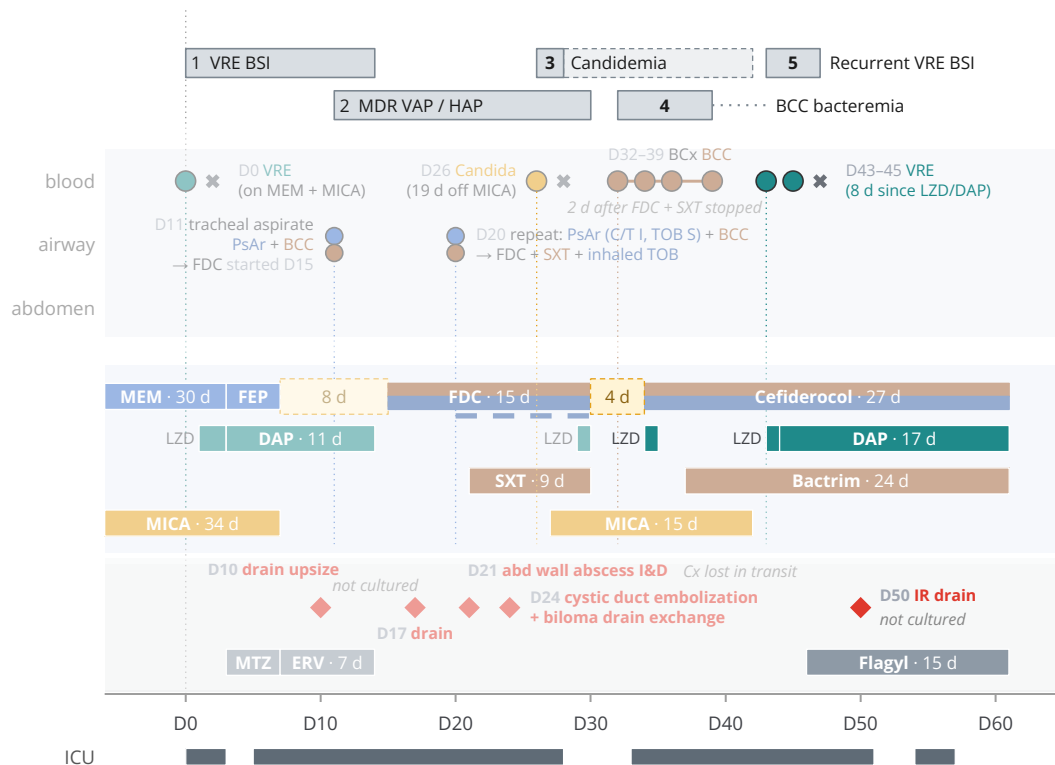
- **Micafungin** & cleared BCx

2 days after stopping **BCC coverage**, develops prolonged **Burkholderia cepacia complex** bacteremia

- Lines exchanged but still BCx (+)
- Proceduralists try to get source control
- No micro sent

Also, we can't get susceptibilities on BCC from the blood, so treating blindly

3-5: Series of bacteremias



Low grade **Candida lusitanae** fungemia

- **Micafungin** & cleared BCx

2 days after stopping **BCC coverage**, develops prolonged **Burkholderia cepacia complex** bacteremia

- Lines exchanged but still BCx (+)
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Also, we can't get susceptibilities on BCC from the blood, so treating blindly

Lastly, the **VRE comes back** in the blood

6: VARD → pneumonias &/or IAI



After prolonged course of abx, deemed stable enough for surgery (**VARD**)

Aspirated in PACU → SICU problem now

- BAL showed **Pseudomonas**
- Started on **Avycaz** (CZA)..?

But gets better anyways → extubated

- 6 days of abx (STOP-IT)

But then develops fever & WBC

- Concern about infected hematoma
- Another long course

Day

Ceftazidime
Ceftaz-avibactam
(**CZA**)

Ceftolozane-tazo (C/T)

Cefiderocol (FDC)

Tobramycin

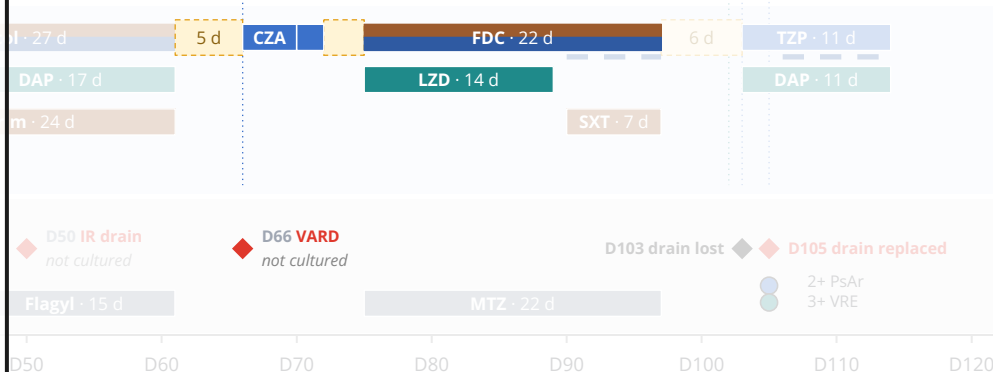
D11

D20

I	R	R
S	R	S
S	S	I
S	S	S
S	S	S

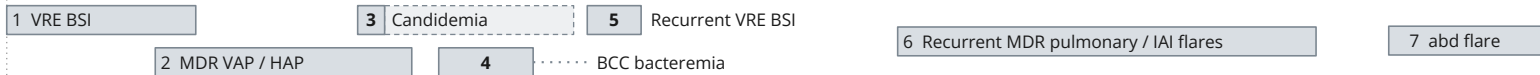
D43-45 VRE
(8 d since LZD/DAP)
D66 BAL post-
(x2 PsAr, low bl)

D105 drain
(VRE 3+, PsAr 2+)



7: Another flare of the belly?

■ P. aeruginosa
 ■ E. faecium (VRE)
 ■ BCC
 ■ Candida
 ⋯ inhaled tobramycin
 ✕ negative blood cx
 no PsAr-directed β-lactam



Cardiac arrest on day 87 with quick ROSC

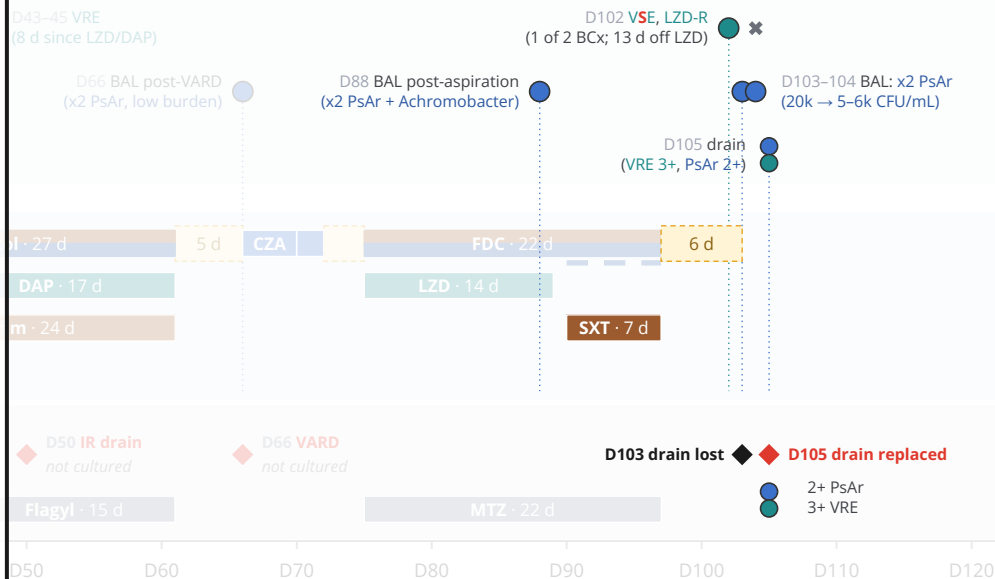
- Pseudomonas from lungs (still??)
- Added on **Bactrim** for 1 wk course

One week after stopping abx: fever, low O2

- BCx: E faecium, linezolid resistant
- BAL: Pseudomonas, susecpt pending

IR drain comes out

- Gets replaced, and micro was sent!



7: Another flare of the belly?

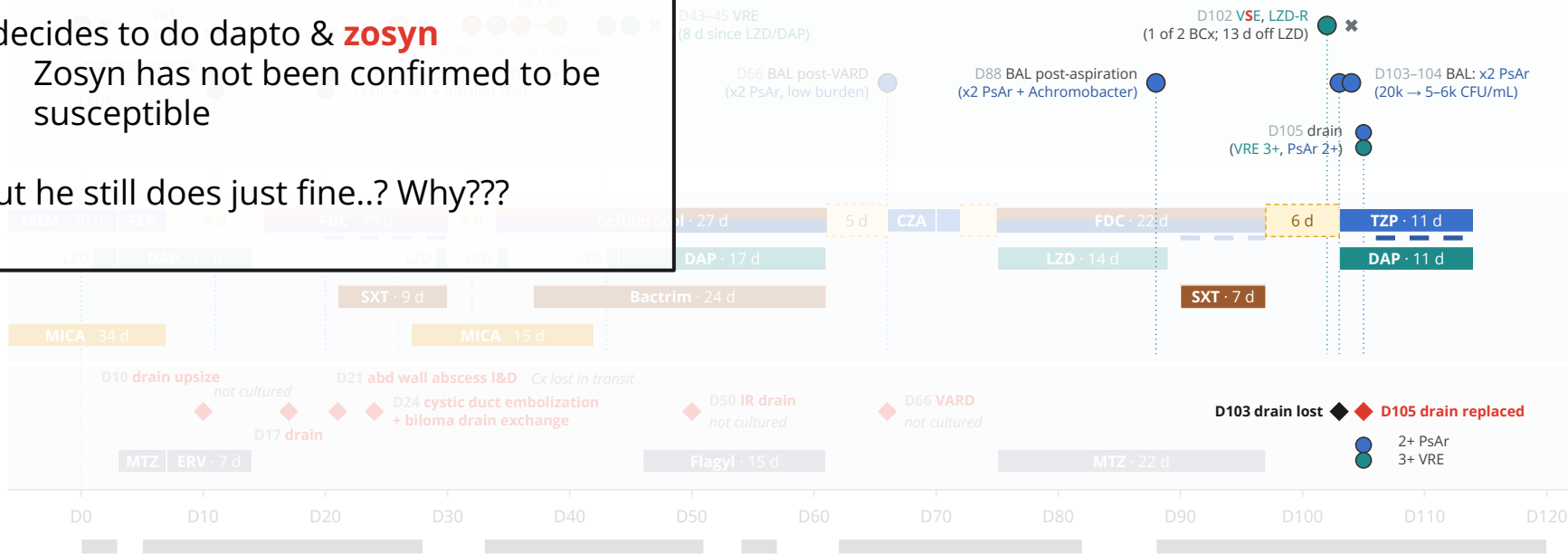
■ P. aeruginosa
 ■ E. faecium (VRE)
 ■ BCC
 ■ Candida
 ⋯ inhaled tobramycin
 ✕ negative blood cx
 no PsAr-directed β-lactam

- 1 VRE BSI
- 2 MDR VAP / HAP
- 3 Candidemia
- 4 BCC bacteremia
- 5 Recurrent VRE BSI
- 6 Recurrent MDR pulmonary / IAI flares
- 7 abd flare

ID decides to do dapto & **zosyn**

- Zosyn has not been confirmed to be susceptible

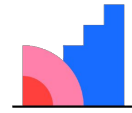
...but he still does just fine...? Why???



Discussion

**[Q1] What % of
infections with a
resistant isolate
still respond?**

Scales slider (0–100%)



Mentimeter

Treated with that drug anyway.

For comparison: about 90% respond
when the isolate is susceptible.

IMAGE: Mentimeter results, [Q-D.1]

The 90-60 rule [1]

Susceptible isolate, treated with that drug



S, and still failed
the 10%

Resistant isolate, treated with that drug anyway



R, and got better
the 60%

The 30-point gap is why we test. The 10% and the 60% are why the test doesn't settle it.

The isolate, not the patient



Objectives

- **Explain** why a clonal population can hold resistant subpopulations, and what that costs the bacterium
- **Describe** what a routine antibiogram samples, and what it misses
- **Apply** the 90-60 rule when a result and the clinical course disagree

How we usually picture it

1

One bacterium divides



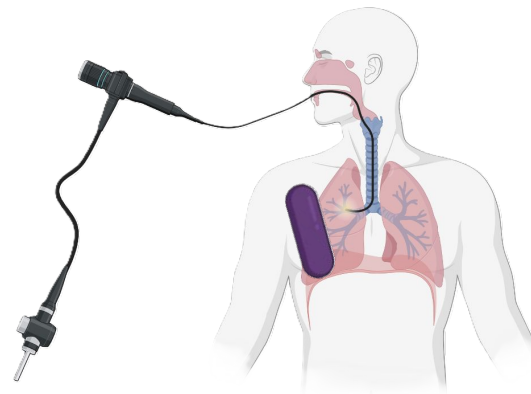
2

Into a large population of identical copies



3

A specimen (here, a BAL) goes to the lab



The model the lab report implies.

How we usually picture it



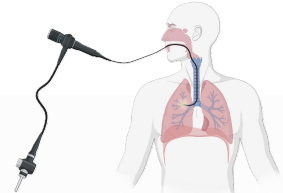
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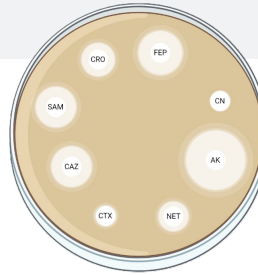
4

What grows on the plate is what's in the patient



5

S = it kills all of them
R = it kills none



6

Give the S drug, and the patient is cured



olies.

Clonal isn't uniform

Variants arise constantly

A large population almost always carries rare, **less susceptible mutants**

In *Pseudomonas*, these are mostly chromosomal changes: porins, AmpC, efflux

It costs the bacterium

Resistance often slows growth. Off the drug, susceptible cells outgrow the resistant ones

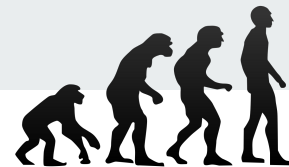
Example: very high gene copy numbers slowed growth by about 40% in lab strains [2]

Heteroresistance

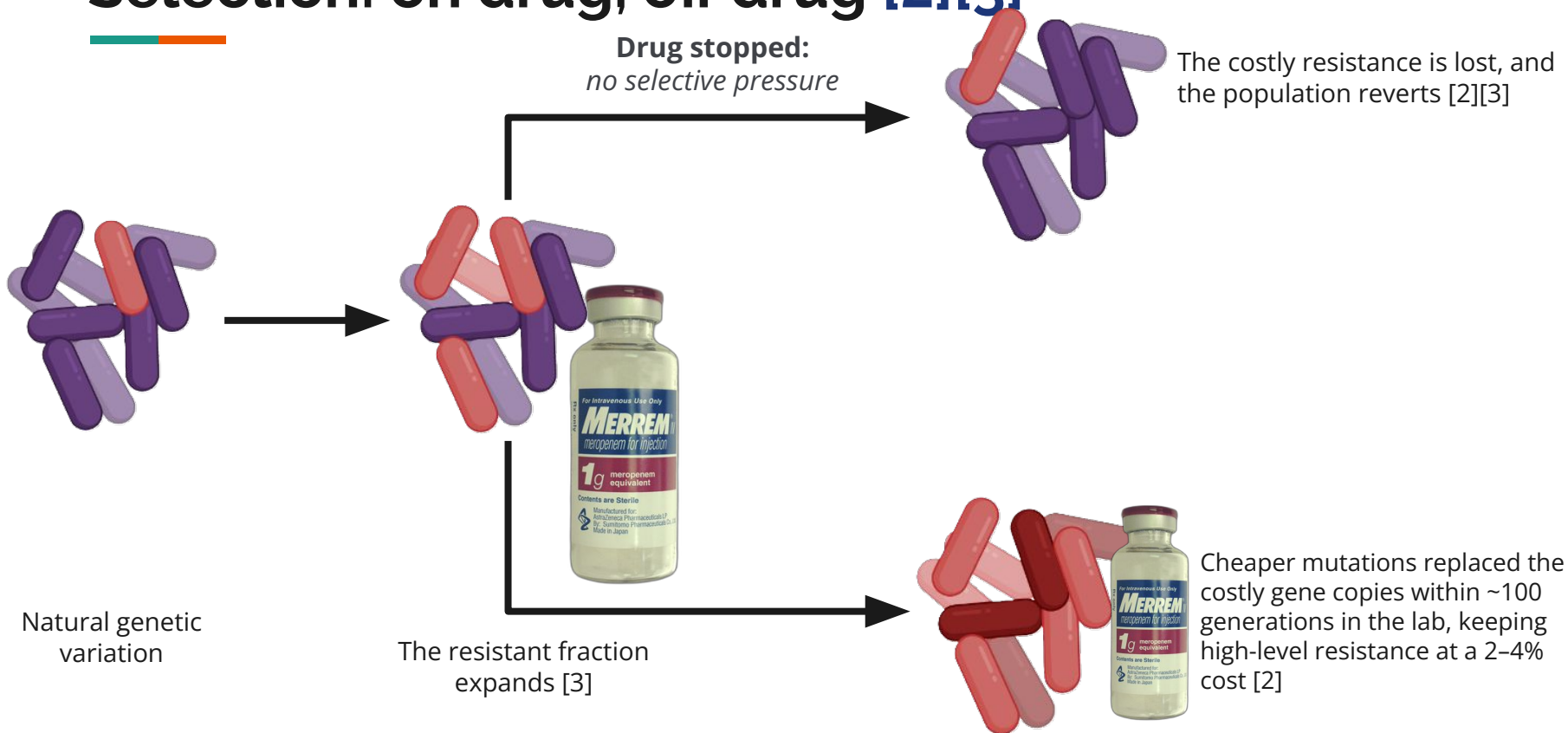
A resistant subpopulation a routine panel can't see. Real, but hard to prove at the bedside [3]

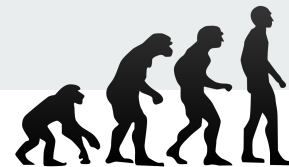
Resistance is a trade-off, not a free upgrade





Selection: on drug, off drug [2][3]





Selection: on drug, off drug [2][3]

Drug stopped:
no selective pressure

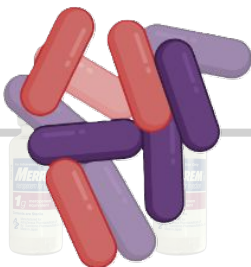
The costly resistance is lost, and the population reverts [2][3]



Natural genetic variation

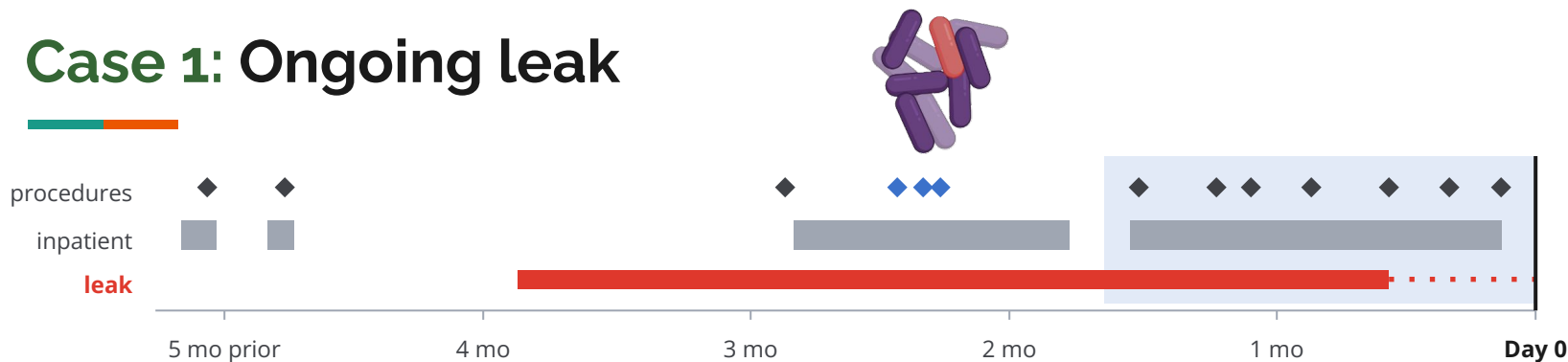
Heteroresistance is **often a stage on the way** to stable resistance (CRE, beta-lactams) [4]

Speculation: low drug levels inside an *undrained collection* may widen that window



Cheaper mutations replaced the costly gene copies within ~100 generations in the lab, keeping high-level resistance at a 2–4% cost [2]

Case 1: Ongoing leak



- **7 weeks prior:** admitted here with lobulated free fluid c/w peritonitis and pancreatitis
- IR drain grew mixed flora; bilateral ureteral stents for compression
- EUS with LAMS: *Pseudomonas aeruginosa* + *Serratia* → Merrem + micafungin; 2 necrosectomies
- **2.5 weeks prior:** ERCP confirmed the **cystic duct leak** → new cystic duct + CBD stents
- Discharged on Merrem + micafungin; readmitted **4 days later (Day 0)**

→ **Day 11:** three *Pseudomonas* populations in the airway, **all meropenem-resistant**

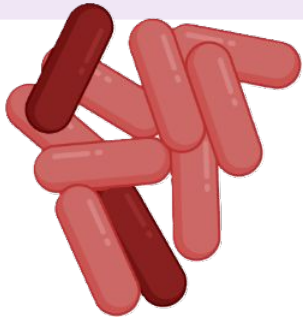
One specimen, more than one answer



Heteroresistance [3]

One strain, with a small resistant subpopulation

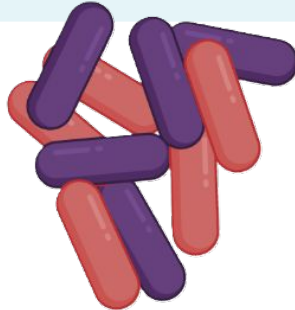
Often unstable: can fade off the drug



Mixed strains

Two or more strains in one specimen

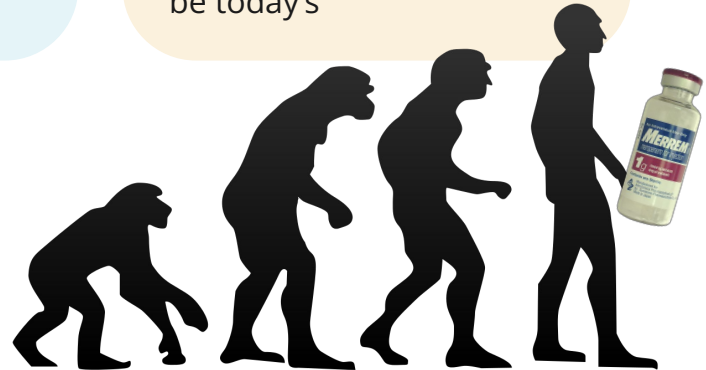
Each can carry different resistance



Evolution

Resistance arises in the patient during therapy

Last week's isolate may not be today's



Why can susceptibility patterns shift?

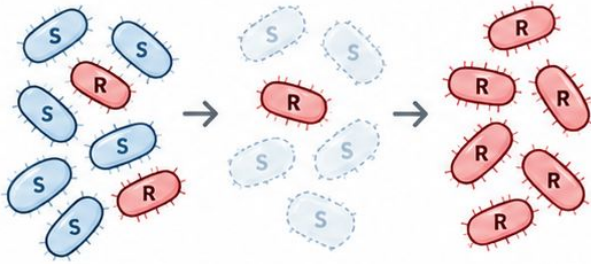
Heteroresistance

One strain, mixed susceptibility

Before therapy

Antibiotic exposure

After selection



A resistant subpopulation becomes enriched during therapy.

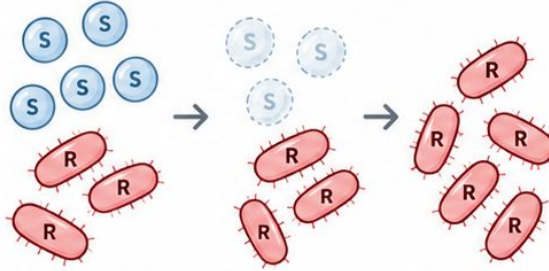
Polyclonal infection

Multiple strains coexist

Before therapy

Antibiotic exposure

After selection



Shifts in which strain is most abundant.

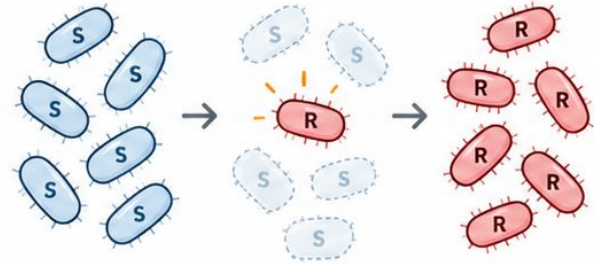
Clonal evolution

Resistance emerges during therapy

Before therapy

Antibiotic exposure

After selection



A newly resistant descendant expands under treatment.

Phenotypic susceptibility changes alone may not distinguish these mechanisms.

How we usually picture it



1 One bacterium divides

2 Into a large population of identical copies

3 **A specimen (here, a BAL) goes to the lab**

4 **What grows on the plate is what's in the patient**

5 S = it kills all of them
R = it kills none

6 Give the S drug, and the patient is cured

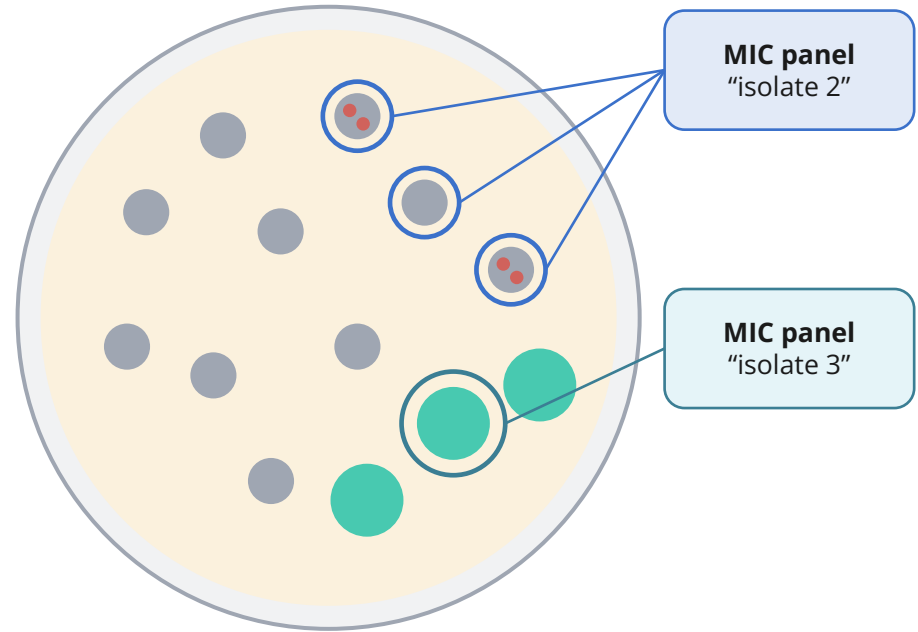
Next: steps 3-4, what the lab actually sees

What goes into an antibiogram

Several colonies that **look alike** are pooled into one inoculum, giving one MIC panel [5]

A colony that **looks different** gets its own panel: your lab's "isolate 2" and "isolate 3"

A game of chance: The plate doesn't have the same selective pressure that is applied to the patient





Let's go back to the micro

1

One bacterium divides

2

Into a large population of identical copies

3

A specimen (here, a BAL) goes to the lab

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What grows on the plate is what's in the patient

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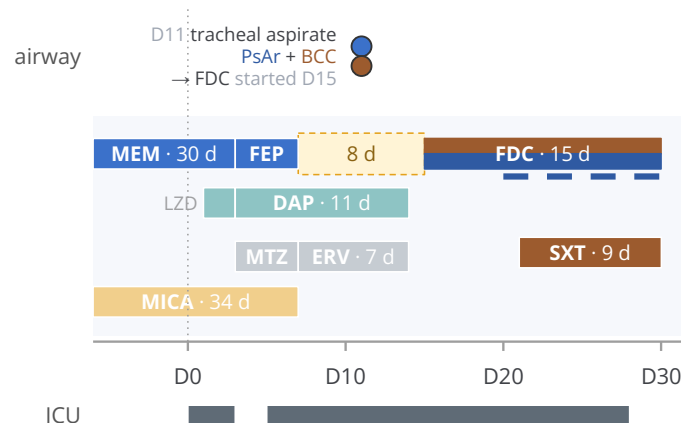
Give the S drug, and the patient is cured

His Pseudomonas: First 3 weeks

— not tested	Day 11 asp. A	Day 11 asp. B
Cefepime	R	R
Ceftazidime	I	R
Pip-tazo	R	R
Meropenem	R	R
Ciprofloxacin	S	I
Levofloxacin	I	R
Ceftaz-avibactam	S	16/4
Ceftolozane-tazo	S	S
Tobramycin	S	S
Cefiderocol	S	S

Day 11: First time he grows a resistant pseudomonas (two phenotypes)

- CRE, as expected since was recently on **Merrem**
- One isolate **R-Avycaz** (ceftaz-avi)
- Started on **Cefiderocol**
 - Due to Burkholderia cepacia complex

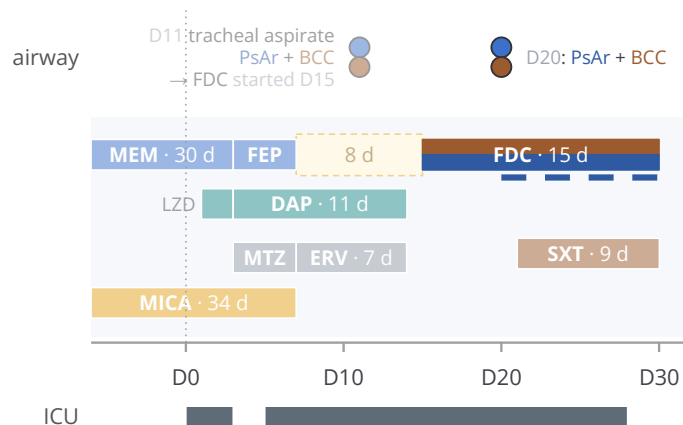


His Pseudomonas: First 3 weeks

— not tested	Day 11 asp. A	Day 11 asp. B	Day 20 asp.
Cefepime	R	R	R
Ceftazidime	I	R	R
Pip-tazo	R	R	R
Meropenem	R	R	R
Ciprofloxacin	S	I	R
Levofloxacin	I	R	R
Ceftaz-avibactam	S	16/4	S
Ceftolozane-tazo	S	S	I
Tobramycin	S	S	S
Cefiderocol	S	S	S

Day 20: Five days into his **Cefiderocol** he grows the **same “bacteria”**

- Now resistant to fluoroquinolones (even though he did not receive any)
- Still **susceptible** to cefiderocol
 - Maybe he just needs a longer course?



His Pseudomonas: After 6 weeks of



	Day 11 asp. A	Day 11 asp. B	Day 20 asp.	Day 66 BAL 2	Day 66 BAL 3
Cefepime	R	R	R	R	R
Ceftazidime	I	R	R	R	R
Pip-tazo	R	R	R	R	R
Meropenem	R	R	R	R	R
Ciprofloxacin	S	I	R	S	I
Levofloxacin	I	R	R	I	I
Ceftaz-avibactam	S	R	S	R	R
Ceftolozane-tazo	S	S	I	I	R
Tobramycin	S	S	S	S	S
Cefiderocol	S	S	S	S	S

Day 66

- Two phenotypes in one BAL
- Has been on **6 weeks** of cefiderocol at this point
Recall prolonged *Burkholderia* bacteremia

Surely it must be R-cefiderocol??

Nope! MIC 0.12

However...

Despite *not having received either* (yet), he is now resistant to:

- **Avycaz** (Ceftaz-avibactam)
- **Zerbaxa** (ceftolozane-tazobactam)

His Pseudomonas: 60-90%

Of course, so you don't know these results immediately

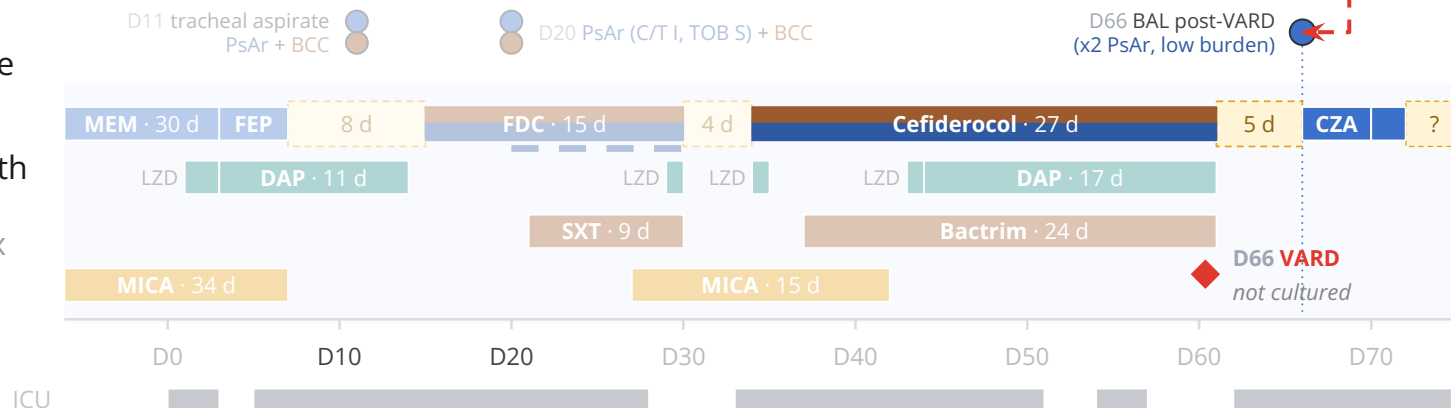
- Team *assumes* that cefiderocol won't work after 6 weeks of exposure (fair)

	Day 11 asp. A	Day 11 asp. B	Day 20 asp.	Day 66 BAL 2	Day 66 BAL 3
Ciprofloxacin	S	I	R		
Levofloxacin	I	R	R		???
Ceftaz-avibactam	S	R	S		
Ceftolozane-tazo	S	S	I		???
Tobramycin	S	S	S		
Cefiderocol	S	S	S		???

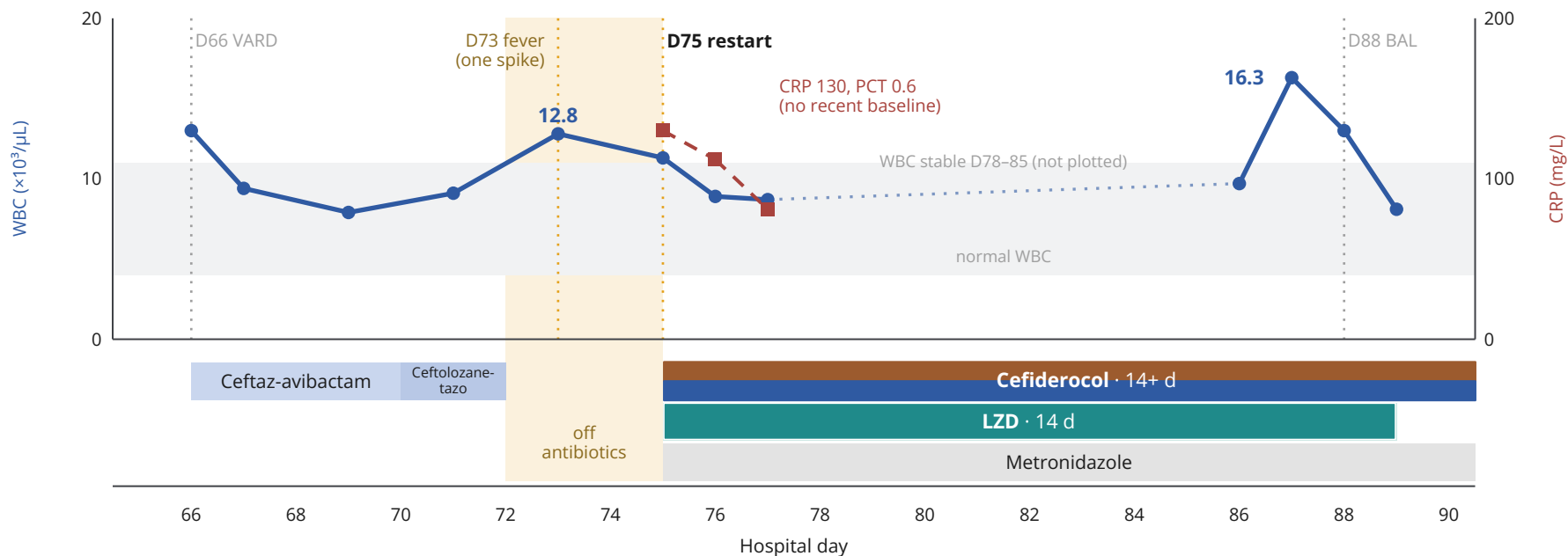
They start him on Avycaz (CZA; ~~c~~eftazidime-~~a~~vibactam)

- Only 2k & 4k cfu on qBAL
- He gets better

- They say they have source control
- I apply STOP-IT with Zerbaxa (the least wrong answer abx wise)



Wrong duration of abx



His Pseudomonas: 8 weeks of



— not tested	Day 11 asp. A	Day 11 asp. B	Day 20 asp.	Day 66 BAL 2	Day 66 BAL 3	Day 88 BAL 2	Day 88 BAL 3
Cefepime	R	R	R	R	R	I	R
Ceftazidime	I	R	R	R	R	I	R
Pip-tazo	R	R	R	R	R	—	—
Meropenem	R	R	R	R	R	R	R
Ciprofloxacin	S	I	R	S	I	S	I
Levofloxacin	I	R	R	I	I	I	R
Ceftaz-avibactam	S	R	S	R	R	S	R
Ceftolozane-tazo	S	S	I	I	R	S	R
Tobramycin	S	S	S	S	S	S	S
Cefiderocol	S	S	S	S	S	S	S

Day 88

Has **PEA arrest** so another BAL is done

- 2,000 cfu Pseudomonas
- 5,000 cfu Pseudomonas

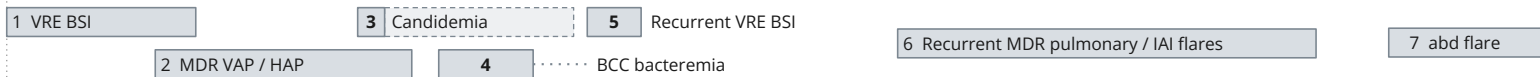
That's 2,000 not >100,000 cfu

Kinda looks like the original

This is the most divergent pair so far (can't call them strains since no sequencing done)

7: Another flare of the belly?

■ P. aeruginosa
 ■ E. faecium (VRE)
 ■ BCC
 ■ Candida
 ⋯ inhaled tobramycin
 ✕ negative blood cx
 no PsAr-directed β-lactam

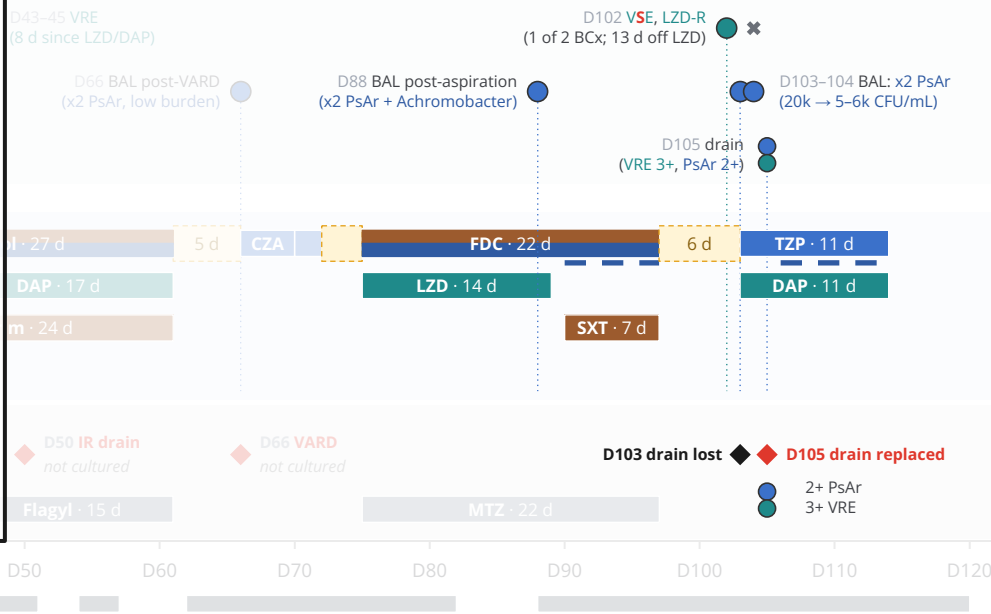


One week after stopping abx: fever, low O2

- BCx: E faecium, linezolid resistant
- BAL: Pseudomonas, susecpt pending

IR drain comes out

- Gets replaced, and micro was sent!



His Pseudomonas, Day 11 to Day 105

— not tested	Day 11 asp. A	Day 11 asp. B	Day 20 asp.	Day 66 BAL 2	Day 66 BAL 3	Day 88 BAL 2	Day 88 BAL 3	Day 103 BAL ×2	Day 105 drain
Cefepime	R	R	R	R	R	I	R	R	R
Ceftazidime	I	R	R	R	R	I	R	R	R
Pip-tazo	R	R	R	R	R	—	—	I	I
Meropenem	R	R	R	R	R	R	R	R	R
Ciprofloxacin	S	I	R	S	I	S	I	R	I
Levofloxacin	I	R	R	I	I	I	R	R	R
Ceftaz-avibactam	S	R	S	R	R	S	R	R	R
Ceftolozane-tazo	S	S	I	I	R	S	R	R	R
Tobramycin	S	S	S	S	S	S	S	S	S
Cefiderocol	S	S	S	S	S	S	S	S	—

Days 103–105

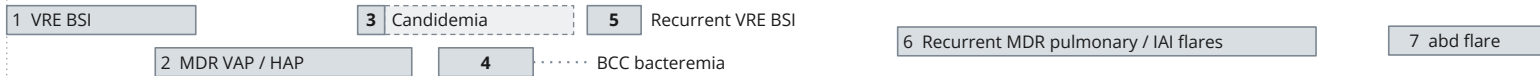
Airway and drain isolates nearly identical, both DTR

Both novel β -lactam combinations now resistant

Phenotypes only: without typing, “same strain” is not established

7: Another flare of the belly?

■ P. aeruginosa
 ■ E. faecium (VRE)
 ■ BCC
 ■ Candida
 ⋯ inhaled tobramycin
 ✕ negative blood cx
 no PsAr-directed β-lactam



One week after stopping abx: fever, low O2

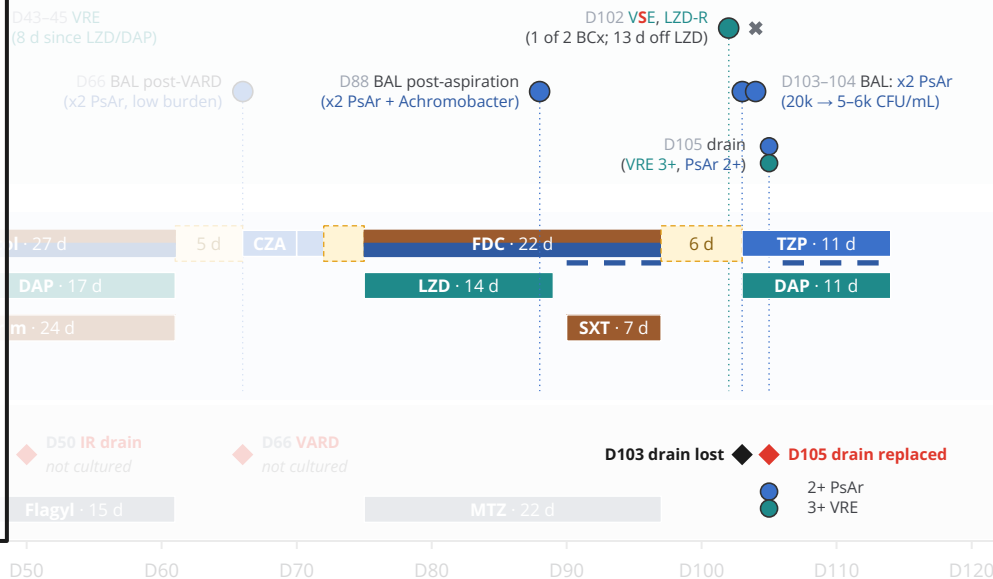
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ID decides to do dapto & **zosyn**

...but he still does just fine..? Why???

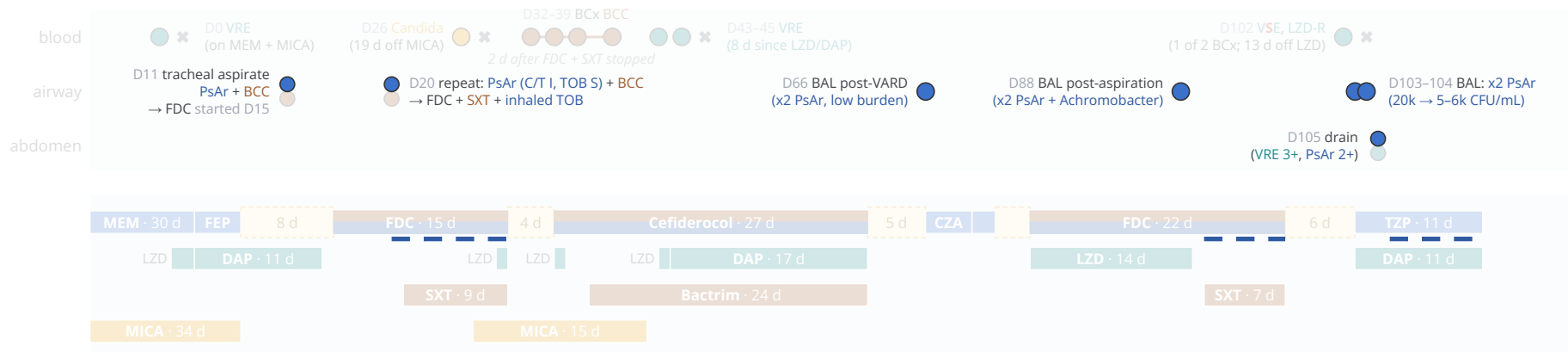


Why this is a weird case

His isolates don't follow the script

Inhaled tobramycin, three courses

S on every isolate since Day
20



His isolates don't follow the script

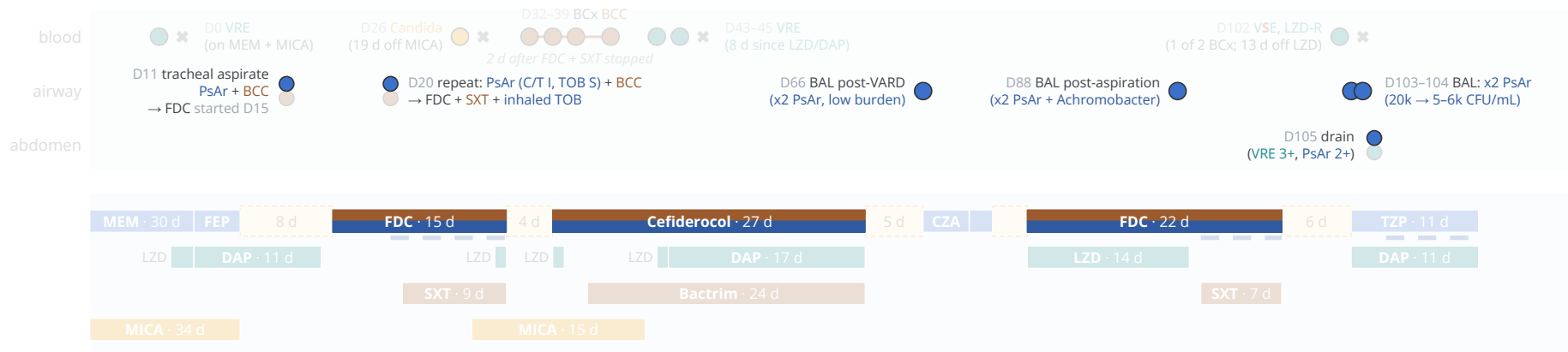
Inhaled tobramycin,
three courses

S on every isolate since Day
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Cefiderocol, ~9 weeks

Still S on Day 103

Cefiderocol · 64 d



His isolates don't follow the script

Inhaled tobramycin, three courses

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— — — —

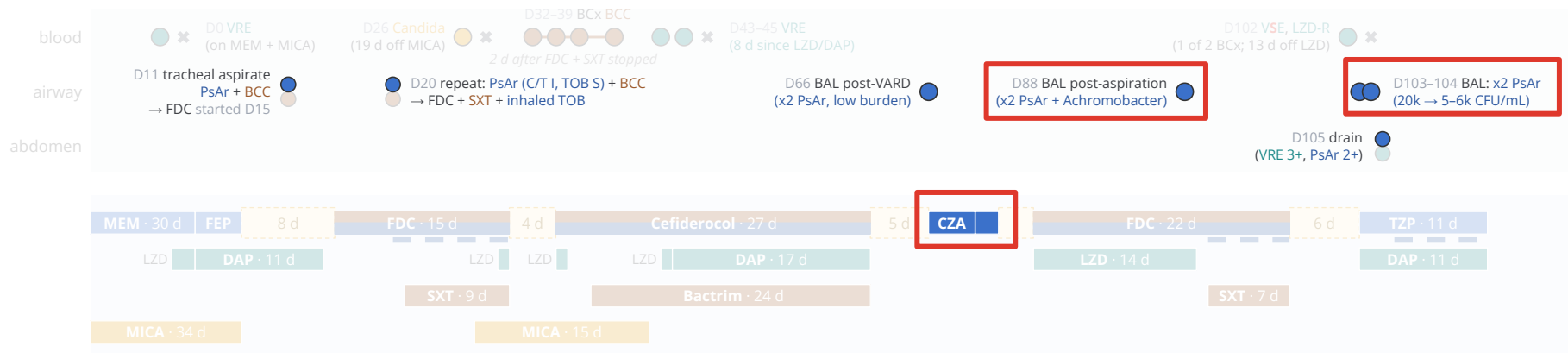
Cefiderocol, ~9 weeks

Still S on Day 103

Cefiderocol · 64 d

Avycaz (CZA) & Zerbaxa (C/T)

- S on a Day 88 isolate
- R by Day 103
- no exposure in between (last was: 6 days, starting Day 66)



How we usually picture it

1

One bacterium divides

2

Into a large population
of identical copies

3

A specimen (here, a
BAL) goes to the lab

4

What grows on the
plate is what's in the
patient

5

S = it kills all of them
R = it kills none

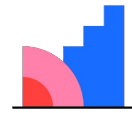
6

Give the S drug, and
the patient is cured

Next: step 5, when S is suspect

[Q2] New Gram-negative rods in the blood. What do you start?

Multiple choice · hypothetical



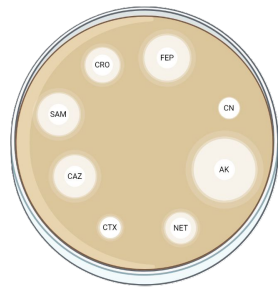
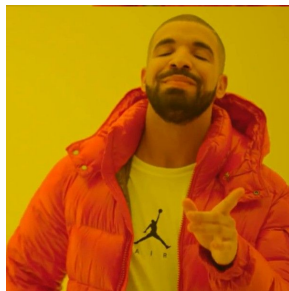
Mentimeter

His most recent *Pseudomonas* (Day 103):
meropenem R, CZA R, C/T R, pip-tazo I,
tobramycin S, cefiderocol S

- A. Cefiderocol
- B. High-dose extended-infusion pip-tazo
- C. Cefiderocol + tobramycin
- D. Something else
- E. At this point, Ivermectin

IMAGE: Mentimeter results, [Q-D.1]

Cefiderocol heteroresistance: S on the disk, failure in mice



407 isolates, two hospitals in China, 2018–2022 [6]

27.9% of carbapenem-resistant *Pseudomonas* were heteroresistant (14.5% overall)

- 73% of heteroresistant isolates tested S by disk diffusion
- Mouse peritonitis: cefiderocol failed against them

First reported as widespread in US isolates [7]

After prolonged exposure, treat a cefiderocol S as a **“soft” susceptible**

Not: “cefiderocol doesn’t work”

Cefiderocol is hard to test [8]

Systematic review (2025) of cefiderocol susceptibility testing methods

41%

**very major errors with
gradient strips**

Authors advise limiting their
use

14%

**very major errors, disks
pooled**

Disks also overcall R: 29%
major errors

75–85%

**essential agreement,
commercial MIC panels**

Target is $\geq 90\%$; the reference
broth method needs
iron-depleted media and lacks
reproducibility

Very major error: the test says S, the reference says R

Resistance can move together [9]

16 patients, before and after ceftolozane-tazobactam

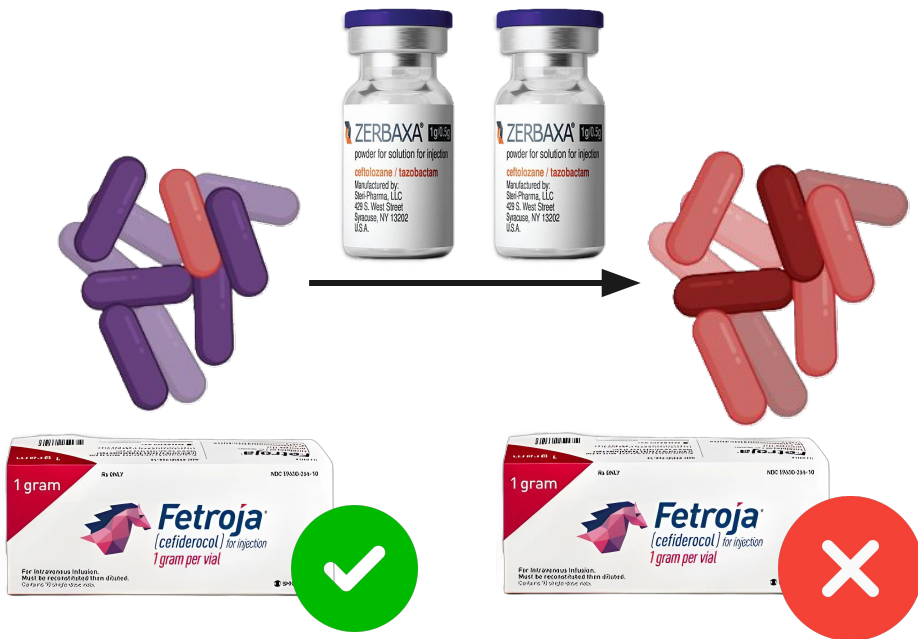
4 of 16 pairs: **cefiderocol MIC rose** ≥ 4 -fold;
only 1 left S

2 isolates with one AmpC change (E247K):

- C/T (Zerbaxa) 0.5 $\rightarrow$ 256
- CZA rose too (16 $\rightarrow$ 64, 8 $\rightarrow$ 32)

Small and exploratory

Zerbaxa drove cefiderocol resistance?



Speculation: the isolate whose cefiderocol MIC rose 4-fold is the one already R to CZA and C/T.
Would have been cool to sequence them

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Our patient

	FDC MIC	CZA	C/T
Day 66 ($\times 2$)	0.12	R, R	I, R
Day 88 #1	0.12	S	S
Day 88 #2	0.5	R	R
Day 103 ($\times 2$)		R, R	R, R

Speculation: was the isolate whose cefiderocol MIC rose 4-fold is the one already R to CZA and C/T?
Would have been cool to sequence them

CREDIBLE-CR: cefiderocol vs BAT [10]

Population: serious carbapenem-resistant Gram-negative infections (HAP/VAP, BSI/sepsis, cUTI); 150 enrolled

Intervention: cefiderocol 2 g q8h **Comparator:** best available therapy (66% colistin-based)

Cefiderocol (n=80)

34% all-cause mortality, end of study

Best available therapy (n=38)

18% all-cause mortality, end of study

Hypothesis (Weiss lab): *cefiderocol heteroresistance could explain the gap. Inferred from regional prevalence; trial isolates not tested [7]*

Counterpoint: APEKS-NP (double-blind, nosocomial pneumonia, n=300): 14-day mortality 12.4% vs 11.6% with high-dose extended-infusion meropenem; non-inferior [11]

One specimen, more than one answer



Heteroresistance [3]

One strain, with a small resistant subpopulation

Often unstable: can fade off the drug



Mixed strains

Two or more strains in one specimen

Each can carry different resistance



Evolution

Resistance arises in the patient during therapy

Last week's isolate may not be today's

Day 88: two Pseudomonas from one BAL, cefiderocol MIC 0.12 and 0.5.

Which card is it? The antibiogram can't say.

This looks familiar

MERINO [12][13]

Ceftriaxone-R *E. coli* / *Klebsiella* bacteremia, all
pip-tazo S

30-day mortality: **12.3%** pip-tazo vs **3.7%**
meropenem [12]

Reanalysis by reference MIC: ~6% weren't S,
and excluding them shrank the gap to 5% (CI
crossed 0) [13]

Inducible AmpC [14]

E. cloacae, *K. aerogenes*, *C. freundii*: test S to
ceftriaxone

Resistance can emerge on therapy (about 1 in
5 in clinical reports)

IDSA: avoid ceftriaxone for invasive infections;
cefepime instead

His *Serratia*: low-risk group (<5%)

Susceptible isolate, treated with that drug

~90% respond

10%

Does BCC susceptibility predict outcome? [15]

Population: 47 patients with *B. cepacia* complex infection (**27 bloodstream**, 20 respiratory); one hospital in Beijing, 2014–2024

Outcome: unfavorable = death, treatment failure, worsening, or discharge for terminal illness. 11 of 47

Analysis: susceptibility to meropenem, ceftazidime, TMP-SMX and minocycline vs outcome, adjusted (Firth and Bayesian regression)

No susceptibility result independently predicted outcome

Only age did: OR 0.86 per year for a favorable outcome (95% CI 0.76–0.94)

No detectable association ≠ no predictive value

Meropenem non-susceptible, unfavorable outcome: OR 1.90 (95% CI 0.45–8.30), unadjusted. With 11 events, that interval runs from half to 8 times the odds

*Authors: “AST results should be interpreted cautiously and integrated with host risk assessment, **source control**, and overall clinical status rather than used in isolation.”*

How we usually picture it



1 One bacterium divides

2 Into a large population of identical copies

3 A specimen (here, a BAL) goes to the lab

4 What grows on the plate is what's in the patient

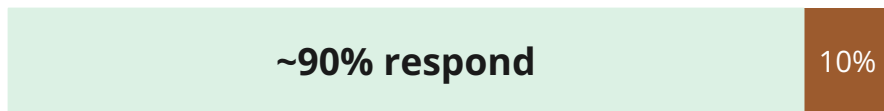
5 S = it kills all of them
R = it kills none

6 **Give the S drug, and the patient is cured**

Next: step 6, back to the patient

The 90-60 rule [1]

Susceptible isolate, treated with that drug



Resistant isolate, treated with that drug anyway



S, and still failed
the 10%

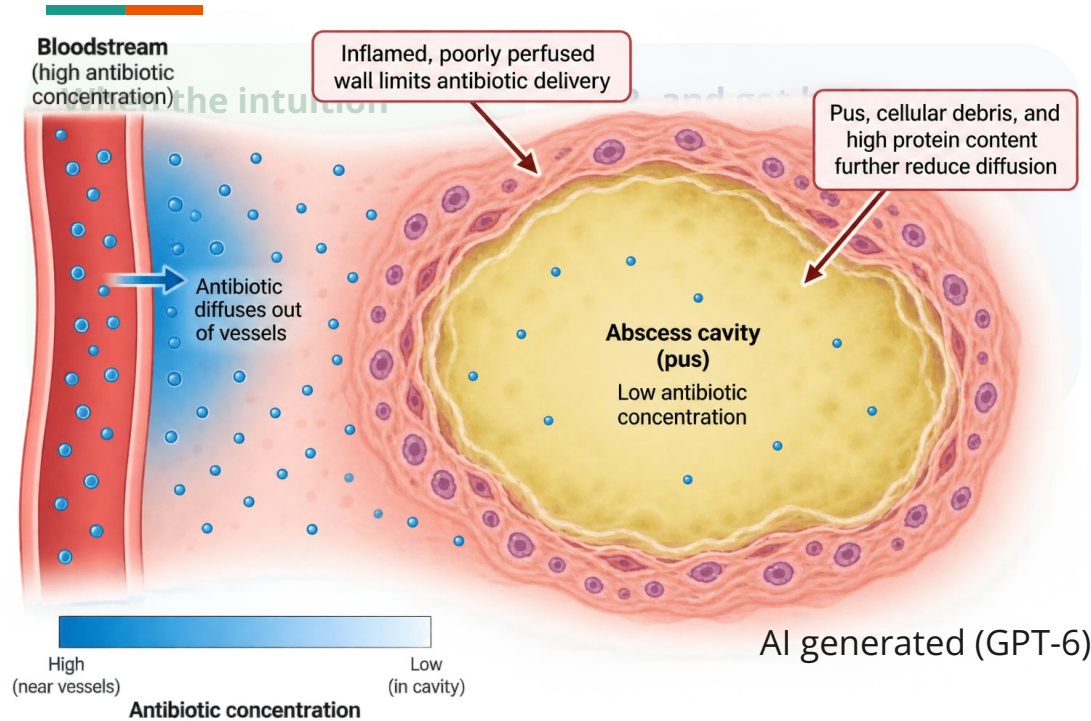
R, and got better
the 60%

The 30-point gap is why we test. The 10% and the 60% are why the test doesn't settle it.

Why an S can still fail

- Host: immune status, comorbidity, severity
- Dose and pharmacokinetics
- Drug penetration to the site
- Inoculum and biofilm
- Heteroresistance, mixed populations
- **An undrained collection**

Cure is more than the drug



AI generated (GPT-6)

Prolonged pressure, no drainage

Survivors are selected;
resistance can become
stable

60-90%

Resistant isolate, treated with that drug anyway

~60% respond

40%



Learning points & take aways

Learning points & take aways



- The antibiogram describes the colonies the lab picked, not the population in the patient. **Heteroresistance, mixed strains and evolution** in the patient **all look the same** on a panel.
- **S isn't cure, and R isn't failure** (90-60). When the result and the patient's course disagree, check the source, host, site and dose before switching drugs to match the panel.
- After long exposure, **treat an S as a soft S**, especially for **cefiderocol**: the testing is unreliable and heteroresistance is common. That doesn't mean the drug doesn't work.
- **Resistance has a cost, but it isn't always temporary**. Off the drug, costly resistance can fade, but compensatory mutations can lock it in. Time off antibiotics doesn't guarantee susceptibility comes back.

Case 1: Overview timeline

