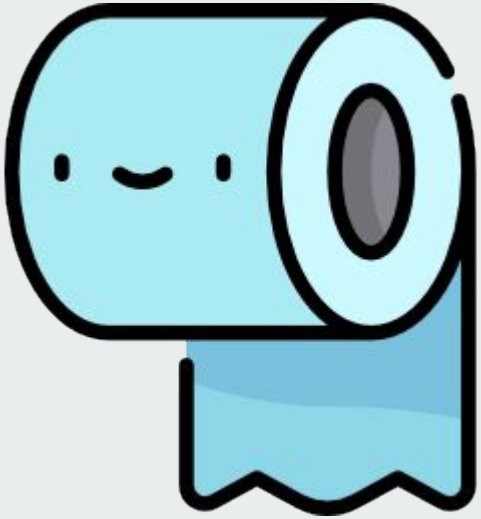
Gut Reactions (in TxID)



CLINID conference
Hunter Ratliff
10/30/2025

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 (poly-positive biofire + norovirus)
Case 2: Start (Hx CDI, fever for IV iron)
Discussion: Objectives

- **Molecular testing**
- **Campylobacter enteritis**
- **Norovirus in SOT** | Nitazoxanide | IVIG | POIG
- **Fever from IV iron**

Takeaway slide

Case #1

Case 1: HPI

A **47 y/o F** with PMH including ESRD s/p DDKT (2021) p/w **diarrhea**

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- Associated with stomach cramps, rare nausea

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- Unintentional* weight loss of 15 pounds
  - *Also started semaglutide (Ozempic) around this time
- No food associations, not waking up with diarrhea

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Was doing “alright” outpatient; only came to the hospital after transplant team found **abnormal renal function** on outpatient labs

Case 1: Transplant history

A **47 y/o F** with PMH including ESRD s/p DDKT (2021) p/w **one month of watery diarrhea**

- Unclear etiology of ESRD (perhaps related to HELLP), was on HD for 7.5 years before transplant
- CMV D (-) / R (-) EBV D+/R+ HCV -/-
  - S/P routine PPx (3 months of valtrex; 1 year of bactrim)
  - No infectious issues
- Currently on tacro & cellcept
  - No Hx of rejection

Case 1: Social history, exposures, & risk factors

Geographic & Travel	• Lives in rural PA with husband & two teenagers. Not around young kids • No travel
Occupational	• Works in a **local diner**, *where she prepares food* • Nobody in the home or workplace have been ill
Substance & needles	• No EtOH, tobacco, or drugs • No needles
Animals	• **Mainly her pet cat** (doesn't do the litter) • Adopted a **pet rabbit** 2 weeks ago • Have chickens & a cow, but she doesn't interact with them
Exposures	• No recent abx • No hx of C diff or MDROs

Case 1: Physical exam

Normal exam

BP	132/84	**Pulse**	77	**SpO2**	99 %
Temp	36.9 °C (98.4 °F)	**RR**	18	**BMI**	38 kg/m^2
General	Alert and oriented, NAD				
HEENT	NCAT; trachea appears midline, no gross LAD; EOMI				
Resp	Normal respiratory effort, symmetric chest rise				
CV	RRR; extremities perfused				
GI	Non-distended; no TTP				
Extremities	No clubbing, cyanosis, or edema				
Neuro/MSK	Moves extremities				
Psych	Normal mood; appropriate affect				

Case 1: Summary

A **47 y/o F** with PMH including ESRD s/p DDKT (2021) p/w **one month of watery diarrhea**.

- No systemic symptoms (besides 15# wt loss)
  - Perhaps confounded by *Ozempic*
- Looks good on exam
  - Only here because of labs
- Cursory exposure history is unrevealing
  - Rabbit → Cryptosporidium (?)

Do you want **additional HPI info** or **a GI biofire**?

Case 1: Additional HPI

- A week before onset of diarrhea, there was **major flooding** around her home
- After the flood, **her spring water was cloudy**
  - They sanitize their water using UV light
  - Didn’t boil the water
- No issues with her septic tank
  - Most of her neighbors also use septic tanks

Case 1: Labs

CBC	Result
WBC	6.0
Hgb	10.7
Platelets	244
Neut %	76%
Lymph %	9%
Eos %	1%

Chem7	Result
Na	137
K	4.1
HCO3	17
BUN	28
Cr	**2.16**
Baseline Cr	**0.95**

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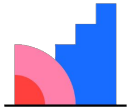
Biofire	Result
Adenovirus	
Astrovirus	
Cyclospora	
Campylobacter	
Cryptosporidium	
E histolytica	
E coli	
Giardia lamblia	

Biofire	Result
Norovirus	
Rotavirus	
Salmonella spp	
Sapovirus	
Shigella	
Vibrio cholerae	
Yersinia spp	

[1.1] Guess the biofire



Mentimeter

- Adenovirus
- Astrovirus
- Norovirus
- Rotavirus or sapovirus
- Campylobacter
- EAEC / EPEC / ETEC / EIEC
- Shigella
- Salmonella
- Vibrio
- Yersinia enterocolitica
- E histolytica
- Giardia or cryptosporidium

[1.1] Guess the results of the GI multiplex PCR

1 Adenovirus ×

2 Astrovirus ×

2 Norovirus ✓

1 Rotavirus or sapovirus ×

4 Campylobacter ✓

5 E coli (EAEC, EPEC, ETEC, EIEC)) ✓

0 Shigella ×

2 Salmonella ×

2 Vibrio ×

2 Yersinia enterocolitica ×

0 E histolytica ×

9 Giardia or cryptosporidium ×

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E histolytica	Neg
E coli	**EPEC**
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Vibrio cholerae	Neg
Yersinia spp	Neg

Stool Cx: *Campylobacter jejuni*
Normal flora, heavy growth on the Campylobacter plate

Case 1: Summary

A **47 y/o F** with PMH including ESRD s/p DDKT (2021, CMV -/-) p/w **one month of watery diarrhea** → AKI. Occurred after recent flooding of her spring water

- Biofire: norovirus, Campylobacter, Enteropathogenic E coli
- Stool Cx: Campylobacter jejuni

Treatment?

Additional diagnostics?

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Treatment?

Additional diagnostics?

What to do if worsens or no improvement?

Case 1: Hospital course

- Started antimicrobial therapy:
  - Azithromycin 500 q24h x 3 days
  - Nitazoxanide 500 q12h x 3 days
- Did not test for:
  - C diff
  - CMV

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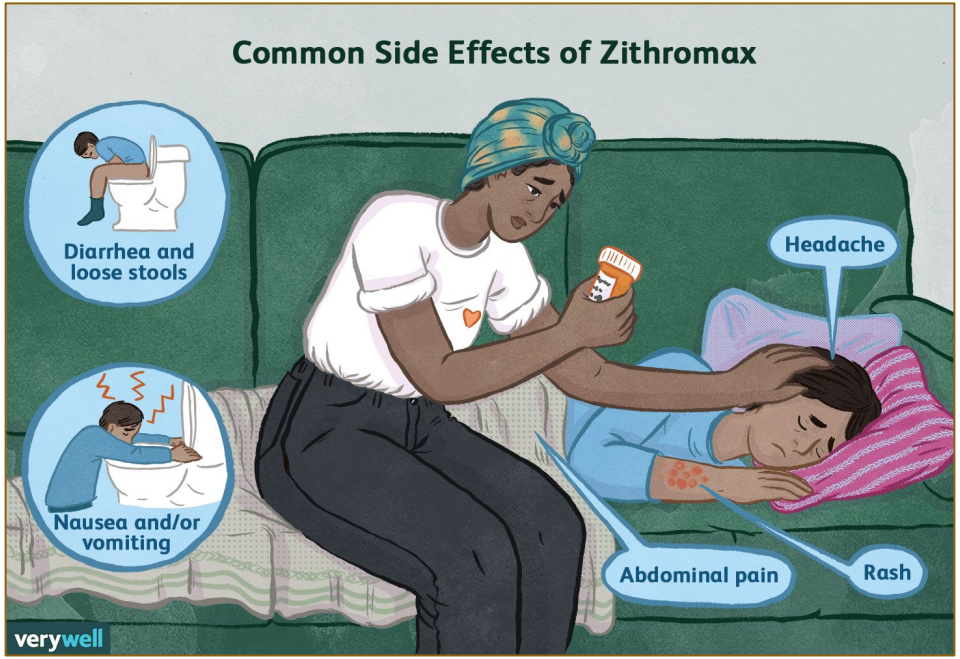
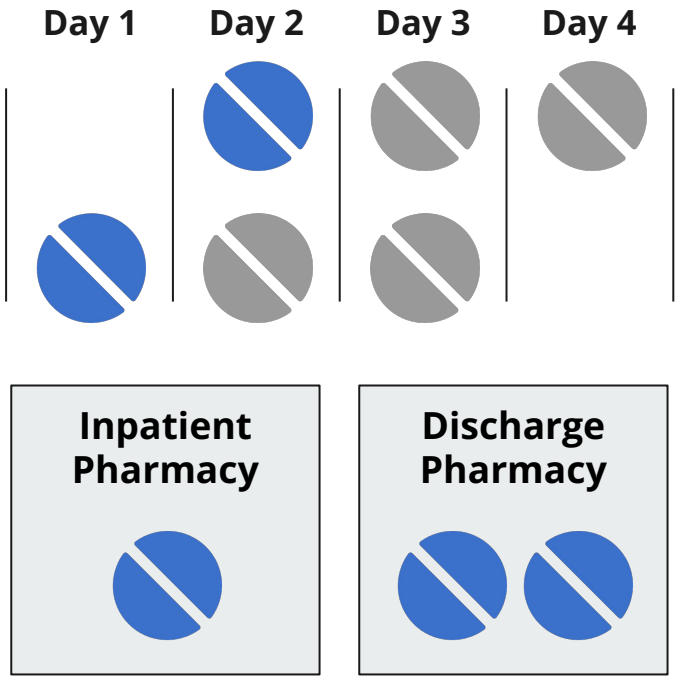
- Did not test for: C diff, CMV
- Reconsulted the **next morning** since **diarrhea had gotten worse**
- Therapeutic ID consult: **All better** by the time we saw the patient
  - Seemed to be transient
  - Perhaps related to **azithromycin**



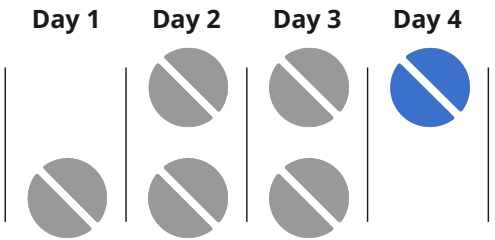
Case 1: Hospital course

- Ready to go home by evening of day 2, but found out that we are **one dose short of nitazoxanide**



Case 1: Hospital course

- Ready to go home by evening of day 2, but found out that we are **one dose short of nitazoxanide**
- After *extensive* Epic chats (during the 6pm hour), will be able to get the last dose to Ruby, but will be 24h
- So there are **two options**:
  - Stay in the hospital an **extra day** to get the medication Meds-to-bed
  - Discharge home, **drive back on day 4** to get last dose from discharge pharmacy



What if there is a third choice?

Three choices

Stay in the hospital an extra day

Each day in the hospital has estimated daily risk of...

- Adverse drug reaction: **0.5%** (1:200)
- Infection: **1.6%** (1:60)
- Ulcer: **0.5%** (1:200)

Any AE: ~ 1 in 50

Hauck & Zhao (2011)
PMID 21945976

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Drive for 3 hours to pick up dose

Around **0.08% to 0.125%** chance of motor vehicle crash

Crash: ~ 1 in 1000

ChatGPT
(insurance and DOT data)

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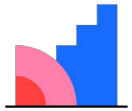
Skip the 6th dose

????

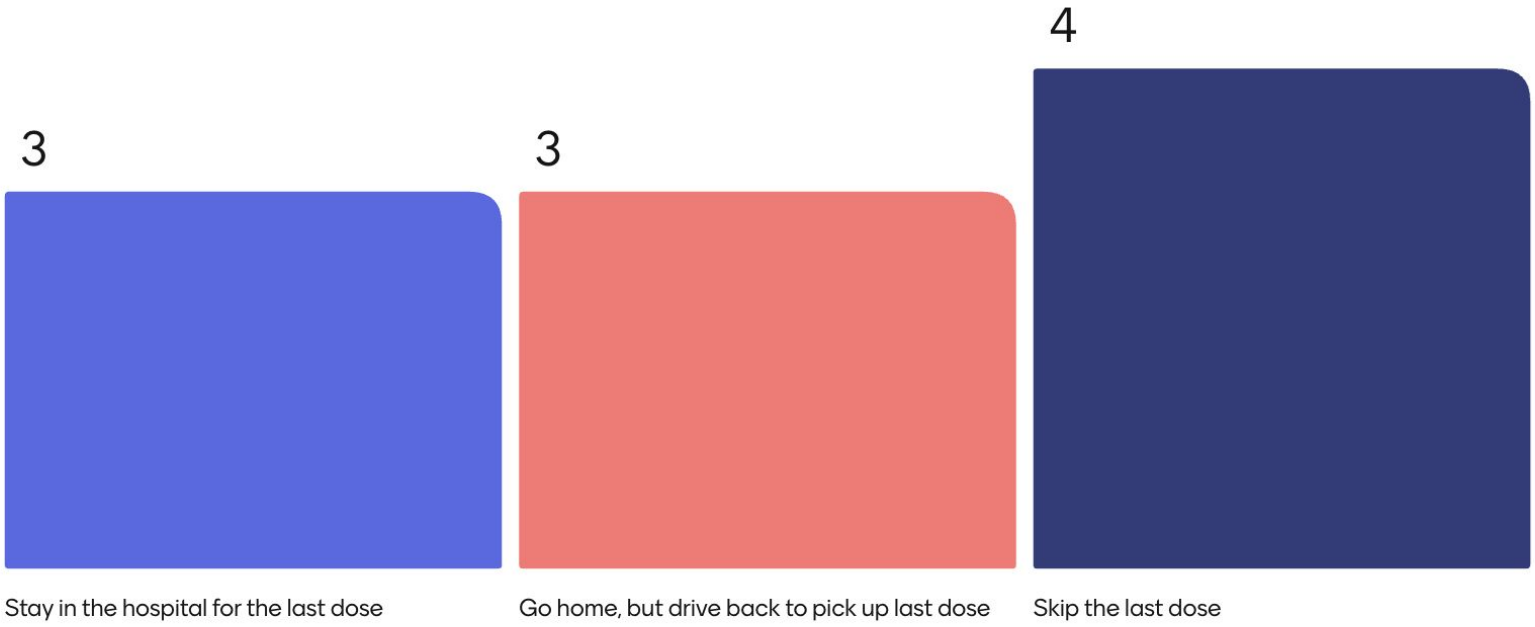
Noro: ???

[1.2] Which is more dangerous: healthcare, driving or norovirus?



Mentimeter

[1.2] What would you recommend?



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This is what the patient picked

Didn't keep her follow up with transplant, but seems to have done fine

No source, but this is what ended up happening

Case #2

Case 2: HPI

A **65 y/o M** with PMH including cirrhosis s/p OLT (2 years ago) w/ recurrent C diff p/w **fever**

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Transplant history

- NASH cirrhosis w/ portal hypertension, hx SBP
- Transplant 20 months ago c/b
  - Explant hemorrhage
  - DVT
  - An episode of C diff
- CMV D(neg) / R(neg)
- EBV +/+
- On tacro

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Splenectomy

Had splenic artery rupture a year ago, requiring splenectomy
...also had C diff at that time

Case 2: Infectious Hx

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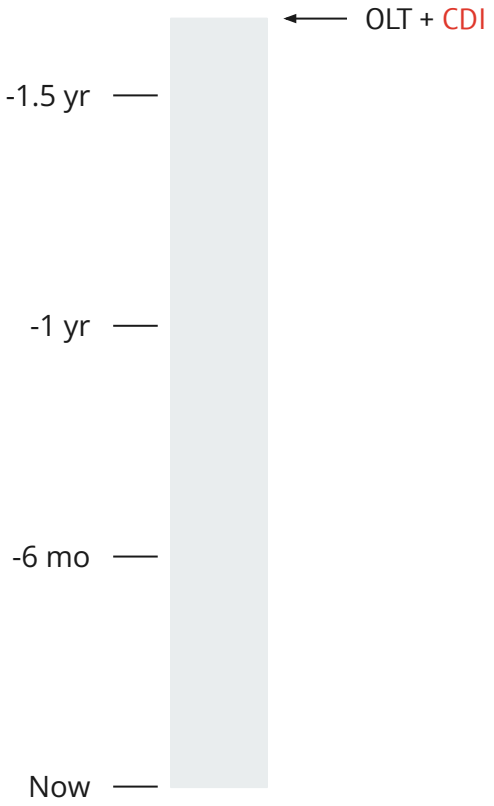

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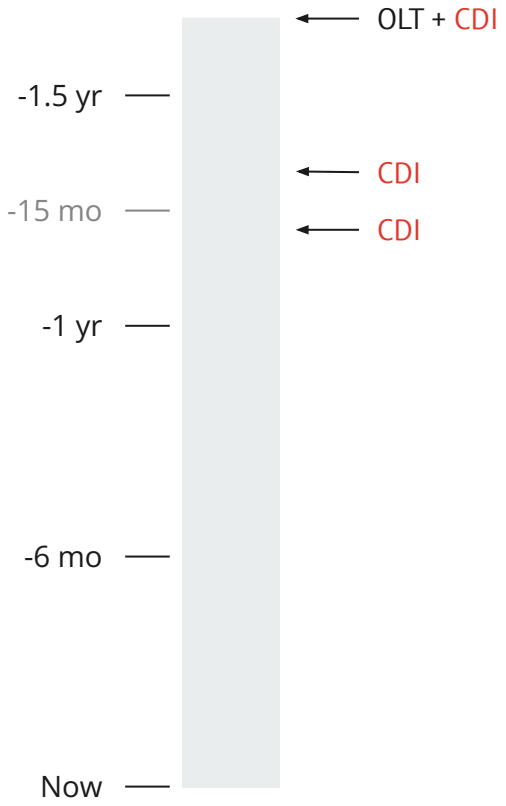
After transplant, **two more C diff episodes**



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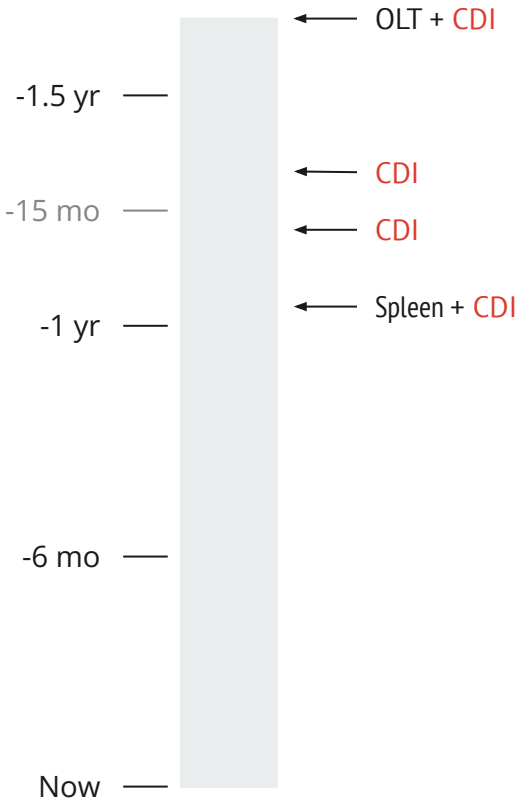

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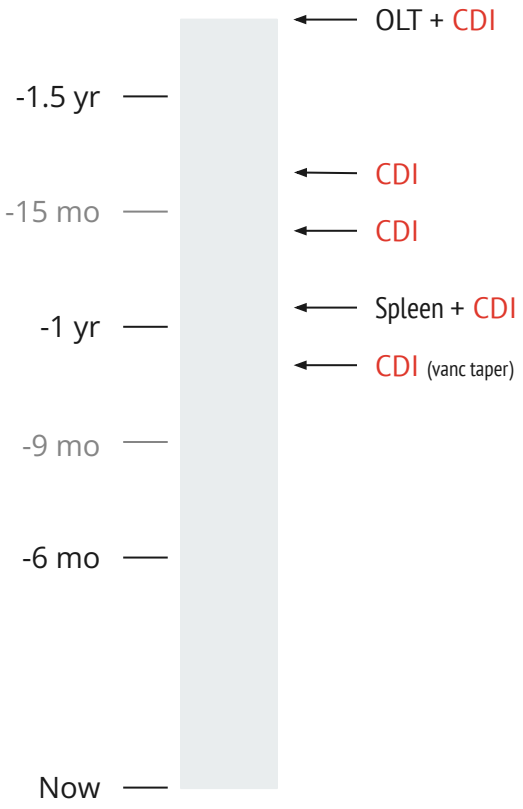
In the first 6 months after transplant, **4 episodes :** Peritransplant (-20mo), (-16 mo), diverticulitis episode (-14.5 mo), splenectomy (-12 mo)

Episode #5: Insurance still denying fidaxomicin, so started on prolonged vanc taper



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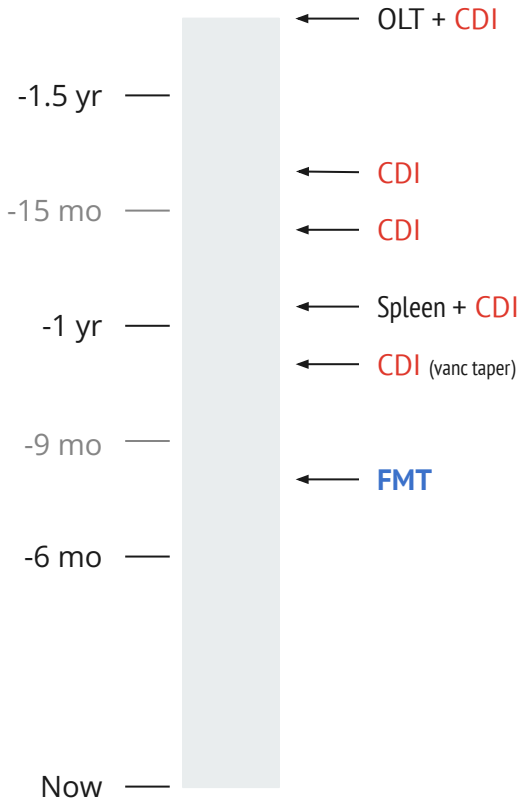

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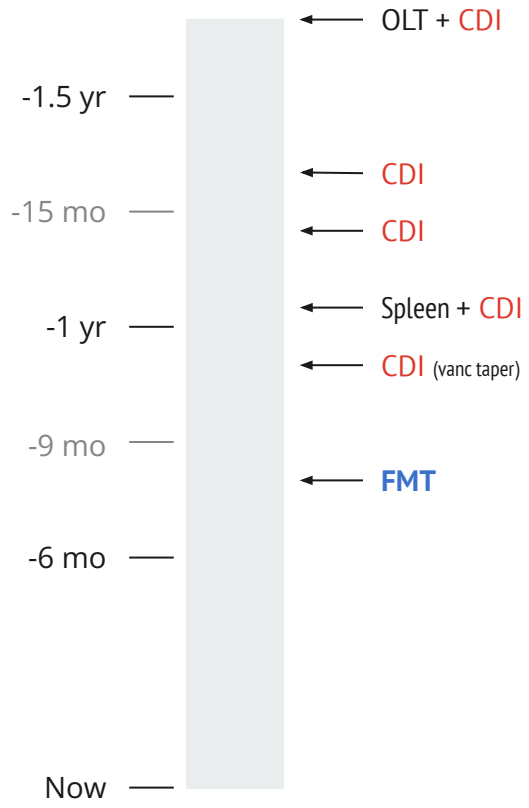
Gets a **fecal microbiota transplant** (insurance doesn't pay for commercial products, so he gets frozen FMT)



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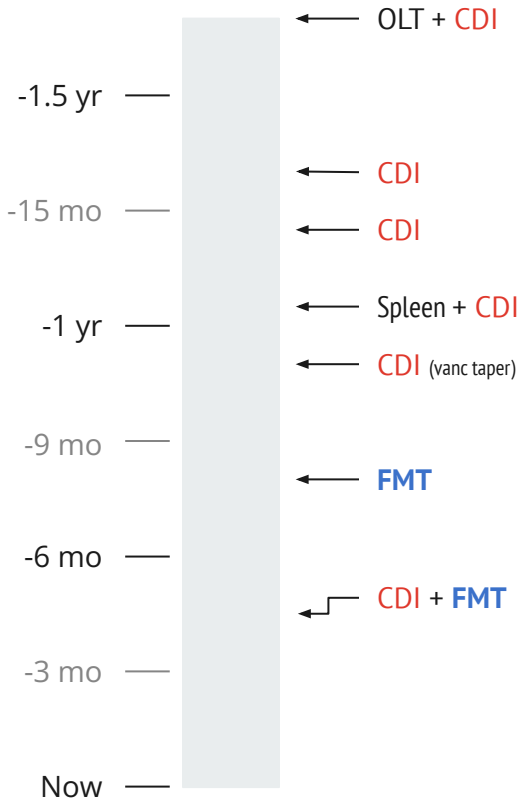
4 months later, ED **Rx Keflex** for toe injury → **fulminant C diff** → gets **FMT #2** (Rebyota)



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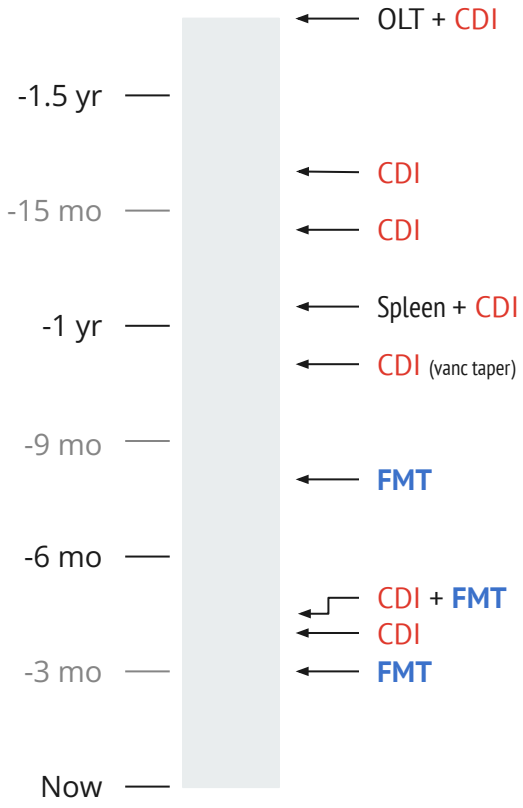

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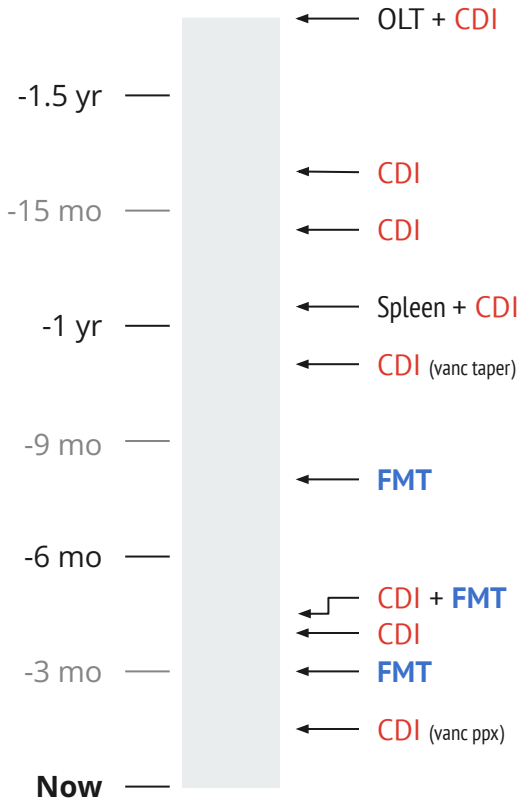
Does well for 6 weeks but then has his **eighth episode of C diff** → prolonged vanc taper followed by **indefinite BID vanco**



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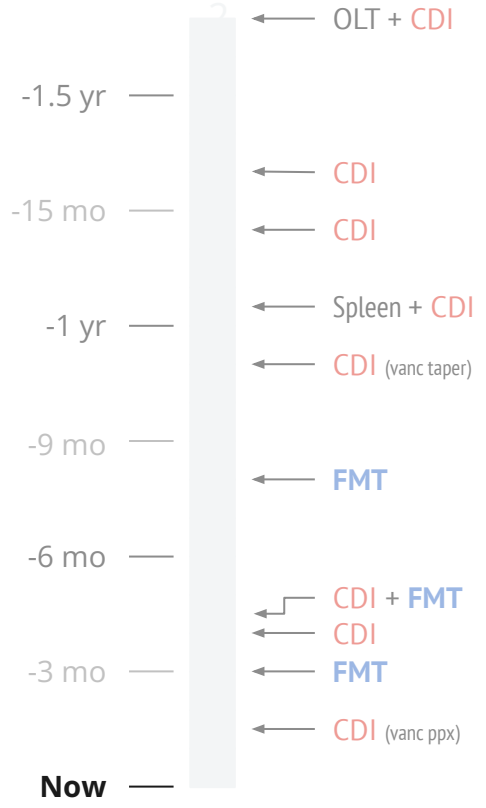
- **Fevers** started yesterday
  - Tmax 102 F
  - Associated **rigors** & **myalgias**



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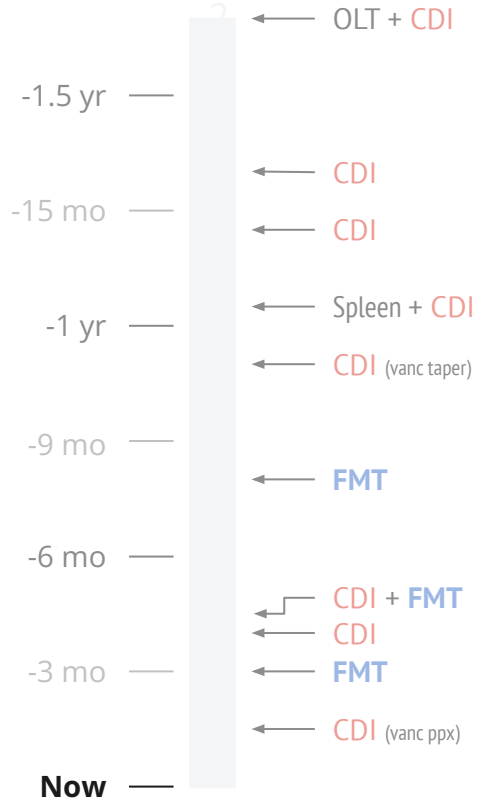

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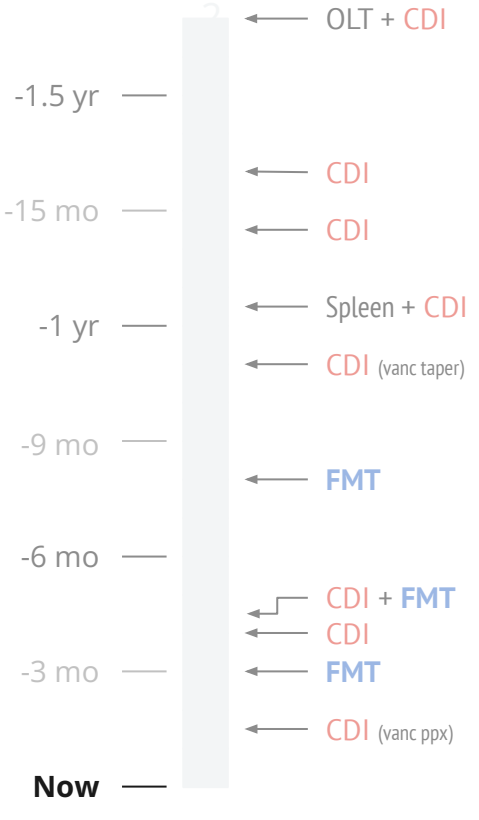

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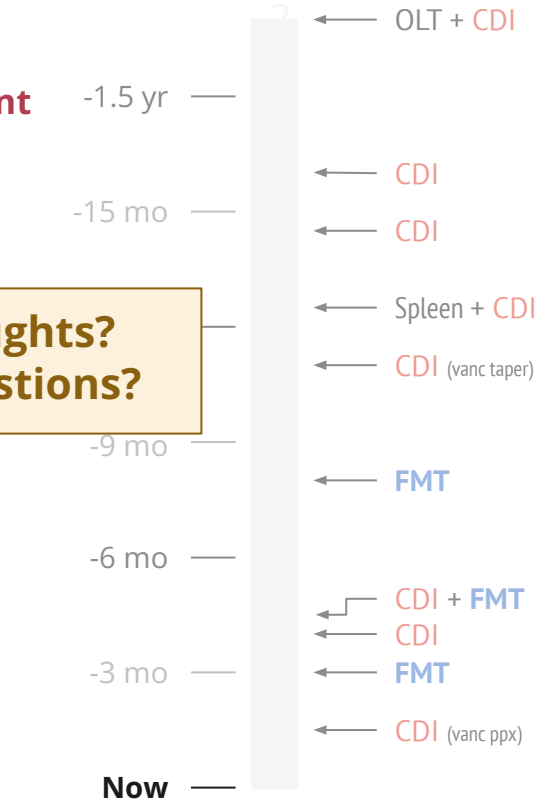
  - Then started having **diarrhea**

Initial thoughts?
Further questions?



Case 2: Social history, exposures, & risk factors

Geographic & Travel	• Lives with wife in rural PA close to Maryland border. Traveled to Alaska & Canada a few years ago, but no recent travel
Occupational	• On disability, used to work in a quarry
Substance & needles	• Rare EtOH use • No tobacco or drugs
Animals	• Indoor/outdoor cats • No bites or scratches

Case 2: Physical exam

BP	**102/50**	**Pulse**	63	**SpO2**	94 %
Temp	**38.3** °C (100.9 °F)	**RR**	18	**BMI**	31 kg/m^2
General	Alert and oriented, NAD				
HEENT	NCAT; trachea appears midline, no gross LAD; EOMI				
Resp	Normal respiratory effort, CTAB				
CV	RRR; extremities perfused				
GI	Non-distended, soft; **no TTP**				
Extremities	No clubbing, cyanosis, or edema; no wounds				
Neuro/MSK	Moves extremities, **no nuchal rigidity**				
Psych	Normal mood; appropriate affect				

Case 2: Initial thoughts

A **65 y/o M** with PMH including cirrhosis s/p OLT (2 years ago) w/ **recurrent C diff**, s/p splenectomy who p/w **fever**.

Fevers started yesterday, **38.3** in ED

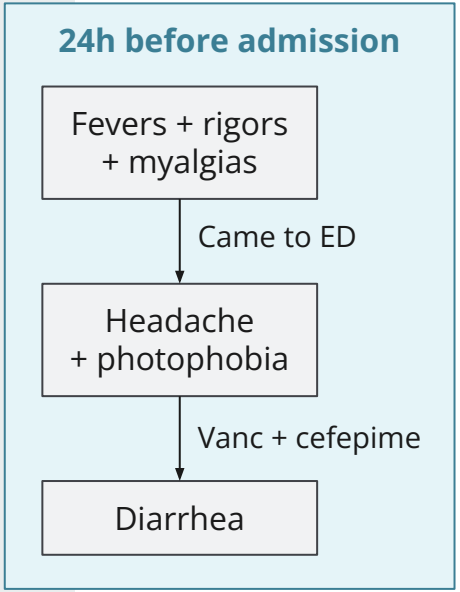
- Tmax 102 F at home
- Associated **rigors** & **myalgias**

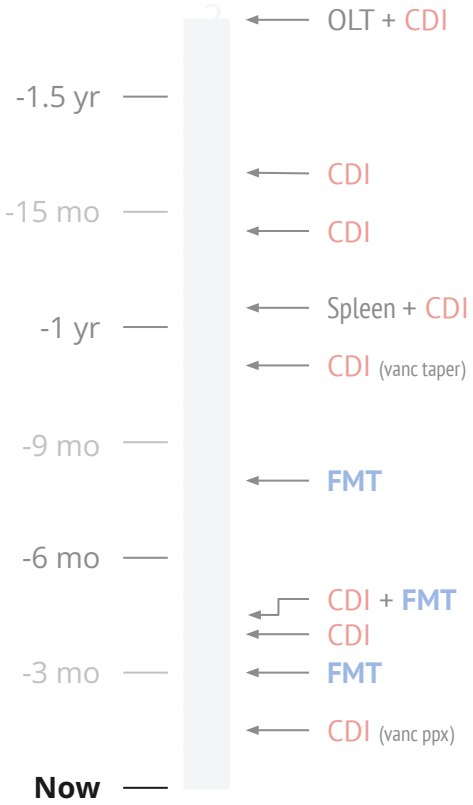
No other symptoms (until he got to the ED)

- Then had **headache** & **photophobia**

Got vanc + cefepime in ED

- Then started having **diarrhea**





Case 2: Further HPI

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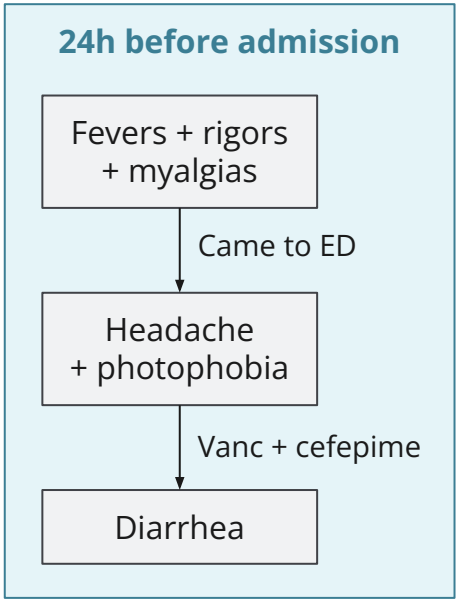
Had issues with his outpatient Rx → been **off vancomycin for ~4 days**



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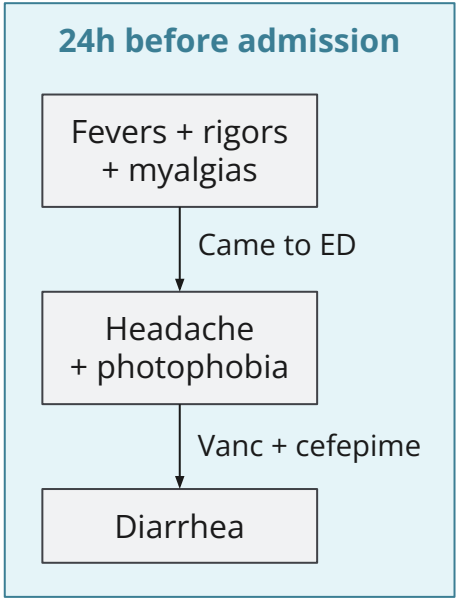

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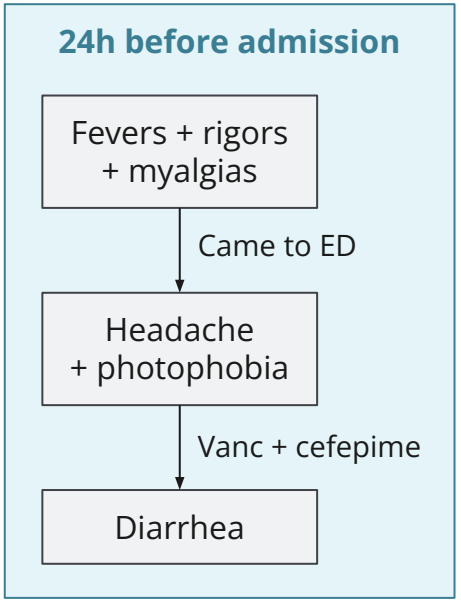
"I always get a bit of a **headache** in these hospital beds, and the **bright hospital lights** always bother me"

- He is struggling to keep his eyes open when the lights are turned on for the exam



Case 2: Labs

CBC	Admit	ED	-1d
WBC	**19.1**	**22.3**	8.8
Hgb	8.7	11.6	11.0
Platelets	261	341	336
Neut %	82%	83%	67%
Lymph %	7%	6%	13%
Eos %	7%	1.3%	7.8%

From day before admission
Obtained for IV iron infusion
Was feeling well at that time

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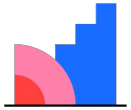
Chem7	Admit	ED	-9d
Na	140	136	140
K	4.3	5.6	5.6
HCO3	**17**	**20**	24
BUN	55	53	54
Cr	**2.83**	**2.73**	**2.7**

LFTs	Admit	ED	-9d
AST	---	25	22
ALT	---	21	18
Alk Phos	---	**122**	115
Bili	---	0.5	0.3
Albumin	---	3.6	3.8

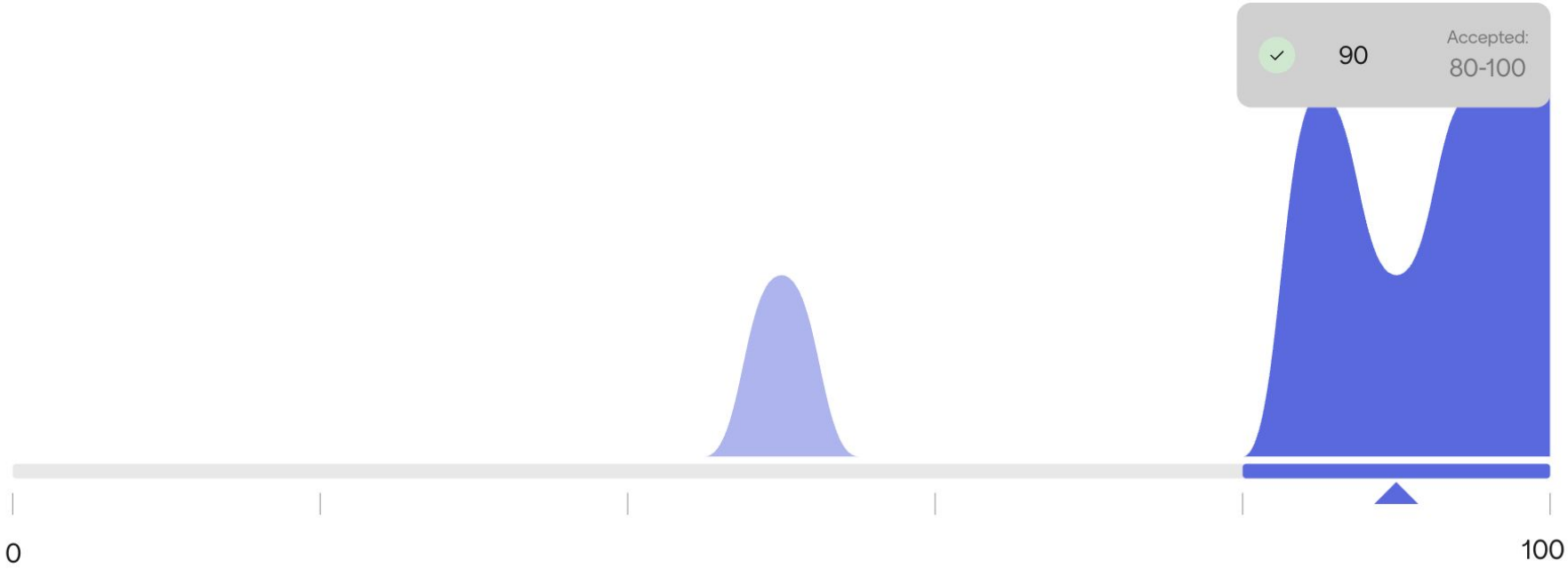
[2.1] Pretest probability of positive C diff screen



Mentimeter

Positive screen being both PCR and toxin positive

[2.1] What is your pre-test probability of a positive C diff screen



[2.2] What antimicrobials to choose?

In addition to IV +/- PO vancomycin

In addition to IV +/- PO vanco

[2.2] In addition to vancomycin, what abx do you pick?

Cefepime 7 Popular	Ceftriaxone 6	Iv metronidazole 3
Flagyl 2	Ceftriaxone 2	Response 1

Case 2: Labs

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C diff	Admit
PCR	**Pos**
Toxin	**Pos**

Case 2: Initial recommendations

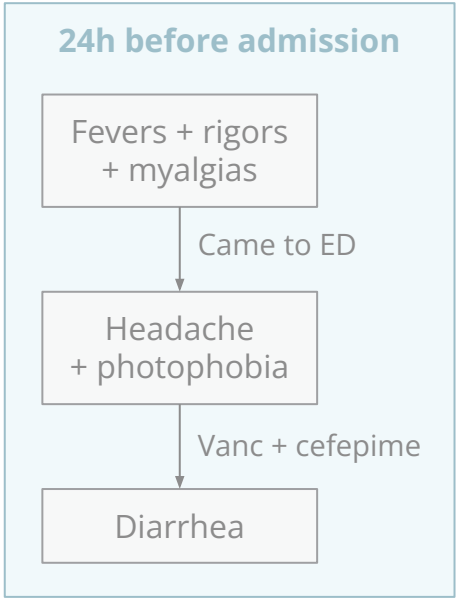
A **65 y/o M** with PMH including cirrhosis s/p OLT (-20 mo) w/ **recurrent C diff** (s/p FMT x3, on indefinite vanco PPx), s/p splenectomy who p/w **one day of fevers** (102 F) with associated rigors

Diagnostic recommendations

- Get **CT C/A/P** to look for source, most worried about GI
- Get **head CT**
- → → **lumbar puncture**
- Send **serum crypto antigen**

Therapeutic recommendations

- Agree with **fidaxomicin** for C diff
- Continue with **vancomycin** (watch AKI)
- Continue **Zosyn**



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Diagnostic recommendations

- Get **CT C/A/P** → **normal**. Rectal wall thickening consistent with diarrheal infection
- Get **head CT** → **normal**
- → → **lumbar puncture** → **delayed**
- Send **serum crypto antigen** → **negative**

Therapeutic recommendations

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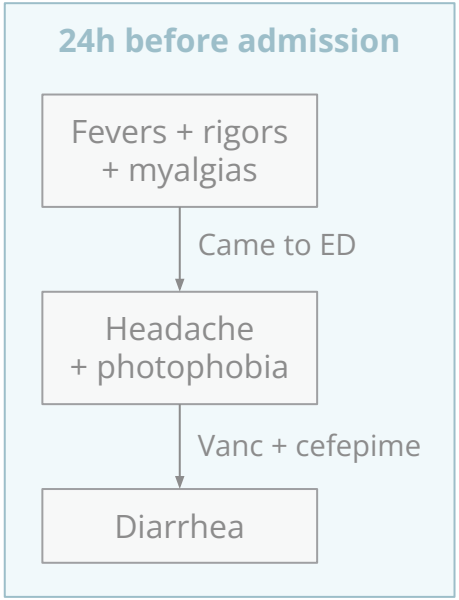

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Diagnostic recommendations

- Get **CT C/A/P → normal**.
- Get **head CT → normal**
- → → **lumbar puncture → delayed**
- Send **serum crypto antigen → negative**

By day 3, he feels **totally back to normal** (& fever free)

Therapeutic recommendations

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- Continue with **vancomycin** (watch AKI)
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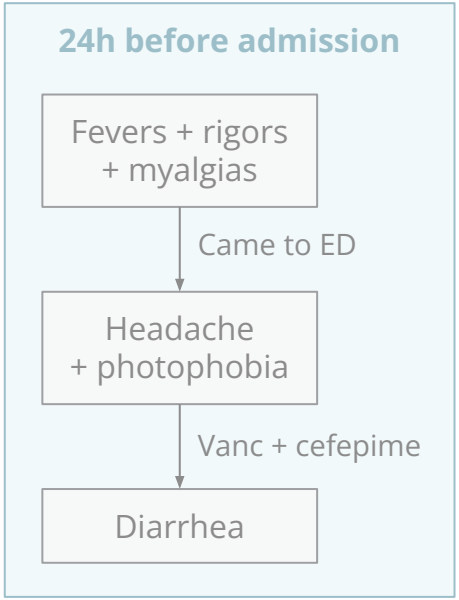

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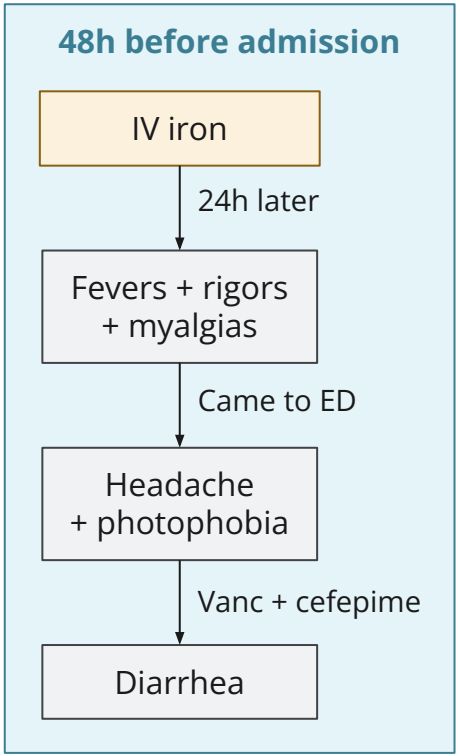
Blood cultures stay negative, and he does quite well on vanc/zosyn

The IV iron

- During his **first IV iron infusion he felt itchy**
- The most *recent infusion* was his **second infusion**



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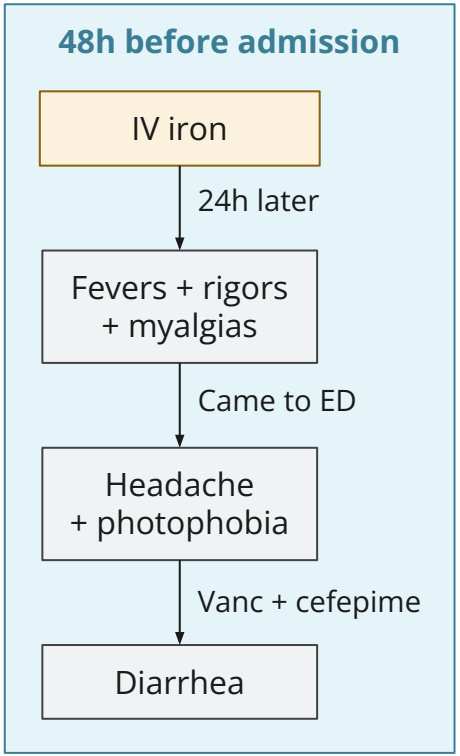
Doing better

Back to normal on **fidaxomicin**, **vancomycin**, and **Zosyn**

Never got an LP though...



Case 2: Treatment course

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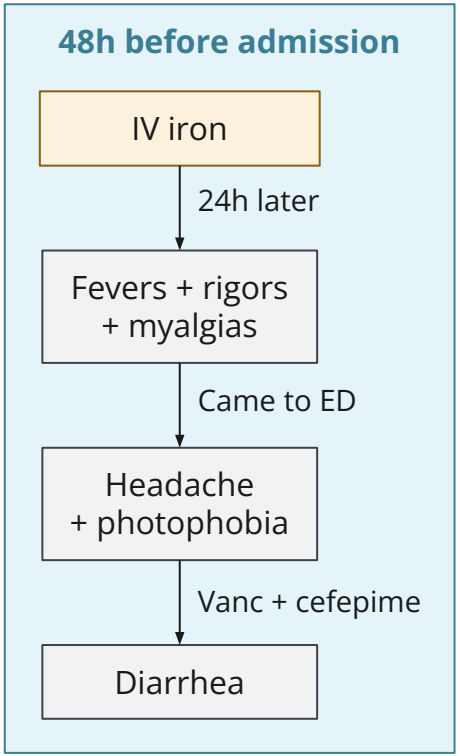
Only localizing symptoms were **CNS** +/- **GI**

- Wanted LP but got better within 24h hours → **LP deferred**
- Diarrhea only after abx → **better w/** few days of **fidaxomicin**



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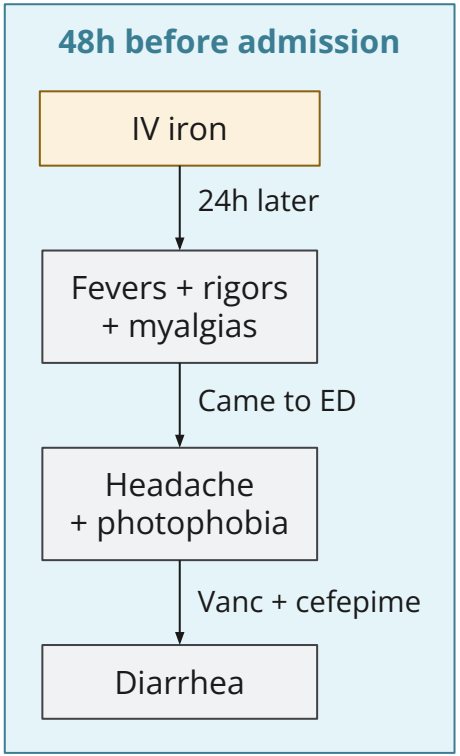
With negative **BCx**, **pan-CT**, **crypto Ag**, & **prompt resolution of Sx**, the benefits of IV antibiotics *outweighed by risks with C diff*

- Stopped vanc/zosyn & **watched off abx** → did well
- **Fidaxomicin** in house → **PO vanc** on d/c (because of insurance)



Discussion

Links to articles discussed here

Learning objectives

- Recognize some pitfalls of **molecular testing** for **infectious diarrhea**, per the 2017 IDSA guidelines
- Review **Campylobacter enteritis** in kidney transplants, with a focus on **treatment** and **risk factors**
- **Appraise the literature** regarding **treatment of norovirus** in solid organ transplant
- Evaluate if **delayed fever from IV iron** may have been the cause of case #2's fever

Molecular testing of infectious diarrhea

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IDSA 2017: Infectious diarrhea diagnostics [1]

Culture independent diagnostic modalities are **double-edged sword**

- **Advantages**: May be **faster diagnosis** → quicker treatment, decreased time in the hospital, maybe saves money

IDSA 2017: Infectious diarrhea diagnostics [1]

Culture independent diagnostic modalities are **double-edged sword**

Recommendation #14
Clinical consideration should be included in the interpretation of results of multiple-pathogen **nucleic acid amplification tests** because these assays detect DNA and **not necessarily viable organisms**

IDSA 2017: Infectious diarrhea diagnostics [1]

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Clinical consideration should be included in the interpretation of results of multiple-pathogen **nucleic acid amplification tests** because these assays detect DNA and **not necessarily viable organisms**

Clinical Hx must fit, especially when PCR is poly-positive

Additional HPI
- Onset of symptoms a week after flooding
  - Spring water looked murky
- Many of neighbors have septic tanks
- Some farms around

Biofire	Result	Does Hx fit?
Campylobacter	Pos	???
E coli	EPEC	???
Norovirus	Pos	???

IDSA 2017: Infectious diarrhea diagnostics [1]

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Multiple reasons to culture:

1. Outbreak investigation
2. Confirming viable pathogens
3. Susceptibility testing

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Multiple reasons to culture:

1. Outbreak investigation
2. Confirming viable pathogens
3. **Susceptibility testing**

Should this be a reflex order?
At least for Campy?

RECOMMENDATIONS

- Please obtain **stool culture** prior to starting azithromycin
- Agree with reducing immunosuppression if able from transplant standpoint

Campylobacter enteritis

- Recognize some pitfalls of **molecular testing** for **infectious diarrhea**, per the 2017 IDSA guidelines
- Review **Campylobacter enteritis** in kidney transplants, with a focus on **treatment** and **risk factors**
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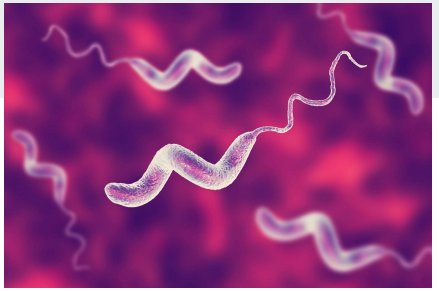
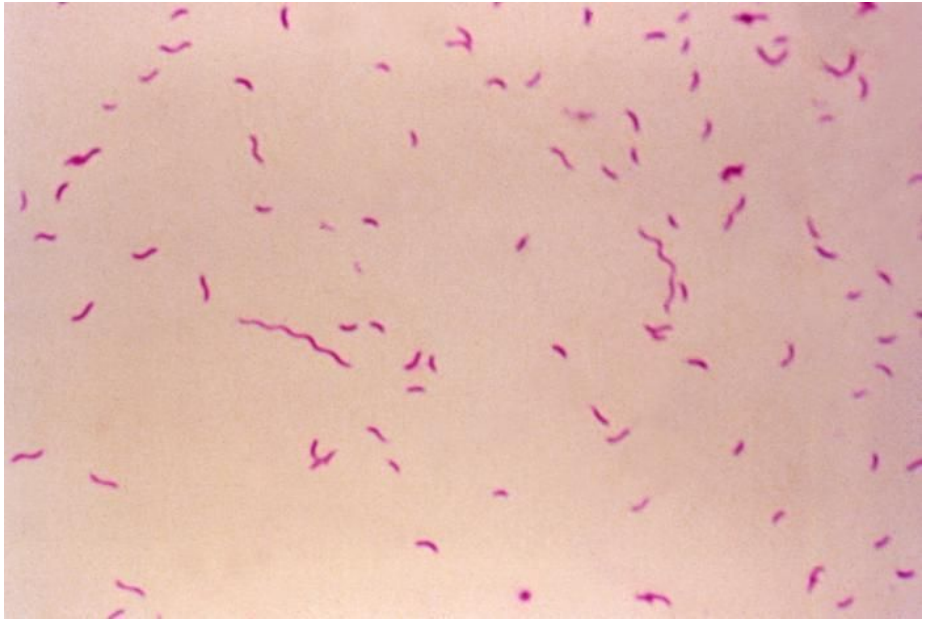


Campylobacter

- Motile, comma shaped, gram negative rod
  - *Kampulos* (Greek) = ‘bent’



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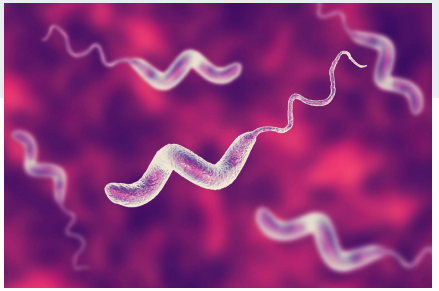

- Motile, comma shaped, gram negative rod
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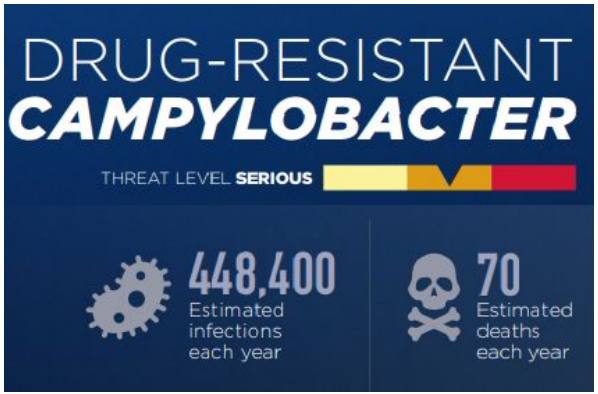
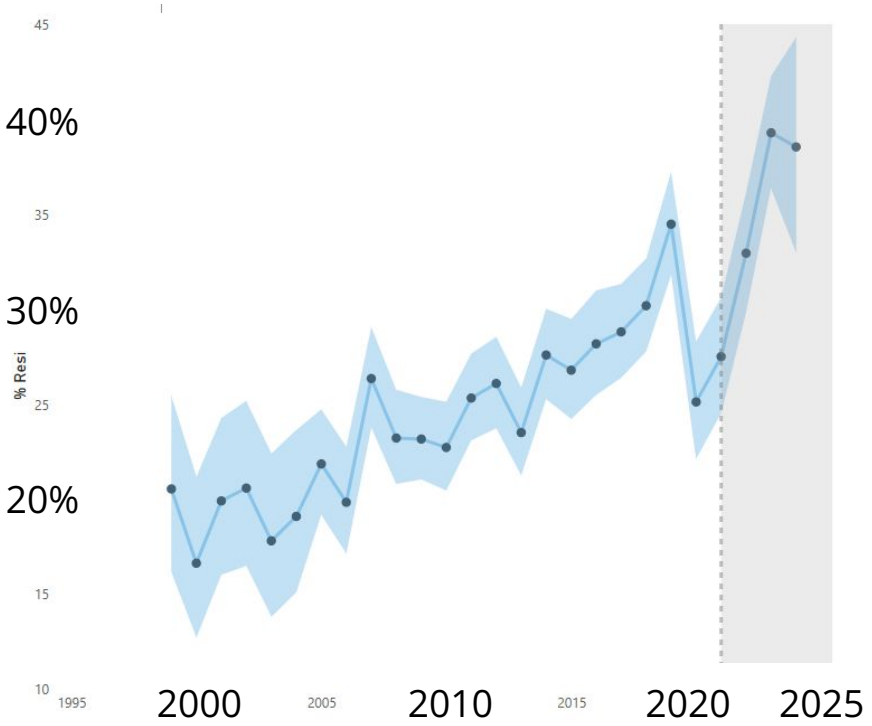
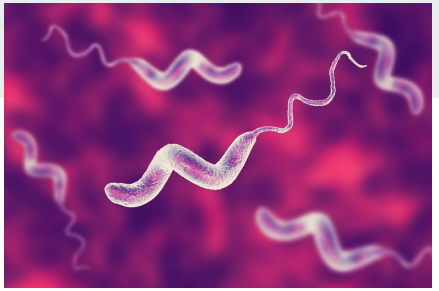
- Over **1 in 3 isolates** tested by CDC are **resistant to fluoroquinolones** [2]

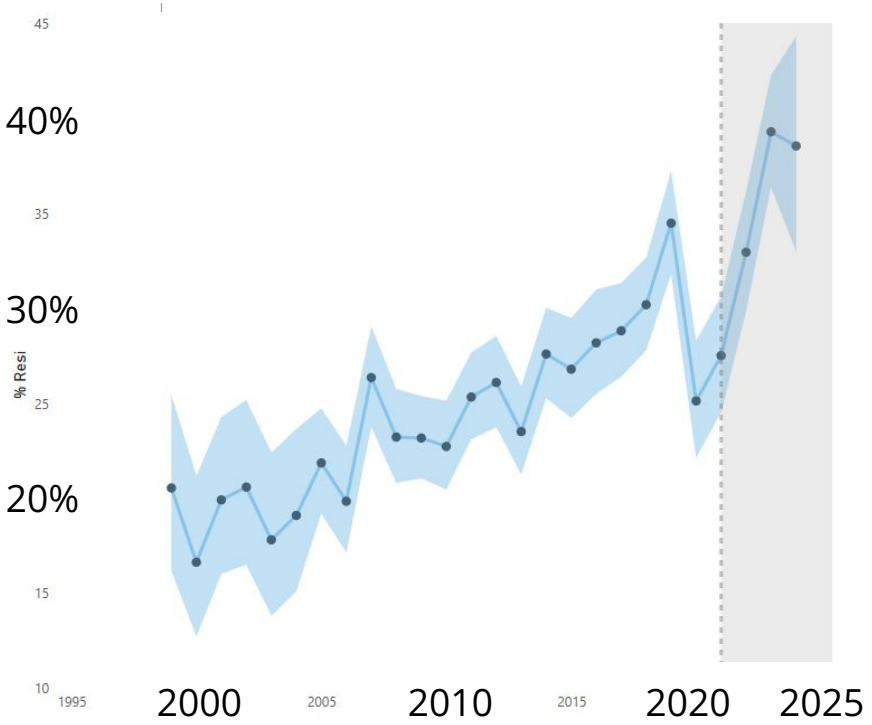




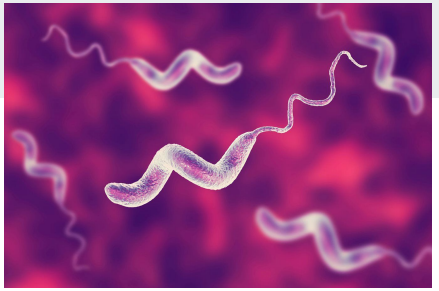


Campylobacter

- Motile, comma shaped, gram negative rod
  - *Kampulos* (Greek) = ‘bent’
- Over **1 in 3 isolates** tested by CDC are **resistant to fluoroquinolones** [2]
- **Macrolides** are **drug of choice**
  - Highly suggest susceptibility testing



Campylobacter in kidney transplant [3]



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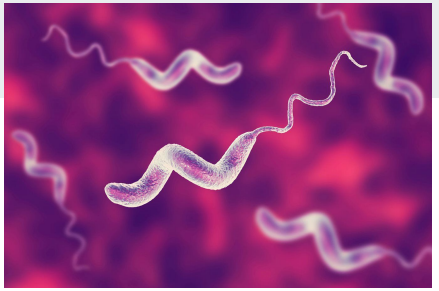
Campylobacter in kidney transplant [3]



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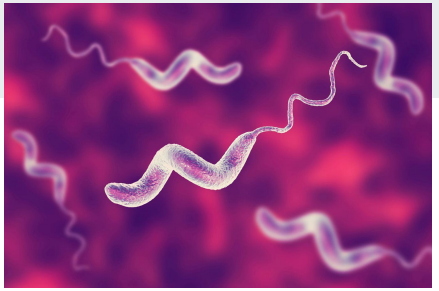
- Patient population: 10 year, multicenter retrospective review of 9 French centers
- Case definition: Positive culture for campylobacter
  - Stool culture (**91%**)
  - Stool PCR (5.8%)
  - Blood culture (4.9%)

Campylobacter in kidney transplant [3]



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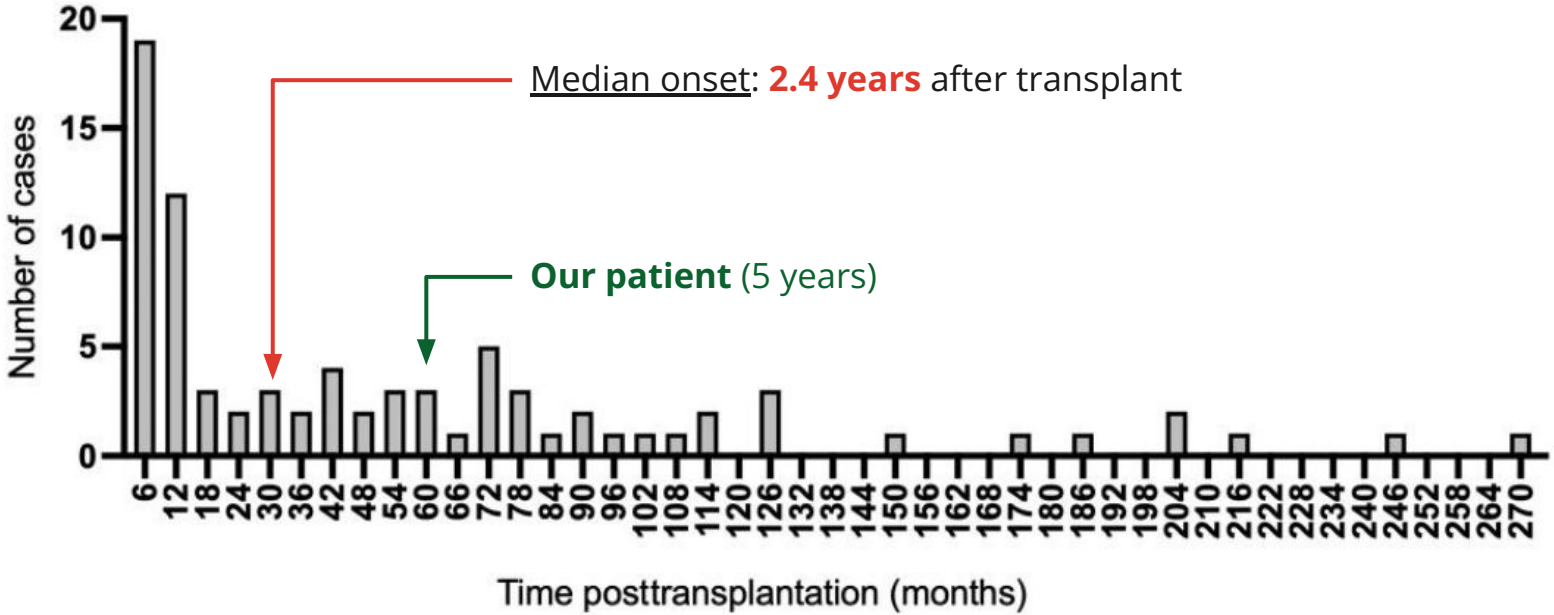
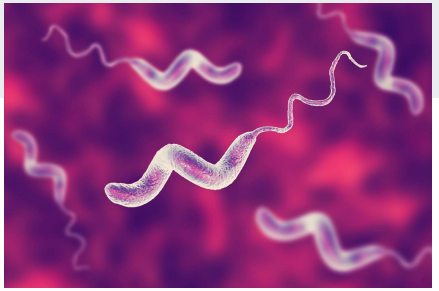


Campylobacter in kidney transplant [3]



Campylobacter is one of the **most common bacterial causes of diarrhea** in kidney transplants, as highlighted in large **matched case-control** by Bos et al (*Open Forum Infect Dis*, 2024)

- Patient population: 10 year, multicenter retrospective review of 9 French centers
- Case definition: Positive culture for campylobacter
  - Stool culture (91%)
  - Stool PCR (5.8%)
  - Blood culture (4.9%)

Cases (n=326) were matched to controls (KT without campylobacter; n=326) at the same center based on date of transplant (+/- 3 months) and similar graft function

Campylobacter in kidney transplant [3]

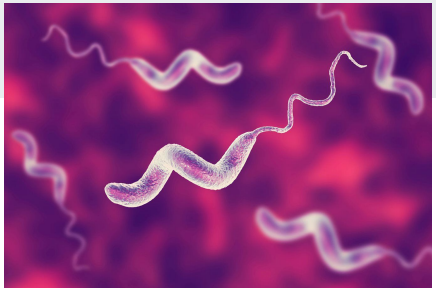
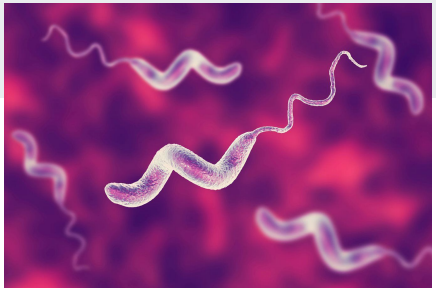


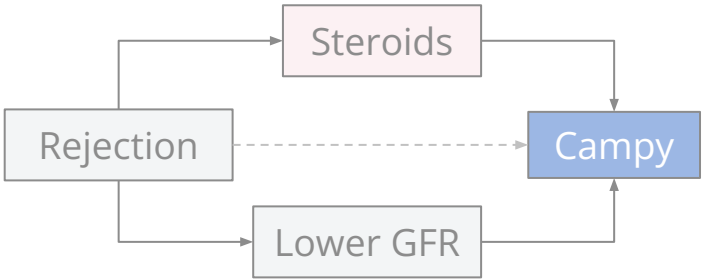
Table 1, select variables	Cases	Controls	Odd Ratio	P value
Age	**58**	55	1.01	0.071
Cancer	**21%**	14%	1.62	**0.021**
Rejection in past year				
Acute	**8.9%**	4.0%	2.27	**0.005**
ABMR	**4.0%**	0.9%	4.65	**0.007**
Tx'ed w/ steroids	**6.7%**	3.0%	2.36	**0.022**
Maintenance IS				
mTORi	**14%**	9.8%	1.54	0.075
Steroids	**76%**	66%	**14.71**	**<0.001**
Lymphocytes count	960	**1400**	0.42	**<0.001**
Baseline eGFR	44.2	**57.5**	0.97	**<0.001**

Campylobacter in kidney transplant [3]



Are steroids the risk factor?

Or is it driven by rejection?



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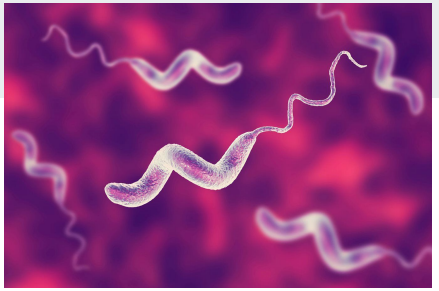
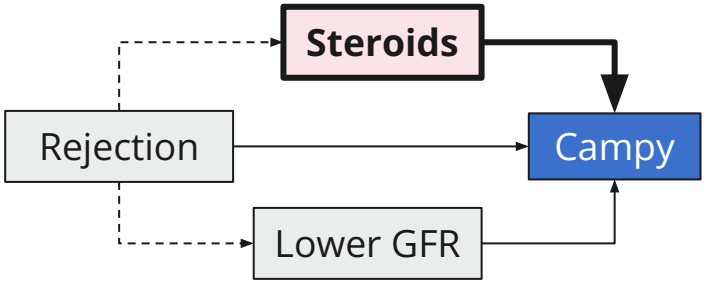


Table 2: Multivariable analyses

Variable	aOR	95% CI	P value
Corticosteroids	**10.22**	4.2 - 30.8	<0.001
Acute rejection	**2.20**	1.03 - 4.95	0.021
Lower lymphocytes count	**2.10**	1.53 - 2.95	<0.001
Lower baseline eGFR	**1.03**	1.02 - 1.04	<0.001



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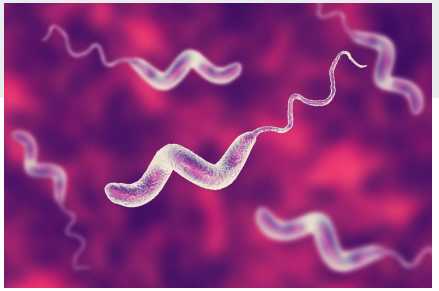


One in four patients had a **co-infection** (n=82)

- CMV (7.7%; n=25)
- Other diarrheal infections (5.3%; n=19)
  - Norovirus (n=9)
  - C diff (n=3)
  - Rotavirus or sapovirus (n=3)
  - Adenovirus (n=3)

Campylobacter in kidney transplant [3]

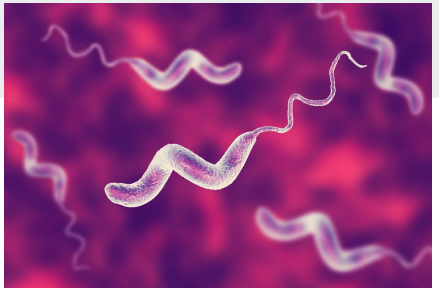


Table 4: First line treatment

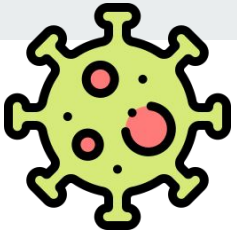
Treatment	Cases	Resistance	Duration
Fluoroquinolones	21% (n=64)	**51%** (24/47)	7.7 (SD 4.3)
Macrolides	40% (n=120)	0% (0/79)	**5.4** (SD 2.5)
No treatment	**11%** (n=33)	N/A	N/A

- Among those **Rx'ed macrolides**: No clinical failures, mean **duration of 5.4 days**
- Among those with ***non-severe disease***, **17% received no antimicrobial treatment**; all had remission without any relapse

Norovirus in SOT

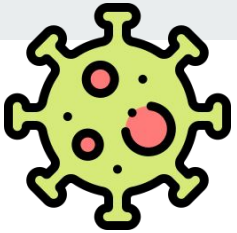
- Recognize some pitfalls of **molecular testing** for **infectious diarrhea**, per the 2017 IDSA guidelines
- Review **Campylobacter enteritis** in kidney transplants, with a focus on **treatment** and **risk factors**
- **Appraise the literature** regarding **treatment of norovirus** in solid organ transplant
- Evaluate if **delayed fever from IV iron** may have been the cause of case #2's fever

Norovirus in transplant



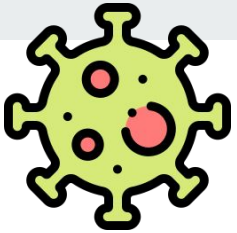
- Highly contagious RNA virus belonging to the Caliciviridae family
  - Genetically, at least 7 genogroups
- Most common cause of gastroenteritis
  - Self-limiting for most
  - May be prolonged / chronic with immunocompromise

Norovirus in transplant



The data is…**not great**

Norovirus in transplant



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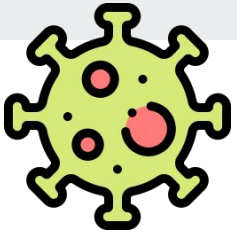
Reducing immunosuppression?

- Reducing immunosuppression is often suggested
- Carries the risk of worsened graft function
- Unclear if immunologically mediated or from consequence of norovirus itself

Norovirus & nitazoxanide



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Reducing immunosuppression?

Nitazoxanide? (NTZ) [4]

- Suggested based on blinded placebo RCT of healthy adults
  - NTZ x3 days -vs- placebo
- Reduced symptom duration 2.5 days → 1.5 days (p=0.03)
  - Only 13 had norovirus

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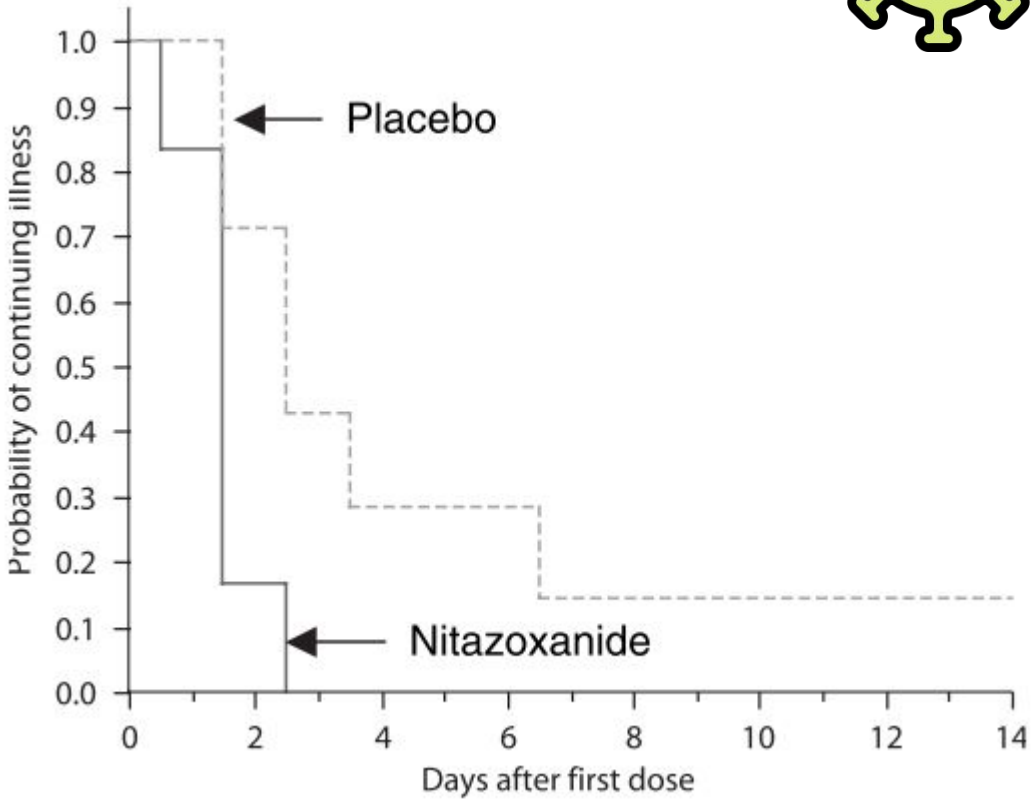
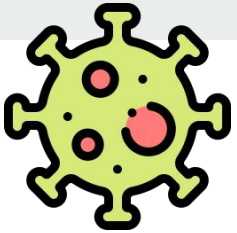


Norovirus & nitazoxanide



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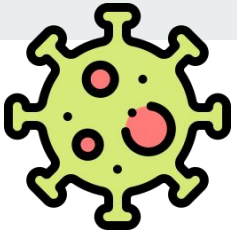
Nitazoxanide? (NTZ) [4]
In 13 healthy adults w/ norovirus, RCT found NTZ x3 days reduced symptom duration 2.5 → 1.5 days (p=0.03)

Issues & limitations with NTZ

- Other (non-randomized) studies have shown some benefit in SOT, but limited by **publication bias**
  - Citation #5 has a good review of other studies, highlighting the mixed results

Norovirus & nitazoxanide



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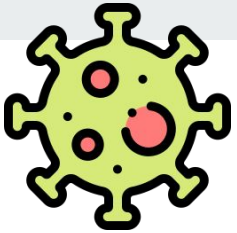
Issues & limitations with NTZ

- Data in SOT limited by **publication bias**
- **No plausible mechanism**
  - Unlike protozoa, viruses do not use anaerobic metabolism
  - Some have proposed that NTZ stimulated host innate immunity, this seems to not be the case [5]

Norovirus & nitazoxanide



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Somebody should do a trial!

Norovirus & nitazo

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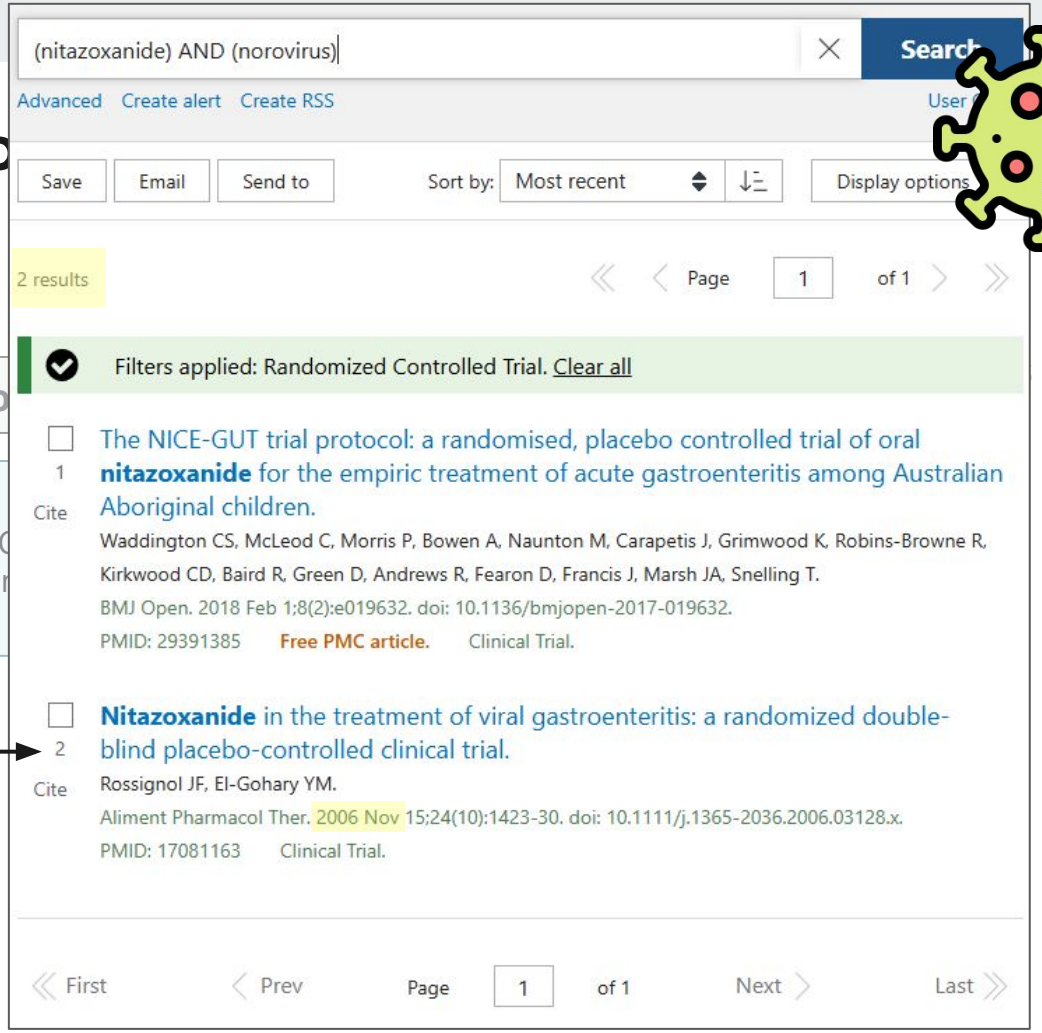
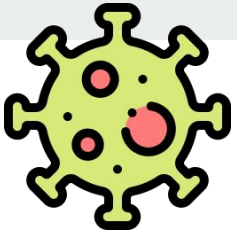


Norovirus & nitazoxanide



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Completed

NNITS-Nitazoxanide for Norovirus in Transplant Patients Study

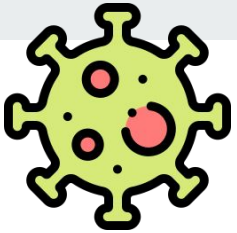
ClinicalTrials.gov ID NCT03395405

Sponsor National Institute of Allergy and Infectious Diseases (NIAID)

Information provided by National Institute of Allergy and Infectious Diseases (NIAID) (Responsible Party)

Last Update Posted 2025-05-21

Norovirus & nitazoxanide



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- Randomized to **28 days of NTZ** vs placebo

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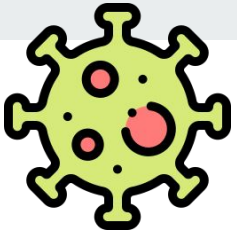

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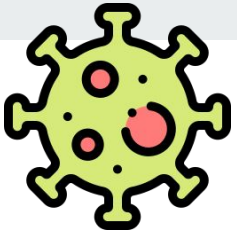
Phase 2, multicenter (including UPMC) **double blinded RCT**; completed in 2021

- Randomized to **28 days of NTZ** vs placebo
- Enrollment ***stopped early*** due to COVID
  - Original target: **160** (total)
  - Actual: **31 patients**
- Results are not published, but available on clinicaltrials.gov (ID: NCT03395405)

Norovirus & nitazoxanide



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	NTZ (n=16)	**Placebo** (n=15)
Completed	12	10
Death	0 (0%)	2 (13%)
Solid organ	15 (94%)	15 (100%)
Time to resolution (95% CI)	19 days (1 - 31)	11 days (2 - 14)
Serious side effects	0 (0%)	2 (13%)

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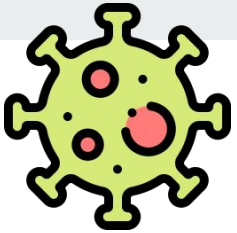

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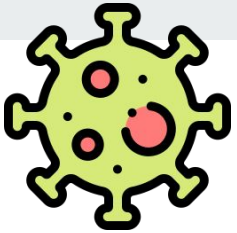
Hazard ratio
0.74 (0.33 - 1.64)
p=0.459

Norovirus in transplant



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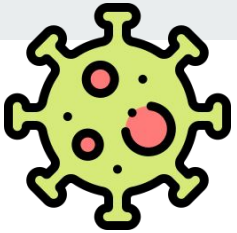

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- 60 kidney transplants
  - 31 with chronic norovirus
- 18 of the patients received IVIG
  - 20 g/day x 3 days
  - All the patients had chronic norovirus

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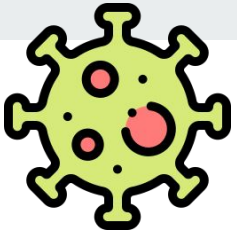

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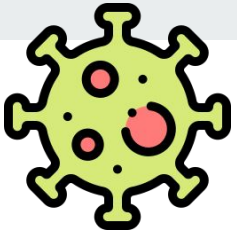
- 72% (n=13) of IVIG patients had no further symptoms or readmissions
  - Most of them (10 in 13) still had positive PCR
- No side effects of IVIG

Norovirus in transplant



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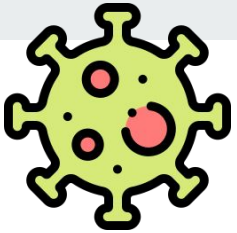

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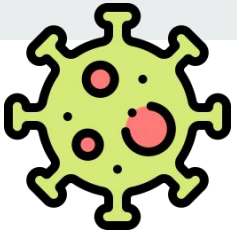
Nair (2023): **No difference at 6 months** [8]

- 79 solid SOT patients
  - 48% had baseline diarrhea
- 9% received IVIG (n=7)
  - Does **not specify** breakdown between **chronic & acute norovirus**
- Improvement at 6 months (p=0.24)
  - IVIG: 71%
  - No IVIG: 88%

Norovirus in transplant



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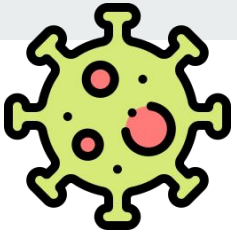
Oral immunoglobulins (POIG)

Oral immunoglobulins have also been used [9]

- Usual dosing is **25 mg/kg** given **q6h for 8 doses**
- Must be given **post-pylorically** (via dobhoff) to avoid stomach acid [13]

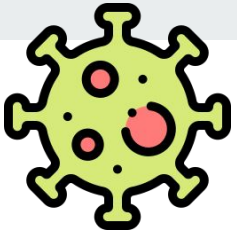
Norovirus in transplant: POIG



Author	Population	Results	Notes
Florescu 2011 [10]	**12 immunocompromised*** **Matched** to w/o POIG	Favored resolution at **7 days** (**OR 65**; p=.078) **No change in total duration** (12.1 vs 11.9 day)	*Mostly **kids with SOT** (small bowel mostly)
Gairard 2014 [11]	Case series of **12 BOLT**	**11 / 12 successfully treated** 1 only mildly improved	**4 patients had recurrence** later on
Nussbaum 2020 [12]	Case series of **9 SOT**	2/3rds had complete resolution by d/c **All patients** had **resolution by 90 days**	Didn't clear the PCR
Buskandar 2025 [13]	Case series of **7 SOT** All had **failed NTZ** therapy	**All had resolution without recurrence** No safety issues	

All studies used 25 mg/kg q6h x 8 doses, with the exception of Buskandar [13] (used 50 mg/kg)

Norovirus in transplant



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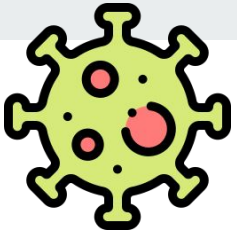
No trials, generally positive results

Oral immunoglobulins have also been used with promising results in one case-control [10] and small (n<15) case series [11, 12, 13]

But, **larger retrospective studies** [14] have **not shown *clear* benefit**

Norovirus in transplant



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Oral immunoglobulins have also been used with promising results in one case-control [10] and small (n<15) case series [11, 12, 13]

But, **larger retrospective studies** [14] have **not shown *clear* benefit**

- Of the 152 SOT patients, only 9 received POIG
- So still not a “large” study *of POIG*

Fever from IV iron?

- Recognize some pitfalls of **molecular testing** for **infectious diarrhea**, per the 2017 IDSA guidelines
- Review **Campylobacter enteritis** in kidney transplants, with a focus on **treatment** and **risk factors**
- Appraise the literature regarding **treatment of norovirus** in solid organ transplant
- Evaluate if **delayed fever** **from IV iron** may have been the cause of case #2's fever

Fevers with IV iron

Not the most common side effect, but has been documented

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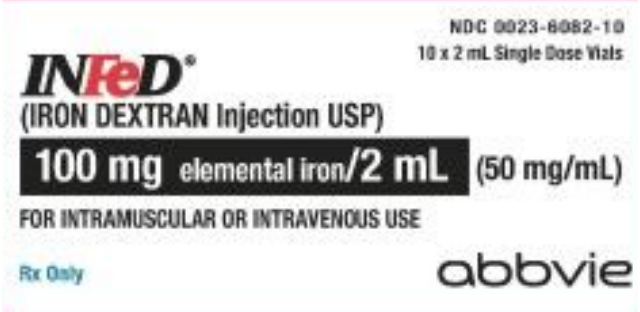
5.2 Delayed Reactions
Large intravenous doses...have been associated with an increased incidence of adverse reactions. The adverse reactions are **frequently delayed** (1 to 2 days) reactions typified by one or more of the following symptoms: arthralgia, **backache**, chills, dizziness, **moderate to high fever** , **headache**, malaise, myalgia, nausea, and vomiting.

- **Iron dextran package insert** [link]



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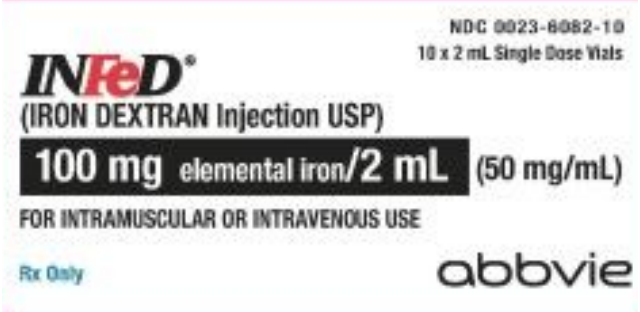
The **onset** is usually **24 to 48 hours** **after administration** and symptoms **generally subside** **within** **3 to 4 days**. The etiology of these reactions is not known.

- **Iron dextran package insert** [link]



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6.1 Adverse Reactions in Clinical Trials
From six trials of patients with CKD

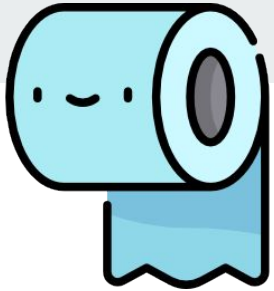
	HD	PD	CKD alone
# Patients	231	75	139
Pyrexia	3.0%	1.3%	0.7% *

* The rate of fevers with PO iron was 0.7%

- **Iron sucrose package insert** [link]

Learning points & take aways

Learning points & take aways



- **Stool PCRs** are great, but **clinical context** and **cultures are still needed** [1]
- Campylobacter is a common etiology of bacterial enteritis in KT, especially if on steroids
- Treat **Campylobacter in KT** similar to immunocompetent folks:
  - **Macrolides first line**, still send for susceptibilities (↑ rates of MDR [2])
  - Limited data suggests **does not need longer duration** and non-severe cases may not need abx [3]
- Treatment of **Norovirus in SOT** really **doesn't have great data**
  - Literature is limited by **publication bias** and being **underpowered**. That said, interventions seem to be **generally safe** (exception: reducing immunosuppression), but **maybe not effective**
  - **Nitazoxanide** had promising trial data for immunocompetent patients [4] but **?worse than placebo** in trial of SOT (unpublished) [6]. In vitro studies suggest it doesn't even help the immune system [5]
  - **IVIG** and **oral IG** (post-pyloric [13]) have plausible mechanisms and could help avoiding changes in immunosuppression. But data is mostly limited to case reports
- **IV iron** has been reported to cause **delayed reactions** (1-2 days later), including **self-resolving fevers**

Slides available on hunterratliff1.com/talk/; Citations available via QR code or via the "citations" button on the website