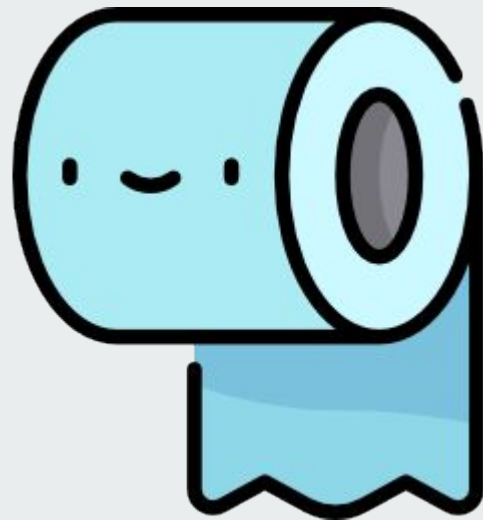




Gut Reactions (in TxID)

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*



Case #1

Case 1: HPI



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

Case 1: HPI



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

- Watery diarrhea x 1 month
 - Pretty bad for first week, stable in past 3 weeks
 - Never any blood
- 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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- No food associations, not waking up with diarrhea

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, <i>where she prepares food</i> • 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

Case 1: Labs



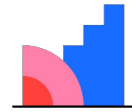
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Biofire	Result
Adenovirus	
Astrovirus	
Cyclospora	
Campylobacter	
Cryptosporidium	
E histolytica	
E coli	
Giardia lamblia	

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

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Campylobacter	Pos
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E histolytica	Neg
E coli	EPEC
Giardia lamblia	Neg

Biofire	Result
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Vibrio cholerae	Neg
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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?

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?

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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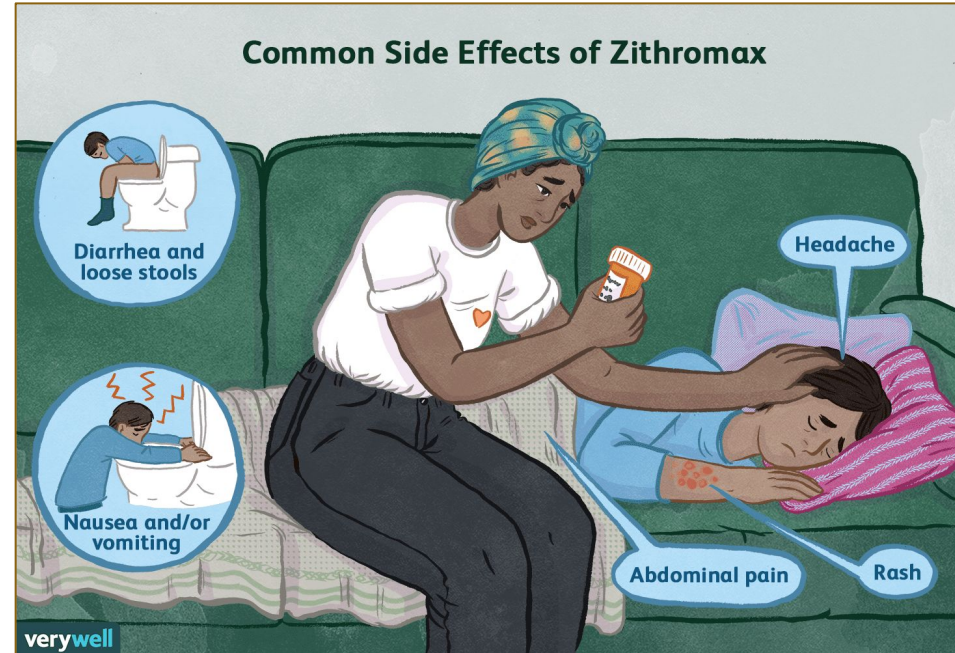
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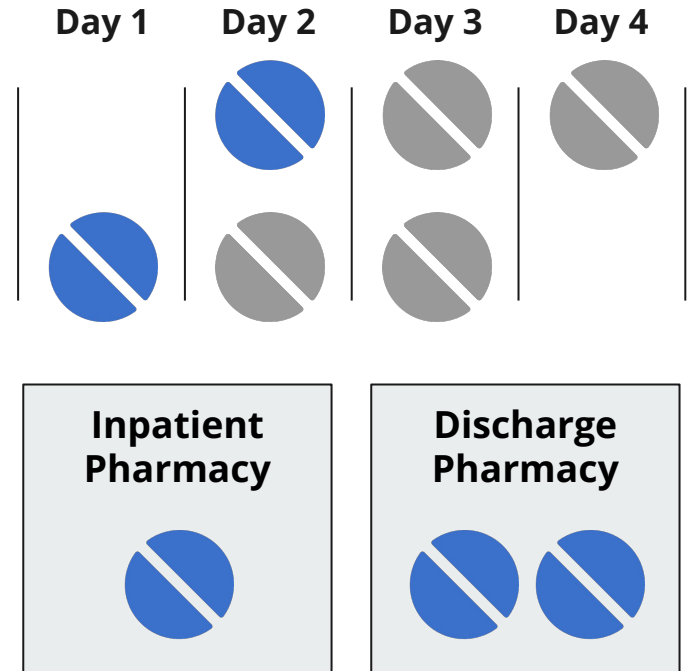
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- Reconsulted the **next morning** since **diarrhea had gotten worse**
- Therapeutic ID consult: **All better** by the time we saw the patient
 - Seemed to be transient
 - Perhaps related to **azithromycin**



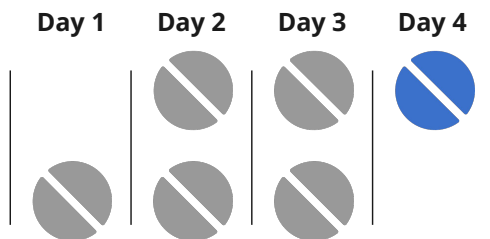
Case 1: Hospital course

- 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)

Three choices

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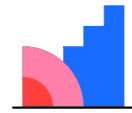
ChatGPT
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Skip the 6th dose

????

Noro: ???

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



Mentimeter

Three choices

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Skip the 6th dose

**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**

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**

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

Case 2: HPI



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- NASH cirrhosis w/ portal hypertension, hx SBP
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Splenectomy

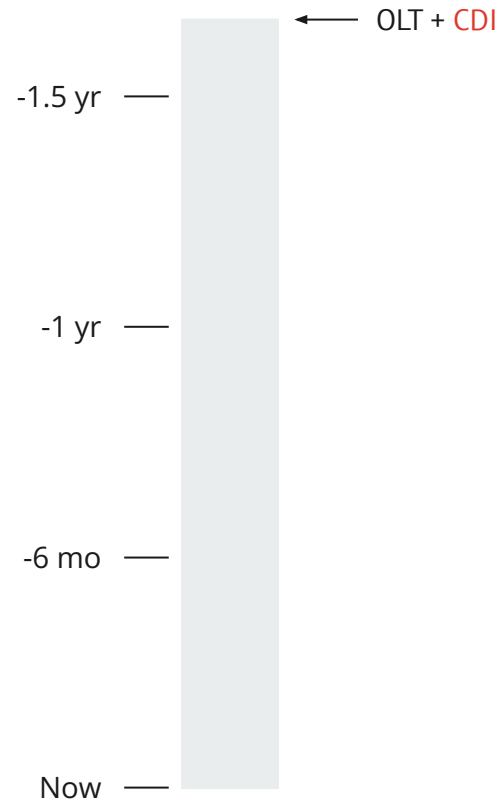
Had splenic artery rupture a year ago, requiring splenectomy
...also had C diff at that time

Case 2: Infectious Hx

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Transplant history

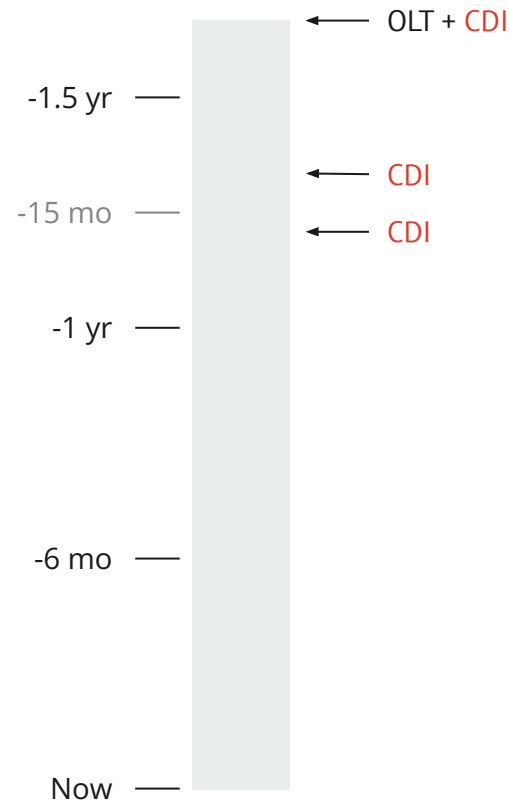
- NASH cirrhosis w/ portal hypertension, hx SBP
- Transplant 20 months ago c/b
 - Explant hemorrhage
 - DVT
 - An **episode of C diff**



Case 2: Infectious Hx

A 65 y/o M s/p OLT (2 years ago) w/ recurrent C diff p/w fever

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



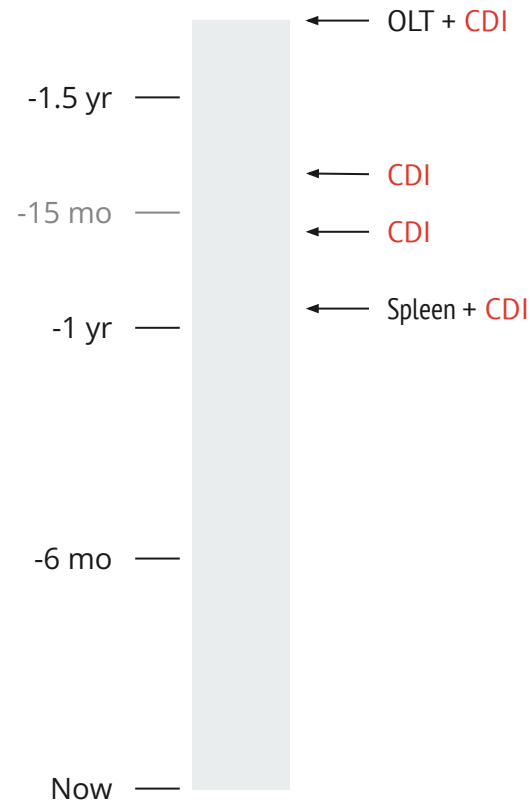
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requiring **splenectomy**
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Case 2: Infectious Hx

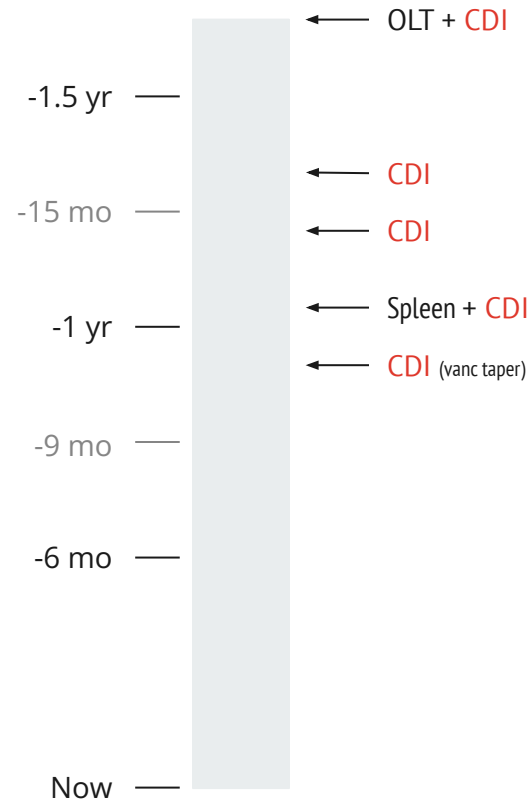
A 65 y/o M s/p OLT (2 years ago) w/ recurrent C diff p/w fever

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



**BlueCross
BlueShield**



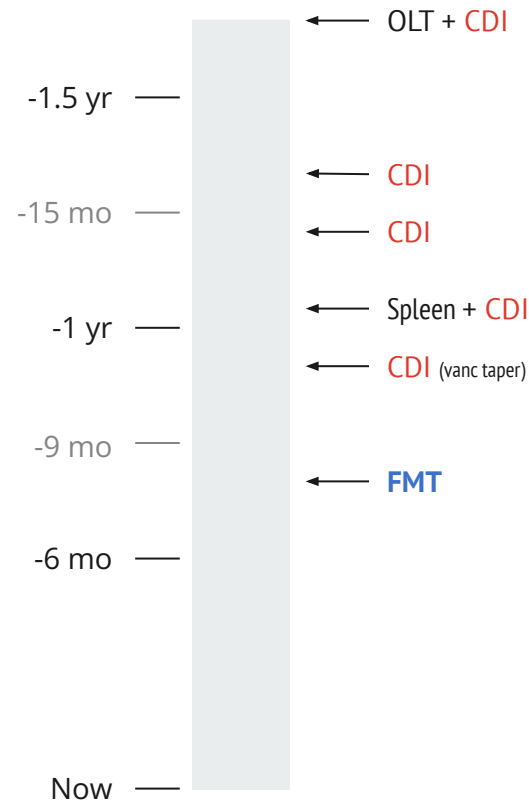
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Gets a **fecal microbiota transplant**



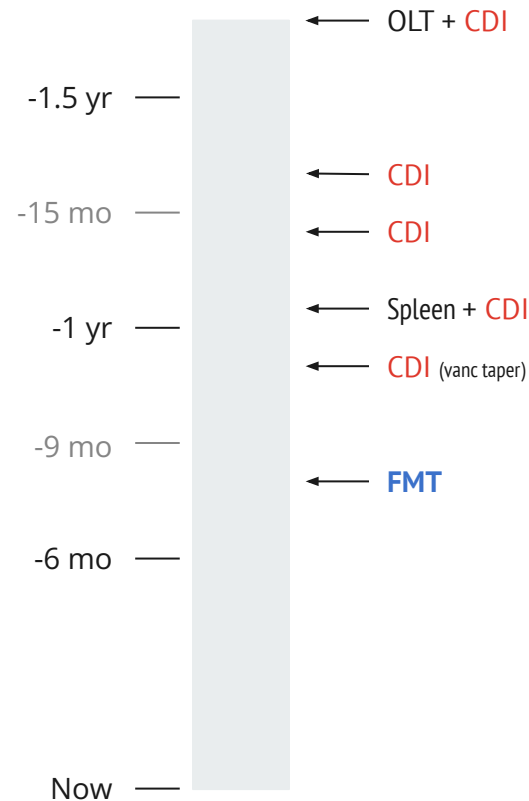
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Gets a **fecal microbiota transplant** (insurance doesn't pay for commercial products, so he gets frozen FMT)



**BlueCross
BlueShield**

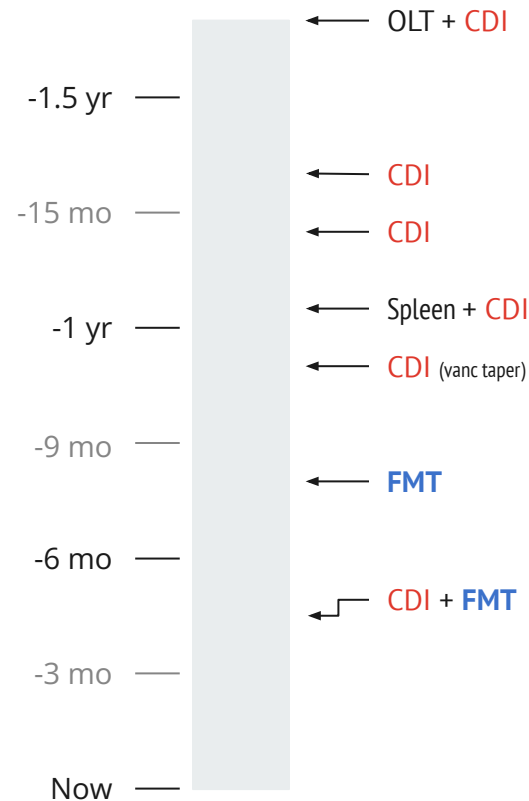
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4 months later, ED **Rx Keflex** for toe injury → **fulminant C diff** → gets **FMT #2** (Rebyota)



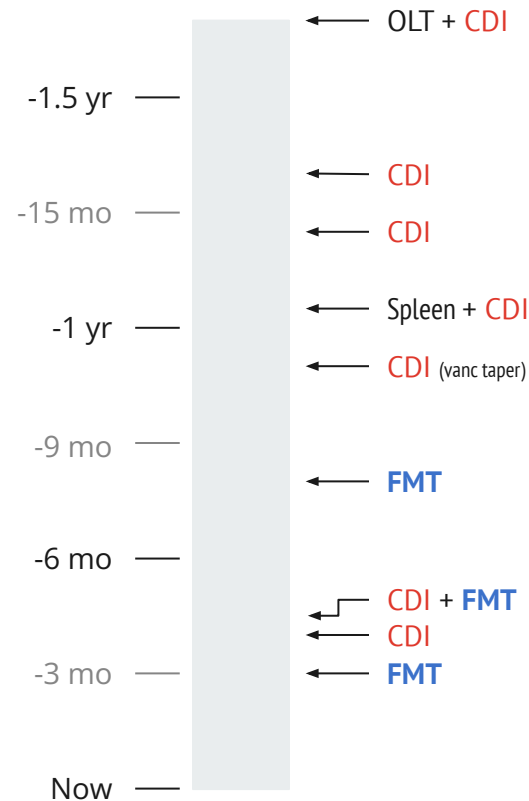
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4 months later, ED **Rx Keflex** for toe injury → **fulminant C diff** → gets **FMT #2** (Rebyota). Doesn't seem to help so gets prolonged vanc taper → **FMT #3** (VOWST)



Case 2: Infectious Hx

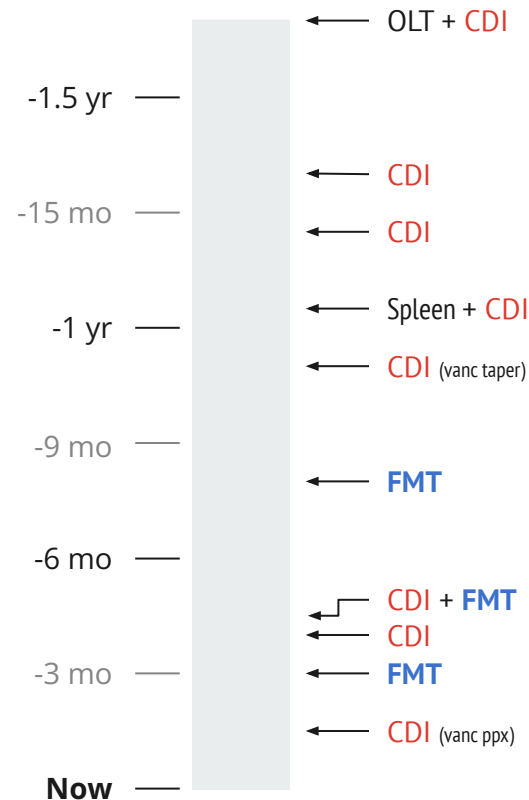
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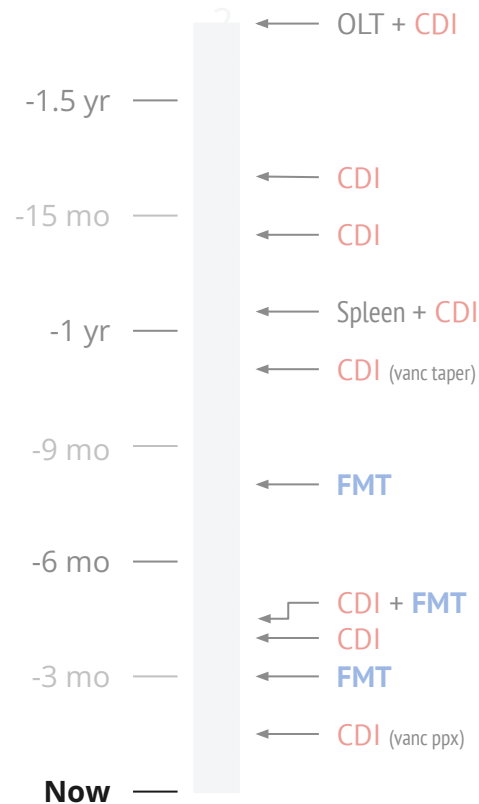
Does well for 6 weeks but then has his **eighth episode of C diff** → prolonged vanc taper followed by **indefinite BID vanco**



Case 2: HPI

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**.

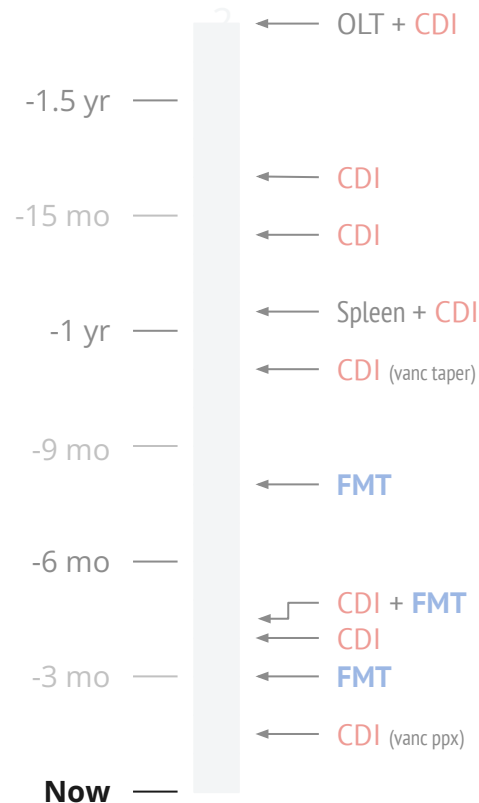
- **Fevers** started yesterday
 - Tmax 102 F
 - Associated **rigors** & **myalgias**



Case 2: HPI

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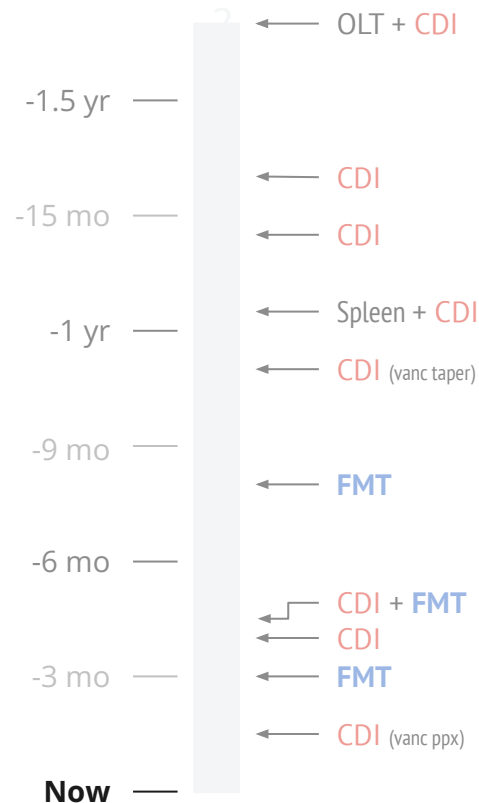
- **Fevers** started yesterday
 - Tmax 102 F
 - Associated **rigors** & **myalgias**
- No other symptoms (until he got to the ED)
 - Then had **headache** & **photophobia**



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- **Fevers** started yesterday
 - Tmax 102 F
 - 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**

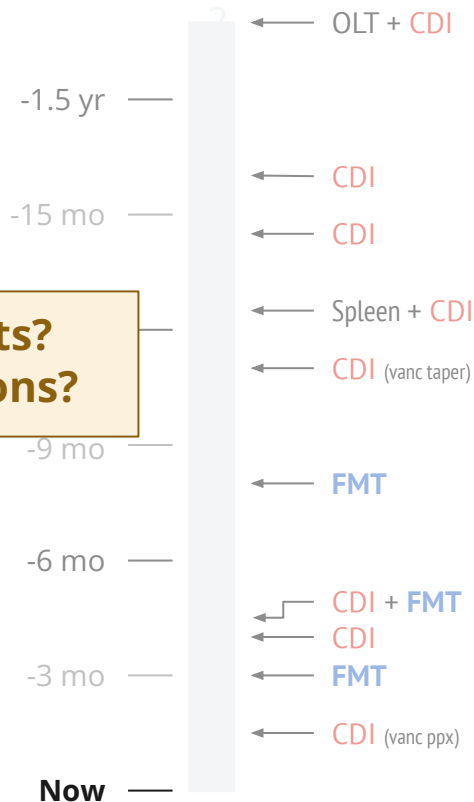


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- No other symptoms (until he got to the ED)
 - Then had **headache** & **photophobia**
- Got vanc + cefepime in ED
 - Then started having **diarrhea**

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**

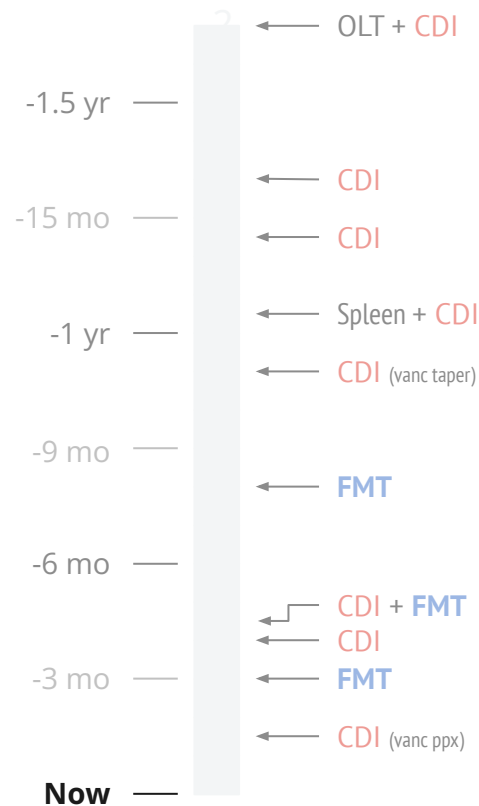
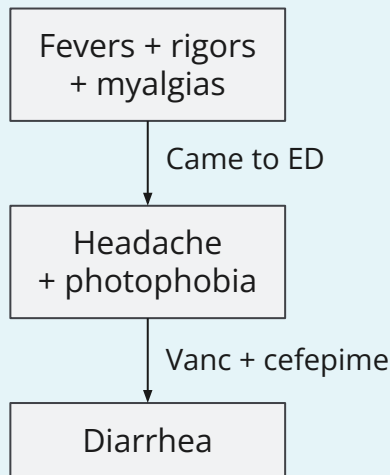
No other symptoms (until he got to the ED)

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

Got vanc + cefepime in ED

- Then started having **diarrhea**

24h before admission



Case 2: Further HPI

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

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

24h before admission

Fevers + rigors
+ myalgias

Came to ED

Headache
+ photophobia

Vanc + cefepime

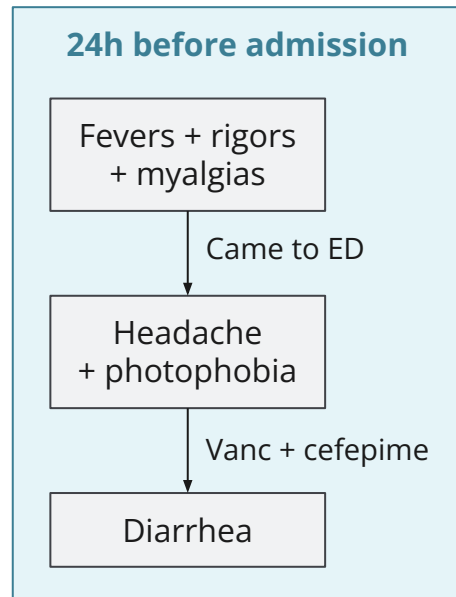
Diarrhea

Case 2: Further HPI

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

- Both he and his wife clarify, it's always **diarrhea *then* fevers** when he has C diff (they don't think he had C diff before coming in)



Case 2: Further HPI

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

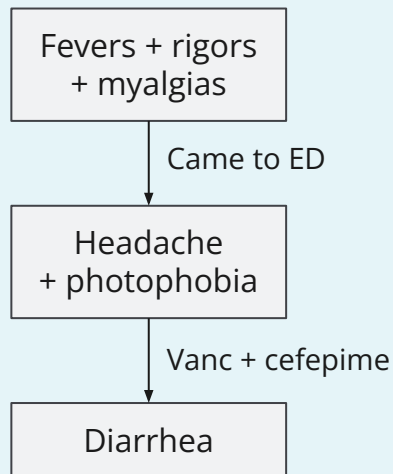
Had issues with his outpatient Rx → been **off vancomycin for ~4 days**

- Both he and his wife clarify, it's always **diarrhea *then* fevers** when he has C diff (they don't think he had C diff before coming in)

"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

24h before admission



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



Case 2: Labs

CBC	Admit	ED	-1d
WBC	19.1	22.3	8.8
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From day before admission

Obtained for IV iron infusion
Was feeling well at that time

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



[2.2] What antimicrobials to choose?



In addition to IV +/- PO vancomycin

Case 2: Labs

CBC	Admit	ED	-1d
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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

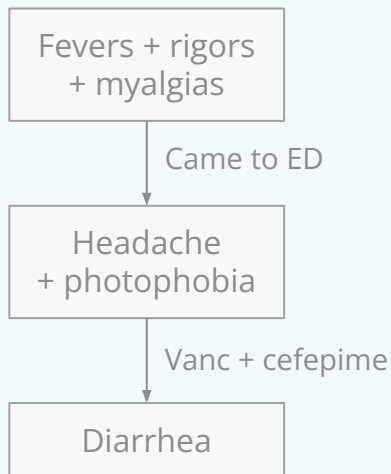
Diagnostic recommendations

- 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**

24h before admission



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

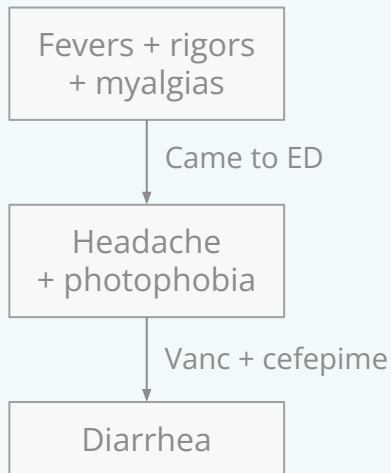
Diagnostic recommendations

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

Therapeutic recommendations

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

24h before admission



Case 2: Initial recommendations

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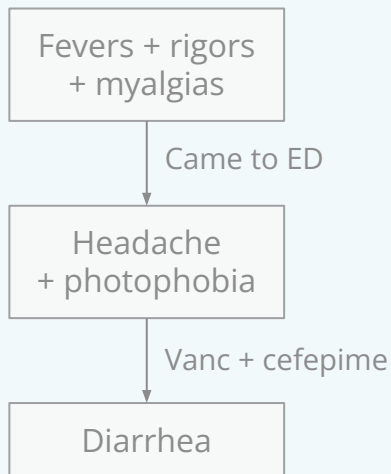
- Get **CT C/A/P** → **normal**.
- Get **head CT** → **normal**
- → → **lumbar puncture** → **delayed**
- Send **serum crypto antigen** → **negative**

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

Therapeutic recommendations

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

24h before admission



Case 2: Timing of symptoms

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 leukocytosis & fevers on admission

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**

48h before admission

IV iron

24h later

Fevers + rigors
+ myalgias

Came to ED

Headache
+ photophobia

Vanc + cefepime

Diarrhea

Case 2: Timing of symptoms

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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**

Doing better

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

Never got an LP though...

48h before admission

IV iron

24h later

Fevers + rigors
+ myalgias

Came to ED

Headache
+ photophobia

Vanc + cefepime

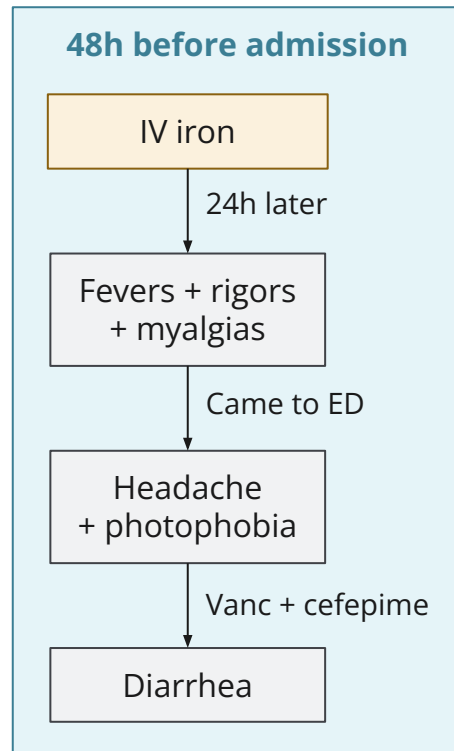
Diarrhea

Case 2: Treatment course

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 leukocytosis & fevers on admission

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



Case 2: Treatment course

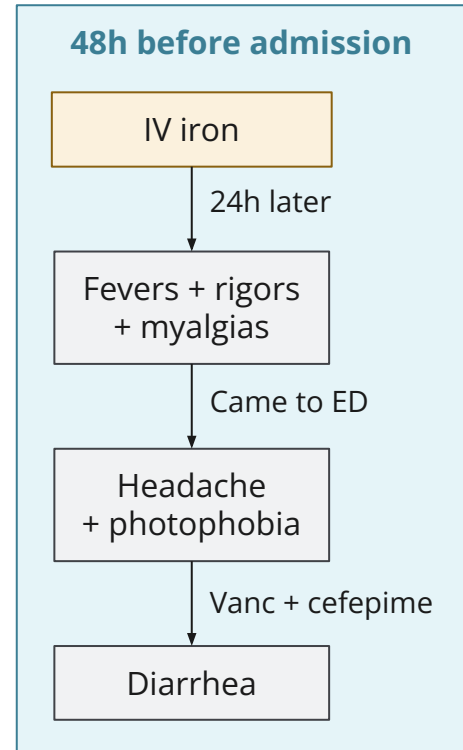
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Only localizing symptoms were **CNS +/- GI**

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

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]



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**

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]



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

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All specimens that test **positive for bacterial pathogens** by culture-independent diagnostic testing...(gastrointestinal tract panels)...should be **cultured in the clinical laboratory**

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Multiple reasons to culture:

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

IDSA 2017: Infectious diarrhea diagnostics ^[1]



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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

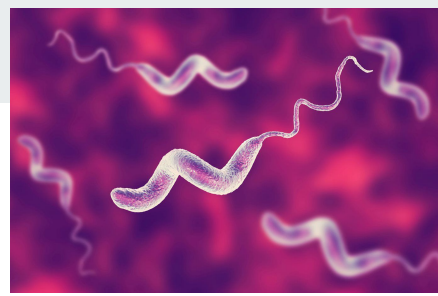
- Please obtain **stool culture** prior to starting azithromycin
- Agree with reducing immunosuppression if able from transplant standpoint



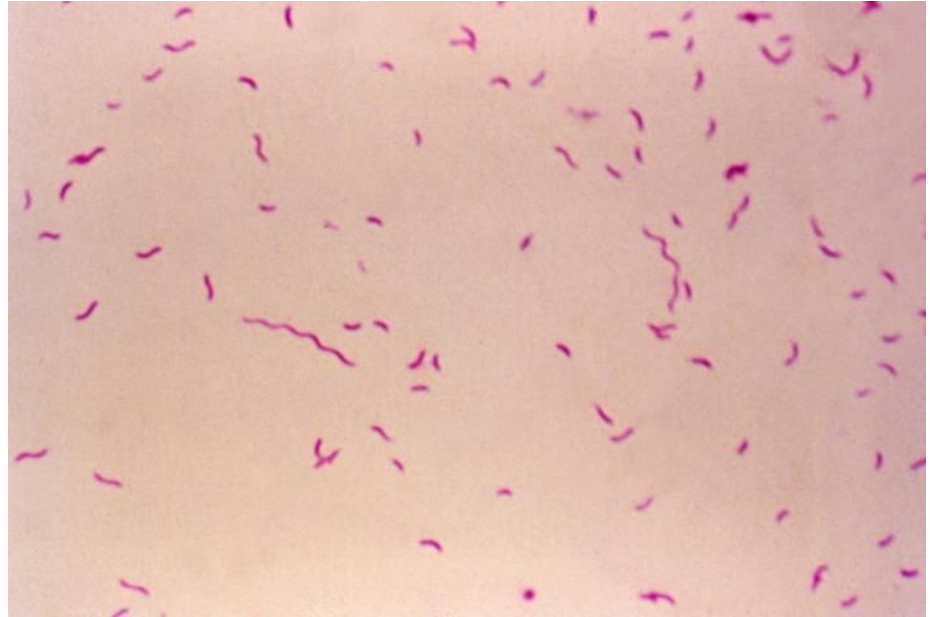
Campylobacter enteritis

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Campylobacter

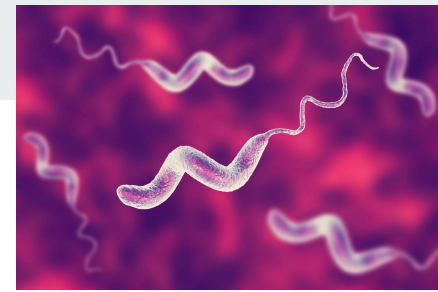
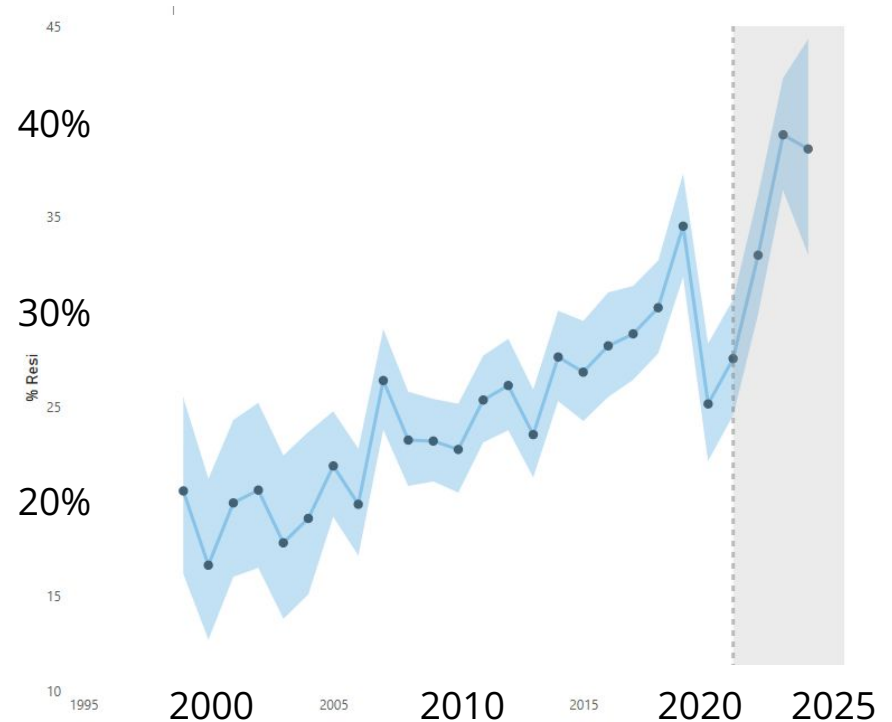


- Motile, comma shaped, gram negative rod
 - *Kampulos* (Greek) = 'bent'

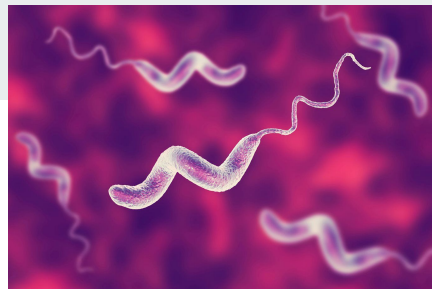


Campylobacter

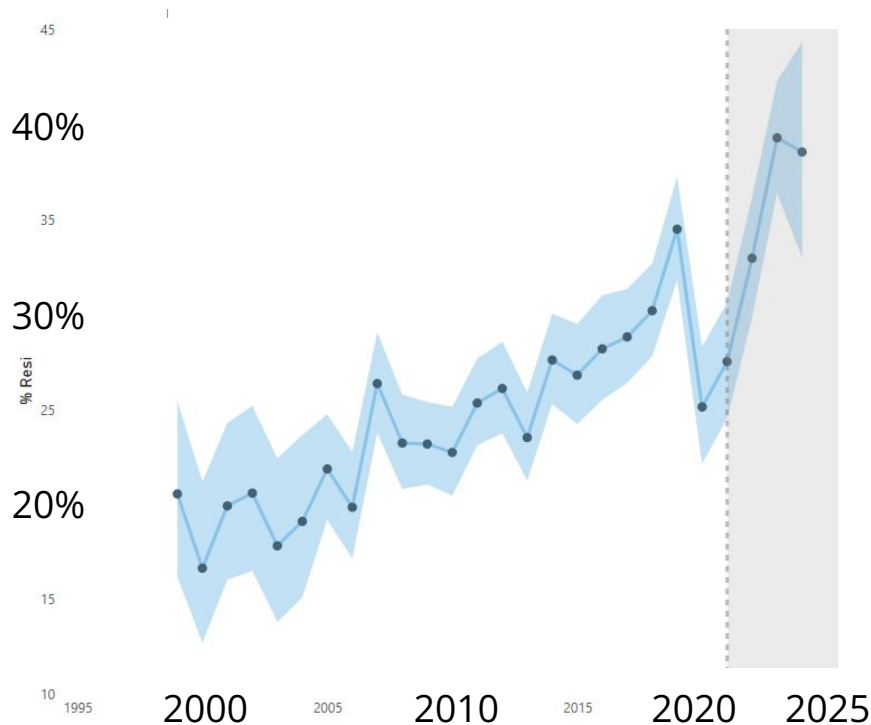
- Motile, comma shaped, gram negative rod
 - *Kampulos* (Greek) = 'bent'
- Over **1 in 3 isolates** tested by CDC are **resistant to fluoroquinolones** [2]



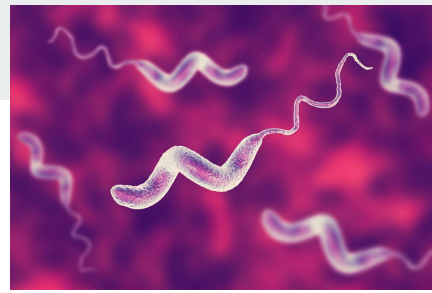
Campylobacter



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- Over **1 in 3 isolates** tested by CDC are **resistant to fluoroquinolones** [2]
- **Macrolides** are **drug of choice**
 - Highly suggest susceptibility testing

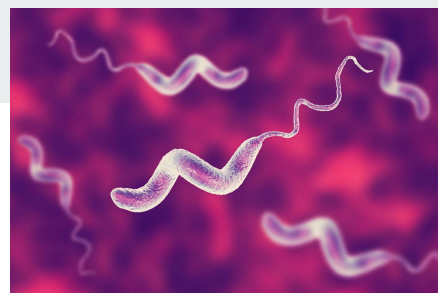


Campylobacter in kidney transplant ^[3]



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)

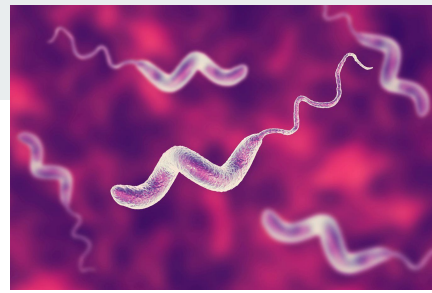
Campylobacter in kidney transplant ^[3]



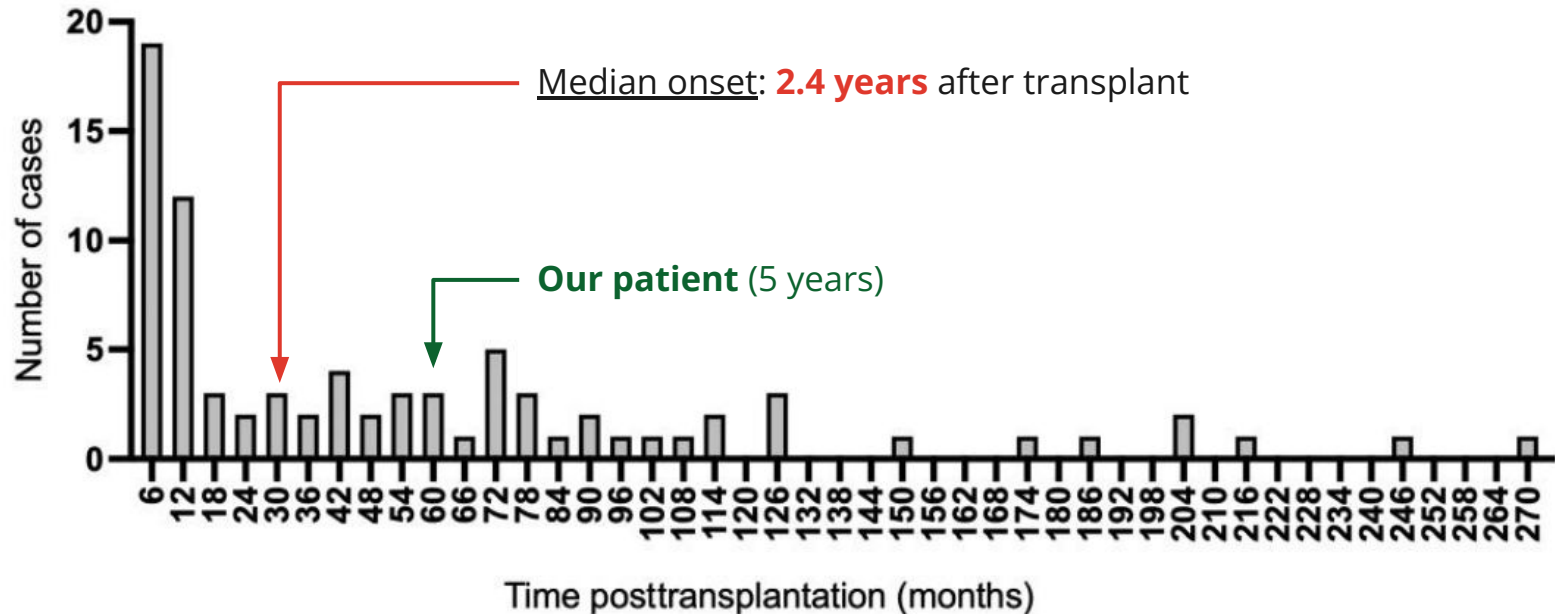
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- Patient population: 10 year, multicenter retrospective review of 9 French centers
- Case definition: Positive culture for campylobacter
 - Stool culture (**91%**)
 - Stool PCR (5.8%)
 - Blood culture (4.9%)

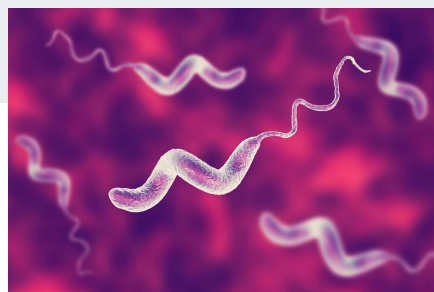
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Cases (n=326) were matched to **controls** (KT **without campylobacter**; n=326) at the same center based on date of transplant (+/- 3 months) and similar graft function

Campylobacter in kidney transplant ^[3]

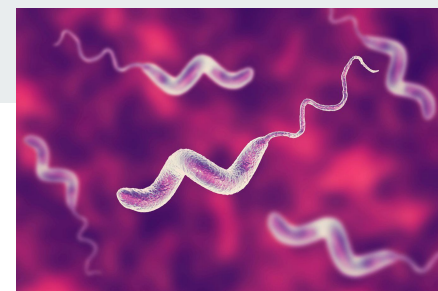
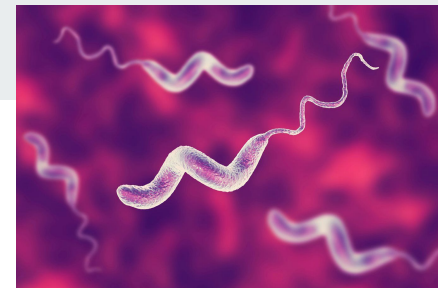


Table 1, select variables	Cases	Controls	Odd Ratio	P value
Age	58	55	1.01	0.071
Cancer	21%	14%	1.62	0.021
Rejection in past year				
Acute	8.9%	4.0%	2.27	0.005
ABMR	4.0%	0.9%	4.65	0.007
Tx'ed w/ steroids	6.7%	3.0%	2.36	0.022
Maintenance IS				
mTORi	14%	9.8%	1.54	0.075
Steroids	76%	66%	14.71	<0.001
Lymphocytes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

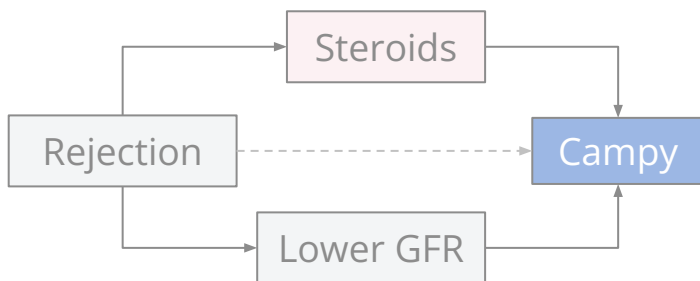


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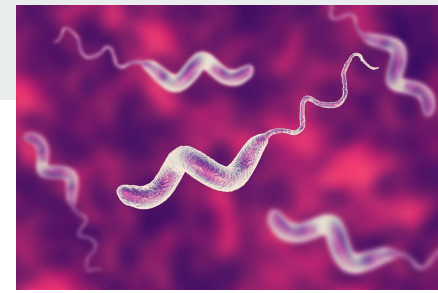
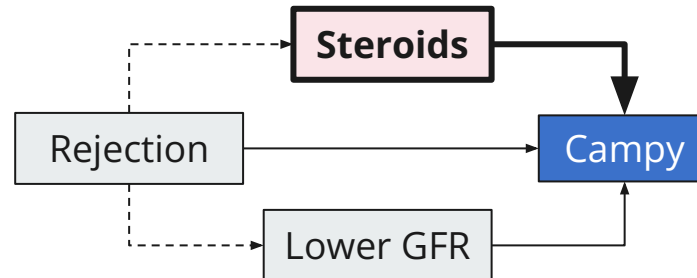
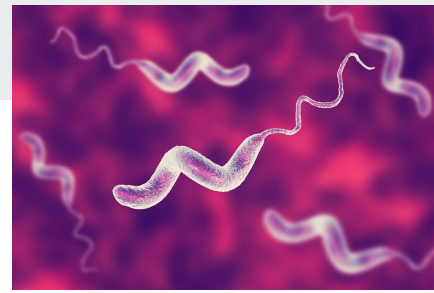


Table 2: Multivariable analyses

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



Campylobacter in kidney transplant ^[3]



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]

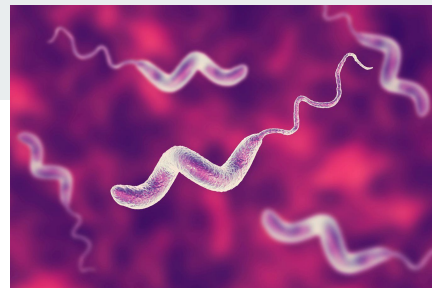


Table 4: First line treatment

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

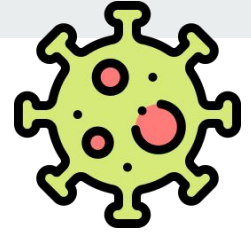
- Among those **Rx'd macrolides**: No clinical failures, mean **duration of 5.4 days**
- Among those with **non-severe disease**, **17% received no antimicrobial treatment**; all had remission without any relapse



Norovirus in SOT

- Recognize some pitfalls of **molecular testing** for infectious diarrhea, per the 2017 IDSA guidelines
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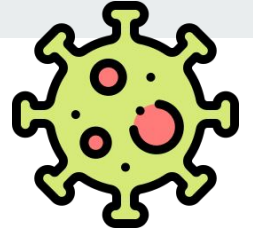
Norovirus in transplant

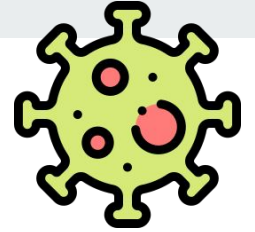


- Highly contagious RNA virus belonging to the Caliciviridae family
 - Genetically, at least 7 genogroups
- Most common cause of gastroenteritis
 - Self-limiting for most
 - May be prolonged / chronic with immunocompromise

Norovirus in transplant

The data is...**not great**



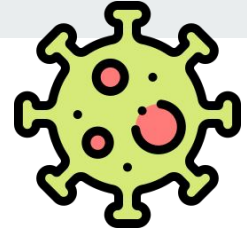


Norovirus in transplant

The data is...**not great**

Reducing immunosuppression?

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



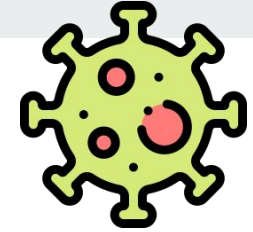
Norovirus & nitazoxanide

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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



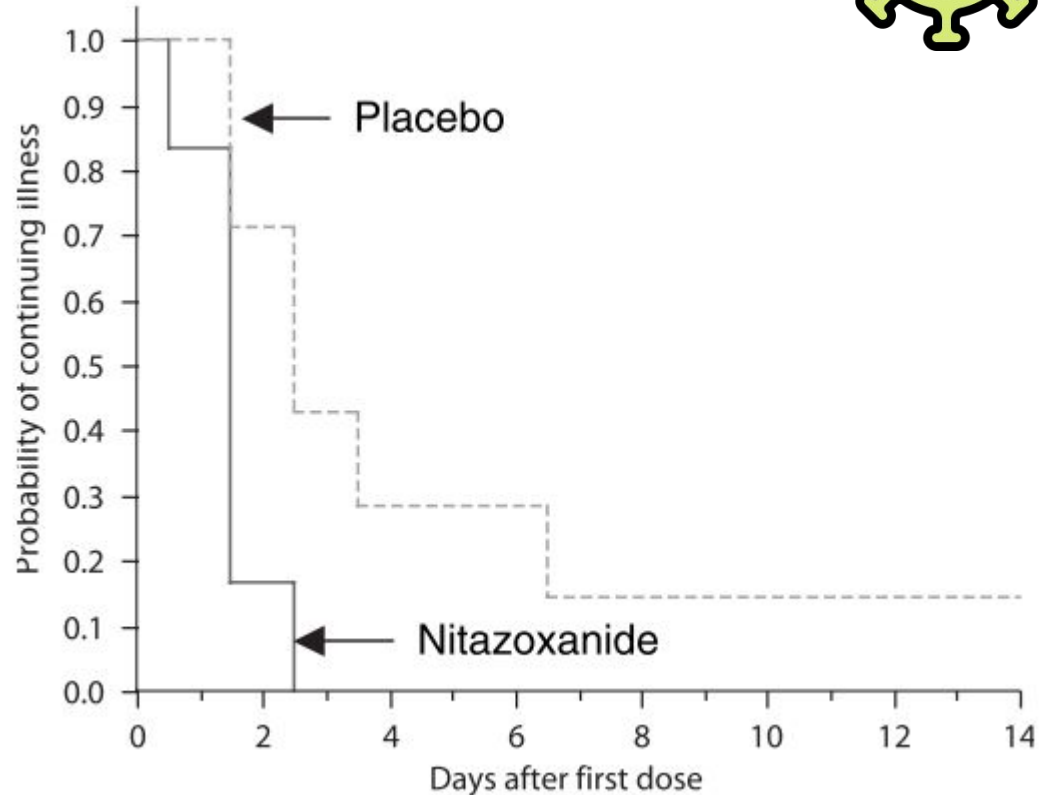
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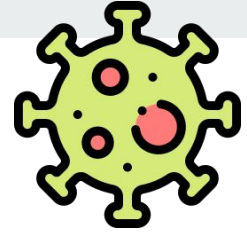
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Norovirus & nitazoxanide

The data is...**not great**

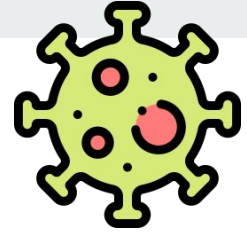
Reducing immunosuppression?

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



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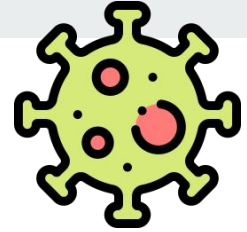
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Issues & limitations with NTZ

- 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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Reducing immunosuppression?

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**Somebody should
do a trial!**

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(nitazoxanide) AND (norovirus)

Advanced Create alert Create RSS User

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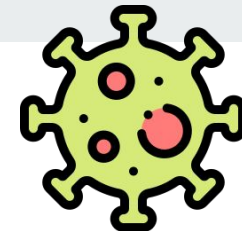
2 results

Filters applied: Randomized Controlled Trial. [Clear all](#)

☐ 1 **The NICE-GUT trial protocol: a randomised, placebo controlled trial of oral nitazoxanide for the empiric treatment of acute gastroenteritis among Australian Aboriginal children.**
Cite: Waddington CS, McLeod C, Morris P, Bowen A, Naunton M, Carapetis J, Grimwood K, Robins-Browne R, Kirkwood CD, Baird R, Green D, Andrews R, Fearon D, Francis J, Marsh JA, Snelling T. BMJ Open. 2018 Feb 1;8(2):e019632. doi: 10.1136/bmjopen-2017-019632. PMID: 29391385 [Free PMC article.](#) Clinical Trial.

☐ 2 **Nitazoxanide in the treatment of viral gastroenteritis: a randomized double-blind placebo-controlled clinical trial.**
Cite: Rossignol JF, El-Gohary YM. Aliment Pharmacol Ther. 2006 Nov 15;24(10):1423-30. doi: 10.1111/j.1365-2036.2006.03128.x. PMID: 17081163 Clinical Trial.

First Prev Page 1 of 1 Next Last



Norovirus & nitazoxanide

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Issues & limitations with NTZ

Reducing immunosuppression?

Completed ⓘ

NNITS-Nitazoxanide for Norovirus in Transplant Patients Study

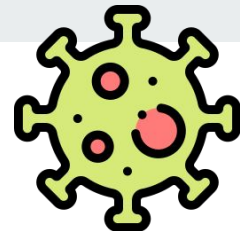
ClinicalTrials.gov ID ⓘ NCT03395405

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

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Norovirus & nitazoxanide

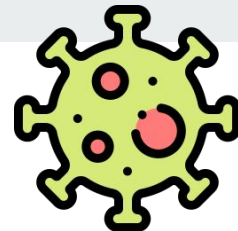
Completed



NNITS-Nitazoxanide for Norovirus in Transplant Patients Study

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

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



Norovirus & nitazoxanide

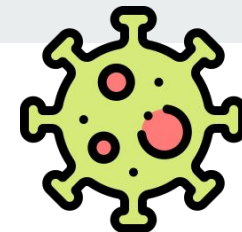
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NNITS-Nitazoxanide for Norovirus in Transplant Patients Study

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](https://clinicaltrials.gov/ct2/show/study/NCT03395405))



Norovirus & nitazoxanide

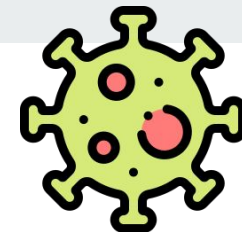
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[NCT03395405](#)

NNITS-Nitazoxanide for Norovirus in Transplant Patients Study

	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%)



Norovirus & nitazoxanide

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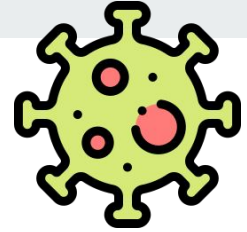


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Hazard ratio
0.74 (0.33 - 1.64)
p=0.459



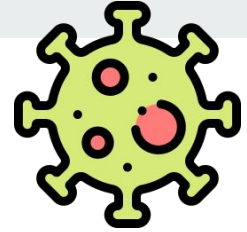
Norovirus in transplant

Reducing immunosuppression?

Nitazoxanide? (NTZ)

Mixed data in limited trials [\[4\]](#)[\[6\]](#)

Intravenous immunoglobulins (IVIG)



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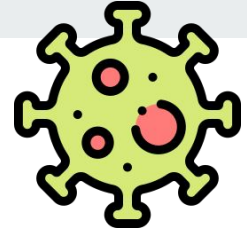
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Gackler (2021): IVIG **might work** [7]

- 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



Norovirus in transplant

Reducing immunosuppression?

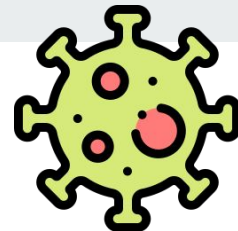
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 - 31 with chronic norovirus
- 18 of the patients received IVIG
 - 20 g/day x 3 days
 - All the patients had chronic norovirus
- 72% (n=13) of IVIG patients had no further symptoms or readmissions
 - Most of them (10 in 13) still had positive PCR
- No side effects of IVIG



Norovirus in transplant

Reducing immunosuppression?

Nitazoxanide? (NTZ)

Mixed data in limited trials [4][6]

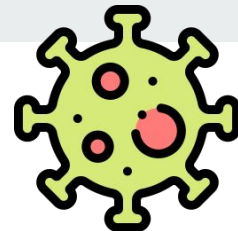
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- 79 solid SOT patients
 - 48% had baseline diarrhea



Norovirus in transplant

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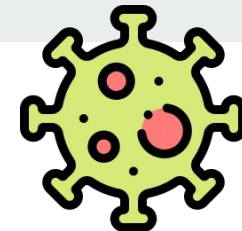
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Nair (2023): **No difference at 6 months** [8]

- 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

Reducing immunosuppression?

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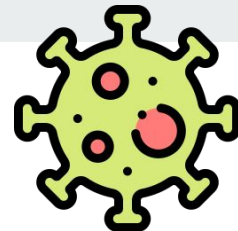
Intravenous immunoglobulins (IVIG)

No trials, mixed results [7][8]

Oral immunoglobulins (POIG)

Oral immunoglobulins have also been used [9]

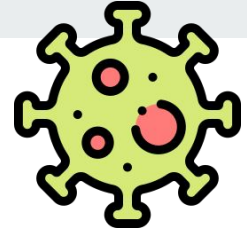
- Usual dosing is **25 mg/kg** given **q6h for 8 doses**
- Must be given **post-pylorically** (via dobhoff) to avoid stomach acid [13]



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

Reducing immunosuppression?

Nitazoxanide? (NTZ)

Mixed data in limited trials [4][6]

Intravenous immunoglobulins (IVIG)

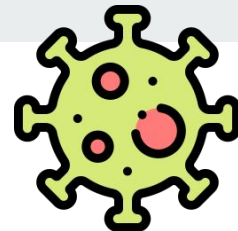
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Oral immunoglobulins (POIG)

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**



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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



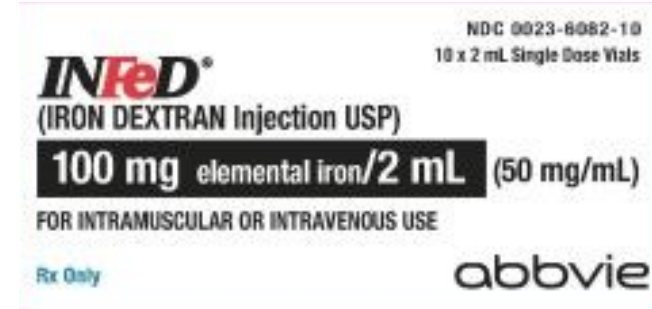
Fevers with IV iron

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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 [\[link\]](#)





Fevers with IV iron

Not the most common side effect, but has been documented

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 [\[link\]](#)

NDC 0517-2340-01

Venofer[®]

(Iron Sucrose) Injection, USP

100 mg Elemental Iron per 5 mL (20 mg/mL)

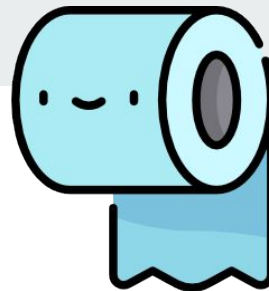
5 mL Single-Dose Vial

Discard Unused Portion

For Intravenous Use Only
Rx Only

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 hunteratliff1.com/talk/; Citations available via QR code or via the "citations" button on the website