DISCLAIMER

Video will be taken at this clinic and potentially used in Project ECHO promotional materials. By attending this clinic, you consent to have your photo taken and allow Project ECHO to use this photo and/or video. If you don't want your photo taken, please let us know.

Thank you!

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Please **DO NOT** disclose any Protected Health Information (PHI)

PHI includes, but is not limited to:

- Patient name
- Date of birth
- Address
- Occupation
- Name of patient's friends/family
- Other identifiable features, i.e. scars, tattoos, hair/eye color

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Antibiotic Stewardship ECHO

AIM Statement: promote appropriate use of antibiotics to improve patients safety and outcomes

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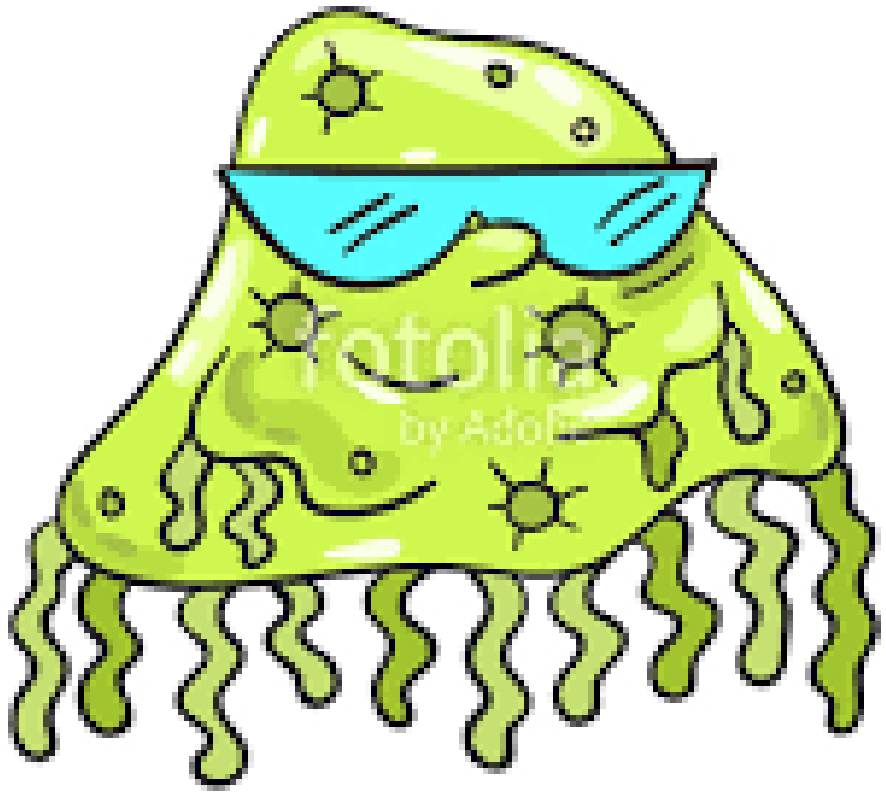
Conflicts of Interest

- None



ASPalooza

11/21/2019

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Patient Case

- 21 yo F G1P0 at 37w6d with no significant PMH who is admitted for non-traumatic acute onset lower pelvic pain with no symptoms of UTI. She gives birth to a health baby boy the next day with no complications. Afterwards, a urinalysis and culture are collected.
- Current medications: simethicone

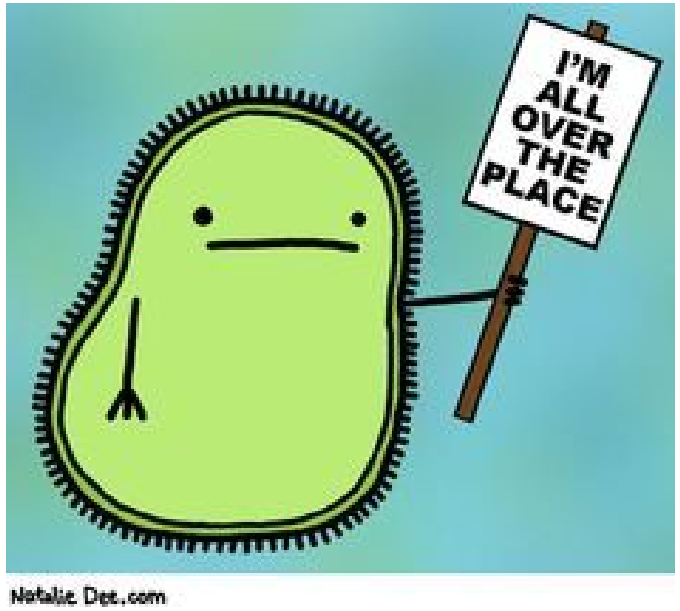
Vitals/Labs	Urinalysis results	Culture Results
T= 98.2^{O}F, HR 80, RR 16, BP116/63, O2 sat = 98% on RA, WBC 7.2 x 10^{9}/L	UA= Nitrite (+), LE (small), WBC 20-50, RBC 2-5, Epithelial cells (few), Bacteria (many)	E. coli >100,000 CFU/mL, resistant only to ampicillin and ampicillin/sulbactam

Should the patient be started on antibiotics?

- Yes
- No

Asymptomatic bacteriuria

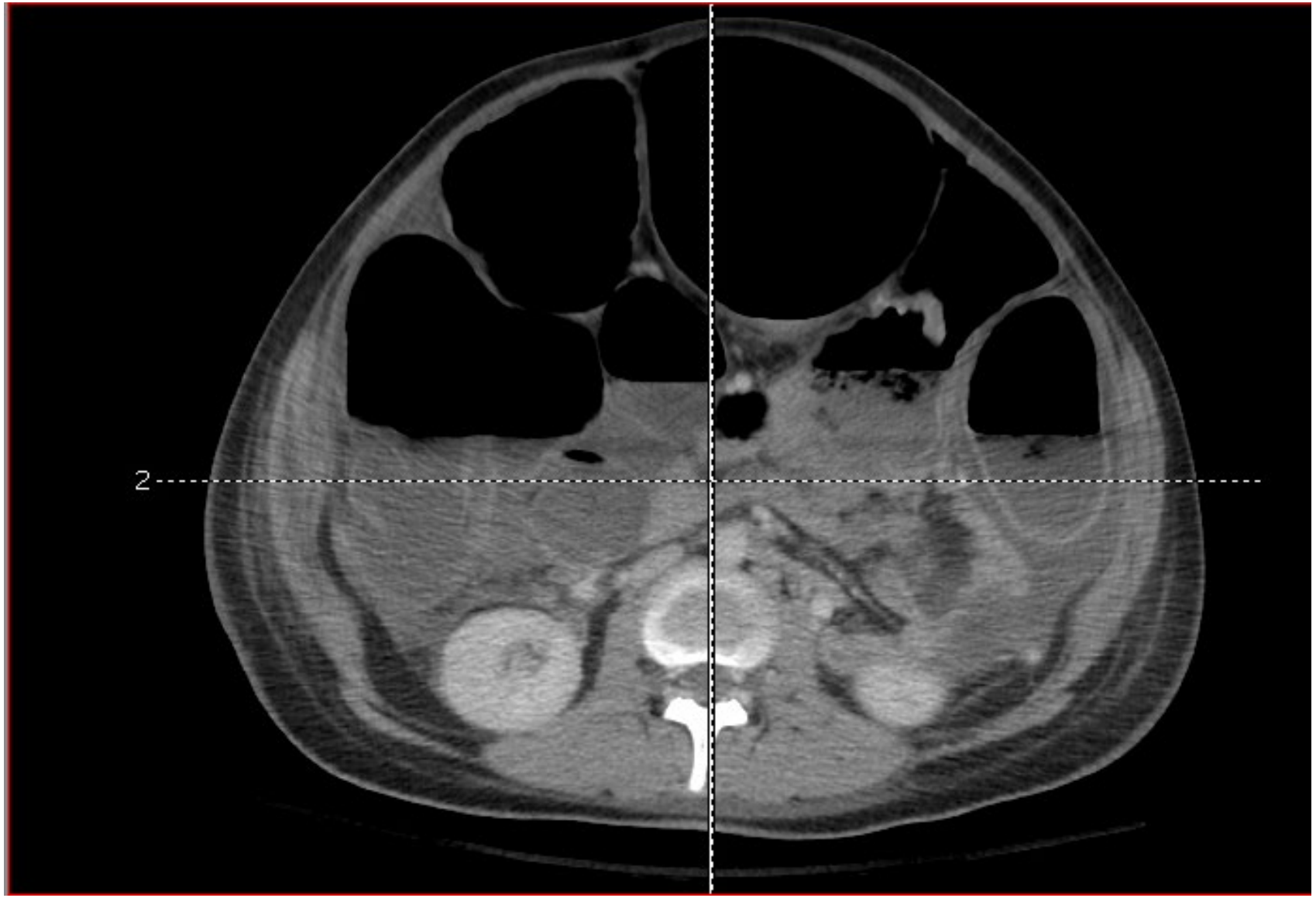
- Presence of bacteria in the urine ($\geq 10^5$ colony-forming units/mL) WITHOUT signs or symptoms of UTI (dysuria, increased frequency, increased urgency, suprapubic pain)
- Should the following patients be treated for asymptomatic bacteriuria, yes or no?
  - Infants and children
  - Healthy non-pregnant women
  - Diabetics
  - Patients with indwelling or suprapubic urinary catheters
  - Elderly and/or functionally impaired
  - Spinal cord injuries
  - Pregnant
  - Undergoing urologic procedure



Patient Case Continued

- The patient is started on a 7 day course of cephalexin 250mg QID x 7 days
- On day 3 of her antibiotic course, she complains of severe abdominal pain with subsequent loose, watery stools (3 within 24 hours)

Vitals	Labs	CT results
T=101.1ºF, BP=86/44, HR 114, RR 16, O2=95% on RA	WBC 14.2, LA 1.6, SCr 0.57, albumin 2.0	Diffuse colonic distension with apparent wall thickening suggesting colitis and probable associated ileus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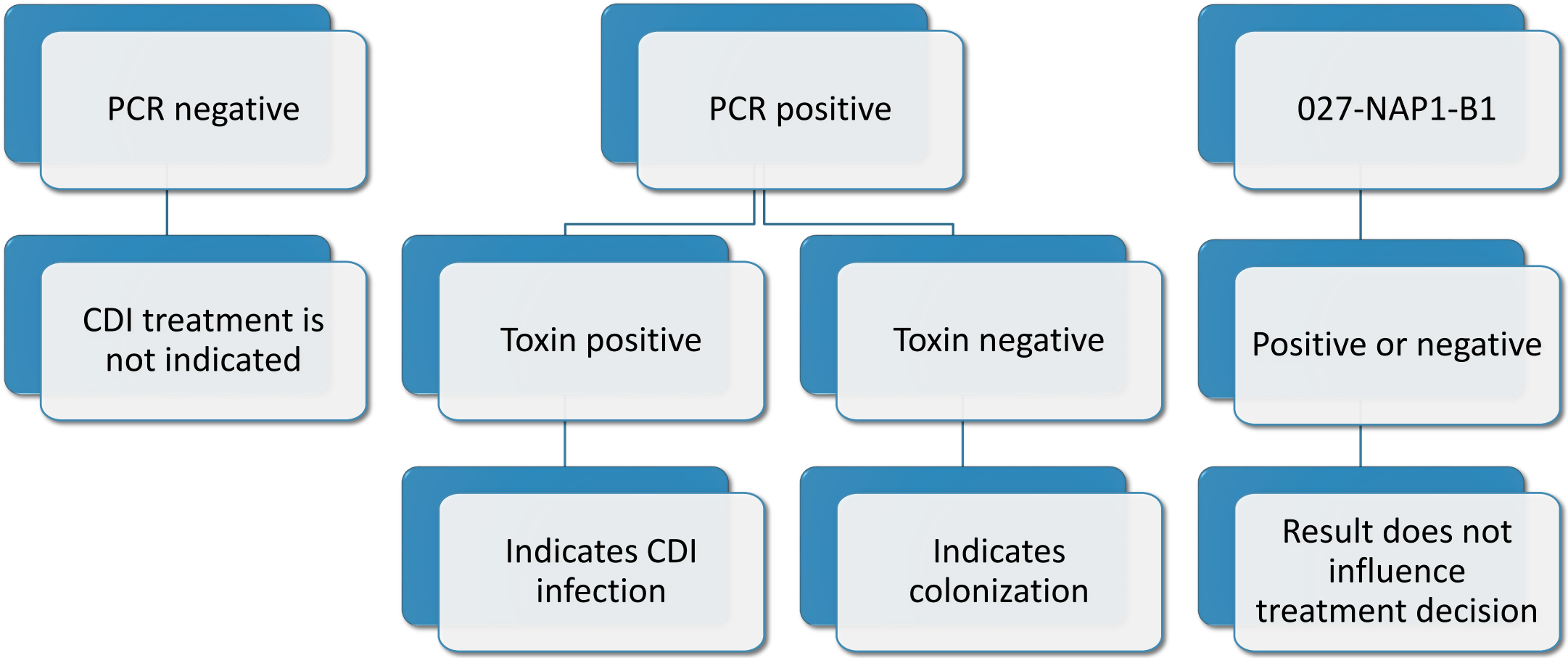
What test would you order next?

C. Diff testing recommendations

- Only submit stool samples from pts with unexplained and new onset $\geq$ 3 unformed stools in 24 hours
  - Check to make sure pt is not receiving laxatives or stool softeners
- Do not perform repeat testing within 7 days
- Do not test for cure

C. Diff testing algorithm



- PCR only tests for the presence of C. diff, it does not mean the pt has active infection
- Toxin tests for the actual toxin itself and makes the diagnosis of C. diff colitis

PCR and toxin tests are positive, which of the following is an appropriate treatment?

- Metronidazole 500mg PO TID X 10 days
- Vancomycin 125mg PO QID x 10 days
- Vancomycin 500mg PO QID + Vancomycin 500mg/100mL enema QID + Metronidazole 500 IV TID

Treatment recommendations for initial episode

Clinical Definition	Treatment Recommendation
Non-severe to Severe	• Vancomycin 125mg PO QID X 10 days Or • Fidaxomicin 200mg PO BID x 10 days • Metronidazole 500mg PO Q8H x 10 days*
Fulminant (hypotension, shock, ileus, megacolon)	• Vancomycin 500mg PO or NG QID PLUS metronidazole 500mg IV Q8H • If ileus consider rectal instillation of vancomycin 500mg/100mL

*Can consider metronidazole 500mg PO TID x 10 days in non-severe cases if the other two agents are unavailable

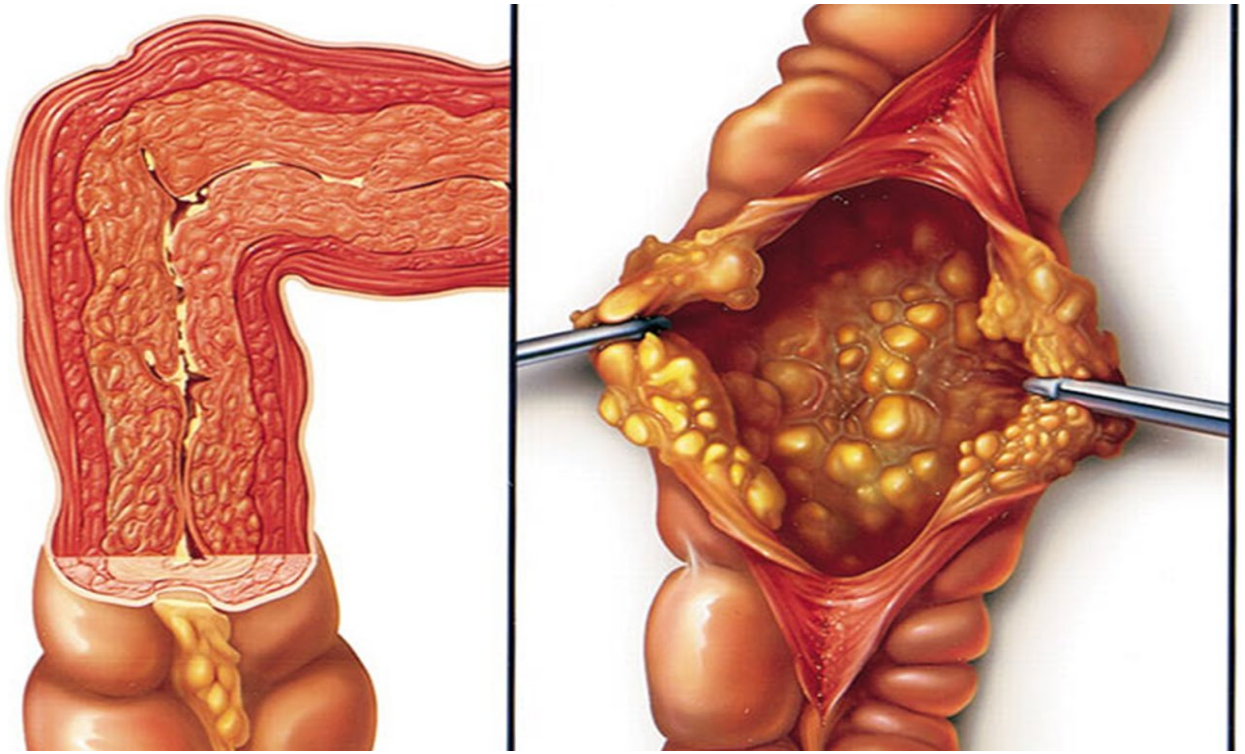
Treatment recommendations for recurrences

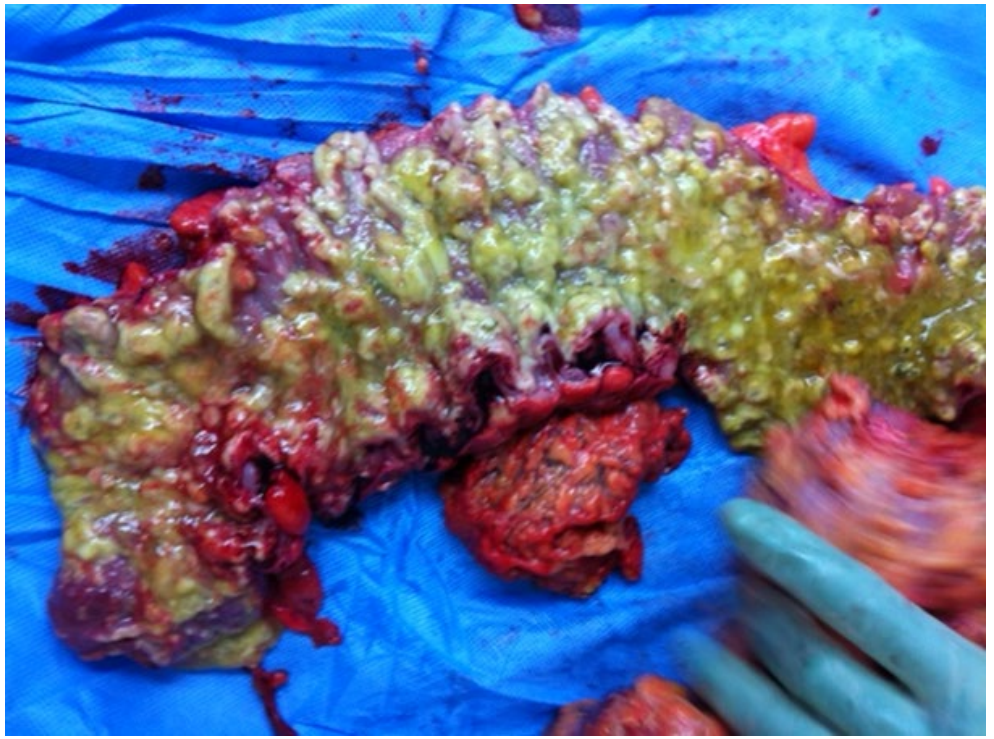
Occurrence	Treatment Recommendation
First recurrence	• 6 week pulsed, tapered vancomycin or • Fidaxomicin 200mg PO BID x 10 days
Second recurrence	• Can consider FMT

Patient case continued

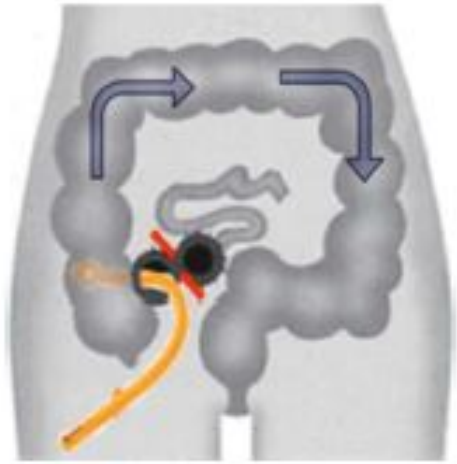
- Pt was taken to OR and found to have a viable colon
- Ileostomy and cecostomy tubes were placed for anterograde vancomycin enemas
- She was started on vancomycin 500mg/100mL anterograde enemas + vancomycin 500mg PO QID + metronidazole 500mg IV Q8H

Usual procedure- sub-total colectomy- 80% mortality with severe morbidity for survivors



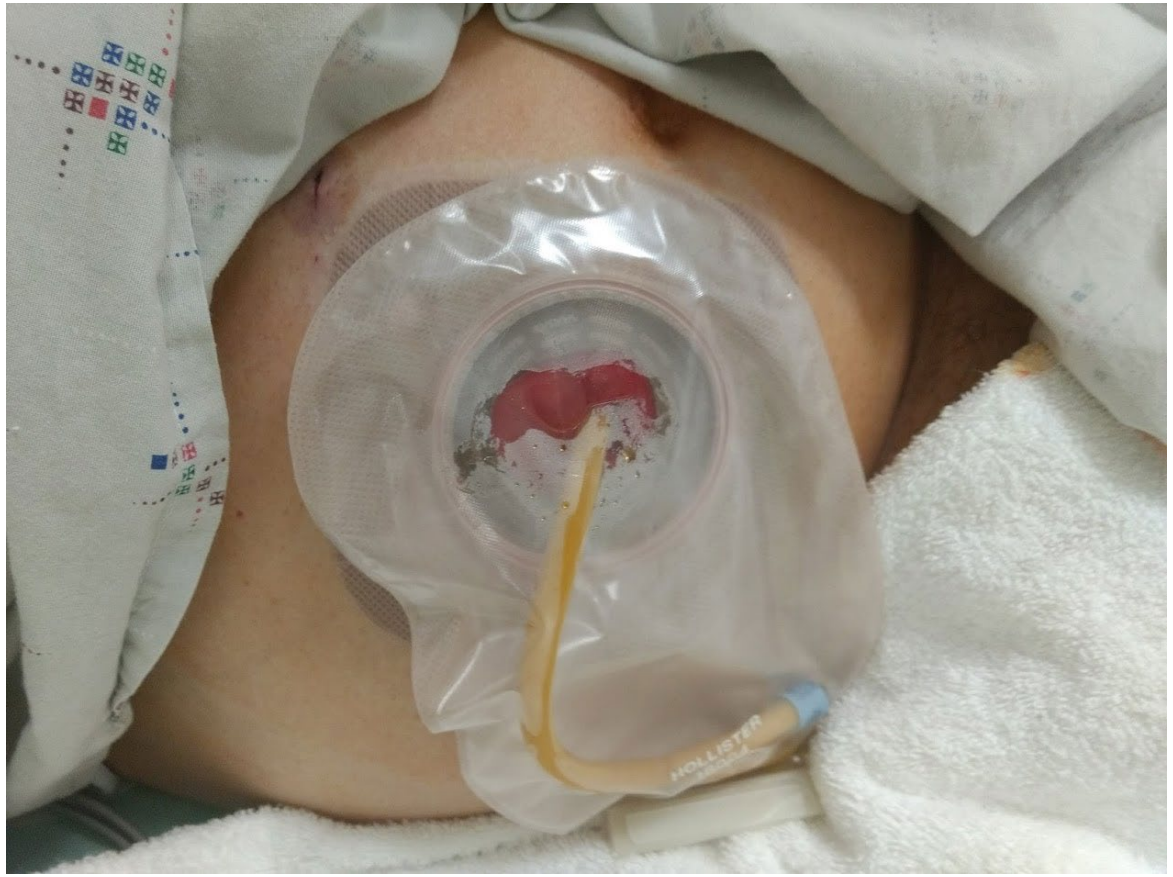


Diverting Loop ileostomy for C. difficle colitis



1. Creation of diverting loop ileostomy
2. Intraoperative antegrade colonic lavage with 8 liters of warmed PEG3350/electrolyte solution via ileostomy.
3. Postoperative antegrade colonic enemas with vancomycin (500 mg in 500 mL X 10 day) via ileostomy

Figure 1 Diverting loop ileostomy and colonic lavage: operative strategy. Reproduced with permission from: Neal MD, Alverdy JC, Hall DE, et al. Diverting loop ileostomy and colonic lavage: an alternative to total abdominal colectomy for the treatment of severe, complicated *Clostridium difficile* associated disease. Ann Surg 2011; 254(3):423–7. Copyright© 2011 Lippincott Williams & Wilkins.



FMT- CAN BE ADMINSTERED VIA Ng TUBE or ileostomy

Patient case f/u

- By day 7 she had improved enough to be transferred to the floor
- She completed 10 days of treatment, then proceeded quickly to tolerating a regular diet
- She was discharged home 2 days after finishing treatment with plans to reverse her ostomy ~6 weeks later

If you were to treat with probiotic, what dose would you use to prevent a recurrence?

- 2 billion CFU
- 6 billion CFU
- 24 billion CFU
- 50 billion CFU

What is a “probiotic”?

- Definition: “Live microorganisms which when administered in adequate amounts **confer a health benefit on the host**”
- Is there ANY evidence these supplements deserve to be called “probiotics”?

Do Probiotics PREVENT C. diff?

"No impact of Probiotics to Reduce *Clostridium difficle* Infection in Hospitalized Patients: A Real-world Experience" MJ Box.et al. Open forum Infect. Disease. Dec 2018.
Scripps Health , San Diego, CA

- Based on the probiotic regimen used in previous studies which claimed positive results, Scripps developed a combination supplement with L. acidophilius, L. casei , and L. rhamnosus
- Large 400 bed community hospital
- Made it available for physicians, at their discretion, to prescribe this probiotic regimen for their patients on iv antibiotics. 1576 patients – about half on probiotics- in the study
- Multi-variate analysis to correct for severity of illness, length of antibiotic treatment, but not by actual antibiotic used.
- No difference in HO-CDI rate (1.8%) in either group

Scripps Hospital Probiotic Study Conclusion:

- “Antibiotic use is the most important modifiable risk factor for HO-CDI in acute care hospitals. The CDC estimates that at least 30% of antibiotic use is unnecessary. Based on these findings, our institution **removed all probiotics from the formulary**. Instead, we **endorse strong antimicrobial stewardship practices** that are shown to be efficacious and caution that probiotics may consume health care resources without adding additional benefit”

Probiotics AFTER fecal transplant?

"Risk of *C. difficile* Infection with Systemic Antimicrobial Therapy Following Successful Stool Transplant: Should we recommend Anti-*C. difficile* Antibiotic Prophylaxis?" Alegretti et al. Digestive Diseases and Sciences January 10 2019 on-line

Looked at long term risks of relapse in patients 1 to 2 years after Fecal transplant (FMT) who needed antibiotics. Is there any evidence to suggest the prophylactic use of either oral vancomycin **or** probiotics reduce risk of relapse when given with antibiotics in these high-risk patients.

This study surprisingly found that in this group of patients with prior FMT receiving antibiotics these interventions had either no benefit (vancomycin) or **increased the risk (with probiotics) of CDI developing!**

Doesn't make sense- Why would probiotics actually be detrimental to these patients ???

Predictors of Clostridioides difficile recurrence across a national cohort of veterans in outpatient, acute, and long-term care settings

Haley J Appaneal, Pharm.D, Aisling R Caffrey, Ph.D, Maya Beganovic, Pharm.D, Sanja Avramovic, Ph.D, Kerry L LaPlante, Pharm.D

American Journal of Health-System Pharmacy, Volume 76, Issue 9, 1 May 2019, Pages 581–590

- VA STUDY RESULTS:

They identified 32 independent predictors of first CDI recurrence among 974 cases and 3,896 matched controls. They found the usual offenders (quinolones, PPIs, cancer etc) increased the risk of C. diff, but also reported "probiotics" prescribed both BEFORE and as well as AFTER CDI treatment increased the relapse rate

"Post-antibiotic Gut Mucosal Microbiome Reconstitution is impaired by Probiotics and Improved by Autologous FMT" Suez, J et. al. Cell Sept 6, 2018 1406-23.

- In this study, researchers wanted to know what happens in the gut when a person follows up a course of antibiotics with probiotic supplements, and how long does the gut microbiome take to get back to a healthy balance after that.
- 21 healthy volunteers took one week of broad spectrum anti-microbial therapy with oral ciprofloxacin and metronidazole to severely disrupt the gut microbiome . They then were assigned to 1 of 3 study arms:

1. 4 weeks of a BID **probiotic supplement** containing all the commonly used bacterial strains
2. **Autologous FMT** with their own stool collected prior to the antibiotic course
3. **No intervention-** watchful waiting

Which group recovered their healthy microbiome the quickest?

Which group took the longest by a long shot to recover and why?

Results

QUICKEST- As expected, the FMT group had quick restoration of their normal microbiome

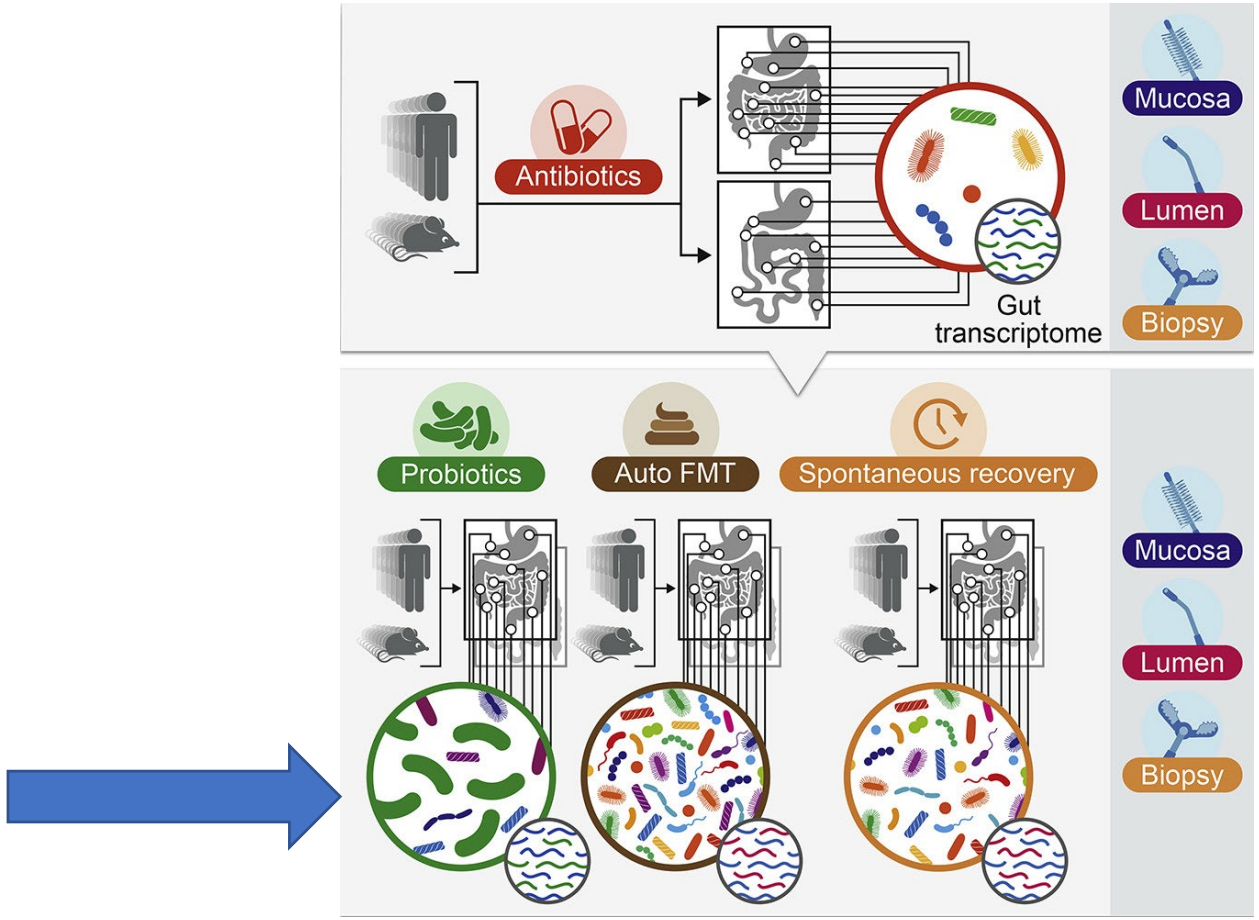
SECOND-The watchful waiting group had recovery of their microbiome, but at a slower pace than the FMT

PROBIOTC GROUP WAY SLOWEST!- With their own microbiome now wiped out, everyone in group 1 who took the probiotic became fully colonized by the probiotics. the probiotic group- took far longer to return to a normal fecal microbiome than the other 2 groups- even after the 6 month f/u period of the study. So the probiotic actually delayed, not enhanced, microbiome recovery

Could that be why in the earlier study the use of probiotics actually increased the risk of C. diff in FMT patients treated with antibiotics ?

Study Conclusion: Probiotics given after a course of antibiotics significantly delays return of the healthy colon microbiome compared to not taking them at all or after receiving a FMT

Intestinal culture-probiotics block recovery of healthy colon microbiome



Case presentation-
68-year-old male cancer patient presents with fever, diarrhea and bacteremia

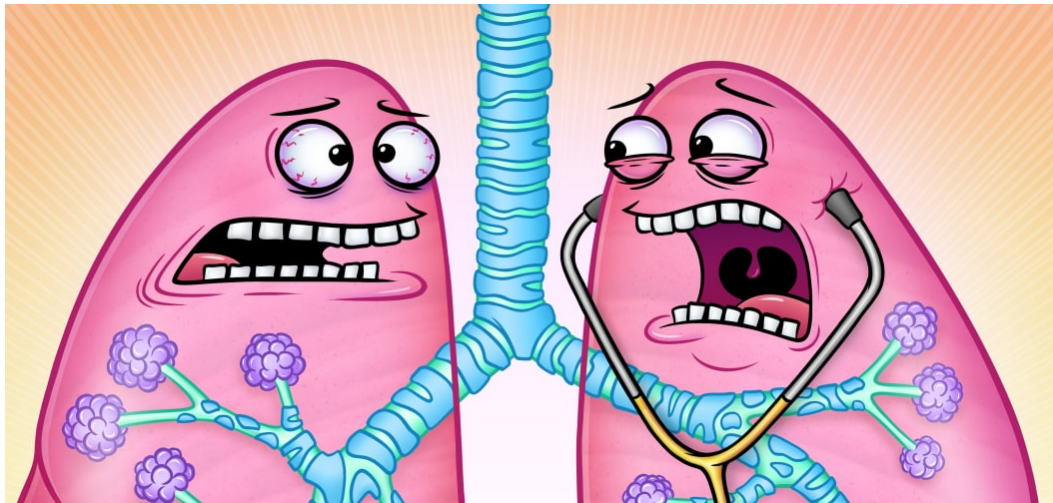
- patient has metastatic colon cancer and is undergoing intensive chemotherapy through a portacath. Just finished cycle # 10 of planned 12, has been getting diarrhea with each cycle. Has been on long-term daily OTC probiotic supplements at his wife's request.
- This cycle he has the usual post-chemo diarrhea, but now accompanied by onset of fever and rigors. Admitted to hospital.
- WBC 34,000. C-diff test negative
- Initially started on empiric broad spectrum antibiotics, then all blood cultures (drawn both via portacath and peripheral sites) become positive for *Lactobacillus* species. We suspected bacterial translocation of the inflamed colon by probiotic supplement
- Porta Cath pulled and patient completes course of ampicillin therapy.
- He and his wife agree he will stop taking "probiotics"

Is there any role for “probiotics” for prevention or treatment of C. diff colitis?
Should we just call it “sour milk” instead?

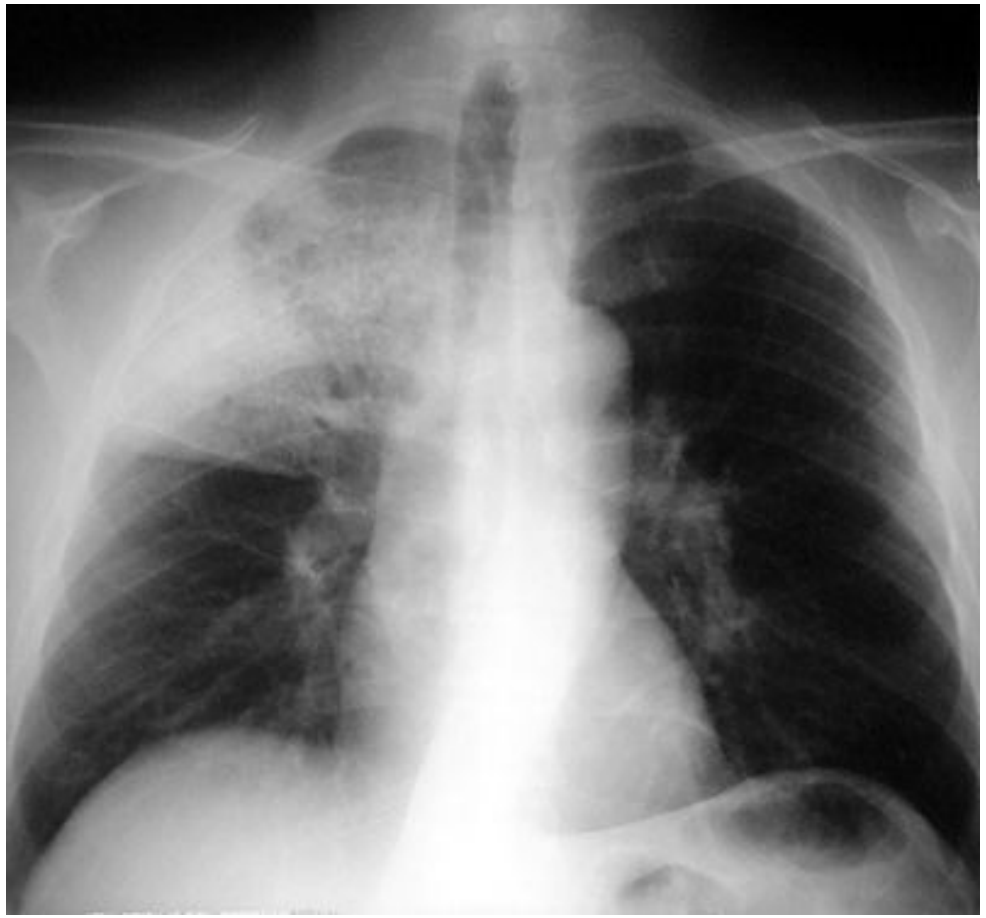
- Is there any evidence that prophylactic use of presently available probiotic formulations reduces risk of antibiotic associated C. diff colitis?
- Not recommended in latest 2017 Guidelines
- Can probiotics cause lactobacillus bacteremia when colitis develops?
- Can probiotics delay recovery of normal fecal microbiome after antibiotic exposure and increase risk of CDI developing ?
- Can probiotics increase the risk of recurrent C. diff in Fecal transplant patients receiving antibiotics ?
- Do probiotics seem like a waste of money?
- Is Antibiotic Stewardship what is critical to prevent CDI???

CAP Case

- 55 yo female with presents to the ED with a 2-day history of progressive fatigue, cough, and SOB
- On physical exam:
  - T = 100.4 degrees F, BP 92/54, HR 124 bpm, RR 40 BPM, O2 sat 82% on RA
  - Decreased air movement in all lung fields
- Labs: WBC 14.4, PLT 213, SCr 0.79, BUN 22, LA 4.1
- CXR: “Right upper lobe infiltrate”
- Respiratory status worsens rapidly and pt is intubated, put on pressors, and admitted to the ICU



Right upper lobe pneumonia



Empiric antibiotics are started. Is there a point in obtaining a procalcitonin for this patient ?

A. Yes – to discontinue antibiotics immediately if procalcitonin is negative (<0.25)
B. Yes – to limit duration of therapy
C. No – empiric antibiotics have been started. All is lost

True or False

- The 2019 CAP Guidelines recommend all patients with CAP, from mild cases to ICU intubated cases, need to have blood and sputum cultures obtained on admission to improve patient's treatment and outcomes

- CXRs must be repeated before discharge to confirm resolving pneumonia

No risk factors for resistant organisms are known in this case. Which of the following is an appropriate initial regimen?

A. Piperacillin-tazobactam (Zosyn) + vancomycin + azithromycin
B. (Azithromycin or doxycycline) + ceftriaxone
C. Levofloxacin

What would be indications for MRSA or Pseudomonas coverage in this patient?

A. Respiratory cultures positive for MRSA or resistant gram- negative organisms (i.e. Pseudomonas) in the past year
B. IV antibiotic use within the past 90 days **AND** severe pneumonia
C. Patient intubated and/or on pressors
D. A and B
E. A, B, and C

You later learn from her family that patient was recently hospitalized and given IV antibiotics for pneumonia. Would you change your answer?

A. Piperacillin-tazobactam (Zosyn) + vancomycin + azithromycin
B. (Azithromycin or Doxycycline) + ceftriaxone
C. Levofloxacin

How long would you treat if all cultures are negative and patient achieves clinical stability within 48-72 hours?

A. 5 days
B. 7 days
C. 10 days
D. 14 days
E. Until repeat CXR clears