Head to Toe Antibiotics:
Treatment Decisions for Common Outpatient Infections

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Disclosure

I have no financial interests or relationships to disclose.

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Head to Toe Antibiotics

- Idea is to examine meaningful antibiotic-related issues and resources for select outpatient conditions
- Remember, each syndrome is normally a hour long CME talk, here we will emphasize a specific aspect of antibiotic care and then move on

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The Five D's of Antimicrobial Stewardship

- Drug
- Dose
- Duration
- De-escalation
- Diagnosis

Emerg Med Clin North Am 2018;36(4):853

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34-year-old Man

- URI was getting better now has 4 days of purulent nasal drainage, congestion and headache
- Has tried decongestants and sinus irrigation
- Otherwise, healthy, no recent antibiotics
- You decide to treat with amoxicillin/clavulanate

How Long Will You Treat?

A. 3 days
B. 5-7 days
C. 10-14 days
D. 21 days
E. I would not have prescribed an antibiotic

IDSA 2012 Guidelines	ENT 2025 Guidelines
X. Should Empiric Antimicrobial Therapy for ABRS Be Administered for 5–7 Days Versus 10–14 Days? ***Recommendations*** 14. The recommended duration of therapy for uncomplicated ABRS in adults is 5–7 days (weak, low-moderate).	*Statement 5. Choice and Duration of Antibiotic for Acute Bacterial Rhinosinusitis (ABRS)* **If a decision is made to treat ABRS with an antibiotic agent, the clinician should prescribe amoxicillin with or without clavulanate as first-line therapy for 5-7 days for most adults.**

Effectiveness and safety of short *vs.* long duration of antibiotic therapy for acute bacterial sinusitis: a meta-analysis of randomized trials

Matthew E. Falagas,[1,2,3] Drosos E. Karageorgopoulos,[1]

12 RCT studies
3-7 days vs 6-10 days
No difference
Efficacy
Microbiologic efficacy
Relapse rates
Adverse effects
When 5 days compared to 10 days
Less adverse effects in 5 day group

Duration — We suggest an initial antibiotic treatment course of five to seven days. We typically give a prescription for seven days but inform patients they can stop after five days if symptoms have improved. Available evidence suggests that response rates with this duration are similar and associated with fewer adverse events than longer courses [3,4]. UpToDate Uncomp ABRS

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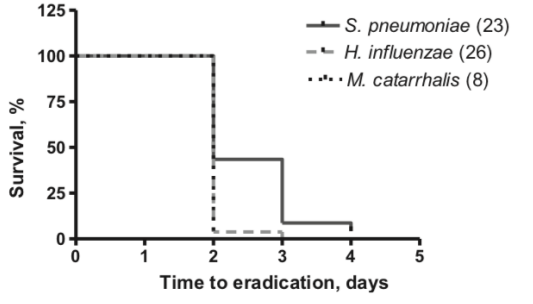

Figure 4. Time to bacterial eradication from the maxillary sinus in patients with acute bacterial rhinosinusitis (ABRS) following initiation of therapy with respiratory fluoroquinolones (N = 50; multiple pathogens were isolated from some patients) [22, 143, 192].

Clin Inf Dis 2012;54(8):e52

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Antibiotic Therapy Duration in US Adults With Sinusitis

Laura M. King, MPH[1]; Guillermo V. Sanchez, PA-C, MPH[1]; Monina Bartoces, PhD[1]; et al

» Author Affiliations | Article Information

JAMA Intern Med. 2018;178(7):992-994. doi:10.1001/jamainternmed.2018.0407

- 70% of courses were 10 days or longer
- When azithromycin scripts (24% of all) were excluded
  - 92% of courses were 10 days or longer
  - 7.6% were for 7 days
  - 0.5% were for 5 days
- No penicillins or tetracyclines were for 5-day courses
- Only 5% of courses were for a 7 day course of a penicillin, tetracycline, or fluoroquinolone

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When Is Sinusitis Not Uncomplicated?

- Comorbidities
  - Immunocompromised, facial trauma, surgery
- Nonstandard pathogens/drug resistance
- Complications of sinusitis
  - Soft tissue, orbital, intracranial
- Frontal, ethmoid?
  - Most discussions focus on maxillary sinusitis

Follow-up no later than the 5-7 day mark. Lack of treatment response or worsening during therapy suggests drug resistance, anatomic or other complicating issue, or the wrong diagnosis.

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68-year-old Woman

- COPD, usually well controlled
- Increased sputum amount and purulence
- Using Oxygen more than normal
- CXR is clear
- You prescribe doxycycline for suspected acute exacerbation of COPD

How Long Will You Treat?

A. 3 days
B. 5 days
C. 7 days
D. 10 days
E. I would not have prescribed an antibiotic

Global Initiative for Chronic Obstructive Lung Disease **2025 REPORT**

- Antibiotics should be used for COPD exacerbations when
  - 3 cardinal symptoms present: increase in dyspnea, sputum volume, and sputum purulence or 2 of these if increased purulence is one
  - Mechanical ventilation (invasive or noninvasive)
- Choice of empiric therapy
  - Amoxicillin/clavulanate, macrolide, doxycycline or in selected pts, quinolone
  - Based on local antibiotic resistance and recency of use
  - Duration for outpatient AECOPD: ≤ 5 days

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Clinical Guidelines | June 2021

Appropriate Use of Short-Course Antibiotics in Common Infections: Best Practice Advice From the American College of Physicians

Best Practice Advice 1:

Clinicians should limit antibiotic treatment duration to 5 days when managing patients with COPD exacerbations and acute uncomplicated bronchitis who have clinical signs of a bacterial infection (presence of increased sputum purulence in addition to increased dyspnea, and/or increased sputum volume).

Annals Int Med 2021;174(6):822

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2025 ATS CAP Clinical Practice Guideline

- Antibiotic duration for CAP
  - "For adult outpatients with CAP who reach clinical stability, we suggest less than 5 days of antibiotics (minimum of 3 days duration) rather than five or more days of antibiotics. This is a conditional recommendation that requires individualization. Overall the committee's certainty in the quality of the evidence was low."

Comment: Guideline is not for patients with immunocompromise. Four studies are cited to support this recommendation using antibiotics and doses that are not considered appropriate treatment by the IDSA/ATS. Reader is referred to Table 1 for individual patient factors that strengthen or weaken recommendations.

Am J Respir Crit care Med 2025 Jul 18.

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			Strengthen	Weaken
3. Antibiotic duration for CAP				
For adult outpatients with CAP who reach clinical stability*, we suggest less than five days of antibiotics (minimum of 3 days duration), rather than five or more days of antibiotics. The duration of antibiotics should be determined based upon daily assessment of clinical stability.	Conditional Low-quality evidence		Higher risk of harm from prolonged antibiotic exposure (History of *C. difficile*, or an antibiotic adverse event) Patient preference to minimize antibiotic exposure	Barriers to self assessment, follow-up, or communication to ensure recovery Organism requiring longer duration (i.e., *Staphylococcus aureus, Pseudomonas aeruginosa*, suspected *Legionella pneumophila* or other intracellular microorganisms)** Radiographic findings (high burden of disease, necrotizing process, dense consolidations) Underlying lung disease (e.g., bronchiectasis, post-obstructive pneumonia, chronic respiratory insufficiency**) Recent Hospitalization or resident in Long-term care**

2025 ATS CAP Guideline. Table 1 excerpt

Am J Respir Crit care Med 2025 Jul 18.

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Antibiotic courses should not be implemented as set duration for all patients determined at presentation, since many patients have contraindications to shorter durations, and time to clinical stability is difficult to predict on presentation. The duration of antibiotics should be determined day by day based on clinical responses.

2025 ATS CAP Guidelines. “For inpatients with non-severe CAP”

Am J Respir Crit care Med 2025 Jul 18.

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Carolina Antimicrobial Stewardship Program

med.unc.edu/casp

Best Practices for Duration of Antimicrobial Therapy for the Most Common Infectious Syndromes

Too often, patients receive longer-than-needed antimicrobial treatment for common infections, when a shorter duration would be equally effective.

Duration recommendations are provided as a general guideline for therapy (IV or PO) with a goal of minimizing unintended consequences to the patient (e.g., precipitating *C. difficile* colitis, development of resistant pathogens, organ dysfunction). Patient-specific factors should influence duration decisions and transition to oral therapy.

SYNDROME	DURATION	COMMENTS	EVIDENCE
Lower respiratory tract infection			
Acute bronchitis	0 days (do not treat, 90% of cases are viral)		
Tracheitis	0 days (do not treat, treatment is not associated with clinical benefit)		
Community-acquired (CAP)	5 days minimum	Consider IV to PO switch if patient <38°C for 48-72 hours and no more than 1 CAP-associated sign of clinical instability	CAP, IDSA (CID 2007;4(S2):S27
Hospital-associated (HAP)	7 days		HAP/VAP, IDSA (CID 2016;63:e61)
Ventilator-associated (VAP)	7 days		
Acute exacerbation of COPD and chronic bronchitis	5 days	Reserve antibiotics for patient with acute exacerbation with physiologic compromise on top of chronic bronchitis or for COPD for patients with physiologic compromise, and worsening sputum purulence and either increased dyspnea or frequency of cough.	Bronchitis/COPD, HEDIS (link), Am Fam Physician 2016; 94:560-65.

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Shorter Is Better

Diagnosis	Short (d)	Long (d)	Result	#RCT
CAP	3-5	5-14	Equal	14
Atypical CAP	1	3	Equal	1
Possible PNA in ICU	3	14-21	Equal	1*
VAP	5-8	10-15	Equal	3
Empyema	14-21	21-42	Equal	2
Cystic Fibrosis Exacerbation	10-14	14-21	Equal	1
Bronchiectasis Exacerbation	8	14	Equal	1
cUTI/Pyelonephritis	5 or 7	10 or 14	Equal	13**
Intra-abd Infection	4	8-10	Equal	3
Complex Appendicitis	1-2	5-6	Equal	2
Bacteremia (non *S. aureus*)	7	14	Equal	4†
Cellulitis/Wound/Abscess	5-6	10	Equal	4‡
Osteomyelitis	42	84	Equal	2
Osteo Removed Implant	28	42	Equal	1
Debrided Diabetic Osteo	10-21	42-90	Equal	2Φ
Septic Arthritis	14	28	Equal	1
Bacterial Meningitis (peds)	4-7	7-14	Equal	6
AECB & Sinusitis	≤5	≥7	Equal	>25
Variceal Bleeding	2-3	5-7	Equal	2
Neutropenic Fever	AFx72h/3 d	+ANC>500/9 d	Equal	2
Post Op Prophylaxis	0-1	1-5	Equal	57Ψ
Erythema Migrans (Lyme)	7-10	14-20	Equal	3
P. vivax Malaria	7	14	Equal	1
Early Syphilis	1 IM	3 IM in 3 wks	Equal	2
Total: 24 Conditions				>150 RCTs

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Home from the Hospital!

52-year-old Woman with Bacteremia

Past history of uterine fibroids, otherwise healthy.

Multiple supplements protein, immune and bone health

Admitted with fever, dysuria, flank pain.

Urine and blood cultures grow *E. coli,* resistant to TMP/SMX but otherwise susceptible.

Started on ceftriaxone. Hospital day 2 improved.

Discharged day 3 with levofloxacin to finish 7 days.

How Can We Be the Best Antibiotic Steward for This Patient?

A. Do a detailed medication reconciliation
B. Order repeat renal US to make sure oral therapy is working
C. Call the hospitalist, stop the quinolone and change to IV ceftriaxone
D. Call the pharmacy, stop the quinolone and change to oral nitrofurantoin

Chavada *et al. BMC Infectious Diseases* (2018) 18:225
https://doi.org/10.1186/s12879-018-3147-0

BMC Infectious Diseases

RESEARCH ARTICLE Open Access

'Careful goodbye at the door': is there role for antimicrobial stewardship interventions for antimicrobial therapy prescribed on hospital discharge?

R. Chavada[1*], J. Davey[2], L. O'Connor[2] and D. Tong[3]

263 antibiotic discharge scripts over a 4 week period

74% Appropriate choice
64% Appropriate dose
64% Appropriate frequency
21% Appropriate duration (71% were too long)
50% Appropriate micro specimens taken
18% Directed therapy based on susceptibility testing

How Would Your Facility Fare?

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Review

Revisiting Oral Fluoroquinolone and Multivalent Cation Drug-Drug Interactions: Are They Still Relevant?

Stuart K. Pitman [1,2,*], Uyen T. P. Hoang [1], Caren H. Wi [1], Mona Alsheikh [1], Dakota A. Hiner [1] and Kelly M. Percival [2]

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check for updates

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Oral fluoroquinolone-multivalent cation drug-drug interactions first came into focus in the latter half of the 1980s as detailed in several case reports, drug-drug interaction studies, and reviews. Today, oral fluoroquinolone-multivalent cation interactions are firmly established. However, unawareness among the healthcare team, perhaps due to the passage of time or due to the presence of drug-interaction-electronic-alert fatigue, may allow for many of these interactions to undergo suboptimal review or even persist unnoticed [9]. This concise and focused review describes the oral fluoroquinolone-multivalent

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Pharmacokinetics vs Pharmacodynamics

- Bioavailability
  - Levofloxacin 99%
  - Moxifloxacin 89%
  - Ciprofloxacin 70%
  - Delafloxacin 59%

Rate and extent to which the active ingredient or active moiety is absorbed from a drug product and becomes available at the site of drug action

- Concentration dependent killing
  - AUC/MIC ratio
  - $C_{MAX)}$/MIC ratio

What does this mean to the clinician? We have to make sure that quinolones are dosed properly and taken properly to optimize AUC and C_{MAX}

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Table 1. Reported area under the concentration-time curve (AUC) and peak concentration (Cmax) alterations with co-administered oral fluoroquinolone-multivalent cation pairs [17,19–21].

Fluoroquinolone	Cation	Mean Reduction in AUC Compared to Quinolone Alone	Mean Reduction in Cmax Compared to Quinolone Alone
Ciprofloxacin	Aluminum with Magnesium	85%	80%
	Aluminum	85%	81%
	Sucralfate	88% [a]	90–96% [a]
	Calcium [b]	41[c]–42%	38[c]–47%
	Iron Preparations [d]	42–64%	33–57%
	Multivitamin Preparation Containing Zinc, Magnesium, Calcium, Manganese, Copper, and Iron	52%	53%
	Multivitamin Preparation Containing Zinc and Copper	23%[e]	Not tested
Levofloxacin	Aluminum Hydroxide	44%	65%
	Magnesium Oxide	22%	38%
	Ferrous Sulfate	19%	45%
	Calcium Carbonate	3%	23%
Moxifloxacin	Sucralfate[f]	60%	71%
	Aluminum Hydroxide and Magnesium Hydroxide	59%	61%
	Ferrous sulfate[g]	39%	59%
	Calcium[h]	3%	16%

Antibiotics 2019;8(3):108

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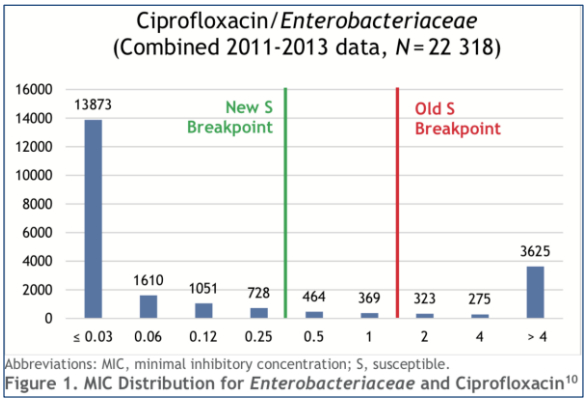
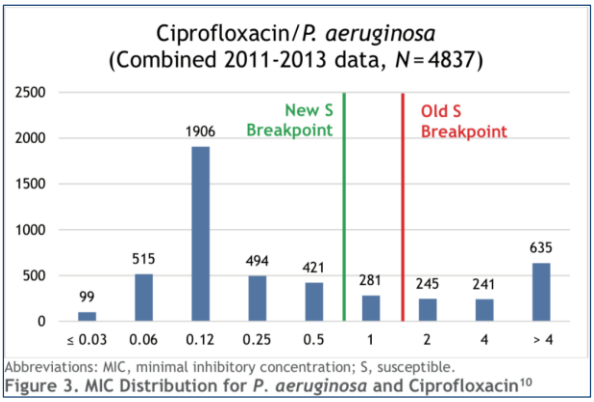
Why *Pseudomonas aeruginosa* Can Get Resistant So Quickly During Therapy



Abbreviations: MIC, minimal inhibitory concentration; S, susceptible.

Figure 1. MIC Distribution for *Enterobacteriaceae* and Ciprofloxacin[10]



Abbreviations: MIC, minimal inhibitory concentration; S, susceptible.

Figure 3. MIC Distribution for *P. aeruginosa* and Ciprofloxacin[10]

clsi.org/media/3011/mr02ed1.pdf

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Table 3. Manufacturer-recommendation dose spacing.

Oral Drug	Administration Recommendation Per Prescribing Information
Delafloxacin [23]	Administer delafloxacin at least 2 h before or 6 h after antacids containing magnesium, or aluminum, with sucralfate, with metal cations such as iron, or with multivitamin preparations containing zinc or iron
Moxifloxacin [35]	Administer moxifloxacin tablets at least 4 h before or 8 h after antacids containing aluminum or magnesium, with sucralfate, with metal cations such as iron, or with multivitamins containing iron or zinc
Ciprofloxacin [37] *	Administer ciprofloxacin at least 2 h before or 6 h after magnesium/aluminum antacids; sucralfate; multivitamin preparations with zinc; or other products containing calcium, iron or zinc
Levofloxacin [38] **	Administer levofloxacin at least 2 h before or 2 h after antacids containing magnesium, aluminum, as well as sucralfate, metal cations such as iron, and multivitamin preparations with zinc

* Applies to both the immediate and extended release tablets; also applies to the oral suspension. ** Applies to both the tablet and oral solution formulations.

Antibiotics 2019;8(3):108

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Fluoroquinolones and Multivalent Cations

Management Options

1. Select a different antibiotic, keep the cation
2. Give the fluoroquinolone IV
3. Temporarily stop, substitute for, or decrease the frequency of the cation
4. Space out the quinolone and cation to avoid interaction

Antibiotics 2019;8(3):108

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Fluoroquinolones and Multivalent Cations

Practical Side

Recognize the interaction by doing a good history

Assess the relative impact of the interaction

Individualize the management strategy

Inpatient vs SNF vs Home – can the plan work everywhere?

"When encountering a drug-drug interaction between an oral multivalent cation and an oral fluroquinolone, the health care team must pause and seriously consider this drug-drug interaction, and chose a management strategy appropriate for the particular interaction and patient"

Antibiotics 2019;8(3):108

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Consider This When Prescribing

- Pressure to decrease fluoroquinolone prescribing
- Means that when we do, the stakes often are higher
  - Early IV to po switch, resistant organism, severe infection
- High bioavailability in theory is only as good as it is today in an individual patient
- Still relevant today? (tetracyclines too)

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78-year-old Man

- Treated for Herpes zoster of his left flank with valacyclovir 1 gram po TID x 10 days
- At day 6 he presents with dyspnea and edema
- Zoster lesions are in various stages of active/healing
- Scr 4.6 mg/dL (baseline 1.8 mg/dL)

Critique?

A. Not the best choice
B. Not the best dose
C. Not the best monitoring
D. B and C

Acyclovir and Herpes

- Acyclovir EC_{50} for VZV is ~ 10-fold greater than HSV
  - Markedly different dosing regimens for each virus
- Bioavailability
  - Acyclovir 15-30%, Valacyclovir 54%
  - AUC_8 valacyclovir 1gm po TID ~ acyclovir 5mg/kg IV q8h
- Renal
  - Dose adjustment needed in renal impairment
  - Toxicity = crystals or AIN can be rapid

Antiviral Therapy of HSV-1 and HSV-2, Kimberlain DW and Whitley RJ. Human Herpesviruses:Biology, Therapy and Immunoprophylaxis, 2007

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Acute kidney injury and acyclovir-associated encephalopathy after administration of valacyclovir in an elderly person with normal renal function

A case report and literature review

Valacyclovir-associated acute kidney injury and encephalopathy in an elderly woman with normal kidney function: a case report

Concurrent Nephrotoxicity and Neurotoxicity Induced by Oral Valacyclovir in a Patient With Previously Normal Kidney Function

ORIGINAL ARTICLE: ACUTE KIDNEY INJURY AND ICU NEPHROLOGY

Associations between Different Antivirals and Hospital-Acquired Acute Kidney Injury in Adults with Herpes Zoster

Literature Revival?

Medicine (Baltimore) 2021;100(21): e26147;CEN Case Reports 2023;12:221-25; Clin J Amer Soc Nephro 2024;19(6):694-703; Cureus 2022;14(3):e23693

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78-year-old Man

- Treated for Herpes zoster of his left flank with valacyclovir 1 gram po TID x 10 days
- At day 4 he presents with dyspnea and leg edema
- Zoster lesions are in various stages of active/healing
- Scr 4.2 mg/dL (baseline 1.8 mg/dL)

Many Considerations When Treating "Uncomplicated" Shingles

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Valacyclovir

- Dose adjust, hydrate, stop optional nephrotoxic meds, and even if baseline renal function is normal FOLLOW the clinical and Scr responses

Table 1 Dosage Adjustments for Adults Renal Insufficiency

	Creatinine Clearance(mL/min)			
	≥ 50	30 to <50	10 to <30	< 10
Herpes Zoster	1000 mg every 8 hours†	1000 mg every 12 hours	1000 mg every 24 hours	500 mg every 24 hours

Acute renal failure: May occur in elderly patients (with or without reduced renal function), patients with underlying renal disease who receive higher-than-recommended doses of VALTREX for their level of renal function, patients who receive concomitant nephrotoxic drugs, or inadequately hydrated patients. Use with caution in elderly patients and reduce dosage in patients with renal impairment. (2.4, 5.2)

Valacyclovir Package Insert 12/2019 accessed at clinicalinfo.hiv.gov

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69-year-old Man

- Successful FMT 2 months ago for highly debilitating recurrent *C.difficile* infection (8 total bouts)
- Scheduled for elective cardiac device procedure
- Standard peri-procedure antibiotic is single dose IV cephalosporin
- He calls you – mortified – that he will be getting an antibiotic

What Could Be Done?

A. Nothing, too late, Epic has him in it's web of templates, protocols, standing orders
B. Call GI, get another MRT ready
C. Call cardiology and GI, maybe even ID, and discuss options

Risks for Recurrent CDI

- Age > 65
- Immunocompromised
- Severity of CDI episode
  - Predicts future events
- History of CDI
  - 20% will get a second bout
  - Half of these will get another…

Pathophysiology

- Colonization
  - Exposure
- Microbiome disruption
  - Antibiotics, chemotherapy, GI tract surgery, other
- Weak immune response
  - Ab to Cdiff toxins

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Early Antibiotic Exposure After FMT

- 349 patients who underwent FMT
  - 12.6% overall failure rate
  - Early antibiotic use (within 8 weeks) was strongest predictor of FMT failure (OR 2.86, 1.16-7.06)
- Most pts (71%) received abx within 4 weeks of FMT
  - 36% UTI, 20% RTI, 12% SSTI
  - Ciprofloxacin, cephalexin, amox/clav most common

CID Allegretti Jan 6 2018, vol 66;1 p 134-35

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Frequently associated	Occasionally associated	Rarely associated
▪ Fluoroquinolones ▪ Clindamycin ▪ Penicillins and combinations (broad spectrum) ▪ Cephalosporins ($2^{nd}/3^{rd}/4^{th}$ generation)* ▪ Carbapenems	▪ Macrolides ▪ Penicillins (narrow spectrum) ▪ Cephalosporins (1^{st} generation) ▪ Trimethoprim-sulfamethoxazole ▪ Sulfonamides	▪ Aminoglycosides ▪ Tetracyclines ▪ Tigecycline ▪ Chloramphenicol ▪ Metronidazole ▪ Vancomycin ▪ Nitrofurantoin

Antimicrobial agents that may induce *Clostridioides difficile* diarrhea and colitis
From Patient Education: Antibiotic-associated diarrhea caused by *Clostridioides difficile* (Beyond the Basics) - UpToDate

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Secondary Vancomycin Prophylaxis

18. Oral vancomycin prophylaxis (OVP) may be considered during subsequent systemic antibiotic use in patients with a history of CDI who are at high risk of recurrence to prevent further recurrence (conditional recommendation, low quality of evidence).

- First time in a guideline (ACG Guideline)
  - 65 or older, or immunocompromised, hosp for severe CDI past 3mos
- Studies and data are mixed, but generally favorable
  - No impact on preventing recurrent CDI in FMT pts exposed to antibiotics in retrospective study (Dig Dis Sci 2019;64(6):1668)
- Vancomycin 125 mg once daily during and until 5 days after completing systemic antibiotics

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What Do You Tell Your Patients After They Have Recovered from C diff?

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Please Be Proactive

- Patient Education "Be Your Own Best PR agent"
  - Carry a letter, be able to tell your history to clinicians
- Colleagues (when future antibiotics are considered)
  - Discuss options for an individual case with the specialists
  - Can we observe closely and not start antibiotics?
- When antibiotics are necessary, consider
  - Secondary vancomycin prophylaxis
  - Using less "C diff-o-genic" antibiotic agents

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69-year-old man

- Successful FMT 2 months ago for highly debilitating recurrent *C. difficile* infection (8 total bouts)
- Scheduled for elective cardiac device procedure
- Standard peri-procedure antibiotic is single dose cefuroxime

- Unfortunately, the single dose cephalosporin lead to a rapid *C. difficile* relapse which necessitated a repeat FMT. Tough lesson learned.

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Head to Toe

A man returns from a trip to Cuba and presents to the primary care clinic. He is prescribed cephalexin for cellulitis.

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Critique?

A. Not the best diagnosis
B. Not the best therapy
C. A and B

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Cutaneous Larva Migrans

- Top 10 (often #1) travel related dermatoses
  - Appears after travel return in 55% of cases
- Larvae of dog or cat hookworm burrows through intact skin but remains in upper dermis since we are the wrong host
- Contaminated sand (beach!)
- Wanders a few mm-few cm each day, very pruritic
- Albendazole or ivermectin

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