ANTIBIOTICS FOR COMMON INFECTIONS

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48th Annual Family Medicine Update
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Big Sky, MT

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OBJECTIVES

- Review oral antimicrobial choice in relation to microbiology and risks.
- Recognize when antimicrobials are indicated in common infections.
- Review antibiotic choice and duration of therapy for common infections such as upper and lower respiratory tract infections, UTIs and skin or soft tissue infection.

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ANTIBIOTIC USE

- **Often overused and used inappropriately**
  - **Up to 50%**
    - Selection, dosing, duration, unnecessary for condition
  - > 25% adult Rxs usually not indicated
- **Inappropriate antibiotic use:**
  - **Leads to adverse drug effects** (eg, hypersensitivity, C. difficile) and mortality
  - **Increases health care cost** (eg, ED visits, Rx)
  - Promotes **antibiotic resistance**

Arch Intern Med 10;170:1314-6 J Antimicrob Chemother. 2014;69(1):234-40
CDC. Grand Rounds: Getting Smart About Antibiotics. MMWR 15;64:871-3
JAMA 16;315:562-70 Editorial. Ann Intern Med 12;157:211-2
Lancet Infect Dis. Online 3/2/16 http://dx.doi.org/10.1016/S1473-3099(16)00065-7

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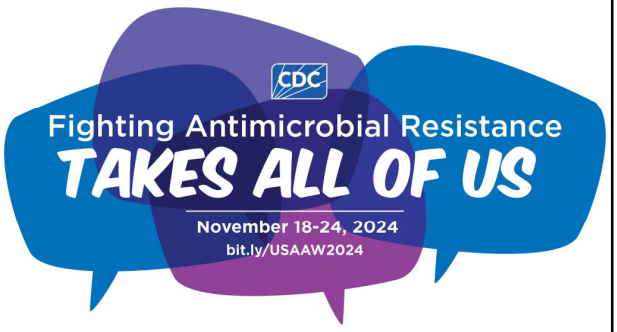

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RISKS WITH ABX USE

- Myth 1: Antibiotics Do No Harm
- Adverse drug events
  - Common cause of Emergency Department visit
  - 20% hospitalized have at least one adverse drug event within 90 days of abx use
- Increased risk of a resistant pathogen
- Increased risk of C. difficile
- Dysbiosis of gut microbiome

Am J Med 22;135:828-35 Infect Dis Clin N Am 22;36:187-202
JAMA Network Open 22;5(5):e2214153

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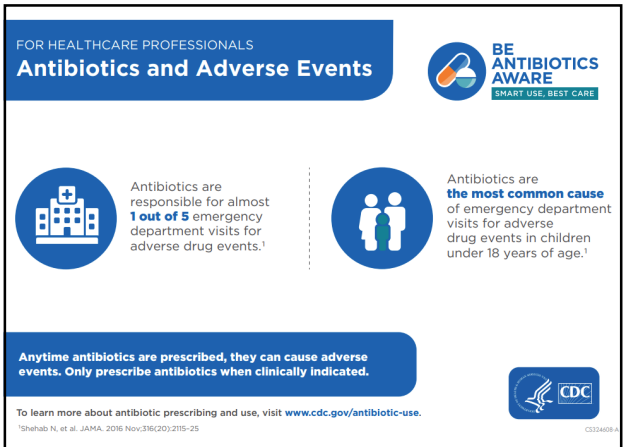

https://www.cdc.gov/antibiotic-use/pdfs/AntibioticSafety-HCP-P.pdf

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ANTIMICROBIAL STEWARDSHIP (AMS)

- "Failure to properly diagnosis and initiate antibiotic therapy in patients with bacterial infections can result in infection progression and adverse outcomes."
- "Conversely, overuse of antibiotics in patients without true infections can also result in patient harm and worsening antimicrobial resistance …"

Emerg Med Clin N Am 24;42:443-59

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EMERGING & ENDURING ANTIMICROBIAL-RESISTANT THREATS INCLUDE:

- Carbapenem-resistant Enterobacterales (CRE)
- **ESBL-producing Enterobacterales**
- Carbapenem-resistant Pseudomonas aeruginosa
- Carbapenem-resistant Acinetobacter baumannii
- Azole-resistant Aspergillus fumigatus
- Antifungal-resistant Candida, including Candida auris
- Drug-resistant Neisseria gonorrhoeae
- Drug-resistant Mycobacterium tuberculosis
- **Drug-resistant Streptococcus pneumoniae**
- **Clostridioides difficile**

https://www.cdc.gov/antimicrobial-resistance-laboratory-networks/php/about/domestic.html

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GRAM-NEGATIVE RESISTANCE

- ESBL-producing organisms
  - 26,000 infections/y – 1,700 deaths/y
- Carbapenem-resistant Enterobacteriaceae (CRE) organisms
  - 2.7% in health-care associated infections
  - > 9,000 infections/y – 900 deaths/y
- Reduced number of antibiotics that are effective

CDC. Antibiotic/antimicrobial resistance. September 8, 2016. https://www.cdc.gov/drugresistance/biggest_threats.html.
Pharmacist's Letter/Pharmacy Technician's Letter/Prescriber Insights. June 2024

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EXTENDED-SPECTRUM ß-LACTAMASES (ESBLs)

- If **confirmed by the lab as ESBL present**
  - **Cephalosporins (except cefoxitin and cefotetan), penicillins (except piperacillin-tazobactam), and aztreonam reported as <u>resistant</u>**
- **Usually susceptible to Carbapenems – drug of choice**; ceftazadime/avibactam, trimethoprim/sulfamethoxazole or fluoroquinolones **may** be susceptible

Infect Dis Clin N Am 21;35:969-94 Microorganisms 23;11:1407
IDSA Gram-neg Guideline 2024. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciae403/7728556?login=false#481562093
Emerg Med Clin N Am 24;42:461-83 Pharmacist's Letter/Prescriber Insights. June 2024

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CASE

- 81 y/o female with frequency and dysuria
  - No fever, chills, abd pain
- h/o UI with urethral bulking injections
- Valsartan; Simvastatin; Alendronate; Budesonide inhaler; Atenolol; Oxybutnynin XL; Cetirizine; ASA; Ca/D
- 122/82; afebrile
  - Exam neg

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- UC E. coli > 10^5
  - R – Amp; Amp/sulb; **Ceftriaxone**; Cipro
  - S – Gent; TMP/SMX; Tobramycin; **Ertapenem**
  - I – Nitrofurantoin
  - **ESBL positive**
    - **Considered resistant – ß-lactams (pens, cephs, aztreonam) EXCEPT carbepenems**

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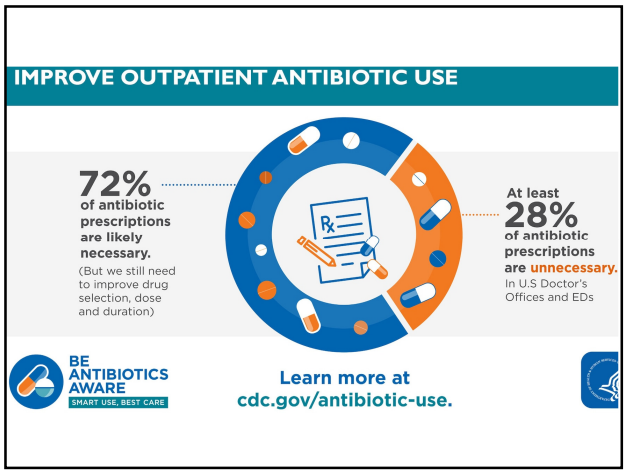

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Common Respiratory Infections	Common Cause			Are Antibiotics Needed?*
	Virus	Virus or Bacteria	Bacteria	
Common cold/runny nose	✓			No
Sore throat (except strep)	✓			No
COVID-19	✓			No
Flu	✓			No
Bronchitis/chest cold (in otherwise healthy children and adults)		✓		No**
Middle ear infection		✓		Maybe
Sinus infection		✓		Maybe
Strep throat			✓	Yes
Whooping cough			✓	Yes

*Antiviral drugs are available for some viral infections, such as COVID-19 or flu.
**Studies show that in otherwise healthy children and adults, antibiotics for bronchitis won't help patients feel better.

iotic prescribing and use, visit www.cdc.gov/antibiotic-use.

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Altru & Sanford Health Systems – 2023 Antibiogram

Gram-pos % susceptible	Penicillin (non-meningitis)	Amp/sulbactam	Oxacillin	Ceftriaxone	Erythromycin	TMP/SXT	Ciprofloxacion	Clindamycin	Doxycycline
S. aureus	24		77		59	96	79	85	98
MRSA						95		81	97
S. epidermidis			49			NR		57	87
S. pneumoniae	98			98	63	73	96	92	70
GABHS	98			100				80	
E. Coli		70		96		84	84		
H. influenzae		84		97	100 Azi	63-72	100		

Sensitive ≥ 90% ≥ 60-90% < 60% or Not Recommended (NR)

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COMMON COLD

- Also called URI
- Viral – Rhinoviruses, coronaviruses
- Nasal congestion, nasal discharge, sneezing, sore throat, cough, low-grade fever
- About 6-10d duration
  - Initially increasing symptoms symptoms then improvement over ± 10d
- **No Antibiotics** (IDSA. Choosing Wisely 2/23/15 http://www.choosingwisely.org) CDC 4/16/24. https://www.cdc.gov/antibiotic-use/hcp/clinical-care/adult-outpatient.html?CDC_AAref_Val=https://www.cdc.gov/antibiotic-use/clinicians/adult-treatment-rec.html

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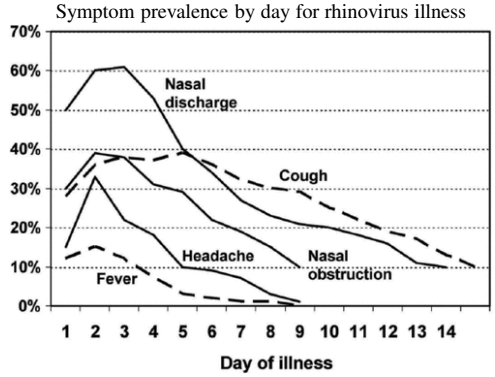
Symptom prevalence by day for rhinovirus illness



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Acute Rhinosinusitis

- **90-98% cases are viral**
- Signs and symptoms are NOT highly sensitive or specific for etiology
- **Acute bacterial develops in ONLY 0.5-2% of all URIs**

Guideline. Otolaryngol Head Neck Surg 15;152(2 suppl):S1-S39
Mayo Clin Proc 11;86:427-43 NEJM 16;375:962-70
Med Clin N Am 21;105:859-70 Med Clin N Am 21;105:199-212
CDC 4/16/24. https://www.cdc.gov/antibiotic-use/hcp/clinical-care/adult-outpatient.html?CDC_AAref_Val=https://www.cdc.gov/antibiotic-use/clinicians/adult-treatment-rec.html

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ACUTE **BACTERIAL** RHINOSINUSITIS ETIOLOGY ADULTS

- **S. pneumoniae 20-43%**
- **H. influenzae 22-36%**
- **M. catarrhalis 2-16%**
- S. aureus 2-13%
- GABHS 2-7%
- Anaerobes 0-12%

IDSA Bacterial Rhinosinusitis Guideline 2012. Otolaryngol Head Neck Surg 15;152(2 suppl):S1-39
Otolaryngol Clin N Am 16;49:927-34 Med Clin N Am 21;105:859-70
Expert Opin Pharmacother 22;23:2013-22

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SUGGESTS ACUTE BACTERIAL

- Any one of the following
  - Persistent s/s compatible with acute rhinosinusitis, **for > 7-10 d** without any clinical improvement
  - **Severe s/s** of high fever (> 39 C) & purulent nasal discharge or facial pain lasting for at least 3-4 d at the beginning of illness
  - **Worsening s/s** with new onset of fever, H/A, or increase in nasal discharge following typical viral URI lasting 5-6 d & were initially improving (''doublesickening'')

IDSA Bacterial Rhinosinusitis Guideline. 2012. http://www.idsociety.org/Organ_System
Curr Allergy Asthma Rep online 6/3/20 https://doi.org/10.1007/s11882-020-00917-5
Med Lett Drugs Ther 23;65:57-62

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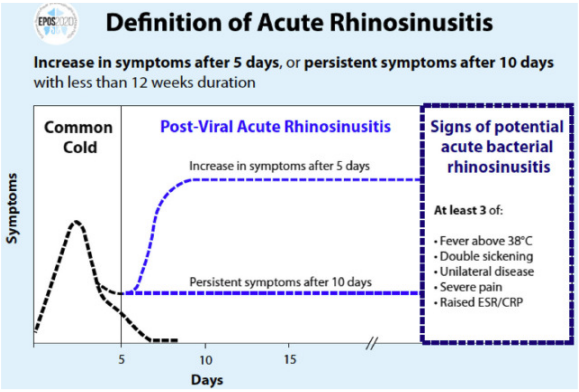
Updated European Position Paper on Rhinosinusitis 2020



Curr Allergy Asthma Rep. online 6/3/20 https://doi.org/10.1007/s11882-020-00917-5

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ACUTE SINUSITIS THERAPY

- 11% of primary care abx-related visits
- Intranasal corticosteroids, decongestants, nasal saline sprays/irrigations
- **If no antibiotics are given**
  - **~66-85% resolve without antibiotics within 7-15d**
- Antibiotics are **often used in 81-98% of cases**
  - Responsible for about 20% of all antibiotic use

American Academy of Otolary-Head/Neck Surgery Guideline. Otolaryngol Head Neck Surg 15;152(no. 2 suppl):S1-S39
NEJM 16;37:962-70 Mayo Clin Proc 11;86:427-43 JAMA 12;307:685-92
Emerg Med Clin N Am 19;37:41-54 Med Clin N Am 21;105:859-70
Med Clin N Am 21;105:199-212

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ANTIBIOTIC CHOICE FOR ACUTE BACTERIAL RHINOSINUSITIS

- If acute bacterial is suggested by history or severity of symptoms
- **1st-line: Amoxicillin (1.5-4 g/d or 90 mg/kg/d) + clavulanate** for 5-10 d
- 2nd-line: Doxycycline, Clinda + 3rd gen ceph, FQ
- Abx failure by 7 d or worsens
  - Change antibiotic

Guideline. Otolaryngol Head Neck Surg 15;152(no. 2 suppl):S1-S39
Emerg Med Clin N Am 19;37:41-54 Expert Opin Pharmacother 22;23:2013-22
Med Lett Drugs Ther 23;65:57-62
CDC 4/16/24. https://www.cdc.gov/antibiotic-use/hcp/clinical-care/adult-outpatient.html?CDC_AAref_Val=https://www.cdc.gov/antibiotic-use/clinicians/adult-treatment-rec.html

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ACUTE BACTERIAL SINUSITIS THERAPY

- **FQ not recommended** as 1st-line
  - PCN allergy alternative
- **Macrolides not recommended** empirically
  - S. pneumoniae resistance (>40%)
- **TMP/SMX not recommended** empirically
  - S. pneumoniae (~30% resistance)
  - H. flu resistance (~50%)

Bacterial Rhinosinusitis Guideline. 2012. http://www.idsociety.org/Organ_System
Guideline. Otolaryngol Head Neck Surg 15;152(Suppl 2):S1-S39
Emerg Med Clin N Am 19;37:41-54 Expert Opin Pharmacother 22;23:2013-22
Med Lett Drugs Ther 23;65:57-62
CDC 4/16/24. https://www.cdc.gov/antibiotic-use/hcp/clinical-care/adult-outpatient.html?CDC_AAref_Val=https://www.cdc.gov/antibiotic-use/clinicians/adult-treatment-rec.html

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CASE

- 22 y/o seen in walk-in clinic with URI symptoms
  - Started with cold symptoms 12 d ago
    - Runny nose and congestion, cough, no fever
    - Symptoms improved (but still present) and 2 days ago had some chills, headache and worsening nasal congestion with thick discharge
- Afebrile, moderate maxillary sinus tenderness
- Acute bacterial sinusitis
  - Azithromycin for 5 days

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CAP

- US ~4M cases/y & causes hospitalization/death
  - 1.5M hospitalizations/y
  - Pneumonia & influenza 8th leading cause of death
  - Mortality ~7-23% within 30 d after hospitalization
  - Accounts for 2.5M deaths worldwide
- Factors that affect mortality in a patient
  - Severity, elderly, male, lung disease, heart disease, CVD, DM, viral RTIs, immunocompromised, smoking, excessive alcolol, inappropriate initial antimicrobial choice

International Journal of Antimicrobial Agents 62 (2023) 106905
NEJM 23;389:632-41 Infect Dis Clin N Am 24;38:35-49

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COMMON PATHOGENS IN CAP*

OUTPATIENT	**INPATIENT (NON-ICU)**	**INPATIENT (ICU)**
S. pneumoniae	S. pneumoniae	S. pneumoniae
H. influenzae	H. influenzae	**S. aureus**
M. pneumoniae	M. pneumoniae	Legionella spp.
C. pneumoniae	C. pneumoniae	Kleb pneumoniae
Viral (Rhinovirus, Influenza, Coronavirus, Adenovirus, RSV, Parainfluenza, Coronavirus)	Legionella spp.	H. influenzae
	Aspiration	P. Aeruginosa
	Viral	Enterobacter spp.
	Fungal	Acinetobacter spp

***Based on site of care. Pathogen not detected in > 50% of patients.**

IDSA/ATS CAP. Clin Infect Dis 07;44:S27–72. Med Clin N Am 11;95:1143-61
Med Clin N Am 19;103:487-501 ATS/IDSA 2019 CAP Guidelines Emerg Med Clin N Am 18;36:665-83
Nature Reviews Disease Primers (2021)7:25 Ann Intern Med 2022 Apr;175:ITC49-64

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RAPID RESPIRATORY DIAGNOSTIC TESTS (RDT)

- **Nucleic amplification test (NAATs)** identification of multiple respiratory pathogens
  - Nasopharyngeal swab
  - Rapid (<2h), sensitivity/specificity >90%, costly
  - High negative predictive value – excludes pathogen if negative
- **An identified virus <u>may</u> allow withholding or rapid deescalation of antibiotics**
  - High risk patient and/or risk of bacterial use abx

Prim Care Clin Office Pract 18;45:485-503 Clin Infect Dis online 5/5/20.
Nature Reviews Disease Primers (2021)7:25 Ann Intern Med 22 Apr;175:ITC49-64
NEJM 23;389:632-41 Infect Dis Clin N Am 24;38:1-17 & 51-63

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CASE - COMP RESP PATHOGEN PANEL Ordered Oct 2024

- **Detected – Human Rhinovirus/Enterovirus**
- Not Detected
  - Adenovirus; Coronavirus HKU1, NL63, 229E, OC43; Human Metapneumovirus; Influenza A, B; Parainfluenza 1, 2, 3, 4; RSV; SARS-CoV-2; Bordetella pertussis, parapertussis; Chlamydia pneumoniae, Mycoplasma pneumoniae
- **Charge $1,199**
  - Allowed amount $548

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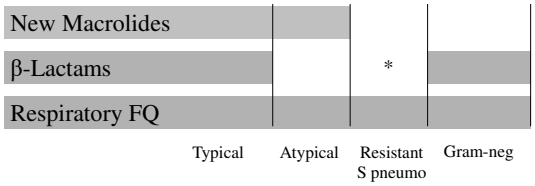
COVERAGE PROFILE IN CAP



*Coverage against S. pneumoniae nonsusceptible varies with dose. Some 2nd & 3rd generation Cephalosporins have coverage.

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INITIAL EMPIRIC CAP THERAPY
OUTPATIENT – Previously healthy

- **No risk factor for resistant pathogens**
- **Amoxicillin** 1 g 3xd (strong rec, mod evidence)
  - Several studies show efficacy despite presumed lack of coverage for atypical organisms
- **Doxycycline 100 mg 2xd** (conditional rec)
- **Azithromycin** (**if local pneumo resistance is <25%**) (conditional rec)

ATS/IDSA CAP Guidelines 2019 Ann Intern Med 2022 Apr;175:ITC49-64
NEJM 23;389:632-41 Med Lett Drugs Ther 23;65:57-62 Infect Dis Clin N Am 24;38:1-17
Emerg Med Clin N Am 24;42:231-47 Sanford Guide 2024

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INITIAL EMPIRIC CAP THERAPY
OUTPATIENT – Comorbidities

- Abx within 3 mon; coexisting diseases; DM; alcoholism; smokers; malignancy; or asplenia
- **Amoxicillin/clavulanate OR cefpodoxime OR cefuroxime AND azithromycin OR doxycycline for 5-7d**
  - Amox does not cover atypical pathogens
- **Levofloxacin**
  - When commonly recommended abx inappropriate

https://www.nice.org.uk/guidance/ng138
ATS/IDSA CAP Guidelines 2019 Ann Intern Med 2022 Apr;175:ITC49-64
NEJM 23;389:632-41 Med Lett Drugs Ther 23;65:57-62 Infect Dis Clin N Am 24;38:1-17
Emerg Med Clin N Am 24;42:231-47 Sanford Guide 2024

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ETIOLOGY ACUTE BRONCHITIS

- **Nonbacterial**
  - **> 90% of uncomplicated acute bronchitis**
  - Influenza A/B, parainfluenza, RSV, corona virus, adenovirus, and rhinoviruses
- Nonviral causes
  - **Bordetella pertussis**, **Mycoplasma pneumoniae**, and C. pneumoniae (TWAR)
  - 5-10% of cases of uncomplicated acute bronchitis

Ann Intern Med 00;133:981-91 Ann Intern Med 01;134:521
Chest 06;129:95S-103S AFP 16;94:560-5 Sanford Guide 2024

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ACUTE BRONCHITIS THERAPY

- **The right antibiotic prescribing rate should be close to 0%**
- Despite viral etiology and abx not recommended in healthy, uncomplicated
  - **Abx are Rx'd 60-70% of the time**
  - **A common inapprop use of abx (Sanford Guide)**
- **Should not use abx for acute uncomplicated bronchitis**

Choosing Wisely Campaign. 2/23/15. http://www.choosingwisely.org/clinician-lists/infectious-diseases-society-antbiotics-for-upper-respiratory-infections/
NIH and Care Excellence. Cough: clinical knowledge summaries. http://cks.nice.org.uk/cough.
JAMA 14;312:2678-9 Am Fam Physician 16;94:560-5 Ann Intern Med 16;164:425-34
J Emerg Med on line 2/27/22 https://doi.org/10.1016/j.jemermed.2022.01.020
Med Lett Drugs Ther 23;65:57-62 Sanford Guide 2024

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PERTUSSIS – IT IS STILL AROUND!

US YTD Dec 14, 2024

2024 32,085 cases

2023 6,479 cases

https://wonder.cdc.gov/nndss/static/2024/50/2024-50-table990.html

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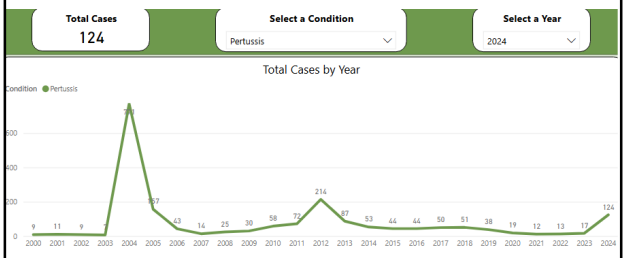
ND PERTUSSIS CASES AS OF DEC 20, 2024



https://www.hhs.nd.gov/health/data

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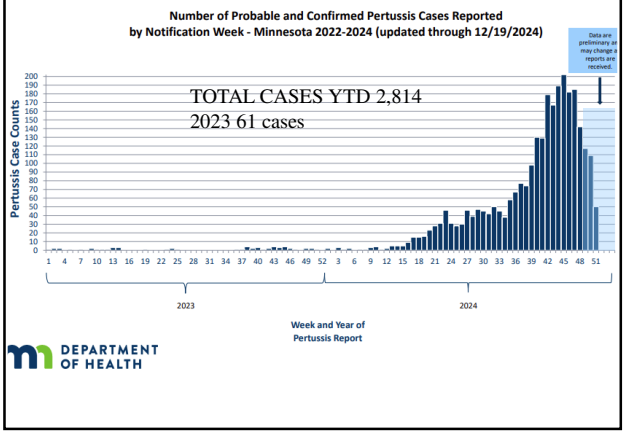

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RECOMMENDED **PERTUSSIS** TREATMENT

- Azithromycin for 5 d
  - Clarithromycin for 7 d
- Alternative agent
  - TMP/SMX for 7 d infant or 14 adult
- **Postexposure prophylaxis**
  - Same as above
  - Antibiotic to close contacts within 3 wks of exposure

MMWR December 9, 2005 / Vol. 54 / No. RR-14. http://www.cdc.gov/mmwr/PDF/rr/rr5414.pdf
Med Clin N Am 13;97:537-52 Sanford Guide 2024

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THINK of pertussis in anyone with the following symptoms, regardless of vaccination history:

- A cough in a person who has been notified of a close exposure to pertussis,
- A paroxysmal cough of any duration, with whooping, post-tussive vomiting/gagging or apnea, or
- A persistent cough of unknown etiology, lasting more than 7 days

MN Dept Health.
http://www.health.state.mn.us/divs/idepc/diseases/pertussis/hcp/managepert.html

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64 y/o Male with Cough

- Admitted with presumed asthma exacerbation
- Increasing symptoms over 3 wks despite oral steroids
  - Multiple ED visits with progressive cough
  - Chest tightness; difficulty eating and sleeping
  - No post-tussive emesis

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64 y/o Male with Cough

- Medical team heard a "whooping" cough
- Azithromycin started
  - Cough and respiratory symptoms improved during the next 5 d
- Lab tests positive for B. pertussis
- Never been vaccinated against pertussis
  - DTaP 1 month after discharge

NEJM 12;366:39

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Acute Exacerbation of Chronic Bronchitis (AECB)

- **Infectious 60-80% – 30-50% bacterial**
  - Frequent (70-85% of all infectious AECB)
    - **H. influenzae, M. catarrhalis, S. pneumoniae**
    - **Viruses** 20-50% (rhinoviruses [most frequent viral], influenza, rhinoviruses, coronaviruses, RSV)
  - **Less frequent** (15-30% of all AECB)
    - **P. aeruginosa, gram-neg Enterobacteriacea, S. aureus**, H. parainfluenzae and hemolyticus, C. pneumoniae, M. pneumoniae, Fungal

Med Clin N Am 12;96:789-809 NEJM 19;381:1257-66 Clin Chest Med 20;41:439-51
GOLD 2024 Med Lett Drugs Ther 23;65:57-62 Sanford Guide 2024

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ANTIBIOTICS INDICATED IN AECB

- **s/s suggesting bacterial infection**
  - **↑dyspnea**
  - **↑ cough with sputum production/volume**
  - **↑ sputum purulence (e.g., green-yellow color)**
    - **94% sensitivity, 52% specificity for high bacterial load**
- **Give antibiotics** for 5-7d
  - **If all 3**
  - **2 of above if includes purulence**
  - No abx if sputum white or clear in color

Med Clin N Am 12;96:789-809 Anaesthesia Intensive Care Med 14;10:460
Ann Intern Med 21;174:822-7 GOLD 2024

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ANTIBIOTICS IN AECB

- **Choice for outpatient** for 5-7d (**5d as effective as longer**)
  - **Mild to moderate COPD**
    - **Amox, Doxycycline, TMP/SMX**
  - **Severe COPD**
    - **Amox/clav; Azithromycin; Levofloxacin**
- **h/o frequent exacerbations, severe COPD and/or mechanical ventilation**
  - Gram-neg (e.g, Pseudomonas) or resistant bacteria
  - **Piperacillin-tazobactam; Cefepime, Levofloxacin**

Med Clin N Am 12;96:789-809. Ann Intern Med 21;174:822-7
Med Lett Drugs Ther 23;65:57-62 GOLD 2024 Sanford Guide 2024

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SYMPTOMATIC UTI TREATMENT FACTORS

- Important in selecting empiric antimicrobials
- Clinical classification and location
  - eg, cystitis, pyelonephritis, prostatitis
- Complexity of infection
  - Complicated or uncomplicated
- Potential pathogen(s) and resistance risk
  - Past UC, recent antibiotic use or hospitalization
- Patient factors
  - Severity (eg. sepsis, bacteremia), allergies, medication cost, co-morbidities

Infect Dis Clin N Am 24,38:295-310

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UNCOMPLICATED UTI

- Includes cystitis and pyelonephritis
- Healthy, no urinary tract abnormalities, not pregnant, premenopausal
  AFP 11;84:771-6 Postgrad Med 20;132:234-50
  - **Nonpregnant females 15-45 y with normal urinary tract and otherwise healthy**
- Low risk for non E.coli, resistant pathogen or treatment failure
  - Predictable response to antibiotics

NEJM 12;366:1028-37 Med Clin N Am 13;97:737-57 Prim Care Clin Office Pract 13;40:687-706
Emerg Med Clin N Am 19;37:707-23 Prim Care Clin Office Pract 19;46:191-202
Postgrad Med 20;132:234-50
Recurrent Uncomplicated UTIs in Women: AUA/CUA/SUFU Guideline 2019
https://www.auanet.org/guidelines/recurrent-uti Urol Clin N Am 22;49:283-97
Infect Dis Clin N Am 24;38:295-310 Infect Dis Clin N Am 24;38:381-93

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COMPLICATED UTI

- **All who do not meet uncomplicated criteria**
  - eg. male, DM, pregnant, catheter, elderly, etc
- > incidence of pathogens other than E. coli and increased antibiotic resistance
- Less predictable response to antibiotics
- Need for empiric broader spectrum antibiotics

NEJM 12;366:1028-37 Prim Care Clin Office Pract 13;40:687-706
Emerg Med Clin N Am 19;37:707-23 Prim Care Clin Office Pract 19;46:191-202
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Recurrent Uncomplicated UTIs in Women: AUA/CUA/SUFU Guideline 2019
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Am J Kidney Dis 23;83:90-100 Infect Dis Clin N Am 24,38:295-310
Infect Dis Clin N Am 24;38:381-93

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BACTERIAL ETIOLOGY

	% Uncomplicated	% Complicated
E. coli	**70-95**	**21-65**
P. mirabolis	1-2	**1-10**
Klebsiella spp	1-2	**2-17**
Citrobactor spp	<1	5
Enterobacter spp	<1	2-10
P. aeruginosa	<1	**2-19**
Other gram-neg	<1	**6-20**
Coagulase-neg Staph	**5-15***	1-4
Enterococci	1-5	**1-23**
Group B Strep	1-3	1-4
S. aureus	<1	1-3
Candida sp	1	7

Infect Dis Clin N Am 03;17:303-32. Prim Care Clin Office Pract 13;40:687-706
Int. J. Mol. Sci. 2023, 24, 10537

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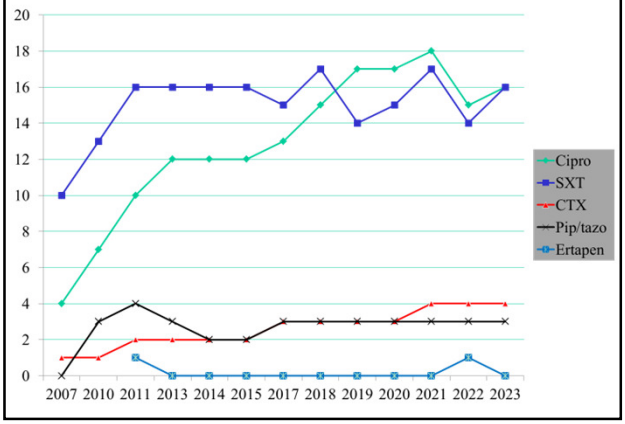
ALTRU ANTIBIOGRAM – E. coli % RESISTANT



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USE OF TMP/SMX IN **CYSTITIS**

- **Traditional 1st-line agent – 3-day regimen**
  - **Increasing resistance** – >20% for E. coli
- Use empirically if **local E. coli resistance < 20%**
- Pregnancy Class C
  - May be used during 2nd & 3rd? trimester (see below)
  - Folic acid antagonist – **avoid in 1st trimester** unless no safe alternative exists & then use folic acid 5 mg/d
  - **Avoid after 32 wks, may cause hyperbilirubinemia**
    - **Displaces bilirubin from albumin**

IDSA Practice Guidelines Clin Infect Dis 11;52:e103-e120. Postgrad Med 20;132:234-50
ACOG committee opinion. September 2017. https://www.acog.org/Clinical-Guidance-and-Publications/Committee-Opinions/Committee-on-Obstetric-Practice/Sulfonamides-Nitrofurantoin-and-Risk-of-Birth-Defects
DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12e. 2023 Obstet Gynecol 23;142:435-45
J Clin Med 2022, 11, 7226

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FQs (Not moxifloxacin) IN CYSTITIS

- **Very good bioavailability; high blood levels**
- Efficacious in **3-d regimens** in cystitis
  - Has been used 1st-line for many years – **BUT**
- High collateral damage
  - Increasing resistance, adverse effects, "overkill", GI tract & C. diff, may increase MRSA
- **Risk may outweigh benefit for treatment of outpatient uncomplicated cystitis** (FDA warning 2018)
- Avoid in pregnancy

IDSA Guidelines. Clin Infect Dis 11;51:e103-e120 Mayo Clin Proc 11;86:477-9
In the Clinic: UTI. Ann Intern Med 10/3/17 Postgrad Med 20;132:234-50
DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12e. 2023

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EMPIRIC THERAPY OF UNCOMPLICATED CYSITIS

- **Preferred**
  - **TMP/SMX DS** 2xd oral or TMP 100 mg 2xd for **3 d**
    - **Don't use if local resistance > 20%** or used within 3 mon
  - **Nitrofurantoin** 100 mg oral 2xd for **5 d**
  - **Fosfomycin** 3 gm oral **single dose**
- Alternative
  - **ß-lactams** oral for **5-7d** (eg, amox/clav, cephalexin, **cefpodoxime**)
  - **Cipro** 250 mg 2xd or **Levo** 250 mg/d oral for **3 d**
    - **Risk may outweigh benefit, no longer 1st-line**
    - Increasing resistance

IDSA Guidelines. Clin Infect Dis 11;51:e103-120 Prim Care Clin Office Pract 19;46:191-202 Emerg Med Clin N Am 19;37:707-23 Postgrad Med 20;132:234-50 Urol Clin N Am 22;49:283-97
Am J Kidney Dis 23;83:90-100 Emerg Med Clin N Am 24;42:209-30
Infect Dis Clin N Am 24;38:295-310

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CASE

- 50s y/o male with bladder spasm presents to office
  - States he has a UTI
  - Quadriplegia, indwelling foley cath x 20y, frequent UTIs
- Nitrofurantoin 100 mg/d X 12 y, Methenamine 1 g 2xd, Cranberry plus vit C
- Afebrile, no CVA tenderness
- UA: nitrite +, WBC 300, bacteria many

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- **TMP/SMX DS 2xd x 10d started empirically**
- **UC: P. aeruginosa**
  - S: Amikacin, Aztreonam, Cefepime, Gent, Meropenem, Pip/tazo, Tobra
  - R: Ciprofloxacin, Nitrofurantoin

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BEFORE INITIATING EMPIRIC ANTIBIOTIC

- **ASSESS COMPLICATED VS UNCOMPLICATED**
- **SYMPTOMATIC VS ASYMPTOMATIC**
- **CYSTITIS VS PYELONEPHRITIS**
- **RECENT ANTIBIOTICS**
- **LOOK FOR PAST UC AND BC TO HELP GUIDE THE SELECTION OF ABX!!!!!!**

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- 1 mon PTA P. aeruginosa x 2
  - S: Amikacin; Cefepime; Cipro; Gent; Meropenem; Pip/Tazo; I: Aztreonam
- 4 mon S. marcescens
  - S: Ceftriaxone; Gent; Tobra
  - R: Cipro; Nitrofurantoin, TMP/SMX
- 7 mon P. aeruginosa
  - S: Cipro; Gent; Pip/Tazo; Tobra; I: Aztreonam
- 11 mon S. marcescens
  - S: Ceftriaxone; Gent; Tobra, TMP/SMX
  - R: Cipro; Nitrofurantoin
- 15 mon S. marcescens x 2
  - S: Ceftriaxone; Gent; Tobra, TMP/SMX
  - R: Cipro; Nitrofurantoin

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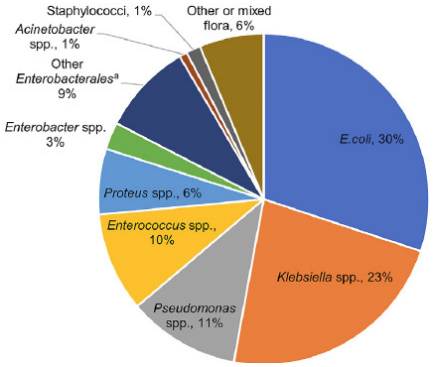
Uropathogens in neurogenic bladder, asymptomatic bacteriuria or UTI



Infect Dis Clin N Am 24;38:381-93

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EMPIRICAL TREATMENT OF ACUTE PYELONEPHRITIS

- **Outpatient**
  - Ciprofloxacin for 7 d or **Levofloxacin** for 5-7 d
    - **1st-line empiric therapy (2nd-line for cystitis)**
    - **If local resistance is < 10-20%**
    - If >10% resistance or patient risk factors increase likelihood of resistance **initial dose of ceftriaxone**, ertapenem or aminoglycoside is often warranted
  - TMP/SMX for 7-14 d if pathogen known susceptible
    - Due to resistance initial dose (above) often warranted
  - Oral 3rd gen Ceph for 10-14d may be effective

IDSA Guidelines. Clin Infect Dis 11;51:e103-e120. NEJM 12;366:1028-37. JAMA 14;311:844-54 Dis-a-Mon 15;61:45-59 In the Clinic: UTI. Ann Intern Med 10/3/17 NEJM 18;378:48-59 Postgrad Med 20;132:234-50 Urol Clin N Am 22;49:283-97 Emerg Med Clin N Am 24;42:209-30 Infect Dis Clin N Am 24,38:295-310

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CASE

- 18 y/o female
  - 2 d onset **dysuria, frequency, urgency and hematuria, nausea, decreased appetite, L back pain**
  - **Cystitis 2 months ago – resolved with TMP/SMX**
- 38C with **L CVA tenderness**
- UA: **Nitrite pos**; protein 300; **WBC 20-50**
- **WBC 14, HCG neg**
- Patient **wants to try outpatient with oral TMP/SMX** since that worked last time
- **Your response** to abx request?

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- **She received Ceftriaxone IM once then Ciprofloxacin oral for 7 days**
  - Will contact patient with culture results
- UC – E. coli
  - **Resistant**: Ampicillin, Ampicillin/Sulbactam, **TMP/SMX**
  - **Sensitive**: Cefazolin, **Ceftriaxone, Ciprofloxacin**, Gentamicin, Nitrofurantoin, Tobramycin

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ASYMPTOMATIC BACTERIURIA (ASB)

- **≥ 1 bacteria in UC at ≥ 10^5 CFU/mL**
  - **Regardless if pyuria is present**
  - **Absence of evidence-based s/s of a UTI**
- For most **no** antibiotic, abx risk > potential benefits
  - Includes elderly, DM, spinal cord, catheterized, peds?
  - **Treatment in elderly does not prolong life**
  - **Treat if becomes symptomatic**
- **Treat**: **pregnant, urologic surgery & instrumentation**, foley removal, renal transplant

Dis-a-Mon 15;61:45-59
IDSA 2019 ASB Guideline. Clinical Infectious Diseases 2019;68:1611-15
Urol Clin N Am 22;49:283-97 Amer J Med 22;135:e236-44
Pediatr Clin N Am 22;69:1099-114 Am J Kidney Dis 23;83:90-100
Emerg Med Clin N Am 24;42:209-30 Infect Dis Clin N Am 24;38:267-76

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COMMON **MISTAKES** IN PRACTICE

- **"All patients with asymptomatic bacteriuria require antibiotic treatment."**
  - There is an overuse of antibiotics that is leading to the emergence of resistance
  - IDSA discourages this practice – except special circumstances

Commentary: Twenty Common Mistakes Made in Daily Clinical Practice
Frishman WH & Alpert JS. AJM 20;133:1-2

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Clostridioides difficile Infection (CDI)

- **New name for Clostridium difficile**
- In 2017 462,100 cases with 20,500 deaths
  - #1 pathogen in health care-associated infections
- Infections often frequent, watery diarrhea
  - Fulminant colitis in 3-8% – Mortality 30-90%
  - **Pseudomembranous colitis (PMC)**
  - Toxic megacolon, Colon perforation, Sepsis
  - Death
    - Linked to ~30,000 deaths/y vs 32,000 in traffic accidents

http://www.cdc.gov/ncidod/dhqp/id_CdiffFAQ_HCP.html. Curr Opin Crit Care 07;13:450-5
NEJM 15;372:1539-48. Infect Dis Clin N Am 23;37:87-102 Sanford Guide 2024
Mayo Clin Proc 24;99:971-9 Surg Clin N Am 24;104:545-56

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C. DIFFICILE PATHOGENESIS

- **GI flora protective to** prevent colonization
  - **Antibiotics disrupt microbiome – dysbiosis**
    - **Most important modifiable risk factor**
    - **20-40% community-acquired without risk factors**
  - **PPI use**
  - **Colonization** with toxigenic strain of C. difficile
  - Toxins A and B (10x more potent) are released
  - **Diarrhea and colitis occur**

J Clin Gastroenterol 07;41:S24–9. Lancet 08;371:1487-8.
NEJM 15;372:1539-48 Infect Dis Clin N Am 23;37:87-102 Mayo Clin Proc 24;99:971-9
Surg Clin N Am 24;104:545-56

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RISK OF C. diff DIARRHEA

High Risk	Moderate Risk	Low Risk
Clindamycin	Other penicillins	Aminoglycosides
	Macrolides	Bacitracin
FQ	TMP/SMX,	Carbapenems
	Sulfonamides	Daptomycin
Cephalosporins	Metronidazole	Nitrofurantoin
	Vancomycin	Rifampin
Broad-spectrum		Rifaximin
PCN (e.g.,		Tetracyclines
amoxicillin)		Tigecycline

J Clin Gastroenterol 07;41:S24–9 J Intensive Care Medicine 14;29:190-9
NEJM 15;372:1539-48 Surg Clin N Am 24;104:545-56

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CASE

- 65 y/o female presents with 3 d of watery diarrhea with flecks of blood
  - At least 11 episodes so far today with diffuse abdominal pain and cramping
  - Also c/o mild nausea, weakness and chills
- 10 d prior received Clindamycin for dental infection
- 115/72; HR 105; 38.2
- WBC 15,750; Cr 1.5 (1.1)
- C. diff – positive

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C. DIFFICILE TREATMENT

- ORAL Vancomycin, Metronidazole or Fidaxomicin
- ORAL Metronidazole was preferred, then ORAL Vancomycin **was** considered preferred therapy

  2017 IDSA/SHEA Guidelines
- **Fidaxomicin (costly) NOW considered preferred therapy OR Vancomycin is**

2021 IDSA/SHEA Guidelines Mayo Clin Proc 24;99:971-9
Gastroenterol Clin N Am 21;50:323-40 Mayo Clin Proc 21;96:2192-2204
Med Lett Drugs Ther 2021;63:137-41 Sanford Guide 2024
Infect Dis Clin N Am 23;37:87-102 Pharmacist's Letter/Prescriber's Letter Feb 2023
Surg Clin N Am 24;104:545-56

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C. diff Recommended Agents

- **Fidaxomicin preferred**
  - **Macrolide – poor absorption**
  - As effective as vanco for initial episode
    - **~40% < recurrence** if without hypervirulent strain
  - **BUT significantly more expensive to treat acute infection – may be cost effective when recurrence cost factored in**

IDSA/SHEA C. Diff Guideline Clin Infect Dis 21;73:e1029-44
Mayo Clin Proc 21;96:2192-2204 Med Lett Drugs Ther 21;63:137-41
Infect Dis Clin N Am 23;37:87-102
Pharmacist's Letter/Prescriber's Letter. February 2023.
Surg Clin N Am 24;104:545-56 Sanford Guide 2024

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CHOICE OF AGENTS

Infection Severity	Clinical Status	Therapy
Initial episode		**Fidaxomicin** 200 mg 2xd X10 d OR Vancomycin 125 mg po 4xd X10d
Non-severe	WBC ≤ 15,000 **&** SCr < 1.5	Alternate: if above not available Metronidazole 500 mg po 3xd 10-14d
Initial episode Fulminant	Hypotension or shock, ileus, megacolon	**Vancomycin 500 mg PO/NG** qid (If ileus, consider adding rectal vanco) **PLUS** **Metronidazole 500 mg IV** q8h (especially if ileus)

2021 C. diff Update by the IDSA & SHEA 2021 ACG Guide Am J Gastroenterol 21;116:1124–47
Med Lett Drugs Ther 2021 Sep 6;63(1632):137-41 Sanford Guide 2024
Infect Dis Clin N Am 23;37:87-102 Pharmacist's Letter/Prescriber's Letter. February 2023
Mayo Clin Proc 24;99:971-9 Surg Clin N Am 24;104:545-56

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COMPARISON OF AGENTS

	Vancomycin	Metronidazole	Fidaxomicin
FDA-approved	Yes	No	Yes
Mild Disease Severe	++++ Superior	++ **Inferior**	++++ Superior
Relapse rate	10-25%	10-25%	**~40% < Vanco**
Cost for 10 d	Capsules 125 mg 4xd: ~$370 Oral Soln (Firvanq): ~$150 IV taken po: ~$65, bitter taste	Tablets 500mg 3xd ~$15	Tablets (Dificid) 200 mg 2xd **~$4,700** **May be cost-effective with < recurrence & improved quality of life**

Adapted from Bartlett JG. Presented at 45th Annual Meeting of IDSA, 10/07. San Diego, CA
Mayo Clin Proc 21;96:2192-2204 Med Lett Drugs Ther 21;63:137-41
Pharmacist's Letter/Prescriber's Letter. February 2023.

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