UWTASP
tele-antimicrobial stewardship program

May 18th, 2021

Agenda:

American College of Physicians: Shorter is better!

- Case Discussions
- Open Discussion

Announcements

June 1st: Patch Dellinger is lecturing! Please invite your colleagues.

Appendicitis: Operate or Antibiotics?

Check out the COVID-19 monoclonal eligibility criteria!

- Obesity or being overweight (for example, BMI >25 kg/m2)

Previously BMI > 35

https://www.fda.gov/media/145611/download

http://pi.lilly.com/eua/bam-and-ete-eua-factsheet-hcp.pdf

Annals of Internal Medicine®

Clinical Guidelines | 6 April 2021

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

FREE

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for the Scientific Medical Policy Committee of the American College of Physicians* View fewer authors

Author, Article and Disclosure Information

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Eligible for CME Point-of-Care

Sections Abstract | PDF | Tools | Share

The cold hard facts

- Primary care physicians prescribe antibiotics in 10% of all outpatient visits
- In 2014, outpatients received more than 250 million courses of antibiotics in the United States
  - at least 30% were considered unnecessary and often continued for too long, particularly for bronchitis and sinusitis

3 Rs of stewardship:

Right drug, Right dose and Right duration

Antibiotic Overuse Consequences

- Antimicrobial overuse drives resistance
- Causes adverse events in up to 20% of patients,
  - Allergic reactions to *Clostridioides difficile* infections
- Antibiotic-resistant infections are a national threat
  - > 2.6 million illnesses and 35 900 deaths annually
- Resistant infections of 6.1 per 10 000 person-days after receipt of antibiotics

Who does this guideline target?

- all internists
- family physicians
- other clinicians

Most patients with these infections will be seen in the outpatient setting

- also apply to patients who present in the inpatient setting.

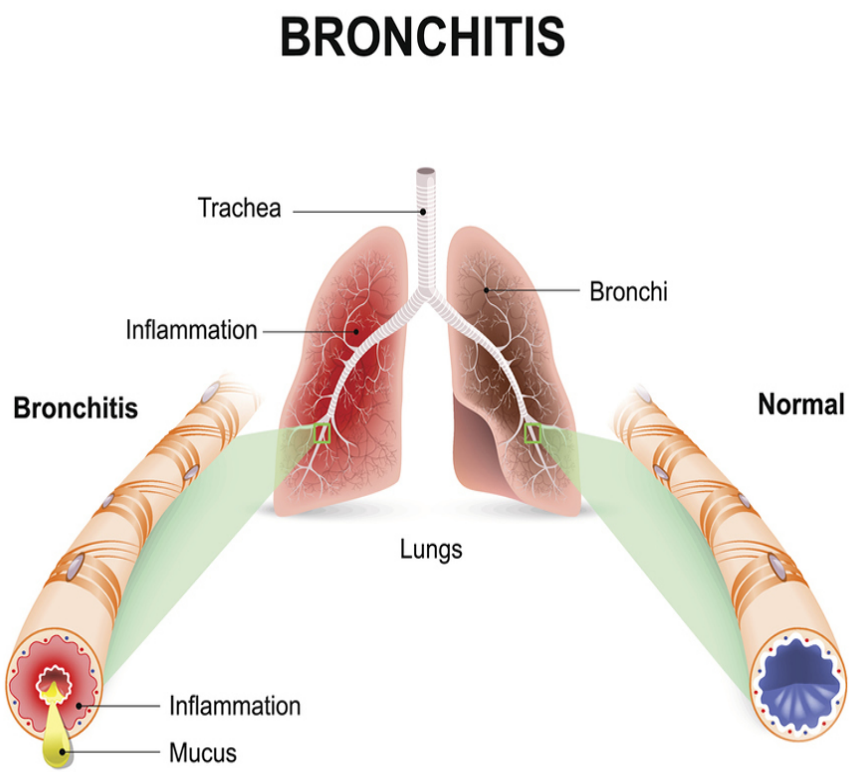
Table. Summary of the ACP Best Practice Advice on Appropriate Use of Short-Course Antibiotics in Common Infections

Condition	Patient Population	Available Guidelines and Evidence*	Best Practice Advice
Acute bronchitis	Adults with COPD	GOLD guideline (18) Meta-analysis of 21 studies comparing ≤5 vs. >5 days (19)	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).
Community-acquired pneumonia	All adults who are not immunocompromised†	IDSA/ATS guideline (20)	Clinicians should prescribe antibiotics for community-acquired pneumonia for a minimum of 5 days. Extension of therapy after 5 days of antibiotics should be guided by validated measures of clinical stability, which include resolution of vital sign abnormalities, ability to eat, and normal mentation.
Urinary tract infection: uncomplicated bacterial cystitis	Nonpregnant adult women†	IDSA/ESCMID guideline (21)	In women with uncomplicated bacterial cystitis, clinicians should prescribe short-course antibiotics with either nitrofurantoin for 5 days, TMP–SMZ for 3 days, or fosfomycin as a single dose.
Urinary tract infection: uncomplicated pyelonephritis	Nonpregnant adults†	IDSA/ESCMID guideline (21) Recent systematic review (22) 3 recent RCTs (23–25)	In men and women with uncomplicated pyelonephritis, clinicians should prescribe short-course therapy either with fluoroquinolones (5 to 7 days) or TMP–SMZ (14 days) based on antibiotic susceptibility.
Nonpurulent cellulitis	All adults	IDSA guideline (26) NICE guideline (27) 1 recent RCT (28)	In patients with nonpurulent cellulitis, clinicians should use a 5- to 6-day course of antibiotics active against streptococci, particularly for patients able to self-monitor and who have close follow-up with primary care.

ATS = American Thoracic Society; COPD = chronic obstructive pulmonary disease; ESCMID = European Society of Clinical Microbiology and Infectious Diseases; GOLD = Global Initiative for Chronic Obstructive Lung Disease; IDSA = Infectious Diseases Society of America; NICE = National Institute for Health and Care Excellence; RCT = randomized controlled trial; TMP–SMZ = trimethoprim–sulfamethoxazole.

* The Scientific Medical Policy Committee prioritized the highest available level of synthesized evidence: clinical guidelines, followed by systematic reviews, and then individual studies.

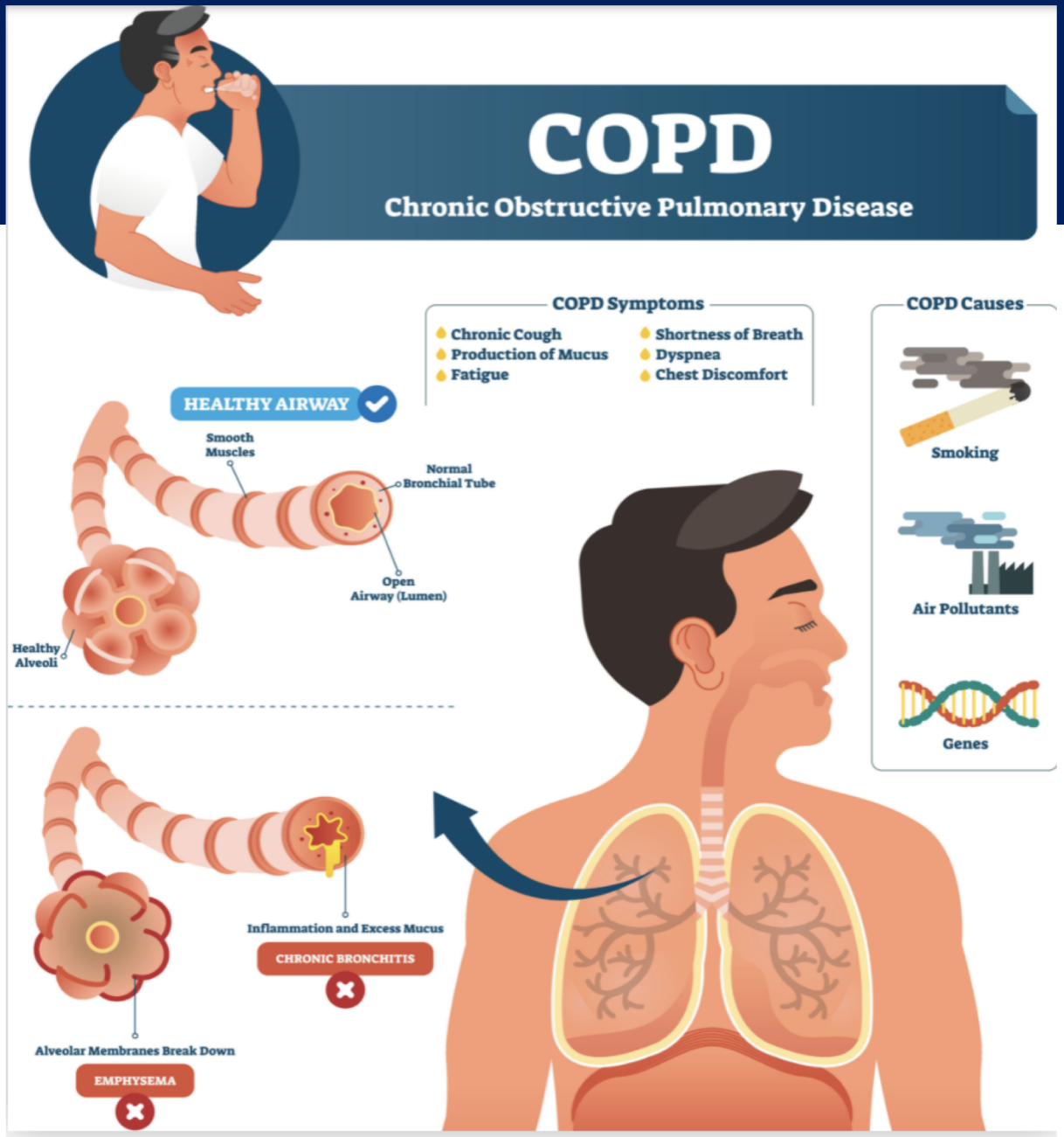
Acute bronchitis in non-COPD



an acute respiratory infection with a normal chest radiograph, is typically a self-limited infection of the large airways, usually caused by a virus

NO ABX, regardless of cough duration

https://www.cdc.gov/antibiotic-use/clinicians/adult-treatment-rec.html



https://www.respiratorylondon.co.uk/chronic-obstructive-pulmonary-disease-copd-previously-known-as-emphysema-and-chronic-bronchitis/

COPD Recommendation

- In COPD, antibiotics are recommended if there is a high pretest probability of a bacterial cause for exacerbation
- The Global Initiative for Chronic Obstructive Lung Disease (GOLD) recommends treating COPD exacerbations with antibiotics in patients who have clinical signs of a bacterial infection
  - presence of increased sputum purulence in addition to increased dyspnea, and/or increased sputum volume

Amoxicillin-clavulanate

Doxycycline

Azithromycin

X 5 days

5 days of Antibiotic Therapy for Bacterial Respiratory Tract Infections

Best Practice Alert 2:

Prescribe antibiotics for CAP for a minimum of 5 days. Extension of therapy after 5 days of antibiotics should be guided by validated measures of clinical stability:

-resolution of VS abnormalities
-ability to eat
-normal mentation

A Plot Twist

THE LANCET
Volume 397, Issue 10280, 27 March–2 April 2021, Pages 1195-1203

Articles

Discontinuing β-lactam treatment after 3 days for patients with community-acquired pneumonia in non-critical care wards (PTC): a double-blind, randomised, placebo-controlled, non-inferiority trial

Dinh et al, 2021

3 Days Non-Inferior to 8 for CAP

Inclusion

Age ≥18 | CAP | Admitted to hospital but not ICU
12/2013 – 02/2018

N =310

Exclusions: severe CAP (abscess, massive pleural effusion, serious chronic respiratory infection), known immunosuppression, HCAP, aspiration pneumonia

Dinh et al, 2021

Randomized at 72h

Afebrile |HR < 100 | SBP >90 | RR < 24 | O2 Sat > 90% | Mentating

152
Placebo

73 years, 20% COPD, 20% HF, 27% with multilobar infiltrate or pleural effusion on CXR

151
B-lactam

Clinical Cure, day 15

Afebrile |Resolved sx (cough, sputum production, SOB, crackles) no add'l abx

117
77%
3 days

9·42% (95% CI –0·38 to 20·04)

102
68%
8 days

"A 3-day treatment regimen seems relevant for approximately 60% of patients admitted to hospital with the strict definition of community-acquired pneumonia…."

Rec #3: UTI 1-5 d, Pyelo 5-14 d

- Women with cystitis
  - 1 day: fosfomycin
  - 3 days: TMP/SMX
  - 5 days: nitrofurantoin

- Women/men with pyelonephritis
  - **5**-7 days: FQ
  - 14 days: TMP/SMX
  - Guided by susceptibility data

5 days of a FQ for Pyelo

- Dinh 2017: RCT 5 vs. 10 days of FQ (oflox, levoflox)
  - 100 patients, similar cure rates, no hospitalization
- Peterson 2008: RCT 5d levo vs. 10d cipro (pyelo, cUTI)
  - 506 patients (311 with pyelo). Similar eradication, clinical cure, relapse
- Klausner 2007: RCT 5d levo vs. 10d cipro (pyelo)
  - 192 patients. Similar eradication, clinical success.

The American Journal of Medicine
Volume 130, Issue 7, July 2017, Pages 842-845

Clinical research study

A Seven-Day Course of TMP-SMX May Be as Effective as a Seven-Day Course of Ciprofloxacin for the Treatment of Pyelonephritis

Miriam T. Fox BS [a], Michael T. Melia MD [b], Rebecca G. Same MD [c], Anna T. Conley BA [d], Pranita D. Tamma MD, MHS [e]

Patients:

- Retrospective review: women with E.coli pyelonephritis
  - 81 received TMP/SMX x 7 days 191 received Cipro x 7 days
- Exclusion: pregnancy, dialysis dependent, bacteria resistant to abx chosen

Outcomes:

- Adjusted odds of recurrent, symptomatic UTI within 30 days: 2.30 (95% CI, 0.71-7.42)

Cellulitis

- **Cellulitis**
  - Diffuse, superficial infection of dermis and subcutaneous tissue
- **Non-purulent vs. purulent cellulitis**
  - Streptococci vs. *S. aureus*
- **Risk factors for MRSA**
  - Penetrating trauma, injection drug use, MRSA colonization

Antibiotic Selection

	MSSA	MRSA	Group A Strep	Dosing
Cephalexin	++++		++++	500mg QID 1000mg BID
Dicloxacillin	++++		++++	500mg QID
Trimethoprim/ sulfamethoxazole	++++	++++	???	1 DS BID
Clindamycin (Inducible resistance)	++++	++	↑↑ Resistance	300mg TID
Doxycycline	++++	++++	Reported resistance	100mg BID

Cellulitis – 5 Day

- **RCT – No difference in clinical response**
  - 5d vs. 10d of levofloxacin
  - 6d vs. 10d of tediazole
  - 6d of tediazole vs. 10d of linezolid
- **2014 IDSA recommendation**
  - Consider extending therapy if lack of improvement after 5d

Hepburn MJ et al JAMA 2004
Prokocimer P, et al. JAMA 2013
Moran GJ et al, Lancet ID 2014
Stevens DL, Clin Infect Dis 2014

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Stewardship Mantra
"Less is More"