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How to Pick the Right Antibiotic Course for Common Infections: A Case-Based Approach

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Disclosures

None

Objectives

Review recommended antimicrobials for common infections

Describe recommended treatment duration for common infections

Antibiotic Resistance

- One of the largest threats to global health
- 2015 World Health Assembly Global Action Plan on resistance
- 2016 United Nations General Assembly
- 2018 WHO Global Antimicrobial Surveillance System (GLASS)

Timeline of Antibiotic Resistance

- Resistance does occur naturally, but misuse of antibiotics accelerates this
- Slow pace of development of newer antimicrobial agents

Timeline of Antibiotic Resistance

Infections once treatable -> harder to eradicate

- Tuberculosis
- Gonorrhea
- Pneumonia

Ramifications

- Longer hospital stays
- Increased mortality
- Higher medical costs

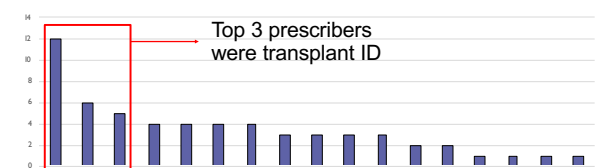
What Reduces Excessive Antimicrobial Use?

Delivery of best available evidence to providers

- High quality
- Latest data
- Applicable to current clinical practice

Offer feedback on antimicrobial prescribing

- Compare with existing guidelines
- Compare with peers



Meropenem Use by Infectious Disease Provider on Service

A healthy 23-year-old woman presents with dysuria and urinary frequency. She is allergic to sulfa. A urine dipstick test is positive for leukocytes and nitrites. Urine pregnancy test is negative.

Which antimicrobial agent is first-line for uncomplicated urinary tract treatment in this patient?

- A. Trimethoprim-sulfamethoxazole
- B. Cephalexin
- C. Ciprofloxacin
- D. Nitrofurantoin
- E. None

Diagnosis

- Need Signs and symptoms
 - Dysuria
 - Frequency
 - Urgency
 - Suprapubic tenderness
 - CVA tenderness
- NON-specific symptoms
 - Fever
 - Hematuria
 - Cognitive changes
 - New onset incontinence in elderly
 - Leukocytosis
 - Sepsis

Clinical
Practice
Guidelines,
CID 2011;
52:e103-20

Uncomplicated UTI

- Recommended first-line antimicrobials:
 - Nitrofurantoin
 - Trimethoprim/sulfamethoxazole
 - Fosfomycin
- Good efficacy
- Minimal "collateral" damage to normal gut microflora (↓ antimicrobial resistance)

FDA Drug Safety Communication:
FDA advises restricting fluoroquinolone antibiotic use for certain
uncomplicated infections

Risks outweigh benefits for patients with:
Uncomplicated acute sinusitis
Acute bronchitis
Urinary tract infections

Due to MSK and CNS side effects

<http://www.fda.gov/Drugs/DrugSafety/ucm500143.htm>

Clinical Pearls: UTI

Diagnosis:
symptoms + pyuria

Consider collateral
damage
(fluoroquinolones,
beta-lactams)

First-line

Nitrofurantoin

TMP/SMX

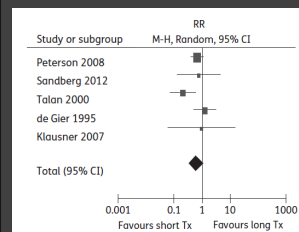
Fosfomycin

A healthy 23 year old woman presents with dysuria and urinary frequency. She is allergic to sulfa. On exam, she is febrile with right-sided flank tenderness. IV Ceftriaxone is begun. Urine cultures +pan-sensitive *E. coli*. Blood cultures are negative.

What is the best treatment regimen?

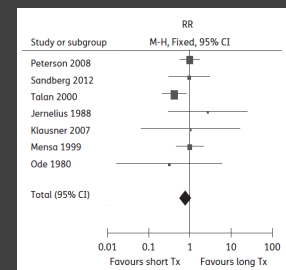
- Ciprofloxacin x 3 days
- Ciprofloxacin x 5 days
- Ciprofloxacin x 7 days
- Ciprofloxacin x 10 days
- Ciprofloxacin x 14 days

Clinical Failure at End of Therapy



Eliakim-Raz et al. J Antimicrob Chemother. 2013

Clinical Failure at End of Follow up



Clinical Pearl: Pyelonephritis

7 days of treatment for acute pyelonephritis is equivalent to longer treatment, including in bacteremic patients.

In patients with urogenital abnormalities, the evidence, although weak, suggests that longer treatment is required.

A 61-year-old otherwise healthy man presents with three days of cough productive of sputum. He is a nonsmoker and has no history of asthma, recent antibiotic use or travel. He is an elementary school teacher. His temperature is 38.5°C, blood pressure is 144/92 mm Hg, respiratory rate is 18 breaths/min, heart rate is 90 bpm, and oxygen saturation is 95% on room air. His CXR is unremarkable.

What is the appropriate antimicrobial to give?

- A. Doxycycline
- B. Azithromycin
- C. Azithromycin + Cefdinir
- D. Levofloxacin
- E. None

Nonspecific cough illness/bronchitis
>90 percent of cases caused by routine respiratory viruses
<10 percent of cases caused by *Bordetella pertussis*, *Chlamydia pneumoniae*, or *Mycoplasma pneumoniae*

When to treat with an antibiotic: presents with prolonged unimproving cough (14 days); should clinically differentiate from pneumonia. Pertussis should be reported to public health authorities. *C. pneumoniae* and *M. pneumoniae* may occur in older children (unusual in those younger than five years).

When not to treat with an antibiotic: nonspecific cough illness

Bronchiolitis/nonspecific URI
>200 viruses, including rhinoviruses, coronaviruses, adenoviruses, respiratory syncytial virus, enteroviruses (coxsackieviruses and echoviruses), influenza viruses, and parainfluenza virus

When not to treat with an antibiotic: sore throat, sneezing, mild cough, fever (generally less than 102°F [39°C], for less than three days), rhinorrhea, nasal congestion, self-limited (typically five to 14 days)

Wong et al. American Family Physician. 2006.

Clinical Pearls: URI

- Acute bronchitis is otherwise healthy adults should not be treated with antimicrobials
- Sputum does not help distinguish between bacterial and viral infection
- A CXR shows an abnormality in the majority of cases of pneumonia

A 61-year-old otherwise healthy man presents with three days of a productive cough and fever without rhinorrhea or sore throat. His temperature is 38.0°C, blood pressure is 144/92 mm Hg, respiratory rate is 22 breaths/min, heart rate is 90 bpm, and oxygen saturation is 95% on room air. Physical examination reveals rales and egophony in the right lower lung field. A chest radiograph shows an infiltrate in the right lower lobe. He is started on oral Levofloxacin.

What is the best treatment duration?

- A. 3 days
- B. 5 days
- C. 7 days
- D. 10 days
- E. No days

Clinical Pearl: CAP

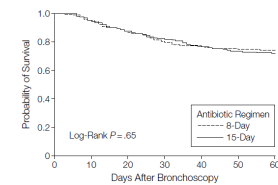
For mild-moderate CAP, no difference between short course (3-5 days) vs long course (7-10 days)

A 62 year man with ischemic cardiomyopathy is admitted to the hospital in cardiogenic shock. He is intubated. He clinically improved with initiation of inotropes and diuresis. On hospital day 5, he spikes a fever and decompensates with increased oxygen requirement. CXR shows a new LLL infiltrate. BAL is done with culture + pan sensitive *Klebsiella pneumonia*. Blood cultures negative. Antimicrobials are narrowed to IV Ceftriaxone. He is extubated 2 days later.

What is the best antimicrobial treatment duration?

- A. 5 days C. 10 days
B. 7 days D. 14 days

Figure 2. Kaplan-Meier Estimates of the Probability of Survival



No. at Risk	0	10	20	30	40	50	60
8-Day Antibiotic Regimen	197	187	172	158	151	148	147
15-Day Antibiotic Regimen	204	194	170	167	157	151	147

Probability of survival is for the 60 days after ventilator-assisted pneumonia onset as a function of the duration of antibiotic administration.

OUTCOME ENDPOINTS IN THE TWO STUDY GROUPS

Variable	Experimental	Standard Therapy	p Value
Length of ICU stay, d			
Mean/median	9.4/4	14.7/9	0.04
Range	1-47	1-91	
Mortality, d			
3	0% (0/39)	7% (3/42)	NS*
14	8% (3/39)	21% (9/42)	NS
30	13% (5/39)	31% (13/42)	NS (0.06)
Resolution of pulmonary infiltrate			NS
Complete resolution	41% (16/39)	21% (9/42)	
Partial resolution	18% (7/39)	14% (6/42)	
Unchanged	18% (7/39)	35% (15/42)	
Worsening	0/39	10% (4/42)	
No follow-up films	23% (9/39)	19% (8/42)	

* NS = not significant, $p > 0.05$.

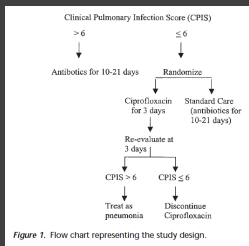


Figure 1. Flow chart representing the study design.

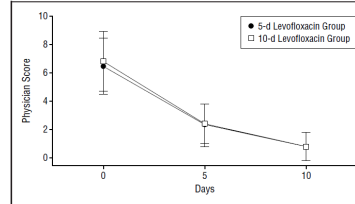
Clinical Pearl: VAP

In patients with VAP with clinical improvement with appropriate antimicrobials, a short course (≤ 8 days) is just as good as a long course (15 days)

Singh et al. Am J Respir Crit Care Med. 2000.

A 35 year old otherwise healthy man presents to clinic with fever, swelling and erythema of the right leg after a fall.
 Temperature 38.2, BP 120/60, HR 90, RR 18
 A 3 x 3 cm area of erythema and soft tissue swelling is present on the anterior right shin without purulent drainage. Oral cephalexin is begun with rapid clinical response within 3 days.
 How long a course of antimicrobials is recommended?

- A. 3 days
- B. 5 days
- C. 7 days
- D. 10 days
- E. No days



Serial physician composite scores for cellulitis with 5 vs 10 days of therapy

Outcome measure

Resolution of cellulitis at 14 days and absence of relapse at 28 days

Hepburn et al. Arch Intern Med. 2004.

Clinical Pearl: Cellulitis

In patients without complicating soft tissue abscess and early evidence of clinical improvement, a short course of antimicrobials (5 days) is no different than a longer course (10 days)

The New Antibiotic Mantra
 – “Shorter Is Better”

Spellberg B. JAMA Intern Med. 2016.

