



Updates in Therapeutics® 2017: Ambulatory Care Pharmacy Preparatory Review and Recertification Course

Infectious Diseases II

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Conflict of Interest Disclosures

No disclosures

Learning Objectives

- Design appropriate pharmacologic and nonpharmacologic treatment regimens for various patient populations with urinary tract infections, prostatitis, community-acquired pneumonia, sinusitis, pharyngitis, otitis media, skin and soft tissue infections, tuberculosis, ophthalmic infections, bone and joint infections, tickborne infections, infective endocarditis, central nervous system infections, antibiotic prophylaxis, infectious diarrhea, and *Clostridium difficile* infections.
 - Identify risk factors and clinical circumstances for antimicrobial resistance.
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Learning Objectives

- Design an antimicrobial therapeutic regimen to treat resistant infections and prevent future development.
 - Apply evidence-based medicine and patient-specific factors to design antimicrobial regimens that are appropriate and cost-effective for the patient.
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Agenda

- Urinary Tract Infections
 - Community-acquired Pneumonia
 - Tuberculosis
 - Upper Respiratory Tract Infections
 - Otitis Media
 - Uncomplicated Skin and Soft Tissue Infections
 - Tick-borne Infections
 - *C. difficile*
 - Bone and Joint Infections
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Urinary Tract Infections

JC is a 25 year old female who presents to her doctor's office complaining of dysuria urinary frequency over the past 3 days. She denies fever or flank pain. She is an otherwise healthy female, no history of UTIs and with no known allergies.

Urinalysis reveals:

hazy urine

WBC of $10^6/\text{mm}^3$

nitrite positive

leukocyte esterase positive

positive protein

10^4 CFU/mL gram-negative rods

How would you treat JC's uncomplicated cystitis?

Urinary Tract Infections

- Most common indication for antimicrobials in women of childbearing age.
- Cystitis/Pyelonephritis
 - Cystitis: lower UTIs involving bladder
 - Pyelonephritis: upper UTIs – kidney
- Uncomplicated: usually girls ages 15 – 45 years
- Complicated
 - Structural abnormalities
 - Men
 - Pregnancy
 - Children

Urinary Tract Infections

■ Etiology

- *E. coli* (75 – 95%)
- Enterobacteriaceae
 - *Proteus mirabilis*
 - *Klebsiella pneumoniae*
- *Staphylococcus saprophyticus*

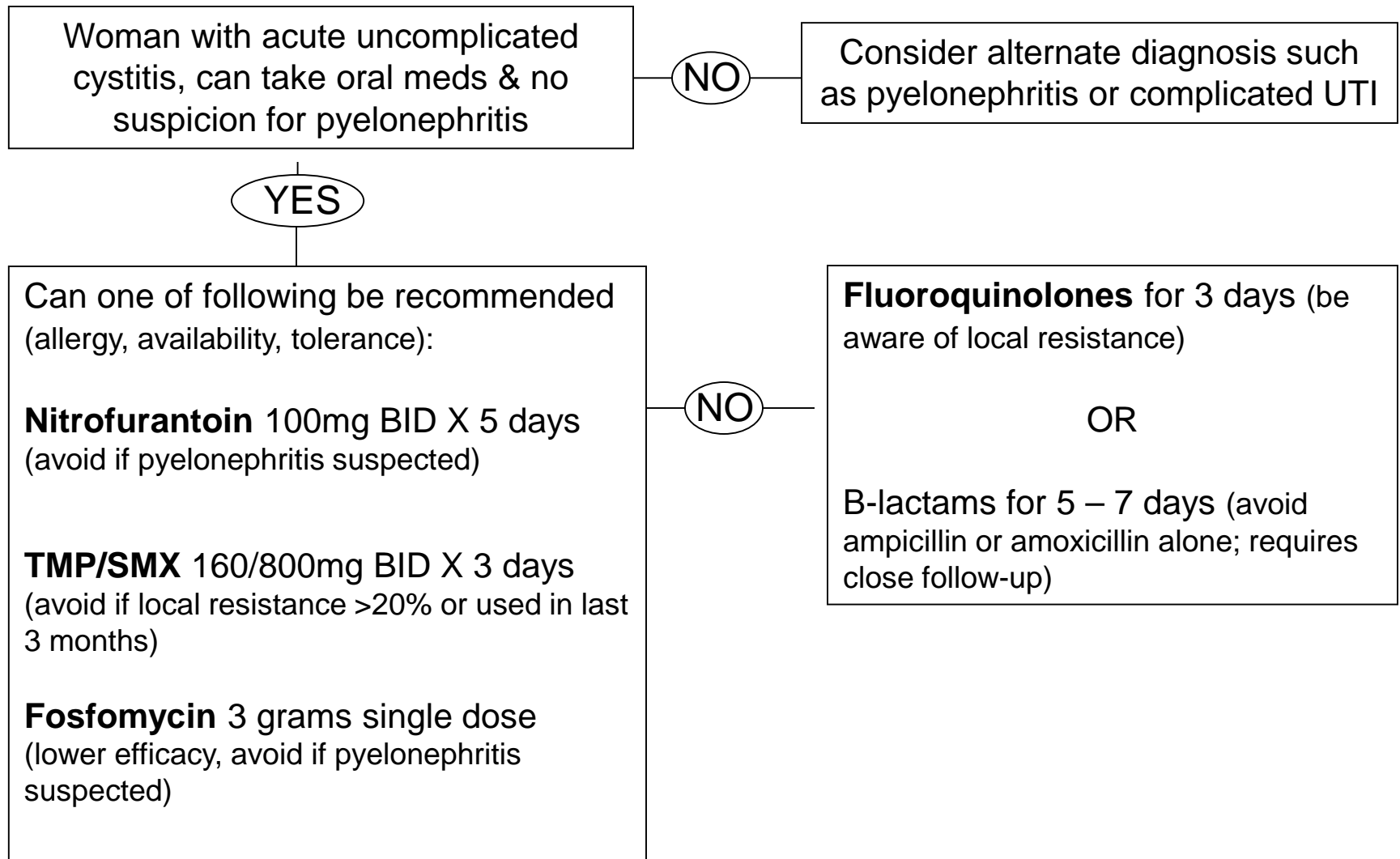
Urinary Tract Infections

- Consideration of *E. coli* Resistance
 - Need to be cognizant of local resistant patterns
 - General Resistance Rates
 - Amoxicillin > 20%
 - Trimethoprim/Sulfamethoxazole ~ $\geq 20\%$
 - Fluoroquinolones < 10%
 - Amoxicillin-clavulanate, 2nd generation oral cephalosporins < 10%
 - Nitrofurantoin & fosfomycin relatively good in vitro susceptibility

Treatment Uncomplicated Cystitis

- Trimethoprim/Sulfamethoxazole 160/800 mg BID
3 day treatment
- Fluoroquinolones
 - Ciprofloxacin 500mg extended release daily or 250mg twice/day
 - Levofloxacin 250mg daily3 day treatment
- Nitrofurantion 100mg BID
5 day treatment
- Fosfomycin 3 grams **Single dose**
- Beta-lactam (Not Amoxicillin)
5 – 7 day treatment

IDSA Guideline Treatment Algorithm



1-799 to 801

Adapted from algorithm in CID 2011; 52(5): e103-e120.

Urinary Tract Infections

- Based off of the 2010 IDSA Guidelines, which of the following is the best option for JC, our 25 year-old, otherwise healthy patient with no known allergies?
 - A. Levofloxacin 250mg once/day X 3 days
 - B. Fosfomycin 3 gram X 3 doses
 - C. Nitrofurantoin 100mg BID X 5 days
 - D. TMP/SMX 160/800mg X one dose

Urinary Tract Infections

- Recurrent and Relapse infections
 - Recurrent Infections – infecting organism is different than original/preceding infection
 - Risks: sexual intercourse, diaphragm & spermicide use
 - Treatment options
 - Self/administered/initiated therapy at onset of symptoms
 - Postcoital therapy
 - Continuous low-dose prophylaxis (when >3 episodes/year)
 - In postmenopausal women, topical estrogen
 - Relapse Infections – persistence of original infection after treatment
 - May indicate renal involvement, structural abnormality
 - May require longer treatment or use of alternative agent

Urinary Tract Infections

W.A. is a 50 year-old woman who presents to the clinic with dysuria and increases urinary frequency the last 2 days. This is her fifth UTI in the past 12 months since going through menopause. Otherwise she is in very good health, and her only drug is a multivitamin daily and loratadine as needed for seasonal allergies. She is very concerned about the frequency of her UTIs and would like to know whether there is any way she can prevent these.

Urinary Tract Infections

- Which intervention is best for W.A.?
 - A. Drink a glass of cranberry juice daily
 - B. Daily topical estrogen cream applied vaginally
 - C. Postcoital voiding after intercourse
 - D. Nitrofurantoin 100mg orally 2 times/day for 6 months

Community-acquired Pneumonia

R.C. is a 60-year-old woman who presents to the clinic with a 4-day history of increasing productive cough, malaise, wheezing, and fever. Her medical history includes type 2 diabetes mellitus for 20 years, congestive heart failure, chronic kidney disease, and osteoarthritis. She states that her only medication allergy is a history of nausea with ciprofloxacin for a UTI several years ago. On examination, she is found to have a temperature of 102.3°F, respiratory rate 22, BP 120/78, & HR 90. She is 5'6" tall and weighs 90kg. Her laboratory values are WNL, except SCr 3.0 mg/L & WBC 18/mm³. A chest radiograph reveals consolidation in the right lower lobe. She is given the diagnosis of CAP.

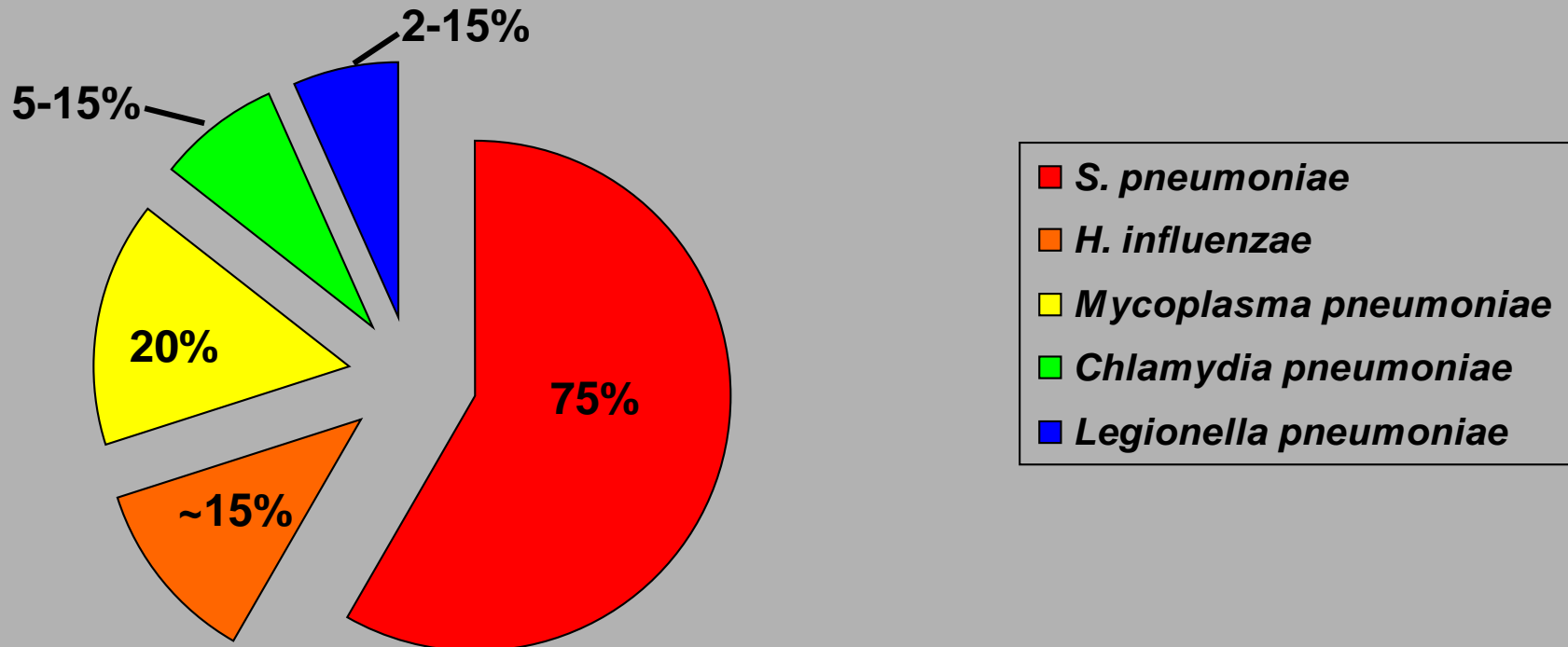
Community-acquired Pneumonia

- Risk factors
 - Age > 65 years
 - Comorbidities (pulmonary, diabetes, CHF, HIV)
 - Smokers
 - Recent antibiotic therapy
- Signs and Symptoms
 - Fever
 - Cough with or without sputum
 - Dyspnea, chest pain, wheezing
 - Myalgia, sweats, rigors

Community-acquired Pneumonia

■ Etiology

- Typical pathogens (*S. pneumoniae*, *H. influenzae*)
- Atypical pathogens (*M. pneumoniae*, *C. pneumoniae*, *Legionella*)



Community-acquired Pneumonia

- Diagnosis
 - Physical exam
 - Chest radiograph
 - Microbiology
 - Not routinely done in outpatient
 - IDSA/ATS 2007 guidelines suggest testing if it will change individual therapy or if previous therapy has failed
 - Scoring Systems
 - Determine if treatment can be in or outpatient treatment
 - CURB-65
 - Pneumonia Severity Index (PSI)

Community-acquired Pneumonia

■ Treatment

- ❑ β -lactams do NOT cover atypical pathogens
- ❑ Macrolides, fluoroquinolones, doxycycline cover typical and atypical pathogens
- ❑ Be cognizant of local resistance patterns
 - Penicillin-resistant *S. pneumoniae*
 - Macrolide or fluoroquinolone *S. pneumoniae* resistance
 - Multi-drug-resistant *S. pneumoniae*
- ❑ Treatment typically 7 – 10 days

Community-acquired Pneumonia

■ Treatment

- Previously healthy/no antimicrobials last 3 months
 - Macrolide (azithromycin, clarithromycin)
 - Doxycycline
- Presence of comorbidities, use of antibiotics last 3 months
 - Respiratory fluoroquinolone (levofloxacin, moxifloxacin, gemifloxacin)
 - β -lactam (high-dose amoxicillin, amoxicillin-clavulanate, or cephalosporin (ceftriaxone, cefpodoxime, cefuroxime) PLUS a macrolide

Community-acquired Pneumonia

- Which of the following is the best empiric option for managing R.C.'s CAP?
 - A. Levofloxacin 750mg orally once daily for 10 days
 - B. Azithromycin 500mg orally once on day 1; then 250mg orally daily for 4 days
 - C. Linezolid 600mg orally 2 times/day for 10 days
 - D. Azithromycin 500mg orally once on day 1, then 250mg orally daily for 4 days plus amoxicillin 500mg orally 2 times/day for 10 days

Tuberculosis

■ Overview

- Tuberculosis (TB) caused by the acid-fast bacilli *Mycobacterium tuberculosis*
- In 2010, the incidence in the USA was 3.2 cases/100,000 population
- Highly contagious spread through airborne transmission
- All infections are not fulminant
 - Latent TB when infection becomes dormant
 - Fulminant when bacteria continues to replicate

Tuberculosis

- At risk populations
 - Immigrants
 - Medically underserved
 - Prison inmates
 - Nursing homes/ long-term care facilities
 - IV drug abusers
 - Immunocompromised (HIV, cancer patients, etc)
 - Healthcare workers

Tuberculosis

E.C. is a 70-kg, 27-year-old male pharmacy resident whose PPD is evaluated after being placed on his left forearm 48 hours ago. It is erythematous, with induration measured at 11 mm.

Tuberculosis

■ Diagnosis - Latent

□ TB Screening

■ PPD – read in 48-72 hours

- $\geq 5\text{mm}$ (HIV, immunosuppressed, recent TB contacts or fibrotic changes on X-ray)
- $\geq 10\text{mm}$ (immigrated to US < 5 years, IVDA, residents & employees in high risk settings, children < 4 years)
- $\geq 15\text{mm}$ (anyone)

■ Blood testing

□ QuantiFERON and T-SPOT

- Patients who have received BCG or will not follow up after PPD placement
- Not as a follow-up for PPD

■ Chest radiograph

Tuberculosis

■ Latent TB treatment

- Baseline labs (LFTs, INR, SCR, BUN, WBC, etc)
- Common Regimens
 - Isoniazid 300 mg daily or 900 mg two or three times weekly for 9 months (*preferred adult treatment*)
 - Isoniazid 300 mg daily or 900 mg two or three times weekly for 6 months (*not in HIV-positive, < 18 years, or with fibrotic lesions*)
 - Rifampin 600 mg daily for 4 months (*if can not tolerate isoniazid*)
 - Isoniazid 15 mg/kg (max 900 mg) PLUS rifapentine 900 mg (if ≥ 50 kg) weekly for 12 weeks administered by DOT (*not if < 2 years, pregnant or may become pregnant, or HIV on ART*)

Tuberculosis

Which is the best recommendation for E.C. at this time?

- A. Tell him to come back next year for an annual PPD because his PPD test results are negative.
- B. Start isoniazid 300 mg orally daily plus vitamin B6 for 9 months.
- C. Start rifampin 600 mg daily for 9 months.
- D. Start isoniazid 900 mg orally daily plus rifapentine 900 mg orally daily for 12 weeks.

Tuberculosis

- Diagnosis Active TB
 - Signs/Symptoms (cough +/- hemoptysis, pleuritic pain, fever, night sweats, weight loss, etc)
 - Laboratory
 - Increased WBC
 - Sputum culture positive for acid-fast bacilli
 - Bacterial growth may take up to 2-4 weeks
 - Nucleic acid amplification assay in 48 hours
 - Drug susceptibility can take up to 4 weeks

Tuberculosis

- Treatment of Active TB
 - Baseline labs
 - Empiric, usually with four-drug regimen especially in areas with high rate of resistance
 - Primary drugs
 - Isoniazid, rifampin (or other rifamycins), pyrazinamide, ethambutol
 - Second-line agents
 - Streptomycin, amikacin, levofloxacin, moxifloxacin
 - Duration
 - 2 months (8 weeks) of primary 4 drug regimen, followed by 4 months (18 weeks) of isoniazid and rifampin if susceptible

Tuberculosis

Drug	Daily Dose (maximum)	Twice Weekly Dose (maximum)	Three Times Weekly Dose (maximum)
Isoniazid (INH)	5 mg/kg (300 mg)	15 mg/kg (900 mg)	15 mg/kg (900 mg)
Rifampin (RIF)	10 mg/kg (600 mg)	10 mg/kg (600 mg)	10 mg/kg (600 mg)
Pyrazinamide (PZA)	> 75 kg = 2.0 gm	> 75 kg = 4.0 gm	> 75 kg = 3.0 gm
Ethambutol (EMB)	> 75 kg = 1.6 gm	> 75 kg = 4.0 gm	> 75 kg = 2.4 gm

Upper Respiratory Tract Infections

- LS is a 35-year-old man who presents to the clinic with a 3-day history of headache, runny nose, nasal congestion, and tooth pain. He is an otherwise healthy man with no allergies or comorbidities. He is given a diagnosis of sinusitis.

Acute Sinusitis

- Primarily viral
 - Differentiation with bacteria is difficult
 - Viral usually resolve in 7 – 10 days, worsening could be bacterial
 - *S. pneumoniae* & *H. influenzae* 70% bacterial cases
- Signs/Symptoms
 - Nasal discharge and/or congestion
 - Facial, sinus and maxillary tooth pain

Acute Sinusitis

- Treatment
 - Most sinus infections are self-limiting
 - Supportive care
 - Nasal or oral decongestants
 - Saline irrigations
 - Avoid antihistamines (dry mucosa)
 - Antimicrobial therapy (when symptoms persistent, severe or worsening after improvement)
 - Amoxicillin/clavulanate first line (*IDSA 2012 guidelines*)
 - Others: tetracyclines (doxycycline, minocycline), respiratory fluoroquinolone
 - Usually treat 5-7days (*IDSA 2012 guidelines*)

Sinusitis

- Which of the following is the best treatment recommendation for L.S.?
 - A. Loratadine 10mg/day for 10 days
 - B. Amoxicillin 1g orally 3 times/day for 10 days
 - C. Azithromycin 500mg orally once on day 1; then 250mg orally daily for 3 days
 - D. Oxymetazoline 2 sprays in each nostril every 12 hours for 3 days

Pharyngitis

TR is a 4-year-old female toddler who presents to the pediatric clinic with a 3-day history of runny nose, sore throat, and fever of 102°F. She lives at home with her mother, father, and 11-year-old brother, and she attends preschool 3 days a week. On physical exam, she weighs 19 kg, and her tonsils are erythematous and inflamed. A throat swab is taken, and her RADT comes back negative for group A streptococcus.

Pharyngitis

- Viruses are most common cause
- Group A *Streptococcus* most common bacterial 15-30%
 - 5-15 year olds
 - Parents of school-age children
- Signs/Symptoms
 - Acute sore throat & pain swallowing
 - Fever
 - Erythema & inflamed tonsils with or without exudates
 - Tender/swollen lymph nodes

Pharyngitis

- Can not determine between viral and bacterial by signs/symptoms
- Diagnosis
 - Throat swab for culture or RADT
 - RADT takes about 15 minutes in clinic

Pharyngitis

■ Treatment

□ Supportive care

- Pain/fever relief with acetaminophen or NSAIDS
- Topical analgesics
- Saltwater gargles

□ Antimicrobials for positive group A *Streptococcus*

- Will see improvement in 24 – 48 hours
- Penicillin drug of choice
 - Oral penicillin VK x 10 days or IM PCN benzathine x 1 dose
 - Amoxicillin orally x 10 days
- Macrolides or 1st generation cephalosporins

Pharyngitis

Which of the following is the most appropriate treatment recommendation for TR?

- A. Penicillin benzathine 0.6million units intramuscularly once
- B. Ibuprofen 150mg (7.5mL of 100/5mL of elixir) as needed
- C. Acyclovir 380 mg (20mg/kg) orally 4 times/day for 10 days
- D. Trimethoprim/sulfamethoxazole 76/380mg (4mg/kg of TMP) orally every 12 hours x 10 days

Otitis Media

- Most common reason for antimicrobial prescriptions in children.
- Risk Factors
 - Siblings
 - Attending daycare
 - Pacifier use
 - Parents or caregivers smoking
- Pathogens
 - Primarily *S. pneumoniae*, *H. influenzae*, *M. catarrhalis*
 - Others: *S. aureus*, *S. pyogenes*, *E. coli*, *Pseudomonas*, anaerobes
 - Viruses

Otitis Media

■ Diagnosis

□ Signs & symptoms

- Abrupt onset of signs and symptoms of AOM (otalgia, fussiness, fever, inconsolability)

□ Middle-ear effusion

- Bulging/non-mobile of tympanic membrane
- Air-fluid level behind tympanic membrane
- Otorrhea

□ Inflammation

- Distinct erythema of the tympanic membrane
- Distinct otalgia

Otitis Media

- JC is a 24 month old male toddler who presents to the pediatric clinic with a 3-day history of fussiness and fever of 102°F. He lives at home with his mother, father, and 5-year-old sister, and attends daycare 3 days a week. On physical exam, he weighs 15 kg, his nasal passages are clear, the right and left tympanic membranes are red and bulging. JC has no known allergies. How should his otitis media be managed?

Otitis Media

- Treatment with antibiotics
 - Otorrhea with AOM
 - AOM with severe symptoms (i.e., toxic appearing, temperature greater than 102.2°F, otalgia greater than 48 hours, uncertain access)
 - Bilateral AOM in children 6 months to 2 years of age
- Treat or observe without treatment for 48-72 hrs
 - Bilateral AOM without otorrhea in children 2 years and older
 - Unilateral AOM without otorrhea in all children regardless of age

Otitis Media





■ Antimicrobial therapy

- ❑ Amoxicillin 80-90 mg/kg/day – if no amoxicillin in 30 days
- ❑ Amoxicillin/clavulanate 90 mg/kg/day of amoxicillin, 6.4 mg/kg/day clavulanate – if amoxicillin in 30 days
- ❑ Cephalosporins (cefdinir, cefuroxime, cefpodoxime) or ceftriaxone if severe
- ❑ Clindamycin alone for *S. pneumoniae* infections, or with cefdinir, cefuroxime, cefpodoxime for *H. influenzae* coverage
- ❑ Macrolides unreliable due to high rates of resistance

Treatment is 5 – 10 days based on age

Otitis Media

Based on the 2013 American Academy of Pediatric Guidelines, which of the following would be best recommendation for managing JC's otitis media?

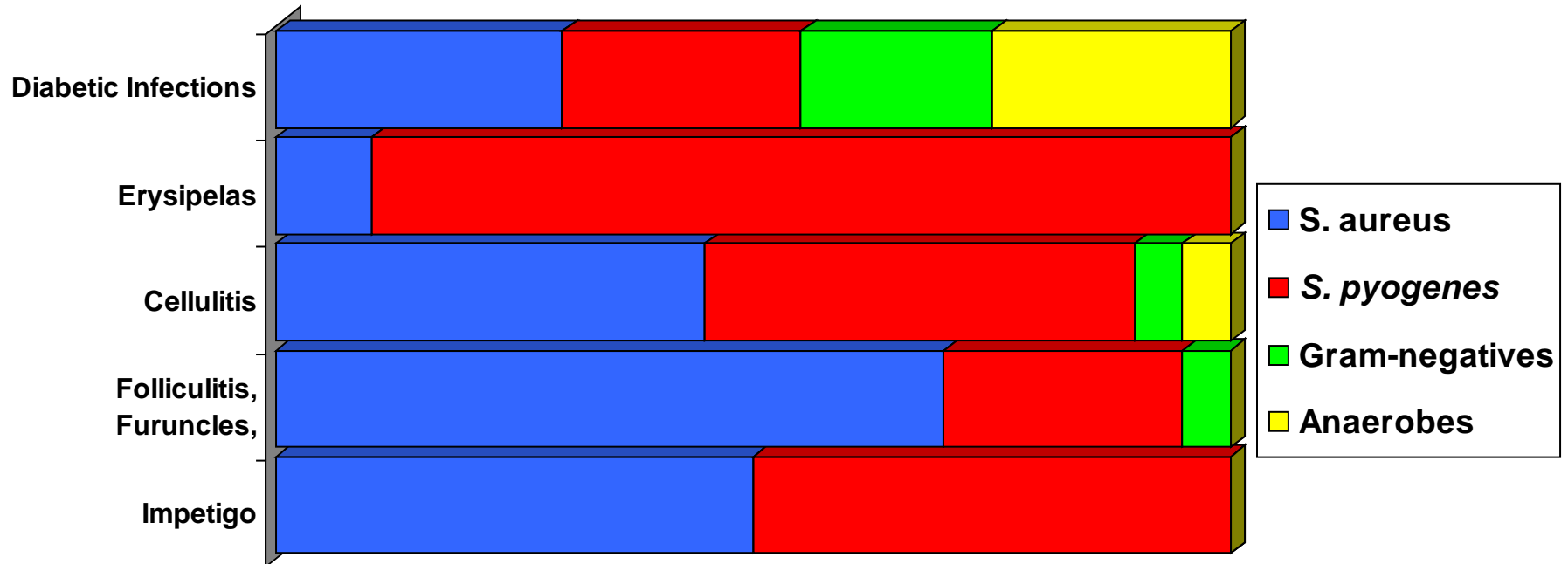
-  A. Clindamycin 150mg divided in 4 doses X 10 days
-  B. Amoxicillin 1500mg divided in 2 doses X 10 days
-  C. Watch and wait for 48 hours
-  D. Azithromycin 150mg X 1 dose, then 280mg daily X 3 days

Uncomplicated Skin & Soft Tissue Infections

- Some of the most common infections seen in community
- Uncomplicated usually involve only the upper layers of skin (epidermis & dermis)
- Common skin infections
 - Impetigo
 - Folliculitis, furuncles, and carbuncles
 - Cellulitis
 - Erysipelas

Uncomplicated Skin & Soft Tissue Infections

Organisms



Impetigo

- Superficial infection with discrete purulent lesions
 - Face & extremities
- Primarily children 2 -5 years old
 - Spread readily with close contact
 - Hot, humid climates
- Treatment for 7 – 10 days
 - Oral antimicrobials (amoxicillin/clavulanate, dicloxacillin, cephalexin, clindamycin)
 - Mupirocin ointment 3 times/day in patients with limited lesions/surface area

Folliculitis, Furuncles, & Carbuncles

MM is a 16-year-old adolescent girl who presents to the clinic with a 24-hour history of a diffuse, itchy rash in both of her legs. She went to a pool party yesterday, and about 10 hours afterward noticed the development of the rash. She has no other symptoms. MM is an otherwise healthy teenager who takes loratadine as needed for allergies. She currently weighs 55kg. On physical exam, significant findings are a diffuse erythematous papular follicular rash. She is given a diagnosis of folliculitis.

Folliculitis, Furuncles, & Carbuncles

■ Folliculitis

- ❑ Superficial inflammation of hair follicle due to infectious and non-infectious causes
- ❑ Pruritic, erythematous papules within 48hrs of infectious exposure

■ Furuncles (abscess or boil)

- ❑ Largely occur in areas of friction or perspiration
- ❑ Firm, tender, red nodule that is painful & usually pus filled
- ❑ Community-acquired MRSA (CA-MRSA) may look like spider bite with necrotic center

■ Carbuncles

- ❑ Swollen, red, deep painful masses commonly back of neck

Folliculitis, Furuncles, & Carbuncles

- Folliculitis – warm saline compresses
- Furuncles & carbuncles: 7-10 day therapy
 - MSSA or *S. pyogenes*
 - ❑ Dicloxacillin 250 – 500mg PO every 6 hours
 - ❑ Cephalexin 250 – 500mg PO every 6 hours
 - ❑ Clindamycin 300 – 600mg PO every 6-8 hours
 - CA-MRSA
 - ❑ TMP/SMX 1-2 DS tablets BID
 - ❑ Doxycycline 100 mg PO BID
 - ❑ Clindamycin (higher resistance rates, inducible resistance)
 - ❑ Linezolid 600mg PO BID
 - ❑ If serious – IV (vancomycin, daptomycin, ceftaroline, dalbavancin, oritavancin)

Folliculitis, Furuncles, & Carbuncles

- Which of the following is the best recommendation for treatment of MM's folliculitis?
 - A. TMP/SMX 1 DS tablet PO 2 times/day for 10 days
 - B. Cephalexin 250 mg PO 4 times/day for 10 days
 - C. Warm saline compresses
 - D. Ciprofloxacin 500 mg PO 2 times/day for 10 days

Cellulitis

- KM is a 32 year-old woman who presents to the clinic with pain, redness, and swelling below her left knee cap. She went to the emergency clinic 2 days ago and was given a prescription for cephalexin, but she states the area keeps getting more painful and red despite the antibiotics. KM is an otherwise healthy woman with no known drug allergies. She works as an elementary teacher and goes to the gym regularly. Physical exam reveals an erythematous and inflamed area with a necrotic center below the left knee cap that is very warm to the touch. KM's vital signs are normal and she is afebrile. I & D are performed in the office, and 15mL of purulent fluid is sent for culture & sensitivities.

Cellulitis

- Acute, diffuse infection of epidermis & dermis
- Usually preceded by trauma, wound, etc
- Signs & Symptoms
 - Infected area red, warm and painful to touch
 - Non-elevated lesions with poorly defined margins
 - Tender lymphadenopathy possible
 - Fever, chills, malaise may be present

Cellulitis

- Treatment for 7 to 10 days
 - Target most likely organisms
 - MSSA or *S. pyogenes*
 - Dicloxacillin 250 – 500mg PO every 6 hours
 - Cephalexin 250 – 500mg PO every 6 hours
 - Clindamycin 300 – 600mg PO every 6-8 hours
 - CA-MRSA
 - TMP/SMX 1-2 DS tablets BID
 - Doxycycline 100 mg PO BID
 - Clindamycin (higher resistance rates, inducible resistance)
 - Linezolid 600mg PO BID
 - If serious – IV (vancomycin, daptomycin, ceftaroline, dalbavancin, oritavancin)

Cellulitis

- Which one of the following is the best recommendation for empiric coverage of KM's cellulitis?
 - A. Penicillin VK 500mg orally every 6hrs for 10 days
 - B. Vancomycin 1 g IV every 12hrs for 10 days
 - C. TMP/SMX 1 DS tablet PO 2 times/day for 10 days
 - D. Dicloxacillin 250mg PO 4 times/day for 10 days

Erysipelas

- Clinically similar to cellulitis
 - Infection is more in upper dermis
 - Clearer demarcation
- Primarily due to *S. pyogenes*
- Treatment for 7 – 10 days
 - Penicillin VK 250 – 500mg every 6hrs
 - Clindamycin 300 – 600mg every 6 -8hrs

Diabetic Foot Infections

- Often polymicrobial
 - Gram-positive (MSSA, MRSA, strep, CNS)
 - Gram-negative (*E. coli*, *Klebsiella* spp., *Proteus* spp., *P. aeruginosa*)
 - Anaerobes (*B. fragilis*, *Peptostreptococcus* spp.)
- Presentation
 - Usually more extensive than they appear
 - Foul smell may be indicative of anaerobes

Diabetic Foot Infections

- Treatment for 7 to 10 days, up to 2 weeks
 - Wound care & antimicrobials
 - Tight glycemic control
 - Mild infections can be treated outpatient from start
 - Assess depth of infection
 - Assess signs of systemic infection / inflammation
 - Uncomplicated treat similarly to non-diabetic

Diabetic Foot Infections

Severity	Description	Antibiotic Options
Mild	Local infection only without involvement of deeper skin structures, no signs of systemic inflammatory response	Dicloxacillin, cephalexin, amoxicillin/clavulanate, clindamycin
Moderate	Local infection with involvement of deeper skin structures but without signs of systemic inflammatory response	Oral options: Amoxicillin/clavulanate, levofloxacin, moxifloxacin Parenteral options: Ampicillin/sulbactam, ertapenem
Severe	Local or extensive infection with signs of systemic inflammatory response	Parenteral options: Vancomycin + antipseudomonal β -lactam (e.g., cefepime, ceftazidime, piperacillin/tazobactam, imipenem/cilastatin, doripenem, meropenem)

Tick Borne Infections

JT is a 23 year old male who goes out for a morning walk in the woods. Upon returning home he notices he has a tick that is attached to his right lower leg. He is very worried about Lyme disease as there are many cases in Wisconsin where he is currently visiting. He calls the clinic to ask what he should do.

Tick Borne Infections

■ Overview

- Lyme disease is the most common tick borne infection in North America and Europe
- Causative pathogen is *Borrelia burgdorferi* transmitted via deer tick bites
- New England, Mid-Atlantic, and parts of Minnesota and Wisconsin have > 20% incidence of *Borrelia burgdorferi*

Lyme disease

- Signs and Symptoms
 - Early manifestations include cutaneous erythema migrans (bull's eye rash) and may be accompanied by flu-like symptoms (fever, chills, fatigue, body aches)
 - Later disease signs/symptoms include joint pain, neurological problems and heart problems

Lyme disease

■ Diagnosis

- Difficult to diagnosis early on unless the tick or characteristic Lyme rash is observed by healthcare professional
- Most signs and symptoms go unrecognized and/or are general to a variety of ailments
- Laboratory tests
 - Enzyme-linked immunosorbent assay (ELISA) to detect *B. burgdorferi* antibodies most common
 - Polymerase chain reaction (PCR) can be run on joints to detect organism

Lyme disease

■ Prophylaxis

- Positively identified infectious tick has been attached ≥ 36 hours
- Start therapy within 72 hours of tick removal
- Therapy
 - Doxycycline 200mg once or 4mg/kg (200mg max) once in children ≥ 8 year
- Closely monitor for rash, flu-like symptoms, joint pain, etc for up to 30 days

Lyme disease

■ Treatment

□ Early disease

- Doxycycline 100 mg orally 2 times/day for 14 days
- Amoxicillin 500 mg orally 3 times/day for 14 days
- Cefuroxime axetil 500 mg orally 2 times/day for 14 days
- Avoid doxycycline in children < 8 years and pregnancy

□ Late Stage Disease (Neurological or Cardiac)

- IV ceftriaxone or cefotaxime for 14 days

□ Lyme arthritis

- Oral antibiotics for 28 days

Tick Borne Infections

■ Prevention

- ❑ Wear protective clothing
- ❑ Tick repellents
- ❑ Check daily for ticks & promptly remove
- ❑ Routine antibiotic prophylaxis for tick bites is NOT recommended

Tick Borne Infections

Which of the following is the most appropriate recommendation for JT based off of the guidelines?

- A. Remove the tick and watch to make sure no rash develops
- B. Go to the emergency room to have the tick removed and examined
- C. Immediately start doxycycline 100 mg orally 2 times/day for 14 days
- D. Remove the tick and bring it in to be identified for species at the clinic

C. difficile

- *C. difficile* infection (CDI) largest culprit antibiotic associated diarrhea and colitis
- Complications: toxic megacolon, leukemoid reactions, septic shock, colectomy, and death
- Increased hospital costs: >\$4,000 per case (conservative estimate)

C. difficile

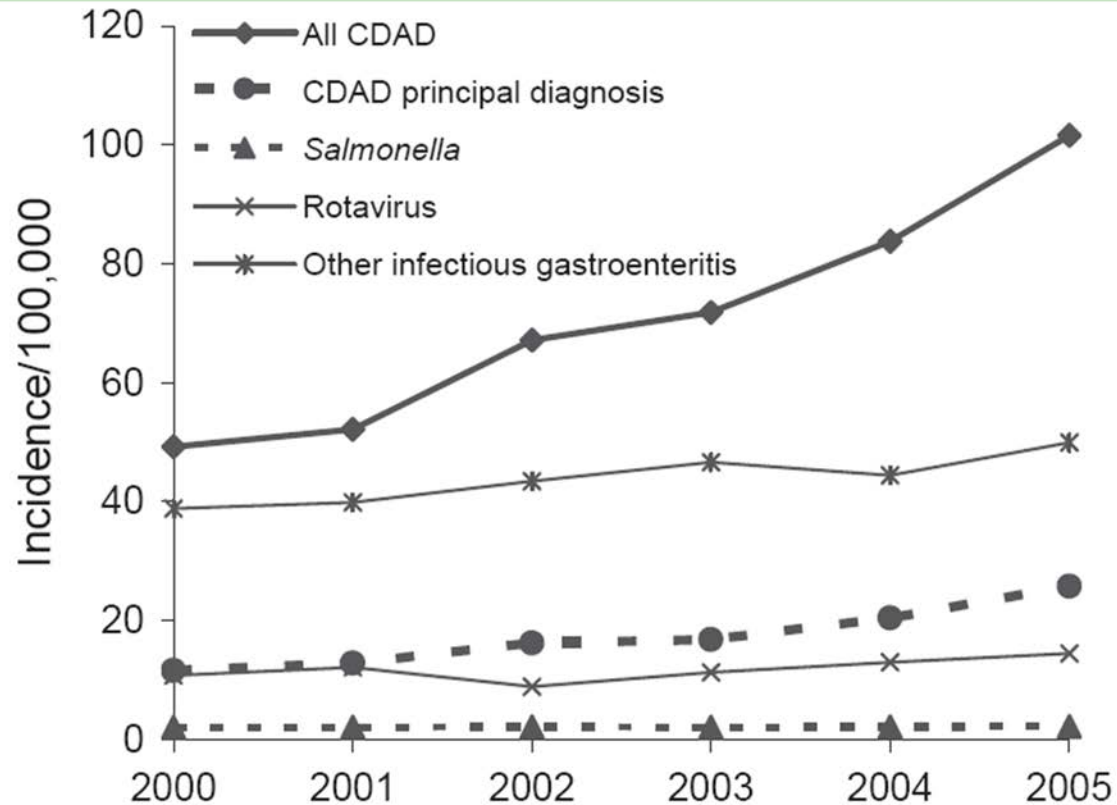


Figure. Annual incidence per 100,000 population of all hospitalizations for *Clostridium difficile*-associated disease (CDAD) compared with hospitalizations for a primary diagnosis of CDAD and with gastroenteritides caused by *Salmonella*, rotavirus, and other unspecified infectious agents, United States, 2000–2005.

C. difficile

■ Toxins

- Produced on pathogenicity locus (PaLoc) of *C. difficile*
 - *tcdA* codes for Toxin A
 - *tcdB* codes for Toxin B
- Hypervirulent Strains
 - Binary Toxin (toxin A & B)
 - *tcdC* deficient (regulator of Toxins A & B)
 - NAP1/BI/027

C. difficile Risk Factors

Host factors

- Increased age
- Immune response



C. diff
Associated
Diarrhea
(CDI)



Pharmacology

- antibiotics
- proton pump inhibitors



Bacteria

- toxin A
- toxin B
- binary toxin



Infection control

- Soap and water
- NO alcohol hand gel



C. difficile

■ Diagnosis

□ Signs and symptoms

- Mild to moderate watery diarrhea
- Leukocytosis

□ Stool testing

- Only test unformed stools
- Culture most sensitive, but will detect non-toxigenic
- Toxin A & B testing for *C. difficile*
 - Tissue culture cytotoxicity assay
 - Enzyme immunoassay
 - Polymerase chain reaction (PCR)

C. difficile

- Determine disease severity
 - Mild to moderate
 - WBC \leq 15,000 mm³, serum creatinine \leq 1.5 times premorbid level
 - Severe
 - WBC $>$ 15,000 mm³, serum creatinine $>$ 1.5 times premorbid level
- Remove offending agent if able
- Avoid antiparistaltics
- Infection control and supportive care

C. Difficile Treatment

Severity	Agent	Dosing
Mild to moderate	Metronidazole	500 mg PO three times daily for 10–14 days
Severe	Vancomycin	125 mg PO four times daily for 10–14 days
Severe with complications	Vancomycin + metronidazole	Vancomycin 500 mg PO four times daily plus metronidazole 500 mg IV every 8 hr, consider rectal vancomycin if ileus

Other options

1. Fidaxomicin 200 mg orally 2 times/day (FDA approved for CDI)
2. Nitazoxanide (Not FDA approved for CDI)
3. Rifaximin (Not FDA approved for CDI)
4. Biotherapy with *Lactobacilli* or *Saccharomyces*?
5. Fecal transplant

C. difficile

AT is a 55 year male who was treated for his first recurrent *C. difficile* infection 3 weeks ago with another round of metronidazole 500 mg orally 3 times/day for 10 days. He has not taken any antibiotics or any other medications in the past 3 weeks, and he now comes to the clinic complaining of severe abdominal pain and frequent loose stools over the past few days. The *C. difficile* toxin immunoassay comes back positive, and she is diagnosed with recurrent CDI again.

C. difficile

■ Recurrence

- First recurrence treat with the same drug as the initial episode
- Second recurrence vancomycin in tapered and/or pulsed regimen
 - Oral taper
- It is not recommended to use metronidazole beyond the first recurrent episode due to possible neurotoxicity

C. difficile

Which of the following is the best recommendation for AT's recurrent infection?

- A. Metronidazole 500 mg orally 3 times/day for 4 weeks
- B. Vancomycin orally tapered over 4 weeks, followed by 4 weeks of pulse dosing
- C. Fidaxomicin 200 mg daily for 10 days
- D. Vancomycin 125 mg orally 4 times/day for 10 days

Bone and Joint Infections

- Osteomyelitis is an inflammatory process with bone destruction due to an infecting organism
- Types
 - Acute (56% of cases) due to infections of recent onset, several days to 1 week
 - Chronic (44% of cases) long standing infections that evolve over months to years with persistence of microorganisms and dead bone
- Risk factors
 - Diabetes, decubitus ulcers, surgery, trauma, IV drug abuse, immunocompromised

Bone and Joint Infections

- Organisms

- *S. aureus* (MSSA and MRSA)
- *S. epidermidis*
- *S. pyogenes*
- Special populations
 - IV drug abusers: *Pseudomonas*
 - Nosocomial exposure: Enterobacteriaceae, *Pseudomonas*
 - Diabetic patients: *S. pneumoniae*, anaerobes

Bone and Joint Infections

■ Diagnosis

□ Signs & symptoms

- Fever, chills, tenderness, redness, decreased motion

□ Laboratory

- Elevated ESR, WBC, C-reactive protein
- Positive blood/tissue cultures

□ Radiography

- Bone changes on radiograph after 10-14 days
- Technetium and gallium scans positive as early as 1 day
- CT and MRI

Bone and Joint Infections

■ Treatment

- Dependent upon likely organisms
 - Nafcillin
 - Cephalosporins
 - Vancomycin for MRSA
 - Addition of rifampin in prosthetic joints
- Length of therapy is usually 4 – 6 weeks in acute osteomyelitis, longer with chronic infections
- Debridement may also be warranted
- Intravenous to oral therapy

Bone and Joint Infections

■ Septic arthritis

- Inflammatory reaction within the joint space leading to persistent purulent effusion within joint
- Risk factors pre-existing arthritis and those for osteomyelitis
- Spread by hematogenous dissemination (majority), adjacent bone infection, direct contamination
- Etiology
 - *S. aureus* (MSSA and MRSA)
 - *Streptococcus* spp.
 - Gram-negatives (*E. coli*, *Pseudomonas* spp.)
 - *Neisseria gonorrhoeae* most common 18 – 30 years old

Bone and Joint Infections

■ Diagnosis

- Signs & symptoms similar to osteomyelitis
- Laboratory
 - Needle aspiration of synovial fluid
 - WBC: 50 – 200 X 10³/mm³
 - Gram stain positive
 - Glucose decreased relative to serum glucose (< 40 mg/dL)
- Imaging shows distention of joint capsule with soft tissue swelling

Bone and Joint Infections

■ Management





- Appropriate antibiotics immediately for 3 to 4 weeks
- Joint drainage and rest
- Antibiotic choices same as osteomyelitis unless gonococcal infection
- *N. gonorrhoeae* treat with ceftriaxone for 7 to 10 days as well as presumptive concomitant treatment for *Chlamydia trachomatis* infection

Bone and Joint Infections

BS is a 23 year old female whom comes into the clinic complaining of fever, severe right knee pain and swelling that started about 3 days ago. She has no memory of any injuries or trauma to her knee. BS is an otherwise healthy, sexually active female with no known drug allergies. On physical exam she has a temperature of 100°F, her right knee has limited mobility with inflammation, erythema, tender and warm to the touch. Laboratory findings reveal a WBC of 15,000 mm³, elevated ESR and CRP. Needle aspiration of the right knee joint shows a WBC of 180,000 mm³ and gram-negative diplococci.

Bone and Joint Infections

Which of the following treatment choices would be best for BS?

-  A. Ceftriaxone 1 gram IM daily for 10 days, plus doxycycline 100 mg PO 2 times/day for 7 days
-  B. Ceftazidime 2 grams IV every 8 hours for 4 weeks
-  C. Ciprofloxacin 750 mg PO 2 times/day for 4 weeks
-  D. Ceftriaxone 1 gram IM daily for 10 days

General Antimicrobial Approach

- Best therapy for patient
 - Effective
 - Compliance
 - Affordable
- Be cognizant of collateral damage
 - Antimicrobial Resistance
 - Treatment of resistant organisms
 - Prevention
 - *C. difficile*
 - Risk with prolonged or broad-spectrum antimicrobials