Infectious Diseases

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Learning Objectives

1. Identify the presenting signs and symptoms, etiology, and risk factors of respiratory tract infections, urinary tract infections, skin and soft tissue infections, osteomyelitis, central nervous system (CNS) infections, intra-abdominal infections, *Clostridium difficile* infections, and endocarditis.

2. Recommend appropriate treatment for patients with respiratory tract infections, urinary tract infections, skin and soft tissue infections, osteomyelitis, CNS infections, intra-abdominal infections, *C. difficile* infections, and endocarditis.

3. Select appropriate preventive therapy for CNS infections, endocarditis, and surgical wound infections.

Self-Assessment Questions

*Answers and explanations to these questions may be found at the end of this chapter.*

1. P.E. is a 56-year-old man who comes to the clinic with a 3-day history of fever, chills, pleuritic chest pain, malaise, and productive cough. In the clinic, his temperature is 102.1°F (38.9°C) (all other vital signs are normal). His chest radiograph reveals consolidation in the right lower lobe. His white blood cell count (WBC) is 14,400 cells/mm³, but all other laboratory values are normal. He is given a diagnosis of community-acquired pneumonia (CAP). He has not received any antibiotics in 5 years and has no chronic disease states. Which is the best empiric therapy for P.E.?

   A. Doxycycline 100 mg orally twice daily.
   B. Cefuroxime axetil 250 mg orally twice daily.
   C. Levofloxacin 750 mg orally daily.
   D. Trimethoprim/sulfamethoxazole double strength orally twice daily.

2. H.W. is a 38-year-old woman who presents with a fever, malaise, dry cough, nasal congestion, and severe headaches. Her symptoms began suddenly 3 days ago, and she has been in bed since then. She reports no other illness in her family, but several people have recently called in sick at work. It is influenza season. Which is best for H.W.?

   A. Azithromycin 500 mg, followed by 250 mg/day orally for 4 more days.
   B. Amoxicillin/clavulanic acid 875 mg orally twice daily for 5 days.
   C. Oseltamivir 75 mg twice daily orally for 5 days.
   D. Symptomatic treatment only.

3. A study is designed to assess the risk of pneumococcal pneumonia in older adults 10 years or more after their pneumococcal vaccination, compared with older adults who have never received the vaccination. Which study design is best?

   A. Case series.
   B. Case-control study.
   C. Prospective cohort study.
   D. Randomized controlled trial.

4. A.B. is a 63-year-old woman who presents to the emergency department with left leg pain and erythema. The pain and erythema have worsened over the past 24 hours, and in the emergency department, large blisters formed and the leg became numb. The left leg is significantly swollen with a large area of erythema and large bullae extending from the thigh to the upper leg. There is crepitus within the soft tissue. A.B. is found to have rapidly progressing necrotizing fasciitis. A.B. has normal renal function and no known drug allergies. Which is the best empiric therapy for A.B.?

   A. Vancomycin 15 mg/kg intravenously every 12 hours.
   B. Piperacillin/tazobactam 4.5 g intravenously every 8 hours.
   C. Vancomycin 15 mg/kg intravenously every 12 hours plus meropenem 1 g intravenously every 8 hours plus clindamycin 900 mg intravenously every 8 hours.
   D. Linezolid 600 mg intravenously every 12 hours plus ceftriaxone 1 g intravenously every 24 hours plus azithromycin 500 mg intravenously daily.
5. N.R. is a 28-year-old woman who presents to the clinic with a 2-day history of dysuria, frequency, and urgency. She has no significant medical history, and the only drug she takes is oral contraceptives. Which is the best empiric therapy for N.R.?
   A. Oral nitrofurantoin extended release (ER) 100 mg twice daily for 3 days.
   B. Oral ciprofloxacin 500 mg twice daily for 7 days.
   C. Oral trimethoprim/sulfamethoxazole double strength twice daily for 3 days.
   D. Oral cephalexin 500 mg four times daily for 3 days.

6. B.Y. is an 85-year-old woman who is bedridden and lives in a nursing home. She is chronically catheterized, and her urinary catheter was last changed 3 weeks ago. Today, her urine is cloudy, and a urinalysis reveals many bacteria. B.Y. is not noticing any symptoms. A urine culture is obtained. Which option is best for B.Y.?
   A. No therapy because she is chronically catheterized and has no symptoms.
   B. No antibiotic therapy, but the catheter should be changed.
   C. Oral ciprofloxacin 500 mg twice daily for 7 days and a new catheter.
   D. Oral ciprofloxacin 500 mg twice daily for 14–21 days without a change in catheter.

7. V.E. is a 44-year-old man who presents to the emergency department with a warm, erythematous, and painful right lower extremity. There is no raised border at the edge of the infection. Three days ago, he scratched his leg on a barbed wire fence on his property. His temperature has been as high as 101.8°F (38°C) with chills. Doppler studies of his lower extremity are negative. Blood cultures are negative. Which is the best empiric therapy for V.E.?
   A. Cefazolin 1 g intravenously every 8 hours. The infection may worsen, and necrotizing fasciitis must be ruled out.
   B. Penicillin G 2 million units intravenously every 4 hours. This is probably erysipelas.
   C. Piperacillin/tazobactam 3.375 g intravenously every 6 hours. Surgical debridement is vitally important.
   D. Enoxaparin 80 mg subcutaneously twice daily and warfarin 5 mg/day orally.

8. R.K. is a 36-year-old woman who presents to the emergency department with a severe headache and neck stiffness. Her temperature is 99.5°F (37.5°C). After a negative computed tomographic scan of the head, a lumbar puncture reveals the following: glucose 54 mg/dL (peripheral, 104 mg/dL), protein 88 mg/dL, and WBC 220 cells/mm³ (100% lymphocytes). The Gram stain reveals no organisms. Which option describes the best therapy for R.K.?
   A. This is aseptic (probably viral) meningitis, and no antibiotics are necessary.
   B. Administer ceftriaxone 2 g intravenously every 12 hours until the cerebrospinal fluid (CSF) cultures are negative for bacteria.
   C. Administer ceftriaxone 2 g intravenously every 12 hours and vancomycin 1000 mg intravenously every 12 hours until the CSF cultures are negative for bacteria.
   D. Administer acyclovir 500 mg intravenously every 8 hours until the CSF culture results are complete.

9. L.G. is a 49-year-old woman with a history of mitral valve prolapse. She presents to her physician’s office with malaise and a low-grade fever. Her physician notes that her murmur is louder than usual and orders blood cultures and an echocardiogram. A large vegetation is observed on L.G.’s mitral valve, and her blood cultures are growing *Enterococcus faecalis* (susceptible to all antibiotics). Which is the best therapy for L.G.?
   A. Penicillin G plus gentamicin for 2 weeks.
   B. Vancomycin plus gentamicin for 2 weeks.
   C. Ampicillin plus gentamicin for 4–6 weeks.
   D. Cefazolin plus gentamicin for 4–6 weeks.
10. N.L. is a 28-year-old woman with no significant medical history. She reports to the emergency department with fever and severe right lower quadrant pain. The pain had been dull for the past few days, but it suddenly became severe during the past 8 hours. Her temperature is 103.5°F (39.7°C), and she has rebound tenderness on abdominal examination. She is taken to surgery immediately, where a perforated appendix is diagnosed and repaired. Which is the best follow-up antibiotic regimen?
   A. Vancomycin 1000 mg intravenously every 12 hours plus metronidazole 500 mg intravenously every 8 hours.
   B. Cefazolin 1 g/day intravenously every 8 hours plus ciprofloxacin 400 mg intravenously every 12 hours.
   C. Ceftriaxone 1 g/day intravenously plus metronidazole 500 mg intravenously every 8 hours.
   D. No antibiotics needed after surgical repair of a perforated appendix.

11. O.R. is a 73-year-old man who presents to the emergency department with a 3-day history of fever, chills, frequency, urgency, and perineal pain. A urinalysis reveals many bacteria. A rectal examination reveals a swollen, tender prostate. He is given a diagnosis of acute bacterial prostatitis. Which is the best regimen for this patient?
   A. Amoxicillin/clavulanate 875 orally twice daily for 7 days.
   B. Trimethoprim/sulfamethoxazole double strength orally twice daily for 14 days.
   C. Cefprozil 500 mg orally twice daily for 21 days.
   D. Ciprofloxacin 500 mg orally twice daily for 28 days.

12. J.M. is a 72-year-old woman with a history of atrial fibrillation, hypertension, a right total hip replacement 8 months earlier, and Crohn disease. She has no drug allergies. She presents to the hospital with increasing pain in her prosthetic hip over the past month. There is concern about hip osteomyelitis. Bone cultures are growing methicillin-sensitive Staphylococcus aureus. J.M. has normal renal function and no known drug allergies. Which is the best antibiotic regimen for this patient with a prosthetic hip infection?
   A. Vancomycin 1000 mg intravenously every 12 hours plus rifampin 300 mg orally twice daily for 2 weeks.
   B. Cefazolin 2 g every 8 hours plus rifampin 300 mg oral twice daily for 6 weeks followed by long-term oral antibiotics.
   C. Nafcillin 1 g every 4 hours for 6 weeks.
   D. Daptomycin 6 mg/kg intravenously daily for 6 weeks followed by long-term oral antibiotics.

13. B.K. is a 58-year-old woman (height 66 inches, weight 82 kg) who is scheduled to undergo a total knee replacement tomorrow. She has no significant medical history and no drug allergies. Which is the best surgical prophylaxis regimen for this patient?
   A. Cefazolin 2 g within 1 hour of the incision and no doses postoperatively.
   B. Cefazolin 2 g within 4 hours of the incision and three doses every 8 hours postoperatively.
   C. Cefazolin 1 g within 1 hour of the incision and three doses every 8 hours postoperatively.
   D. Cefazolin 1 g within 4 hours of the incision and no doses postoperatively.
BPS Pharmacotherapy Specialty Examination Content Outline

This chapter covers the following sections of the Pharmacotherapy Specialty Examination Content Outline:

1. Domain 1: Patient-Specific Pharmacotherapy
   a. Task 1: Knowledge statements: 1–7, 11–12, 15; Task 5: Knowledge statement: 4
   b. Systems and Patient Care Problems:
      i. Pneumonia
      ii. Influenza
      iii. Sinusitis
      iv. Urinary Tract Infections
      v. Skin and Soft Tissue Infections
      vi. Diabetic Foot Infections
      vii. Osteomyelitis
      viii. Central Nervous System Infections
      ix. Endocarditis
      x. Peritonitis/Intra-Abdominal Infections
      xi. *Clostridium difficile* Infection
      xii. Medical/Surgical Prophylaxis

2. Domain 2: Retrieval, Generation, Interpretation and Dissemination of Knowledge in Pharmacotherapy; Task 2: Knowledge statements: 1–5
I. RESPIRATORY TRACT INFECTIONS

A. Pneumonia
   1. Pneumonia is the most common cause of death attributable to infectious diseases (very high rates in older adults) and in the top 10 causes of death in the United States.
   2. Hospital-acquired pneumonia (HAP) is the second most common nosocomial infection (0.6%–1.1% of all hospitalized patients). There is a higher incidence in patients in the intensive care unit recovering from thoracic or upper abdominal surgery and in older adults.
   3. Mortality rates
      a. Community-acquired pneumonia (CAP) without hospitalization: Less than 1%
      b. CAP with hospitalization: About 14%
      c. Ventilator-associated pneumonia (VAP): About 20%–50%

B. Community-Acquired Pneumonia
   1. Definition: Acute infection of the pulmonary parenchyma, accompanied by an acute infiltrate consistent with pneumonia on chest radiograph or auscultatory findings, acquired in the community. Patients must not have been hospitalized recently, nor had regular exposure to the health care system.
   2. Symptoms of CAP are listed below. Older adults often have fewer and less severe findings (mental status changes are common).
      a. Fever or hypothermia
      b. Rigors
      c. Sweats
      d. New cough with or without sputum (90%)
      e. Chest discomfort (50%)
      f. Onset of dyspnea (66%)
      g. Fatigue, myalgias, abdominal pain, anorexia, and headache
   3. Predictors of a complicated course of CAP are listed below. Hospitalization should be based on the severity-of-illness scores (e.g., CURB-65, pneumonia severity index).
      a. Age older than 65 years
      b. Comorbid illness (diabetes mellitus, congestive heart failure, lung disease, renal failure, liver disease)
      c. High temperature: more than 101°F (38°C)
      d. Bacteremia
      e. Altered mental status
      f. Immunosuppression (e.g., steroid use, cancer)
      g. High-risk etiology (Staphylococcus aureus, Legionella, gram-negative bacilli, anaerobic aspiration)
      h. Multilobe involvement or pleural effusions
   4. Severity-of-illness scoring systems in CAP
      a. CURB-65 (Tables 1 and 2)
Table 1. CURB-65 Scoring

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confusion</td>
<td>1</td>
</tr>
<tr>
<td>Urea &gt; 19 mg/dL</td>
<td>1</td>
</tr>
<tr>
<td>Respiratory rate ≥ 30 breaths/minute</td>
<td>1</td>
</tr>
<tr>
<td>SBP &lt; 90 mm Hg, DBP ≤ 60 mm Hg</td>
<td>1</td>
</tr>
<tr>
<td>Age ≥ 65 yr</td>
<td>1</td>
</tr>
</tbody>
</table>

*CRB-65 (without a blood urea nitrogen concentration) is useful in a primary practice setting.

DBP = diastolic blood pressure; SBP = systolic blood pressure.

Table 2. CURB-65 Location of Therapy

<table>
<thead>
<tr>
<th>Score</th>
<th>Risk of Death at 30 Days (%)</th>
<th>Location of Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.7</td>
<td>Treat as outpatient</td>
</tr>
<tr>
<td>1</td>
<td>2.1</td>
<td>Treat as outpatient</td>
</tr>
<tr>
<td>2</td>
<td>9.2</td>
<td>Outpatient or inpatient</td>
</tr>
<tr>
<td>3</td>
<td>14.5</td>
<td>Inpatient (± ICU)</td>
</tr>
<tr>
<td>4</td>
<td>40.0</td>
<td>Inpatient (± ICU)</td>
</tr>
<tr>
<td>5</td>
<td>57.0</td>
<td>Inpatient (± ICU)</td>
</tr>
</tbody>
</table>

ICU = intensive care unit.

b. Pneumonia severity index (or Pneumonia Patient Outcomes Research Team score)
   i. Evaluates 20 patient characteristics
   ii. Assesses risk of mortality, similar to CURB-65
   iii. Has predictive ability similar to that of CURB-65 but better in patients with lower mortality risk

C. HAP and VAP
   1. HAP: Pneumonia in a nonventilated patient that occurs 48 hours or more after admission and was not incubating at the time of admission
   2. VAP: Pneumonia that arises more than 48 hours after endotracheal intubation
   3. Health care–associated pneumonia (HCAP): Pneumonia developing in a patient who has had recent significant contact with the health care system. Not included in the 2016 HAP/VAP guidelines. Patients should be assessed for multidrug-resistant (MDR) organisms.
   4. Risk factors for nosocomial pneumonia
      a. Intubation and mechanical ventilation
      b. Supine patient position
      c. Enteral feeding
      d. Oropharyngeal colonization
      e. Stress bleeding prophylaxis
      f. Blood transfusion
      g. Hyperglycemia
      h. Immunosuppression or corticosteroids
      i. Surgical procedures: thoracoabdominal, upper abdominal, thoracic
j. Immobilization  
k. Nasogastric tubes  
l. Previous antibiotic therapy  
m. Admission to the intensive care unit  
n. Advanced age  
o. Underlying chronic lung disease

D. Microbiology (Table 3)

Table 3. Incidence of Pneumonia by Organism

<table>
<thead>
<tr>
<th>Community Acquired (%)</th>
<th>Hospital Acquired (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unidentifiable</td>
<td>Unidentifiable</td>
</tr>
<tr>
<td><em>Mycoplasma pneumoniae</em></td>
<td>40–60</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>13–37</td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em></td>
<td>9–20</td>
</tr>
<tr>
<td><em>Chlamydia pneumoniae</em></td>
<td>3–10</td>
</tr>
<tr>
<td><em>Legionella pneumophila</em></td>
<td>1–17</td>
</tr>
<tr>
<td>Viruses</td>
<td>Common</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>0.7–13</td>
</tr>
<tr>
<td>Moraxella catarrhalis</td>
<td>Common</td>
</tr>
<tr>
<td>Anaerobes</td>
<td>Common</td>
</tr>
<tr>
<td>Gram-negative bacilli</td>
<td>Uncommon</td>
</tr>
<tr>
<td>(e.g., <em>Klebsiella pneumoniae</em>)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Community Acquired (%)</th>
<th>Hospital Acquired (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>50</td>
</tr>
<tr>
<td><em>Enterobacter spp.</em></td>
<td>10</td>
</tr>
<tr>
<td><em>K. pneumoniae</em></td>
<td>8</td>
</tr>
<tr>
<td><em>Candida spp.</em></td>
<td>5</td>
</tr>
<tr>
<td><em>Acinetobacter spp.</em></td>
<td>4</td>
</tr>
<tr>
<td><em>Serratia marcescens</em></td>
<td>3</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>2</td>
</tr>
<tr>
<td><em>S. pneumoniae</em></td>
<td>1</td>
</tr>
</tbody>
</table>

Specific populations in community-acquired pneumonia:
- Alcoholism: *S. pneumoniae*, oral anaerobes, gram-negative bacilli (e.g., *Klebsiella*)  
- Nursing home: *S. pneumoniae*, *H. influenzae*, gram-negative bacilli, *S. aureus*  
- COPD: *S. pneumoniae*, *H. influenzae*, *M. catarrhalis*  
- Postinfluenza: *H. influenzae*, *S. aureus*, *S. pneumoniae*  
- Exposure to water: *Legionella*  
- Poor oral hygiene: oral anaerobes  
- HIV infection: *Pneumocystis jirovecii*, *S. pneumoniae*, *M. pneumoniae*, *Mycobacterium*

Issues in hospital-acquired pneumonia:
- *P. aeruginosa* is transmitted by health care workers’ hands or respiratory equipment  
- *S. aureus* is transmitted by health care workers’ hands  
- Enterobacteriaceae endogenously colonize hospitalized patients’ airways (healthy people seldom have gram-negative upper airway colonization)  
- Stress changes respiratory epithelial cells so that gram-negative organisms can adhere  
- Up to 70% of patients in the intensive care unit have gram-negative upper airway colonization, and 25% of them become infected through aspiration

COPD = chronic obstructive pulmonary disease; HIV = human immunodeficiency virus.
Patient Case
1. R.L. is a 68-year-old man who presents to the emergency department with coughing and shortness of breath. His symptoms, which began 4 days ago, have worsened during the past 24 hours. He is coughing up yellow-green sputum, and he has chills, with a temperature of 102.4°F (39°C). His medical history includes coronary artery disease with a myocardial infarction 5 years ago, congestive heart failure, hypertension, and osteoarthritis. He rarely drinks alcohol and has not smoked since his myocardial infarction. He lives at home with his wife. His medications on admission include lisinopril 10 mg/day, hydrochlorothiazide 25 mg/day, and acetaminophen 650 mg four times/day. On physical examination, he is alert and oriented, with the following vital signs: temperature 101.8°F (38°C), heart rate 100 beats/minute, respiratory rate 32 breaths/minute, and blood pressure 142/94 mm Hg. His laboratory results are normal except for blood urea nitrogen (BUN) 32 mg/dL (serum creatinine [Scr] 1.23 mg/dL). A chest radiograph reveals infiltrates in the right lower lobe. A sputum specimen is not available. If R.L. were hospitalized, which would be the best empiric therapy for him?
A. Ampicillin/sulbactam 1.5 g intravenously every 6 hours.
B. Piperacillin/tazobactam 4.5 g intravenously every 6 hours plus gentamicin 180 mg intravenously every 12 hours.
C. Ceftriaxone 1 g intravenously every 24 hours plus azithromycin 500 mg intravenously every 24 hours.
D. Doxycycline 100 mg intravenously every 12 hours.

E. Therapy: Pneumonia
1. CAP
   a. Empiric treatment of nonhospitalized patients
      i. Previously healthy and no antibiotic therapy in the past 3 months
         (a) Macrolide (clarithromycin or azithromycin if Haemophilus influenzae is suspected)
         (b) Doxycycline
         (c) If local high-level macrolide resistance (minimum inhibitory concentration [MIC] of 16 mcg/mL or greater) exceeds 25%, use regimen from below.
      ii. Comorbidities (chronic obstructive pulmonary disease [COPD], diabetes mellitus, chronic renal or liver failure, congestive heart failure, malignancy, asplenia, or immunosuppression) or recent antibiotic therapy (within the past 3 months)
         (a) Respiratory fluoroquinolone (moxifloxacin, gemifloxacin, or levofloxacin [750 mg])
         (b) Macrolide (or doxycycline) with high-dose amoxicillin (1 g three times/day) or amoxicillin/clavulanate (2 g twice daily) or a cephalosporin (ceftriaxone, cefuroxime, or cefpodoxime)
   b. Empiric treatment of hospitalized patients with moderately severe pneumonia
      i. Respiratory fluoroquinolone (moxifloxacin, gemifloxacin [oral only], or levofloxacin [750 mg])
      ii. Ampicillin, ceftriaxone, or cefotaxime (ertapenem in select patients) plus a macrolide (or doxycycline)
      iii. Corticosteroids (unknown optimal agent, dose, or duration) decrease risk of mechanical ventilation and acute respiratory distress syndrome and decrease hospital stay by about 1 day; greater incidence of hyperglycemia requiring treatment. Typical doses are prednisone or methylprednisolone 20–50 mg daily for 7 days.
   c. Empiric treatment of hospitalized patients with severe pneumonia necessitating intensive care unit treatment (may need to add other antibiotics if Pseudomonas aeruginosa or methicillin-resistant S. aureus [MRSA] is suspected)
      i. Ampicillin/sulbactam plus either a respiratory fluoroquinolone or azithromycin
      ii. Ceftriaxone plus either a respiratory fluoroquinolone or azithromycin
      iii. Cefotaxime plus either a respiratory fluoroquinolone or azithromycin
d. Treatment duration: At least 5 days, with 48–72 hours afebrile and no more than one sign of clinical instability (elevated temperature, heart rate, or respiratory rate; decreased systolic blood pressure; or arterial oxygen saturation) before therapy discontinuation

**Patient Case**

2. B.P. is a 66-year-old woman who underwent a two-vessel coronary artery bypass graft 8 days ago and has been on a ventilator in the surgical intensive care unit since then. Her temperature is now rising and her chest radiograph reveals a new infiltrate in the right lower lobe. Her medical history includes coronary artery disease with a myocardial infarction 2 years ago, COPD, and hypertension. All antipseudomonal antibiotics in the institution are active against at least 90% of strains. B.P. has no known drug allergies. Which is the best empiric therapy for B.P.?

A. Ceftriaxone 1 g intravenously every 24 hours plus gentamicin 7 mg/kg intravenously every 24 hours plus linezolid 600 mg intravenously every 12 hours.

B. Piperacillin/tazobactam 4.5 g intravenously every 6 hours.

C. Levofoxacin 750 mg intravenously every 24 hours plus linezolid 600 mg intravenously every 12 hours.

D. Cefepime 2 g intravenously every 8 hours plus tobramycin 7 mg/kg intravenously every 24 hours plus vancomycin 15 mg/kg intravenously every 12 hours.

2. VAP
   a. Empiric regimen should include antibiotics with activity against *S. aureus*, *P. aeruginosa*, and other gram-negative organisms.
      - Options for single agents: Piperacillin/tazobactam, cefepime, levofoxacin, imipenem or meropenem.
   b. Two antibiotics with activity against *P. aeruginosa* should be included if the patient has risk factors for MDR organisms (see below) or if *P. aeruginosa* resistance in the hospital unit to the antibiotic considered for monotherapy is greater than 10%.
      i. Options for first agent: Antipseudomonal β-lactam (ceftazidime, cefepime, imipenem, meropenem, piperacillin/tazobactam, or aztreonam)
      ii. Options for second agent: Aminoglycoside, fluoroquinolone (ciprofloxacin, levofoxacin) or colistin (aztreonam may be used with another β-lactam if no other second option is available)
   c. An antibiotic with activity against MRSA should be included if the patient has risk factors for MDR organisms (see below) or if MRSA incidence in the hospital unit is greater than 10%–20%.
      Note: In locations where the prevalence of MRSA respiratory infections is low, a negative MRSA nasal screen suggests that MRSA antibiotics are unnecessary empirically. Locations with a high prevalence of MRSA respiratory infections should follow the rule above.
      i. Options if MRSA activity necessary: Vancomycin or linezolid
      ii. If an MRSA agent is used, then ceftazidime and aztreonam are potential alternative choices for the anti-pseudomonal agent.
   d. Ideally, dose antibiotics based on pharmacokinetic/pharmacodynamic data, including antibiotic serum concentrations, extended infusions of β-lactams and weight based dosing of aminoglycosides
   e. Antibiotics should be de-escalated on the basis of culture results. Antibiotic therapy for *P. aeruginosa* can be de-escalated to one active agent on the basis of culture and sensitivity results.
   f. Treatment duration: 7-day course is recommended for all infections.
   g. Risk factors for MDR organisms
      i. Intravenous antibiotic therapy within the past 90 days
      ii. Hospitalization of 5 days or more (VAP only)
      iii. Septic shock at time of VAP (VAP only)
iv. Acute respiratory distress syndrome preceding VAP (VAP only)
v. Acute renal replacement therapy before VAP (VAP only)

3. HAP
   a. Empiric regimen should include antibiotics with activity against *S. aureus, P. aeruginosa*, and
      other gram-negative organisms.
      - Options for single agents: Piperacillin/tazobactam, cefepime, levofloxacin, imipenem or
        meropenem.
   b. Two antibiotics with activity against *P. aeruginosa* should be included if the patient has received
      antibiotics in the past 90 days or has a high risk of mortality (indicated by the need for ventilator
      support or septic shock). In addition, use two agents for patients with respiratory cultures grow-
      ing several and predominantly gram-negative organisms or patients with structural lung disease
      (bronchiectasis or cystic fibrosis).
      i. Options for first agent: Antipseudomonal β-lactam (ceftazidime, cefepime, imipenem, mero-
         penem, piperacillin/tazobactam, or aztreonam)
      ii. Options for second agent: Aminoglycoside, fluoroquinolone (ciprofloxacin, levofloxacin), or
          colistin (aztreonam may be used with another β-lactam if no other second option is available)
      iii. Aminoglycosides should not be used as monotherapy.
   c. An antibiotic with activity against MRSA should be included if the patient has risk factors for
      MDR organisms, if MRSA incidence in the hospital unit is greater than 10%–20%, or if the patient
      is at a high mortality risk. See statement in VAP section regarding MRSA nasal screening.
      i. Options if MRSA activity necessary: Vancomycin or linezolid
      ii. If a MRSA agent is used, then ceftazidime and aztreonam are potential alternative choices for
          the anti-pseudomonal agent.
      iii. Use oxacillin, nafcillin, or cefazolin for proven MSSA infections.
   d. Ideally, dose antibiotics according to pharmacokinetic/pharmacodynamic data, including anti-
      biotic serum concentrations, extended infusions of β-lactams, and weight-based dosing of
      aminoglycosides.
   e. Antibiotics should be de-escalated according to culture results. Antibiotic therapy for *P. aeruginosa*
      can be de-escalated to one active agent on the basis of culture and sensitivity results.
   f. Treatment duration: A 7-day course is recommended for all infections.

4. HCAP
   a. Treat with CAP guideline regimens (appropriate in over 90% of patients).
   b. Rationale for not using broad-spectrum antibiotics universally
      i. HCAP criteria poorly predict MDR organisms
      ii. HCAP mortality associated more with age and comorbidities
      iii. Use of broad-spectrum antibiotics for all patients with HCAP leads to overtreatment.
   c. When to add Pseudomonas coverage (any one of the following):
      i. COPD/structural lung disease with history of repeated antibiotics
      ii. Chronic corticosteroid use (more than 20mg/day prednisone for more than 14 days)
      iii. 3 or more of the following pneumonia risk factors:
          (a) Hospitalization for more than 2 days in previous 90 days
          (b) Antibiotic use during the previous 90 days
          (c) Non-ambulatory status
          (d) Patient receiving tube feedings
          (e) Immunocompromised status
          (f) Use of gastric acid suppressive agents
d. When to add MRSA coverage (two or more of the following):
   i. Long-term hemodialysis
   ii. Prior MRSA infection or colonization
   iii. Heart failure
   iv. Any one of the following pneumonia risk factors:
      (a) Hospitalization for more than 2 days in previous 90 days
      (b) Antibiotic use during the previous 90 days
      (c) Non-ambulatory status
      (d) Patient receiving tube feedings
      (e) Immunocompromised status
      (f) Use of gastric acid suppressive agents

F. Antibiotic Resistance
1. Innate resistance – Based on characteristics of the microorganism (e.g., *P. aeruginosa* has innate resistance to vancomycin)
2. Acquired resistance
   a. Mutations – Chromosomal alterations passed to daughter cells only
   b. Horizontal gene transfer
      i. Plasmids – Extrachromosomal DNA that codes for resistance; mobile; can code for resistance to multiple antibiotics
      ii. Transposons – Resistance genes transferred within or between chromosomal DNA or plasmids
      iii. Integrons – DNA component that contains a site where a gene cassette that codes for resistance can be integrated into the bacterial DNA
3. Mechanisms of resistance
   a. Decreased uptake
      i. β-Lactams
      ii. Fluoroquinolones
      iii. Aminoglycosides (especially *Pseudomonas*)
   b. Enzyme modification and degradation
      i. β-Lactamases (see Table 4)
      ii. Aminoglycoside hydrolytic enzymes (e.g., acetyltransferase, phosphotransferase, adenyl transferase) – Enteric gram-negative bacteria
   c. Altered target site
      i. β-Lactams (e.g., altered penicillin-binding proteins (PBPs), *mecA*) – *Staphylococcus, Streptococcus*, and *Enterococcus*
      ii. Glycopeptides (e.g., van*A* and van*B*) – Vancomycin resistance in *Enterococcus*
      iii. Fluoroquinolones (e.g., *gyrA* and *parC* mutations)
      iv. Ribosomal mutations (e.g., macrolides, tetracyclines)
      v. Sulfonamides (e.g., altered genes encoding dihydropteroate synthase)
      vi. Trimethoprim (e.g., altered genes encoding dihydrofolate reductase or overproduction of dihydrofolate reductase)
   d. Efflux pumps
      i. Macrolides (e.g., *mef*-encoded efflux in *Streptococcus*)
      ii. Fluoroquinolones
      iii. Tetracyclines
Table 4. β-Lactamases

<table>
<thead>
<tr>
<th>Molecular Class</th>
<th>Category Name</th>
<th>Target</th>
<th>Examples</th>
<th>Effective Inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Serine β-lactamases</td>
<td>Penicillins, cephalosporins, aztreonam, carbapenems</td>
<td>TEM family; SHV family; CTX-M family; most ESBLs; CRE (KPC)</td>
<td>Avibactam, clavulanic acid, sulbactam, tazobactam</td>
</tr>
<tr>
<td>B</td>
<td>Metallo β-lactamases</td>
<td>Carbapenems</td>
<td>IMP family, VIM family; CRE (NDM-I)</td>
<td>None</td>
</tr>
<tr>
<td>C</td>
<td>Serine β-lactamases</td>
<td>Cephalosporins</td>
<td>Amp C</td>
<td>Avibactam</td>
</tr>
<tr>
<td>D</td>
<td>Serine β-lactamases</td>
<td>Extended-spectrum cephalosporins, carbapenems</td>
<td>CRE (OXA family)</td>
<td>Avibactam; ±clavulanic acid; ±tazobactam</td>
</tr>
</tbody>
</table>

CRE = carbapenem-resistant Enterobacteriaceae; ESBL = extended-spectrum β-lactamase; KPC = Klebsiella pneumoniae carbapenemase; NDM = New Delhi metallo-β-lactamase; OXA = oxacillinase; VIM = Verona integron-encoded metallo-β-lactamase.

G. Influenza

1. Characteristics of influenza infection
   a. Epidemic with significant mortality
   b. Epidemics begin abruptly → peak in 2–3 weeks → resolve in 5–6 weeks.
   c. Occurs almost exclusively in the winter
   d. Average overall attack rates of 10%–20%
   e. Mortality greatest in those older than 65 years (especially with heart and lung disease): More than 80% of deaths caused by influenza are from this age group (20,000 deaths a year in the United States).

2. Is it a cold or the flu? (Table 5)

Table 5. Differentiating the Symptoms of Cold and Influenza

<table>
<thead>
<tr>
<th>Signs and Symptoms</th>
<th>Influenza</th>
<th>Cold</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>Sudden</td>
<td>Gradual</td>
</tr>
<tr>
<td>Temperature</td>
<td>Characteristic, high (&gt; 101°F [38°C]) of 3–4 days’ duration</td>
<td>Occasional</td>
</tr>
<tr>
<td>Cough</td>
<td>Dry; can become severe</td>
<td>Hacking</td>
</tr>
<tr>
<td>Headache</td>
<td>Prominent</td>
<td>Occasional</td>
</tr>
<tr>
<td>Myalgia (muscle aches and pains)</td>
<td>Usual; often severe</td>
<td>Slight</td>
</tr>
<tr>
<td>Tiredness and weakness</td>
<td>Can last 2–3 wk</td>
<td>Very mild</td>
</tr>
<tr>
<td>Extreme exhaustion</td>
<td>Early and prominent</td>
<td>Never</td>
</tr>
<tr>
<td>Chest discomfort</td>
<td>Common</td>
<td>Mild to moderate</td>
</tr>
<tr>
<td>Stuffy nose</td>
<td>Sometimes</td>
<td>Common</td>
</tr>
<tr>
<td>Sneezing</td>
<td>Sometimes</td>
<td>Usual</td>
</tr>
<tr>
<td>Sore throat</td>
<td>Sometimes</td>
<td>Common</td>
</tr>
</tbody>
</table>
3. Pathophysiology
   a. Type A
      i. Influenza further grouped by variations in hemagglutinin and neuraminidase (e.g., H1N1, H3N2)
      ii. Changes through antigenic drift or shift
         (a) Drift: Annual, gradual change caused by mutations, substitutions, and deletions
         (b) Shift: Less common dramatic change leading to pandemics
      iii. Causes epidemics every 1–3 years
   b. Type B
      i. Type B influenza carries one form of hemagglutinin and one form of neuraminidase, both of which are less likely to mutate than the hemagglutinin and neuraminidase of type A influenza.
      ii. Changes through antigenic drift (minor mutations from year to year); when enough drifts occur, an epidemic is likely.
      iii. Causes epidemics every 5 years

4. Therapy
   a. Treatment indicated in patients with confirmed or suspected influenza and the following conditions (use only the neuraminidase inhibitors):
      i. Hospitalized patients
      ii. Severe, complicated, or progressive illness
      iii. High risk of influenza complications
         (a) Patients younger than 2 years or 65 years and older
         (b) Patients with chronic disease states: Pulmonary (including asthma), cardiovascular (except hypertension alone), renal, hepatic, hematologic (including sickle cell disease), metabolic disorders (including diabetes mellitus), or neurologic and neurodevelopment conditions
         (c) Immunosuppressed patients
         (d) Pregnant women
         (e) Patients younger than 19 years who are receiving long-term aspirin therapy
         (f) American Indians and Alaska Natives
         (g) Patients who are morbidly obese
         (h) Residents of nursing homes and other long-term care facilities
      iv. Treatment may be considered for those without risk factors according to clinical judgment (must initiate within 48 hours).
   b. Amantadines
      i. Amantadine (Symmetrel), rimantadine (Flumadine)
      ii. Inhibit viral uncoating and release of viral nucleic acid by inhibiting M2 protein
         (a) Never effective against influenza B virus
         (b) Not recommended for treatment because of current universal resistance in influenza A
   c. Neuraminidase inhibitors
      i. Oseltamivir (Tamiflu), Zanamivir (Relenza), peramivir (Rapivab)
      ii. Inhibit neuraminidase; symptoms resolve 1–1.5 days sooner
      iii. Adverse effects
         (a) Oseltamivir: Gastrointestinal (GI) (nausea and vomiting), central nervous system (CNS) (anxiety, headache, insomnia, etc.)
         (b) Zanamivir: Bronchospasm, cough (not recommended in patients with asthma or COPD)
         (c) Peramivir: Diarrhea; aspartate aminotransferase, alanine aminotransferase, creatinine phosphokinase, glucose elevation
iv. Dosage
   (a) Oseltamivir: 75 mg orally twice daily for 5 days; decrease dosage to 30 mg twice daily orally in patients with a creatinine clearance (CrCl) of 31–60 mL/minute/1.73 m² and 30 mg once daily orally in patients with a CrCl of 11–30 mL/minute/1.73 m².
   (b) Zanamivir: Two inhalations (5 mg/inhalation) twice daily for 5 days
   (c) Peramivir: 600 mg intravenously once; decrease dose to 200 and 100 mg in patients with a CrCl less than 50 and 30 mL/minute/1.73 m², respectively
   (d) Initiate within 48 hours of symptom onset.

5. Prevention
   a. Chemoprophylaxis only for influenza-related complications in patients at very high risk (e.g., severely immunosuppressed patients) who cannot be protected by the vaccine when a high risk of exposure exists
   b. Amantadine, rimantadine: Not recommended for prevention because of current universal resistance
   c. Neuraminidase inhibitors
      i. Oseltamivir (Tamiflu)
         (a) Oseltamivir administered 75 mg/day orally for 6 weeks during peak influenza season had 74% protective efficacy (as prophylaxis in unvaccinated people).
         (b) Begin oseltamivir 75 mg/day orally within 2 days of close contact with an infected person and continue for no more than 10 days.
      ii. Zanamivir (Relenza)
         (a) Zanamivir 10 mg/day through inhalation for 4 weeks during peak influenza season had 67% protective efficacy (as prophylaxis in unvaccinated people).
         (b) Begin zanamivir 10 mg/day within 5 days of community outbreak and continue for 4 weeks during peak influenza season.

Patient Case
3. S.C. is a 46-year-old woman who presents to the clinic with purulent nasal discharge, nasal and facial congestion, headaches, fever, and dental pain. Her symptoms began about 10 days ago, improved after about 4 days, and then worsened again a few days later. Which is the best empiric therapy for S.C.?
   A. Cefpodoxime 200 mg orally twice daily.
   B. Clindamycin 300 mg orally four times daily.
   C. Amoxicillin/clavulanate 875 mg/125 mg orally every 12 hours.
   D. No antibiotic therapy needed because this is a typical viral infection.

H. Sinusitis
1. Definition and etiology
   a. Inflammation of the mucosal lining of the nasal passage and paranasal sinuses lasting up to 4 weeks
   b. Many different causes, including viruses, bacteria, and fungi
   c. Viruses account for more than 90% of cases, whereas bacteria account for less than 10%.
2. Diagnosis
   a. Presence of at least two major symptoms or one major and two or more minor symptoms (Table 6)

Table 6. Symptoms Associated with Diagnosis of Sinusitis

<table>
<thead>
<tr>
<th>Major Symptoms</th>
<th>Minor Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Purulent anterior nasal discharge</td>
<td>Headache</td>
</tr>
<tr>
<td>Purulent or discolored posterior nasal discharge</td>
<td>Ear pain, pressure, or fullness</td>
</tr>
<tr>
<td>Nasal congestion or obstruction</td>
<td>Halitosis</td>
</tr>
<tr>
<td>Facial congestion or fullness</td>
<td>Dental pain</td>
</tr>
<tr>
<td>Facial pain or pressure</td>
<td>Cough</td>
</tr>
<tr>
<td>Hyposmia or anosmia</td>
<td>Fever (for subacute or chronic sinusitis)</td>
</tr>
<tr>
<td>Fever (for acute sinusitis only)</td>
<td>Fatigue</td>
</tr>
</tbody>
</table>

   b. Viral or bacterial? (Table 7)

Table 7. Differentiating Viral from Bacterial Sinusitis

<table>
<thead>
<tr>
<th></th>
<th>Viral</th>
<th>Bacterial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms</td>
<td>Nasal discharge, congestion, and scratchy throat</td>
<td>Nasal discharge, congestion, and scratchy throat</td>
</tr>
<tr>
<td>Nasal discharge</td>
<td>Clear to purulent to clear; purulence not present until days 4–5</td>
<td>Persistent purulent discharge (&gt; 10 days) or early and severe (first 3–4 days) or increased on days 5–6 after typical viral infection (“double-sickening”)</td>
</tr>
<tr>
<td>Fever</td>
<td>None (or early in course, resolving in 48 hr)</td>
<td>High temperature (≥ 39°C) and early (first 3–4 days)</td>
</tr>
<tr>
<td>Other symptoms</td>
<td>Headache, facial pain, and myalgia (resolving in 48 hr)</td>
<td>Headache, facial pain, myalgia, daytime cough</td>
</tr>
<tr>
<td>Peak symptoms</td>
<td>Days 3–6</td>
<td>Persistent &gt; 10 days or early and severe (first 3–4 days) or improved symptoms that worsen on days 5–6</td>
</tr>
<tr>
<td>Duration</td>
<td>5–10 days</td>
<td>In general, &gt; 10 days</td>
</tr>
</tbody>
</table>

3. Treatment
   a. Begin antibiotics as soon as bacterial sinusitis is diagnosed (see criteria in Table 7).
   b. First-line therapy
      i. Amoxicillin/clavulanate
      ii. High-dose amoxicillin/clavulanate (2 g twice daily in adults or 90 mg/kg/day divided twice daily) in
         (a) Geographic regions with high endemic rates (greater than 10%) of invasive penicillin-nonsusceptible S. pneumoniae
         (b) Those with a severe infection (e.g., evidence of systemic toxicity with a temperature of 39°C or higher and a threat of suppurative complications)
         (c) Attendance at day care
         (d) Age younger than 2 years or older than 65 years
         (e) Recent hospitalization
         (f) Antibiotic use within the past month
         (g) Those who are immunocompromised
c. Second-line therapy
   i. Respiratory fluoroquinolone (including children with type I hypersensitivity to penicillin) –
      Because of serious adverse effects, avoid if there are other treatment options.
   ii. Doxycycline
   iii. Cefixime or cefpodoxime with clindamycin (for children with non-type I hypersensitivity to
      penicillin)
   iv. Intranasal saline irrigation as adjunctive therapy
   v. Intranasal corticosteroids as adjunctive therapy in patients with allergic rhinitis

d. Therapy duration
   i. Adults: 5–7 days
   ii. Children: 10–14 days

II. URINARY TRACT INFECTIONS

A. Introduction
   1. Most common bacterial infection in humans: 7 million office visits per year; 1 million hospitalizations
   2. Many women (15%–20%) will have a urinary tract infection (UTI) during their lifetime.
   3. 1–50 years of age: UTIs occur predominantly in women; after 50: men are increasingly affected because
      of prostate problems

B. Microbiology (Table 8)

Table 8. Incidence of Urinary Tract Infections by Organism

<table>
<thead>
<tr>
<th>Community Acquired (%)</th>
<th>Nosocomial (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Escherichia coli</em></td>
<td>73</td>
</tr>
<tr>
<td><em>Staphylococcus saprophyticus</em></td>
<td>13</td>
</tr>
<tr>
<td><em>Proteus mirabilis</em></td>
<td>5</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td>4</td>
</tr>
<tr>
<td><em>Enterococcus</em></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>E. coli</td>
</tr>
<tr>
<td></td>
<td>31</td>
</tr>
<tr>
<td></td>
<td><em>Pseudomonas aeruginosa</em></td>
</tr>
<tr>
<td></td>
<td>Other gram-negative bacilli</td>
</tr>
<tr>
<td></td>
<td><em>K. pneumoniae</em></td>
</tr>
<tr>
<td></td>
<td><em>Staphylococcus aureus</em></td>
</tr>
<tr>
<td></td>
<td><em>P. mirabilis</em></td>
</tr>
<tr>
<td></td>
<td><em>Enterococcus</em></td>
</tr>
<tr>
<td></td>
<td>Fungal</td>
</tr>
</tbody>
</table>

C. Predisposing Factors
   1. Age
   2. Female sex
   3. Diabetes mellitus
   4. Pregnancy
   5. Immunosuppression
   6. Urinary tract instrumentation
   7. Urinary tract obstruction
   8. Renal disease, renal transplantation
   9. Neurologic dysfunction
Patient Case

4. G.N. is a 62-year-old woman who presents to the emergency department with a 3-day history of urinary frequency and dysuria. During the past 24 hours, she has had nausea, vomiting, and flank pain. G.N. has a history of type 2 diabetes, which is poorly controlled, with some diabetes-related complications. G.N. also has hypertension and a history of several episodes of deep venous thrombosis. Her medications include glyburide 5 mg/day orally, enalapril 10 mg orally twice daily, warfarin 3 mg/day orally, and metoclopramide 10 mg four times/day. On physical examination, she is alert and oriented, with the following vital signs: temperature 102.8°F (39°C), heart rate 120 beats/minute, respiratory rate 16 breaths/minute, supine blood pressure 140/75 mm Hg, and standing blood pressure 110/60 mm Hg. Her laboratory values are within normal limits except for elevated international normalized ratio 2.7, BUN 26 mg/dL, SCr 1.88 mg/dL, and WBC 12,000 cells/mm³ (78 polymorphonuclear leukocytes, 7 band neutrophils, 10 lymphocytes, and 5 monocytes). Her urinalysis reveals turbidity, 2+ glucose, pH 7.0, protein 100 mg/dL, 50–100 WBCs, positive nitrates, 3–5 red blood cells, and many bacteria and positive casts. Which is the best empiric therapy for G.N.?

A. Trimethoprim/sulfamethoxazole double strength orally twice daily; duration of antibiotics 7 days. Monitor INR carefully.
B. Ciprofloxacin 400 mg intravenously twice daily and then 500 mg orally twice daily; duration of antibiotics 7 days. Monitor INR carefully.
C. Gentamicin 140 mg intravenously every 24 hours; duration of antibiotics 3 days.
D. Tigecycline 100 mg once, then 50 mg every 12 hours and then doxycycline 100 mg twice daily; duration of antibiotics 10 days.

D. Clinical Presentation
1. Lower UTI: Cystitis (older adults may have only nonspecific symptoms, such as mental status changes, abdominal pain, and decreased eating or drinking)
   a. Dysuria
   b. Frequent urination
   c. Urgency
   d. Occasionally, gross hematuria
2. Upper UTI: Pyelonephritis (older adults may have only nonspecific symptoms, such as mental status changes, abdominal pain, and decreased eating or drinking)
   a. Frequency, dysuria, hematuria
   b. Suprapubic pain
   c. Costovertebral angle tenderness; flank pain
   d. Fever, chills
   e. Elevated WBC
   f. Nausea, vomiting
3. Factors associated with or used to define complicated UTI (UTI involving a structural or functional abnormality)
   a. Male sex
   b. Hospital acquired
   c. Pregnancy
   d. Anatomic abnormality of the urinary tract
   e. Poorly controlled diabetes mellitus
   f. Recent antimicrobial use
   g. Indwelling urinary catheter
   h. Recent urinary tract instrumentation
   i. Immunosuppression
4. Recurrent cystitis
   a. Relapse: Infection with the same organism within 14 days of discontinuing antibiotics for the preceding UTI
   b. Reinfection: Infection with a completely different organism; most common cause of recurrent cystitis

E. Diagnosis: Urinalysis (blood cultures will be positive in 20% of patients with upper UTIs)
   1. Pyuria (WBC greater than 10 cells/mm\(^3\))
   2. Bacteriuria (more than \(10^2\) colony-forming units per milliliter is diagnostic)
   3. Red blood cells
   4. Cloudiness
   5. Nitrite positive (\(E. coli, Proteus, Klebsiella\))
   6. Leukocyte esterase positive
   7. Casts (if pyelonephritis)
   8. Note: patient must also have symptoms; diagnosis cannot be made on urinalysis results alone.

F. Therapy
   1. Uncomplicated cystitis
      a. Recommended therapy
         i. Trimethoprim/sulfamethoxazole 160 mg/800 mg twice daily for 3 days. Avoid if resistance prevalence is known to exceed 20% or if used for UTI in previous 3 months.
         ii. Nitrofurantoin 100 mg twice daily for 5 days (ineffective in patients with a CrCl less than 30 mL/minute/1.73 m\(^2\))
         iii. Fosfomycin 3 g, one dose
      b. Alternatives
         i. Fluoroquinolones for 3 days – Because of serious adverse effects, avoid fluoroquinolones if there are other treatment options.
         ii. \(\beta\)-Lactams for 5–7 days
   2. Uncomplicated pyelonephritis
      a. Outpatient therapy (if patient is not immunocompromised or does not have nausea and vomiting)
         i. Trimethoprim/sulfamethoxazole for 14 days
         ii. Fluoroquinolone for 5–7 days – Because of serious adverse effects, avoid fluoroquinolones if there are other treatment options.
         iii. \(\beta\)-Lactam for 10–14 days (less effective than first two options)
      b. Uropathogen resistance greater than 10%: Use initial dose of an intravenous, long-acting \(\beta\)-lactam (e.g., ceftriaxone) or once-daily aminoglycoside.
   3. Complicated UTIs
      a. Outpatient therapy
         i. Trimethoprim/sulfamethoxazole for 7-14 days
         ii. Fluoroquinolone for 5–7 days
         iii. Amoxicillin-clavulanate for 7–14 days
      b. Inpatient therapy
         i. Fluoroquinolone
         ii. Aminoglycoside
         iii. Ceftriaxone (consider a \(\beta\)-Lactam with anti-pseudomonal activity in patients recently hospitalized or with urinary catheters or living in nursing homes)
      c. Therapy duration: 5–14 days (5 days with levofloxacin)
4. Pregnancy (pregnant women should be screened for bacteriuria and treated, even if asymptomatic)
   a. Antibiotic options
      i. Amoxicillin/clavulanate for 3-5 days
      ii. Nitrofurantoin (avoid at term if other options available) for five days
      iii. Cephalexin or cefpodoxime for 3-5 days
      iv. Fosfomycin single dose
   b. Antibiotics to avoid
      i. Fluoroquinolones
      ii. Tetracyclines
      iii. Aminoglycosides
      iv. Trimethoprim/sulfamethoxazole (used frequently but avoidance recommended, especially during the late third trimester)

5. Recurrent cystitis
   a. Relapse
      i. Assess for pharmacologic reason for treatment failure.
      ii. Longer treatment (for 2–6 weeks, depending on length of initial course)
   b. Reinfaction (reassess need for continuous prophylactic antibiotics every 6–12 months)
      i. If patient has two or fewer UTIs in 1 year, use patient-initiated therapy for symptomatic episodes (3-day treatment regimens).
      ii. If patient has three or more UTIs in 1 year and they are temporally related to sexual activity, use post-intercourse prophylaxis with trimethoprim/sulfamethoxazole single strength, cephalexin 250 mg, or nitrofurantoin 50–100 mg and counsel on voiding after intercourse.
      iii. If patient has three or more UTIs in 1 year that are not related to sexual activity, use daily or three times per week prophylaxis with trimethoprim 100 mg, trimethoprim/sulfamethoxazole single strength, cephalexin 250 mg, or nitrofurantoin 50–100 mg.

6. Catheter-related UTIs
   a. Short-term indwelling catheters
      i. About 5% of patients develop a UTI per each day of catheterization.
      ii. By 30 days, 75%–95% of patients with an indwelling catheter will have bacteriuria.
      iii. Preventive antimicrobial therapy is not recommended; it only increases the chance of selecting out resistant organisms.
      iv. Asymptomatic patients with bacteriuria should not be treated.
      v. Symptomatic patients with bacteriuria should be treated with 7 days of antibiotics if symptoms resolve promptly and with 10–14 days of antibiotics if there is a delayed response (both durations whether or not catheter removed). Treat for 5 days with levofloxacin if the patient is not severely ill; treat for 3 days in women 65 years and younger who have their catheters removed and who do not have upper urinary tract symptoms.
      vi. The most common organisms are E. coli (21.4%), Candida spp. (21.0%), Enterococcus spp. (14.9%), P. aeruginosa (10.0%), K. pneumoniae (7.7%), and Enterobacter spp. (4.1%).
   b. Long-term indwelling catheters
      i. Almost all patients will be bacteriuric with two to five organisms.
      ii. Asymptomatic patients should not be treated. Catheters do not need to be replaced.
      iii. Symptomatic patients should be treated for a short period (7 days) to prevent resistance, and catheter replacement may be indicated.

7. Prostatitis and epididymitis
   a. Acute bacterial prostatitis
      i. Primarily gram-negative organisms
ii. Therapy duration, 4 weeks  
   (a) Trimethoprim/sulfamethoxazole  
   (b) Fluoroquinolones  

b. Chronic bacterial prostatitis  
i. Difficult to treat  
ii. Therapy duration, 1–4 months  
   (a) Trimethoprim/sulfamethoxazole  
   (b) Fluoroquinolones  

8. Epididymitis  
a. Older than 35 years, probably caused by enteric organisms  
i. Therapy duration: 10 days to 4 weeks  
ii. Antibiotics: trimethoprim/sulfamethoxazole or fluoroquinolones  
b. Younger than 35 years, probably gonococcal or chlamydial infection  
i. Therapy duration: 10 days  
ii. Antibiotics: ceftriaxone 250 mg intramuscularly once plus doxycycline 100 mg twice daily  

III. SKIN AND SKIN STRUCTURE INFECTIONS  

A. Cellulitis  
1. Description  
a. Acute spreading skin infection that involves primarily the deep dermis and subcutaneous fat  
b. Non-elevated, poorly defined margins  
c. Warmth, pain, erythema and edema, and tender lymphadenopathy  
d. Malaise, fever, and chills  
e. Usually, patient has had previous minor trauma, abrasions, ulcers, or surgery (could be tinea infections, psoriasis, or eczema).  
f. Often, patients have impaired lymphatic drainage.  
2. Microorganism: Usually *Streptococcus pyogenes* and occasionally *S. aureus* (rarely other organisms); blood cultures are rarely positive and not routinely recommended unless severe systemic symptoms are present or the patient is immunosuppressed  
3. Treatment: 5–10 days (may extend therapy if infection has not improved)  
a. Penicillin G if definitely streptococcal  
b. First-generation cephalosporin (cefazolin, cephalexin)  
c. Ceftriaxone  
d. Clindamycin  
e. Treat empirically for MRSA if associated with penetrating trauma, injection drug use, purulent drainage, nasal colonization with MRSA, concurrent evidence of MRSA infection elsewhere or systemic inflammatory response syndrome (SIRS) criteria (severe nonpurulent).  
i. Outpatient: Clindamycin, trimethoprim/sulfamethoxazole (add β-lactam for *Streptococcus*), doxycycline (add β-lactam for *Streptococcus*)  
ii. Inpatient: Vancomycin, linezolid, daptomycin, or telavancin  

B. Erysipelas  
1. Description  
a. Acute spreading skin infection that involves primarily the superficial dermis  
b. Spreads rapidly through the lymphatic system in the skin (patients may have impaired lymphatic drainage)
c. Usually occurs in infants and older adults
d. Usually occurs on the legs and feet (facial erysipelas can occur, but this is less common)
e. Warmth, erythema, and pain
f. Edge of infection is elevated and sharply demarcated from the surrounding tissue.
g. Systemic signs of infection are common, but blood cultures are positive only 5% of the time.

2. Microorganism: Group A *Streptococcus (S. pyogenes)*, but occasionally groups G, C, and B are seen

3. Treatment: 5 days (may extend therapy if infection has not improved)
   a. Penicillin G
   b. Clindamycin

C. Necrotizing Fasciitis

1. Description
   a. Acute, necrotizing cellulitis that involves the subcutaneous fat and superficial fascia
   b. Infection extensively alters surrounding tissue, leading to cutaneous anesthesia or gangrene.
   c. Very painful (pain out of proportion to appearance)
   d. Streptococcal infection: Either spontaneous or attributable to varicella, minor trauma (cuts, burns, and splinters), surgical procedures, or muscle strain; mixed infection generally secondary to abdominal surgery or trauma
   e. Significant systemic symptoms, including shock and organ failure

2. Microorganisms
   a. *S. pyogenes*
   b. Mixed infection with facultative and anaerobic bacteria

3. Treatment
   a. Surgical debridement: Most important therapy and often repeated debridement is necessary
   b. Antibiotics are not curative; given in addition to surgery (if used early, may be effective alone)
   c. Empiric therapy: Vancomycin or linezolid plus piperacillin/tazobactam or a carbapenem or ceftriaxone with metronidazole
   d. If group A streptococci, *S. aureus*, or clostridia suspected, clindamycin should be included in the empiric regimen to suppress streptococcal toxin and cytokine production
   e. Streptococcal necrotizing fasciitis: High-dose intravenous penicillin plus clindamycin

### Patient Case

5. G.N. returns to the clinic in 6 months with no urinary symptoms, but her chief concern is now an ulcer on her right foot. She recently returned from a vacation in Florida and thinks she might have stepped on something while walking barefoot on the beach. Her foot is not sore but is red and swollen around the deep ulcer. Her medications are the same as before. Vital signs are stable, and there is nothing significant on physical examination except for the right foot ulcer. Laboratory values are within normal limits (SCr 0.86 mg/dL). Which is the best empiric therapy for G.N.?

A. Nafcillin 2 g intravenously every 6 hours; duration of antibiotics 6–12 weeks.
B. Tobramycin 120 mg intravenously every 12 hours plus levofloxacin 750 mg intravenously every 24 hours; duration of antibiotics 1–2 weeks.
C. Ampicillin/sulbactam 3 g intravenously every 6 hours; duration of antibiotics 2–3 weeks.
D. Below-the-knee amputation followed by ceftriaxone 1 g intravenously every 24 hours; duration of antibiotics 1 week.
IV. DIABETIC FOOT INFECTIONS

A. Epidemiology
   1. 25% of people with diabetes develop foot infections.
   2. 1 in 15 needs amputation.

B. Etiology
   1. Neuropathy: Motor and autonomic
      a. Mechanical or thermal injuries lead to ulcerations without patient knowledge.
      b. Gait disturbances and foot deformities; maldistribution of weight on the foot
      c. Diminished sweating, causing dry, cracked skin
   2. Vasculopathy: Decreased lower limb perfusion
   3. Immunologic defects: Cellular and humoral

C. Causative Organisms: In general, polymicrobial (average, 2.1–5.8 microorganisms)
   1. S. aureus
   2. Group A and B Streptococcus
   3. Enterococcus
   4. Proteus
   5. E. coli
   6. Klebsiella
   7. Enterobacter
   8. P. aeruginosa
   9. Bacteroides fragilis
   10. Peptostreptococcus

D. Therapy
   1. Preventive therapy
      a. Examine feet daily for calluses, blisters, trauma, and so forth.
      b. Wear properly fitting shoes.
      c. Do not walk barefoot.
      d. Keep feet clean and dry.
      e. Have toenails cut properly.
   2. Antimicrobial therapy
      a. Mild infections (and no antibiotics in the past month), defined as local infection involving only the skin and the subcutaneous tissue, with no SIRS criteria and erythema of 2 cm or less
         i. No MRSA risk factors: Penicillinase-resistant penicillin, first-generation cephalosporin, fluoroquinolone, or clindamycin
         ii. MRSA risk factors (see below): Doxycycline or trimethoprim/sulfamethoxazole
      b. Moderate to severe infections, defined as local infection with erythema greater than 2 cm, or involving structures deeper than skin and subcutaneous tissues without (moderate) or with (severe) SIRS criteria
         i. Ampicillin/sulbactam
         ii. Ertapenem
         iii. Cefoxitin
         iv. Moxifloxacin alone or ciprofloxacin/levofloxacin plus clindamycin
         v. Tigecycline
vi. If risk of *P. aeruginosa* (uncommon in diabetic foot infections and often a nonpathogenic colonizer), use piperacillin/tazobactam, ceftazidime, cefepime, or carbapenem. Risk factors for *Pseudomonas* include high local prevalence of *Pseudomonas* infection, warm climate, frequent exposure of the foot to water, a severe infection, and failure of previous therapy with non-pseudomonal antibiotics.

vii. If risk of MRSA, use vancomycin, linezolid, or daptomycin. Risk factors for MRSA include history of MRSA infection or colonization, high local prevalence of MRSA, or a severe infection.

c. Treatment duration: 1–2 weeks for mild infections and 2–3 weeks for moderate to severe infections. Extended duration is needed for osteomyelitis; after amputation treatment, duration is 2–5 days if there is no remaining infected tissue or 4 weeks or more if infected tissue remains.

E. Surgical Therapy

1. Drainage and debridement (appropriate wound care) are very important.

2. Amputation is often necessary; if infection is discovered early, can maintain structural integrity of the foot.

### Patient Case

6. W.A. is a 55-year-old man who presents with weight loss, malaise, and severe back pain and spasms that have progressed during the past 2 months. He has also experienced loss of sensation in his lower extremities. Four months before this admission, he had surgery for a fractured tibia, followed by an infection treated with unknown antibiotics. W.A. has hypertension and a history of diverticulitis. On physical examination, he is alert and oriented, with the following vital signs: temperature 99.4°F (37.4°C), heart rate 88 beats/minute, respiratory rate 14 breaths/minute, and blood pressure 130/85 mm Hg. His laboratory values are within normal limits, except for WBC 14,300 cells/mm³, erythrocyte sedimentation rate 89 mm/hour, and C-reactive protein 12 mg/dL. Magnetic resonance imaging reveals bony destruction of lumbar vertebrae 1 and 2, which is confirmed by a bone scan. A computed tomography–guided bone biopsy reveals gram-positive cocci in clusters. Which is the best therapy for W.A.?

A. Vancomycin 15 mg/kg intravenously every 12 hours; duration of antibiotics 6 weeks.

B. Nafcillin 2 g intravenously every 6 hours; duration of antibiotics 2 weeks.

C. Levofloxacin 750 mg orally every 24 hours; duration of antibiotics 6 weeks.

D. Ampicillin/sulbactam 3 g intravenously every 6 hours; duration of antibiotics 2 weeks.

### V. OSTEOMYELITIS

A. Introduction

1. Infection of the bone with subsequent bone destruction

2. About 20 cases per 100,000 people
B. Characteristics (Table 9)

Table 9. Characteristics of Osteomyelitis

<table>
<thead>
<tr>
<th></th>
<th>Hematogenous Spread</th>
<th>Contiguous Spread</th>
<th>Vascular Insufficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definition</td>
<td>Spread of bacteria through the bloodstream from a distant site</td>
<td>Spread of bacteria from an adjacent tissue infection or by direct inoculation</td>
<td>Infection results from insufficient blood supply to fight the bacteria</td>
</tr>
<tr>
<td>Patient population</td>
<td>Children (&lt; 16 yr): femur, tibia, humerus</td>
<td>Adults (25–50 yr): femur, tibia, skull</td>
<td>Adults (&gt; 50 yr)</td>
</tr>
<tr>
<td>Predisposing factors</td>
<td>Bacteremia (e.g., IV catheters, IVDU, skin infections, URI)</td>
<td>Open reduction of fractures</td>
<td>Diabetes</td>
</tr>
<tr>
<td></td>
<td>Sick cell anemia</td>
<td>Gunshot wound</td>
<td>PVD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dental or sinus infections</td>
<td>Post-CABG ( sternum)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Soft tissue infections</td>
<td></td>
</tr>
<tr>
<td>Common pathogens</td>
<td>Usually monomicrobial</td>
<td>Usually mixed infection:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Children: <em>Staphylococcus aureus</em> (60%–90%), <em>Staphylococcus epidermidis</em>, <em>Streptococcus pyogenes</em>, <em>Streptococcus pneumoniae</em>, <em>Haemophilus influenzae</em>, <em>Pseudomonas aeruginosa</em>, <em>Enterobacter</em>, <em>Escherichia coli</em> (all &lt; 5%)</td>
<td><em>S. aureus</em> (60%), <em>S. epidermidis</em>, <em>Streptococcus</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Adults: <em>S. aureus</em> and gram-negative bacilli</td>
<td><em>Gram-negative bacilli:</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sick cell anemia: <em>Salmonella</em> (67%), <em>S. aureus</em>, <em>S. pneumoniae</em></td>
<td><em>P. aeruginosa</em> (foot punctures), <em>Proteus</em>, <em>Klebsiella, E. coli</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td>IVDU: <em>P. aeruginosa</em></td>
<td>Anaerobic (human bites, decubitus ulcers)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Infected prosthesis:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>S. aureus</em>, <em>S. epidermidis</em></td>
</tr>
</tbody>
</table>

CABG = coronary artery bypass graft; IV = intravenous; IVDU = intravenous drug use; PVD = pulmonary vascular disease; URI = upper respiratory infection.

C. Clinical Presentation
1. Signs and symptoms
   a. Fever and chills
   b. Localized pain, tenderness, and swelling
   c. Neurologic symptoms if spinal cord compression
2. Laboratory tests
   a. Elevated WBC
   b. Elevated erythrocyte sedimentation rate
   c. Elevated C-reactive protein
3. Diagnostic tests
   a. Radiographic tests: Positive results lag behind infectious process.
   b. Computed tomography and magnetic resonance imaging scans
   c. Radionuclide imaging: Positive as soon as 24–48 hours after infectious process begins.

D. Empiric Therapy
1. Pediatric (neonate therapy should be tailored to the patient)
   a. Cefazolin
   b. Nafcillin, oxacillin
   c. Clindamycin (use if prevalence of MRSA in community is 10% or more)
   d. Vancomycin (use if prevalence of MRSA and clindamycin-resistant *S. aureus* in community is 10% or more)
2. Adults
   a. Nafcillin, oxacillin, cefazolin, ceftriaxone, clindamycin, or vancomycin (alternatives linezolid or daptomycin)
   b. Choose additional antibiotics according to patient-specific characteristics.

3. Patients with sickle cell anemia: Ceftriaxone/cefotaxime or ciprofloxacin/levofoxacin (no studies assessing best empiric therapy)

4. Prosthetic joint infections
   a. Debridement and retention of prosthesis or one-stage exchange of prosthesis
      i. Staphylococcal: Pathogen-specific intravenous therapy plus rifampin 300–450 mg twice daily for 2–6 weeks, followed by rifampin plus ciprofloxacin or levofloxacin for 3 months (hip, elbow, shoulder, ankle prosthesis) or 6 months (knee prosthesis)
      ii. Non-staphylococcal: Pathogen-specific intravenous (or highly bioavailable oral) therapy for 4–6 weeks, followed by indefinite oral suppression therapy
   b. Resection of prosthesis with or without planned reimplantation or amputation
      i. Pathogen-specific intravenous (or highly bioavailable oral) therapy for 4–6 weeks
      ii. Only 24–48 hours of antibiotic therapy after amputation if all infected tissue is removed

E. Therapy Length
   1. Acute osteomyelitis: 4–6 weeks
   2. Chronic osteomyelitis: 6–8 weeks of parenteral therapy and 3–12 months of oral therapy

F. Criteria for Effective Oral Therapy for Osteomyelitis
   1. High bioavailability antibiotic is available.
   2. Adherence
   3. Identified organism that is highly susceptible to the oral antibiotic used
   4. C-reactive protein less than 2.0 mg/dL
   5. Adequate surgical debridement
   6. Resolving clinical course

VI. CENTRAL NERVOUS SYSTEM INFECTIONS

A. Meningitis: Introduction
   1. Incidence: About 8.6 cases per 100,000 people
   2. Occurs more often in male than in female patients
   3. More common in children
B. Microbiology (Table 10)
   1. Bacterial (septic meningitis)

Table 10. Bacterial Etiology of Meningitis, Based on Age

<table>
<thead>
<tr>
<th>Age</th>
<th>Most Likely Organisms</th>
<th>Less Common Organisms</th>
</tr>
</thead>
</table>
| < 1 mo (newborns) | *Streptococcus agalactiae*  
*Listeria monocytogenes*  
*Streptococcus pneumoniae*  
*Neisseria meningitidis* | *Escherichia coli, Klebsiella spp.*  
*Herpes simplex type 2* |
| 1–23 mo         | *Streptococcus pneumoniae*  
*Neisseria meningitidis*  
*Haemophilus influenzae*  
*Streptococcus agalactiae* | *Viruses*  
*E. coli* |
| 2–50 yr         | *N. meningitidis*  
*S. pneumoniae* | *H. influenzae*  
*Viruses* |
| > 50 yr         | *S. pneumoniae*  
*N. meningitidis* | *L. monocytogenes, Streptococcus agalactiae,*  
*H. influenzae, aerobic gram-negative bacilli, viruses* |

2. Other causes (aseptic meningitis)
   a. Viral
   b. Fungal
   c. Parasitic
   d. Tubercular
   e. Syphilis
   f. Drugs (e.g., trimethoprim/sulfamethoxazole, ibuprofen)

C. Predisposing Factors
   1. Head trauma
   2. Immunosuppression
   3. CNS shunts
   4. Cerebrospinal fluid (CSF) fistula or leak
   5. Neurosurgical patients
   6. Alcoholism
   7. Local infections
      a. Sinusitis
      b. Otitis media
      c. Pharyngitis
      d. Bacterial pneumonia
   8. Splenectomized patients
   9. Sickle cell disease
   10. Congenital defects

D. Clinical Presentation
   1. Symptoms
      a. Fever, chills
      b. Headache, backache, nuchal rigidity, mental status changes, photophobia
      c. Nausea, vomiting, anorexia, poor feeding habits (infants)
      d. Petechiae or purpura (*Neisseria meningitidis* meningitis)
2. Physical signs
   a. Brudzinski sign
   b. Kernig sign
   c. Bulging fontanel

E. Diagnosis
   1. History and physical examination
   2. Blood cultures
   3. Lumbar puncture
      a. Elevated opening pressure
      b. Composition in bacterial meningitis (Table 11)

<table>
<thead>
<tr>
<th>Table 11. CSF Changes in Bacterial Meningitis</th>
</tr>
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<tbody>
<tr>
<td>Component</td>
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<tr>
<td>---------------------</td>
</tr>
<tr>
<td>Glucose</td>
</tr>
<tr>
<td>Protein</td>
</tr>
<tr>
<td>WBC</td>
</tr>
<tr>
<td>pH</td>
</tr>
<tr>
<td>Lactic acid</td>
</tr>
</tbody>
</table>

CSF = cerebrospinal fluid.

   c. CSF stains and studies
      i. Gram stain (microorganisms): Helps identify organism in 60%–90% of cases
      ii. Latex agglutination: High sensitivity, 50%–100%, for common organisms
          (a) Not recommended routinely
          (b) Most useful in patients pretreated with antibiotics with subsequent negative CSF Gram stains and cultures
      iii. Acid-fast staining (tubercular meningitis)
      iv. India ink test (Cryptococcus)
      v. Cryptococcal antigen
      vi. Herpes simplex virus polymerase chain reaction

4. Laboratory findings
   a. Elevated WBC with a left shift
   b. CSF Gram stain
   c. CSF cultures (positive in 75%–80% of bacterial meningitis cases)
   d. Blood cultures (±)
   e. C-reactive protein concentrations: High negative predictive value
Patient Case
7. D.M. is a 21-year-old university student who presents to the emergency department with the worst headache of his life. During the past few days, he has felt slightly ill but has been able to go to class regularly and eat and drink adequately. This morning, he awoke with a terrible headache and pain whenever he moved his neck. He has no significant medical history and takes no medications. He cannot remember the last time he received a vaccination. On physical examination, he is in extreme pain (10/10) with the following vital signs: temperature 102.4°F (39.1°C), heart rate 110 beats/minute, respiratory rate 18 breaths/minute, and blood pressure 130/75 mm Hg. His laboratory values are within normal limits, except for WBC 22,500 cells/mm³ (82 polymorphonuclear leukocytes, 11 band neutrophils, 5 lymphocytes, and 2 monocytes). A computed tomography scan of the head is normal, so a lumbar puncture is performed with the following results: glucose 44 mg/dL (peripheral, 110), protein 220 mg/dL, and WBC 800 cells/mm³ (85% neutrophils, 15% lymphocytes). Which is the best empiric therapy for D.M.?

A. Penicillin G 4 million units intravenously every 4 hours.
B. Ceftriaxone 2 g intravenously every 12 hours.
C. Ceftriaxone 2 g intravenously every 12 hours plus dexamethasone 10 mg intravenously every 6 hours.
D. Ceftriaxone 2 g intravenously every 12 hours plus vancomycin 1000 mg intravenously every 8 hours plus dexamethasone 10 mg intravenously every 6 hours.

F. Empiric Therapy
1. Neonates younger than 1 month
   a. Ampicillin plus aminoglycoside or
   b. Ampicillin plus cefotaxime
2. Infants (1–23 months): Third-generation cephalosporin (cefotaxime or ceftriaxone) plus vancomycin*
3. Children and adults (2–50 years): Third-generation cephalosporin (cefotaxime or ceftriaxone) plus vancomycin*
4. Older adults (50 years and older): Third-generation cephalosporin (cefotaxime or ceftriaxone) plus vancomycin* plus ampicillin
5. Penetrating head trauma, neurosurgery, or CSF shunt: Vancomycin plus cefepime, ceftazidime, or meropenem
   *Vancomycin added for activity against highly drug resistant S. pneumoniae.

G. Therapy for Common Pathogens
1. S. pneumoniae
   a. An MIC to penicillin of 0.1 mcg/mL or less
      i. Penicillin G 4 million units intravenously every 4 hours
      ii. Ampicillin 2 g intravenously every 4 hours
      iii. Alternative: Third-generation cephalosporin (cefotaxime 2 g intravenously every 4–6 hours or ceftriaxone 2 g intravenously every 12 hours) or chloramphenicol 1–1.5 g intravenously every 6 hours
   b. An MIC to penicillin of 0.1–1.0 mcg/mL
      i. Third-generation cephalosporin (cefotaxime or ceftriaxone)
      ii. Alternative: Cefepime 2 g intravenously every 8 hours or meropenem 2 g intravenously every 8 hours
   c. An MIC to penicillin of 2.0 mcg/mL or greater
      i. Vancomycin 15–20 mg/kg intravenously every 8–12 hours plus a third-generation cephalosporin (cefotaxime or ceftriaxone)
      ii. Alternative: Moxifloxacin 400 mg intravenously every 24 hours
2. *N. meningitidis*
   a. An MIC to penicillin of less than 0.1 mcg/mL
      i. Penicillin G
      ii. Ampicillin
      iii. Alternative: Third-generation cephalosporin (cefotaxime or ceftriaxone) or chloramphenicol
   b. An MIC 0.1–1.0 mcg/mL
      i. Third-generation cephalosporin (cefotaxime or ceftriaxone)
      ii. Alternative: Chloramphenicol, fluoroquinolone, or meropenem

3. *H. influenzae*
   a. β-Lactamase negative
      i. Ampicillin
      ii. Alternative: Third-generation cephalosporin (cefotaxime or ceftriaxone), cefepime, chloramphenicol, or fluoroquinolone
   b. β-Lactamase positive
      i. Third-generation cephalosporin (cefotaxime or ceftriaxone)
      ii. Alternative: Cefepime, chloramphenicol, or fluoroquinolone

4. *Streptococcus agalactiae*
   a. Penicillin G
   b. Ampicillin
   c. Alternative: Third-generation cephalosporin (cefotaxime or ceftriaxone)

5. *Listeria monocytogenes*
   a. Penicillin G
   b. Ampicillin
   c. Alternative: Trimethoprim/sulfamethoxazole 5 mg/kg intravenously every 6–12 hours or meropenem

H. Therapy Length: Based on clinical experience, not on clinical data
   1. *N. meningitidis*: 7 days
   2. *H. influenzae*: 7 days
   3. *S. pneumoniae*: 10–14 days
   4. *S. agalactiae*: 14–21 days
   5. *Listeria monocytogenes*: 21 days or more

I. Adjunctive Corticosteroid Therapy
   1. Risks and benefits
      a. Significantly less hearing loss and other neurologic sequelae in children receiving dexamethasone for *H. influenzae* meningitis
      b. Significantly improved outcomes, including decreased mortality, in adults receiving dexamethasone for *S. pneumoniae* meningitis
      c. May decrease antibiotic penetration (decreased penetration of vancomycin in animals after dexamethasone)
   2. Dosage and administration
      a. Give corticosteroids 10–20 minutes before or at same time as first dose of antibiotics.
      b. Dexamethasone 0.15 mg/kg every 6 hours for 2–4 days
      c. Use in children with *H. influenzae* meningitis or in adults with pneumococcal meningitis; however, may need to initiate before knowing specific causative bacteria.
Patient Case
8. D.M.’s CSF cultures grew *N. meningitidis*, and now there is concern about prophylaxis. Which is the best recommendation for meningitis prophylaxis?

A. The health care providers in close contact with D.M. should receive rifampin 600 mg orally every 12 hours for four doses.

B. Everyone in D.M.’s dormitory and in all of his classes should receive rifampin 600 mg orally every 24 hours for 4 days.

C. Everyone in the emergency department at the time of D.M.’s presentation should receive the meningococcal conjugate vaccine.

D. Everyone in the emergency department at the time of D.M.’s presentation should receive rifampin 600 mg orally every 12 hours for four doses.

J. Chemoprophylaxis
   1. *N. meningitidis*
      For close contacts (household or day care) and exposure to oral secretions of index case
      a. Rifampin
         i. Adults: 600 mg every 12 hours, four doses
         ii. Children: 10 mg/kg every 12 hours, four doses
         iii. Infants (younger than 1 month): 5 mg/kg every 12 hours, four doses
      b. Ciprofloxacin 500 mg orally, one dose (adults only)
      c. Ceftriaxone 125–250 mg intramuscularly, one dose
   2. *H. influenzae*
      For all close contacts in households with unvaccinated or immunocompromised children
      a. Adults: Rifampin 600 mg/day for 4 days
      b. Children (1 month to 12 years): Rifampin 20 mg/kg/day for 4 days
      c. Infants younger than 1 month: Rifampin 10 mg/kg/day for 4 days

K. Brain Abscess
   1. Pathophysiology
      a. Direct extension or retrograde septic phlebitis from otitis media, mastoiditis, sinusitis, and facial cellulitis
      b. Hematogenous: Particularly lung abscess or infective endocarditis: 3%–20% have no detectable focus.
   2. Signs and symptoms
      a. Expanding intracranial mass lesion: Focal neurologic deficits
      b. Headache
      c. Fever
      d. Seizures
      e. Mortality is about 50%.
   3. Microbiology
      a. Usually polymicrobial
      b. *Streptococcus* spp. in 50%–60%
      c. Anaerobes in about 40%
4. Therapy
   a. Incision and drainage: By craniotomy or stereotaxic needle aspiration
   b. Suggested empiric regimens based on source of infection
      i. Otitis media or mastoiditis: Metronidazole plus third-generation cephalosporin
      ii. Sinusitis: Metronidazole plus third-generation cephalosporin
      iii. Dental sepsis: Penicillin plus metronidazole
      iv. Trauma or neurosurgery: Vancomycin plus third-generation cephalosporin
      v. Lung abscess, empyema: Penicillin plus metronidazole plus sulfonamide
      vi. Unknown: Vancomycin plus metronidazole plus third-generation cephalosporin
   c. Corticosteroids if elevated intracranial pressure

Patient Case
9. T.S. is a 48-year-old man who presents to the emergency department with fever, chills, nausea and vomiting, anorexia, lymphangitis in his right hand, and lower back pain. He has no significant medical history except for kidney stones 4 years ago. He has no known drug allergies. He is homeless and was an intravenous drug abuser (heroin) for the past year but quit 2 weeks ago. On physical examination, he is alert and oriented, with the following vital signs: temperature 100.8°F (38°C), heart rate 114 beats/minute, respiratory rate 12 breaths/minute, and blood pressure 127/78 mm Hg. He has a faint systolic ejection murmur, and his right hand is erythematous and swollen. His laboratory values are all within normal limits. He had an HIV test 1 year ago, which was negative. One blood culture was obtained in the emergency department that later grew MSSA. Two more cultures were obtained 24 hours after the first culture and are now both growing gram-positive cocci in clusters. A transesophageal echocardiogram reveals vegetation on the mitral valve. Which is the best therapeutic regimen for T.S.?
   A. Nafcillin intravenous therapy; antibiotic duration 7–10 days.
   B. Nafcillin intravenously plus rifampin plus gentamicin therapy; antibiotic duration 6 weeks or longer.
   C. Nafcillin intravenously plus gentamicin intravenous therapy; antibiotic duration 2 weeks of both antibiotics.
   D. Nafcillin intravenously; antibiotic duration 6 weeks.
VII. ENDOCARDITIS

A. Introduction
1. Infection of the heart valves or other endocardial tissue
2. Platelet-fibrin complex becomes infected with microorganisms: Vegetation
3. Main risk factors include mitral valve prolapse, prosthetic valves, and intravenous drug abuse.
4. Three or four cases per 100,000 people per year

B. Presentation and Clinical Findings
1. Signs and symptoms
   a. Fever: Low grade and remittent
   b. Cutaneous manifestations (50% of patients): Petechiae (including conjunctival), Janeway lesions, splinter hemorrhage
   c. Cardiac murmur (90% of patients)
   d. Arthralgias, myalgias, low back pain, arthritis
   e. Fatigue, anorexia, weight loss, night sweats
2. Laboratory findings
   a. Anemia: Normochromic, normocytic
   b. Leukocytosis
   c. Elevated erythrocyte sedimentation rate and C-reactive protein
   d. Positive blood culture in 78%–95% of patients
3. Complications
   a. Congestive heart failure: 38%–60% of patients
   b. Emboli: 22%–43% of patients
   c. Mycotic aneurysm: 5%–10% of patients

C. Microbiology (Table 12)
1. Three to five blood cultures of at least 10 mL each should be obtained during the first 24–48 hours.
2. Empiric therapy should be initiated only in acutely ill patients. In these patients, three blood samples should be obtained during a 15- to 20-minute period before antibiotics are initiated.

Table 12. Incidence of Microorganisms in Endocarditis

<table>
<thead>
<tr>
<th>Organism</th>
<th>Incidence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptococcus</td>
<td>50</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>25</td>
</tr>
<tr>
<td>Enterococcus</td>
<td>8</td>
</tr>
<tr>
<td>Coagulase-negative <em>Staphylococcus</em></td>
<td>7</td>
</tr>
<tr>
<td>Gram-negative bacilli</td>
<td>6</td>
</tr>
<tr>
<td>Candida albicans</td>
<td>2</td>
</tr>
</tbody>
</table>
### Table 13. Treatment Recommendation for Endocarditis

<table>
<thead>
<tr>
<th>Organism</th>
<th>Recommended Therapy</th>
<th>Length of Therapy (wk)</th>
<th>Native Valve</th>
<th>Prosthetic Valve</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Viridans streptococci</strong> (with PCN MIC ≤ 0.12 mcg/mL)</td>
<td>PCN G</td>
<td>4</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PCN G + gentamicin</td>
<td>2</td>
<td>6&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ceftriaxone</td>
<td>4</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ceftriaxone + gentamicin</td>
<td>2</td>
<td>6&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vancomycin (only if unable to tolerate PCN or ceftriaxone)</td>
<td>4</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td><strong>Viridans streptococci</strong> (with PCN MIC &gt; 0.12 mcg/mL)</td>
<td>PCN G + gentamicin</td>
<td>4&lt;sup&gt;b&lt;/sup&gt;</td>
<td>6&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ceftriaxone (+ gentamicin if PCN MIC &gt; 0.5 mcg/ml)</td>
<td>4</td>
<td>6&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vancomycin (only if unable to tolerate PCN or ceftriaxone)</td>
<td>4</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td><strong>Staphylococcus, methicillin sensitive</strong></td>
<td>Oxacillin or nafcillin</td>
<td>6</td>
<td>≥ 6&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Plus gentamicin and rifampin in prosthetic valves</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cefazolin (only for nonanaphylactic penicillin allergy)</td>
<td>6</td>
<td>≥ 6&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Plus gentamicin and rifampin in prosthetic valves</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vancomycin (only if severe PCN allergy)</td>
<td>6</td>
<td>≥ 6&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Plus gentamicin and rifampin in prosthetic valves</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Staphylococcus, methicillin resistant</strong></td>
<td>Vancomycin</td>
<td>6</td>
<td>≥ 6&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vancomycin (only if severe PCN allergy)</td>
<td>6</td>
<td>≥ 6&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Plus gentamicin and rifampin in prosthetic valves</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Daptomycin (not for prosthetic valves)</td>
<td>6</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td><strong>Enterococcus</strong></td>
<td>PCN G or ampicillin + gentamicin</td>
<td>4–6</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td><strong>Enterococcus, PCN resistant</strong></td>
<td>Vancomycin + gentamicin</td>
<td>6</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td><strong>Enterococcus, PCN, aminoglycoside, and vancomycin resistant</strong></td>
<td>Vancomycin + gentamicin</td>
<td>6</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td><strong>Enterococcus, PCN resistant</strong></td>
<td>Linezolid</td>
<td>&gt; 6</td>
<td>&gt; 6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Daptomycin</td>
<td>&gt; 6</td>
<td>&gt; 6</td>
<td></td>
</tr>
<tr>
<td><strong>Enterococcus, vancomycin resistant</strong></td>
<td>Ampicillin</td>
<td>6</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td><strong>Enterococcus, vancomycin resistant</strong></td>
<td>Ampicillin/sublactam</td>
<td>4</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fluoroquinolone (ciprofloxacin, levofloxacin, moxifloxacin)</td>
<td>4</td>
<td>6</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup>Gentamicin can be added for 2 wk if CrCl is greater than 30 mL/minute/1.73 m<sup>2</sup>.  
<sup>b</sup>Gentamicin for 2 wk.  
<sup>c</sup>Gentamicin for 6 wk.  

HACEK = *Haemophilus, Actinobacillus, Cardiobacterium, Eikenella, Kingella*; MIC = minimum inhibitory concentration; PCN = penicillin.
E. Prophylaxis (Table 14)

Table 14. Endocarditis Prophylaxis

<table>
<thead>
<tr>
<th>Conditions in Which Prophylaxis Is Necessary</th>
<th>Dental Procedures That Require Prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prosthetic cardiac valves including bioprosthetic and homograft valves</td>
<td>Any dental procedure that involves the gingival tissues or periapical region of a tooth and for procedures that perforate the oral mucosa</td>
</tr>
<tr>
<td>Previous bacterial endocarditis</td>
<td></td>
</tr>
<tr>
<td>Congenital heart disease</td>
<td></td>
</tr>
<tr>
<td>Unrepaired cyanotic congenital heart disease</td>
<td></td>
</tr>
<tr>
<td>Completely repaired congenital heart defect with prosthetic material or device, during the first 6 months after the procedure</td>
<td></td>
</tr>
<tr>
<td>Repaired congenital heart disease with residual defects adjacent to or at the site of a prosthetic patch or device</td>
<td></td>
</tr>
<tr>
<td>Cardiac transplant recipients who develop cardiac valvulopathy</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other Procedures That Require Prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory tract</td>
</tr>
<tr>
<td>Tonsillectomy or adenoidectomy</td>
</tr>
<tr>
<td>Surgical operations that involve an incision or biopsy of the respiratory mucosa</td>
</tr>
</tbody>
</table>

F. Recommended Prophylaxis for Dental or Respiratory Tract Procedures (Table 15)

Table 15. Prophylaxis for Dental or Respiratory Tract Procedures

<table>
<thead>
<tr>
<th>Situation</th>
<th>Agent</th>
<th>Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard general prophylaxis</td>
<td>Amoxicillin</td>
<td>Adults: 2 g; children: 50 mg/kg 1 hr before procedure</td>
</tr>
<tr>
<td>Unable to take oral medications</td>
<td>Ampicillin</td>
<td>Adults: 2 g IM/IV; children: 50 mg/kg IM/IV within 30 min before procedure</td>
</tr>
<tr>
<td></td>
<td>Cefazolin or ceftriaxone</td>
<td>Adults: 1 g IM/IV; children: 50 mg/kg IM/IV within 30 minutes before procedure</td>
</tr>
<tr>
<td>Allergic to penicillin</td>
<td>Clindamycin</td>
<td>Adults: 600 mg; children: 20 mg/kg 1 hr before procedure</td>
</tr>
<tr>
<td></td>
<td>Cephalexin</td>
<td>Adults: 2 g; children: 50 mg/kg 1 hr before procedure</td>
</tr>
<tr>
<td></td>
<td>Azithromycin or clarithromycin</td>
<td>Adults: 500 mg; children: 15 mg/kg 1 hr before procedure</td>
</tr>
<tr>
<td>Allergic to penicillin and unable to take oral medications</td>
<td>Clindamycin</td>
<td>Adults: 600 mg; children: 20 mg/kg IV within 30 min before procedure</td>
</tr>
<tr>
<td></td>
<td>Cefazolin or ceftriaxone</td>
<td>Adults: 1 g IM/IV; children: 50 mg/kg IM/IV within 30 min before procedure</td>
</tr>
</tbody>
</table>

IM = intramuscularly; IV = intravenously.

Patient Case

10. Six months after treatment of his endocarditis, T.S. is visiting his dentist for a tooth extraction. Which antibiotic is best for prophylaxis?

A. Tooth extractions do not warrant endocarditis prophylaxis.

B. Administer amoxicillin 2 g 1 hour before the extraction.

C. Administer amoxicillin 3 g 1 hour before the extraction and 1.5 g 6 hours for four doses after the extraction.

D. T.S. is not at increased risk of endocarditis and does not need prophylactic antibiotics.
VIII. PERITONITIS AND INTRA-ABDOMINAL INFECTIONS

A. Introduction
   1. Definition: Inflammation of the peritoneum (serous membrane lining the abdominal cavity)
   2. Types
      a. Primary: Spontaneous or idiopathic, no primary focus of infection
      b. Secondary: Occurs secondary to an abdominal process

B. Primary Peritonitis: Spontaneous Bacterial Peritonitis (see the “Gastrointestinal Disorders” chapter)

C. Secondary Peritonitis
   1. Etiology:
      a. Peptic ulcer perforation
      b. Perforation of a GI organ
      c. Appendicitis
      d. Endometritis secondary to intrauterine device
      e. Bile peritonitis
      f. Pancreatitis
      g. Operative contamination
      h. Diverticulitis
      i. Intestinal neoplasms
      j. Secondary to peritoneal dialysis
   2. Microbiology of intra-abdominal infections
      a. Stomach and proximal small intestine: Aerobic and facultative gram-positive and gram-negative organisms
      b. Ileum: \textit{E. coli}, \textit{Enterococcus}, anaerobes
      c. Large intestine: Obligate anaerobes (i.e., \textit{Bacteroides}, \textit{Clostridium perfringens}), aerobic and facultative gram-positive and gram-negative organisms (i.e., \textit{E. coli}, \textit{Streptococcus}, \textit{Enterococcus}, \textit{Klebsiella}, \textit{Proteus}, \textit{Enterobacter})
   3. Clinical manifestations and diagnosis
      a. Fever, tachycardia
      b. Elevated WBC
      c. Abdominal pain aggravated by motion, rebound tenderness
      d. Bowel paralysis
      e. Pain with breathing
      f. Decreased renal perfusion
      g. Ascitic fluid
         i. Protein: High (more than 3 g/dL); exudate fluid
         ii. WBCs: Many, primarily granulocytes

D. Therapy: Secondary Peritonitis
   1. Therapy or prophylaxis should be limited in
      a. Bowel injuries caused by trauma that are repaired within 12 hours (treat for less than 24 hours)
      b. Intraoperative contamination by enteric contents (treat for less than 24 hours)
      c. Perforations of the stomach, duodenum, and proximal jejunum (unless patient is on antacid therapy or has malignancy) (prophylactic antibiotics for less than 24 hours)
      d. Acute appendicitis without evidence of perforation, abscess, or peritonitis (treat for less than 24 hours)
2. Mild to moderate community-acquired infection
   a. Cefoxitin
   b. Cefazolin, cefuroxime, ceftriaxone, or cefotaxime plus metronidazole
   c. Erta penem
   d. Moxifloxacin
   e. Ciprofloxacin or levofloxacin plus metronidazole
   f. Tigecycline

3. High-risk or severe* community-acquired or health care–acquired infection
   a. Piperacillin/tazobactam
   b. Ceftazidime or cefepime plus metronidazole
   c. Imipenem/cilastatin, meropenem, or doripenem
   d. Ciprofloxacin or levofloxacin plus metronidazole (not for health care–acquired infections)
   e. Consider adding an aminoglycoside when extended-spectrum β-lactamase–producing Enterobacteriaceae or P. aeruginosa is of concern (health care–acquired infections only).
   f. Consider adding vancomycin for MRSA (health care–acquired infections only)

*High-risk or severe is defined as APACHE II score greater than 15, poor nutritional status, significant cardiovascular disease, an inability to achieve adequate source control or immunosuppression.

4. Therapy duration: 4 days (when source control is complete)

IX. CLOSTRIDIUM DIFFICILE INFECTION

Patient Case
11. R.K. is a 72-year-old man who presents to the emergency department with a 2-day history of redness and swelling of his upper right extremity. He scraped his arm while clearing some brush in his yard. Although the scratch was initially healing, the area around the injury has become red and warm to the touch over the past few days, and the redness appears to be spreading. His medical history includes gastroesophageal reflux disease, hypertension, hyperlipidemia, and osteoarthritis. R.K. is taking pantoprazole 40 mg oral daily, lisinopril 20 mg oral daily, atorvastatin 40 mg oral daily, and acetaminophen 500 mg oral as needed. R.K. has no known drug allergies. R.K. is hospitalized and sent home after a few days with a prescription for oral clindamycin for his cellulitis. Two weeks after completing therapy for his cellulitis, R.K. has watery diarrhea. R.K. goes to the emergency department, and his C. difficile toxin is positive. His WBC is 24,500 cells/mm³, albumin is 2.8 g/dL, and SCr is 1.74 mg/dL (normally around 0.90 mg/dL). Which is the best therapeutic regimen for R.K.?
   A. Metronidazole 500 mg orally three times daily for 7 days total.
   B. Vancomycin 125 mg orally four times daily for 10 days total.
   C. Fidaxomicin 200 mg orally twice daily for 14 days total.
   D. Rifaximin 400 mg orally twice daily for 7 days total.

A. Introduction
1. Clostridium difficile is transmitted by the fecal-oral route.
2. Overgrowth in the GI tract occurs after antibiotic therapy.
3. Risk factors: Hospital stays, medical comorbidities (e.g., oncology, inflammatory bowel disease, chronic kidney disease, organ transplant), extremes of age, immunodeficiency states, use of broad-spectrum antibiotics, use of proton pump inhibitors
4. Production of endotoxins A and B causes pathogenesis.
5. Symptoms: Watery diarrhea, abdominal pain, leukocytosis, GI tract complications
6. Definition of severe disease:
   a. Infectious Diseases Society of America: WBC 15,000–20,000 cells/mm$^3$ or more, SCr more than 1.5 times normal (complicated if hypotension or shock, ileus or megacolon)
   b. American College of Gastroenterology: Serum albumin less than 3 g/dL plus either WBC of 15,000 cells/mm$^3$ or greater or abdominal tenderness

7. BI/NAP1 strain produces more enterotoxin, produces binary toxin, has increased sporulation capacity, and is resistant to fluoroquinolones. Increased risk of metronidazole failure, morbidity, and mortality

B. Therapy

1. Initial episode and first recurrence
   a. Mild to moderate infection
      i. Metronidazole 500 mg orally three times a day for 10–14 days
      ii. Vancomycin orally can be used if metronidazole cannot be used.
   b. Severe infection
      i. Vancomycin 125 mg orally four times a day for 10–14 days
      ii. Fidaxomicin 200 mg orally twice daily for 10 days: No difference in clinical cure rates compared with vancomycin but lower incidence of recurrence
   c. Severe and complicated infection: Vancomycin 500 mg orally four times a day plus metronidazole 500 mg intravenously every 8 hours for 10–14 days (if complete ileus, add vancomycin per rectum 500 mg in 500 mL of saline as an enema four times a day)

2. Second and third recurrences
   a. Consider fidaxomicin if not already given.
   b. Taper therapy: Vancomycin 125 mg orally four times a day for 14 days, twice daily for 7 days, and daily for 7 days
   c. Pulse therapy: Recommended vancomycin course of therapy for initial episode (for 10–14 days), followed by vancomycin every other day for 8 days, and then every 3 days for 15 days
   d. Consider rifaximin 400 mg twice daily for 14 days or nitazoxanide 500 mg twice daily for 10 days if above options fail.
   e. Consider fecal transplant

3. Recurrence prevention with bezlotoxumab
   a. Human monoclonal antibody that binds to C. difficile toxin B preventing recurrent infections.
   b. Indicated in patients who are at high risk of recurrence.
   c. Dose: 10mg/kg intravenously as a single 60 minute infusion given during standard antibiotic therapy (does NOT replace standard antibiotic therapy)
   d. Lower incidence of recurrent C. difficile infection in 12 weeks (17% vs. 27%)

Patient Case

12. You are a pharmacist who works closely with the surgery department to optimize therapy for patients undergoing surgical procedures at your institution. The surgeons provide you with principles of surgical prophylaxis that they believe are appropriate. Which is the best practice for optimizing surgical prophylaxis?

A. Antibiotics should be redosed for extended surgical procedures; redose if the surgery lasts longer than 4 hours or involves considerable blood loss.

B. All patients should be given antibiotics for 24 hours after the procedure; this will optimize prophylaxis.

C. Preoperative antibiotics can be given up to 4 hours before the incision; this will make giving the antibiotics logistically easier.

D. Vancomycin is the antibiotic of choice for surgical wound prophylaxis because of its long half-life and activity against MRSA.
X. SURGICAL PROPHYLAXIS

A. Introduction
   1. Prophylaxis: Administering the putative agent before bacterial contamination occurs
   2. Early therapy: Immediate or prompt institution of therapy as soon as the patient presents; usually, contamination or infection will have preceded the initiation of therapy (e.g., dirty wounds).

B. Classification of Surgical Procedures (Table 16)

Table 16. Classification of Surgical Procedures

<table>
<thead>
<tr>
<th>Surgical Procedure</th>
<th>Infection Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clean: No entry is made in the respiratory, GI, or genitourinary tracts or in the oropharyngeal cavity</td>
<td>1–4</td>
</tr>
<tr>
<td>In general, it is elective with no break in technique and no inflammation encountered</td>
<td></td>
</tr>
<tr>
<td>Clean contaminated: Entry in the respiratory, GI, genitourinary, or biliary tracts or oropharyngeal cavity without unusual contamination</td>
<td>5–15</td>
</tr>
<tr>
<td>Includes clean procedures with a minor break in technique</td>
<td></td>
</tr>
<tr>
<td>Contaminated: Includes fresh traumatic wounds, gross spillage from the GI tract (without a mechanical bowel preparation), a major break in technique, or incisions encountering acute, nonpurulent inflammation</td>
<td>16–25</td>
</tr>
<tr>
<td>Dirty: Includes procedures involving old traumatic wounds, perforated viscera, or clinically evident infection</td>
<td>30–100</td>
</tr>
</tbody>
</table>

C. Risk Factors for Postoperative Wound Infections
   1. Bacterial contamination
      a. Exogenous sources: Flaw in aseptic technique
      b. Endogenous sources
         i. Most important except in clean procedures
         ii. Patient flora causes infection.
   2. Host resistance
      a. Extremes of age
      b. Nutrition (i.e., malnourished patients)
      c. Obesity
      d. Diabetes mellitus (decreased wound healing and increased risk of infection)
      e. Immunocompromised
      f. Hypoxemia
      g. Remote infection
      h. Presence of foreign body
         i. Healthy person tolerates inoculum of \(10^5\).
         ii. In presence of foreign body, only \(10^2\) are needed.

D. Indications for Surgical Prophylaxis
   1. Common postoperative infection with low morbidity
   2. Uncommon postoperative infection with significant morbidity and mortality
E. Principles of Prophylaxis (Figure 1)

1. Timing: Antibiotics must be present in the tissues at the time of bacterial contamination (incision) and throughout the operative period; on-call dosing is not acceptable.
   a. Administering antibiotics earlier than immediately preoperatively (within 60 minutes before incision or 60–120 minutes if using vancomycin or a fluoroquinolone) is unnecessary.
   b. Initiating antibiotics postoperatively is no more effective than administering no prophylaxis.
   c. Antibiotics should be redosed for extended surgical procedures.
   d. Redose if the surgery lasts longer than 4 hours (or more than 2 half-lives of the antibiotic) or involves considerable blood loss.


2. Dosage
   a. Adequate dosing is necessary to prevent postoperative skin infections. Obese patients have a higher incidence of postoperative infections.
   b. Appropriate dosing
      i. Cefazolin: 2 g (3 g for patients weighing 120 kg or more)
      ii. Ceftriaxone, cefotetan, cefoxitin: 2 g
      iii. Clindamycin: 900 mg
      iv. Vancomycin: 15 mg/kg

3. Duration
   a. Most procedures, including GI, orthopedic, and gynecologic procedures, warrant antibiotics only as long as the patient is in the operating room; administration beyond surgical closure is not necessary.
   b. Cardiac procedures may warrant 24 hours of antibiotics after surgery.

4. Spectrum
   a. Need only activity against skin flora unless the operation violates a hollow viscus mucosa
   b. GI, genitourinary, hepatobiliary, and some pulmonary operations warrant additional antibiotics.
   c. Colorectal surgery is one procedure in which broad-spectrum aerobic and anaerobic coverage is most effective.
   d. Try to avoid a drug that may be needed for therapy if infection occurs.
5. Adverse reactions and bacterial resistance
   a. Antibiotic prophylaxis should not cause greater morbidity than the infection it prevents.
   b. Overuse may lead to resistance, which could prevent further use of the antibiotic for surgical prophylaxis or other infections (duration of administration is an important factor).

6. Cost
   a. Prophylaxis can account for a substantial portion of the antibiotic budget.
   b. Must be weighed against the cost of treating one person with a postoperative infection

F. Antibiotic Prophylaxis in Specific Surgical Procedures

Note: For patients colonized with MRSA, a single preoperative dose of vancomycin can be added.

1. GI
   a. Gastric or duodenal
      i. Because of acidity, little normal flora
      ii. Rates of intragastric organisms and postoperative infections increase with increasing pH.
      iii. Indicated for morbid obesity, esophageal obstruction, decreased gastric acidity, or decreased GI motility
      iv. Recommendation: Cefazolin 2 g before induction
   b. Biliary
      i. Biliary tract normally has no organisms.
      ii. Indicated for high-risk patients. (Often, intraoperative cholangiography reveals unexpected common duct stones, so some studies recommend using antibiotics in all biliary surgery. In addition, studies have shown an increase in infection rates without risk factors.)
         (a) Acute cholecystitis
         (b) Obstructive jaundice
         (c) Common duct stones
         (d) Age older than 70 years
      iii. Recommendation: Cefazolin, cefoxitin, cefotetan, or ceftriaxone 2 g or ampicillin/sulbactam 3 g before induction
   c. Appendectomy
      i. Acutely inflamed or normal appendix: Less than 10% risk
      ii. Evidence of perforation: More than 50% risk (treatment necessary)
      iii. If perforated appendix, treat for 3–7 days.
      iv. Recommendation: Cefoxitin or cefotetan 2 g (or cefazolin plus metronidazole) before induction
   d. Colorectal
      i. A 30%–77% infection rate without antibiotics
      ii. One of the few surgical procedures in which coverage for aerobes and anaerobes has proved most effective
      iii. Preoperative antibiotics
         (a) Combined oral and parenteral regimens may be better than parenteral regimens alone.
         (b) Oral regimens are inexpensive; however, some data suggest they are less effective when used alone (without parenteral agents), have greater toxicity, and may increase the risk of C. difficile infections.
   e. Recommendation
      i. Cefazolin or ceftriaxone 2 g plus metronidazole (or cefoxitin or cefotetan 2 g or ampicillin/sulbactam or ertapenem or gentamicin/tobramycin 5 mg/kg plus clindamycin 900 mg–metronidazole 500 mg) before induction
      ii. With or without neomycin 1 g and erythromycin 1 g at 19, 18, and 9 hours before surgery or neomycin 2 g and metronidazole 2 g at 13 and 9 hours before surgery
      iii. Mechanical bowel preparation is not recommended and may be harmful.
2. Obstetrics and gynecology
   a. Vaginal or abdominal hysterectomy
      i. Antibiotics are most effective in vaginal hysterectomies but generally are given for both procedures.
      ii. Recommendation: Cefazolin or cefoxitin or cefotetan 2 g (or ampicillin/sulbactam) before induction
   b. Cesarean section. Recommendation: Cefazolin 2 g after the cord is clamped

3. Cardiothoracic
   a. Cardiac surgery
      i. Antibiotics decrease the risk of mediastinitis.
      ii. Recommendation: Cefazolin or cefuroxime 2 g preinduction (plus intraoperative doses), if MRSA is probable or patient has been hospitalized, use vancomycin
   b. Pulmonary resection (i.e., lobectomy and pneumonectomy). Recommendation: Cefazolin 2 g before induction (or ampicillin/sulbactam or vancomycin)
   c. Vascular surgery
      i. High mortality with infected grafts
      ii. Recommendation: Cefazolin 2 g before induction and every 8 hours for three doses; if MRSA is probable, use vancomycin

4. Orthopedic
   a. Prophylaxis is indicated when surgery involves prosthetic materials (i.e., total hip or knee, nail, or plate).
      b. Recommendation: Cefazolin 2 g before induction (or vancomycin)

5. Head and neck
   a. Indicated for major surgical procedures when an incision is made through the oral or pharyngeal mucosa
   b. Recommendation: Cefazolin or cefuroxime 2 g plus metronidazole or ampicillin/sulbactam 3 g or clindamycin 900 mg before induction

6. Urologic
   a. In general, not recommended
   b. Indicated if patient has a positive urine culture before surgery (should treat and then operate)
   c. If therapy is unsuccessful, cover for the infecting organism and operate.
REFERENCES

Respiratory Tract Infections

Urinary Tract Infections

Skin and Soft Tissue Infections

Osteomyelitis

Central Nervous System Infections

Endocarditis
Intra-Abdominal Infections


Clostridium difficile Infections


Surgical Prophylaxis

ANSWERS AND EXPLANATIONS TO PATIENT CASES

1. **Answer: C**
   Although ampicillin/sulbactam has good activity against *H. influenzae*, *Moraxella catarrhalis*, and *S. pneumoniae* (but not drug-resistant *S. pneumoniae* [DRSP]), it has no activity against atypical organisms (*L. pneumophila*, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*). Current recommendations are to include a macrolide with a β-lactam antibiotic for hospitalized patients with CAP (Answer A is incorrect). Piperacillin/tazobactam has good activity against *H. influenzae*, *M. catarrhalis*, and *S. pneumoniae* (but not DRSP) and, with gentamicin, is excellent for pneumonia caused by most gram-negative organisms. However, this increased activity is not necessary for CAP, and the combination has no activity against atypical organisms (Answer B is incorrect). Ceftriaxone plus azithromycin is the best initial choice. It has excellent activity against atypical organisms (because of azithromycin), *H. influenzae*, *M. catarrhalis*, and *S. pneumoniae* (even intermediate DRSP) (Answer C is correct). Although doxycycline has activity against atypical organisms and most of the typical organisms that cause CAP, it is not recommended as monotherapy in hospitalized patients. In addition, its activity against *S. pneumoniae* may be limited (if the patient lives in an area with extensive DRSP). Doxycycline would not be the best initial choice (Answer D is incorrect).

2. **Answer: D**
   Ceftriaxone plus gentamicin plus linezolid is not good empiric therapy because ceftriaxone has no activity against *P. aeruginosa*. Because the patient has been in a hospital for 5 days or more (8 days at this point), she is at increased risk of MDR organisms, specifically *P. aeruginosa* and MRSA (Answer A is incorrect). Although piperacillin/tazobactam has good activity against most common causes of nosocomial pneumonia (including *P. aeruginosa*), the most recent guidelines recommend two antibiotics with activity against *P. aeruginosa* for patients with risk factors for MDR organisms. She also needs an antibiotic with MRSA activity (Answer B is incorrect). Levofloxacin has activity against *P. aeruginosa*, but two drugs should be used (Answer C is incorrect). Cefepime plus tobramycin plus vancomycin is the best empiric therapy because it includes two antibiotics with activity against *P. aeruginosa* and another agent for MRSA (Answer D is correct).

3. **Answer: C**
   This patient has symptoms suggestive of bacterial sinusitis, including two major symptoms and a few minor symptoms. That the symptoms improved and then worsened suggests a bacterial sinusitis that followed a viral infection (Answer D is incorrect). Although the combination of cefpodoxime and clindamycin is an option for sinusitis in penicillin-allergic patients, it is not recommended to give either of these alone for treatment (Answers A and B are incorrect). The best option is amoxicillin/clavulanate, which has activity against organisms commonly seen in bacterial sinusitis and is considered a first-line agent (Answer C is correct).

4. **Answer: B**
   Although the treatment duration is correct for this patient’s diagnosis (7 days), oral trimethoprim/sulfamethoxazole is inappropriate for complicated pyelonephritis. It will also interact with warfarin, increasing the risk of bleeding. (Answer A is incorrect). Ciprofloxacin 400 mg intravenously twice daily and then 500 mg orally twice daily for 7 days is an appropriate choice and duration (7–14 days) for this complicated pyelonephritis (it may also interact with warfarin but to a lesser extent than trimethoprim/sulfamethoxazole). It would be expected to have activity against the common organisms causing complicated pyelonephritis (Answer B is correct). Gentamicin for 3 days is too short a treatment duration (Answer C is incorrect). Tigecycline, followed by doxycycline, is not recommended for complicated pyelonephritis (although tigecycline is found unchanged in the urine) (Answer D is incorrect).

5. **Answer: C**
   Nafcillin has excellent activity against gram-positive organisms, but it would miss the gram-negative organisms and anaerobes often involved in moderate to severe diabetic foot infections (Answer A is incorrect). Tobramycin and levofloxacin would be good against aerobic organisms, but levofloxacin has only limited activity against anaerobes. Tobramycin may also not be a good choice for a patient with diabetes mellitus with long-term complications (because of the increased risk of nephrotoxicity) (Answer B is incorrect). β-Lactamase inhibitor combinations are good agents because they have activity against the organisms that are often involved. At this time, a regimen active
against \textit{P. aeruginosa} is probably not necessary. Treatment duration may need to be extended if the bone is involved (Answer C is correct). Aggressive antibiotic treatment often prevents the need for an amputation (Answer D is incorrect).

6. Answer: A

Because sensitivities of the gram-positive organism are still unknown, vancomycin is the best choice. In addition, the therapy duration for osteomyelitis is 4–6 weeks (Answer A is correct). Therefore, the 2-week duration with nafcillin is too short (Answer B is incorrect). Although levofloxacin is advantageous because it can be given orally, it will probably not achieve adequate bone concentrations to eradicate \textit{S. aureus} (the most likely organism) (Answer C is incorrect). Ampicillin/sulbactam is effective against \textit{S. aureus} (except for MRSA); its broad spectrum of activity is not necessary in this situation, and the duration is too short (Answer D is incorrect).

7. Answer: D

From his presentation and laboratory values, this patient has bacterial meningitis. The gram-negative coci on Gram stain are probably \textit{N. meningitidis}. Penicillin is effective against \textit{N. meningitidis}; however, some strains are resistant, and until culture results are received, it is unwise to use this agent alone (Answer A is incorrect). Ceftriaxone is the appropriate empiric antibiotic therapy in this situation; however, vancomycin is generally added empirically because of its activity against highly penicillin-resistant \textit{S. pneumoniae} (Answer B and C is incorrect). Dexamethasone is primarily beneficial in adults with pneumococcal meningitis, but it should be included empirically until culture results are finalized (Answer D is correct). Vancomycin and dexamethasone can be discontinued when pneumococcal meningitis is ruled out.

8. Answer: A

Only people in close contact to a patient with meningococcal meningitis need prophylaxis (primarily those who live closely with the patient and those who are exposed to oral secretions) (Answer B and D are incorrect). The correct regimen is rifampin 600 mg every 12 hours for four doses (Answer A is correct). Although the vaccine is a good idea for those at future risk of acquiring this infection (e.g., college students living in dormitories), its use during an outbreak is very limited (Answer C is incorrect).

9. Answer: D

A treatment duration of 7-10 days is too short for \textit{S. aureus} endocarditis in the mitral position (Answer A is incorrect). Only streptococcal endocarditis can be treated for 2 weeks. Although nafcillin intravenously plus rifampin plus gentamicin therapy for 6 weeks or longer is an appropriate duration for MSSA, the rifampin and gentamicin need not be added in patients with native valve endocarditis (Answer B is incorrect). Nafcillin intravenously plus gentamicin intravenously for 2 weeks is too short for \textit{S. aureus} endocarditis (Answer C is incorrect). Nafcillin intravenously for 6 weeks is the recommended treatment for MSSA endocarditis (Answer D is correct).

10. Answer: B

This patient is at increased risk of endocarditis because of his history of the disease (Answer D is incorrect). Tooth extractions warrant prophylaxis for those at risk (Answer A is incorrect) Amoxicillin 2 g, 1 hour before the tooth extraction, is the current recommended dose (Answer B is correct). The 2-g dose is adequate for protection, and a follow-up dose is not needed. Amoxicillin 3 g 1 hour before the extraction and 1.5 g 6 hours for four doses after the extraction is the older recommended dose. A follow-up dose is not needed (Answer C is incorrect).

11. Answer: B

This patient is having a severe episode of \textit{C. difficile} diarrhea, as demonstrated by his low albumin, high WBC, and elevated SCr. Therefore, metronidazole is not the optimal choice (and the duration is too short) (Answer A is incorrect). Fidaxomicin and rifaximin are not first-line agents (Answers C and D are incorrect). Fidaxomicin could be used first line in patients who are at high risk of recurrence, but the duration of 14 days is too long. The best therapy for this patient is vancomycin for 10 days (Answer B is correct).

12. Answer: A

Redosing antibiotics for surgical prophylaxis is very important, especially for antibiotics with short half-lives, for extended surgical procedures, or for when there is extensive blood loss (Answer A is correct).
Antibiotics given beyond the surgical procedure are generally unnecessary and only increase the potential for adverse drug reactions and resistant bacteria (Answer B is incorrect). Although preoperative antibiotics given up to 4 hours before the incision may improve the logistics of administering surgical prophylaxis, study results show that antibiotics must be given as close to the time of the incision as possible (definitely within 2 hours) (Answer C is incorrect). Vancomycin should not be used routinely for surgical prophylaxis. The Centers for Disease Control and Prevention does not recommend the use of vancomycin for "routine surgical prophylaxis other than in a patient with life-threatening allergy to β-lactam antibiotics.” (Answer D is incorrect).
ANSWERS AND EXPLANATIONS TO SELF-ASSESSMENT QUESTIONS

1. Answer: A
The patient has CAP that does not require hospitalization (CURB-65 score is 1 at most [no mention of mental status]). Because he has not received any antibiotics in the past 3 months and has no comorbidities, he is at low risk of DRSP. Therefore, the drug of choice is either a macrolide or doxycycline (Answer A is correct). Cefuroxime is not recommended for the treatment of CAP (Answer B is incorrect). Fluoroquinolones are recommended only if the patient has had recent antibiotics or has comorbidities (Answer C is incorrect). Trimethoprim/sulfamethoxazole is not used for CAP (Answer D is incorrect).

2. Answer: D
The symptoms of this patient (high temperature, malaise, dry cough, nasal congestion, and severe headaches) are most consistent with influenza; therefore, an antibacterial agent would not affect recovery (Answers A and B are incorrect). Oselamivir should be initiated within 48 hours of symptom onset, so because this patient is more than 3 days out from symptom onset, oselamivir will not affect recovery (Answer C is incorrect). Because of the viral etiology and time since symptom onset, symptomatic treatment is all that is indicated (Answer D is correct).

3. Answer: B
A case-control study would be the most appropriate study design because it is the most ethical, cost-effective, timely method (Answer B is correct). A stronger study design—for instance, a prospective cohort study or a randomized controlled trial—has many disadvantages if used to answer this question. In a prospective cohort study, too many patients would need to be observed because of the low incidence of confirmed pneumococcal pneumonia. This study would be too costly and take too long to complete (Answer C is incorrect). Randomized controlled trials also have many disadvantages in this situation. First, patients would need to be vaccinated and then observed for at least 10 years. Second, too many patients would need to be observed because of the low incidence of confirmed pneumococcal pneumonia. Third, it would be unethical to randomly assign half of the patients to no vaccination. This study would therefore be too costly, unethical, and time-consuming (Answer D is incorrect).

A case series would evaluate only a few patients given a diagnosis of pneumococcal pneumonia 10 years or more after vaccination. It would not provide comparative data, nor would it provide a strong study design (Answer A is incorrect).

4. Answer: C
Although necrotizing fasciitis can be caused by Streptococcus only, it is often a mixed infection that includes gram-positive, gram-negative, and anaerobic bacteria. Therefore, in addition to urgent surgical debridement, it must be treated empirically with broad-spectrum antibiotics. It is recommended that one of those antibiotics have activity against P. aeruginosa. Clindamycin therapy is also recommended initially to decrease the production of toxin by Streptococcus. Because vancomycin alone has no activity against gram-negative organisms and does not decrease toxin production, it is not the best empiric agent (Answer A is incorrect). Moreover, piperacillin/tazobactam alone has no activity against MRSA and does not decrease toxin production (Answer B is incorrect). Although there are some data that azithromycin may also decrease toxin production, it is not the best empiric agent (Answer C is incorrect). The best empiric option is vancomycin plus meropenem plus clindamycin (Answer C is correct).

5. Answer: C
Although nitrofurantoin is a recommended first-line agent, the therapy duration is too short for its use (Answer A is incorrect). Because this patient has no contraindications to the use of trimethoprim/sulfamethoxazole or nitrofurantoin, and trimethoprim/sulfamethoxazole resistance rates are not mentioned as being high, fluoroquinolones would not be considered appropriate as first-line therapy in this particular case (Answer B is incorrect). In addition, 7 days of therapy is not necessary. The best choice for this patient is trimethoprim/sulfamethoxazole double strength twice daily orally for 3 days. The patient should be counseled about the potential interaction between antibiotics and oral contraceptives (Answer C is correct). β-Lactams are not as effective as trimethoprim/sulfamethoxazole, and data are limited on their use for 3 days (Answer D is incorrect).
6. Answer: A
For the asymptomatic patient who is bedridden and chronically catheterized, with cloudy urine and bacteria revealed by urinalysis, no therapy is indicated (Answer A is correct). All patients with chronic urinary catheters will be bacteriuric. Because this patient is asymptomatic, the catheter does not need to be replaced (Answer B is incorrect). If she were symptomatic, catheter replacement might be indicated. Antibiotics are not indicated; however, a 7-day course would be appropriate if treatment were instituted (Answer C and D are incorrect). A long course of treatment only increases the risk of acquiring resistant organisms.

7. Answer: A
Because cellulitis (which the patient appears to have) is usually caused by Streptococcus or Staphylococcus, cefazolin is the drug of choice (vancomycin could be initiated empirically if MRSA were a concern in this patient) (Answer A is correct). Necrotizing fasciitis must be ruled out because other organisms may be involved, and surgery would be crucial. Although penicillin is the treatment of choice for erysipelas, the patient probably has acute cellulitis (there is no raised border at the edge of the infection, which indicates erysipelas) (Answer B is incorrect). Although piperacillin/tazobactam has activity against both Streptococcus and Staphylococcus, this treatment is too broad spectrum for an acute cellulitis (Answer C is incorrect). Because Doppler studies are negative, the likelihood of a deep venous thrombosis is low (Answer D is incorrect).

8. Answer: C
Even if a patient is believed to have aseptic meningitis after analysis of the CSF, antibiotics must be given until CSF cultures are negative (Answer A is incorrect). In empiric therapy for bacterial meningitis in adults (i.e., when the CSF Gram stain is negative), ceftriaxone should be used in combination with vancomycin (Answer B is incorrect). The vancomycin is necessary for activity against resistant S. pneumoniae (Answer C is correct). Although the symptoms and CSF results are similar to what is expected for herpes simplex encephalitis, the use of acyclovir alone in this patient is inappropriate. Antibacterials must be used as well. Viral meningitis is generally caused by coxsackievirus, echovirus, and enterovirus, which are not treated with acyclovir (Answer D is incorrect).

9. Answer: C
Enterococcal endocarditis should be treated for 4–6 weeks. The 2-week treatment regimen is indicated only for streptococcal endocarditis (Answer A is incorrect). There is also no indication that the patient is penicillin allergic; thus, vancomycin should not be used as first-line treatment (Answer B is incorrect). Ampicillin plus gentamicin for 4–6 weeks is the regimen of choice for penicillin-susceptible enterococcal endocarditis (Answer C is correct). Cephalosporins have no activity against Enterococcus; therefore, the regimen with cefazolin is inappropriate (Answer D is incorrect).

10. Answer: C
A perforated appendix requires antibiotics after surgery for an intra-abdominal infection (Answer D is incorrect). The combination of vancomycin and metronidazole does not have adequate activity against aerobic, gram-negative organisms (e.g., E. coli) (Answer A is incorrect). The combination of cefazolin and ciprofloxacin does not have adequate activity against anaerobic organisms (e.g., B. fragilis group) (Answer B is incorrect). Ceftriaxone plus metronidazole is a good choice for intra-abdominal infections, although it has limited activity against Enterococcus (Answer C is correct).

11. Answer: D
β-Lactam antibiotics are not recommended first-line agents for patients with acute bacterial prostatitis. Therefore, amoxicillin/clavulanate and cefprozil are not the best options in this patient (Answers A and C are incorrect). Although trimethoprim/sulfamethoxazole is an appropriate antibiotic, 14 days of treatment is too short for prostatitis. Treatment duration should be 4 weeks (Answer B is incorrect). Fluoroquinolones are an appropriate antibiotic class for prostatitis, and the 28-day duration is also appropriate (Answer D is correct).

12. Answer: B
Because the organism causing the infection is known to be MSSA, using vancomycin or daptomycin is unnecessary. They both can potentially cause serious toxicities, and daptomycin is expensive (Answers A and D are incorrect). Both nafcillin and cefazolin are appropriate choices for MSSA osteomyelitis; however, because this infection involves a prosthetic joint rifampin must be combined with the primary antibiotic, and
this combination must continue for 2–6 weeks (Answer C is incorrect). This must be followed with 3 months of appropriate oral antibiotics. (Answer B is correct).

13. **Answer: A**

For any orthopedic surgical procedures in which prosthetic materials will be implanted, surgical prophylaxis is necessary. The preferred agent is cefazolin, although vancomycin may be used in patients with allergies. The recommended dosage of cefazolin is at least 2 g (3 g for those weighing more than 120 kg) (Answers C and D are incorrect). Antibiotics must be present in the tissues at the time of incision, and it is best to administer the agent within 1 hour of the incision (Answer A is correct). Because orthopedic procedures tend to be shorter procedures, redosing is probably unnecessary. Administering antibiotics beyond surgical closure is unnecessary (Answer B is incorrect).