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Evidence-Based Guidelines For Evaluation And Antimicrobial Therapy For Common Emergency Department Infections

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CME Objectives

Upon completion of this article, you should be able to:

1. Describe the epidemiology, microbiology, and clinical features of several common ED infections.
2. Risk-stratify and select treatment strategies for common ED infections.
3. Select appropriate empiric antibiotic therapy for pneumonia, UTI, intra-abdominal infections. and SSTI.

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Abstract

Infections are among the most common diagnoses in the emergency department (ED), and antibiotics are among the most frequently prescribed drugs. Community-acquired pneumonia (CAP) and healthcare-associated pneumonia (HCAP) are frequently encountered in the ED, and pneumonia is the seventh leading cause of death in the United States. Cystitis, pyelonephritis, and complicated urinary tract infection (UTI) are often treated in the ED, with UTI being one of the most common reasons for healthy young women to require antimicrobial treatment. Intra-abdominal infections have an incidence of 3.5 million cases per year in the United States, and emergency clinicians must make complex decisions regarding appropriate evaluation and management. Skin and soft-tissue infections (SSTIs) are common, their incidence in the ED has been rising, and the emergence of methicillin-resistant *Staphylococcus aureus* (MRSA) infection has altered their management.

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Timely diagnosis and management of infectious disease, including proper antimicrobial treatment, is an important goal of emergency care. This issue of *Emergency Medicine Practice* reviews the available evidence and consensus guidelines for the management of common infectious diseases presenting to the ED and presents recommendations for treatment.

Case Presentations

At 7:00 on a Monday morning, the day begins with a full line-up of "to be seen." A 35-year-old female with no past medical history presents to the ED complaining of cough and shortness of breath for 2 days that is progressively worsening. On physical examination, she is febrile with an oxygen saturation of 94% on room air and decreased breath sounds at the right base. You order a chest x-ray that shows right lower lobe consolidation.

The second patient on your tracking board is a 70-year-old female with fever, nausea, and back pain for 3 days. She is accompanied by her daughter, who states her mother hasn't been herself today and that she had a similar presentation when she had a UTI 2 years ago. She is febrile to 38.3°C (101°F), oriented x2, with left costovertebral angle tenderness. Her urine dipstick is positive for leukocyte esterase and nitrites.

In the next bed, you are evaluating a 23-year-old male who has had a painful, swollen right forearm for 2 days. He reports a subjective fever earlier in the evening, but no other systemic symptoms. He denies any past medical history and has no IV drug abuse and no history of diabetes. He is afebrile with normal vital signs. A 6-cm area of erythema, induration, and tenderness is noted on his proximal forearm with a 2-cm central fluctuant, raised area. He has full range of motion at the elbow.

Just as you sit down for a cup of coffee, the triage nurse notifies you that she just received an 85-year-old male from a nursing home that was sent in for evaluation for fever. He has a history of insulin-dependent diabetes mellitus, hypertension, and dementia. On physical examination, he is febrile, with otherwise normal vital signs. His abdomen is slightly distended, soft, but diffusely tender to palpation.

Four infectious disease cases in a row — it feels like an epidemic. You reflect on the challenge of choosing the right antibiotic in the age of emerging pathogens and how the right choice may be the difference between a good or bad outcome.

Introduction

Clinicians who treat infectious diseases in the ED need to apply a vast amount of knowledge regarding not only which antibiotics are appropriate in a particular situation, but also the relevant microbiology, diagnostic testing, and pathophysiology of the underlying disease. Timely diagnosis and management of infectious disease, including proper antimicrobial treatment in the ED, has been shown to decrease morbidity and mortality in bacterial meningitis and sepsis[1] and should be a goal of emergency care. To facilitate proper broad-spectrum coverage for initial antibiotic administration while decreasing unnecessary antibiotic use and propagating the emerging problem of multidrug-resistant organisms, evidence-based guidelines have been developed by the Infectious Diseases Society of America (IDSA) in collaboration with multiple specialty societies.

Knowledge of these guidelines and proper empiric therapy is of utmost importance to the emergency clinician when treating common and uncommon infections. Familiarity with comorbidities and risk factors for multidrug-resistant organisms and complicated infections as well as clinical decision rules to help guide diagnostic modalities, surgical consultation, and admission criteria for intravenous (IV) antibiotics may also be helpful in ensuring patients receive the best chances for proper diagnosis and appropriate treatment. This issue of *Emergency Medicine Practice* focuses on common infectious diseases presenting to the ED and reviews the current literature and guidelines.

Critical Appraisal Of The Literature

For this evidence-based review article, an extensive search of the PubMed database, Ovid MEDLINE®, and the Cochrane Database of Systematic Reviews was performed. A search for relevant guidelines was performed via the Agency for Healthcare Research and Quality National Guideline Clearinghouse. A thorough review of consensus guidelines and evaluation of their citations was undertaken. An online search of the IDSA website, the Centers for Disease and Control and Prevention (CDC) website, and the American College of Emergency Physicians (ACEP) website was performed.

Recommendations were formulated, to a large degree, from the available relevant guidelines of the IDSA. These include the joint recommendations for the management of pneumonia from the IDSA and the American Thoracic Society (ATS), the 2005 "Guidelines for the Management of Adults with Hospital-Acquired, Ventilator-Associated, and Healthcare-Associated Pneumonia," and the 2007 "Community-Acquired Pneumonia in Adults: Guidelines for Management." The authors also thoroughly reviewed the 2010 "Guidelines for the Selection of Anti-Infective Agents for Complicated Intra-Abdominal Infections," "International Clinical Practice Guidelines for Antimicrobial Treatment of Acute Uncomplicated Cystitis and Pyelonephritis in Women," the 2009 "Diagnosis, Prevention, and Treatment of Catheter-Associated Urinary Tract Infections in Adults," and the 2005 Association of Medical Microbiology and Infectious Disease

Canada Guidelines Committee's "Complicated Urinary Tract Infection in Adults." For skin infections, the 2005 "Practice Guidelines for the Diagnosis and Management of Skin and Soft-Tissue Infections" and the 2011 "Management of Patients with Infections Caused by Methicillin-Resistant *Staphylococcus aureus:* Clinical Practice Guidelines by the Infectious Diseases Society of America (IDSA)" were reviewed. Information for skin and soft-tissue infections was also obtained from the October 2010 *Emergency Medicine Practice* Issue, "Emergency Department Infections in the Era of CA-MRSA."

Table 1 outlines the grading system for rating the recommendations in clinical guidelines that is used by IDSA and the United States Public Health Service.

Abbreviations And Acronyms

ACEP: American College of Emergency Physicians
ATS: American Thoracic Society
CA-MRSA: Community-acquired MRSA
CAP: Community-acquired pneumonia
CA-UTI: Catheter-associated urinary tract infection
ESCMID: European Society of Clinical Microbiology and Infectious Disease
ED: Emergency department
HA-MRSA: Hospital-acquired MRSA
HAP: Hospital-acquired pneumonia
HCAP: Healthcare-associated pneumonia
IDSA: Infectious Diseases Society of America
IV: Intravenous
MRSA: Methicillin-resistant *Staphylococcus aureus*
MSSA: Methicillin-sensitive *Staphylococcus aureus*
PSI: Pneumonia severity index
SSTI: Skin and soft-tissue infection
UTI: Urinary tract infection
VAP: Ventilator-associated pneumonia

Table 1. Infectious Diseases Society Of America–US Public Health Service Grading System For Rating Recommendations In Clinical Guidelines[2]

Category, Grade	Definition
Strength of Recommendation	
A	Good evidence to support a recommendation for use
B	Moderate evidence to support a recommendation for use
C	Poor evidence to support a recommendation
D	Moderate evidence to support a recommendation against use
E	Good evidence to support a recommendation against use
Quality of Evidence	
I	Evidence from ≥ 1 properly randomized controlled trial
II	Evidence from ≥ 1 well-designed clinical trial, without randomization; from cohort or case-controlled analytic studies (preferably from > 1 center); from multiple time-series; or from dramatic results of uncontrolled experiments
III	Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

Epidemiology

Each year, approximately 5% of all patients presenting to the ED are febrile at triage. Infections including pneumonia, UTI, and cellulitis/abscesses are among the most common admitting diagnoses, and approximately 10% overall receive a hospital discharge diagnosis associated with an infectious disease.[3]

Because antibiotics are among the most frequently prescribed and administered drugs in the ED, the emergency clinician is an antibiotic steward and must make rational and appropriate antibiotic decisions. Early and appropriate antibiotic administration optimizes patient outcomes. Additional factors that must be considered in choosing an antibiotic include minimizing toxicity, reducing the development of resistance (ie, preserving antibiotic effectiveness), and containing cost. Additional considerations in choosing empiric antibiotic treatment include knowledge of typical pathogens, regional or local antibiogram susceptibility patterns, tissue penetration and concentration, consensus guidelines, and availability/formulary issues. The emergency clinician must remain current as resistance patterns and antibiotic availability change.

Pharmacology Of Antibiotics

Antibiotics work by either killing bacteria (bactericidal action) or inhibiting their growth (bacteriostatic action). Their mechanism of action can be categorized as disrupting cell wall synthesis (beta-lactams, vancomycin, bacitracin, polymixins), inhibiting protein synthesis (aminoglycosides, tetracyclines, oxazolidones), or inhibiting nucleic acid synthesis (quinolones, rifampin, metronidazole, sulfonamides). In general, most antibiotics that disrupt cell wall or nucleic acid synthesis are bacteriocidal, while those that inhibit protein synthesis tend to be bacteriostatic (with the exception of aminoglycosides). This is of particular importance when treating serious infectious such as endocarditis, meningitis, or neutropenia, when bacteriocidal regimens are preferred.

Some combinations of antibiotics can achieve enhanced bacteriocidal activity when used together and achieve better clinical outcomes in treating gram-negative sepsis.[4-5] Using combinations of antibiotics with different mechanisms of action can also broaden the spectrum of coverage, thus increasing the likelihood of appropriate therapy for multidrug-resistant pathogens, as well as decreasing the

Table 2. Spectrum Of Activity Of Commonly Used Antibiotics[8,9]

Mechanism of Antibiotic	Activity of Antibiotic
Cell Wall Inhibitors	
Natural penicillins Benzylpenicillin (penicillin G) phenoxymethyl penicillin (penicillin LV)	• Gram(+) cocci including beta-hemolytic streptococci and meningococci • Gram(+) rods, *Neisseria*, spirochetes, anaerobes (except *Bacteroides fragilis*)
Penicillinase-resistant penicillins Methicillin, nafcillin, oxacillin, cloxacillin, dicloxacillin	Enhanced activity against staphylococci
Broad-spectrum penicillins • Aminopenicillins (ampicillin, amoxicillin) • Carboxypenicillins (carbenicillin, ticarcillin) • Ureidopenicillins (piperacillin)	• Enhanced activity against some gram(+) rods including *H influenzae, E coli, Proteus, Salmonella,* and *Shigella* • Ticarcillin and piperacillin include activity against *P aeruginosa* and *K pneumoniae*
Beta-lactam with beta-lactamase inhibitor Ampicillin-sulbactam, amoxicillin-clavulanate, ticarcillin-clavulanate, piperacillin-tazobactam	• Improved activity against beta-lactamase-producing staphylococci and selected gram(-) rods • Piperacillin/tazobactam is most active
First-generation cephalosporins Cephalexin, cephalothin, cefazolin, cephapirin, cephradine	• Activity equivalent to oxacillin against gram(+) bacteria • Some gram(-) activity (eg, *E coli, Klebsiella, P mirabilis*)
Second-generation cephalosporins Cefaclor, cefuroxime	Improved gram(-) activity to include *Enterobacter, Citrobacter,* and *Proteus* spp
Extended-spectrum cephamycins Cefotetan, cefoxitin	• Similar to second-generation cephalosporins • Less susceptible to beta-lactamases
Third-generation cephalosporins Cefixime, cefotaxime, ceftriaxone, ceftazidime	• Improved gram(-) activity • Weak coverage of *Pseudomonas*
Fourth-generation cephalosporins Cefepime, cefpirome	• Marginally improved gram(-) activity • Covers *Pseudomonas*
Carbapenems Imipenem, meropenem, ertapenem, doripenem	Broad-spectrum against most aerobic and anaerobic gram(+) and gram(-) except oxacillin-resistant staphylococci, most *E faecium*, selected gram(-) rods, and some *Pseudomonas*
Monobactam Aztreonam	• Selective aerobic gram(-) rods including *Enterobacteriaceae* and *Pseudomonas* • Inactive against anaerobes or gram(+) cocci • No cross-reactivity to penicillins
Protein Synthesis Inhibitors	
Aminoglycosides Streptomycin, kanamycin, gentamicin, tobramycin, amikacin	• Gram(-) rods • Tobramycin slightly more active than gentamicin against *Pseudomonas;* amikacin most active • Streptomycin and gentamicin combined with cell-wall-active antibiotic to treat *Enterococcus*
Tetracyclines Tetracycline, doxycycline, minocycline	Gram(+) and gram(-) (*Neisseria,* some Enterobacteriaceae), mycoplasmas, *Chlamydophila,* chlamydiae, and rickettsiae
Glycylcyclines Tigecycline	• Similar to tetracyclines but gram(+) activity • Gram(+) cocci skin infections and facultative and anaerobic intra-abdominal infections
Oxazolidinone Linezolid	*Staphylococcus* (including methicillin-resistant and vancomycin-intermediate strains), *Enterococcus, Streptococcus,* gram(+) rods, and *Clostridium* and anaerobic cocci
Macrolides Azithromycin, erythromycin, clarithromycin	• Gram(+) and some gram(-) bacteria, *Neisseria, Legionella, Mycoplasma, Chlamydia, Chlamydophila, Treponema,* and *Rickettsia* • Clarithromycin and azithromycin active against some mycobacteria
Ketolides Telithromycin	Similar to macrolides, also covers some macrolide-resistant staphylococci, *Streptococcus pneumonia*, and enterococci
Lincosamide Clindamycin	Aerobic gram(+) cocci and anaerobes including *Clostridium perfringens,* and *Bacteroides fragilis*
Chloramphenicol	*Haemophilus influenzae* meningitis, typhoid fever, anaerobic infections (especially *Bacteroides fragilis*)
Nucleic Acid Inhibitors	
Broad-spectrum fluoroquinolones Ciprofloxacin, levofloxacin, ofloxacin	• Gram(+) and gram(-) bacteria • Some activity against *Pseudomonas aeruginosa* and some atypicals
Extended-spectrum fluoroquinolones Gatifloxacin, clinafloxacin, moxifloxacin, trovafloxacin	• Enhanced gram(+) coverage (streptococci and enterococci) • Some gram(-) rods and anaerobic coverage
Metronidazole	Anaerobes and certain parasites and protozoa such as *Giardia* and *Trichomonas*
Nitrofurantoin	Gram(+) and gram(-) coverage only in the lower urinary tract
Trimethoprim-sulfamethoxazole	• Gram(+) and gram(-), protozoals • Useful for urinary tract infections, *Pneumocystis* pneumonia, shigellosis, and MRSA
Rifampin	Primarily for treatment of tuberculosis or prophylaxis in close contacts with *N meningitides* or *H influenzae* meningitis

Abbreviation: MRSA, methicillin-resistant *Staphylococcus aureus*.

development of resistance.[6-7] **Table 2 (see page xx)** describes the spectrum of activity of commonly used antibiotics to help guide empiric antibiotic regimens.

Additional factors influencing appropriate selection of antibiotics include its penetration, or ability to reach target tissues; bioavailability via mechanism of administration; metabolism and excretion; and toxicity. Common antibiotics that may need renal and liver dosing adjustments are included in **Table 3**.

Pneumonia

Pneumonia is the seventh leading cause of death in the United States, accounting for 1.7 million hospital admissions annually,[10] and consequently has become the focus of many organizations including The Joint Commission and Centers for Medicare & Medicaid Services (CMS) as a way to decrease costs of hospital admission through increased quality measures. Core measures for patients admitted with the diagnosis of pneumonia evaluated through the ED have been created, including blood culture collection prior to first antibiotic administration, administration of initial antibiotics within 6 hours of arrival to the ED, and appropriate empiric antibiotic selection.[11,12] (Note: as of January 1, 2012, The Joint Commission retired the core measure requiring antibiotics to be administered within 6 hours of ED arrival.) For more information on National Quality Measures, see the EB Medicine Research Report, "Quality And Performance Measurement: A Guide For Emergency Physicians."

Pneumonia is described as 4 different entities based on patient factors and where the pneumonia was acquired, reflecting the differences in pathogens and drug resistance patterns. **(See Tables 4-6 for common antibiotic regimens for pneumonia.)**

Table 3. Antibiotics That Require Dosage Adjustments In Liver Or Kidney Disease

Renal Disease
- Some cephalosporins (mostly third-generation cephalosporins)
- Clindamycin
- Chloramphenicol
- Metronidazole
- Nafcillin

Liver Disease
- Most cephalosporins
- Aminoglycosides
- Macrolides
- Fluoroquinolones
- Penicillins

Table 4. Common Antibiotic Regimens For Outpatient Treatment Of Community-Acquired Pneumonia[51,52]

Antibiotic	Adult Dosage	Comments/Caveats
Outpatient Treatment, No Comorbidities		
Macrolides		
Azithromycin	500 mg PO, then 250 mg PO daily x 4 days Extended-release 2 g x1 dose	Macrolides are first-line therapy
Clarithromycin	500 mg PO twice daily 1 g extended-release daily x 7 days	
Doxycycline	100 mg PO twice daily x 7-10 days	
Outpatient Treatment, Patient With Comorbidities or Recent Antibiotics		
Fluoroquinolone		
Moxifloxacin	400 mg PO daily x 7-10 days	If recent antibiotics, choose alternate therapy from prior
Levofloxacin	750 mg PO daily x 5 days	
Beta-lactam		
Amoxicillin	1 g PO 3 times daily x 7 days	
Amoxicillin-clavulanate	1000/62.5 mg PO 2 tabs twice daily x 7 days	
Cefpodoxime	200 mg PO twice daily x 7 days	
Cefprozil	500 mg PO twice daily x 7 days	
Cefdinir	300 mg PO twice daily x 7 days	
PLUS		
Macrolide		
Azithromycin	500 mg PO, then 250 mg PO daily x 4 days Extended-release 2 g x1 dose	
Clarithromycin	500 mg PO twice daily Extended-release 1 g daily x 7 days	
OR		
Doxycycline	100 mg PO twice daily x 7-10 days	

Abbreviations: g, gram; mg, milligram; PO, by mouth; q, every.

Clinical Pathway For Treatment Of Pneumonia

- Fever, cough, dyspnea, pleuritic chest pain
- Acute infiltrate on chest radiography

ICU candidate?
- Septic shock requiring vasopressors
- Acute respiratory failure
- 3 or more minor ICU criteria:
  - Respiratory rate > 30
  - PaO_2/FiO_2 < 250
  - Multilobar infiltrates
  - Confusion
  - BUN > 20 mg/dL
  - Leukopenia
  - Thrombocytopenia
  - Hypothermia
  - Hypotension requiring aggressive resuscitation

NO → **Inpatient therapy?**
- CURB 65 ≥ 2
- PSI ≥ 4
- Patient factors requiring hospitalization

NO → Presence of comorbidities, antibiotics in previous 3 months, or other risk factors for drug-resistant *S pneumoniae*?

Comorbidities:
- Chronic heart, lung or renal disease
- Diabetes mellitus
- Alcoholism
- Malignancy
- Asplenia
- Immunosuppressing condition or drugs

NO
- A macrolide **(Level I Evidence)**
  OR
- Doxycycline **(Level III Evidence)**

YES
- Respiratory fluoroquinolone **(Level I Evidence)**
  OR
- Beta-lactam **PLUS** a macrolide **(Level II Evidence)**
  OR
- Beta-lactam **PLUS** doxycycline **(Level II Evidence)**

YES → **HCAP risk factors?**
- Hospitalization for 2 or more days of the past 90 days
- Resides in nursing home or long-term care facility
- Received chemotherapy, IV antibiotics, or wound care within the prior 30 days
- Attended a hospital or hemodialysis clinic in the last 30 days

NO

Collect blood cultures, consider sputum cultures
- Respiratory fluoroquinolone **(Level I Evidence)**
  OR
- Beta-lactam **PLUS** a macrolide **(Level II Evidence)**
  OR
- Beta-lactam **PLUS** doxycycline **(Level III Evidence)**

YES

Collect blood cultures, consider sputum cultures;
HCAP empiric antibiotic coverage: **(Level II Evidence)**
- Antipseudomonal cephalosporin*
  OR
  Antipseudomonal carbapenem*
  OR
  Beta-lactam/beta-lactamase inhibitor*
  PLUS
- Antipseudomonal fluoroquinolone
  OR
  Aminoglycoside
  PLUS
- MRSA coverage (linezolid or vancomycin)
  CONSIDER
- *Legionella pneumophila* coverage (macrolide or fluoroquinolone instead of aminoglycoside)

*For penicillin-allergic patients, substitute aztreonam.

YES
- Begin resuscitative efforts
- Collect blood and sputum cultures
- Start broad-spectrum antibiotics:
  - Beta-lactam **PLUS** azithromycin **(Level II Evidence)**
    OR
  - Beta-lactam* **PLUS** a fluoroquinolone **(Level I Evidence)**

If *Pseudomonas* risk factors:
- Antipseudomonal beta-lactam* **PLUS** a fluoroquinolone
  OR
- Antipseudomonal beta-lactam* **PLUS** an aminoglycoside **PLUS** azithromycin
  OR
- Antipseudomonal beta-lactam* **PLUS** an aminoglycoside **PLUS** an antipneumococcal fluoroquinolone **(Level III Evidence)**

*For penicillin-allergic patients, substitute aztreonam for the above beta-lactam.

In regions with high rate (> 25%) of infection with high-level macrolide-resistant *S pneumoniae,* consider alternative agents in above recommendations for any patient **(Level III Evidence)**

Abbreviations: BUN, blood urea nitrogen; CURB-65, Confusion, Uremia, Respiratory rate, low Blood pressure, age 65 years or greater; FiO_2, fraction of inspired oxygen; HCAP, healthcare-associated pneumonia; ICU, intensive care unit; IV, intravenous; PaO_2, arterial oxygen pressure; PSI, pneumonia severity index.

For class of evidence definitions, see Table 1, page 3.

Table 5. Common Antibiotic Regimens For Inpatient Treatment Of Community-Acquired Pneumonia[51,52]

Antibiotic	Adult Dosage	Comments/Caveats
Inpatient Treatment, Non-ICU		
Fluoroquinolones		
Moxifloxacin	400 mg PO/IV q24 hours	
Levofloxacin	750 mg PO/IV q24 hours	
Beta-lactam		
Cefotaxime	1 g IV q8 hours	
Ceftriaxone	1 g IV q24 hours	
Ertapenem	1 g IV q24 hours	
PLUS		
Macrolide		
Azithromycin	500 mg PO/IV q24 hours	
Clarithromycin	500 mg PO q12 hours 1 g extended-release q24 hours	
OR		
Doxycycline	100 mg PO/IV q12 hours	
Inpatient Treatment, ICU		
Beta-lactam		• In severe penicillin allergy, use aztreonam 2 g IV q6-8 hours and fluoroquinolone
Cefotaxime	2 g IV q8 hours	• See above for azithromycin and fluoroquinolone dosing
Ceftriaxone	1 g IV q24 hours	
Ampicillin-sulbactam	3 g IV q6 hours	
PLUS		
Azithromycin		
OR		
Fluoroquinolone		
Inpatient Treatment, ICU, *Pseudomonas* Risk Factors		
Antipneumococcal, antipseudomonal beta-lactam		• In severe penicillin allergy, substitute aztreonam 2 g IV q6-8 hours in place of beta-lactam
Piperacillin-tazobactam	4.5 g IV q6 hours or 3.375 g IV q4 hours	
Cefepime	1-2 g IV q8 hours	
Imipenem	1 g IV q6-8 hours	
Meropenem	2 g IV q8 hours	
PLUS		
Antipseudomonal fluoroquinolone		
Ciprofloxacin	400 mg IV q8 hours	
Levofloxacin	750 mg IV q24 hours	
Antipneumococcal, antipseudomonal beta-lactam		• In severe penicillin allergy, substitute aztreonam 2 g IV q6-8 hours in place of beta-lactam
PLUS		
Aminoglycoside		
Gentamicin	3 mg/kg load, then 2 mg/kg IV q8 hours	• See above for antipneumococcal, antipseudomonal beta-lactam, azithromycin, and antipseudomonal fluoroquinolone dosing
Tobramycin	3 mg/kg load, then 2 mg/kg IV q8 hours	
Amikacin	8-12 mg/kg load, then 8 mg/kg IV q8 hours	
PLUS		
Azithromycin		
OR		
Antipseudomonal fluoroquinolone		

Abbreviations: g, gram; ICU, intensive care unit; IV, intravenous; kg, kilogram; mg, milligram; PO, by mouth; q, every.

Hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP) occur in hospitalized patients, whereas community-acquired pneumonia (CAP) and healthcare-associated pneumonia (HCAP) are more typically treated through the ED.

Community-acquired pneumonia is an acute pulmonary infection in an ambulatory patient who is not living in a long-term care facility for 14 or more days before presentation and does not meet the criteria for HCAP. Healthcare-associated pneumonia includes patients hospitalized for 2 or more days within 90 days of the infection, patients who reside in a nursing home or long-term care facility, and/or who received chemotherapy, IV antibiotics, or wound care within the prior 30 days or attended a hospital or hemodialysis clinic in the past 30 days.[13]

Healthcare-associated pneumonia is more similar, epidemiologically, to HAP and VAP, with high risk for multidrug-resistant pathogens and a mortality rate significantly higher than that for CAP.[14-16]

The IDSA and ATS joined to develop unified HAP/VAP/HCAP guidelines in 2004 and CAP guidelines in 2007. The following recommendations are adapted from the guidelines.

Initial Emergency Department Evaluation And Management For Pneumonia

Emergency department evaluation focuses on the presence of signs and symptoms consistent with pneumonia such as fever, cough, dyspnea, and pleuritic chest pain. Patient comorbidities, recent antibiotic use, recent hospitalizations or frequent exposure to healthcare and multidrug-resistant organisms (such as in nursing homes, assisted living facilities, and/or hemodialysis units) are necessary for empiric antimicrobial decisions. Vital sign abnormalities such as fever, hypotension, tachypnea, and hypoxia should be addressed with proper resuscitation.

Diagnostic Studies For Pneumonia

Tachypnea and bronchial breath sounds may point towards pneumonia, but they are less sensitive or specific than chest radiography. For patients in whom pneumonia is suspected based on presence of fever, cough, tachypnea, or pleuritic chest pain, perform a chest radiograph early to establish the diagnosis and aid in differentiating CAP from other causes of cough and fever such as acute bronchitis. Computed tomography (CT) scans may be more sensitive than radiography, but the clinical significance of a CT diagnosis of pneumonia after a negative chest radiograph is unclear.

Evidence-Based Recommendations: Diagnostic Studies For Pneumonia

In addition to a constellation of suggestive clinical features, a demonstrable infiltrate by chest radiograph or other imaging technique, with or without supporting microbiological data, is required for the diagnosis of pneumonia. **(B-III)**

Blood And Sputum Cultures For Pneumonia

Routine use of blood cultures in all patients admitted with CAP yields positive results in only 5% to 14% of cases, rarely leads to improved outcomes or choices in antibiotic regimens, and may lead to

Table 6. Common Antibiotic Regimens For Treatment Of Healthcare-Associated Pneumonia[51,52]

Antibiotic	Adult Dosage	Comments/Caveats
Antipseudomonal beta-lactam		
Cefepime	1-2 g IV q8-12 hours	• In severe penicillin allergy, use aztreonam 2 g IV q6-8 hours in and fluoroquinolone
Ceftazidime	2 g IV q8 hours	
Imipenem	500 mg q6 hours or 1g q8 hours	
Meropenem	1 g q8 hours	• To cover *Legionella pneumophila*, use the fluoroquinolone-containing regimen or add a macrolide to the aminoglycoside regimen
Piperacillin-tazobactam	4.5 g q6 hours	
PLUS		
Antipseudomonal fluoroquinolone		
Ciprofloxacin	400 mg q8 hours	
Levofloxacin	750 mg q24 hours	
OR		
Aminoglycoside		
Gentamicin	3 mg/kg load, then 2 mg/kg IV q8 hours	
Tobramycin	3 mg/kg load, then 2 mg/kg IV q8 hours	
Amikacin	8-12 mg/kg load, then 8 mg/kg IV q8 hours	
PLUS		
MRSA coverage		
Vancomycin	15 mg/kg q12 hours	
Linezolid	600 mg q12 hours	

Abbreviations: g, gram; IV, intravenous; kg, kilogram; mg, milligram; PO, by mouth; q, every.

false-positive results that complicate the patient's clinical course. The strongest indications for blood cultures are severe CAP and in immunocompromised patients, or those with significant comorbidities, as these patients are more likely to be infected with pathogens other than *S pneumoniae.* Antibiotic administration decreases blood culture yield, and blood cultures should be obtained prior to antibiotic treatment in all admitted patients with pneumonia in accordance with core measures.[17] (Note: this is still part of core measure PN-3b.)

Sputum Gram stain and cultures also tend to be of low yield, as their quality is influenced by ability to collect an adequate patient specimen, transport, rapid processing, cytologic criteria, absence of prior antibiotic therapy, and skill in interpretation. Culture yield is significantly higher with endotracheal aspirates, bronchoscopic sampling, or transthoracic needle aspiration. Culture and Gram stain of intubated patients with severe CAP is recommended.

Evidence-Based Recommendations: Cultures

- Pretreatment blood samples for culture and an expectorated sputum sample for stain and culture (in patients with a productive cough) should be obtained from hospitalized patients with: ICU admission, cavitary infiltrates, leukopenia, active alcohol abuse, chronic or severe liver disease, asplenia, positive pneumococcal urinary antigen test, or pleural effusion, but they are optional for patients without these conditions. **(B-I)**
- Pretreatment Gram stain and culture of expectorated sputum should be performed only if a good-quality specimen can be obtained and quality performance measures for collection, transport, and processing of samples can be met. **(B-I)**
- Patients with severe CAP should at least have blood samples drawn for culture, urinary antigen tests for *Legionella pneumophila* and *Streptococcus pneumoniae* performed, and expectorated sputum samples collected for culture. For intubated patients, an endotracheal aspirate sample should be obtained. **(B-II)**

Site-Of-Care Decisions For Pneumonia

Identifying which patients may be treated safely as outpatients can reduce unnecessary costs. Inpatient treatment for pneumonia can cost up to 25 times that of outpatient therapy and consumes an estimated $8.4 to $10 billion annually for treatment.[18]

Severity of illness can be prognosticated through scores such as the CURB-65 criteria (**C**onfusion, **U**remia, **R**espiratory rate, low **B**lood pressure, age **65** years or greater) or the pneumonia severity index (PSI), which can help identify which patients may be safely discharged and treated as outpatients with the proper follow-up and outpatient resources. The goal of admission is to decrease mortality associated with pneumonia. Both CURB-65 and PSI stratify patients into risk classes, which can then be used to predict mortality. CURB-65 is widely used and easy to calculate, but it does not take into account exacerbation of co-morbid conditions, such as an asthma exacerbation or uncontrolled diabetes, and the possible need to admit based on these factors.

Approximately 10% of patients with CAP require ICU admission, but predicting which patients would benefit from ICU monitoring is not straightforward among patients who do not meet major criteria (shock or respiratory failure).

Evidence-Based Recommendations: Site-Of-Care Decisions For Pneumonia

Hospital Admission Decision

- Severity-of-illness scores such as the CURB-65 criteria or prognostic models such as the pneumonia severity index (PSI) can be used to identify patients with CAP who may be candidates for outpatient treatment. **(A-I)**
- Objective criteria or scores should always be supplemented with physician determination of subjective factors, including the ability to safely and reliably take oral medication and the availability of outpatient support resources. **(A-II)**

Intensive Care Unit Admission Decision

- Direct admission to an intensive care unit (ICU) is required for patients with septic shock requiring vasopressors or with acute respiratory failure requiring intubation and mechanical ventilation (major criteria). **(A-II)**
- Direct admission to an ICU or high-level monitoring unit is recommended for patients with 3 of the following minor criteria for severe CAP **(B-II)**:
  - Respiratory rate > 30 breaths/min
  - Arterial oxygen pressure/fracture of inspired oxygen (PaO_2/FiO_2) ratio < 250
  - Multilobar infiltrates
  - Confusion
  - Blood urea nitrogen > 20 mg/dL
  - Leukopenia
  - Thrombocytopenia
  - Hypothermia
  - Hypotension requiring aggressive fluid resuscitation

Empiric Antimicrobial Therapy For Community-Acquired Pneumonia

The major goal of antimicrobial therapy is eradication of the infecting organism with clinical resolution of the pneumonia. Recommendations for empiric therapy are based on common pathogens given patient

risk factors; however, this may vary regionally due to local susceptibility patterns and should be compared to the last-performed hospital antibiograms.

Evidence-Based Recommendations: Community-Acquired Pneumonia

Outpatient Treatment

1. Previously healthy with no antibiotics within the prior 3 months:
   - A macrolide **(A-I)**
     OR
   - Doxycycline **(C-III)**

2. Comorbid conditions such as chronic heart, lung, liver or renal disease, diabetes mellitus, alcoholism, malignancy, asplenia, immunosuppressing conditions, use of immunosuppressing drugs, or use of antibiotics within prior 3 months (an alternative from a different class should be selected)
   - A respiratory fluoroquinolone **(A-I)**
     OR
   - A beta-lactam plus a macrolide **(A-I)** or doxycycline **(C-II)**

   If > 25% rate of infection with high-level macrolide-resistant *Streptococcus pneumoniae*, consider use of alternative agents above in level 2 for patients without comorbidities **(B-III)**

Inpatients, Non-ICU Treatment

- A respiratory fluoroquinolone **(A-I)**
  OR
- A beta-lactam plus a macrolide **(A-I)** or doxycycline **(C-III)**

Inpatients, ICU Treatment

- A beta-lactam plus azithromycin (A-II)
  OR
- A beta-lactam* plus a respiratory fluoroquinolone **(A-I)**

Special Concerns

If *Pseudomonas* is a consideration:

- An antipneumococcal, antipseudomonal beta-lactam* (piperacillin-tazobactam, cefepime, imipenem, or meropenem)
  PLUS ciprofloxacin or levofloxacin
  or
  An aminoglycoside and azithromycin **(B-III)**

If CA-MRSA is a consideration, add vancomycin or linezolid **(B-III)**

*For penicillin-allergic patients, substitute aztreonam for the above beta-lactam **(B-III)**

Healthcare-Associated Pneumonia

Evidence-Based Recommendations: Healthcare-Associated Pneumonia

Additional coverage for multidrug-resistant pathogens including *Pseudomonas aeruginosa, Klebsiella pneumoniae, Acinetobacter* species

- Antipseudomonal cephalosporin
  OR
  Antipseudomonal carbapenem
  OR
  Beta-lactam/beta-lactamase inhibitor*

PLUS

- Antipseudomonal fluoroquinolone
  OR
  Aminoglycoside

PLUS

- MRSA coverage

CONSIDER

- *Legionella pneumophila* coverage

*For penicillin-allergic patients, substitute aztreonam for the above beta-lactam **(B-III)**

Urinary Tract Infection

Urinary tract infections are some of the most common indications for prescribing antibiotics to otherwise healthy women, with estimated numbers as high as 8,000,000 episodes per year.[19] One out of 3 women will require treatment for a UTI before the age of 24, and 40% to 50% of women will have a UTI during their lifetime.[20] Uncomplicated cystitis and pyelonephritis include UTIs in structurally and functionally normal urinary tracts in premenopausal nonpregnant women without significant comorbidities.[21]

Complicated UTI occurs among males, pregnant women, and individuals with structural or functional anatomic abnormalities of the genitourinary tract, including (but not limited to) congenital abnormalities, renal stones, urologic procedures, indwelling catheters, neurogenic bladder, and renal transplant.[22] Pregnant women are at increased risk of UTIs,[23] which, if untreated, can lead to complications such as pyelonephritis, low-birthweight infants, premature delivery, and occasionally stillbirth.[24]

In 1999, the IDSA issued its first clinical practice guideline on uncomplicated cystitis and pyelonephritis; however, antibiotic resistance among common pathogens has increased and improved studies looking at antibiotic resistance and clinical outcomes have

been reported, leading to the 2010 update in collaboration with the European Society of Clinical Microbiology and Infectious Disease (ESCMID). There are a number of review articles regarding empiric antimicrobial therapy for urinary tract infections in pregnancy but no current evidence-based guidelines. The Association of Medical Microbiology and Infectious Disease Canada released guidelines for complicated urinary tract infection in adults in 2005. **(See Tables 7-10 for common antibiotic regimens for UTI.)**

Initial Emergency Department Evaluation And Management For Urinary Tract Infection

Suspect acute cystitis in patients who present with urinary frequency, urgency, dysuria, hematuria, and suprapubic discomfort. Perform a focused evaluation to assess the patient for history of frequent or prior UTIs caused by multidrug-resistant organisms and comorbid conditions that may complicate antimicrobial therapy including pregnancy, diabetes, presence of indwelling urological devices, renal

Table 7. Common Antibiotic Regimens For Uncomplicated Urinary Tract Infection[51,52]

Antibiotic	Adult Dosage	Comments/Caveats
Uncomplicated Cystitis		
Nitrofurantoin macrocrystals	100 mg PO twice daily x 5 days	• First-line therapies
Trimethoprim-sulfamethoxazole	160/800 mg PO twice daily x 3 days	• Avoid nitrofurantoin and fosfomycin in suspected early pyelonephritis due to poor tissue penetration
Fosfomycin trometamol	3 g PO once	
Fluoroquinolones		• Alternative therapies
Ciprofloxacin	250 mg PO twice daily x 3 days	• Cephalexin less-well-studied
Ofloxacin	200 mg PO twice daily x 3 days	
Levofloxacin	250 mg PO once daily x 3 days	
Beta-lactams		
Amoxicillin-clavulanate	875/125 mg PO twice daily x 5-7 days	
Cefpodoxime proxetil	100 mg PO twice daily x3 days	
Cephalexin	250 mg PO 4 times daily x 5-7 days	
Uncomplicated Pyelonephritis, Outpatient Therapy		
Fluoroquinolones		• If fluoroquinolone resistance < 10%, oral ciprofloxacin with initial IV dose: Ciprofloxacin Ceftriaxone 24-hour dose gentamicin or tobramycin
Ciprofloxacin	500 mg PO twice daily x 7 days	
	1 g extended-release PO once daily x 7 days	
Levofloxacin	750 mg PO once daily x 5 days	
Trimethoprim-sulfamethoxazole	160/800 mg PO twice daily x 14 days	• Once-daily fluoroquinolone can be used if fluoroquinolone resistance < 10%. If fluoroquinolone resistance > 10%, initial IV dose: Ceftriaxone 24-hour dose gentamicin or tobramycin
Beta-lactams		
Amoxicillin-clavulanate	875/125 mg PO twice daily x 14 days	
Cefpodoxime proxetil	200 mg PO twice daily x 14 days	
Cephalexin	500 mg PO four times daily x 14 days	
Initial IV dose		• If susceptibility to trimethoprim-sulfamethoxazole unknown, or oral beta-lactam is used, an initial IV dose: Ceftriaxone 24-hour dose gentamicin or tobramycin
Ciprofloxacin	400 mg IV	
Ceftriaxone	1 g IV	
Gentamicin	5-7 mg/kg IV	
Tobramycin	5-7 mg/kg IV	
Uncomplicated Pyelonephritis, Inpatient Therapy		
Fluoroquinolones		
Ciprofloxacin	400 mg IV q12 hours	
Levofloxacin	750 mg IVq24 hours	
Beta-lactams		
Ampicillin-sulbactam	3 g IV q6 hours	
Ampicillin + gentamicin	2 g IV q6 hours + 2 mg/kg load then 1.7-2 mg/kg q8 hours	
Ceftriaxone	1 g IV q24 hours	
Cefotaxime	1-2 g IV q8 hours	
Ceftazidime	1-2 g IV q8-12 hours	

Abbreviations: g, gram; IV, intravenous; kg, kilogram; mg, milligram; PO, by mouth; q, every.

Clinical Pathway For Treatment Of Cystitis And Pyelonephritis

- Urinary frequency, urgency, dysuria, suprapubic tenderness
- Indwelling urological device with unexplained fever or altered mental status
- Pyuria (leukocyte esterase, nitrates, white cell casts)

High-risk for treatment failure?
- Male gender
- Structural or functional anatomic abnormalities
- Renal stones
- Indwelling catheters
- Renal transplant
- Neurogenic bladder
- Recent urologic procedure

NO

YES

Complicated UTI

Send urine culture and sensitivity studies

(Level III Evidence)

Empiric Therapy:

Broaden coverage to include gram(+) and gram(-) bacteria, consider *Pseudomonas, Enterococcus*
- Fluoroquinolone (ciprofloxacin, levofloxacin, ofloxacin)
- Trimethoprim-sulfamethoxazole
- Cephalosporins
- Antipseudomonal cephalosporin (ceftazidime, cefepime)
- Ampicillin + gentamicin
- Carbapenems

Signs and symptoms of systemic infection?

Fever, nausea, vomiting, costovertebral angle tenderness?

NO

YES

Cystitis
(Level I Evidence)

- Nitrofurantoin monohydrate/macrocrystals* *(Pregnancy Category B)*
- Trimethoprim-sulfamethoxazole *(Pregnancy Category C)*
- Fosfomycin trometamol* *(Pregnancy Category B)*

*Avoid if early pyelonephritis suspected

Alternative regimens if none of above can be used based on availability, allergies, or tolerance:
- Fluoroquinolones (ciprofloxacin, ofloxacin, levofloxacin) *(Pregnancy Category C)*
- Beta-lactams (amoxicillin-clavulanate, cefdinir, cefaclor, cefpodoxime-proxetil). Cephalexin may also be appropriate **(Level III Evidence)** *(Pregnancy Category B)*

Pyelonephritis

Send urine culture and sensitivity studies

(Level III Evidence)

Inpatient therapy?
- Sepsis
- Pregnancy
- Urinary tract obstruction
- Persistent vomiting
- Poor outpatient follow-up

NO

YES

Outpatient Therapy:
- Ciprofloxacin (if community resistance < 10%) Consider initial dose of IV ciprofloxacin, ceftriaxone **(Level I Evidence)**, or aminoglycoside **(Level III Evidence)** *(Pregnancy Category C)*
- Once-daily oral fluoroquinolone (if community resistance < 10%) **(Level II Evidence)** If resistance > 10%, initial dose of IV ceftriaxone or aminoglycoside **(Level III Evidence)** *(Pregnancy Category C)*
- Trimethoprim-sulfamethoxazole **(Level I Evidence)** If susceptibility is not known, initial dose of IV ceftriaxone or aminoglycoside **(Level III Evidence)** *(Pregnancy Category C)*
- Oral beta-lactam agents Less effective than other agents. **(Level III Evidence)** Initial dose of IV ceftriaxone or aminoglycoside **(Level III Evidence)** *(Pregnancy Category B)*

Inpatient Parenteral Therapy:
(Level III Evidence)

- Fluoroquinolone *(Pregnancy Category C)*
- Aminoglycoside +/- ampicillin or extended-spectrum penicillin *(Pregnancy Categories: Ampicillin-B, Gentamicin-D)*
- Extended-spectrum cephalosporin *(Pregnancy Category B)*
- Carbapenem *(Pregnancy Categories: Imipenem-C Doripenem, Meropenem-B)*

Consider CT or ultrasound to evaluate for obstruction or complicating factors

Abbreviations: CT, computed tomography; IV, intravenous.

For class of evidence definitions, see Table 1, page 3.

transplant, or chronic immunosuppressed states. Patients with catheter-associated UTI (CA-UTI) or spinal cord injury may not present with classic symptoms of dysuria, urinary frequency, or urgency, but they may have new or worsening fever, rigors, or altered mental status. Signs of systemic infection such as fever, nausea or vomiting, and costovertebral angle tenderness should raise suspicion for pyelonephritis and a need to consider inpatient treatment for IV antibiotics and a longer duration of therapy.

Common microbes implicated in uncomplicated cystitis and pyelonephritis mainly consist of *E coli* (75%–95%), with occasional other species of Enterobacteriaceae, such as *Proteus mirabilis* and *Klebsiella pneumoniae*, and *Staphylococcus saprophyticus*. In particular, local antimicrobial susceptibility patterns of *E coli* should be considered in empirical antimicrobial selection for uncomplicated UTI. Since the resistance patterns of *E coli* strains causing uncomplicated UTI vary considerably between regions and countries, a specific treatment recommendation may not be universally suitable for all regions or countries. Other species are rarely isolated in uncomplicated UTI; however, gram-negative and gram-positive species including *Proteus mirabilis, Providencia stuartii, Morganella morganii, Enterococcus,* and *Pseudomonas aeruginosa* can be present in up to 40% of complicated UTIs.[22,25]

Diagnostic Studies For Urinary Tract Infection

A urine pregnancy test should be performed on all women of childbearing age. Urinalysis and urine culture confirm the diagnosis of UTI. The gold standard for the diagnosis of significant bacteriuria consistent with acute uncomplicated cystitis is a urine culture with at least 1000 colony-forming units (CFU)/mm^3, or > 10,000 CFU/mm^3 for the diagnosis of acute uncomplicated pyelonephritis and UTI in men.[26]

In the ED setting, it is not feasible to withhold antibiotics until results of urine cultures, as they may take 24-48 hours. Studies looking at point-of-care testing such as the urine dipstick have found 82% to 98% sensitivity in detecting UTI when compared to urine cultures positive for > 100,000 CFU/mm^3.[27]

Specific imaging such as noncontrast CT scan of the abdomen and pelvis or renal ultrasound may be indicated to evaluate for complicated UTI, but it is not routine.

Table 8. Common Antibiotic Regimens For Complicated Urinary Tract Infection[51,52]

Antibiotic	Adult Dosage	Comments/Caveats
Mildly Ill, Lower Tract Infections Only		
Trimethoprim-sulfamethoxazole	160/800 mg PO twice daily x 7 days	**Complicated UTI** includes patients at high risk for treatment failure:
Fluoroquinolones		• Male gender
Levofloxacin	750 mg PO once daily x 5 days	• Structural or functional anatomic abnormalities
Ciprofloxacin	500 mg PO twice daily x 7 days	• Renal stones
		• Indwelling catheters
		• Renal transplant
		• Neurogenic bladder
		• Recent urologic procedures
Mild to Moderately Ill		
Fluoroquinolones		• Not for patients from long-term care facility, recent fluoroquinolone exposure, or areas with high fluoroquinolone resistance
Levofloxacin	750 mg PO once daily x 5 days	
Ciprofloxacin	500 mg PO twice daily x 10-14 days	
Severely Ill or Not Fluoroquinolone Candidate		
Beta-lactams		
Cefepime	2 g IV q12 hours	
Ceftazidime	2 g IV q8 hours	
Imipenem	500 mg IV q6 hours	
Meropenem	1 g IV q8 hours	
Doripenem	500 mg IV q8 hours	
Piperacillin-tazobactam	3.375 - 4.5 g IV q6 hours	
Ampicillin + gentamicin	2 g IV q6 hours + 3 mg/kg load, then 2 mg/kg IV q8 hours	

Abbreviations: g, gram; IV, intravenous; kg, kilogram; mg, milligram; PO, by mouth; q, every.

Evidence-Based Recommendations: Diagnostic Studies For Urinary Tract Infection

- Pyuria in a urine specimen, in the absence of symptoms, is not an indication for antimicrobial therapy. **(A-II)**
- The diagnosis of symptomatic UTI in patients without indwelling urological devices should be considered only when localizing genitourinary signs or symptoms are present. **(A-III)**
- Patients who fail to respond to therapy or who present with severe manifestations, including sepsis syndrome, should have urgent evaluation with imaging to exclude obstruction, abscess, or other abnormalities requiring immediate intervention. **(A-II)**

Cultures For Urinary Tract Infection

Blood cultures are positive in 20% of patients with pyelonephritis; however, this has not been shown to change antibiotic therapy, and in an otherwise healthy person, it does not indicate a more complicated course.[28,29] Blood cultures should be sent only if there is diagnostic uncertainty, the patient is immunosuppressed, or a hematogenous source is suspected.[30]

Urine cultures are positive in 90% of patients with pyelonephritis and should be obtained before starting antimicrobial therapy. Because CA-UTIs are often polymicrobial and caused by multidrug-resistant pathogens, urine cultures are recommended prior to treatment to confirm appropriate coverage by an empirical regimen and to help tailor antibiotic therapy based on susceptibility data.

Evidence-Based Recommendations: Cultures For Urinary Tract Infection

- In patients suspected of having pyelonephritis, a urine culture and susceptibility test should always be performed, and initial empiric therapy should be tailored appropriately on the basis of the likely infecting uropathogen. **(B-III)**
- A urine specimen should be obtained for culture and susceptibility testing before initial antimicrobial therapy for complicated UTIs. **(A-III)**
- If an indwelling catheter has been in place for more than 2 weeks at the onset of CA-UTI, the catheter should be replaced to hasten resolution of symptoms and reduce risk of subsequent CA-UTI. **(A-I)**
- To help guide treatment, the urine culture should be obtained from a freshly placed catheter prior to the initiation of antimicrobial therapy. **(A-II)**

Site-Of-Care Decisions For Urinary Tract Infections

A 1988 retrospective chart review cost-benefit analysis compared outpatient therapy to inpatient therapy for acute pyelonephritis and found a > 90% success in outpatient treatment despite the presence of diabetes, age > 50, pregnancy, renal calculi, fever > 38.9°C (102.2°F), and leukocytosis > 15,000 mm^3. It was suggested that parenteral therapy and inpatient hospitalization may be beneficial for patients with acute pyelonephritis if they have persistent vomiting, suspected sepsis, diagnostic uncertainty, or urinary tract obstruction. Relative indications for hospitalization include age > 60, anatomic urinary tract abnormality, immunocompromised state (diabetes mellitus, malignancy, sickle cell anemia, organ transplant recipients), inadequate access to outpatient follow-up, frailty, or poor social support.[30]

Pyelonephritis during pregnancy can progress to maternal sepsis, preterm labor, and premature delivery, and early aggressive treatment is important in preventing complications. Hospitalization is often indicated, although it may not always be necessary. Two randomized clinical trials examining outpatient therapy with cephalosporins compared to standard IV therapy found no difference between the 2 groups in success of therapy or birth complications.[31,32] The American College of Obstetricians and Gynecologist (ACOG) recommends parenteral antimicrobial therapy for pregnant patients until the patient is afebrile, followed by oral therapy to complete a 10-day course of therapy.[33]

Evidence-Based Recommendations: Site-Of-Care Decisions For Urinary Tract Infections

- Patients sufficiently ill to require hospitalization (high fever, high white blood cell count, vomiting, dehydration, or evidence of sepsis) or those who fail to improve during an initial outpatient treatment period should be admitted to the hospital and treated with IV antimicrobials. **(A-II)**
- Parenteral therapy is indicated if patients are unable to tolerate oral therapy, have impaired gastrointestinal absorption, have hemodynamic instability, or if the infecting organism is known or suspected to be resistant to oral agents. **(A-I)**

Empiric Antimicrobial Therapy For Urinary Tract Infection

Acute Uncomplicated Cystitis

Evidence-Based Recommendations: Acute Uncomplicated Cystitis

- Nitrofurantoin monohydrate/macrocrystals is an appropriate choice for therapy due to minimal resistance, decreased side effects, and increased efficacy comparable to 3 days of trimethoprim-sulfamethoxazole. **(A-I)**
- Trimethoprim-sulfamethoxazole DS is an appropriate choice for therapy if local resistance rates do not exceed 20% or if the infecting strain is known to be susceptible. **(A-I)**
- Fosfomycin trometamol is an appropriate choice for therapy where it is available due to minimal resistance and limited side effects, but it appears to have inferior efficacy. **(A-I)**
- Fluoroquinolones (ofloxacin, ciprofloxacin, levofloxacin) are highly efficacious regimens **(A-I)** but due to the propensity for adverse side effects and the critical utilization for more serious infections other than cystitis, these agents should be considered as alternative regimens. **(A-III)**
- Beta-lactams are appropriate choices for therapy when other recommended agents cannot be used, but they generally have inferior efficacy and more adverse effects **(B-I).** Cephalexin is less well-studied but may also be appropriate in certain settings. **(B-III)**

Pyelonephritis

Evidence-Based Recommendations: Acute Uncomplicated Pyelonephritis

<u>Outpatient Treatment</u>

- Oral ciprofloxacin with or without initial dose of IV ciprofloxacin if resistance of community uropathogens to fluoroquinolones is < 10%. **(A-I)**
  OR
  Initial dose of ceftriaxone or a consolidated 24-hour dose of an aminoglycoside. **(B-III)**
- A once-daily oral fluoroquinolone if the resistance of community uropathogens to fluoroquinolones is < 10%. **(B-II)**
  If the local fluoroquinolone resistance exceeds 10%, an initial IV dose of 1 g ceftriaxone or a consolidated 24-hour dose of an aminoglycoside is recommended. **(B-III)**
- Oral trimethoprim-sulfamethoxazole if the pathogen is known to be susceptible.
  If the susceptibility is not known, an initial IV dose of 1 g ceftriaxone or a consolidated 24-hour dose of an aminoglycoside is recommended. **(B-III)**
- Oral beta-lactam agents are less effective than other available agents for treatment of pyelonephritis. **(B-III)**
  If an oral beta-lactam agent is used, an initial IV dose of 1 g ceftriaxone or a consolidated 24-hour dose of an aminoglycoside is recommended. **(B-III)**

<u>Inpatient Treatment</u>

- Initial therapy with an IV antimicrobial regimen such as a fluoroquinolone, aminoglycoside with or without ampicillin, extended-spectrum cephalosporin, extended-spectrum penicillin with or without an aminoglycoside, or a carbapenem. Choice should be based on local resistance data and tailored on the basis of susceptibility results. **(B-III)**

Complicated Urinary Tract Infection

Studies generally report equivalent outcomes for treatment of complicated UTI; however, patients with resistant isolates are generally excluded from evaluation, and the relevance of these studies to empiric antibiotic regimens is unclear. The Association of Medical Microbiology and Infectious Disease Canada review of comparative studies of complicated UTI recommends fluoroquinolones with high urinary penetration as the preferred treatment (eg, levofloxacin, ciprofloxacin). Trimethoprim-sulfamethoxazole and cephalosporins were also effective; amoxicillin or ampicillin remained the therapy of choice for susceptible enterococci and group B streptococcal infection. Nitrofurantoin was found to be effective for treatment of lower UTI, but it was not effective for upper tract infection or infection with *Klebsiella pneumoniae, P mirabilis,* or *P aeruginosa,* and it should be avoided in patients with renal failure.

Urinary Tract Infection In Pregnancy

A 2011 Cochrane review examining 10 studies including 1125 pregnant women with UTI found insufficient data to recommend any specific drug regimen and concluded that all of the antibiotics studied were very effective in decreasing birth complications with very rare adverse events.[34] The choice of antibiotics should be guided by local resistance patterns and patient factors.

Table 9. Common Antibiotic Regimens For Inpatient Treatment Of Pyelonephritis During Pregnancy[37]

Antibiotic	Pregnancy Category	Dosage
Cefazolin	B	1-2 g IV q6-8 hours
Cefuroxime	B	1 g IV q8 hours
Ceftriaxone	B	1-2 g IV or IM q24 hours
Ampicillin + gentamicin	Ampicillin: B Gentamicin: D	Ampicillin: 2 g IV q6 hours Gentamicin: 3-5 mg/kg/day IV in 3 divided doses

Note: Conversion to oral agent (such as cephalexin 500 mg, 4 times per day or cefuroxime 250 mg 2 times per day) is indicated upon discharge.

Abbreviations: g, gram; kg, kilogram; IM, intramuscular; IV, intravenous.

Evidence-Based Recommendations: Complicated Urinary Tract Infection

- The duration of therapy should be 7 days for individuals with lower tract symptoms and 10 to 14 days for individuals presenting with upper tract symptoms or sepsis syndrome. **(B-III)**
- Selection of empiric antimicrobial therapy should be individualized, considering patient tolerance, clinical presentation, recent prior antimicrobial exposure, prior urine culture results, and known or suspected institutional susceptibilities. **(A-II)**[22]

Intra-Abdominal Infection

Evidence-based guidelines prepared by the IDSA in conjunction with the Surgical Infection Society were published in 2010 as an update to the original 2002 and 2003 guidelines on diagnosis and management of complicated intra-abdominal infection. **(See Tables 11 and 12 for common antibiotic regimens for intra-abdominal infection.)**

Intra-abdominal infection in the United States has an average incidence of 3.5 million cases per year, and it is the second most common cause of infectious disease mortality in the ICU, with mortality rates as high as 60% among those with well-established infection complicated by multisystem organ failure.[38,39]

Complicated intra-abdominal infections are those that extend beyond the hollow viscus or organ of origin into the peritoneal space and are associated with either abscess formation or peritonitis. Successful treatment of complicated intra-abdominal infections relies on early diagnosis, rapid and appropriate antimicrobials, and timely source control through surgical intervention, when feasible.

Table 10. Common Antibiotic Regimens For Urinary Tract Infection During Pregnancy[27,35,36]

Antibiotic	Pregnancy Category	Dosage	Comment
Nitrofurantoin macrocrystals	B	100 mg PO, twice daily	• Not active against *Proteus* spp; may cause hemolytic anemia in glucose-6-phosphate dehydrogenase deficiency
Cephalexin	B	250 mg PO, 2 to 4 times per day	• Not active against *Enterococcus* spp
Fosfomycin	B	3-g sachet PO, 1-time dose	
Amoxicillin-clavulanic acid	B	250 mg PO, 4 times per day	

Abbreviations: g, gram; mg, milligram; spp, species.

Initial Emergency Department Evaluation And Management Of Intra-Abdominal Infection

Intra-abdominal infections typically present as abdominal pain coupled with symptoms of gastrointestinal dysfunction such as anorexia, nausea, vomiting, bloating, and obstipation. These are often — but not always — accompanied by signs of inflammation such as pain, tenderness, fever, tachycardia, and tachypnea. Emergency department evaluation should focus on these features, in addition to the physical examination, to create a differential diagnosis and assess the severity of the infection.

This assessment should allow for appropriate decision-making regarding the need for and intensity of resuscitation, further diagnostic testing, initiation of proper antimicrobial therapy, and whether emergent surgical intervention is required. Patients at high risk for treatment failure may be identified by APACHE II scores > 15, or other clinical features that may predict failure of source control for intra-abdominal infection:

- Delay in initial intervention (> 24 hours)
- Advanced age
- Comorbidity and degree of organ dysfunction
- Low albumin level
- Poor nutritional status
- Degree of peritoneal involvement or diffuse peritonitis
- Inability to achieve adequate debridement or control of drainage
- Presence of malignancy

Table 11. Common Antibiotic Regimens For Treatment Of Community-Acquired Complicated Intra-Abdominal Infection[51,52]

Antibiotic	Adult Dosage	Comments/Caveats
Mild- to-Moderate Biliary Infection		
Cefazolin	1-2 g IV q8 hours	• Empiric coverage of *Enterococcus* is not necessary
Cefuroxime	750 mg IV q8 hours	
Ceftriaxone	1-2 g IV q24 hours	
Mild-to-Moderate Extra-Biliary Infection		
Single Agent Therapy:		• Empiric coverage of *Enterococcus* is not necessary
Cefoxitin	1-2 g IV q6 hours	
Ertapenem	1 g IV q24 hours	
Moxifloxacin	400 mg IV/PO q24 hours	
Tigecycline	100 mg IV first dose, then 50 mg IV q12 hours	
Ticarcillin-clavulanic acid	3.1 g IV q6 hours	
Combination Therapy:		
Cefazolin	1-2 g IV q8 hours	
Cefuroxime	750 mg IV q8 hours	
Ceftriaxone	2 g IV q24 hours	
Ciprofloxacin	400 mg IV q12 hours	
Levofloxacin	750 mg IV q24 hours	
PLUS		
Metronidazole	500 mg IV q6-8 hours or 1 g IV q12 hours	
Community-Acquired Severe Intra-Abdominal Infection, Biliary, and Extra-Biliary Infections		
Single Agent Therapy:		• Empiric coverage of *Enterococcus* is recommended
Imipenem-cilastatin	250-500 mg IV q6-8 hours	
Meropenem	1 g IV q8 hours	
Doripenem	500 mg IV q8 hours	
Piperacillin-tazobactam	3.375 g IV q6 hours or 4.5 g IV q8 hours	
Combination Therapy:		
Ciprofloxacin	400 mg IV q12 hours	
Levofloxacin	750 mg IV q24 hours	
Cefepime	2 g IV q8 hours	
Ceftazidime	2 g IV q8 hours	
PLUS		
Metronidazole	500 mg IV q6-8 hours or 1 g IV q12 hours	

Abbreviations: g, gram; IV, intravenous; mg, milligram; PO, by mouth; q, every.

Evidence-Based Recommendations: Empiric Antimicrobial Therapy For Intra-Abdominal Infections

Mild-To-Moderate Community-Acquired Infection

- Empiric treatment should be active against enteric gram(-) aerobic and facultative bacilli and enteric gram(+) streptococci. **(A-I)**
- Empiric coverage of *Enterococcus* is not necessary. **(A-I)**
- Ampicillin-sulbactam is not recommended for use because of high resistance among community-acquired *E coli.* **(B-II)**
- Cefotetan and clindamycin are not recommended for use because of increasing resistance among the *Bacteroides fragilis* group. **(B-II)**

Biliary Infection

- Anaerobic therapy is not indicated unless a biliary-enteric anastomosis is present. **(B-II)**
- For community-acquired biliary infection, antimicrobial activity against *Enterococcus* is not required unless the patient is immunosuppressed, particularly those with hepatic transplantation. **(B-III)**

Mild-To-Moderate Severity Infection (Level II Evidence)

- Consider blood cultures for epidemiologic studies or in high-resistance areas
- CT scan or ultrasound as clinically indicated
- Surgical consultation

Empiric Antimicrobial Therapy: Biliary Infection (Level II Evidence)

- Cefazolin, cefuroxime, or ceftriaxone

Extra-Biliary Infection

- Coverage for obligate anaerobic bacilli should be provided for distal small bowel, appendiceal, and colon-derived infection and for more proximal gastrointestinal perforations in the presence of obstruction or paralytic ileus. **(A-I)**

Empiric Antimicrobial Therapy: Extra-Biliary Infection (Level I Evidence)

- **Single Agent:** Cefoxitin, ertapenem, moxifloxacin, tigecycline, or ticarcillin-clavulanic acid
- **Combination:** Cefazolin, cefuroxime, ceftriaxone, cefotaxime, ciprofloxacin, or levofloxacin **PLUS** metronidazole
  Empiric coverage of *Enterococcus* is not necessary **(Level I Evidence)**

Severe/High-Risk Community-Acquired Infection

- Empiric use of antimicrobial regimens with broad-spectrum activity against gram(-) organisms is recommended for patients with high-severity community-acquired intra-abdominal infection, as defined by APACHE II scores > 15 or other high-risk variables predicting failure of source control. **(A-I)**
- Quinolone-resistant *E coli* have become common in some communities, and fluoroquinolones should not be used unless hospital data indicate > 90% susceptibility. **(A-II)**
- Empiric use of agents effective against enterococci is recommended. **(B-II)**
- Antifungal therapy is recommended if *Candida* is grown from intra-abdominal cultures. **(B-II)**

Empiric Antimicrobial Therapy: Biliary And Extra-Biliary Infection (Level I Evidence)

- **Single Agent:** Imipenem-cilastatin, meropenem, doripenem, or piperacillin-tazobactam
- **Combination:** Ciprofloxacin, levofloxacin, or cefepime PLUS metronidazole
  Can also use ceftazidime in extra-biliary infections
  Empiric coverage of *Enterococcus* is recommended. **(Level II Evidence)**

Severe Healthcare-Associated Infection

- Empiric antibiotic therapy should be driven by local microbiologic results. **(A-II)**
- Empiric coverage should include expanded spectra of activity against gram(-) aerobic and facultative bacilli. **(B-III)**
- Antifungal therapy is recommended if *Candida* is grown from intra-abdominal cultures. **(B-II)**
- Empiric use of agents effective against enterococci is recommended. **(B-II)**
- Empiric therapy directed against vancomycin-resistant *Enterococcus faecium* is not recommended unless the patient is at very high risk for an infection caused by this organism (ie, liver transplant recipient with intra-abdominal infection of hepatobiliary origin or a patient known to be colonized). **(B-III)**
- Empiric coverage directed against MRSA should be provided to patients who are known to be colonized or at risk of infection due to prior treatment failure and significant antibiotic exposure. **(B-II)**

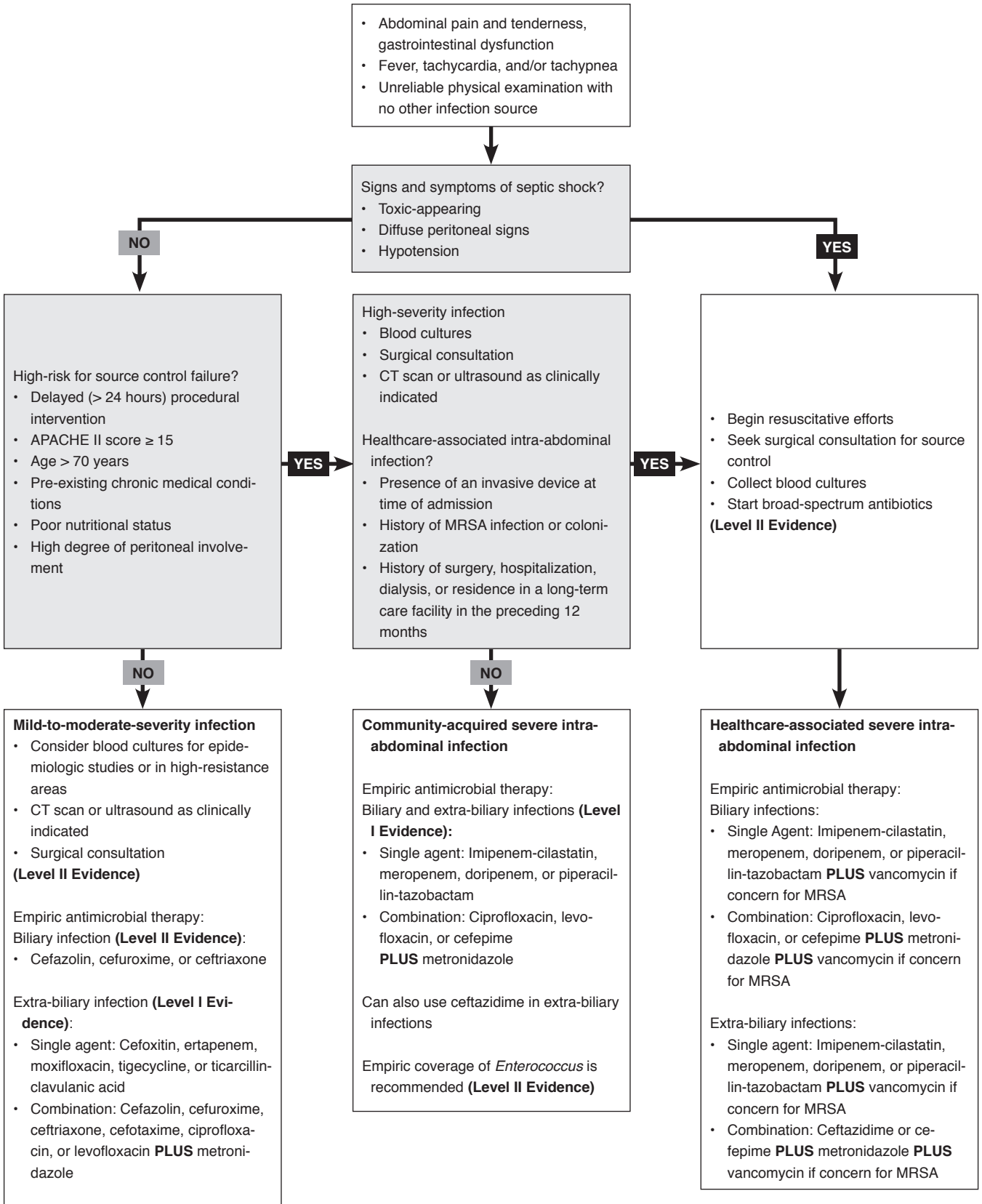
Empiric Antimicrobial Therapy: Biliary Infection

- **Single Agent:** Imipenem-cilastatin, meropenem, doripenem, or piperacillin-tazobactam
- **Combination:** Ciprofloxacin, levofloxacin, or cefepime **PLUS** metronidazole **PLUS** vancomycin if concern for MRSA

Empiric Antimicrobial Therapy: Extra-Biliary Infection

- **Single Agent:** Imipenem-cilastatin, meropenem, doripenem, or piperacillin-tazobactam
- **Combination:** Ceftazidime or cefepime **PLUS** metronidazole **PLUS** vancomycin if concern for MRSA

Clinical Pathway For Treatment Of Complicated Intra-Abdominal Infection



Abbreviations: CT, computed tomography; MRSA, methicillin-resistant *Staphylococcus aureus*.
For class of evidence definitions, see Table 1, page 3.

Clinical features and risk factors for resistant bacteria and healthcare-associated intra-abdominal infection should be elicited from the patient. Healthcare-associated infection includes adult patients who have close association with acute-care hospitals or reside in chronic-care settings,[40] and it can be further described as "community-onset" and "hospital-onset." Community-onset involves patients with at least 1 of the following healthcare risk factors: presence of an invasive device at time of admission, history of MRSA infection or colonization, or history of surgery, hospitalization, dialysis, or residence in a long-term care facility in the 12 months preceding the culture date. Hospital-onset infection includes patients with positive culture results from a normally sterile site obtained > 48 hours after hospital admission, and it may include patients with community-onset risk factors.

Surgical consultation should be sought for appropriate source control procedures to drain infected foci, control ongoing peritoneal contamination, and restore anatomic and physiological function. Acute peritonitis is best treated surgically rather than with percutaneous drainage. Patients with a perforated viscus and diffuse peritonitis cannot be fully resuscitated until ongoing peritoneal soiling has been controlled, and such resuscitation efforts should be continued intra-operatively. It may be appropriate to delay surgical intervention up to 1 day for patients who are hemodynamically stable without peritonitis, and select patients with a well-circumscribed focus of infection may be treated with antimicrobial therapy alone, provided very close clinical follow-up is possible.

Table 12. Common Antibiotic Regimens For Treatment Of Hospital-Acquired Complicated Intra-Abdominal Infection[51,52]

Antibiotic	Adult Dosage	Comments/Caveats
Healthcare-Associated Severe Biliary Infection		
Single-Agent Therapy:		• **Healthcare-associated intra-abdominal infection:** ▪ Presence of an invasive device at time of admission ▪ History of MRSA infection or colonization ▪ History of surgery, hospitalization, dialysis, or residence in a long-term care facility in the preceding 12 months • **Add vancomycin if concern for MRSA:** 15 mg/kg IV q12 hours
Imipenem-cilastatin	500 mg IV q6 hours	
Meropenem	1 g IV q8 hours	
Doripenem	500 mg IV q8 hours	
Piperacillin-tazobactam	3.375 g IV q6 hours or 4.5 g IV q8 hours	
Combination Therapy:		
Ciprofloxacin	400 mg IV q12 hours	
Levofloxacin	750 mg IV q24 hours	
Cefepime	2 g IV q8 hours	
PLUS		
Metronidazole	500 mg IV q6-8 hours or 1 g IV q12 hours	
Healthcare-Associated Severe Extra-Biliary Infection		
Single Agent Therapy:		• **Add vancomycin if concern for MRSA:** 15 mg/kg IV q12 hours
Imipenem-cilastatin	500 mg IV q6 hours	
Meropenem	1 g IV q8 hours	
Doripenem	500 mg IV q8 hours	
Piperacillin-tazobactam	3.375 g IV q6 hours or 4.5 g IV q8 hours	
Combination Therapy:		
Ceftazidime	2 g IV q8 hours	
Cefepime	2 g IV q8 hours	
PLUS		
Metronidazole	500 mg IV q6 hours or 1 g IV q12 hours	

Abbreviations: g, gram; IV, intravenous; kg, kilogram; mg, milligram; MRSA, methicillin-resistant *Staphylococcus aureus*; PO, by mouth; q, every.

Evidence-Based Recommendations: Initial Evaluation For Intra-Abdominal Infection

- Routine history, physical examination, and laboratory studies will identify most patients with suspected intra-abdominal infection for whom further evaluation and management is warranted. **(A-II)**
- For selected patients with unreliable physical examination findings, such as those with an obtunded mental status, spinal cord injury, or those immunosuppressed by disease or therapy, intra-abdominal infection should be considered if the patient presents with evidence of infection from an undetermined source. **(B-III)**
- Patients should undergo rapid restoration of intravascular volume and additional measures as needed to promote physiologic stability. **(A-II)**
- An appropriate source control procedure to drain infected foci, control ongoing peritoneal contamination, and restore anatomic and physiologic function is recommended for nearly all patients. **(B-II)**
- Patients with diffuse peritonitis should undergo an emergency surgical procedure as soon as possible, even if ongoing resuscitative efforts need to be continued during the procedure. **(B-II)**

Diagnostic Studies For Intra-Abdominal Infection

In general, helical CT scanning is the preferred imaging modality. The only studies looking at sensitivity and specificity of CT scanning for intra-abdominal infection is for appendicitis, in which pooled data showed a sensitivity and specificity of 94% and 94%, respectively, for CT studies, and 83% and 94%, respectively, for ultrasound studies.[41]

Ultrasonography detects cholelithiasis in approximately 98% of patients who have stones, with cholecystitis diagnosed by the concomitant presence of gallbladder wall thickening, pericholecystic fluid, or ultrasonographic Murphy sign. Hepatobiliary scintigraphy is also an acceptable method for diagnosing acute cholecystitis.

Evidence-Based Recommendations: Diagnostic Studies For Intra-Abdominal Infection

- Further diagnostic testing is unnecessary in patients with obvious signs of diffuse peritonitis and in whom immediate surgical intervention is to be performed. **(B-III)**
- In adult patients not undergoing immediate laparotomy, CT scan is the imaging modality of choice to determine the presence of an intra-abdominal infection and its source. **(A-II)**
- Ultrasonography is the first imaging technique used for suspected acute cholecystitis or cholangitis. **(A-I)**

Cultures For Intra-Abdominal Infection

Routine blood cultures are seldom useful for diagnosing community-acquired intra-abdominal infection, and they rarely provide information that alters outcome or antibiotic choice. Cultures do add to epidemiologic data on pathogen and resistance patterns. Though they may not necessarily benefit the individual, they can help identify local areas with significant antimicrobial resistance to specific antibiotics and change local treatment guidelines.

Patients with severe community-acquired or healthcare-acquired intra-abdominal infections may benefit from Gram stains to identify gram-positive cocci or yeast that would lead to additional empiric antimicrobial therapy before definitive culture results are available.

Evidence-Based Recommendations: Cultures For Intra-Abdominal Infection

- Blood cultures do not provide additional clinically relevant information for patients with community-acquired intra-abdominal infection and are therefore not routinely recommended for such patients. **(B-III)**
- If a patient appears clinically toxic or is immunocompromised, knowledge of bacteremia may be helpful in determining duration of antimicrobial therapy. **(B-III)**
- Routine aerobic and anaerobic cultures from lower-risk patients with community-acquired infection are considered optional in the individual patient but may be of value in detecting epidemiologic changes in the resistance patterns of pathogens and in guiding follow-up oral therapy. **(B-II)**
- If there is a significant resistance (ie, in 1%-20% of isolates) of a common community isolate to an antimicrobial regimen, routine culture and susceptibility studies should be obtained for community-acquired intra-abdominal infections. **(B-III)**
- Healthcare-associated intra-abdominal infections are commonly caused by more-resistant microbes. Use of culture and susceptibility results to determine antimicrobial therapy in high-severity community-acquired or healthcare-associated infection should be based on pathogenic potential and density of identified organisms. **(B-III)**

Skin And Soft-Tissue Infection

Between 1997 and 2005, the overall rate of patient visits for skin and soft-tissue infections to primary care offices and EDs increased from 32.1 to 48.1 visits per 1000 population and reached 14.2 million visits by 2005, representing 3% of all ED visits.[42] During this same time frame, the use of antibiotics to treat CA-MRSA increased to over 38% of all prescriptions for SSTI.[43] CA-MRSA is the most common pathogen isolated from purulent infections.[44,45]

In 2005, the IDSA published "Practice Guidelines for the Diagnosis and Management of Skin and Soft-Tissue Infections" to create specific recommendations for therapy, given the wide array of microbes and clinical presentations that may cause soft-tissue infections. The guideline includes empiric antibiotic therapy for impetigo, erysipelas, and cellulitis; necrotizing infections; infections following human or animal bites; surgical site infections; and infections in the immunocompromised hosts. The October 2010 issue of *Emergency Medicine Practice* provides further detail about skin and soft-tissue infections in the era of CA-MRSA.[46] In 2011, IDSA published the guideline "Management of Patients with Infections Caused by Methicillin-Resistant *Staphylococcus aureus.*" **(See Tables 13-15 for common antibiotic regimens for SSTI.)**

Emergency Department Evaluation For Skin And Soft-Tissue Infection

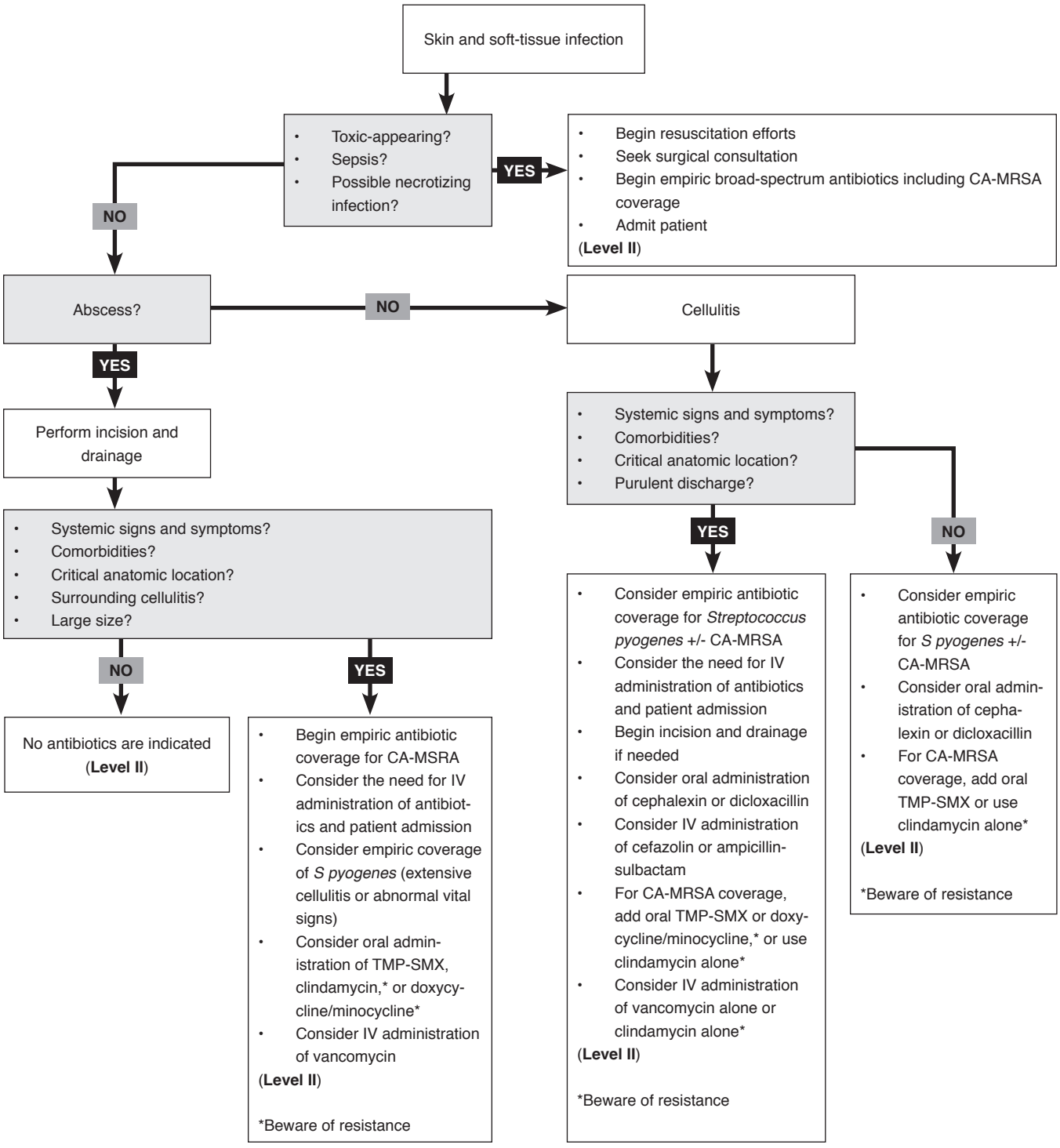
Evaluation begins with a targeted history and physical examination to elicit the onset of infection, inciting injury, and suggestions of systemic illness. Modification of antimicrobial therapy will differ depending on comorbidities, which may include immunodeficiency such as diabetes or HIV, recent

Table 13. Common Antibiotic Regimens for Outpatient Treatment Of Skin And Soft-Tissue Infections[51,52]

Antibiotic	Adult Dosage	Comments/Caveats
Cellulitis, Oral Therapy		
Beta-hemolytic *Streptococcus* coverage:		• Empiric therapy for *Streptococcus pyogenes* (beta-hemolytic streptococcus) is recommended • Azithromycin or clindamycin for severe penicillin allergy
Cephalexin	500 mg PO 4 times daily x 7-10 days	
Dicloxacillin	500 mg PO 4 times daily x 7-10 days	
Azithromycin	500 mg PO x 1 dose than 250 mg PO daily x 4 days	
Clindamycin	300 mg PO 3 times daily x 7-10 days	
CA-MRSA coverage:		• If comorbidities, purulent drainage, or in critical anatomic location, add empiric coverage for CA-MRSA • Clindamycin is bacteriostatic, potential for cross-resistance and emergence of resistance in erythromycin-resistant strains; inducible resistance in MRSA
Doxycycline or minocycline	100 mg PO twice daily x 7-10 days	
Trimethoprim-sulfamethoxazole	160/800 mg PO 1-2 tabs twice daily x 7-10 days	
Clindamycin	300 mg PO 3 times daily x 7-10 days	

Abbreviations: g, gram; IV, intravenous; kg, kilogram; mg, milligram; MRSA, methicillin-resistant *Staphylococcus aureus*; PO, by mouth; q, every.

Clinical Pathway For Treatment Of Skin And Soft-Tissue Infections



Abbreviations: CA-MRSA, community-acquired methicillin-resistant *Staphylococcus aureus;* IV, intravenous; TMP-SMX, trimethoprim-sulfamethoxazole.

For class of evidence definitions, see Table 1, page 3.

antibiotics, or recent hospitalization.

Recognition of signs and symptoms of systemic toxicity such as fever or hypothermia, tachycardia, hypotension, delirium, or lethargy are crucial in assessing the need for resuscitation and the seriousness of an infection. Presence of purulence may increase suspicion for infection with CA-MRSA. CA-MRSA is the most frequent isolate from purulent infections in ED patients.[43] Severe, deep soft-tissue and necrotizing infections must be considered, including recognition of the following:

- Pain disproportionate to physical findings
- Violaceous bullae
- Cutaneous hemorrhage
- Skin sloughing
- Skin anesthesia
- Rapid progression
- Gas in the soft tissues

Diagnostic Studies For Skin And Soft-Tissue Infection

Ultrasonography can be a useful adjunct to help identify deep abscesses, differentiate cellulitis from an abscess, and guide drainage.

Patients with systemic signs of toxicity may warrant the following diagnostic tests: blood culture and susceptibility, complete blood cell count with differential, electrolytes and creatinine, bicarbonate, creatinine phosphokinase, and C-reactive protein levels. In patients with hypotension and/or one of the following abnormalities, consider hospitalization and definitive etiologic diagnosis via Gram stain, culture of needle aspiration or punch biopsy, and surgical consultation for inspection, exploration, and/or drainage:

- Elevated creatinine level
- Low serum bicarbonate level
- Elevated creatinine phosphokinase level (2-3 times the upper limit of normal)
- Marked left shift
- C-reactive protein level > 13 mg/L

The above laboratory results can also be used to calculate the Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score.[47] Different laboratory values are assigned points, and a total score is obtained, with a maximum score of 13. A score of greater than 6 has a positive predictive value of 92% (95% CI, 84.3%-96.0%) and a negative predictive value of 96% (95% CI, 92.6%-97.9%) for necrotizing fasciitis. The LRINEC score has not been prospectively validated, and the ability to identify necrotizing fasciitis early in its clinical course when it is not already apparent on history and physical examination is unproven.[48,49]

In patients with concern for necrotizing infections, early surgical consultation is crucial for diagnosis and debridement. Diagnosis may be made via CT scan or magnetic resonance imaging (MRI). These studies may show edema extending along the fascial plane in necrotizing fasciitis or gas in the tissues with clostridial myonecrosis, but requesting such studies may delay definitive diagnosis and treatment.

Cultures For Skin And Soft-Tissue Infection

Prior to the emergence of CA-MRSA, routine wound cultures of abscesses were not necessary; however, some experts are recommending cultures of complicated abscesses for patients requiring admission and for immunocompromised hosts.[50]

Evidence-Based Recommendations: Skin and Soft-Tissue Infections

- Penicillin, either orally or parenterally, is the treatment of choice for erysipelas. **(A-I)**
- For cellulitis, a penicillinase-resistant semisynthetic penicillin or a first-generation cephalosporin should be selected unless streptococci or staphylococci resistance is common in the community. **(A-I)**
- Effective treatment of abscesses entails incision, thorough evacuation of the pus, and probing the cavity to break up loculations **(A-I)**. Gram stain, culture, and systemic antibiotics are rarely indicated unless there is extensive surrounding cellulitis, fever, multiple lesions, severely impaired host defenses, or cutaneous gangrene. **(E-III)**
- Linezolid, daptomycin, and vancomycin have excellent efficacy in skin and soft-tissue infections against MRSA, but they should be reserved for patients who require hospitalization or have not responded to prior therapy **(A-I)**. Clindamycin has excellent antistaphylococcal activity, including MRSA, but there is the potential for inducible resistance to MRSA, as well as emergence of resistance in strains already resistant to erythromycin. Trimethoprim-sulfamethoxazole has also been used to treat MRSA infections.
- Surgical intervention is the major therapeutic modality in cases of necrotizing fasciitis. **(A-III)**
- The best choice for antibiotics for community-acquired mixed, necrotizing infections is a combination of ampicillin-sulbactam plus clindamycin plus ciprofloxacin. **(A-III)**
- Necrotizing fasciitis and/or streptococcal toxic shock syndrome caused by group A streptococci should be treated with clindamycin and penicillin. **(A-II)**

Table 14. Common Antibiotic Regimens For Inpatient Treatment Of Skin And Soft-Tissue Infections[51,52]

Antibiotic	Adult Dosage	Comments/Caveats
Complicated Cellulitis and Abscess, Parenteral Therapy		
Beta-hemolytic *Streptococcus* and MSSA Coverage		• Empiric therapy for *Streptococcus pyogenes* **and** CA-MRSA is recommended
Nafcillin	2 g IV q4 hours	
Oxacillin	2 g IV q4 hours	• Clindamycin is bacteriostatic, potential for cross-resistance and emergence of resistance in erythromycin-resistant strains; inducible resistance in MRSA
Cefazolin	1 g IV q8 hours	
Ceftriaxone	1-2 g IV q24 hours	
Cefotaxime	1-2 g IV q8 hours	
Clindamycin	600 mg IV q8 hours	
CA-MRSA Coverage		
Clindamycin	600 mg IV q8 hours	
Linezolid	600 mg IV q12 hours	
Vancomycin	15 mg/kg IV q12 hours	

Abbreviations: CA-MRSA, community-acquired MRSA; g, gram; IV, intravenous; kg, kilogram; mg, milligram; MRSA, methicillin-resistant *Staphylococcus aureus;* MSSA, methicillin-sensitive *Staphylococcus aureus;* PO, by mouth; q, every.

Table 15. Common Antibiotic Regimens For Treatment Of Necrotizing Skin And Soft-Tissue Infections[51,52]

Antibiotic	Adult Dosage	Comments/Caveats
Mixed Infection		
Ampicillin-sulbactam **OR** Piperacillin-tazobactam **PLUS** Clindamycin **PLUS** Ciprofloxacin	1.5-3 g IV q6-8 hours 3.375 g IV q6-8 hours 600 mg IV q8 hours 400 mg IV q12 hours	• For penicillin allergy: Clindamycin or metronidazole with an aminoglycoside or fluoroquinolone • Consider addition of clindamycin to regimen; added benefit of toxin suppression and cytokine production modulation in group A streptococcal infection
Imipenem-cilastatin	1 g IV q6-8 hours	
Meropenem	1 g IV q8 hours	• **Add MRSA coverage to all regimens**
Ertapenem	1 g IV q24 hours	
Cefotaxime **PLUS** Metronidazole **OR** Clindamycin	2 g IV q6 hours 500 mg IV q6 hours 600 mg IV q8 hours	
MRSA Coverage		
Vancomycin Clindamycin* Linezolid	15 mg/kg IV q12 hours 600 mg IV q8 hours 600 mg IV q12 hours	* Clindamycin is bacteriostatic, potential for cross-resistance and emergence of resistance in erythromycin-resistant strains; inducible resistance in MRSA

Abbreviations: g, gram; IV, intravenous; kg, kilogram; mg, milligram; MRSA, methicillin-resistant *Staphylococcus aureus*; PO, by mouth; q, every.

Summary

Emergency clinicians must be knowledgeable and remain current regarding guidelines and recommended empiric antimicrobial regimens for ED infections. It is important to risk stratify patients with infections, taking into consideration comorbidities and factors that increase the likelihood of multidrug-resistant organisms, and as well as awareness of local antimicrobial resistance patterns. Timely diagnosis and initiation of empiric antibiotic therapy is important in improving outcome in ED infections.

Case Conclusions

The 35-year-old female was young and healthy, and therefore a decision was made for outpatient management that included coverage for atypical organisms. In the ED, 500 mg of azithromycin was administered and a prescription for 4 additional days at 250-mg-per-day dosing was provided. She was given strict instructions to return if she felt more shortness of breath or worse in any way. You found out that she followed up with her primary care doctor in 3 days, feeling much better.

The 70-year old female was presumed to have a mild delirium induced by her UTI. She was given IV ciprofloxacin, and her mental status returned to normal on hospital day 2. Her urine culture grew E coli sensitive to fluoroquinolones, and she was discharged on oral ciprofloxacin on hospital day 4.

The 23-year-old with the infected forearm had the abscess incised and drained in the ED. Because there was also a surrounding cellulitis, he was given oral trimethoprim-sulfamethoxazole and instructed to return for a wound check. His arm was markedly improved by a day 3 wound check, and his wound culture was positive for CA-MRSA.

Risk Management Pitfalls For Antibiotics In The Emergency Department

1. **"I treated the UTI with nitrofurantoin. I didn't know it wouldn't work."**
   Males and patients with pyelonephritis should not be treated with nitrofurantoin. Due to tissue penetration issues, it should be used only for women with uncomplicated cystitis.

2. **"I treated the patient from the nursing home with urosepsis with cefazolin - that should have been adequate, since most UTIs are caused by** *E coli.***"**
   Remember that nursing home patients and those recently hospitalized may have more resistant bacteria and need antimicrobials with broader coverage.

3. **"He had a hazy, ill-defined possible infiltrate and was otherwise healthy, so I discharged him on amoxicillin-clavulanate."**
   This is incomplete coverage for pneumonia. Remember to cover for atypical pathogens with azithromycin, doxycycline, or a respiratory fluoroquinolone.

4. **"She had a small area of localized infection on her abdominal wall, so I treated her by prescribing coverage for CA-MRSA with trimethoprim-sulfamethoxazole. I can't believe how bad it looked when she came back 3 days later."**
   Incision and drainage is the mainstay of treatment for abscesses.

5. **"Do you remember the diabetic patient with the inner-thigh infection you treated yesterday? He came back today in septic shock."**
   Don't forget to consider necrotizing infections when treating skin and soft-tissue infections. Early on, these may not show classic signs and symptoms. Early recognition requires a high degree of clinical suspicion. When in doubt, obtain specialty consultation.

6. **"The patient had a fever and left-lower-quadrant tenderness, so I recommended antibiotics for diverticulitis. How should I have known he would come back with an acute abdomen?"**
   Patients with possible diverticulitis may develop serious complications, such as abscess formation. They should undergo diagnostic imaging.

7. **"I gave antibiotics in the ED right after I evaluated the patient. It wasn't my fault the CT didn't get done for 12 hours and the appendix perfed."**
   A patient with an acute abdomen should have timely surgical consultation, not just antibiotic treatment.

8. **"She was sent from the nursing home with a fever, and her x-ray had an infiltrate, so I treated with azithromycin and admitted her. I can't believe she was intubated the next day."**
   Remember that nursing home patients have healthcare-associated pneumonia and need more broad-spectrum coverage.

The 85-year-old from the nursing home had a CT of the abdomen and pelvis that revealed diverticulitis with no evidence of abscess or perforation. Treatment with cefepime and metronidazole was initiated, and he was admitted. The hospital discharge summary indicated that he defervesced after 4 days and was sent back to the nursing home on day 8.

References

Evidence-based medicine requires a critical appraisal of the literature based upon study methodology and number of subjects. Not all references are equally robust. The findings of a large, prospective, randomized, and blinded trial should carry more weight than a case report.

To help the reader judge the strength of each reference, pertinent information about the study, such as the type of study and the number of patients in the study, will be included in bold type following the reference, where available.

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CME Questions

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1. Which of the following antibiotics is not recommended as monotherapy for CAP?
a. Doxycycline
b. Trimethoprim-sulfamethoxazole
c. Azithromycin
d. Levofloxacin

2. Which is the best antibiotic regimen for a 65-year-old male with diabetes, hypertension, and cirrhosis, presenting with 3 days of a productive cough and a chest x-ray with a left-lower-lobe infiltrate?
a. Azithromycin 500 mg on day 1, then 250 mg for 4 days
b. Nitrofurantoin 100 mg bid for 7 days
c. Ceftriaxone 1-2 g IV daily and azithromycin 500 mg PO/IV daily
d. Cefepime 1 g IV daily and vancomycin 1 g IV every 12 hours

3. Which of the following is the most likely pathogen in a previously healthy 25-year-old female presenting with acute pyelonephritis?
a. *Enterococcus*
b. *Pseudomonas aeruginosa*
c. *Escherichia coli*
d. *Staphylococcus aureus*
e. *Bacteroides fragilis*

4. **A 60-year-old male with longstanding constipation but otherwise healthy presents with nausea with abdominal pain for 4 days. He is febrile 38.3°C (101°F) with left-lower-quadrant tenderness, and a WBC count of 18,000, with a left shift. A CT scan of the abdomen and pelvis is pending. Which of the following is the best antibiotic regimen for this patient?**
   a. Imipenem-cilastatin
   b. Cefazolin
   c. Clindamycin
   d. Ciprofloxacin and metronidazole
   e. Hold antibiotics until a definitive diagnosis can be made

5. **Which of the following is the most common cause of purulent SSTIs?**
   a. *Streptococcus pyogenes*
   b. MSSA
   c. CA-MRSA
   d. *Staphylococcus epidermidis*
   e. *Haemophilus influenzae*

6. **In a previously healthy patient with a purulent drainage lesion with an extensive area of surrounding cellulitis, which of the following antibiotics is the best choice?**
   a. Cephalexin
   b. Amoxicillin-clavulanate
   c. Rifampin
   d. Clindamycin

7. **Which of the following does not increase the suspicion for a necrotizing soft-tissue infection?**
   a. Well-demarcated margins
   b. Rapid progression
   c. Violaceous bullae
   d. Gas in the tissue

In This Month's *Pediatric Emergency Medicine Practice*

The Young Child With Lower Gastrointestinal Bleeding Or Intussusception

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Lower gastrointestinal (LGI) bleeding in the pediatric patient 5 years of age or younger is an uncommon ED presentation that causes anxiety and concern both in the child's family and in the clinician. A report from Boston Children's Hospital in the early 1990s showed that rectal bleeding was a presenting complaint in 0.3% of pediatric patients who visited the emergency department (ED) within a 1-year period. The emergency clinician may find this presentation daunting, since the differential diagnosis of LGI bleeding includes numerous age-specific disorders not found in the adult population, ranging from self-limited anal fissures to surgical emergencies. The time to diagnosis and reduction will influence morbidity and mortality in these patients; hence, the emergency clinician should have a high index of suspicion as well as knowledge of current evidence for diagnosis and treatment. This issue of *Pediatric Emergency Medicine Practice* reviews the common differential diagnoses of LGI bleeding in children younger than 5 years of age, relying on the best available evidence from the literature. Readers will be able to apply clinically appropriate guidelines regarding diagnosis and treatment in an effective and patient-specific manner. In particular, this article focuses on the challenge of evaluating and managing the pediatric patient with intussusception.

***Pediatric Emergency Medicine Practice* subscribers:** Access this article at no charge at www.ebmedicine.net/PEMP.

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Coming Soon In *EM Critical Care*

Emergency Ultrasound In Patients With Respiratory Distress

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Emergency ultrasound is a highly valuable and readily learned tool for practicing emergency clinicians that has expanded rapidly since its introduction to emergency medicine more than 20 years ago. In the past decade, emergency ultrasound has progressed from 6 to 11 primary indications and has become a mandated competency for emergency medicine residents graduating from an ACGME-accredited training program. Patients who are critically ill can have multiple focused ultrasound examinations that, when considered together, provide crucial, time-dependent information at the bedside, which will improve diagnostic certainty and guide management.

This issue of ***EMCC*** will provide an evidence-based approach to the use of ultrasound in the evaluation of the critically ill patient with respiratory distress and hypotension. Two clinical scenarios will be presented: the progressively dyspneic patient with a history of COPD and decompensated heart failure and the acutely dyspneic patient with hypotension. These scenarios were chosen because they are commonly encountered in clinical practice and require rapid, complex decision making that is augmented with the use of emergency ultrasound. The evidence supporting emergency ultrasound for diagnosis of pulmonary edema, pneumothorax, left ventricular dysfunction, and right ventricular dysfunction will be presented, and the technique for image acquisition will be discussed.

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Emergency Medicine Practice has been accepted for indexing on PubMed

We at EB Medicine are proud to announce that our inaugural publication, *Emergency Medicine Practice,* has been accepted by the National Library of Medicine for MEDLINE® indexing. This means that all 2011 and future issues of *Emergency Medicine Practice* will be indexed on PubMed. This is an important breakthrough for our publication, and we are extremely pleased to have received this recognition.

To read a letter from Dr. Andy Jagoda, Editor-in-Chief, about this exciting achievement, please visit www.ebmedicine.net/MEDLINEletter.

All of our readers have played an instrumental role in ensuring the publication's high quality, and we greatly appreciate your support.

—THE EB MEDICINE TEAM

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Needs Assessment: The need for this educational activity was determined by a survey of medical staff, including the editorial board of this publication; review of morbidity and mortality data from the CDC, AHA, NCHS, and ACEP; and evaluation of prior activities for emergency physicians.

Target Audience: This enduring material is designed for emergency medicine physicians, physician assistants, nurse practitioners, and residents.

Goals: Upon completion of this article, you should be able to: (1) demonstrate medical decision-making based on the strongest clinical evidence; (2) cost-effectively diagnose and treat the most critical ED presentations; and (3) describe the most common medicolegal pitfalls for each topic covered.

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