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antibiotic guidelines

Treatment Recommendations for Adult Inpatients

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Introduction

Antibiotic resistance is now a major issue confronting healthcare providers and their patients. Changing antibiotic resistance patterns, rising antibiotic costs and the introduction of new antibiotics have made selecting optimal antibiotic regimens more difficult now than ever before. Furthermore, history has taught us that if we do not use antibiotics carefully, they will lose their efficacy. As a response to these challenges, the Johns Hopkins Antibiotic Management Program was created in July 2001. Headed by an Infectious Disease physician (Sara Cosgrove, M.D., M.S.) and an Infectious Disease pharmacist (Edina Avdic, Pharm.D., M.B.A), the mission of the program is to ensure that every patient at Hopkins on antibiotics gets optimal therapy. These guidelines are a step in that direction. The guidelines were initially developed by Arjun Srinivasan, M.D., and Alpa Patel, Pharm.D., in 2002 and have been revised and expanded annually.

These guidelines are based on current literature reviews, including national guidelines and consensus statements, current microbiologic data from the Hopkins lab, and Hopkins’ faculty expert opinion. Faculty from various departments have reviewed and approved these guidelines. As you will see, in addition to antibiotic recommendations, the guidelines also contain information about diagnosis and other useful management tips.

As the name implies, these are only **guidelines**, and we anticipate that occasionally, departures from them will be necessary. When these cases arise, we will be interested in knowing why the departure is necessary. We want to learn about new approaches and new data as they become available so that we may update the guidelines as needed. You should also document the reasons for the departure in the patient’s chart.

Finally, please let us know if there are sections that you think could be improved, and also let us know if there is more information you would like to see included. Our goal is for the Antibiotic Management Program to be a useful service in optimizing antibiotic use at Hopkins. We welcome your thoughts and comments to 443-287-4570 (7-4570) or to: abxmgmt@jhmi.edu.

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How to use this guide
- Each section begins by giving recommendations for the choice and dose of antibiotics for the particular infection.
- **ALL DOSES IN THE TEXT ARE FOR ADULTS WITH NORMAL RENAL AND HEPATIC FUNCTION.**
  - If your patient does NOT have normal renal or hepatic function, please refer to the sections on antibiotic dosing to determine the correct dose.
- Following the antibiotic recommendations, we have tried to include some important treatment notes that explain a bit about WHY the particular antibiotics were chosen and that provide some important tips on diagnosis and management. PLEASE glance at these notes when you are treating infections, as we think the information will prove helpful. All references are on file in the office of the Antibiotic Management Program (7-4570).

Important phone numbers
- Antibiotic approval: 3-9ABX (3-9229)
  - Please note that text pages alone are NOT sufficient and MUST include a call-back phone and pager number.
  - ALL orders for restricted antibiotics MUST be approved unless they are part of a pre-printed order sheet.
  - Please see page 7 for more information about obtaining approval.
- Antibiotic Management Program: 7-4570
- Infectious Diseases Consults: 3-8026
- Osler 2 pharmacy: 5-6150
- Carnegie 6 pharmacy: 5-6505
- Weinberg pharmacy: 5-8998
- Microbiology lab: 5-6510

A word from our lawyers
The recommendations given in this guide are meant to serve as treatment guidelines. They should NOT supplant clinical judgment or Infectious Diseases consultation when indicated. The recommendations were developed for use at The Johns Hopkins Hospital and thus may not be appropriate for other settings. We have attempted to verify that all information is correct but because of ongoing research, things may change. If there is any doubt, please verify the information in the guide by calling the antibiotics pager (3-9ABX) or Infectious Diseases (3-8026). **Also, please note that these guidelines contain cost information that is confidential. Copies of the book <u>should not</u> be distributed outside of the institution without permission.**

Adult Inpatient Antibiotic Approval Form

Abdominal Infections

☐ 1a Biliary tract infection – community-acquired, mild/mod. ill
☐ 1b Biliary tract infection – severely ill and/or nosocomial
☐ 2a Diverticulitis – community-acquired, mild/mod. ill
☐ 2b Diverticulitis – severely ill and/or nosocomial
☐ 3a Peritonitis – community-acquired, mild/mod. ill
☐ 3b Peritonitis – severely ill and/or nosocomial
☐ 4 Crohn's disease – stable patient admitted on daily oral ciprofloxacin
☐ 5a Spontaneous Bacterial Peritonitis (SBP), treatment

Central Nervous System Infections

☐ 7a Meningitis – community-acquired
☐ 7b Meningitis – hospital-acquired/post-operative

Skin And Soft Tissue Infections

☐ 9 Cellulitis
☐ 10 Diabetic foot infection – mild
☐ 10a Diabetic foot infection – moderate
☐ 10b Diabetic foot infection – severe
☐ 11a Surgical site infection – following clean procedure
☐ 11b Surgical site infection – following contaminated procedure

Pneumonias

☐ 13 Community-acquired pneumonia – infiltrate required
☐ 13b Hospital-acquired pneumonia – infiltrate required
☐ 14 Ventilator associated pneumonia – infiltrate required

Urinary Tract Infections- note criteria in guidelines

☐ 15 Cystitis – bacterial – symptomatic; Bactrim preferred
☐ 16 Pyelonephritis
☐ 17 Cystitis – fungal

Fluconazole

☐ 18_a HIV positive, esophageal candidiasis
☐ 18_b Medical oncology patient, esophageal candidiasis
☐ 19 HIV positive, admitted on daily fluconazole
☐ 20 Liver/pancreas transplant, admitted on daily fluconazole

Vancomycin

☐ 21 ≥ 2 sets of blood cultures with Gram (+) cocci in clusters
☐ 22 Severe PCN allergy & infection with MSSA or Enterococcus – culture from a sterile site or abscess within prior 72 h. required
☐ 23a Proven infection with MRSA – culture from a sterile site or abscess within prior 72 h. required
☐ 23b Proven infection with Ampicillin-resistant Enterococcus – culture from a sterile site or abscess within prior 72 h. required
☐ 24 PCN allergy in patient needing prophylaxis for cardiac, vascular, or orthopedic (joint replacement, spinal fusion, ORIF only) surgery (NO more than one pre-op and one post-op dose)

Obtaining ID approval

The use of restricted and non-formulary antimicrobials requires pre-approval from Infectious Diseases. This approval can be obtained by any of the following methods.

Approval method	Notes
Adult Inpatient Antibiotic Approval Form	This form allows the use of specific agents for specific indications. For therapies not recommended on the reverse side of the form, approval should be obtained via the pager. **Please note that it is NOT an order form and MUST be accompanied by an order.**
3-9ABX (3-9229)	The pager is answered between 8 a.m. and 10 p.m. Call the ID consult pager (3-8026) if you fail to get a response from the ID approval pager within 10 minutes.

Overnight Approval	Restricted antibiotics ordered between 10 p.m. and 8 a.m. must be approved by noon the following morning.
	• Doses will be dispensed to last until noon
	• Methods to obtain approval
	  • Antibiotic Approval Form (see above)
	  • Page ID approval (3-9229) after 8 a.m.
	• Please remember to sign out the need for approval if you go off shift before 8 a.m.

Liposomal Amphotericin B Approval Form	This form should be completed for all patients meeting criteria for AmBisome®. For circumstances not delineated on the form, approval for AmBisome® can be obtained via the pager, or after consultation with ID.
Ordersets (e.g. neutropenic fever, etc.)	These forms are P&T-approved for specific agents and specific indications.

2.1 Obtaining ID approval

Selected formulary antimicrobials and restriction status

The following list applies to ALL adult floors and includes the status of both oral and injectable dosage forms, unless otherwise noted.

Unrestricted		Restricted (requires ID approval)
Amoxicillin	Minocycline	Amikacin
Amoxicillin/ clavulanate	Nitrofurantoin	Ampicillin/sulbactam (Unasyn®)
Ampicillin IV	Norfloxacin	Azithromycin IV[1]
Azithromycin PO	Oxacillin	Aztreonam
Cefazolin	Penicillin V/G	Cefepime
Cefotetan	Piperacillin	Ceftazidime
Cefoxitin	Rifampin	Chloramphenicol
Cefpodoxime	Streptomycin	Ciprofloxacin
Ceftriaxone	Tobramycin	Colistin IV
Cefuroxime IV	Trimethoprim/ sulfamethoxazole	Daptomycin*
Cephalexin		Fosfomycin
Clarithromycin		Linezolid
Clindamycin (IV dose: 600 mg every 8H)		Meropenem
Dicloxacillin		Moxifloxacin
Doxycycline		Nitazoxanide‡
Ertapenem		Piperacillin/tazobactam (Zosyn®)
Erythromycin		Quinupristin/ dalfopristin (Synercid®)
Gentamicin		Tigecycline
Metronidazole		Vancomycin
Amphotericin B deoxycholate (Fungizone®)		Liposomal amphotericin B (AmBisome®)[2]
Flucytosine		Micafungin
Itraconazole oral solution		Fluconazole[3]
		Posaconazole†
		Voriconazole

*Approval should be obtained from Antibiotic Management Program
†Approval should be obtained from Antibiotic Management Program, Polk Service Fellow/Attending, or ID consult service after full consultation
‡Approval should be obtained from Polk Service or ID Consult

Exceptions – the following drugs DO NOT require ID approval under specific conditions:

1. Azithromycin IV, when used as a single dose for chlamydial infection, when used weekly for MAI prophylaxis, or when ordered Monday, Wednesday, and Friday as a continuation of outpatient therapy in lung transplant or cystic fibrosis patients.
2. Liposomal amphotericin B (AmBisome®), if criteria on the AmBisome® Form are met and form is submitted to pharmacy.
3. Oral Fluconazole, when used as a single-dose treatment for vulvovaginal candidiasis or when used in compliance with the SICU/WICU protocol.

Restricted antimicrobials that are ordered as part of a P&T-approved critical pathway or order set do NOT require ID approval.

REMINDER: the use of non-formulary antimicrobials is strongly discouraged. ID approval MUST be obtained for ALL non-formulary antimicrobials.

NOTE: Formulary antivirals (e.g. Acyclovir, Ganciclovir) do NOT require ID approval.

Antibiotics

Ampicillin/sulbactam (Unasyn®)

Ampicillin/sulbactam is a beta-lactam/beta-lactamase inhibitor combination antibiotic. It has activity against MSSA, streptococci, entercocci, and anaerobes. Its activity against Gram-negative organisms is limited; an increasing number of *E. coli* and *Proteus* isolates are now resistant.

Acceptable uses

- Treatment of human or animal bites if IV therapy is needed
- Treatment of oral infections
- Treatment of lung abscess
- Treatment of culture negative endocarditis

Unacceptable uses

- Empiric treatment of biliary tract infections, diverticulitis, or secondary/peritonitis/GI perforation (use can be considered only in infections with organisms that are proven to be susceptible)

Dose

- 1.5-3 g IV Q6H
- 3 g IV Q4H for multi-drug resistant *Acinetobacter* (see p. 93)

Colistin (Colistimethate)

Colistin is a polymixin antibiotic. It has *in vitro* activity against *Acinetobacter spp.* and *Pseudomonas spp.* but does NOT have activity against *Proteus, Serratia, Providentia, Burkholderia,* Gram-negative cocci, Gram-positive organisms, or anaerobes.

Acceptable uses

- Management of infections due to multi-drug resistant *Acinetobacter* and *Pseudomonas* on a case by case basis.

Unacceptable uses

- Monotherapy for empiric treatment of suspected Gram-negative infections

Dose

- 5 mg/kg/day divided in 2 doses, must adjust for worsening renal function and dialysis (see p. 142 for dose adjustment recommendation).

Toxicity

- Renal impairment, neuromuscular blockade, neurotoxicity
- Monitoring: BUN, creatinine twice-weekly

Daptomycin

Daptomycin is a lipopeptide antibiotic. It has activity against most strains of staphylococci and streptococci (including MRSA and VRE). It does NOT have activity against Gram-negative organisms.

Acceptable uses (Cases must be discussed with Infectious Diseases and Antibiotic Management Program)

- Bacteremia or endocarditis caused by MRSA or Methicillin-resistant coagulase-negative staphylococci in a patient with serious allergy to Vancomycin
- Therapy for MRSA infections other than pneumonia in which the MIC of Vancomycin is > 2 mcg/mL
- Bacteremia or endocarditis caused by MRSA in a patient failing Vancomycin therapy as defined by:
  - Clinical decompensation after 3–4 days
  - Failure to clear blood cultures after 7–9 days despite Vancomycin troughs of 15–20 mcg/mL
  - Select cases in which the MIC of Vancomycin is 2 mcg/mL
- Salvage therapy for VRE infections other than pneumonia, on a case by case basis

Unacceptable uses

- Daptomycin should NOT be used for treatment of pneumonia due to its inactivation by pulmonary surfactant.
- Initial therapy for Gram-positive infections
- VRE colonization of the urine, respiratory tract, wounds, or drains

Dose

- Bacteremia: 6–12 mg/kg IV Q 24H
- Endocarditis: 6–12 mg/kg IV Q 24H
- Dose adjustment is necessary for CrCl < 30 ml/min (see p. 142 for dose adjustment recommendation).

Toxicity

- Myopathy (defined as CK ≥ 10 times the upper limit of normal without symptoms or ≥ 5 times the upper limit of normal with symptoms).
- Monitoring: CK weekly, more frequently during initial therapy.

References:
Daptomycin in *S. aureus* bacteremia and infective endocarditis: N Engl J Med 2006; 355: 653–65.

Ertapenem

Ertapenem is a carbapenem antibiotic. It has *in vitro* activity against many Gram-negative organisms including those that produce extended spectrum beta-lactamases (ESBL), but it does not have activity against *Pseudomonas spp. or Acinetobacter spp.* Its anaerobic and Gram-positive activity is similar to that of other carbapenems, except it does not have activity against *Enteroccocus spp.*

Acceptable uses

- Mild to moderate intra-abdominal infections (biliary tract infections, diverticulitis, secondary peritonitis/GI perforation)
- Moderate diabetic foot infections without osteomyelitis
- Moderate surgical-site infections following contaminated procedure
- Urinary tract infections caused by ESBL-producing organisms
- Pyelonephritis in a patient who is not severely ill

Unacceptable uses

- Severe infections in which *Pseudomonas spp.* are suspected.

Dose

- 1 g IV or IM Q24H, must adjust for worsening renal function and dialysis (see p. 142 for dose adjustment recommendation)

Toxicity

- Diarrhea, nausea, headache, phlebitis/thrombophlebitis

Fosfomycin

Fosfomycin is a synthetic, broad-spectrum, bactericidal antibiotic with *in vitro* activity against large number of gram-negative and gram-positive organisms including *E. coli*, *Klebsiella spp.*, *Proteus spp. Pseudomonas spp.*, and VRE. It does not have activity against *Acinetobacter spp.* Fosfomycin is available in an oral formulation only in the U.S. and its pharmacokinetics allow for one-time dosing.

Acceptable uses

- Management of uncomplicated UTI in patients with multiple antibiotic allergies and when oral therapy is indicated.
- Uncomplicated UTI due to VRE
- Salvage therapy for UTI due to multi-drug resistant Gram-negative organisms (e.g. *Pseudomonas spp.*) on case by case basis.

NOTE: Susceptibility to Fosfomycin should be confirmed prior to initiation of therapy.

Unacceptable uses

- Fosfomycin should NOT be used for management of any infections outside of the urinary tract because it does not achieve adequate concentrations at other sites.

Dose

- Uncomplicated UTI: 3 g (1 sachet) PO once.
- Complicated UTI: 3 g (1 sachet) PO every 2-3 days (up to 21 days of treatment)

3.1 Agent-specific guidelines: Antibiotics

- Frequency adjustment may be necessary in patients with CrCl < 50 mL/min. Contact the Antibiotic Management Program for dosing recommendations.
- Powder should be mixed with 90–120 mL of cool water, stirred to dissolve and administered immediately.

Toxicity
- Diarrhea, nausea, headache, dizziness, asthenia and dyspepsia

Linezolid

Acceptable uses
- Documented Vancomycin intermediate *Staphylococcus aureus* (VISA) or Vancomycin resistant *Staphylococcus aureus* (VRSA) infection
- Documented MRSA or Methicillin-resistant coagulase-negative staphylococcal infection in a patient with serious allergy to Vancomycin
- Documented MRSA or Methicillin-resistant coagulase-negative staphylococcal infection in a patient failing Vancomycin therapy (as defined below):
  - Bacteremia/endocarditis: failure to clear blood cultures after 7–9 days despite Vancomycin troughs of 15–20 mcg/mL. Should be used in combination with another agent
  - Pneumonia: worsening infiltrate or pulmonary status in a patient with documented MRSA pneumonia after 2 to 3 days or if the MIC of Vancomycin is 2 mcg/mL.
    Cases should be discussed with Infectious Diseases or Antibiotic Management.
- High suspicion of CA-MRSA necrotizing pneumonia in a seriously ill patient
- Documented VRE infection
- Gram-positive cocci in chains in blood cultures in an ICU, or oncology transplant patient known to be colonized with VRE

Unacceptable uses
- Prophylaxis
- Initial therapy for staphylococcal infection
- VRE colonization of the stool, urine, respiratory tract, wounds, or drains

Dose
- 600 mg IV/PO Q12H
- Skin and skin-structure infections: 400 mg IV/PO Q12H

Toxicity
- Bone marrow suppression (usually occurs within first 2 weeks of therapy)
- Optic neuritis and irreversible sensory motor polyneuropathy (usually occurs with prolonged therapy > 28 days)

3.1 Agent-specific guidelines: Antibiotics

- Case reports of lactic acidosis
- Case reports of serotonin syndrome when co-administered with serotonergic agents (SSRIs, TCAs, MAOIs, etc.)
- Monitoring: CBC weekly

Rifaximin

Rifaximin is a nonabsorbable, semi-synthetic antibiotic derived from rifamycin that is FDA approved for treatment of travelers' diarrhea caused by noninvasive strains of *E. coli*. It may be used as an alternative to lactulose for hepatic encephalopathy (HE) in patients meeting the criteria below. It is not on the formulary at JHH and requires ID approval.

Acceptable uses

Hepatic encephalopathy in patients meeting the following criteria:
- Refractory to lactulose: patient continues to experience HE symptoms despite receiving lactulose at a dose that obtains 2–3 loose stools per day.
- Intolerance to lactulose: patient requiring maintenance therapy with ≥ 4 loose stools per day despite dosage reductions.

Dose
- 200–800 mg PO Q8H

Toxicity
- Diarrhea, abdominal pain, headache. Rare hypersensitivity reactions (dermatitis, rash, angioneurotic edema, urticaria, and pruritis) have been reported in post-marketing trials.

Tigecycline

Tigecycline is a tetracycline derivative called a glycylcycline. It has *in vitro* activity against most strains of staphylococci and streptococci (including MRSA and VRE), anaerobes, and many Gram-negative organisms with the exception of *Proteus spp.* and *Pseudomonas aeruginosa*. It is FDA approved for skin and skin-structure infections and intra-abdominal infections.

NOTE: Peak serum concentrations of Tigecycline do not exceed 1 mcg/mL which limits its use for treatment of bacteremia

Acceptable uses
- Management of intra-abdominal infections in patients with contraindications to both beta-lactams and fluoroquinolones
- Management of infections due to multi-drug resistant Gram-negative organisms including *Acinetobacter spp.* and *Stenotrophomonas maltophilia* on a case by case basis
- Salvage therapy for MRSA/VRE infections on a case by case basis

Dose
- 100 mg IV once, then 50 mg IV Q12H
- 100 mg IV once, then 35 mg IV Q12H if severe hepatic impairment (Child - Pugh 10–15)

Toxicity
- Nausea and vomiting

Vancomycin

At The Johns Hopkins Hospital in 2008, 58% of *S. aureus* isolates in adult patients were resistant to Oxacillin. These data suggest that empiric use of Vancomycin is advisable for an ill patient with suspected *S. aureus* infection. However, Vancomycin should be stopped if culture data do not indicate a need for continued definitive therapy (see below). **Limiting prolonged or inappropriate use of Vancomycin is essential.** There are few instances when continued use of Vancomycin is appropriate in the absence of positive cultures. The following are recommendations for empiric, definitive, and prophylactic Vancomycin use:

Acceptable empiric use

NOTE: therapy should be discontinued within 72 hours if criteria for definitive therapy (see below) are not met:

- Treatment of suspected community- or nosocomially acquired bacterial meningitis
- Treatment of ventilator-associated pneumonia
- Treatment of peritoneal dialysis-related peritonitis in a severely ill patient
- Treatment of sepsis in a patient at risk for MRSA bacteremia [catheter in place, indwelling hardware, known colonization with MRSA, transfer from a nursing home or subacute facility, recent (within 3 months) or current prolonged hospitalization > 2 weeks]
- Treatment of surgical-site infection following placement of hardware
- Treatment of severe diabetic foot infection in a patient at risk for MRSA
- Treatment of necrotizing fasciitis
- Treatment of suspected endocarditis in a moderately or severely ill patient after appropriate blood cultures are obtained (injection-drug users with low-grade fevers and no clinical evidence of endocarditis or sepsis should NOT receive empiric Vancomycin)
- Treatment of Gram-positive cocci in clusters in ≥ 1 set of blood cultures in a moderately or severely ill patient
- Treatment of Gram-positive cocci in clusters or chains in ≥ 2 sets of blood cultures in any patient

3.1 Agent-specific guidelines: Antibiotics

Acceptable use for definitive INTRAVENOUS therapy

- Proven infection with beta-lactam resistant organisms
  - MRSA
  - Methicillin-resistant coagulase-negative staphylococcus
  - Ampicillin-resistant enterococcus (if Vancomycin susceptible)
  - Ceftriaxone-resistant *S. pneumoniae* (CSF only)
- Treatment of infections caused by Gram-positive organisms in patients who have serious allergies to beta-lactam agents (see p. 118 for discussion of penicillin allergy)

Acceptable use for definitive ORAL therapy

- *Clostridium difficile* infection (see CDI section, p. 35)

Acceptable use for prophylaxis

- Prophylaxis for cardiac, vascular or orthopedic (joint replacement, spinal fusion, ORIF ONLY) surgery in patients with severe PCN allergy (no more than one pre-op and one post-op dose)

Unacceptable uses for Vancomycin

- Continued empiric use for presumed infection with negative cultures
- Treatment of a single-positive blood culture for coagulase-negative staphylococci
- Routine surgical prophylaxis
- Empiric treatment for first fever in neutropenic patients without evidence of catheter-related bloodstream infection, severe mucositis, or history of MRSA
- Prophylaxis for infection or colonization of indwelling intravascular catheters
- Selective decontamination of the digestive tract
- Eradication of MRSA colonization
- Routine prophylaxis for patients on continuous ambulatory peritoneal dialysis or hemodialysis
- Treatment (chosen for dosing convenience) of infections caused by beta-lactam sensitive organisms in patients who have renal failure
- Use of Vancomycin solution for topical application or irrigation

Antifungals

Definitions	
Definite	invasive aspergillosis is established by positive culture or histopathology for aspergillosis from tissue obtained during an invasive procedure. Washings, brushings, or suctioning of secretions do NOT represent invasive procedures.
Probable	aspergillosis is indicated by a positive galactomannan assay from serum or BAL or positive culture for aspergillus species AND clinical evidence suggestive of aspergillosis.
Possible	aspergillosis is indicated by a positive galactomannan assay from serum or BAL or radiographic findings highly suggestive of aspergillosis in a compatible host (follow-up diagnostic studies are highly recommended).
Refractory	means disease progression or failure to improve despite at least 96 hours of treatment with Voriconazole or an IV Amphotericin B product (deoxycholate or lipid-based product).

Liposomal Amphotericin B (AmBisome®)

Patients must meet one or more of the criteria below to receive AmBisome® unless otherwise approved by ID

1. Patients currently experiencing or with history of toxicity related to conventional Amphotericin B administration
   - Infusional toxicity (defined as 2 episodes of rigors despite premedication with diphenhydramine, acetaminophen, and either hydrocortisone or dexamethasone)
   - Acute renal failure (defined as doubling of serum creatinine from baseline or urine output < 0.5 mL/kg/hour for > 2 hours despite adequate fluid resuscitation)

2. Patients with renal disease – NOT ESRD ON DIALYSIS
   - Estimated or collected CrCl ≤ 40 mL/min
   - Acute renal failure (doubling of serum creatinine from baseline or urine output < 0.5 mL/kg/hour for > 2 hours despite adequate fluid resuscitation)
   - Renal transplant, single kidney, lupus nephritis

3. Patients at risk for renal failure
   - Age ≥ 65
   - ICU patient with sepsis
   - End-stage liver disease
   - Multiple myeloma/amyloidosis
   - Active tumor lysis syndrome
   - Allogeneic BMT/HSCT until hematopoietic recovery and discontinuation of immune suppression
   - Patient receiving or about to receive cytarabine (ARA-C) within 48 hours
   - Concurrent nephrotoxic therapy
     Aminoglycosides, Colistin, Foscarnet, Cidofovir, Cyclosporine, Tacrolimus, Carboplatin, Cisplatin, high-dose Methotrexate (> 1000 mg/m^2/dose)

4. Patients receiving long-course, high-dose therapy with Amphotericin B, defined as ≥ 2 weeks
   - Definite or probable aspergillosis or zygomycosis requiring long-term therapy
   - Neutropenic fever in patients expected to have prolonged neutropenia (≥ 4 weeks)

For dosing in patients with neutropenic fever, see p. 111.

Micafungin

NOTE: Micafungin does not have activity against Cryptococcus.

Aspergillosis

- **Acceptable uses**
  - Infusional toxicity or acute renal failure on AmBisome® and intolerance to Voriconazole defined as serious hepatoxicity, persistent visual disturbance, or allergic reaction.
  - Refractory disease- for use in combination with Voriconazole or AmBisome® for **definite** or **probable** invasive pulmonary aspergillosis in patients who are refractory to Voriconazole or AmBisome® alone.
- **Unacceptable uses**
  - Micafungin alone or in combination with other antifungal agents is not recommended for empiric therapy in patients with CT findings suggestive of aspergillosis (e.g., **possible** aspergillosis) without plans for diagnostic studies.
  - Micafungin does not have good *in vitro activity* against zygomycoses (Mucor, Rhizopus, Cunninghamella, etc.).

Candidiasis

- **Acceptable uses**
  - Treatment of invasive candidiasis due to *C. glabrata* or *C. krusei*.
  - Treatment of invasive candidiasis in patients who are NOT clinically stable due to candidemia or have received prior long-term azole therapy.

- Alternative treatment of recurrent esophageal candidiasis.
- Alternative treatment of endocarditis.

- **Unacceptable uses**
  - Micafungin has poor penetration into the CNS and urinary tract. It should be avoided for infections involving those sites.
  - Monotherapy for zygomycoses (Mucor, Rhizopus, Cunninghamella, etc.).

Neutropenic Fever
- Micafungin can be used for neutropenic fever in patients who are not suspected to have aspergillosis or zygomycosis.

Dose
- Candidemia, invasive candidiasis, neutropenic fever: 100 mg IV Q24H
- Candidal endocarditis: 150 mg IV Q24H
- Recurrent esophageal candidiasis: 150 mg IV Q24H
- Invasive aspergillosis: 100–150 mg IV Q24H

Drug Interactions
- Close monitoring is recommended when Micafungin is used with the following agents concomitantly:
  - Sirolimus – levels of Sirolimus may be increased, monitor for Sirolimus toxicity
  - Nifedipine – levels of Nifedipine may be increased, monitor for Nifedipine toxicity
  - Itraconazole – levels of Itraconazole maybe increased, monitor for Itraconazole toxicity

Toxicity
- Infusion-related reactions (rash, pruritis), phlebitis, headache, nausea and vomiting, and elevations in hepatic enzymes.
- Monitoring: AST/ALT/bilirubin at baseline and every 1–2 weeks after.

Posaconazole

Posaconazole is a broad spectrum azole anti-fungal agent. It has *in vitro* activity against *Candida, Aspergillus, Zygomycosis* and *Fusarium spp.*

Acceptable uses
- Treatment of invasive zygomycosis in combination with Amphotericin B
- Monotherapy for zygomycosis after 7 days of combination therapy with Amphotericin B

3.2 Agent-specific guidelines: Antifungals

NOTE: Posaconazole requires up to 7 days to achieve steady state concentrations. ID Consult is required.

Unacceptable uses
- Candidiasis/Neutropenic fever
- Primary treatment of aspergillosis

Dose (Only available as oral suspension)
NOTE: Each dose should be given with a full meal or with liquid nutritional supplements if patients cannot tolerate full meals.
- Loading dose: 200 mg PO Q6H for 7 days
- Maintenance dose: 400 mg PO Q8–Q12H

Drug Interactions
- Posaconazole is an inhibitor and is metabolized by cytochrome P4503A4; therefore, co-administration with other agents that are cytochrome P450 substrates, inducers, or inhibitors will result in significant drug interactions.
- **You must check for potential drug interactions when initiating Posaconazole therapy or starting a new medication in patients already receiving Posaconazole therapy.**
- Administration of the following agents with Posaconazole is contraindicated:
  - Terfenadine, Astemizole, Pimozide, Cisapride, Quinidine, Sirolimus, Halofantrine and ergot alkaloids
- Posaconazole inhibits metabolism of the following agents. Dose reductions and close monitoring are recommended when Posaconazole is used with agents concomitantly:
  - Tacrolimus – reduce Tacrolimus dose to ⅓ and monitor levels
  - Cyclosporine – reduce Cyclosporine dose to ¾ and monitor drug levels
  - Midazolam – consider dose reducing
  - Cimetidine, Rifabutin, Efavirenz and Phenytoin – unless the benefit outweighs the risk, **AVOID** concomitant use. If used together, monitor effect of the drugs and consider decreasing dose when Posaconazole is added
  - Statins (avoid Lovastatin and Simvastatin), vinca alkaloids, calcium channel blockers, Digoxin, Atazanavir, Ritanovir, QTc prolonging drugs (e.g. Amiodarone and Erythromycin) – monitor effect of the drugs and consider decreasing dose when Posaconazole is added
  - Cimetidine, Rifabutin, Phenytoin, Efavirenz, Esomeprazole, Metoclopramide may decrease Posaconazole blood levels.

Toxicity
- GI upset (~40%), headaches, elevation in hepatic enzymes. Rare but serious effects include QTc prolongation.
- Monitoring: AST/ALT/bilirubin at baseline and every 1–2 weeks after

References:
Clinical efficacy of new antifungal agents: Curr Opin Microbiol. 2006;9:483-88
Posaconazole: a broad spectrum triazole antifungal: Lancet Infect Dis. 2005; 5:775-85

Voriconazole

NOTE: Voriconazole does not cover zygomycoses (Mucor, Rhizopus, Cunninghamella, etc.).

Acceptable uses
- **Aspergillosis** (please refer to the definitions on p. 16).
  - ***Oncologic neutropenic and BMT populations:***
    1) **Definite** (biopsy-proven) invasive non-zygomycete filamentous fungal infections
    2) **Probable** invasive non-zygomycete filamentous fungal infections
    3) Empiric therapy in patients with ***possible*** aspergillosis (follow-up diagnostic studies are highly recommended)
  - ***Other patient populations:***
    Definite infections or as otherwise deemed appropriate after consultation with the Infectious Diseases service or the Antibiotic Management Program.
- ***Pseudallescheria boydii (Scedosporium spp.), Fusarium spp.***
  Voriconazole is recommended as first-line therapy.
- Alternative therapy for *C. krusei* if susceptible and oral therapy is desired in stable patient.

Unacceptable uses
- **Candidiasis / Neutropenic fever**
  Voriconazole should not be used as first-line therapy for the treatment of candidiasis or for empiric therapy in patients with neutropenic fever.

Dose
- Loading dose: 6 mg/kg IV/PO Q12H x 2 doses
- Maintenance dose: 4 mg/kg IV/PO Q12H
  - Patients receiving concomitant **Phenytoin** or **Efavirenz** should receive following maintenance doses of Voriconazole due to induced hepatic clearance by Phenytoin and Efavirenz.
    - Intravenous: 5 mg/kg Q12H
    - Oral: 400 mg Q12H (wt. ≥ 40 kg) OR 200 mg Q12H (wt. < 40 kg)
    - Efavirenz dose should be decreased to 300 mg PO daily.
    - Monitor Phenytoin levels and adverse events.

3.2 Agent-specific guidelines: Antifungals

- Dose escalation may be necessary for some patients due to subtherapeutic levels.

Therapeutic monitoring
- Obtaining Voriconazole trough levels should be considered in patients who are:
  - not responding to therapy after at least 5 days of therapy using a mg/kg dosing strategy
  - receiving concomitant drugs that may increase or decrease Voriconazole levels
  - experiencing adverse events due to Voriconazole
  - experiencing GI dysfunction
- Voriconazole trough levels should be obtained 5–7 days after start of therapy
- Goal trough: 1–5.5 mcg/mL. Levels < 1 mcg/mL have been associated with clinical failures and levels >5.5 mcg/mL with toxicity.

Drug Interactions
- Voriconazole is an inhibitor and is metabolized by cytochrome P450; therefore, co-administration with other agents that are cytochrome P450 substrates, inducers, or inhibitors will result in significant drug interactions.
- **You must check for potential drug interactions when initiating Voriconazole therapy or starting a new medication in patients already receiving Voriconazole therapy.**
- Administration of the following agents with Voriconazole is contraindicated:
  - Sirolimus, Rifampin, Rifabutin, Carbamazepine, Terfenadine, Astemizole, Cisapride, Pimozide, Quinidine, long-acting barbiturates, Ritonavir (400 mg BID), St. John's Wort, and ergot alkaloids
- Voriconazole inhibits metabolism of the following agents; dose reductions and close monitoring are recommended when Voriconazole is used with agents concomitantly:
  - Tacrolimus – reduce Tacrolimus dose to ⅓ and monitor levels
  - Cyclosporine – reduce Cyclosporine dose to ½ and monitor drug levels
  - Omeprazole – reduce Omeprazole dose to ½
  - Warfarin – monitor PT, INR levels
  - Ritonavir low dose (100 mg Q12H) – avoid this combination unless benefit outweighs risk.
  - Sulfonylureas, statins (avoid Lovastatin and Simvastatin), vinca alkaloids, calcium channel blockers, benzodiazepines (avoid midazolam and triazolam), oral contraceptives, Alfentanil, and Methadone – monitor effect of the drugs and consider decreasing dose when Voriconazole is added.

Toxicity

- Visual disturbances (~30%) usually self-limited, rash, fever, elevations in hepatic enzymes.
- Monitoring: AST/ALT/bilirubin at baseline and every 1–2 weeks after

References:
Voriconzole: Clin Infect Dis 2003; 36:630
Voriconazole in neutropenic fever: N Engl J Med 2002;346(4):225.
Voriconazole TDM: CID 2008; 46:201

Interpreting the microbiology report

Interpretation of preliminary microbiology data

Gram-positive cocci	Gram-negative cocci
Aerobic In clusters • Coagulase (+): *S. aureus* • Coagulase (–): *S. epidermidis*, *S. lugdunensis* In pairs/chains • Diplococcus, Quellung positive: *S. pneumoniae* • Alpha-hemolytic: Viridans group *Streptococci*, *Enterococcus* (*faecalis* and *faecium*) • Beta-hemolytic: Group A strep (*S. pyogenes*), Group B strep (*S. agalactiae*), Group C, D, G strep **Anaerobic:** *Peptostreptococcus spp.*	**Aerobic** Diplococcus: *N. meningiditis*, *N. gonorrhea*, *Moraxella catarrhalis* Cocco-bacillus: *H. flu*, *Acinetobacter spp.*, HACEK organisms **Anaerobic:** *Veillonella spp.*
Gram-positive rods	**Gram-negative rods**
Aerobic Large: *Bacillus spp.* Cocco-bacillus: *Listeria monocytogenes*, *Lactobacillus spp.* Small, pleomorphic: *Corynebacterium spp.* Branching filaments: *Nocardia spp.*, *Streptomyces spp.* **Anaerobic** Large: *Clostridium spp.* Small, pleomorphic: *P. acnes*, *Actinomyces spp.*	**Aerobic** Lactose fermenting: *Citrobacter spp.*, *Enterobacter spp.*, *E. coli*, *Klebsiella spp.*, *Serratia spp.** Non-lactose fermenting • Oxidase (–): *Acinetobacter spp.*, *Burkholderia spp.*, *E. coli* (rare), *Proteus spp.*, *Salmonella spp.*, *Shigella spp.*, *Serratia spp.**, *Stenotrophomonas maltophilia* • Oxidase (+): *P. aeruginosa*, *Aeromonas spp.*, *Vibrio spp.*, *Campylobacter spp.* (curved) **Anaerobic:** *Bacteroides spp.*, *Fusobacterium spp.*, *Prevotella spp.*

* *Serratia spp.* can appear initially as non-lactose fermenting due to slow fermentation.

The Johns Hopkins microbiology laboratory utilizes standard reference methods for determining susceptibility. The majority of isolates are tested by the automated system.

The minimal inhibitory concentration (MIC) value represents the concentration of the antimicrobial agent required at the site of infection for inhibition of the organism.

The MIC of each antibiotic tested against the organism is reported with one of three interpretations S (susceptible), I (intermediate), or R (resistant). The highest MIC which is still considered susceptible represents the breakpoint concentration. This is the highest MIC which is usually associated with clinical efficacy. MICs which are ½–⅛ the

breakpoint MIC are more frequently utilized to treat infections where antibiotic penetration is variable or poor (endocarditis, meningitis, osteomyelitis, pneumonia, etc.). Similarly, organisms yielding antibiotic MICs at the breakpoint frequently possess or have acquired a low-level resistance determinant with the potential for selection of high-level expression and resistance. This is most notable with cephalosporins and *Enterobacter spp., Serratia spp., Morganella spp., Providencia spp., Citrobacter spp.* and *Pseudomonas aeruginosa*. These organisms all possess a chromosomal beta-lactamase which frequently will be over-expressed during therapy despite initial *in vitro* susceptibility. The intermediate (I) category includes isolates with MICs that approach attainable blood and tissue levels, but response rates may be lower than fully susceptible isolates. Clinical efficacy can potentially be expected in body sites where the drug is concentrated (e.g., aminoglycosides and beta-lactams in urine) or when a higher dose of the drug can be used (e.g., beta-lactams). The resistant (R) category indicates the organism will not be inhibited by usually achievable systemic concentrations of the antibiotic of normal doses.

NOTE: MIC values vary from one drug to another and from one bacteria to another, and thus MIC values are NOT comparable between antibiotics or between organisms.

Biliary tract infections – cholecystitis and cholangitis

TREATMENT

Community-acquired infections in patients without previous biliary procedures AND who are not severely ill

- Cefotetan 1 g IV Q12H
  OR
- Ertapenem 1 g IV Q24H
  OR
- PCN allergy: Ciprofloxacin 400 mg IV Q12H PLUS Metronidazole 500 mg IV Q8H
  OR
- PO regimen: Amoxicillin/clavulanate 875 mg PO BID

Hospital-acquired infections OR patients with prior biliary procedures OR patients who are severely ill

- Piperacillin/tazobactam 3.375 g IV Q6H
  OR
- PCN allergy: Ciprofloxacin 400 mg IV Q12H PLUS Metronidazole 500 mg IV Q8H

In severely ill patients with cholangitis and complicated cholecystitis, **adequate biliary drainage** is crucial as antibiotics will not enter bile in the presence of obstruction.

Duration

- Uncomplicated cholecystitis: treat only until obstruction is relieved. NO post-procedure antibiotics are necessary if the obstruction is successfully relieved.
- Complicated cholecystitis: 5–10 days. Trend is now favoring shorter regimens.
- Biliary sepsis: 5–14 days. Shorter course favored if source controlled. Average duration is 7 days.

TREATMENT NOTES

Microbiology

- Gram-negative rods – *E. coli, Klebsiella spp., Proteus spp., P. aeruginosa* (mainly in patients already on broad-spectrum antibiotics or those who have undergone prior procedures)
- Anaerobes – *Bacteroides spp.*, generally in more serious infections, or in patients with a history of biliary manipulations
- *Enterococcus spp.* – treatment not always indicated; use clinical judgment
- Yeast – rare

Special circumstances
- In cases of uncomplicated acute cholecystitis, antibiotics should be given until the biliary obstruction is relieved (either by surgery, ERCP, or percutaneous drain. Treatment of enterococci is controversial. They should be treated if recovered in severely ill patients but specific enterococcal coverage is often not needed in mild/moderate disease.
- Yeast generally should be treated only if they are recovered from biliary cultures, not empirically.

Reference:
Biliary tract infections: Drugs 1999;57(1):81-91.
IDSA Guidelines for Intra-abdominal Infections: Clin Infect Dis 2003;37:997.

Diverticulitis

TREATMENT

Mild/moderate infections – can be oral if patient can take PO
- Amoxicillin/clavulanate 875 mg PO Q12H
  OR
- Cefotetan 1 g IV Q12H
  OR
- Ertapenem 1 g IV Q24H
  OR
- PCN allergy: [Ciprofloxacin 400 mg IV Q12H OR Ciprofloxacin 500 mg PO Q12H] PLUS Metronidazole 500 mg IV/PO Q8H

Severe infections
- Ampicillin 2 g IV Q6H PLUS Gentamicin (see dosing sections) PLUS Metronidazole 500 mg IV Q8H
  OR
- Piperacillin/tazobactam 3.375 g IV Q6H
  OR
- PCN allergy: Ciprofloxacin 400 mg IV Q12H PLUS Metronidazole 500 mg IV Q8H

Duration
- Treat for 7–10 days.

TREATMENT NOTES

Microbiology
- Almost all infections are polymicrobial
- Most commonly isolated aerobic organisms – *E. coli, K. pneumoniae, Enterobacter spp., Proteus spp., Enterococcus spp.*
- Most commonly isolated anaerobic organisms – *B. fragilis, Prevotella, Peptostreptococci*

Other considerations
CT scan is important in assessing need for drainage in severe disease. Some patients will present with diffuse peritonitis and pneumoperitoneum.

Reference:
IDSA Guidelines for Intra-abdominal Infections: Clin Infect Dis 2003;37:997.

Pancreatitis

TREATMENT
- Mild to moderate pancreatitis – no antibiotics
- Severe acute pancreatitis (SAP)* – no *prophylactic* antibiotics
  - No necrosis – no antibiotics
  - Sterile pancreatic necrosis – no antibiotics
  - Infected pancreatic necrosis* – empiric antibiotic therapy as defined below:
    - Meropenem 1 g IV Q8H
      OR
    - PCN allergy: Ciprofloxacin 400 mg IV Q12H PLUS Metronidazole 500 mg IV Q8H

*** Definitions**
- **Severe acute pancreatitis (SAP)** is defined as pancreatitis associated with one or more of the following:
  - > 30% pancreatic necrosis
  - APACHE II ≥ 8
  - More than 3 Ranson's criteria

Ranson's criteria to predict severity of acute pancreatitis

Zero Hours	
Age	> 55
WBC	> 16,000/mm^3
Blood glucose	> 200 mg/dL
Lactate dehydrogenase	> 350 U/L
Aspartate aminotransferase (AST)	> 250 U/L

48 Hours	
Hematocrit	Fall by ≥ 10 percent
Blood urea nitrogen	Increase by ≥ 5 mg/dL despite fluids
Serum calcium	< 8 mg/dL
pO_2	< 60 mmHg
Base deficit	> 4 MEq/L
Fluid sequestration	> 6000 mL

5.1 Abdominal infections

- **Infected pancreatic necrosis is defined as one or both of the following:**
  - CT scan with gas
  - Percutaneous aspirate or surgical specimen with organisms evident on gram stain or culture

Duration

For infected pancreatic necrosis, continue antibiotics for 14 days after source control is obtained. Continuation of antibiotics beyond this time places the patient at risk for colonization or infection with resistant organisms and drug toxicity.

TREATMENT NOTES

- Penicillins and cephalosporins penetrate poorly into the pancreas
- Infection develops in 30–50% of patients with necrosis documented by CT scan or at the time of surgery.
- Peak incidence of infection occurs in the 3rd week of disease
- Prophylactic antibiotics have been associated with a change in the spectrum of pancreatic isolates from enteric Gram-negatives to Gram-positive organisms and fungi.
- There is insufficient evidence to recommend selective gut decontamination in management of pancreatitis.

References:
Lack of utility of prophylactic antibiotics: Ann Surg 2007;245:674.
Guidelines for management of SAP: Crit Care Med 2004;32:2524.
Ranson's criteria: Surg Gynecol Obstet 1974;139:69.

Peritonitis

DEFINITIONS

Primary peritonitis is spontaneous infection of the peritoneal cavity, usually associated with liver disease and ascites [spontaneous bacteria peritonitis (SBP)].
Secondary peritonitis is infection of the peritoneal cavity due to spillage of organisms into the peritoneum, usually associated with GI perforation.
Tertiary peritonitis is a recurrent infection of the peritoneal cavity following an episode of secondary peritonitis.

Primary peritonitis/Spontaneous bacterial peritonitis (SBP)

TREATMENT

- Ceftriaxone 1 g IV Q24H is preferred.
- Amoxicillin/clavulanic acid 875 mg PO BID is the preferred oral regimen.
- Moxifloxacin 400 mg IV/PO Q24H can be used in PCN-allergic patients who have NOT been taking fluoroquinolone for SBP prophylaxis.

Duration

- Treat for 5 days.

PROPHYLAXIS

Cirrhotic patients with gastrointestinal hemorrhage

- Norfloxacin 400 mg PO BID for 7 days
- Ceftriaxone 1 g IV Q24H can be used only if patient is NPO, then switch to Norfloxacin 400 mg PO BID once bleeding is controlled

Non-bleeding cirrhotic patients with ascites

- Norfloxacin 400 mg PO daily

  OR
- TMP/SMX 1 DS PO once daily

TREATMENT NOTES

Microbiology

- Gram-negative rods (Enterobacteriaceae, esp. *E. coli* and *K. pneumoniae*), *S. pneumoniae*, enterococci, and other streptococci.
- Polymicrobial infection should prompt suspicion of GI perforation.

Diagnostic criteria

- 250 PMN per mm^3 of ascitic fluid.
- Positive culture with < 250 PMN should prompt repeat tap. If PMN > 250 OR culture remains positive, patient should be treated.

Follow-up
- Consider repeat paracentesis after 48 hours of therapy.
- Consider changing antibiotics if ascites fluid PMN has not dropped by 25% after 48 hours and/or patient is not clinically responding.

Notes on prophylaxis against SBP
- All patients with cirrhosis and upper GI bleed should receive prophylaxis for 7 days (50% develop SBP after bleed).
- Patients who get SBP should get lifelong prophylaxis to prevent future episodes (40–70% risk of recurrence in 1 year).
- Prophylaxis should be considered for those with low protein concentrations in ascites (< 10 g/L) or immunosuppression but must be carefully weighed against the risk of resistance.

Reference:
Diagnosis, treatment and prophylaxis of SBP: J Hepatol 2000;32:142.
Management of variceal hemorrhage in cirrhosis: Hepatology 2007;46:922–38.

Secondary peritonitis/GI perforation

TREATMENT

Perforation of esophagus, stomach, small bowel, colon, or appendix

Patient mild to moderately ill
- Cefotetan 1 g IV Q12H
  OR
- Ampicillin 2 g IV Q6H PLUS Gentamicin (see dosing section) PLUS Metronidazole 500 mg IV Q8H
  OR
- Ertapenem 1 g IV Q24H
  OR
- PCN allergy: Ciprofloxacin 400 mg IV Q12H PLUS Metronidazole 500 mg IV Q8H

Patient severely ill or immunosuppressed
- Piperacillin/tazobactam 3.375 g IV Q6H
  OR
- PCN allergy: Ciprofloxacin 400 mg IV Q12H PLUS Metronidazole 500 mg IV Q8H

Empiric antifungal therapy is generally not indicated for GI perforation unless patient has one of the following risk factors:

Esophageal perforation, immunosuppression, prolonged antacid or antibiotic therapy, prolonged hospitalization, persistent GI leak.

Recommendations for patients who are clinically stable and have not received prior long-term azole therapy:
- Fluconazole 400-800 mg IV/PO Q24H
  OR
- Amphotericin B 0.7 mg/kg IV Q24H

Recommendations for patients who are NOT clinically stable or have received prior long-term azole therapy:
- Micafungin 100 mg IV Q24H
  OR
- AmBisome® 3 mg/kg IV Q24H

Duration of therapy for secondary peritonitis/GI perforation

	Stomach	Small Bowel	Colon	Appendix
Uncomplicated				
Definition	Operated on within 24 hours	Operated on within 12 hours	Operated on within 12 hours	Non-necrotic or gangrenous appendix
Duration	24–48 hours	24–48 hours	24–48 hours	24 hours
Complicated				
Definition	Late operation or no operation; or necrotic/gangrenous appendix			
Duration	5-7 days			

TREATMENT NOTES
- Causative agents for small bowel, colon, appendix: anaerobes (esp. *B. fragilis*), Enterobacteriaceae (esp. *E. coli, K. pneumoniae, Enterobacter spp., Proteus spp.*); infections usually polymicrobial.
- Pathogens causing tertiary peritonitis are variable and are often resistant to or not covered by the initial antimicrobial regimen; thus, a change in antimicrobials is advised.
- A change in antimicrobials therapy should be considered in patients with hospital-acquired infections who are already on antimicrobials.
- Treatment of enterococci remains controversial but may be of benefit in critically ill patients.
- Treatment of *Candida spp.* is generally indicated only when they are recovered from blood or are the primary organism in the peritoneal culture.
- Postoperative antibiotics for appendicitis are unnecessary unless there is clinical evidence of peritonitis, abscess, or gangrene.
- Antibiotics are adjunctive to source control, which is an absolute necessity.
- Lack of source control is defined as on-going contamination and/or an undrained collection of infection.

Peritonitis related to peritoneal dialysis

TREATMENT

Mild to moderate illness: intraperitoneal therapy is preferred in most cases.

Anuric patient

- Cefazolin 15 mg/kg in one bag Q24H (1 g if patient < 65 kg) PLUS
- Gentamicin 2 mg/kg in one bag loading dose, then Gentamicin 0.6 mg/kg in one bag Q24H

Patient with urine output > 100 mL/day

- Ceftazidime 1 g in one bag Q24H

Severe illness: systemic therapy is preferred.

- FIRST DOSE: Vancomycin (see dosing section, p. 138) IV PLUS ONE of the following:
  [Gentamicin 2 mg/kg IV OR Ceftazidime 1 g IV OR Ciprofloxacin 400 mg IV]
- MAINTENANCE DOSE: Dose per drug levels and/or renal function (See dosing section p. 138 and p. 142)

Duration of tailored therapy: 10–14 days

TREATMENT NOTES

Microbiology

- Most cases caused by contamination of the catheter
- Cultures may be negative in 5–20%
- Gram-positive cocci (*S. aureus*, coagulase-negative staphylococci, *Enterococcus spp.*), Gram-negative rods, yeast (much less common)

Diagnosis

- All patients with suspected PD-related peritonitis should have PD fluid sampled for **cell count, differential, gram stain, culture AND amylase.** WBC > 100/mm^3 with > 50% PMN suggests infection.
- Elevated amylase suggests pancreatitis or bowel perforation.
- In symptomatic patients with cloudy fluid accompanied by abdominal pain and/or fever, empiric treatment should be started given the high likelihood of infection.
- In symptomatic patients with clear fluid, another PD fluid exchange, with a dwell time of at least 2 hours, should be sampled. The decision to start empiric therapy in these cases will depend on how sick the patient appears.
- In asymptomatic patients with cloudy fluid, it is reasonable to delay therapy pending the results of cell count, gram stain, and culture.

References:
ISPD Guidelines for Peritoneal Dialysis-related Infections: Perit Dial Int 2005;25:107.

Clostridium difficile infection (CDI)

TREATMENT

- **STOP ALL ANTIMICROBIAL AGENTS WHENEVER POSSIBLE.**
- Oral therapy must be used whenever possible as the efficacy of IV Metronidazole is poorly established for CDI and there is no efficacy of IV Vancomycin for CDI.

Treatment depends on clinical severity

Infection severity	Clinical manifestations
Asymptomatic carriage	*C. difficile* antigen or PCR positive without diarrhea, ileus, or colitis
Mild or moderate	*C. difficile* PCR positive with diarrhea but no manifestations of severe disease
Severe	*C. difficile* PCR positive with diarrhea and one or more of the following **attributable to CDI:** • WBC ≥ 15,000 • Increase in serum creatinine > 50% from baseline
Severe Complicated	Criteria as above plus one or more of the following **attributable to CDI:** • Hypotension • Ileus • Toxic megacolon or pancolitis on CT • Perforation • Need for colectomy • ICU admission for severe disease

Infection Severity	Treatment
Asymptomatic carriage	Do NOT treat; treatment can promote relapsing disease
Mild or moderate	• Metronidazole 500 mg PO/NGT Q8H Unable to tolerate oral therapy • Metronidazole 500 mg IV Q8H (suboptimal; see note at start of CDI section above)
Severe	• Vancomycin solution 125-250 mg PO/NGT Q6H (preferred) **OR** • Vancomycin capsules 125 mg PO Q6H
Severe Complicated	• Consult surgery for evaluation for colectomy and ID • Vancomycin solution 500 mg by NGT Q6H PLUS Metronidazole 500 mg IV Q8H Unable to tolerate oral therapy or complete ileus • Vancomycin 500 mg in 100 ml NS Q6H as retention enema via Foley catheter in rectum + Metronidazole 500 mg IV Q8H

Other indications for oral Vancomycin use
- No response to oral Metronidazole after 5 days of therapy
- Second episode of recurrent disease
- Patients with significant side effects to Metronidazole
- Patients who are pregnant
- Consider in patients > 80 years given reports of increased morbidity from CDI.

Duration
- 10–14 days

Recurrent disease
- Resistance to Metronidazole or Vancomycin has not been documented conclusively.
- Recurrent disease after a complete course of therapy occurs in ~ 25% of patients. Relapse is due to failure to eradicate spores (60%) or acquisition of a new strain (40%). Document recurrent disease with repeat stool testing.
- First recurrence should be treated the same as the initial episode.
- Second recurrence should be treated with Vancomycin taper followed by pulse dosing.
- If serious or multiple recurrences, consult ID.

Vancomycin taper regimen
125 mg 4 times daily x 10–14 days
125 mg BID X 7 days
125 mg daily X 7 days
125 mg every 2–3 days for 2–8 weeks (pulse dosing)

TREATMENT NOTES

Diagnosis
- Do NOT send stool for *C. difficile* testing if patients do not have diarrhea, ileus, or colitis.
- Stool for *C. difficile* testing should be collected prior to starting treatment for *C. difficile*.
- Specimens should be hand carried to the laboratory as soon as possible after collection. If they cannot be transported promptly, the samples should be refrigerated.
- Specimens collected outside of the institution should be transported at 4° C to avoid degradation of toxin which can lead to false negative results.
- The JHH microbiology lab uses a two-step algorithm for *C. difficile* detection. Stools are screened with an assay that detects an antigen produced by both toxigenic (i.e. disease causing) and non-toxigenic (i.e. non-disease causing) strains. The negative predictive value of this test is 95%. Antigen-positive samples are automatically tested for *C. difficile* toxin B gene using a real-time PCR assay. The sensitivity of the real time PCR is 91% compared to cell culture neutralization and 84% compared to toxigenic culture.
- There is limited utility to sending repeat *C. difficile* tests. If the antigen or toxin tests are negative and clinical suspicion is high for CDI, collect a repeat stool sample and call the microbiology lab to ask for a toxigenic stool culture for *C. difficile*. Stool samples should be sent before therapy for *C. difficile* is initiated.

Management
- Surgical intervention for total colectomy should be considered early if patient is clinically unstable secondary to CDI.
- Most patients with severe CDI should undergo abdominal CT to rule out toxic megacolon or pancolitis.
- Early therapy appears to be important, especially in elderly patients. It may be necessary to discontinue the offending agent and initiate therapy with Metronidazole or Vancomycin while the toxin assay is pending.
- Do NOT send follow-up *C. difficile* toxins to document resolution of disease.
- Do not use antimotility agents.
- The offending antimicrobial agents should be discontinued. If antimicrobials are still required, it is best to avoid Clindamycin, cephalosporins, and fluoroquinolones.
- Prophylactic use of oral Metronidazole or Vancomycin in patients receiving antimicrobial therapy for treatment of underlying infection (other than CDI) is not recommended and may increase the patient's risk for CDI.

References:
Diagnosis of CDI: Clin Infect Dis 2008; 46:S12-8.
Treatment of CDI: Clin Infect Dis 2008; 46:S32-42.
Lack of utility of treating CDI carriers: Ann Intern Med 1992; 117:297-302.
Colectomy in CDI: Ann Surg 2007; 245:267-72.

5.2 *Clostridium difficile* infection (CDI)

Infectious diarrhea

- **For treatment of *C. difficile* infection, see p. 35.**
- Carefully assess the patient before prescribing antimicrobials.
- Most infectious diarrhea is self limited and only requires supportive management.
- Treatment with antibiotics is not recommended for most mild-moderate disease; see specific indications in table below.
- Viral pathogens, such as Norovirus and Rotavirus commonly cause diarrhea and do not require antibiotics.
- Antibiotic use may lead to adverse outcomes (e.g. hemolytic uremic syndrome with Shiga toxin-producing *E. coli*).
- Antimotility agents should not be used in patients with bloody diarrhea, fever, or elevated WBC.

Microbiology

- Common non-viral pathogens in acute community-acquired diarrhea: *Salmonella, Shigella*, Shiga toxin-producing *E. coli, Campylobacter, C. difficile* (usually with antibiotic exposure).
- Nosocomial diarrhea: *C. difficile*
- Persistent diarrhea if immunocompromised (most likely causes vary depending on type of immunocompromise): *Giardia, Cryptosporidium, Cyclospora, Isospora, Microsporidia*, Cytomegalovirus (CMV).

Diagnosis

- Not every diarrheal illness requires stool culture. Decision to test should be based on suspicion for specific pathogens and/or clinical judgment of illness severity.
- Patients with febrile diarrheal illnesses with clinical features of moderate to severe disease should receive empiric therapy only after a fecal specimen is obtained for appropriate testing.
- Fecal specimens from patients hospitalized for > 3 days should not be submitted for routine stool culture unless a high suspicion for specific pathogen exists and/or if the patient is immunocompromised.
- Multiple stool examinations for ova and parasites (O&P) are of low yield.
- Fecal leukocyte/lactoferrin assessments should not be used to determine the therapeutic approach.

Treatment of infectious diarrhea

Organism/Indications for treatment	Treatment
Bacteria	
Campylobacter spp. Treatment recommended for: • Severe illness • Age < 6 months or > 50 years • Gross blood in stool • High fever • Worsening or relapsing symptoms • Pregnancy • Immunocompromised host	• Azithromycin 500 mg PO daily for 1–3 days
E. coli (enterotoxigenic, enteropathogenic, enteroinvasive) or **empiric therapy of traveler's diarrhea**	• Norfloxacin 400 mg PO BID **OR** • Ciprofloxacin 500 mg PO BID **OR** **Duration:** 1–3 days
Shiga toxin producing *E. coli* (including *E. coli* 0157:H7)	Treatment not recommended. Antibiotic use associated with development of hemolytic uremic syndrome.
Non-typhoid *Salmonella spp.* Treatment recommended for: • Severe illness requiring hospitalization • Age < 6 months or > 50 years • Bacteremia • Presence of prostheses • Valvular heart disease • Severe atherosclerosis • Malignancy or other immunocompromise	• Norfloxacin 400 mg PO BID (not for bacteremia) **OR** • Ciprofloxacin 500 mg PO BID **OR** • TMP/SMX 160/800 mg PO BID (if susceptible) **OR** • Ceftriaxone 1g IV Q24H **Duration:** 5–7 days; 14 days for immunocompromised host
Shigella spp. Treatment always recommended even if result returns when patient is asymptomatic.	• TMP/SMX 160/800 mg PO BID (if susceptible) **OR** • Norfloxacin 400 mg PO BID (not for bacteremia) **OR** • Ciprofloxacin 500 mg PO BID **Duration:** 3 days; 7 days for immuno-compromised host
Vibrio parahaemolyticus Note: Associated with shellfish consumption Treatment recommended for severe illness	• Ciprofloxacin 500 mg PO BID x 3 days
Yersinia spp. Treatment recommmended for: • Immunocompromised host • Bacteremia • Pseudoappendicitis syndrome	• TMP/SMX 160/800 mg PO BID x 3–5 days (if susceptible) **OR** • Ciprofloxacin 500 mg PO BID x 3 days **OR** • Doxycycline 100 mg PO BID x 3 days (not for bacteremia)

5.3 Infectious diarrhea

Parasites	
Entamoeba histolytica Treat all (even asymptomatic) *E. dispar & E. moshkovskii* infections do not require treatment	• Metronidazole 750 mg PO TID x 5–10 days **OR** • Tinidazole 1 g PO Q12H x 3 days • **PLUS** all patients should receive Paromomycin 500 mg PO TID x 7 days after the course of 1st agent complete **Asymptomatic patients** • Paromomycin 500 mg PO TID x 7 days
Giardia spp.	• Metronidazole 250-500 mg PO TID x 7–10 days **OR** • Tinidazole 2 g PO once

References:
IDSA Guidelines for Management of Infectious Diarrhea; Clin Infect Dis 2001;32:331–50.
Infectious diarrhea in developed and developing countries: J Clin Gastroenterol 2005:39:757–773.

Helicobacter pylori infection

Established indications for testing for *H. pylori* and treating positive patients

- Active peptic ulcer disease (PUD) – gastric or duodenal
- Confirmed history of PUD (not previously treated for *H. pylori*)
- Gastric MALT lymphoma (low grade)
- Following resection of gastric cancer
- Family history of gastric cancer

Other indications where testing for *H. pylori* and treating positive patients can be considered: nonulcer dyspepsia, GERD, persons using NSAID, unexplained iron deficiency anemia, family members of patients with *H. pylori* with mild dyspepsia.

First-line treatment

- Amoxicillin 1 g PO Q12H PLUS Clarithromycin 500 mg PO Q12H PLUS Pantoprazole 40 mg PO Q12H
  OR
- PCN allergy
  - Clarithromycin 500 mg PO Q12H PLUS Metronidazole 500 mg PO Q12H PLUS Pantoprazole 40 mg PO Q12H
    OR
  - Tetracycline 500 mg PO Q6H PLUS Metronidazole 500 mg PO Q8H PLUS Bismuth subsalicylate 525 mg PO Q6H PLUS Pantoprazole 40 mg PO Q12H

- **Duration:** 10–14 days

Documented recurrence of *H. pylori* disease

- If possible, avoid antibiotics previously used to treat *H. pylori*
- Tetracycline 500 mg PO Q6H PLUS Metronidazole 500 mg PO Q8H PLUS Bismuth subsalicylate 525 mg PO Q6H PLUS Pantoprazole 40 mg PO Q12H

- **Duration:** 14 days

TREATMENT NOTES

Diagnosis

- PPIs and antibiotics should be withheld for at least 2 weeks prior to testing.
- *H. pylori* stool antigen is the only FDA approved test (>90% sensitivity and specificity).
- Urea breath test may be optimal but not commonly available.
- Endoscopy PLUS rapid urease test (80–95% sensitivity; 92–100% specificity).
- *H. pylori* serology does not document current infection.

Management

- First line treatment eradication rates estimated between 70–80%. Failure most often due to Clarithromycin resistance and/or non-adherence.
- H2-receptor antagonists (e.g., ranitidine) can be substituted for the PPI if patients are unable to tolerate PPIs or if drug interactions are a concern.
- Amoxicillin PLUS Tetracycline can NOT be used together in treatment due to low response rates.
- In patients with positive test results endoscopy is mandatory for age > 45-50 years, presence of mass GI bleeding, anemia, weight loss, or family history of gastric cancer.
- Test of cure is recommended > 4–8 weeks post treatment.

References:
Maastricht III Consensus Report. *Gut* 2007;56:772-781.
ACG Guidelines. *Am J Gastroenterol* 2007;102:1808-1825.

Management of catheter-associated bloodstream infections (CA-BSI)

Diagnosis

- If there is more than minimal erythema or ANY purulence at the exit site, the catheter is likely infected. It should be removed and replaced at a different site.
- Two sets of blood cultures should be drawn with AT LEAST one (and preferably both) from peripheral sites. Blood cultures drawn through non-tunneled catheters are more likely to yield contaminants. One set of cultures may be drawn through a catheter if it is **tunneled**.
- The utility of cultures of the catheter itself is not well defined, and should ONLY be sent when there is a clinical suspicion of infection, NOT routinely when lines are removed. They MUST be accompanied by two sets of blood cultures obtained as detailed above.
  - Technique: The exit site should be cleaned with alcohol. The catheter should be grasped a few centimeters proximal to the exit site. A 5 cm segment of catheter including the intradermal segment just distal to the insertion site should be cut off with sterile scissors and placed in a sterile container.
- In instances where the blood and catheter are cultured at the same time and the blood cultures are negative but the catheter culture is positive, antibiotics are generally not recommended, even for patients with valvular heart disease or immunosuppression.
  - The exception is patients whose catheter tips grow *S. aureus* and have negative blood cultures. These patients should receive 5–7 days of antibiotics.
  - All patients should be followed closely, and repeat cultures should be sent if clincally indicated.
- When a catheter-associated BSI is associated with catheter dysfunction, consider the possibility of suppurative thrombophlebitis.

Management

- Antibiotics should generally be withheld in febrile patients with intravenous catheters and no other clear source of infection pending the results of blood cultures. Exceptions include immunosuppressed or critically ill patients, patients with valve replacement or other hardware in place, or instances where there is pus at the catheter site.

Empiric treatment – immunosuppressed or critically ill patients

- Vancomycin (see dosing section, p. 138) ± [Cefepime 1 g IV Q8H OR Piperacillin/tazobactam 4.5 g IV Q6H]

  OR
- PCN allergy: Vancomycin (see dosing section, p. 138) ± Ciprofloxacin 400 mg IV Q8H

Empiric treatment – Gram-positive cocci in clusters in 2 or more sets of blood cultures

• Vancomycin (see dosing section, p. 138)

NOTE: The microbiology lab performs a coagulase and thermonuclease test on all Gram-positive cocci in clusters isolated from blood cultures within 3 hours. A note is placed in EPR if the tests are positive, indicating *S. aureus*. No EPR note is generated if the tests are negative, indicating coagulase-negative staphylococci in the majority of cases (90%). If a patient has one set of blood cultures growing Gram-positive cocci in clusters that are not coagulase-positive then treatment should be withheld and additional blood cultures obtained in the majority of situations.

Coagulase-negative staphylococci (CoNS)

NOTE: Single positive cultures of CoNS should NOT be treated unless they are confirmed by follow-up cultures, the patient is immunosuppressed and/or critically ill, or the patient has implanted hardware. In these cases, treatment can be started but repeat cultures should be sent PRIOR to initiation of therapy to confirm the diagnosis.

• Vancomycin (see dosing section, p. 138)

Change to

• Oxacillin 2 g IV Q4H if susceptible (preferred to Vancomycin)

Duration:

• 5–7 days if catheter removed (preferred)
• 10–14 days if catheter salvage attempt

Staphylococcus aureus

• Vancomycin (see dosing section, p. 138)

Change to

• Oxacillin 2 g IV Q4H if susceptible
OR
• Non-anaphylactic PCN allergy: Cefazolin 2 g IV Q8H
OR
• Anaphylactic PCN allergy or MRSA: Vancomycin (see dosing section, p. 138)

TREATMENT NOTES

• Remove catheter. High relapse rates if catheter is not removed.
• Vancomycin is inferior to Oxacillin for treatment of MSSA.
• Patients with *S. aureus* bacteremia should have an echocardiogram to rule out endocarditis. Transthoracic echo is acceptable only if the study adequately views the left-sided valves; most experts recommend TEE.
• 14 days is the minimum course of therapy for *S. aureus* bacteremia and should only be considered if endocarditis and other metastatic infection have been ruled out.
• Linezolid should not be used as monotherapy for treatment of *S. aureus* bacteremia

Enterococcus faecalis

NOTE: Can be contaminants. Draw repeat cultures to confirm before starting treatment. All *E. faecalis* blood isolates at JHH are susceptible to Ampicillin, which should be used unless the patient has a PCN allergy.

• Ampicillin 2 g IV Q4H ± Gentamicin 1 mg/kg IV Q8H (see treatment notes below)
OR
• PCN allergy: Vancomycin (see dosing section p. 138) ± Gentamicin 1 mg/kg IV Q8H (see treatment notes below)

Duration: 10–14 days

Enterococcus faecium

NOTE: Can be contaminants. Draw repeat cultures to confirm before starting treatment. The majority (78%) of *E. faecium* blood isolates at JHH are resistant to Vancomycin. If the isolate is susceptible to Ampicillin or Vancomycin, these agents should be used preferentially at the doses listed above for *E. faecalis* bacteremia.

• Linezolid 600 mg IV/PO Q12H
OR
• Quinupristin/dalfopristin 7.5 mg/kg Q8H

TREATMENT NOTES

• Consider echocardiogram if there is persistent bacteremia (> 3 days) on antibiotics.
• Do not use Gentamicin if the lab reports no synergy with a cell wall agent.
• If synergy is present, Gentamicin should be added to Ampicillin or Vancomycin in the treatment of endocarditis; however, the addition of Gentamicin does not appear to change outcomes in CA-BSI caused by Enterococcus in the absence of endocarditis if catheter has been removed.
• Do not use Gentamicin with Linezolid or Quinupristin/dalfopristin given lack of supportive evidence for synergy.

Gram-negative bacilli

• Cefepime 1 g IV Q8H
OR
• Piperacillin/tazobactam 4.5 g IV Q6H

5.5 Catheter-associated bloodstream infections

OR

• PCN allergy: Ciprofloxacin 400 mg IV Q8H

These are anti-pseudomonal doses. Lower the doses (Piperacillin/tazobactam 3.375 g IV Q6H, or Ciprofloxacin [400 mg IV Q12H or 500 mg PO Q12H]) if *Pseudomonas* is NOT recovered and organisms are NOT susceptible to agents with a narrower spectrum of activity.

Duration: 10–14 days

TREATMENT NOTES

• Catheters are less commonly the source of the infection; however, most advocate catheter removal if the catheter is the source.

Candida spp.

• Refer to p. 99 for treatment of candidemia

GENERAL TREATMENT NOTES ON CATHETER-ASSOCIATED BSIs

Microbiology – most common pathogens: Coagulase-negative staphylococci, Enterococci, *S. aureus*, Gram-negative bacilli, *Candida* species

Catheter salvage

• Catheter removal is STRONGLY recommended for infections with *S. aureus*, yeast and *Pseudomonas*, as the chance of catheter salvage is low and the risks of ongoing infection can be high.
• Catheters associated with tunnel infections CANNOT be salvaged and should be removed.
• Catheter salvage can be considered in CA-BSIs caused by coagulase-negative staphylococci if the patient is clinically stable.
• When catheter salvage is attempted, antibiotics should be given through the infected line.
• Duration of treatment for catheter salvage is similar to duration of treatment when the catheter is removed.
• Antibiotic lock therapy, in which an antibiotic is infused into the catheter and left in place, can be considered in the treatment of tunneled catheter infections due to less virulent pathogens such as CoNS and some Gram-negatives. Call the Antibiotic Management Program (7-4570) for details.

Reference:
IDSA Guidelines for the Diagnosis and Management of Intravascular Catheter-related Infections: Clin Infect Dis 2009;49:1-45.

Treatment of native valve endocarditis

NOTES:

• Beta-lactams are **highly preferable** to Vancomycin if the organism is susceptible and if the patient is not severely allergic. Some advocate PCN desensitization for allergic patients.
• Infectious Diseases consultation is advised for cases of left-sided infective endocarditis and prosthetic valve endocarditis, particularly in those in which the preferred antibiotic cannot be used or in which the organism is resistant to usual therapy.
• Therapeutic monitoring:
  • Vancomycin
    • Goal trough level: 15–20 mcg/mL
  • Gentamicin for Gram-positive synergy
    • Daily dosing
      • Goal trough level: <1 mcg/mL
    • Traditional dosing (Q8H)
      • Goal peak level: 3–4 mcg/mL
      • Goal trough level: <1 mcg/mL
  • See p. 132 and p. 138 for details

Viridans streptococci or *S. bovis* with PCN MIC ≤ 0.12 mcg/mL

• Penicillin G 3 million units IV Q4H for 4 weeks
OR
• Ceftriaxone 2 g IV/IM Q24H for 4 weeks
OR
• [Penicillin G 3 million units IV Q4H OR Ceftriaxone 2 g IV/IM Q24H for 2 weeks] PLUS Gentamicin 3 mg/kg IV Q24H for 2 weeks
OR
• PCN allergy: Vancomycin (see dosing section, p. 138) for 4 weeks

Criteria for 2 week treatment:
• Patient does not have cardiac or extracardiac abscess
• CrCl >20 mL/min
• Patient does not have impaired 8th cranial nerve function
• Patient does not have *Abiotrophia*, *Granulicatella*, or *Gemella spp.* infection

Viridans streptococci or *S. bovis* with PCN MIC > 0.12 mcg/mL and ≤ 0.5 mcg/mL

• [Penicillin G 4 million units IV Q4H OR Ceftriaxone 2 g IV/IM Q24H for 4 weeks] PLUS Gentamicin 3 mg/kg IV Q24H for the first 2 weeks of therapy

OR
- PCN allergy: Vancomycin (see dosing section, p. 138) for 4 weeks

Viridans streptococci or *S. bovis* with PCN MIC > 0.5 mcg/mL
- Treat as Enterococcal endocarditis

TREATMENT NOTES
- All patients with *S. bovis* endocarditis should undergo GI work-up to rule out underlying cancer.

***Staphylococcus aureus* – Methicillin susceptible, native valve, right-sided involvement only**
- Oxacillin 2 g IV Q4H for 2 weeks
  - Use Nafcillin for Oxacillin-induced hepatitis

Criteria for 2-week treatment:
  - ADEQUATE transthoracic echo (TTE) or transesophageal echo (TEE) to rule out left-sided involvement, as some series report a high frequency of left-sided disease
  - Treatment is with Oxacillin or Nafcillin
  - Patient does not have AIDS (CD4 < 200)
  - Patient does not have a vascular prosthesis (dialysis graft, etc)
  - Blood cultures are negative within 4 days after starting therapy
  - There is no evidence of embolic disease OTHER than septic pulmonary emboli
  - Vegetations are all < 2 cm in size
- If patient does not meet criteria for 2-week treatment, treat as MSSA, native valve, left-sided endocarditis
- Oral treatment with Ciprofloxacin 750 mg BID PLUS Rifampin 300 mg BID for 4 weeks has been effective in 2 studies BUT has never been studied in the outpatient setting where compliance may be problematic

***Staphylococcus aureus* – Methicillin susceptible, native valve, left-sided involvement**
- Oxacillin 2 g IV Q4H

  OR
- Non-anaphylactic PCN allergy: Cefazolin 2 g IV Q8H

  OR
- Anaphylactic PCN allergy: Strongly consider PCN desensitization or Vancomycin (see dosing section, p. 138)
- The addition of Gentamicin to a beta-lactam may help clear blood cultures faster but does not appear to affect mortality. It particularly should be avoided in the elderly and in those with baseline renal impairment.

***Staphylococcus aureus* – Methicillin resistant, native valve**
- Vancomycin (see dosing section, p. 138)

Duration
- Uncomplicated: 4 weeks
- Complicated (perivalvular abscess formation, metastatic complication, poor controlled diabetes mellitus, MRSA): 6 weeks
- ID and cardiac surgery consults recommended for complicated diseases

***S. pneumoniae*, and Group A streptococci**
- Penicillin G 3 million units IV Q4H for 4 weeks

  OR
- Ceftriaxone 2 g IV Q24H for 4 weeks

  OR
- Cefazolin 2 g IV Q8H for 4 weeks

  OR
- Anaphylactic PCN allergy: Vancomycin (see dosing section, p. 138) for 4 weeks
- For *S. pneumoniae*, if PCN MIC ≥ 0.1, consult ID

Groups B, C and G streptococci
- Penicillin G 3 million units IV Q4H for 4–6 weeks ± Gentamicin 3 mg/kg IV Q24H for the first 2 weeks of therapy

  OR
- Cefazolin 2 g IV Q8H for 4–6 weeks ± Gentamicin 3 mg/kg IV Q24H for the first 2 weeks of therapy

  OR
- Anaphylactic PCN allergy: Vancomycin (see dosing section, p. 138) for 4–6 weeks ± Gentamicin 3 mg/kg IV Q24H for the first 2 weeks of therapy
- Consider an ID Consult

Enterococci with PCN MIC ≤ 16 mcg/mL AND Gentamicin MIC ≤ 500 mcg/mL
- [Ampicillin 2 g IV Q4H OR Penicillin G 4 million units IV Q4H] PLUS Gentamicin 1 mg/kg IV Q8H BOTH for 4–6 weeks

  OR
- PCN allergy: Strongly consider PCN desensitization if PCN allergy is anaphylactic or Vancomycin (see dosing section, p. 138) PLUS Gentamicin 1 mg/kg IV Q8H BOTH for 4–6 weeks
- Treat for 4 weeks only when symptoms have been present for < 3 months AND there is a prompt response to therapy

- If PCN susceptible and Gentamicin resistant but Streptomycin susceptible, substitute Streptomycin 7.5 mg IV/IM Q12H for Gentamicin

Enterococci – PCN, Vancomycin, or Aminoglycoside resistant
- Consult ID

HACEK organisms (*Haemophilus parainfluenzae, H. aphrophilus, Actinobacillus actinomycetemcomitans, Cardiobacterium hominus, Eikenella corrodens, Kingella kingae*)

- Ceftriaxone 2 g IV/IM Q24H for 4 weeks
  OR
- Ampicillin/sulbactam 3 g IV Q6H for 4 weeks
  OR
- Anaphylactic PCN allergy: Consult ID

Gram-negative organisms, culture negative endocarditis, or fungal endocarditis
- Consult ID

Treatment of prosthetic valve endocarditis

- Generally caused by staphylococci in the first 1–2 years following valve replacement (both *S. aureus* and coagulase-negative staph). Etiologies are similar to native valve infections 2 or more years post-op.
- Medical treatment alone is often NOT effective.
- All patients should have a TEE.

Empiric therapy
- Vancomycin (see dosing section, p. 138) PLUS Gentamicin 1 mg/kg IV Q8H
  AND
- Rifampin 300 mg PO Q8H after blood cultures have cleared

Viridans streptococci or *S. bovis* with PCN MIC ≤ 0.12 mcg/mL
- [Penicillin G 4 million units IV Q4H OR Ceftriaxone 2 g IV/IM Q24H] for 6 weeks ± Gentamicin 3 mg/kg IV Q24H for first 2 weeks of therapy
  OR
- PCN allergy: Vancomycin (see dosing section, p. 138) for 6 weeks

Viridans streptococci or *S. bovis* with PCN MIC > 0.12 mcg/mL
- [Penicillin G 4 million units IV Q4H OR Ceftriaxone 2 g IV/IM Q24H] PLUS Gentamicin 3 mg/kg IV Q24H for 6 weeks

OR
- PCN allergy: Vancomycin (see dosing section, p. 138) for 6 weeks

***Staphylococcus aureus*—Methicillin susceptible**
- Oxacillin 2 g IV Q4H for 6 weeks PLUS Gentamicin 1 mg/kg IV Q8H for 1st 2 weeks of therapy
  AND
- Rifampin 300 mg PO Q8H for 6 weeks after blood cultures have cleared
- ID and cardiac surgery consults recommended

Staphylococcus aureus – Methicillin resistant or Coagulase-negative Staphylococci*
- Vancomycin (see dosing section, p. 138) for 6 weeks PLUS Gentamicin 1 mg/kg IV Q8H for the first 2 weeks of therapy
  AND
- Rifampin 300 mg PO Q8H for 6 weeks after blood cultures have cleared

* If coagulase-negative staphylococci is susceptible to Oxacillin with MIC ≤ 0.5, then treat as *S. aureus* – Methicillin susceptible.
- ID and cardiac surgery consults recommended

Gram-negative organisms or culture negative endocarditis
- Consult ID

DUKE CRITERIA FOR INFECTIVE ENDOCARDITIS

Diagnostic criteria (Modified Duke criteria)
Definite endocarditis
- Presence of 2 major criteria OR 1 major AND 3 minor OR 5 minor

Possible endocarditis
- Presence of 1 major AND 1 minor OR 3 minor criteria

Rejected endocarditis
- Firm alternate diagnosis that explains ALL manifestations of IE (**NOTE:** simply having another infection does NOT exclude endocarditis)

Major criteria
Microbiologic
- Two separate blood cultures positive for a typical organism: viridans streptococci, *S. bovis*, HACEK, *S. aureus*, *Enterococcus* spp.
- Persistent bacteremia with any organism as evidenced by: 2 positive blood cultures drawn at least 12 hours apart OR 3/3 positive blood cultures with at least 1 hour between the first and last OR the majority of more than 4 cultures positive from any time period.

- Positive *Coxiella burnetti* (Q fever) culture or serology.

Echocardiographic (TEE strongly recommended for prosthetic valve)

- Vegetation (on valve or supporting structure OR in path of regurgitant jet)
- Abscess
- New dehiscence of prosthetic valve

Physical exam

- NEW regurgitant murmur (worsening of old murmur is NOT sufficient)

Minor criteria

- Predisposing condition: previous endocarditis, injection drug use, prosthetic valve, ventricular septal defect, coarctation of the aorta, calcified valve, patent ductus, mitral valve prolapse with regurgitation, IHSS or other valvular heart disease
- Fever ≥ 38.0°C (100.4°F)
- Embolic events: arterial or pulmonary emboli, conjunctival hemorrhage, retinal hemorrhage, splinter hemorrhage, intracranial hemorrhage, mycotic aneurysm
- Immunologic phenomenon: Osler nodes, glomerulonephritis, positive rheumatoid factor
- Positive blood cultures that don't meet criteria above OR serologic evidence of active infection with an organism known to cause endocarditis BUT single positive cultures for coagulase-negative staphylococci are NOT considered even a minor criterion

References:
Oral therapy: Am J Med 1996; 101:68-76.
Short course therapy: Ann Intern Med 1994; 121:873-6.
Duke criteria: Clin Infect Dis 2000; 30:633-8.
AHA Scientific Statement on Infective Endocardits: Circulation 2005; 111(23):e394-434.
TEE in *S. aureus* bacteremia: J Am Coll Cardiol 1997; 30: 1072-8.

Meningitis – Empiric treatment

TREATMENT

- **ANTIBIOTICS SHOULD BE STARTED AS SOON AS THE POSSIBILITY OF BACTERIAL MENINGITIS BECOMES EVIDENT, IDEALLY WITHIN 30 MINUTES.**
- **DO NOT WAIT FOR CT SCAN OR LP RESULTS. IF LP MUST BE DELAYED, GET BLOOD CULTURES AND START THERAPY.**
- Adjust therapy once pathogen and susceptibilities are known.
- Some advocate penicillin desensitization for pathogen-specific therapy in patients with severe allergies (p. 118).
- **Antibiotic doses are higher for CNS infections (p. 57).**
- Infectious Diseases consultation is advised for all CNS infections, particularly those in which the preferred antibiotic cannot be used or in which the organism is resistant to usual therapy.

Empiric therapy

Host	Pathogens	Preferred Abx	Alternative for serious PCN allergy (ID consult recommended)
Immunocompetent*, age < 50	*S. pneumo, N. mening, H. influenzae*	Vancomycin PLUS Ceftriaxone	Chloramphenicol PLUS Vancomycin
Immunocompetent*, age > 50	*S. pneumo, Listeria, H. influenzae, N. mening, Group B streptococci*	Vancomycin PLUS Ceftriaxone PLUS Ampicillin	Chloramphenicol PLUS Vancomycin PLUS TMP/SMX
Immuno-compromised*+	*S. pneumo, N. mening, H. influenzae, Listeria,* (Gram-negatives)	Vancomycin PLUS Cefepime PLUS Ampicillin	Vancomycin PLUS TMP/SMX PLUS Ciprofloxacin
Post neurosurgery or penetrating head trauma	*S. pneumo* (if CSF leak), *H. influenzae, Staphylococci,* Gram-negatives	Vancomycin PLUS Cefepime	Vancomycin PLUS Ciprofloxacin
Infected shunt	*S. aureus,* coagulase-negative staphylococci, Gram-negatives (rare)	Vancomycin PLUS Cefepime	Vancomycin PLUS Ciprofloxacin

+ Immunocompromised is defined as HIV infection or AIDS, receiving immunosuppressive therapy, or after transplantation. In patients with HIV infection, nonbacterial causes of meningitis must be considered, particularly cryptococcal meningitis.

*** Use of Dexamethasone**

- Addition of dexamethasone is recommended in all adult patients with suspected pneumococcal meningitis (note that this will be most adult patients).
- Dose: 0.15 mg/kg IV Q6H for 2–4 days
- The first dose must be administered 10–20 minutes before or concomitant with the first dose of antibiotics.

- Administration of antibiotics should not be delayed to give dexamethasone.
- Dexamethasone should not be given to patients who have already started antibiotics.
- Continue dexamethasone only if the CSF gram stain shows Gram-positive diplococci or if blood or CSF grows *S. pneumoniae*

Pathogen-specific therapy

Pathogens	Preferred	Alternative for serious PCN allergy (ID consult recommended)
S. pneumo PCN MIC ≤ 0.06 µg/ml AND/OR Ceftriaxone MIC <0.5 µg/ml	Penicillin OR Ceftriaxone	Vancomycin OR Chloramphenicol*
S. pneumo PCN MIC >0.1–1 µg/ml AND Ceftriaxone MIC <1 µg/ml (ID consult recommended)	Ceftriaxone	Moxifloxacin OR Linezolid
S. pneumo PCN MIC > 1 µg/ml AND/OR Ceftriaxone MIC ≥1 µg/ml (ID consult recommended)	Ceftriaxone PLUS Vancomycin PLUS Rifampin	Moxifloxacin OR Linezolid
N. meningitidis PCN susceptible (MIC < 0.1)	Penicillin OR Ceftriaxone+	Chloramphenicol*
H. flu Non β-lactamase producer	Ampicillin OR Ceftriaxone	Chloramphenicol* OR Ciprofloxacin
H. flu β-lactamase producer	Ceftriaxone	Chloramphenicol* OR Ciprofloxacin
Listeria	Ampicillin ± Gentamicin‡	TMP/SMX
P. aeruginosa (ID consult recommended)	Cefepime OR Meropenem	Any 2 of the following: Ciprofloxacin, Tobramycin‡, Aztreonam
E. coli and other Enterobacteriaceae	Ceftriaxone ± Ciprofloxacin	Aztreonam OR Ciprofloxacin OR TMP/SMX
S. aureus–MSSA	Oxacillin	Vancomycin
S. aureus–MRSA	Vancomycin	
Coagulase-negative staphylococci if Oxacillin MIC ≤ 0.25	Oxacillin	Vancomycin
Coagulase-negative staphylococci Oxacillin MIC > 0.25	Vancomycin	
Enterococcus	Ampicillin PLUS Gentamicin‡	Vancomycin PLUS Gentamicin‡
Candida species	Amphotericin B	
Cryptococcus	Preferred: Amphotericin B +/- Flucytosine Alternative: Fluconazole	

* Consider penicillin desensitization
\+ Must give Ciprofloxacin 500 mg once to eradicate carrier state if PCN used as treatment
‡ Administer aminoglycosides systemically, not intrathecally

TREATMENT NOTES

Indications for head CT prior to LP
- History of CNS diseases (mass lesion, CVA)
- New-onset seizure (≤ 1 week)
- Papilledema
- Altered consciousness
- Focal neurologic deficit

Duration
- STOP treatment if LP culture obtained prior to antibiotic therapy is negative at 48 hours OR no PMNs on cell count
- *S. pneumoniae*: 10–14 days
- *N. meningitidis*: 7 days
- *Listeria*: 21 days
- *H. influenzae*: 7 days
- Gram-negative bacilli: 21 days

Adjunctive therapy
- Consider intracranial pressure monitoring in patients with impaired mental status.

Encephalitis

- Herpes viruses (HSV, VZV) remain the predominant causes of treatable encephalitis.
- CSF PCRs are rapid diagnostic tests and appear quite sensitive and specific.
- Have low threshold to treat if suspected as untreated mortality exceeds 70%.
- Treatment: Acyclovir 10 mg/kg IV Q8H for 14–21 days

Brain abscess

- Empiric treatment is guided by suspected source and underlying condition. While therapy should be adjusted based on culture results, anaerobic coverage should ALWAYS continue even if none are grown.

Source/ Condition	Pathogens	Preferred	Alternative for serious PCN allergy (ID consult recommended)
Unknown	*S. aureus*, Streptococci, Gram-negatives, Anaerobes	Vancomycin PLUS Ceftriaxone PLUS Metronidazole	Vancomycin PLUS Ciprofloxacin PLUS Metronidazole
Sinusitis	Streptococci (incl. *S. pneumoniae*), Anaerobes	[Penicillin OR Ceftriaxone] PLUS Metronidazole	Vancomycin PLUS Metronidazole
Chronic otitis	Gram-negatives, Streptococci Anaerobes	Cefepime PLUS Metronidazole	Aztreonam PLUS Metronidazole PLUS Vancomycin
Post neurosurgery	Staphylococci, Gram negatives	Vancomycin PLUS Cefepime	Vancomycin PLUS Ciprofloxacin
Cyanotic heart disease	Streptococci (esp. *S. viridans*)	Penicillin OR Ceftriaxone	Vancomycin

References:
IDSA Guidelines for Bacterial Meningitis: Clin Infect Dis 2004;39:1267.
Dexamethasone in adults with bacterial meningitis: N Eng J Med 2002;347:1549.

CNS shunt infection

Diagnosis

- Culture of cerebrospinal fluid remains the mainstay of diagnosis. Clinical symptoms may be mild and/or non-specific, and CSF chemistries and leukocyte counts may be normal.

Empiric Therapy

- Vancomycin (see dosing section, p. 138) PLUS Cefepime 2 g IV Q8H
  OR
- PCN Allergy: Vancomycin (see dosing section, p. 138) PLUS Ciprofloxacin 400 mg IV Q8H

TREATMENT NOTES

- **ID consult recommended for assistance with timing of shunt replacement and length of the antibiotic therapy.**
- Removal of all components of the infected shunt with external ventricular drainage or intermittent ventricular taps in combination with the appropriate intravenous antibiotic therapy leads to the highest effective cure rates. Success rates are substantially lower when the infected shunt components are not removed.
- The role of intraventricular antibiotics is controversial, and generally limited to refractory cases or cases in which shunt removal is not possible. Intraventricular injection should be administered only by experienced physicians.

References:
IDSA Guidelines for the Management of Bacterial Meningitis: Clin Infect Dis 2004;39:1267.
Therapy in cerebrospinal fluid shunt infection. Neurosurgery 1980;7:459.

Antimicrobial doses for CNS infections – normal renal function

Antibiotics

- Aminoglycosides: see section on "Traditional dosing of aminoglycosides" (p. 134)
- Ampicillin: 2 g IV Q4H
- Aztreonam: 2 g IV Q6H
- Ceftriaxone: 2 g IV Q12H
- Cefepime: 2 g IV Q8H
- Chloramphenicol: 1000–1500 mg IV Q6H (reduce dose for hepatic dysfunction)
- Ciprofloxacin: 400 mg IV Q8H (based on limited data)
- Moxifloxacin 400 mg IV Q24H
- Meropenem 2 g IV Q8H
- Metronidazole: 500 mg IV Q6H
- Oxacillin: 2 gm IV Q4H
- Penicillin: 4 million units IV Q4H (24 million units per day)
- Rifampin: 600 mg IV Q12–24H
- TMP/SMX: 5 mg/kg (TMP component) IV Q6H
- Vancomycin: load with 25–35 mg/kg, then 15–20 mg/kg Q8–12H (minimum 1 g Q12H)
  - Vancomycin should be administered to maintain serum trough concentrations close to 20 mcg/mL.

Antifungals

- Amphotericin 0.7–1 mg/kg IV Q24H
- AmBisome® 5 mg/kg IV Q24H
- Flucytosine 25 mg/kg PO Q6H

Intraventricular antibiotics (ID consult recommended)

- Amikacin 30 mg Q24H (contains preservative)
- Gentamicin 5 mg Q24H
- Tobramycin 5 mg Q24H
- Vancomycin 20 mg Q24H

5.7 Central nervous system infections

Pelvic inflammatory disease

- **Includes salpingitis, tubo-ovarian abscess and pelvic peritonitis.**
- **For treatment of post-operative peritonitis or wound infection, see p. 32 and p. 84.**

TREATMENT

Patient not severely ill

- Cefotetan 2 g IV Q12H PLUS Doxycycline* 100 mg PO BID
  OR
- PCN allergy (preferred): Clindamycin 600-900 mg IV Q8H PLUS Gentamicin (see dosing section or OB protocol)
  OR
- PCN allergy†: Moxifloxacin 400 mg PO ± Metronidazole 500 mg PO BID for 14 days

Patient severely ill

- Piperacillin/tazobactam 3.375 g IV Q6H PLUS Doxycycline* 100 mg PO BID for 14 days
  OR
- PCN allergy†: Moxifloxacin 400 mg IV Q24H PLUS Metronidazole 500 mg IV Q8H for 14 days

Step-down therapy once patient is afebrile

- Preferred: Doxycycline 100 mg PO BID ± [Clindamycin 450 mg PO QID **OR** Metronidazole 500 mg PO BID] to complete 14 days total
  OR
- Moxifloxacin† 400 mg PO ± Metronidazole 500 mg PO BID to complete 14 days total

* Azithromycin 500 mg IV once, then 250 mg PO daily x 6 days can be used in the case of Doxycycline contraindication or intolerance
† Given CDC recommendations to avoid use of fluoroquinolones for *N. gonorrhoeae* because of increased resistance, this regimen should be considered only if other regimens are contraindicated. Rates of resistance in Baltimore City are ~5%.

TREATMENT NOTES

Microbiology: *N. gonorrhoeae, C. trachomatis, Gardnerella* spp, *Ureaplasma urealyticum,* Anaerobes (*Prevotella* spp., *B. fragilis*), Gram-negative rods, Streptococci

Treatment of partners

- All women diagnosed with acute PID should be offered HIV testing.
- Male partners of women who have PID caused by C. *trachomatis* and/or *N. gonorrhoeae* often are asymptomatic.
- Sex partners (male or female) of patients who have PID should be examined and treated empirically for *C. trachomatis* and *N. gonorrhoeae* if they have had sexual contact with the patient during the 60 days preceding onset of symptoms in the patient, regardless of the pathogens isolated from the patient.

Endomyometritis

TREATMENT

- Same as for PID but no need for addition of Doxycycline/Azithromycin

Duration

- Treat until patient afebrile for 24–48 hours

Uncomplicated gonococcal urethritis, cervicitis, proctitis

TREATMENT

- Ceftriaxone 125 mg IM once
  OR
- Cefpodoxime 400 mg PO once
  OR
- Cefixime 400 mg PO once
  OR
- Severe PCN allergy ONLY: Ciprofloxacin 500 mg PO once (The patient must return for a test of cure if this regimen is used given emergence of fluoroquinolone resistance among *N. gonorrhoeae* isolates.)

TREATMENT NOTES

- Patients should also be treated for *C. trachomatis* with Doxycycline 100 mg PO BID for 7 days OR Azithromycin 1 g PO once.

References:
Sexually transmitted diseases treatment guidelines: CDC 2006.

Septic pelvic thrombophlebitis

Blood cultures will be positive in the vast majority of cases. Thus, **treatment should be tailored to the culture results.**

TREATMENT

For patients not already on antibiotics
- Cefotetan 2 g IV Q12H
  OR
- Ceftriaxone 1 g IV Q24H PLUS Metronidazole 500 mg IV Q8H
  OR
- PCN allergy: [Ciprofloxacin 400 mg IV OR 500 mg PO Q12H] PLUS Metronidazole 500 mg IV/PO Q8H

If patient has already been on broad-spectrum antibiotics
- Piperacillin/tazobactam 3.375 g IV Q6H

Special considerations in pelvic thrombophlebitis
- Addition of heparin is controversial. Consider if febrile after 72 hours on antibiotics
- Surgery may be needed for refractory cases

TREATMENT NOTES

Microbiology: Anaerobes, Streptococci, Enterobacteriaceae

Diagnosis
- Persistent bacteremia is a major clue to the diagnosis.
- Pelvic thrombophlebitis is generally associated with pregnancy or GYN procedures.
- CT scan is helpful for diagnosis.

COPD exacerbations

Uncomplicated
- Patient presenting with increased cough, sputum volume, sputum purulence, and dyspnea relative to baseline and none of the risk factors for complicated exacerbation.
  - Doxycycline 100 mg PO BID
    OR
  - TMP/SMX 1 DS tab PO BID
    OR
  - Amoxicillin 500 mg PO TID (see treatment notes below)

Complicated
- Patient presenting with increased cough, sputum volume, sputum purulence, and dyspnea relative to baseline and at least one of the following: FEV_1 < 50% predicted, more than 4 exacerbations in last 12 months, significant coronary artery disease or heart failure, use of home oxygen, chronic oral steroid use, or antibiotic use in the past three months.
  - Azithromycin 500 mg PO/IV Q24H
    OR
  - Amoxicillin/clavulanate 875 mg PO BID
    OR
  - Cefuroxime 750 mg IV Q8H

TREATMENT NOTES

Microbiology
- Predominantly *H. influenzae*, *M. catarrhalis*, *S. pneumoniae*
- Gram-negative enteric bacilli suspected only in complicated patients

Management
- At JHH 25% of *H. influenzae* are resistant to Amoxicillin; most *M. catarrhalis* isolates are beta-lactamase producers and resistant to Amoxicillin.
- Patients failing therapy should have sputum Gram-stain and culture.
- Empiric use of fluoroquinolones is discouraged and should only be considered if past or present microbiologic evidence indicates infection with a pathogen(s) that is resistant to standard therapy (e.g. *Pseudomonas spp.*, Enterobacteriaceae).
- IV antibiotics should only be used if the patient cannot tolerate PO antibiotics.
- Antibiotics are not indicated for asthma flares in the absence of pneumonia.

References:
American College of Physicians Position Paper: Ann Intern Med 2001; 134:600.
Canadian guidelines: Can Respir J. 2003; 10, Suppl B:3B.

Community-acquired pneumonia in hospitalized patients

TREATMENT

Empiric Treatment – patient NOT in the ICU

- Ceftriaxone 1 g IV Q24H PLUS Azithromycin 500 mg IV/PO once daily
  OR
- Moxifloxacin 400 mg IV/PO Q24H

In non-critically ill patients, consider switch to oral agents as soon as patient is clinically improving and eating (see next page for oral options and doses).

Empiric treatment – patient in the ICU

Not at risk for infection with *Pseudomonas* (see risks on next page)

- Ceftriaxone 1 g IV Q24H PLUS Azithromycin 500 mg IV Q24H
  OR
- PCN allergy: Moxifloxacin 400 mg IV Q24H

At risk for infection with *Pseudomonas* (see risks on next page)

- Piperacillin/tazobactam 4.5 g IV Q6H PLUS Azithromycin 500 mg IV Q24H (preferred if *Pseudomonas* most likely)
  OR
- Cefepime 1 g IV Q8H PLUS Azithromycin 500 mg IV Q24H (preferred if *S. pneumoniae* most likely)
  OR
- Severe PCN allergy: Moxifloxacin 400 mg IV Q24H PLUS Aztreonam 2 g IV Q8H
- Sputum gram stain may help determine if *Pseudomonas* is present.
- **Narrow coverage** ([Ceftriaxone PLUS Azithromycin] OR Moxifloxacin) if *Pseudomonas* is NOT present on culture at 48 hours.
- The benefits of combination therapy in the treatment of *Pseudomonas* are not well documented; if it is desired, then consider giving it for the first 5 days of therapy. Please see the section on "Combination therapy of Gram-negative bacterial infections" (p. 120).

Risks for *Pseudomonas*

- Prolonged hospital or long-term care facility stay (≥ 5 days)
- Structural disease of lung (e.g., CF, bronchiectasis)
- Steroid Rx (>10 mg prednisone/day)
- Broad-spectrum abx for >7 days in past month
- AIDS (CD4 < 50)
- Granulocytopenia (ANC < 500)

Other causes of pneumonia

- Suspected aspiration: additional empiric coverage for aspiration is justified only in classic aspiration syndromes suggested by loss of consciousness (overdose, seizure) PLUS gingival disease or esophogeal motility disorder. Ceftriaxone, Cefepime, and Moxifloxacin have adequate activity against most oral anaerobes. For classic aspiration, Clindamycin 600 mg IV Q8H can be added to regimens not containing Piperacillin/tazobactam.
- Community-acquired MRSA: Necrotizing pneumonia with cavitation in absence of risk factors for aspiration listed above is concerning for CA-MRSA pneumonia, particularly if associated with a preceding or concomitant influenza-like illness. In these cases, Linezolid 600 mg IV/PO Q12H can be added while awaiting culture data. Infectious diseases consult is strongly recommended. Use of Linezolid monotherapy for MRSA bacteremia, even if associated with a pulmonary source, is not recommended. In the absence of necrotizing pneumonia with cavitation, empiric coverage for CA-MRSA can be deferred until sputum and blood culture results return given their high diagnostic yield for CA-MRSA.

Pathogen-specific treatments and duration

- Susceptibility results should be considered when choosing an agent.
- *S. pneumoniae:* IV: Penicillin G OR Cefuroxime OR Ceftriaxone; PO: Amoxicillin OR Cefpodoxime OR Azithromycin. Treatment for 5–10 days based on clinical stability. Moxifloxacin should not be used routinely as step-down therapy for pneumococcal pneumonia if the organism is susceptible to beta-lactams.
- *L. pneumophila:* Azithromycin for 7–10 days OR Moxifloxacin for 10–21 days.
- *H. influenzae:* Doxycycline OR Amoxicillin/clavulanate OR Cefuroxime are preferred. Other options include Ceftriaxone OR Cefpodoxime OR Moxifloxacin. Treat for 5–10 days.
- *B. anthracis* or pneumonic plague or tularemia (**get ID consult, 3-8026;** see p. 130).

Empiric step-down therapy

In absence of microbiologic data, oral options may be selected based on initial regimen:

Initial	Step-down (preferred)	Step-down (alternate)
Ceftriaxone PLUS Azithromycin	Azithromycin	Doxycycline
Moxifloxacin	Moxifloxacin	Azithromycin OR Doxycycline

Doses of oral agents

Oral Agent	Dose	Duration*
Amoxicillin	1 g PO three times daily	5–10
Amoxicillin/clavulanate XR†	2 g PO twice daily	5–10
Azithromycin	500 mg PO once daily	5‡
Cefixime (suspension)	400 mg PO once daily	5–10
Cefpodoxime	200 mg PO twice daily	5–10
Cefuroxime axetil	500 mg PO twice daily	5–10
Doxycycline	100 mg PO twice daily	5–10
Moxifloxacin	400 mg PO once daily	5–7

*Treat for a minimum of 5 days (include therapy before oral switch). Therapy can be stopped after the patient is afebrile for 48–72 hours and has no more than one of the following signs and symptoms: HR > 100 beats/min, RR > 24 breaths/min, BP < 90 mmHg, 0_2sat < 90%, altered mental status. Therapy >5 days without a clinical reason should be avoided.
†Preferred for step-down therapy of aspiration pneumonia
‡Due to long half-life

TREATMENT NOTES

Diagnosis

- Immunocompetent patients MUST have a chest X-ray infiltrate to meet diagnostic criteria for pneumonia.
- Sputum and blood cultures should be sent on all patients admitted to the hospital BEFORE antibiotics are given.
- The legionella urine antigen is the test of choice for diagnosing legionella infection. However, this test detects only *L. pneumophila* serogroup 1, which is responsible for 70–80% of infections.

Resolution of symptoms

- Cough and chest X-ray abnormalities may take 4–6 weeks to improve. There is NO need to extend antibiotics if the patient is doing well otherwise (e.g., no fever).

Other considerations

- Consider Influenza during season (November through March) and test and treat appropriately (see p. 71).
- Consider anthrax infection in pneumonia patients with widened mediastinum on chest X-ray. Consult ID (3-8026) for diagnostic recommendations.

References:
IDSA/ATS Consensus Guidelines for CAP: Clin Infect Dis 2007;44:S27.

Healthcare-acquired pneumonia (NOT ventilator-associated)

NOTE: If the patient is on antibiotic therapy or has recently been on antibiotic therapy, choose an agent from a different class.

TREATMENT

Empiric treatment

No risk factors for infection with *Pseudomonas* (see risks below)

- Ceftriaxone* 1 g Q24H
  OR
- Moxifloxacin 400 mg IV/PO Q24H

At risk for infection with *Pseudomonas* (see risks below)

- Piperacillin/tazobactam* 4.5 g IV Q6H
  NOTE: lower dose to Piperacillin/tazobactam 3.375 g IV Q6H if *Pseudomonas* is NOT recovered
  OR
- Cefepime* 1g IV Q8H
  OR
- PCN allergy: Ciprofloxacin 400 mg IV Q8H PLUS Clindamycin 600 mg IV Q8H

* IF the patient is on immunosuppressive medications or is neutropenic, ADD Azithromycin 500 mg IV/PO Q24H to cover *Legionella*

Risk factors for *Pseudomonas* infection:

- Prolonged hospital or long-term care facility stay (≥ 5 days)
- Steroid use (> 10 mg prednisone per day)
- Broad spectrum antibiotics for > 7 days in past month
- Structural lung disease
- AIDS (CD4 < 50)
- Granulocytopenia (ANC < 500)

TREATMENT NOTES

Microbiology

- Gram-negative rods or Enterobacteriaceae (e.g. *Klebsiella, E.coli, Serratia*)
- Anaerobes
- *Legionella*
- *S. aureus* (MRSA and MSSA)
- *Pseudomonas* IF risk factors present (see above)
- Enterococci and candida species are often isolated from the sputum in hospitalized patients. In general, they should be considered to be colonizing organisms and should not be treated with antimicrobials.

Antimicrobial management of "aspiration events"

- Prophylactic antibiotics ARE NOT recommended for patients who are at increased risk for aspiration.
- Immediate treatment is indicated for patients who have small-bowel obstructions or are on acid suppression therapy given the increased risk of gastric colonization.
- Antibiotic treatment of patients who develop fever, leukocytosis and infiltrates in the 1st 48 hours after an aspiration is likely unnecessary since most aspiration pneumonias are chemical and antibiotic treatment may only select for more resistant organisms.
- Treatment IS recommended for patients who have symptoms for more than 48 hours or who are severely ill.

References:
Aspiration pneumonitis and aspiration pneumonia: N Engl J Med 2001;344(9):665.
ATS/IDSA Guidelines for HAP/VAP: AJRCCM 2005;171:388.

Ventilator-associated pneumonia (VAP)

- Sputum cultures should be obtained **PRIOR TO STARTING OR CHANGING ANTIBIOTICS** by endotracheal suction or invasive techniques. ET suction appears just as sensitive but less specific than invasive methods.
- **Empiric treatment MUST be narrowed as soon as sputum culture results are known.**
- If the patient is on antibiotic therapy or has recently been on antibiotic therapy, choose an agent from a different class.

Optimal treatment can likely be based on severity of illness as determined by the Clinical Pulmonary Infection Score (CPIS).

Calculating the Clinical Pulmonary Infection Score (CPIS)

	0 points	1 points	2 points
Temperature (°C)	36.5 to 38.4	38.5 to 38.9	≤ 36.4 or ≥ 39
Peripheral WBC	4,000 – 11,000	< 4,000 or > 11,000 *> 50% bands: add 1 extra point*	
Tracheal secretions	None	Non-purulent	Purulent
Chest X-ray	No infiltrate	Diffuse or patchy infiltrates	Localized infiltrate
Progression of infiltrate from prior radiographs	None		Progression (ARDS, CHF thought unlikely)
Culture of ET suction	No growth/light growth	Heavy growth *Same bacteria on gram stain: add 1 extra point*	
Oxygenation (PaO2/FiO2)	> 240 or ARDS		≤ 240 and no ARDS

TREATMENT

If the CPIS is ≤ 6

- VAP is unlikely.
- In a study by Singh et al, patients with a CPIS ≤ 6 received 3 days of a fluoroquinolone which was stopped at day 3 if the CPIS remained ≤ 6. These patients had NO increase in mortality or ICU stay, but they did develop fewer superinfections.
- Ciprofloxacin 400 mg IV Q12 for 3 days can be considered.

If the CPIS is > 6

- **Treatment MUST be narrowed based on culture results.**
- Vancomycin (see dosing section, p. 138) PLUS [Piperacillin/tazobactam 4.5 g IV Q6H* **OR** Cefepime 1 g IV q8H] ± Tobramycin (see dosing section, p. 132)
  OR
- PCN allergy: Vancomycin (see dosing section, p. 138) PLUS Ciprofloxacin 400 mg IV Q8H PLUS Tobramycin (see dosing section, p. 132)

*** This is an anti-pseudomonal dose. LOWER the dose (Piperacillin/tazobactam 3.375 g IV Q6H) if *Pseudomonas* is NOT recovered**

If the patient is immunocompromised, consider ADDING Azithromycin 500 mg Q24H to Piperacillin/tazobactam to cover *Legionella*

Tobramycin is recommended as a second agent to broaden empiric coverage rather than fluoroquinolones because of high rates of resistance to fluoroquinolones in the institution.

Antimicrobial therapy should be tailored once susceptibilities are known. Vancomycin should be stopped if resistant Gram-positive organisms are not recovered. Gram-negative coverage can be reduced to a single susceptible agent in most cases. The benefits of combination therapy in the treatment of *Pseudomonas* are not well documented; if it is desired, then consider giving it for the first 5 days of therapy. Please see the section on "Combination therapy of Gram-negative infections" (p. 120).

Duration

- **8 days** if the patient has clinical improvement
- If symptoms persist at 8 days consider alternative source and/or bronchoscopy with quantitative cultures
- VAP associated with *S. aureus* bacteremia should be treated for at least 14 days

TREATMENT NOTES

Microbiology

- *Staphylococcus aureus* (MRSA and MSSA), *Pseudomonas aeruginosa,* other Gram-negative bacilli, *Legionella*
- Enterococci and candida species are often isolated from the sputum in hospitalized patients. In general, they should be considered to be colonizing organisms and should not be treated with antimicrobials.

Diagnosis

- VAP is difficult to diagnose.
- Bacteria in endotracheal suction may represent tracheal colonization and NOT infection.
- Quantitative cultures of BAL fluid can help distinguish between colonization and infection; ≥ 10^4 cfu/ml is considered significant growth.

Other considerations

- Tracheal colonization of Gram-negatives and *S. aureus* is not eradicated even though lower airways are sterilized. Thus, post-treatment cultures in the absence of clinical deterioration (fever, rising WBC, new infiltrates, worsening ventilatory status) are not recommended.
- Inadequate initial treatment of VAP is associated with higher mortality (even if treatment is changed once culture results are known).

References:
ATS/IDSA Guidelines for HAP/HAV: AJRCCM 2005;171:388.
Clinical response to VAP: AJRCCM 2001;163:1371-1375.
VAP: Arch Intern Med 2000;160:1926-6.
Mini-BAL: Chest 1998;113:412-20.
CPIS score: Am Rev Respir Dis 1991;143:1121–1129.
Determining course of therapy using CPIS Score: Am J Respir Crit Care Med 2000; 162: 505, Intensive Care Med 2004; 30: 735–738.

Antibiotic selection and dosing for cystic fibrosis patients

- Therapy should be based on culture and susceptibility data when available; the agent with the narrowest spectrum of activity should be selected preferentially
- If possible, stop failing antibiotics when initiating new antibiotics
- High doses of antibiotics should be used to maximize lung penetration and reduce the risk of emergence of resistance (see below)

TREATMENT NOTES FOR SPECIFIC ORGANISMS

- ***Pseudomonas aeruginosa***
  - Piperacillin, Cefepime, and Ceftazidime should be used preferentially to Meropenem to minimize the induction of resistance to beta-lactams by Meropenem
  - These agents are generally combined with high-dose aminoglycosides based on *in vitro* evidence that there is synergy against *Pseudomonas*
  - For patients with penicillin allergy, Ciprofloxacin or Aztreonam can be combined with an aminoglycoside; desensitization to beta-lactams or carbapenems should be strongly considered
  - In patients intolerant or resistant to aminoglycosides, Colistin can be added
  - Continuous infusion of beta-lactams can be considered in some patients; call the Antibiotic Management Program (7-4570) to discuss
  - Inhaled Tobramycin and Colistin can be used as adjunctive therapy
- ***Stenotrophomonas maltophilia***
  - *S. maltophilia* isolated from sputum usually represents colonization.
  - If superinfection is suspected, TMP/SMX is the first line agent.
  - Minocycline (if susceptible) may be used in patients who are allergic or intolerant or resistant to TMP/SMX.
- ***Staphylococcus aureus***
  - *S. aureus* isolated from sputum can indicate colonization or infection.
  - Whether treating colonization with *S. aureus* in CF patients improves outcomes is an area of active research, although historically such colonization has not been successfully eradicated with antimicrobial therapy. If this is attempted, possible agents include Dicloxacillin, Cefazolin or Cephalexin for MSSA and Clindamycin, TMP/SMX, and Minocycline for MRSA.
  - Oxacillin is the drug of choice for MSSA pneumonia; Vancomycin or Linezolid can be used for MRSA pneumonia.

Antibiotic doses for cystic fibrosis infections – normal renal function

- Ceftazidime: 2 g IV Q8H
- Piperacillin: 4 g IV Q4H
- Piperacillin/tazobactam: 3.375 g IV Q4H
- Cefepime: 2 g IV Q8H
- Meropenem: 2 g IV Q8H
- Ciprofloxacin: 750 mg PO Q12H OR 400 mg IV Q8H
- Aztreonam: 2 g IV Q8H
- Ticarcillin/clavulanate: 3.1 g IV Q4H
- TMP/SMX for *S. maltophilia:* 5 mg/kg IV/PO Q8H
- TMP/SMX for *S. aureus:* 2 DS tablets PO BID
- Colistin: 3-6 mg/kg/day IV divided in 3 doses
- Inhaled Tobramycin (TOBI®): 300 mg Q12H
- Inhaled Colistin: 75-150 mg Q12H depending on the delivery system

Intravenous Tobramycin dosing and monitoring:

- Loading dose: 10 mg/kg/day given over 1 hour.
- Peak is recommended after first dose, 1 hour after the end of infusion with goal of 20-30 and trough at 23 hours with goal < 1 mcg/mL.
- Doses can be increased up to 12 mg/kg/day if adequate peaks are not achieved. If trough is too low or too high, interval should be changed.

Seasonal influenza diagnosis and management

Diagnosis:

- Respiratory virus testing should be considered in individuals with fever (T >38.0° C) and influenza-like symptoms of myalgia, arthralgia, headache, and/or sore throat.
- Information about specific diagnostic approaches can be found on the HEIC web site (www.hopkinsmedicine.org/heic)

Treatment for inpatients:

- Should be considered for confirmed cases with symptom onset in the past 48 hours.
- Consideration can be given to treating immunocompromised patients who are outside of the 48 hour window, although no data exist to show significant benefit at this point.
- Antiviral choice is dependent on the susceptibility of circulating strains which may vary from season to season (see www.hopkinsmedicine.org/amp for current recommendations).

Antiviral agents

Medication	Adult dosing	Side effects	Notes
Oseltamivir	**Treatment:** 75 mg PO twice a day for 5 days **Prophylaxis:** 75 mg PO once a day	Common: nausea, vomiting Severe: hypersensitivity, neuropsychiatric	Dose adjustment needed for GFR <30 mL/min
Zanamivir	**Treatment:** 10 mg (2 oral inhalations) twice daily for 5 days **Prophylaxis:** 10 mg (2 oral inhalations) once a day	Common: diarrhea, nausea, cough, headache, and dizziness Severe: bronchospasm, hypersensitivity, (laryngeal edema, facial swelling)	Should NOT be used in patients with chronic underlying airway diseases
Amantadine	**Treatment/Prophylaxis:** 100 mg PO twice a day or 200 mg once daily	Common: nervousness, anxiety, difficulty concentrating, lightheadedness, nausea Severe: hypersensitivity, neuropsychiatric	Dose adjustment needed for GFR <50 mL/min
Rimantadine	**Treatment/Prophylaxis:** < 65 y/o 100 mg PO twice a day ≥ 65 y/o 100 mg PO once daily	Common: nervousness, anxiety, difficulty concentrating, lightheadedness, nausea Severe: hypersensitivity, neuropsychiatric	Dose adjustment needed for GFR ≤ 10 mL/min and severe hepatic dysfunction

Infection Control:

- All individuals with suspected influenza infection should be placed on droplet precautions. A private room is required, unless patients are cohorted. When outside of their room (i.e. during transport) patients should wear a mask.
- All health care workers should receive the influenza vaccine yearly.
- Personnel with direct patient care or working in clinical areas who have not received the influenza vaccine are required to wear a mask when within 3 feet of a patient.
- Employees who are febrile or have flu-like symptoms must stay home. If they become sick while at work, they must go to Occupational Health Services.
- Employees who have cold symptoms, such as cough and runny nose, WITHOUT fever should wear a surgical mask during patient contact.
- If an unvaccinated HCW is exposed to a patient with documented influenza who was not on Droplet Precautions, notify HEIC and call Occupational Health (OH) immediately. OH will decide whether to recommend post-exposure prophylaxis.

Notes:

- These recommendations are meant to apply to inpatient care of patients with seasonal influenza.
- Recommendations on diagnosis and management of novel influenza strains will be provided by Antibiotic Management and HEIC as circumstances arise and may vary from those listed here.

Tuberculosis (TB) Infection

Definitions	
Acid fast bacilli (AFB)	Bacteria including *Mycobacterium tuberculosis* and non-tuberculous mycobacteria (NTM) that are detected in clinical specimens by direct microscopy using an acid-fast stain • Negative AFB smear does not rule out active TB; cultures may yield results after 6–8 weeks
Tuberculin skin test (TST)	Intradermal injection of purified protein derivative (PPD) and measurement of induration diameter in 48–72 hours for diagnosis of latent TB infection (also positive in most active TB cases). Criteria for a positive test are: • ≥ 5 mm – high risk of developing active TB (e.g. HIV infection, close contact of TB case, immunocompromised) • ≥ 10 mm – other risk factors for TB infection (HCW, IDU, DM) • ≥ 15 mm – no risk factors for TB
Latent TB infection (LTBI)	Previous infection with TB that has been contained by the host immune response • Patients may have a positive TST or suggestive radiographic findings such as calcified granulomata or minimal apical scarring, but do not have symptoms of active TB disease • Not infectious and does not require isolation
Active TB disease	Active replication of *M. tuberculosis* causing pulmonary or extrapulmonary symptoms and/or signs. • Confirmed by positive AFB smear, MTD test or culture • Requires airborne isolation

When to suspect active TB disease

High-risk individuals

- Recent exposure to a person with known TB; history of a positive TST; HIV infection; injection or non-injection drug use; foreign birth or residence in a region in which TB incidence is high; residents and employees of high-risk congregate settings (e.g. prisons); membership in a medically underserved, low-income population; anti-TNF alpha therapy

Clinical syndromes

- Cough of ≥2 wk duration, with at least one additional symptom, including fever, night sweats, weight loss, or hemoptysis
- Any unexplained respiratory illness of ≥2 wk duration in a patient at high risk for TB
- Any patient with HIV infection and unexplained cough and fever
- Any patient on anti-TNF alpha therapy with unexplained fever
- Community-acquired pneumonia which has not improved after 7 days of appropriate treatment
- Incidental findings on chest radiograph suggestive of TB (even if symptoms are minimal or absent) in a patient at high risk for TB

Radiographic findings

- Primary TB (often unrecognized): Can resemble CAP and involve any lobes; hilar adenopathy, pleural effusions are common; cavitation is uncommon. Findings often resolve after 1–2 months. These are common findings in patients with advanced HIV infection and TB.
- Reactivation TB: Infiltrates with or without cavitation in the upper lobes or the superior segments of the lower lobes; hilar adenopathy is variable; CT scan may have "tree-in-bud" appearance.

Diagnosis

- Patients with characteristic syndromes and radiographic findings should have expectorated sputum obtained for AFB smear and culture.
- Sensitivity of AFB smear on expectorated sputum is 50–70%; it is lower in HIV+ patients. Morning expectorated sputum, induced sputum, bronchoscopy have higher sensitivity. AFB culture of lower respiratory tract specimens is considered the gold standard.
- AFB smear and culture should be obtained regardless of CXR findings in patients with high clinical suspicion, HIV infection or other immunocompromised states. CXR is normal in approximately 10% of HIV-infected patients with pulmonary TB.

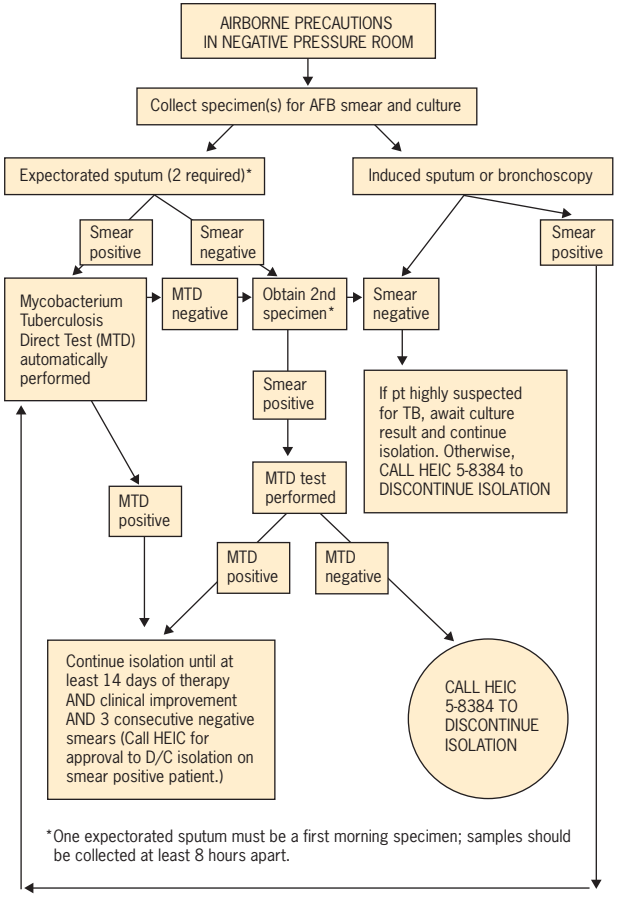
Infection prevention and control precautions

Airborne precautions are required in the following cases:

- Suspicion of disease sufficiently high to warrant obtaining sputum AFB smear/culture as described above
- Positive AFB smear or culture until diagnosis of TB vs. NTM is confirmed
- Known active pulmonary or laryngeal TB (if patient is currently on TB treatment, consult with HEIC and patient's local health department to obtain treatment history in order to determine if infectious at the time of current hospitalization; in meantime airborne precautions are required)

5.11 Tuberculosis (TB) infection

Algorithm when active TB is suspected



TREATMENT

Active TB

- ID consult is strongly recommended
- Therapy should be initiated for patients with positive AFB smear and clinical findings consistent with active TB.
- Therapy should be considered for patients with negative AFB smears when suspicion of TB is high and no alternate diagnosis exists. Multiple specimens should be obtained for culture prior to treatment.
- Four drugs are necessary for initial phase (2 months).
  - Isoniazid (INH) 300* mg (5 mg/kg) PO daily
  - Rifampin (RIF) 600* mg (10 mg/kg) PO daily
  - Pyrazinamide (PZA) 1000 mg PO daily (40–55 kg) OR 1500 mg PO daily (56–75 kg) OR 2000* mg PO daily (76–90 kg)
  - Ethambutol (EMB) 800 mg PO daily (40–55 kg) OR 1200 mg PO daily (56–75 kg) OR 1600* mg PO daily (76–90 kg)

  *Max dose regardless of weight.
- Pyridoxine 25 mg PO daily is recommended to prevent INH associated peripheral neuropathy in patients with HIV, malnutrition, alcohol abuse, diabetes mellitus, renal failure or in pregnant or breastfeeding women.

Latent TB

- Treatment for latent tuberculosis should not be started in the hospital setting without a clear follow-up plan.

Drug toxicity and monitoring

- Isoniazid: asymptomatic elevation in hepatic enzymes, serious and fatal hepatitis, peripheral neurotoxicity
- Rifampin: orange discoloration of body fluids, hepatotoxicity, pruritis with or without rash
- Pyrazinamide: hepatotoxicity, nongouty polyarthralgia, asymptomatic hyperuricemia, acute gouty arthritis
- Ethambutol: retrobulbar and peripheral neuritis
- Monitoring: baseline hepatic transaminases, bilirubin, alkaline phosphatase, creatinine and CBC are recommended for all adults initiating TB treatment. Monthly hepatic panel is recommended for patients with baseline abnormalities, history of liver disease or viral hepatitis, chronic alcohol consumption, HIV, IVDU, pregnancy or immediate post-partum state or those taking other potentially hepatotoxic medications. Therapy should be discontinued immediately if AST and ALT are >3 times the upper limit of normal (ULN) in the presence of jaundice or hepatitis symptoms or >5 times the ULN in the absence of symptoms.

References:
ATS/IDSA/CDC Guidelines for diagnosis of TB: Am J Respir Care Med 2000;161:1376.
ATS/IDSA/CDC Guidelines for treatment of TB: MMWR;52:RR-11.

Sepsis in the ICU patient with no clear source

NOTE: Refer to specific sections of these guidelines for empiric treatment recommendations for specific sources of infection

EMPIRIC TREATMENT

Cultures MUST be sent to help guide therapy.

- [Piperacillin/tazobactam 4.5 g IV Q6H **OR** Cefepime 1 g IV q8H] ± Vancomycin (see dosing section, p. 138) (if at risk for MRSA) ± Tobramycin (see dosing section, p. 132)
  OR
- Severe PCN allergy: [Aztreonam 2 g IV Q8H **OR** Ciprofloxacin 400 mg IV Q8H] PLUS Tobramycin (see dosing section, p. 132) PLUS Vancomycin (see dosing section, p. 138)

Risk factors for MRSA

- Central venous catheter in place
- Other indwelling hardware
- Known colonization with MRSA
- Recent (within 3 months) or current prolonged hospitalization > 2 weeks
- Transfer from a nursing home or subacute facility
- Injection drug use

TREATMENT NOTES

- For patients with renal insufficiency or aminoglycoside intolerance, a beta-lactam may be combined with a fluoroquinolone **IF** 2 agents are needed (see section on “double coverage” p. 120).
- Potential sources (e.g., pneumonia, peritonitis, etc.) should be considered when selecting therapy.
- Empiric therapy is ONLY appropriate while cultures are pending (72 hours max).
- Vancomycin should almost always be stopped if no resistant Gram-positive organisms are recovered in cultures.

Cellulitis

NOTE: The majority of cellulitis seen at JHH is associated with purulent drainage. The most common etiology of cellulitis with purulent drainage is *S. aureus*, although Group A streptococci and other streptococcal species can also present in this manner.

TREATMENT

The following regimens include coverage for MSSA, MRSA and streptococci:

Oral Regimens

- Clindamycin 300 mg PO TID
  OR
- TMP/SMX 1–2 DS tab PO BID PLUS Amoxicillin 500 mg PO TID*
  OR
- [Doxycycline 100 mg PO BID OR Minocycline 100 mg PO BID] PLUS Amoxicillin 500 mg PO TID*

*TMP/SMX, Doxycycline, and Minocycline have poor activity against Group A streptococci.

Parenteral regimens

- Clindamycin 600 mg IV Q8H (mild disease)
  OR
- Vancomycin (see dosing section, p. 138) (moderate to severe disease or nosocomial acquisition)

Duration: 7–10 days

TREATMENT NOTES

Microbiology

- *S. aureus* and Streptococci (especially group A)
- Rare causes of cellulitis are discussed below

Management

- Always elevate the affected extremity. Treatment failure is more commonly due to failure to elevate than failure of antibiotics.
- Improvement of erythema can take days, especially in patients with lymphedema, because dead bacteria in the skin continue to induce inflammation.
- The microbiology lab routinely tests *S. aureus* isolates for inducible Clindamycin resistance and this testing is reflected in the reported susceptibility data.
- Resistance to fluoroquinolones in *S. aureus* is common and develops quickly; > 85% of MRSA isolates are resistant to fluoroquinolones.

Monotherapy with fluoroquinolones for *S. aureus* infections is not recommended.
- Rifampin should NEVER be used as monotherapy because resistance develops rapidly.
- There is no evidence that Linezolid is superior to TMP/SMX, Doxycycline, or Clindamycin in the management of skin and skin-structure infection or osteomyelitis. Linezolid should only be considered when the *S. aureus* isolate is resistant to or the patient is intolerant of these agents.

Other causes of cellulitis in select patient populations
- With bullae, vesicles, and ulcers after exposure to seawater or raw oysters, consider *Vibrio vulnificus*, especially in patients with liver disease. Rare, but rapidly fatal if untreated. Treat with Ceftriaxone 1 g IV Q24H PLUS Doxycycline 100 mg PO BID.
- Neutropenic, solid organ transplant, and cirrhotic patients may have cellulitis due to Gram-negative organisms. Consider expanding coverage in these cases.
- If eschar, consider angioinvasive organisms (GNR, aspergillosis, mold). ID consult is recommended.
- Animal and human bites: *Pasteurella multocida* should be covered in cat and dog bites. Treat with Amoxicillin/clavulanate 875 mg PO BID OR Ampicillin/sulbactam 1.5–3 g IV Q6H. If PCN allergy: Moxifloxacin 400 mg PO/IV Q24H.

Cutaneous abscess

- Incision and drainage (I&D) is the primary treatment for a cutaneous abscess.
- Lesions that appear superficial can often have associated abscess formation that is not clearly appreciated without debridement of the wound or, on occasion, additional imaging.
- At the time of I&D, a sample should be obtained for culture and sensitivity testing.
- Most studies that have been published to date suggest that antibiotics are adjunct to I&D in the management of uncomplicated skin abscesses caused by CA-MRSA.
- Indications for antimicrobial therapy in patients with cutaneous abscesses:
  - Severe or rapidly progressive infections
  - The presence of extensive associated cellulitis
  - Signs and symptoms of systemic illness
  - Diabetes or other immune suppression
  - Advanced age
  - Location of the abscess in an area where complete drainage is difficult
  - Lack of response to incision and drainage alone
- Therapy should be given **before** incision and drainage in patients with prosthetic heart valves or other conditions placing them at high risk for endocarditis.

TREATMENT

If antibiotic treatment is thought to be necessary, regimens are the same as for cellulitis above. If CA-MRSA is strongly suspected, can consider not adding Amoxicillin to TMP/SMX, Doxycycline, or Minocycline.

Management of recurrent MRSA skin infections

1. **Education regarding approaches to personal and hand hygiene**
   - Practice frequent hand hygiene with soap and water and/or alcohol based hand gels, especially after touching infected skin or wound bandages.
   - Cover draining wounds with clean, dry bandages
   - Do not share personal items (e.g. razors; used towels and clothing before washing)
   - Regular bathing
   - Avoid all shaving
   - Launder clothing, sheets, towels in hottest suitable temperature
   - Clean all personal sporting clothing/equipment
2. **Decontamination of the environment**
   - Clean high touch areas in the bathroom with a disinfectant active against *S. aureus* daily (e.g. 10% dilute bleach).
3. **Topical decolonization (consider if a patient has ≥ 2 episodes in 1 year or other household members develop infection)**
   - Mupirocin twice daily for 5 days may be considered in patients with documented evidence of MRSA nasal colonization; Mupirocin therapy should be initiated after resolution of acute infection. Mupirocin should not be used in patients or patients' family members who are not documented to have MRSA nasal colonization.
   - Bathing or showering with chlorhexidine or hexachlorophine (or dilute bleach baths) every other day for 1 week then twice weekly; do not get these substances into ears or eyes
   - Systemic antibiotics are NOT recommended solely for decolonization
4. **Evaluation of other family members**
   - Intra-family transmission should be assessed and if present, all members should participate in hygiene and decolonization

5.13 Skin and soft-tissue infections

strategies above, starting at that same time and after the acute infection is controlled.

NOTE: Data on efficacy and durability of the decontamination and decolonization strategies described above are limited.

References:
TMP/SMX for MRSA: Ann Intern Med 1992;117:390-8.
Management of CA-MRSA: http://www.cdc.gov/ncidod/dhqp/ar_mrsa_ca.html.

Diabetic foot infections

TREATMENT

Treatment depends on clinical severity

Infection Severity	Clinical Manifestations
Uninfected	No purulence or inflammation*
Mild	Presence of purulence and ≥ 1 signs of inflammation* and cellulitis (if present) ≤ 2 cm around ulcer limited to skin or superficial subcutaneous tissue
Moderate	Same as mild PLUS at least one of the following: > 2 cm of cellulitis, lymphangitic streaking, spread beneath the superficial fascia, deep tissue abscess, gangrene, involvement of muscle, tendon, joint, or bone
Severe	Any of above PLUS systemic toxicity or metabolic instability

*erythema, pain, tenderness, warmth, induration

MILD INFECTIONS

Oral regimens

- Cephalexin 500 mg PO QID
  OR
- Clindamycin 300 mg PO TID (covers MRSA)
  OR
- Amoxicillin/clavulanate 875 mg PO BID

Parenteral regimens

- Clindamycin 600 mg IV Q8H (covers MRSA)
  OR
- Oxacillin 1-2 g IV Q4H
  OR
- Cefazolin 1 g IV Q8H

MODERATE INFECTIONS

- Cefotetan 1 g IV Q12H
  OR
- Ertapenem 1 g Q24H
  OR
- [Ciprofloxacin* 500 mg PO BID OR Ciprofloxacin* 400 mg IV Q12H] PLUS ONE of the following [Clindamycin 600 mg IV Q8H/300 mg PO TID OR Metronidazole 500 mg IV/PO TID]

* BUT avoid fluoroquinolones in patients who were on them as outpatients

If patient at risk for MRSA, add Vancomycin to regimens that do not include Clindamycin.

Risk factors for MRSA

- History of colonization or infection with MRSA
- Recent (within 3 months) or current prolonged hospitalization > 2 weeks
- Transfer from a nursing home or subacute facility
- Injection drug use

SEVERE INFECTIONS

- Pipercillin/tazobactam 4.5 g IV Q6H
  OR
- Ciprofloxacin* 400 mg IV Q12H PLUS Clindamycin 600 mg IV Q8H

* BUT avoid fluoroquinolones in patients who were on them as outpatients.

If patient at risk for MRSA (see above)

- Piperacillin/tazobactam 4.5 g IV Q6H PLUS Vancomycin (see dosing section, p. 138)
  OR
- Ciprofloxacin* 400 mg IV Q12H PLUS Metronidazole 500 mg IV Q8H PLUS Vancomycin (see dosing section, p. 138)

* BUT avoid fluoroquinolones in patients who were on them as outpatients

TREATMENT NOTES

Management

- A multidisciplinary approach to management should include wound care consultation, assessment of vascular supply, vascular and/or general surgery consultation and infectious diseases consultation.
- Consider necrotizing fasciitis in patients who are severely ill.
- Antibiotic therapy should be narrowed based on culture results.

Microbiology
- Cellulitis without open wound or infected ulcer, antibiotic naïve: beta-hemolytic streptococci, *S. aureus*
- Infected ulcer, chronic or previously treated with antibiotics: *S. aureus*, beta-hemolytic streptococci, Enterobacteriaceae
- Exposure to soaking, whirlpool, hot tub: usually polymicrobial, may involve *Pseudomonas*
- Chronic wounds with prolonged exposure to antibiotics: aerobic Gram-positive cocci (GPC), diptheroids, Enterobacteriaceae, other Gram-negative rods (GNR) including *Pseudomonas*
- Necrosis or gangrene: mixed aerobic GPC and GNR, anaerobes

Diagnosis
- Cultures of the ulcer base after debridement can help guide therapy. Biopsy of unexposed bone is NOT recommended. Avoid swabbing non-debrided ulcers or wound drainage.
- Ulcer floor should be probed carefully. If bone can be touched with a metal probe then the patient should be treated for osteomyelitis with antibiotics in addition to surgical debridement.
- Plantar fasciitis and a deep foot-space infection can be present. Consider imaging to look for deep infections.
- Putrid discharge is diagnostic of the presence of anaerobes.
- MRI is more sensitive and specific than other modalities for detection of soft-tissue lesions and osteomyelitis.

Duration
- Duration of treatment will depend on rapidity of response and presence of adequate blood supply.
- Likely need shorter treatment with adequate surgical intervention (7–10 days post-op) and longer for osteomyelitis.
- Change to oral regimen when patient is stable.

Reference:
IDSA Guidelines: Clin Infect Dis 2004;39:885-910.

Surgical-site infections (SSI)

TREATMENT

Infections following clean procedures (e.g. orthopedic joint replacements, open reduction of closed fractures, vascular procedures, median sternotomy, craniotomy, breast and hernia procedures)

- Oxacillin 1–2 g IV Q4H
  OR
- Cefazolin 1 g IV Q8H
  OR
- PCN allergy: Clindamycin 600 mg IV Q8H
  OR
- Involvement of hardware: Vancomycin (see dosing section, p. 138)

Exception: Saphenous vein graft harvest site infections should be treated with Cefotetan 1 g IV Q12H OR Ertapenem 1 g IV Q24H

Infections following contaminated procedures (GI/GU procedures, oropharyngeal procedures, obstetrical and gynecology procedures)

Patients not on broad-spectrum antibiotics at time of surgery and not severely ill
- Cefotetan 1 g IV Q12H
  OR
- Ertapenem 1 g IV Q24H
  OR
- PCN allergy: [Ciprofloxacin 500 mg PO BID OR Ciprofloxacin 400 mg IV Q12H] PLUS Clindamycin 600 mg IV Q8H

Patients on broad-spectrum antibiotics at time of surgery or severely ill
- Piperacillin/tazobactam 3.375 g IV Q6H ± Vancomycin (see dosing section, p. 138) (if hardware present or MRSA suspected)
  OR
- PCN allergy: Vancomycin (see dosing section, p. 138) PLUS [Ciprofloxacin 500 mg PO BID OR Ciprofloxacin 400 mg IV Q12H] PLUS Metronidazole 500 mg IV/PO Q8H

Deep fascia involvement
- Treat as necrotizing fasciitis (see subsequent section)

TREATMENT NOTES

Microbiology
- Following clean procedures (no entry of GI/GU tracts)
  - *Staphylococcus aureus*
  - Streptococci, group A (especially with early onset, < 72 hours)
  - Coagulase-negative staphylococci
- Following clean-contaminated and contaminated procedures (entry of GI/GU tracts with or without gross contamination)
  - Organisms above
  - Gram-negative rods
  - Anaerobes (consider *Clostridia* spp. in early-onset infection, 1–2 days)
- Generally, empiric use of Vancomycin is not indicated because the percentage of SSIs caused by MRSA is low at Johns Hopkins Hospital (10–20%)

5.13 Skin and soft-tissue infections

Risk factors for MRSA
- History of colonization or infection with MRSA
- Recent (within 3 months) or current prolonged hospitalization >2 weeks
- Transfer from a nursing home or subacute facility
- Injection drug use

Other management issues
- Many advocate that ALL infected wounds be explored both to debride and to assess depth of involvement.
- Superficial infections may be adequately treated with debridement alone.
- Deeper infections (cellulitis, panniculitis) need adjunctive antibiotics.
- Infections that extend to the fascia should be managed as necrotizing fasciitis.
- Patients with hypotension should have their wounds explored even if they are unremarkable on physical exam.

Serious, deep-tissue infections (necrotizing fasciitis)

THESE ARE SURGICAL EMERGENCIES!
ANTIBIOTICS ARE ONLY AN ADJUNCT TO PROMPT DEBRIDEMENT!
ID should also be consulted (3-8026)

TREATMENT (adjunct to surgery)
- Vancomycin (see dosing section, p. 138) PLUS [Piperacillin/tazobactam 3.375 g IV Q6H OR Cefepime 1 g IV Q8H] PLUS Clindamycin 600-900 mg IV Q8H
  OR
- PCN allergy: Vancomycin (see dosing section, p. 138) PLUS Ciprofloxacin 400 mg IV Q12H PLUS Clindamycin 600-900 mg IV Q8H

TREATMENT NOTES

Conventional nomenclature and microbiology
Pyomyositis
- *S. aureus* most commonly
- Clostridial myonecrosis – *Clostridia* spp. (esp. *C. perfringens*)
- Group A streptococcal myonecrosis

Fasciitis
- Type 1 – Polymicrobial infections with anaerobes, streptococci and Gram-negative rods (Fournier's gangrene is a type 1 necrotizing fasciitis of the perineum)
- Type 2 – Group A streptococci predominate
- Cases of fasciitis caused by community-associated MRSA strains have been reported

Diagnosis
- Can be difficult – gas production is not universal and is generally absent in streptococcal diseases.
- Maintain high index of suspicion when:
  - Patients are very ill from cellulitis (hypotension, toxic appearance)
  - Pain out of proportion to physical findings
  - Anesthesia over affected area
  - Risk factors such as diabetes, recent surgery or obesity
  - Findings such as skin necrosis or bullae
  - Putrid discharge with thin, "dishwater" pus
- CT scan can help with diagnosis but if suspicion is moderate to high, surgical exploration is the preferred diagnostic test. DO NOT delay surgical intervention to obtain CT.

5.13 Skin and soft-tissue infections

Bacterial urinary tract infections (UTI)

NOTES:

- The diagnosis of a UTI in inpatients can be difficult.
- Signs and symptoms, the presence of a urinary catheter, and the quality of specimen collection must be considered before initiation of treatment.
- Collection of cultures in the absence of signs and symptoms should be avoided.
- All recommendations are for empiric treatment; narrow coverage based on susceptibilities.

Management of patients WITHOUT a urinary catheter

NOTE: Ciprofloxacin has been removed as an empiric treatment recommendation for in-patients with non-catheter associated UTI at JHH due to the low rate of *E. coli* susceptibility (59%). Use of Ciprofloxacin can be considered in patients with known-susceptible isolates or with non-lactose fermenting organisms in the urine.

Category	Definition	Empiric treatment
Asymptomatic bacteriuria	Positive urine culture with no signs or symptoms	No treatment unless the patient is: • Pregnant • About to undergo a urologic procedure • Post renal transplant • Neutropenic
Acute cystitis	Signs and symptoms (e.g. dysuria, urgency frequency, suprapubic pain) AND pyuria (>5–10 WBC/hpf) AND positive urine culture ≥100,000 colonies	Uncomplicated: female, no urologic abnormalities, no stones, no catheter • TMP/SMX 1 DS tab PO Q12H for 3 days **OR** • Cephalexin 500 mg PO Q6H for 7 days **OR** • Nitrofurantoin (Macrobid®) 100 mg PO Q12H for 5 days (do NOT use in patients with CrCl <40 ml/min)
		Complicated: male gender, possible stones, urologic abnormalities, pregnancy Same regimens as above except duration is 7–14 days
Acute pyelonephritis	Signs and symptoms (e.g. fever, flank pain) AND pyuria AND positive urine culture ≥100,000 colonies Many patients will have other evidence of upper tract disease (i.e. leukocytosis, WBC casts, or abnormalities upon imaging)	Patient not severely ill • Ertapenem 1 g IV Q24H **OR** • Ceftriaxone 1 g IV Q24H • Duration 7–14 days
		Patient severely ill or hospitalized >48 H • Cefepime 1 g IV Q8H **OR** • PCN allergy: Aztreonam 1 g IV Q8H • Duration: 7–14 days
Urosepsis	SIRS with urinary source of infection	• Cefepime 1 g IV Q8H **OR** • PCN allergy: Aztreonam 1 g IV Q8H • Duration: 7–14 days

DIAGNOSIS

Specimen collection: The urethral area should be cleaned with an antiseptic cloth and the urine sample should be collected midstream or obtained by fresh catheterization. Specimens collected using a drainage bag or taken from a collection hat are not reliable and should not be sent.

Interpretation of the urinalysis (U/A) and urine culture

- Urinalysis and urine cultures must be interpreted together in context of symptoms
- **Urinalysis/microscopy:**
  - Dipstick
    - Nitrites indicate bacteria in the urine
    - Leukocyte esterase indicates white blood cells in the urine
    - Bacteria: presence of bacteria on urinalysis should be interpreted with caution and is not generally useful
  - Pyuria (more sensitive than leukocyte esterase): >5–10 WBC/hpf or >27 WBC/microliter

Urine cultures:

- If U/A is negative for pyuria, positive cultures are likely contamination
- Positive cultures with pyuria are defined as ≥100,000 (10^5) colonies. This cutoff is the most sensitive for a true UTI. Situations in which lower colony counts < 10^5 are significant include: patients who are already on antibiotics at the time of culture, symptomatic young women, suprapubic aspiration, and men with pyuria.

TREATMENT NOTES

- Sterile pyuria (positive U/A, but negative urine cultures) usually requires no treatment, although if the patient has received antibiotics, the patient may still have a UTI. If sterile pyuria persists consider other causes (e.g. interstitial nephritis or cystitis, fastidious organisms).
- Follow-up urine cultures or U/A are only warranted for ongoing symptoms. They should NOT be acquired routinely to monitor response to therapy.
- See below for discussion of treatment options for VRE and renal concentrations of antibiotics.

Management of patients WITH a urinary catheter

Category	Definition	Empiric treatment
Asymptomatic bacteriuria	Positive urine culture with no signs or symptoms of infection NOTE: obtaining routine cultures in asymptomatic patients is not recommended	Remove the catheter No treatment unless the patient is: • Pregnant • About to undergo a urologic procedure • Post renal transplant • Neutropenic Antibiotics do not decrease asymptomatic bacteriuria or prevent subsequent development of UTI
Catheter-associated UTI (CA-UTI)	Signs and symptoms (fever with no other source is the most common; patients may also have suprapubic or flank pain) AND pyuria (>5–10 WBC/hpf) AND positive urine culture ≥100,000 colonies (see information below regarding significant colony counts)	• Remove (PREFERRED) or replace catheter in all symptomatic patients Patient stable with no evidence of upper tract disease: • If catheter removed, consider observation alone **OR** • Ertapenem 1 g IV Q24H **OR** • Ceftriaxone 1 g IV Q24H **OR** • Ciprofloxacin 500 mg PO BID or 400 mg IV Q12H (avoid in pregnancy and in patients with prior exposure to quinolones) • Duration: see treatment notes below Patient severely ill, with evidence of upper tract disease, or hospitalized >48 H: • Cefepime 1 g IV Q8H **OR** • PCN allergy: Aztreonam 1 g IV Q8H • Duration: 7–14 days

DIAGNOSIS

Specimen collection: urine sample should be drawn in a sterile fashion from fresh catheter specimen. It should be drawn from either the catheter itself or through the port designed specifically for this purpose, **NOT** from the urine collection bag. Specimen collection is critical since colonization of the Foley bag or actual catheter is common.

Symptoms: Catheterized patients often lack typical symptoms of dysuria, although fever, suprapubic pain, and flank pain may still be present.

Interpretation of the urinalysis (U/A) and urine culture

- Pyuria**:** defined as >5–10 WBC/hpf or >27 WBC/microliter. In the presence of a catheter, pyuria or positive cultures are not always a reliable indicator of infection. Lack of pyuria suggests no active infection.
- Positive urine culture: ≥100,000 colonies is the most specific for true CA-UTI. Some experts state that ≥ 1,000 colonies represent significant bacteriuria; however, if this count is used, there should be a strong suspicion of CA-UTI based on symptoms and absence of infection at another site.

TREATMENT NOTES
- Remove catheter whenever possible
- The duration of treatment has not been well studied for CA-UTI.
- Assess the degree of illness, comorbidities, and clinical response to determine duration of therapy. As a general guide:
  - If the catheter is removed and the patient is not severely ill and has good response to treatment: 5–7 days
  - If catheter remains present or the patient is severely ill (e.g. urosepsis) or has pyelonephritis: 7–14 days

Treatment of Enterococci
- Almost all *E. faecalis* isolates are susceptible to Amoxicillin 500 mg PO TID OR Ampicillin 1 g IV Q6H and should be treated with these agents. For patients with PCN allergy: Nitrofurantoin (Macrobid®) 100 mg PO Q12H (do NOT use in patients with CrCl < 40 mL/min).
- *E. faecium* (often Vancomycin resistant)
  - Nitrofurantoin (Macrobid®) 100 mg PO Q12H if susceptible (do NOT use in patients with CrCl < 40 mL/min).
  - Tetracycline 500 mg PO Q6H if susceptible
  - Fosfomycin 3 g PO once (if female without catheter or catheter is removed; ask the micro lab for susceptibility)
  - Linezolid 600 mg PO BID OR Fosfomycin 3 g PO every 2–3 days (max 21 days) if complicated UTI or catheter can not be removed

Renal excretion/concentration of selected antibiotics
Good (≥60%): aminoglycosides, Amoxicillin, Amoxicillin/clavulanate, Fosfomycin, Cefazolin, Cefepime, Cephelexin, Ciprofloxacin, Colistin, Ertapenem, Trimethoprim/sulfamethoxazole, Vancomycin, Amphotericin B, Fluconazole, Flucytosine
Variable (30-60%): Cefpodoxime, Linezolid (30%), Doxycycline (29–55%), Ceftriaxone, Tetracycline (~60%)
Poor (<30%): Azithromycin, Clindamycin, Moxifloxacin, Oxacillin, Tigecycline, Micafungin, Posaconazole, Voriconazole

References:
Pyuria and urinary catheters: Arch Int Med 2000;160(5):673-77.
IDSA Guidelines for treatment of uncomplicated acute bacterial cystitis and pyelonephritis in women: Clin Infect Dis 1999;29:745.
European and Asian guidelines on management and prevention of CA-UTI: Int J Antimicrob Agents 2008; 31S:S68.

Resistant Gram-negative infections

Patients with infection or colonization with the resistant organisms listed below should be placed on CONTACT precautions (see isolation chart on p. 125)

Extended spectrum beta-lactamase (ESBL)-producing organisms
- ESBLs are enzymes that confer resistance to all penicillins, cephalosporins, and Aztreonam.
- They are most commonly seen in *K. pneumoniae* and *K. oxytoca, E. coli,* and *P. mirabilis*, and these organisms are automatically screened by the JHH microbiology lab for the presence of ESBLs.
- Risk factors for infection or colonization: recent hospitalization at an institution with a high rate of ESBLs, residence in a long-term care facility and prolonged use of broad spectrum antibiotics.

Treatment:
- Meropenem 1 g IV Q8H (2 g IV Q8H for CNS infections) should be used for ALL severe infections if the organism is susceptible.
- Ertapenem 1 g IV Q24H can be used for uncomplicated UTI or soft tissue infection with adequate source control if the organism is susceptible.
- Ciprofloxacin or TMP/SMX can be used as alternatives to Ertapenem for uncomplicated UTI or soft tissue infection with adequate source control if the organism is susceptible. Nitrofurantoin may also be used for uncomplicated UTI if the organism is susceptible.

Carbapenemase-producing Enterobacteriacae
- Carbapenemases are enzymes that confer resistance to all penicillins, cephalosporins, carbapenems and Aztreonam.
- Enterobacteriaceae are automatically screened by the JHH microbiology lab and a modified Hodge test is conducted to confirm the presence of carbapenemases.

Hodge test result	Susceptibility on panel	Reporting
Hodge test (+)	Resistant	Reported as resistant
Hodge test (+)	Susceptible or Intermediate	MIC only without interpretation*
Hodge test (-)	Susceptible, Intermediate or Resistant	Reported as tested, no carbapenemase production

*Infections caused by organisms that are modified-Hodge test positive in the susceptible or intermediate range may respond to extended infusions of Meropenem in combination with an aminoglycoside. Consult ID or Antibiotic Management for recommendations.

Treatment:
- If Hodge test (+) and Meropenem susceptible or intermediate: Meropenem 2 g IV Q8H infused over 3 hours PLUS aminoglycoside if MIC within susceptible or intermediate range.
- If carbapenem resistant and Colistin susceptible: Colistin 2.5 mg/kg IV Q12H can be used for serious infections
- Alternatives for Colistin-resistant organisms include aminoglycosides and Tigecycline (do not use either as monotherapy for bacteremia).

Multi-drug resistant (MDR) gram-negative organisms: defined as organisms susceptible to NO MORE than ONE of the following antibiotic classes: carbapenems, aminoglycosides, fluoroquinolones, penicillins, or cephalosporins. **Note:** susceptibility to sulfonamides, tetracyclines, polymixins, and Sulbactam are NOT considered in this definition

Treatment

MDR *Pseudomonas aeruginosa*	MDR *Acinetobacter baumannii/calcoaceticus complex*
• Anti-pseudomonal β-lactam PLUS aminoglycoside if synergy predicted or confirmed **OR** • Colistin (if susceptible)	• β-lactam PLUS aminoglycoside if synergy predicted or confirmed **OR** • Colistin (if susceptible) **OR** • Ampicillin/sulbactam (if susceptible) PLUS aminoglycoside (Sulbactam component has *in vitro* activity against *Acinetobacter* spp.) **OR** • Tigecycline (if susceptible; for infections other than bacteremia)

*Combination therapy should be considered in severe infections.

Synergy testing:
- Consult ID or Antibiotic Management to request synergy testing.
- If the organism is intermediate to a beta-lactam and susceptible to aminoglycosides, synergy can be assumed.
- If the organism is resistant to beta-lactams and susceptible or intermediate to aminoglycosides, request synergy testing.

Antibiotic doses for MDR and carbapenemase-producing infections – normal renal function
- Meropenem: 2 g IV Q8H, infuse over 3 hours
- Cefepime: 2 g IV bolus loading dose over 30 minutes, then 6 g IV as continuous infusion over 24 hours
- Ceftazidime: 2 g IV bolus loading dose over 30 minutes, then 6 g IV as continuous infusion over 24 hours
- Piperacillin/tazobactam: 3.375 g IV bolus loading dose over 30 minutes, then continuous infusion 3.375 g IV Q4H infused over 4 hours **OR** 4.5 g IV Q6H, infuse over 4 hours
- Piperacillin: 4 g IV bolus loading dose over 30 minutes, then continuous infusion 4 g IV Q4H infused over 4 hours
- Colistin: 2.5 mg/kg IV Q12H (for additional information, see p. 9)
- Ampicillin/sulbactam: 3 g IV Q4H (for MDR *A. baumannii* only)
- Aminoglycosides (for dosing, see p. 132)
- Tigecycline 100 mg IV once, then 50 mg IV Q12H (for MDR non-bacteremic *A. baumannii* only)

References:
ESBLs and clinical outcomes. Clin Infect Dis 2006:42;S164.
Current therapies for *P. aeruginosa*. Crit Care Clin 2008;24:261.
MMWR: Guidance for control of infections with carbapenem – resistant or carbapemase – producing *Enterobacteriaceae* in acute care facilities; 2009, March; 58(10): 256-260.

5.15 Resistant Gram-negative infections

Candidiasis in the non-neutropenic patients

Oropharyngeal disease (thrush)

Initial treatment
- Clotrimazole 10 mg troche 5 times a day

OR
- Nystatin suspension 500,000 units/5mL 4 times a day

Recurrent or intractable disease
- Fluconazole 100–200 mg PO once daily

Duration: 5–10 days

NOTE: If refractory to Fluconazole consider fungal culture and susceptibilities

Esophageal candidiasis

Initial treatment
- Fluconazole 200–400 mg IV/PO once daily

Duration: 14–21 days

Relapse
- Fluconazole 400–800 mg IV/PO once daily

Refractory to Fluconazole 800 mg daily (fungal culture and susceptibilities are recommended)
- Micafungin 150 mg IV once daily

OR
- Amphotericin B 0.3–0.7 mg/kg IV once daily

OR
- Oral therapy: Itraconazole oral solution 200 mg daily

Duration: 14–21 days

Candiduria

- Urinary catheter removal will resolve the candiduria in 40% of cases.

TREATMENT

Asymptomatic cystitis
- Therapy not usually indicated
- Consider in the following conditions (see regimens under "symptomatic cystitis"):
  - Neutropenic patients
  - Renal transplant
  - Urinary obstruction or abnormal GU tract
  - When recovered in urine prior to urologic procedures
  - When recovered in urine prior to surgery to implant hardware (joints, valves, etc.)

Symptomatic cystitis

Preferred therapy
- Fluconazole 200 mg IV/PO once daily

Duration: 7–14 days

Fluconazole-resistant organism suspected or confirmed
- Amphotericin B 0.3-0.6 mg/kg IV once daily

Duration: 1–7 days

Pyelonephritis

NOTE: Candida pyelonephritis is usually secondary to hematogenous spread except for patients with renal transplant or abnormalities of the urogenital tract.

Preferred therapy
- Fluconazole 200–400 mg IV/PO once daily

Duration: 14 days

Fluconazole-resistant organism suspected or confirmed
- Amphotericin B 0.5–0.7 mg/kg IV once daily

OR
- Micafungin 100 mg IV once daily

Duration: 14 days

TREATMENT NOTES

- Remove urinary catheter if possible.
- Therapy of candiduria in the non-neutropenic, non-ICU catheterized patient has not been shown to be beneficial and promotes resistance.
- AmBisome®, Voriconazole, Itraconazole, and Posaconazole are not recommended due to poor penetration into the urinary tract.
- Micafungin penetrates poorly in the urine, but does penetrate into renal tissue.
- Amphotericin B bladder washes are not recommended.

Candida vaginitis

Initial Therapy
- Fluconazole 150 mg PO X 1 dose

OR
- Miconazole 2% cream 5 g intravaginally once daily X 7 days

Recurrent (> 4 episodes/year of symptomatic infection)
- Fluconazole 150 mg PO Q72H X 3 doses, then 150 mg a week X 6 months

Candidemia

- YEAST IN A BLOOD CULTURE SHOULD NOT BE CONSIDERED A CONTAMINANT.

NOTE: Micafungin does not have activity against Cryptococcus

TREATMENT

Unspeciated candidemia

Patients who are clinically stable and have not received prior long-term azole therapy
- Fluconazole 800 mg IV/PO X 1 dose, then 400 mg IV/PO once daily

Patients who are NOT clinically stable due to Candidemia or have received prior long-term azole therapy
- Micafungin 100 mg IV once daily

If the yeast is *C. albicans* or *C. glabrata* based on PNA FISH results, follow the recommendations for *C. albicans* or *C. glabrata* noted below. Otherwise, await speciation before modifying therapy as recommended below, unless the patient becomes clinically unstable on Fluconazole.

Candida albicans
- Fluconazole 800 mg IV/PO X 1 dose, then 400 mg IV/PO once daily

Patients who are NOT clinically stable due to Candidemia or have received prior long-term azole therapy
- Micafungin 100 mg IV once daily

Patients should be transitioned to Fluconazole once stable.

Candida glabrata
- Micafungin 100 mg IV once daily

OR
- Fluconazole 800 mg IV/PO X 1 dose, then 400 mg IV/PO once daily IF the isolate is susceptible with MIC ≤ 8 mcg/mL and the patient is stable.

If isolate is intermediate to Fluconazole and oral therapy is desired, consult ID. Other azoles such Voriconazole should not be used in Fluconazole-resistant strains due to the same mechanism of resistance.

Candida krusei
- Micafungin 100 mg IV once daily

Fluconazole should NEVER be used to treat infections due to *C. krusei* because the organism has intrinsic resistance to Fluconazole. This mechanism of resistance is not shared with Voriconazole; therefore, oral Voriconazole can be used if isolate is susceptible (for dosing see Voriconazole specific guidelines, p. 20).

Candida lusitaniae

• Fluconazole 800 mg IV/PO X 1 dose, then 400 mg IV/PO once daily

C. lusitaniae is resistant to Amphotericin B in approximately 20% of cases.

Candida parapsilosis

• Fluconazole 800 mg IV/PO X 1 dose, then 400 mg IV/PO once daily

Fluconazole-intermediate isolate

• Fluconazole 800 mg IV/PO once daily

Fluconazole-resistant isolate

• Micafungin 100 mg IV once daily

If the patient is not responding to Micafungin then consider changing to Amphotericin B. The minimum inhibitory concentrations (MICs) of echinocandins are higher for *C. parapsilosis* than any other *Candida spp.*; this has led to concern that some infections with *C. parapsilosis* may not respond well to echinocandins.

Candida tropicalis

• Fluconazole 800 mg IV/PO X 1 dose, then 400 mg IV/PO once daily

Fluconazole-intermediate isolate

• Fluconazole 800 mg IV/PO once daily

Fluconazole-resistant isolate

• Micafungin 100 mg IV once daily

TREATMENT NOTES

Amphotericin B use in Candidemia

• Amphotericin B is highly effective against all *Candida* spp. except for *C. lusitaniae*; however, azoles and echinocandins are favored in susceptible strains over Amphotericin B products due to toxicity.

Doses for Candidemia

• Amphotericin B 0.7 mg/kg IV once daily
OR
• AmBisome® 3 mg/kg IV once daily (if patient cannot tolerate conventional Amphotericin B)

Duration

• 14 days following documented clearance of blood cultures and clinical symptoms
• Patients with persistent candidemia and/or metastatic complications (e.g. endophthalmitis, endocarditis) need a longer duration of therapy and evaluation by Ophthalmology and ID.

Microbiology

Fluconazole susceptibilities (%) of fungal isolates in blood at JHH, 8/2007–4/2009

Organism	#	S (%)	I (%)	R (%)
C. albicans	30	100	0	0
C. glabrata	35	31	54	15
C. parapsilosis	14	100	0	0
C. tropicalis	10	80	10	10

S – susceptible (MIC ≤ 8); I – intermediate (MIC = 16-32); R – resistant (MIC ≥ 64)

Non-pharmacologic management

• Removal of all existing central venous catheters is highly recommended.
• Patients should have blood cultures daily or every other day until candidemia is cleared.
• Patients should have an ophthalmologic examination to exclude candidal endophthalmitis prior to discharge, preferably once the candidemia is controlled.
• Echocardiography can be considered if the patient has persistent candidemia on appropriate therapy.

Endophthalmitis

• Management in conjunction with Ophthalmology
• Due to poor CNS and vitreal penetration, treatment with echinocandins is NOT recommended.

Preferred therapy

• Amphotericin B 1 mg/kg IV once daily ± Flucytosine 25 mg/kg PO Q6H
OR
• AmBisome® 5 mg/kg IV once daily ± Flucytosine 25 mg/kg PO Q6H

Alternate therapy

• Fluconazole 400-800 mg/kg IV/PO once daily ± Flucytosine 25 mg/kg PO Q6H

Duration: 4–6 weeks

Endocarditis

Consultation with ID and Cardiac Surgery is recommended. Surgical valve replacement is considered a critical component for cure. If the patient is not a candidate for surgery then life-long Fluconazole suppression is likely required.

5.16 Candidiasis in the non-neutropenic patient

Preferred therapy
- Amphotericin B 1 mg/kg IV once daily
  OR
- AmBisome® 5 mg/kg IV once daily

Alternative therapy
- Micafungin 150 mg IV once daily

Duration: 6 weeks or longer

Notes on antifungal susceptibility testing
- Susceptibility testing for Fluconazole, Itraconazole, Voriconazole, Flucytosine, and Micafungin is performed routinely on the first yeast isolate recovered from blood.
- Fluconazole and Micafungin susceptibility are reported on all isolates.
- Susceptibility testing for conventional Amphotericin B is done routinely for *C. lusitaniae* and *C. guillermondii*, and for other organisms by request.
- If the organism is intermediate (I) to Fluconazole, then 800 mg IV/PO once daily can be used. This choice is NOT recommended in an immunocompromised patient, in a patient who is clinically unstable due to candidemia, in a patient with *C. glabrata* candidemia or in patients with endocarditis, meningitis or endophthalmitis.
- Susceptibility testing should be considered when:
  - Mucocutaneous candidiasis is refractory to Fluconazole
  - Treating osteomyelitis, meningitis, or endophthalmitis with Fluconazole
  - Blood cultures are persistently positive on Fluconazole
- Non-routine susceptibility testing can be arranged by calling the mycology lab at 5-6148

References:
IDSA Guidelines for Treatment of Candidiasis: Clin Infect Dis 2009;48:503-535.

Fluconazole prophylaxis

Pending further research, Fluconazole prophylaxis should be limited to the following settings:
- Patients expected to remain in the **SICU or WICU** for ≥ 72 hours (Criteria from Hopkins SICU prophylaxis study; prophylaxis in other ICUs has NOT been studied and is NOT recommended).
- Neutropenic patients undergoing bone marrow transplantation (see p. 99).
- Patients who are post-op from liver or pancreas transplants.

Dose and route
- ALL treatment should be **PO or per feeding tube.** IV prophylaxis is NOT recommended (based on Hopkins study).
- Fluconazole 800 mg PO load then 400 mg PO once daily. IF creatinine clearance less than 25 mL/min, then maintenance dose is 200 mg PO once daily.

Duration
- For SICU and WICU patients, **prophylaxis should be stopped on transfer out of the unit.**

TREATMENT NOTES

- Fluconazole prophylaxis has been ineffective in some groups and should be limited to those listed above.
- Use of Fluconazole has led to the emergence of resistant *Candida spp.*

Reference:
Fluconazole prophylaxis in surgical patients: Ann Surg 2001;233:542.

Pre-operative and pre-procedure antibiotic prophylaxis

Drug	Usual dose	Redosing during procedure
Cefazolin	2 g	Q4H (Q2H for cardiac surgery)
Cefotetan	2 g	Q8H
Clindamycin	600 mg	Q8H
Ciprofloxacin	400 mg	Q8H
Gentamicin	5 mg/kg	None
Metronidazole	500 mg	Q8H
Vancomycin	< 70 kg: 1 g 71-99 kg: 1.25 g > 100 kg: 1.5 g	Q12H

Important notes

- **Timing is crucial. Antibiotics must be in the skin when the incision is made to be effective. They should be given NO more than 1 hour before the procedure.**
- Cephalosporins can be administered over 3–5 min IV push just before the procedure and will achieve appropriate skin levels in minutes. Vancomycin and Ciprofloxacin must be given over ONE HOUR and must be COMPLETELY infused before the incision is made. Clindamycin should be infused over 10–20 min.
- Post-procedure doses are generally NOT needed (exceptions are noted in table). Single doses pre-procedure have been as effective as post-procedure doses in all studies.
- Patients receiving pre-operative antibiotics generally do NOT need additional antibiotics for endocarditis prophylaxis.
- Prophylaxis for patients already on antibiotics:
  - For antibiotics other than Vancomycin: Hold standing dose until 1 hour before incision
  - For Vancomycin: Redose a full dose if 8 hours have passed since the last dose or a half dose if fewer than 8 hours have passed in patient with normal renal function

Procedure	Pre-op prophylaxis recommendations
Urologic surgery	
Transrectal prostate biopsy	Cefotetan PCN allergy: Ciprofloxacin
Transurethral surgery (e.g. TURP, TURBT, ureteroscopy, cystouretoscopy)	Cefazolin PCN allergy: Gentamicin
Lithotripsy	Cefazolin PCN allergy: Gentamicin
Nephrectomy or radical prostatectomy	Cefazolin PCN allergy: Clindamycin
Radical cystectomy, cystoprostatectomy or anterior exenteration	Cefotetan PCN allergy: Clindamycin PLUS Gentamicin
Penile or other prostheses	Cefazolin OR [Vancomycin ± Gentamicin] PCN allergy: [Clindamycin OR Vancomycin] ± Gentamicin
Head and neck surgery	
Major procedure with incision of oral or pharyngeal or sinus mucosa	Cefotetan or Clindamycin PCN allergy: Clindamycin
Major neck dissection or parotid dissection	Cefazolin PCN allergy: Clindamycin
Thyroid/parathyroid surgery	Prophylaxis not recommended
Tonsillectomy	Prophylaxis not recommended
Cardiac surgery/procedure	
Median sternotomy/uncomplicated heart transplant	Cefazolin PCN allergy: Vancomycin ± Gentamicin
Median sternotomy/heart transplant – previous VAD or MRSA colonization/infection	Cefazolin PLUS Vancomycin PCN allergy: Vancomycin ± Gentamicin
Pacemaker placement	Cefazolin PCN allergy: Clindamycin
Lung transplant	Piperacillin/tazobactam 4.5 g IV Q6H PCN allergy: Vancomycin PLUS Ciprofloxacin If CF patient: please confirm with transplant ID
LVAD/BIVAD placement	Vancomycin PLUS Ciprofloxacin PLUS Fluconazole for 48 hours
Vascular surgery	
All procedures	Cefazolin PCN allergy: Vancomycin Prophylaxis not recommended for carotid surgery unless risk of infection thought to be high
Thoracic surgery	
All cases except esophageal	Cefazolin PCN allergy: Clindamycin
Esophageal cases	Cefotetan PCN allergy: Clindamycin
Neurosurgery	
Craniotomy (including shunt placement)	Cefazolin PCN allergy: Clindamycin
Spinal fusion	Cefazolin PCN allergy: Clindamycin OR Vancomycin
Laminectomy	Cefazolin PCN allergy: Clindamycin

Procedure	Pre-op prophylaxis recommendations
Gynecologic surgery	
Cesarean section	Cefazolin PCN allergy: Clindamycin
Hysterectomy (abdominal or vaginal)	Uncomplicated: Cefazolin Complicated: Cefotetan PCN allergy: Clindamycin PLUS Gentamicin
Repair of cystocele or rectocele	Cefazolin PCN allergy: Clindamycin
Orthopedic surgery	
Joint replacement	Cefazolin PCN allergy: Vancomycin
Open reduction of fracture	Cefazolin PCN allergy: Vancomycin
Lower limb amputation	Cefotetan PCN allergy: Clindamycin PLUS Gentamicin
Spinal fusion	Cefazolin PCN allergy: Clindamycin OR Vancomycin
Laminectomy	Cefazolin PCN allergy: Clindamycin
Arthroscopic surgery	No data to support prophylaxis
General surgery	
Inguinal hernia repair	Uncomplicated: Prophylaxis not recommended Complicated, recurrent, or emergent: Cefotetan PCN allergy: Clindamycin ± Gentamicin
PEG	Cefazolin OR Cefotetan PCN allergy: Clindamycin ± Gentamicin
Gastrectomy/hepatectomy/ cholecystectomy	Cefotetan PCN allergy: Clindamycin ± Gentamicin
Small bowel or colon surgery	Cefotetan PCN allergy: Clindamycin PLUS Gentamicin
Whipple procedure or pancreatectomy	Cefotetan PCN allergy: Clindamycin PLUS Ciprofloxacin
Appendectomy (uncomplicated), if complicated or perforated, treat as secondary peritonitis	Cefotetan PCN allergy: Clindamycin PLUS Gentamicin
Penetrating abdominal trauma	Cefotetan PCN allergy: Clindamycin PLUS Gentamicin
Mastectomy	Prophylaxis not recommended
Mastectomy with lymph node dissection	Cefazolin PCN allergy: Clindamycin
Plastic surgery	
Tissue expander insertion/all flaps	Cefazolin PCN allergy: Clindamycin
Rhinoplasty	No prophylaxis OR Cefazolin PCN allergy: No prophylaxis OR Clindamycin

Procedure	Pre-op prophylaxis recommendations
Transplant surgery	
Pancreas or pancreas/kidney transplant	Cefotetan PCN allergy: Clindamycin PLUS Ciprofloxacin
Renal transplant/adult live donor	Cefazolin PCN allergy: Clindamycin
Liver transplant	Cefotetan PCN allergy: Clindamycin PLUS Ciprofloxacin
Interventional radiology procedures	
Biliary/GI procedures	Cefotetan PCN allergy: Gentamicin PLUS Metronidazole
Liver chemoembolization or percutaneous ablation with history of biliary surgery or instrumentation	Cefotetan PCN allergy: Clindamycin PLUS Gentamicin
Liver, renal, lung† chemoembolization or percutaneous ablation	Prophylaxis not recommended
Fibroid/uterine artery embolization	Prophylaxis not recommended
Vascular malformation embolization	Prophylaxis not recommended unless necrotic skin then Cefazolin or PCN allergy: Clindamycin
Lymphangiogram embolization (not ablation)	Cefazolin PCN allergy: Clindamycin
Urologic procedures	Cefazolin PCN allergy: Gentamicin
Placement of implantable access port (e.g., Mediport®)	Cefazolin PCN allergy: Clindamycin
Placement of tunneled catheters	Prophylaxis not recommended

†Pretreatment w/antibiotics can be considered for patients w/COPD or h/o recurrent post-obstructive pneumonia

Prophylaxis against bacterial endocarditis

NOTES:
- These recommendations are new as of May 2007 and represent a significant departure from previously published guidelines.
- Patients who have received antibiotics for surgical prophylaxis do not need additional prophylaxis for endocarditis.

Antibiotic prophylaxis solely to prevent endocarditis is not recommended for GU or GI tract procedures.

Cardiac conditions associated with a high risk of endocarditis for which prophylaxis is recommended prior to some dental and respiratory tract procedures and procedures involving infected skin or musculoskeletal tissue
- Prosthetic cardiac valve
- Previous episode of infective endocarditis
- Congenital heart disease (CHD)
  - Unrepaired cyanotic CHD, including palliative shunts and conduits
  - Completely repaired congenital heart defect with prosthetic material or device, whether placed by surgery or by catheter intervention, during the first 6 months after the procedure
  - Repaired CHD with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device
- Cardiac transplantation recipients who develop cardiac valvulopathy

Antibiotic prophylaxis is recommended for the following dental procedures ONLY:
- Manipulation of gingival tissues or periapical region of teeth
- Perforation of oral mucosa

Antibiotic prophylaxis is recommended for the following respiratory tract procedures ONLY:
- Incision or biopsy of the respiratory mucosa

Antibiotic regimens
- Amoxicillin 2 g PO 1 hour before procedure
  OR
- PCN allergy: Clindamycin 600 mg PO 1 hour before procedure
  OR
- PCN allergy: Azithromycin 500 mg PO 1 hour before procedure
  OR
- Patient unable to take oral medication: Ampicillin 2 g IM/IV 1 hour before procedure OR Cefazolin 1 g IM/IV 5 minute push prior to procedure

Reference:
AHA Guidelines for Prevention of Infective Endocarditis: Circulation 2007; 115(15):e408.

Prophylactic antimicrobials for patients with solid organ transplants

NOTE: PCP, anti-viral, anti-fungal prophylaxis is generally restarted in patients starting therapy for acute rejection. All doses assume normal renal function; dose modifications may be indicated for reduced CrCl

Kidney, kidney-pancreas, pancreas, liver transplants		
Indication	Agent and dose	Duration
Anti-viral prophylaxis (CMV, HSV, VZV)		
CMV D-/R-	Acyclovir 400 mg PO BID	3 months
CMV D+/R+	Valgancyclovir 450 mg PO daily	3 months
CMV D-/R+	Valgancyclovir 450 mg PO daily	3 months
CMV D+/R-	Valgancyclovir 900 mg PO daily	6 months
Anti-fungal prophylaxis		
Kidney	Clotrimazole troches 10 mg PO Q6H or Nystatin suspension 500,000 units/15 mL Q6H	1 month
Pancreas and kidney	Fluconazole 400 mg PO daily	1 month
Liver	Fluconazole 400 mg PO daily	3 months
PCP prophylaxis	First line: TMP/SMX one SS tablet PO daily Second line: Atovaquone 1500 mg PO daily	6 months

Treatment notes: TMP/SMX therapy reduces risk of infection with *Listeria* spp., *Nocardia* spp., and Toxoplasmosis, but does not eliminate risk. For splenectomized patients, antibacterial prophylaxis with Penicillin (or Doxycycline if PCN allergy) is recommended for 1 year.

Heart transplants		
Indication	Agent and dose	Duration
Anti-viral prophylaxis (CMV, HSV, VZV)		
CMV D-/R-	No prophylaxis unless HSV IgG or VZV IgG positive. If positive serology, Valacyclovir 500 mg PO BID OR Acyclovir 400 mg PO BID	3 months
CMV D+/R+	Valganciclovir 900 mg PO daily	3 months
CMV D-/R+	Valganciclovir 900 mg PO daily	3 months
CMV D+/R-	Valganciclovir 900 mg PO daily	6 months
Anti-fungal prophylaxis	Nystatin suspension 500,000 units Q6H	1 month
PCP prophylaxis	First line: TMP/SMX SS one tablet PO daily OR TMP/SMX one DS tablet PO three times/week Second line: Dapsone 100 mg PO daily (sulfa allergy)	12 months
Toxoplasmosis prophylaxis		
Toxo D-/R+ OR D+/R+	First line: TMP/SMX one SS tablet PO daily OR TMP/SMX one DS tablet PO three times/week. Second line: Dapsone 100 mg PO daily PLUS Pyrimethamine and Leucovorin	12 months
Toxo D+/R-	TMP/SMX one DS tablet PO three times/week	Lifelong

D = donor, R = recipient, (–) = seronegative, (+) = seropositive

(continues)

5.17 Guidelines for use of prophylactic antimicrobials

Lung transplants		
Indication	Agent and dose	Duration
Anti-viral prophylaxis		
CMV D-/R-	No prophylaxis unless HSV IgG or VZV IgG positive. If positive serology, Valacyclovir 500 mg PO BID OR Acyclovir 400 mg PO BID	3 months
CMV D-/R+ OR D+/R+	Ganciclovir 5 mg/kg IV Q24H x 14 days, then Valganciclovir 900 mg PO daily x 78 days	3 months
CMV D+/R-	Ganciclovir 5 mg/kg IV Q12H x 14 days, then 5 mg/kg IV Q24H x 78 days	3 months
Anti-fungal prophylaxis		
No Aspergillus colonization	Inhaled Amphotericin B per protocol	During the initial hospitalization
	Nystatin 5 mL swabbed in mouth Q6H OR Clotrimazole troches 10 mg PO Q6H	1 month post D/C
Aspergillus colonization	Voriconazole 200 mg twice daily	3–6 months
PCP prophylaxis	First line: TMP/SMX one DS tablet PO three times/week Second line: Dapsone 100 mg PO daily (sulfa allergy) Second line: Atovaquone 1500 mg PO daily (sulfa allergy & G6PD deficiency)	At least 12 months

D = donor, R = recipient, (–) = seronegative, (+) = seropositive

Neutropenic fever

NOTE: These guidelines were developed for use in BMT and leukemia patients and may not be fully applicable in other instances.

Definitions

- Neutropenia: ANC < 500/mm^3
- Fever: Temp > 38.0° C times two at least 2 hours apart OR
  Temp > 38.3° C times one

TREATMENT

Always tailor antibiotics based on susceptibility profiles

If the patient is hypotensive or otherwise unstable, see "Treatment of clinically unstable patients" (p. 112).

Initial fever

- Piperacillin/tazobactam 3.375 g IV Q4H (preferred if *Pseudomonas* expected)
  OR
- Cefepime 2 g IV Q8H
  OR
- Serious allergy to PCN, defined as anaphylaxis or Stevens-Johnson syndrome: Strongly consider allergy consult to verify allergy in patients with unclear histories (see section on penicillin allergy)
  - Ciprofloxacin 400 mg IV Q8H PLUS [Aztreonam 2 g IV Q8H **OR** Tobramycin (see dosing section, p. 132)] PLUS Vancomycin (see dosing section, p. 138)

NOTES:

- Discontinue mucositis prophylaxis (Ampicillin or Vancomycin) when antibiotics are started to treat fevers, BUT continue Norfloxacin for GI decontamination.
- Consider adding Vancomycin in non-PCN allergic patients if a serious catheter-related infection is suspected (e.g., there is warmth and redness at the catheter site).

For patients who remain febrile or develop a new fever after 72 hours on antibiotics above and are NOT hypotensive ("Second fever"):

- Continue antibiotics above and ADD
  OR
- AmBisome® 3 mg/kg IV Q24H (for patients with a history of neutropenia ≤ 10 days and without evidence of fungal infection)

OR

- AmBisome® 5 mg/kg IV Q24H (for patients with a history of neutropenia > 10 days or evidence of fungal infection)

NOTE: Discontinue Fluconazole if AmBisome® or Micafungin are started.

For patients who remain febrile or develop a new fever after 72 hours on both antibacterial agents AND Amphotericin B but are NOT hypotensive ("third fever"):

Option 1:

- Add Vancomycin (see dosing section, p. 138) IF and ONLY IF the patient has a documented Gram-positive infection that is susceptible only to Vancomycin.

Option 2:

- Continue current regimen (some patients will take longer to defervesce)

Option 3:

- No PCN allergy: STOP Piperacillin/tazobactam or Cefepime and START Meropenem 1 g IV Q8H.
- PCN allergy: STOP Aztreonam or Tobramycin and START Amikacin (see dosing section, p. 132)

Antibiotic treatment of patients who are CLINICALLY UNSTABLE due to a possible infectious cause at ANY time during neutropenia:

Transplant ID consult recommended

- AmBisome® 5 mg/kg IV Q24H PLUS
- Vancomycin (see dosing section, p. 138) PLUS
- Amikacin 8 mg/kg IV Q8H (see dosing section, p. 132, AND "Treatment notes," below) PLUS
- Meropenem 1 g IV Q8H

For patients with severe PCN allergy, replace Meropenem with:

- [Aztreonam 2 g IV Q8H or Ciprofloxacin 400 mg IV Q8H]

TREATMENT NOTES

- Antibiotics should ALWAYS be narrowed based on positive cultures.
- It is recommended that all patients receiving aminoglycosides have levels obtained around the third dose:
  - A **trough** level should be drawn just prior to administration of the third dose.
  - A **peak** level should be drawn 30 minutes after the infusion of the third dose.
  - If the patient is critically ill and has an unclear volume status, some advocate obtaining a peak level after the first dose to ensure efficacy.

Prophylactic antimicrobials for patients with expected prolonged neutropenia

1. Bone marrow transplant patients

Indication	Agent and dose	Duration
GI decontamination	Norfloxacin 400 mg PO BID	Day zero until ANC > 500/mm^3
Candida prophylaxis	Fluconazole 400 mg PO once daily	Day zero until ANC > 500/mm^3
Anti-viral prophylaxis (if HSV or VZV IgG positive or pending)	Valacyclovir 500 mg PO TID [If unable to take PO Acyclovir 250 mg/m^2 IV Q12H]	Day zero until day 28
Streptococcal prophylaxis for patients with mucositis*	Ampicillin 2 g IV Q6H [If severe PCN allergy Vancomycin 1 g IV Q12H]	Day zero until "First Fever" antibiotics are started OR mucositis is < grade 2

* For outpatients: Amoxicillin 500 mg PO TID (if PO tolerated) **OR** Vancomycin 1 g IV Q12H (if PCN allergy) **OR** no prophylaxis (see treatment notes on the next page)

2. Leukemia patients

Indication	Agent and dose	Duration
GI decontamination	Norfloxacin 400 mg PO BID	Day 1 until ANC > 100/mm^3
Anti-viral prophylaxis (if HSV Ig G positive or pending)	Valacyclovir 500 mg PO TID [If unable to take PO Acyclovir 250 mg/m^2 IV Q12H]	Day 1 until ANC > 100/mm^3
Streptococcal prophylaxis for patients with mucositis*	Ampicillin 2 g IV Q6H [If severe PCN allergy Vancomycin 1 g IV Q12H]	Day 8 of chemotherapy until "First Fever" antibiotics are started OR ANC > 100/mm^3 on the way up
PCP prophylaxis (ALL, CLL, lymphoma and myeloma pts only)	Bactrim 1 SS once daily OR [If Sulfa allergy Dapsone 100 mg once daily]	Until immunosuppression resolves

* For outpatients: Amoxicillin 500 mg PO TID (if PO tolerated) **OR** Vancomycin 1 g IV Q12H (if PCN allergy) **OR** no prophylaxis (see treatment notes below)

3. Solid tumor patients

The use of prophylactic antibiotics in neutropenic patients who have solid tumors has not been studied formally and is not routinely recommended.

5.18 Guidelines for use of antimicrobials in neutropenic hosts

TREATMENT NOTES

- There is some controversy surrounding the utility of anti-streptococcal prophylaxis in patients with mucositis.

Guidelines for the use of antifungal agents in hematologic malignancy patients

Filamentous fungi

TREATMENT

***Aspergillus* spp.**

Initial therapy

- Voriconazole 6 mg/kg IV/PO Q12H times two doses then 4 mg/kg IV/PO Q12H (see Voriconazole guidelines, p. 20, for more information).
  OR
- AmBisome® 5 mg/kg IV Q24H

NOTES:

- Voriconazole is considered by many to be the first-line treatment of suspected filamentous fungal infections in the immunocompromised host as most of these infections are caused by *Aspergillus* species. Although the data are limited, Voriconazole appears more effective than Amphotericin for this very serious infection.
- Combination antifungal therapy is not recommended for empiric therapy of aspergillosis.

Treatment failure

- The Tucker ID consult service (#4-0242) should be involved in these cases to assist in antifungal selection and eligibility for ongoing clinical trials.
- Treatment failure defined as:
  - Persistent fever beyond 96 hours
  - Worsening clinical status at ANY time after starting therapy defined as: hypotension, worsening respiratory status, evidence of embolization
  - Worsening radiologic findings
  - Patients receiving Voriconazole should be appropriately dosed using actual body weight (mg/kg) and have therapeutic levels before being considered treatment failures. See p. 20 for dosing and therapeutic monitoring.
- Micafungin PLUS [Voriconazole OR AmBisome®]

NOTE: There is no convincing evidence to suggest that any of the agents would be superior in patients who fail to respond to the first agent. *In vitro* data suggest that Micafungin in combination with Voriconazole may be the most effective approach in those who fail to respond to Voriconazole alone.

***Fusarium* spp.**

- ID consult should be involved in these cases.
- Voriconazole 6 mg/kg IV/PO Q12H times two doses then 4 mg/kg IV/PO Q12H (see Voriconazole guidelines, p. 20, for more information). Dose escalation may be necessary for some patients.

Pseudallescheria boydii (Scedosporium spp.)

- Voriconazole 6 mg/kg IV/PO Q12H times two doses then 4 mg/kg IV/PO Q12H (see Voriconazole guidelines, p. 20, for more information).

NOTE:

- Treatment with other agents has yielded disappointing results. Voriconazole appears to be the best option but the data are limited.

Zygomycoses (*Mucor, Rhizopus, Cunninghamella,* etc.).

- AmBisome® 5 mg/kg IV once daily
- Posaconazole 200 mg PO Q6H for 7 days then 400 mg PO Q8H – Q12H can be considered in combination with AmBisome® in the acutely ill patient or for outpatient monotherapy once the patient is stable. ID consult required.
- Surgical debridement and correction of underlying risk factors (e.g. acidosis, hyperglycemia) are critical.
- Voriconazole and Micafungin should not be used as a single agent.

Candida

TREATMENT

- YEAST IN A BLOOD CULTURE SHOULD NEVER BE CONSIDERED A CONTAMINANT.
  - See sections below on empiric therapy and on pathogen-specific therapy.

Unspeciated candidemia

- Micafungin 100 mg IV Q24H
  OR
- AmBisome® 3–5 mg/kg IV Q24H

If the yeast is *C. albicans* or *C. glabrata,* the recommendations for *C. albicans* noted below can be followed. If the yeast is not *C. albicans,* await speciation before modifying therapy as recommended below.

5.18 Guidelines for use of antimicrobials in neutropenic hosts

NOTE: Micafungin does not cover Cryptococcus

Candida albicans

- Micafungin 100 mg IV Q24H
  OR
- AmBisome® 3–5 mg/kg IV Q24H

NOTE: Patients who are clinically stable and no longer neutropenic can be switched to Fluconazole if the organism is susceptible.

Candida glabrata

- Micafungin 100 mg IV Q24H
  OR
- AmBisome® 3–5 mg/kg IV Q24H

Candida krusei

- Micafungin 100 mg IV Q24H
  OR
- AmBisome® 5 mg/kg IV Q24H

NOTE: *C. krusei* is intrinsically resistant to Fluconazole and these infections can be difficult to treat. In stable patients, Voriconazole can be used if susceptible and oral therapy is desired. (See p. 20 for dosing).

Candida parapsilosis

- AmBisome® 3–5 mg/kg IV Q24H

NOTES:

- Most *C. parapsilosis* isolates remain susceptible to Fluconazole, which can be used in stable and non-neutropenic patients.
- There are limited data that suggest that Micafungin may be inferior to Amphotericin B in these infections.

Candida tropicalis

- Micafungin 100 mg IV Q24H
  OR
- AmBisome® 3–5 mg/kg IV Q24H

TREATMENT NOTES

Microbiology

Candidemia at The Johns Hopkins Hospital Oncology Center—8/2007–4/2009

Organism	#	Fluconazole susceptibility
C. albicans	4	4/4
C. glabrata	3	2/3
C. parapsilosis	2	2/2
C. tropicalis	9	9/9

S – susceptible (MIC ≤ 8); I – intermediate (MIC = 16–32); R – resistant (MIC ≥ 64)

Notes on antifungal susceptibility testing

- Susceptibility testing for Fluconazole, Itraconazole, Voriconazole, Flucytosine (5-FC), and Micafungin is performed routinely on the first yeast isolate recovered from blood.
- Fluconazole and Micafungin susceptibilities are reported on all blood isolates.
- If the isolate is resistant (R) or dose-dependent susceptible (DD-S) to Fluconazole, then Micafungin susceptibility will be reported.
- Susceptibility testing for conventional Amphotericin B is done routinely for *C. lusitaniae* and *C. guillermondii* and for other organisms by request.
- Susceptibility testing should be considered when:
  - Mucocutaneous candidiasis is refractory to Fluconazole
  - Treating osteomyelitis, meningitis, or endophthalmitis with Fluconazole
  - Blood cultures are persistently positive on Fluconazole
- Non-routine susceptibility testing can be arranged by calling the mycology lab at 5-6148

Reference:
IDSA Guidelines for Treatment of Candidiasis: Clin Infect Dis 2009;48:503.

Approach to the patient with a history of penicillin allergy

Penicillin reactions – Incidence

- 80-90% of patients who report they are "allergic" to PCN actually have negative skin tests and are not at increased risk of an allergic reaction.
- Penicillin reactions of some type occur in 0.7 to 10% of all patients who get the drug.
  - BUT: The incidence of anaphylactic reactions is 0.004% to 0.015%.
- Rates of cross-reaction allergies to cephalosporins are unknown but thought to be low.
- Rates of PCN and carbapenem skin test cross reactivity are 47%, although clinical rates of hypersensitivity reactions in patients with reported PCN allergy who receive carbapenems are 9–11%.
- Cross reactions to monobactams (Aztreonam) do NOT appear to occur.

Penicillin skin testing

- When done correctly, is highly predictive of serious, anaphylactic reactions.
- Patients with a negative skin test are NOT at risk for anaphylactic reactions.
- Rarely, skin test negative patients may get mild hives and itching following penicillin administration but these RESOLVE with continued treatment.
- Skin tests cannot predict dermatologic or GI reactions or drug fevers.

Penicillin reactions—Types

- **Immediate** (type 1) – Anaphylaxis, hypotension, laryngeal edema, wheezing, angioedema, urticaria
  - Almost always occur **within 1 hour** of administration. Hypotension **always** occurs soon after administration
  - Can be predicted by skin tests
- **Accelerated** – Laryngeal edema, wheezing, angioedema, urticaria (NOT hypotension)
  - Occur within 1-72 hours of administration
  - Can be predicted by skin tests
- **Late** – Rash (maculopapular or morbilliform or contact dermatitis), destruction of RBC, WBC, platelets, serum sickness
  - Almost always occur after 72 hours of administration
  - Rashes sometimes go away despite continued treatment
  - Maculopapular and morbilliform rashes DO NOT progress to Stevens-Johnson syndrome
  - Late reactions are NOT predicted by skin tests
- **Stevens-Johnson Syndrome** – exfoliative dermatitis with mucous membrane involvement

6.1 Approach to the patient with a history of penicillin allergy

  - Almost always occur after 72 hours of administration
  - NOT predicted by a history of rash OR by skin tests

Approach to the patient with reported penicillin allergy

- Brief, focused history can be VERY helpful.
- Questions to ask:
  1. How long after beginning penicillin did the reaction occur?
  2. Was there any wheezing, throat or mouth swelling, urticaria?
  3. If a rash occurred, what was the nature of the rash? Where was it and what did it look like?
  4. Was the patient on other medications at the time of the reaction?
  5. Since then, has the patient ever received another penicillin or cephalosporin (ask about trade names like: Augmentin, Keflex, Trimox, Ceftin, Vantin)?
  6. If the patient received a beta-lactam, what happened?

Interpreting the history of the patient reporting penicillin allergy

- **ANY patient who has a history consistent with an immediate reaction (laryngeal edema, wheezing, angioedema, urticaria) SHOULD NOT receive beta-lactams without undergoing skin testing first EVEN IF they have received beta-lactams with no problems after the serious reaction.**
  - Patients who report non-anaphylactic reactions and have received other penicillins without problems DO NOT have penicillin allergy and are not at increased risk for an allergic reaction compared to the general population.
  - Patients who report non-anaphylactic reactions and have received cephalosporins can get cephalosporins but not necessarily PCNs.
  - Patients who report a history of a non-urticarial rash that is NOT consistent with Stevens-Johnson syndrome (target lesions with mucous membrane inflammation) after more then 72 hours of getting penicillin are not at increased risk for an adverse reaction. They should, however, be watched closely for development of rashes.
  - Patients who report reactions consistent with serum sickness (rare) can receive either penicillins or cephalosporins with careful monitoring for recurrence.
  - Patients who report GI symptoms (diarrhea, nausea) probably do not have penicillin allergy and do not appear to be at increased risk for an adverse reaction. They should be closely observed for recurrent symptoms and be given supportive therapy if they occur.

References:
JAMA 2001;285:2498.
Use of carbapenems in patients with PCN allergy: J Antimicrob. Chemother 2004;54: 1155–7.
Ann Intern Med 2007;146:266–9.

Combination therapy or "double-coverage" of Gram-negative bacterial infections

Reasons to consider combination therapy

Synergy

- Occurs when inhibitory or bactericidal activity of combination therapy is greater than would be expected from the sum of the activities of the individual agents
- Synergy for Gram-negative infections is of major value only when the bacterium is resistant to one or both of the drugs in the combination.
- Synergy has been best established for beta-lactam and aminoglycoside combinations.
- Synergy between other drug combinations is less predictable and has unclear clinical significance.

Prevention of emergence of resistance

- Emergence of resistance on therapy is uncommon, occurring in 5–10% of infections treated.
- Emergence of resistance to beta-lactams while on therapy with these agents occurs in ~20% of patients infected with organisms with inducible beta-lactamases (*Serratia*, *Enterobacter*, *Citrobacter*, *Acinetobacter*); beta-lactams are best avoided in these patients if other options are available.
- Emergence of resistance is more common in pneumonia and osteomyelitis due to decreased antibiotic penetration at these sites; attention should be given to appropriate dosing in these patients.
- The addition of additional agents may lead to increased toxicity from adverse drug reactions.

Broadening empiric coverage in the event that the causative organism is resistant to one agent

- Should be considered in patients with life-threatening infections (ventilator-associated pneumonia, sepsis).
- Second agent should offer additional coverage and generally will be an aminoglycoside at JHH.
- Coverage MUST be narrowed based on culture results; negative cultures can be used to rule out infections with most organisms.

Data Regarding Combination Therapy

- An early study by Hilf suggested that combination therapy was superior to monotherapy in patients with *Pseudomonas* bacteremia BUT 84% of monotherapy patients received inadequate monotherapy with an aminoglycoside. Five more recent studies have not shown a difference in mortality when patients received appropriate monotherapy for *Pseudomonas* bacteremia.
- Recent prospective studies have not shown a benefit to combination therapy over monotherapy in the treatment of serious Gram-negative infections in both non-neutropenic AND neutropenic patients.
- Two recent meta-analysis showed no difference in outcomes of patients with sepsis or febrile neutropenia treated with beta-lactams alone vs beta-lactam/aminoglycoside combinations although patients in the latter group had a higher incidence of nephrotoxicity.

Recommendations for use of combination therapy

- Data suggest that monotherapy is sufficient for the treatment of most Gram-negative infections.
- The use of 2 agents to treat proven or suspected Gram-negative infections should be limited to the following situations:
  1. **Empiric treatment** of serious infections manifested by hypotension, pressor dependence or mechanical ventilation (primarily to broaden spectrum).
  2. **Documented infection** with a resistant Gram-negative organism (particularly *Pseudomonas*, *Acinetobacter*, *Citrobacter*, *Enterobacter*, and *Serratia*) when antibiotic penetration to the site of infection is poor (pneumonia, osteomyelitis). Consideration can be given to stopping one of the agents after 5–7 days of therapy when the bacterial burden has decreased.
  3. **Documented infection** with a highly resistant organism after synergy testing shows an advantage to a beta-lactam/aminoglycoside combination. Call ID to discuss synergy testing (3-8026).
- The second agent should be an aminoglycoside in most cases. Fluoroquinolone resistance is common among Gram-negative organisms at JHH.
- Double beta-lactam combinations should not be used.

References:
Am J Med 1989;87:540.
Antimicrob Agents Chemother 1994;38(6):1309.
Antimicrob Agents Chemother 1997;41:1127.
BMJ 2003;326:1111.
BMJ 2004;328:668.
Clin Infect Dis 1995;20(5):1217.
Int J Antimicrob Agents 1999;11:7.
Pharmacother 1995;15(3):279.

6.2 "Double coverage"

Hospital Epidemiology and Infection Control (HEIC)

- HEIC is located is located in Osler 425, phone 5-8384
- Office hours are Monday-Friday, 8:00 a.m. to 5:30 p.m.
- After hours, an Infection Control Practitioner (ICP) can be reached by pager at 3-3855
- Consult the HEIC Web site (www.hopkinsmedicine.org/heic) for detailed isolation charts, HEIC policies, and surveillance information

Hand hygiene

- Hand hygiene measures are the single most important strategy for preventing healthcare-associated infections.
- If hands are not visibly soiled, then alcohol-based hand sanitizers are recommended for cleaning. If hands are visibly soiled, wash hands with soap and water for 10–15 seconds.
- Hand hygiene is required upon entering a patient room, upon exiting, and between patients in a semi-private room.
- Use soap and water upon exiting the room of a patient with *C. difficile* infection.
- No artificial fingernails are permitted for any staff member who has patient contact.

Bloodborne pathogen exposures (needlestick or other exposure)

The prompt treatment of injuries and exposures is vital to prevent the transmission of disease. Whatever the exposure, IMMEDIATE cleaning of the exposure site is the first priority.

- Skin wounds should be cleaned with soap and water
- Mucous membranes should be flushed thoroughly with water
- Eyes should be irrigated with a liter of normal saline

After cleaning the exposure site, call 5-STIX (5-7849) and follow instructions to contact the ID physician. Workplace injuries should be reported immediately on the "Employee Report of Incident Form" and to the **Occupational Injury Clinic** (Blalock 139, Monday–Friday, 7:30 a.m. to 4 p.m., 5-6433).

Communicable diseases—exposures and reporting

HEIC should be notified:

- If patients or HCWs are exposed to a communicable disease (i.e. meningococcal disease, varicella, TB etc.)
- About HCWs with acute hepatitis A, B or C, Salmonella, or pneumonia requiring hospital admission
- About any unusual occurrence of disease or cluster, particularly diseases that have the potential to expose many susceptible individuals
- Suspicion or diagnoses of the following diseases (diseases with ☎ require immediate notification by phone or pager). If disease is in a HCW, notify HEIC and Occupational Health (98 N. Broadway, Suite 421, Monday–Friday, 7:30 a.m. to 4:00 p.m., 5-6211) immediately

Anthrax ☎	Rabies ☎
Avian Influenza ☎	Ricin toxin ☎
Botulism ☎	Rubella (German measles)
Brucellosis	Salmonellosis
Creutzfeldt-Jakob disease (CJD) ☎	SARS ☎
Diphtheria ☎	Scabies
Glanders ☎	Shigellosis
Highly resistant organisms (i.e. VISA, VRSA) ☎	Smallpox (orthopox viruses) ☎
Legionellosis	Streptococcal Group A or B invasive disease ☎
Measles (rubeola) ☎	Tuberculosis ☎
Meningococcal disease ☎	Tularemia ☎
Monkeypox ☎	Varicella (chickenpox or disseminated zoster) ☎
Mumps	Viral hemorrhagic fever ☎
Pertussis ☎	Yellow Fever ☎
Plague ☎	
Poliomyelitis	
Q Fever	

Physicians are required to report communicable disease to the Baltimore City Health Department (410-396-4436, fax: 410-625-0688). For a complete list of communicable diseases, see the HEIC Web site, the DHMH Web site, www.dhmh.state.md.us/ or the BCHD Web site, www.baltimorecity.gov/government/health/index.html.

Infection control precautions

Standard Precautions

All employees must follow Standard Precautions for all patients as follows:

• Routine hand hygiene	• Bag contaminated linen at point of use
• Consistent and correct glove use	• Regular cleaning of environmental surfaces
• Appropriate use of gowns to prevent contamination of uniform/clothing	• Routine cleaning or disposal of patient-care equipment
• Appropriate use of masks, eye protection and face shields (i.e., when suctioning, or when splash likely)	• Strict adherence to occupational safety requirements

IC admission codes

Used to inform HCWs of the need for isolation on readmission to JHH based on the following code system:

Code	Precautions	Reason for Precautions
IC01	Contact	Vancomycin Resistant Enterococcus (VRE)
IC02	Contact	Methicillin Resistant *Staphylococcus aureus* (MRSA)
IC03	Maximum	Vancomycin Resistant *Staphylococcus aureus* (VRSA) OR Vancomycin Intermediate *Staphylococcus aureus* (VISA)
IC04	Contact + Airborne	Chickenpox or disseminated zoster
IC05	Airborne, Neg. Pressure	MDR Tuberculosis
IC06	Infection Control use only	
IC07	Contact, Private Room	Both VRE and MRSA
IC08	Contact, Specified location	*Burkholderia cepacia*
IC09	Contact, Private room	MDR Acinetobacter
IC10	Contact, Private room	MDR Gram negative rod

JHH Precautions Categories

These precaution categories must be used in addition to Standard Precautions. The following table includes general requirements for precaution categories. The complete table and the type of isolation required for each organism can be found on the HEIC website. If recommendations on this table cannot be followed, please refer to the HEIC website or contact HEIC.

(sign color)	Contact Precautions (pink)	Droplet Precautions (orange)	Airborne Precautions (blue)	Maximun Precautions (red)
Private room	Required unless cohorted	Required unless cohorted*	Required	Required unless cohorted
Door closed	No	No	Yes	Yes
Mask/Eye Protection	No	If within 3 feet of patient	PAPR or N95† to enter room‡	No, unless organism is in sputum
Gown and Gloves	To enter room	To enter room	No	To enter room
One to One Nursing	No	No	No	Yes
Examples	MRSA, *C.diff*, zoster§	Influenza, bacterial meningitis	TB, disseminated zoster§	VISA/VRSA, used at the discretion of HEIC

* Required for pertussis and diphtheria
† Fittesting is required to use an N95 mask for airborne precautions
‡ HCWs who are Varicella-immune do not have to wear a PAPR or N95 if patient is in isolation for zoster or chickenpox
§ Disseminated zoster, zoster in an immunocompromised host, and chickenpox require both Contact and Airborne Precautions

Disease-specific infection control recommendations

Creutzfeldt-Jakob disease (CJD)

CJD, variant CJD and other diseases caused by prions are resistant to a number of standard sterilization and disinfection procedures. Iatrogenic transmission of CJD has been associated with percutaneous exposure to medical instruments contaminated with prion/central nervous system (CNS) tissue residues, transplantation of CNS and corneal tissues and recipients of human growth hormone and gonadotropin. Transmission of CJD has not been associated with environmental contamination or from person-to-person via skin contact. The following additional precautions must be made when processing equipment that could be contaminated with prion related material:

- Notify HEIC immediately of any suspected or confirmed CJD case and refer to the CJD policy on the HEIC Web site.
- Use disposable equipment whenever possible.
- Label all laboratory and pathology requisitions as suspected CJD and notify the lab before sending specimens.
- The following are considered highly infective and should be handled with extreme caution: brain, spinal cord, and optic tissues
- The following should be handled as high infectivity even though they are considered to be of lower infectivity: CSF, kidney, liver, lung, lymph nodes, spleen, placenta, tonsillar tissue, olfactory tissue, and blood.

Methicillin-resistant *Staphylococcus aureus* (MRSA)

Routine active surveillance cultures for MRSA are performed to track patients with MRSA. Surveillance culture results are found in the electronic patient record with the test name "MRSA Surv. Cult." When a culture is positive for MRSA the patient is placed on **Contact Precautions.** The results are to be used for isolation purposes, not to guide therapy or clinical care. **The overwhelming majority of positive surveillance cultures represents colonization, not infection, and should not prompt any antimicrobial therapy.**

Surveillance cultures should be obtained upon admission and weekly in the following units: MICU, OSL-8, WICU, CSICU, SICU/IMC, Nel-7, WGA-5, WGB-5, WGC-5, WGD-5, NCCU, CCU/CCP, PICU.

A swab of the anterior nares should be obtained and sent for culture.

To remove a patient from MRSA precautions, cultures from the original site of infection and 2 nares cultures taken ≥ 72 hours apart must be negative. Nares cultures should not be sent if the patient has received antibiotics active against MRSA in the previous 48 hours. Once this is accomplished, call HEIC to review culture data and initiate deflagging.

7.3 Disease-specific infection control recommendations

Pertussis

All patients with pertussis should be placed on **Droplet Precautions** for five days from the start of therapy. If the patient is not on therapy, Droplet Precautions should be continued for three weeks from the onset of cough. Private room is required.

Treatment:

- Azithromycin 500 mg PO once on day 1, then 250 mg PO daily on days 2–5
  OR
- Macrolide allergy: TMP/SMX 1 DS tablet PO BID for 14 days

Prophylaxis with the above regimens is required for all household contacts within three weeks of exposure. Use the same antibiotic as for treatment. All household contacts and HCWs with exposure to the patient should also have up-to-date immunizations for *Bordetella pertussis*, although vaccination does not provide post-exposure prophylaxis.

Scabies

All patients with conventional or Norwegian scabies should be placed on **Contact Precautions.** Norwegian scabies is a severe form of heavy mite infestation.

- Private room required unless cohorted.
- Patients with conventional scabies must be treated with a scabicide once, and the precautions may be discontinued 24 hours after the treatment is completed.
- Patients with Norwegian scabies require 2 treatments with a scabicide 1 week apart. The precautions may be discontinued 24 hours after the second treatment is completed.
- Infested clothing and linen should be sealed in a plastic bag for 48 hours. The mite will not survive off a human host for more than 48 hours. Clothing/patient belongings should be sent home with the patient's family/caretaker. Linens and clothing should be washed in the washing machine on the hot cycle.
- If prolonged skin-to-skin contact occurs with a scabies patient, prophylactic treatment is required. Healthcare workers should contact HEIC if an exposure is suspected.

Vancomycin-resistant enterocci (VRE)

Routine active surveillance cultures for VRE are performed to track patients with VRE. Surveillance culture results are found in the electronic patient record with the test name "Bacteriology-Stool-VRE Stool Surv.

Cult." When a culture grows VRE, the patient is flagged for **Contact Precautions.** The results are to be used for isolation purposes, not to guide therapy or clinical care. **The overwhelming majority of positive surveillance cultures represents colonization, not infection, and should not prompt any antimicrobial therapy.**

Surveillance cultures should be obtained upon admission and weekly in the following units: MICU, OSL-8, WICU, CSICU, SICU/IMC, Nel-7, WGA-5, WGB-5, WGC-5, WGD-5, NCCU, PICU.

A peri-rectal swab should be obtained and sent for culture.

The patient must be off antibiotics for ≥ 48 hours and cultures from original site of infection AND 3 stool or perirectal cultures taken ≥ 1 week apart must be negative. Once this is accomplished, call HEIC to review culture data and initiate deflagging.

Varicella-Zoster

Immunocompetent patients with disseminated zoster and all immunosuppressed patients with zoster need **Contact AND Airborne Precautions**. The following definitions apply to patients with zoster:

- **Immunosuppressed:** bone marrow transplant within the past year; acute leukemia; lymphomas under treatment; solid organ transplant recipients; patients receiving cytotoxic or immunosuppressive treatments, including long-standing steroid treatment; HIV+ patients with CD4 ≤ 200
- **Disseminated:** lesions outside of 2 contiguous dermatomes

Central vascular access device (VAD) recommendations

All healthcare workers who place central lines are required to take the online VAD training (see HEIC Web site). To prevent central VAD-related infections follow the central line bundle:

Insertion

- Clean hands thoroughly
- ChloraPrep® for patient skin antisepsis
- Subclavian is the preferred site for central line insertion
- Use full barrier precautions and aseptic technique
- Lines placed emergently should be changed as soon as the patient is medically stable

Care

- Change a semipermeable transparent central line dressing every 7 days, unless it is damp, loose or soiled, in which case change the dressing immediately
- Change peripheral IV site and tubing every 96 hours
- Remove line as soon as possible

Please refer to the VAD policy on the HEIC Web site for more details.

Evidenced-based recommendations for prevention of surgical site infections (SSI)

Pre-operative interventions

- Identify and treat remote site infections
- Postpone elective procedures until remote infection is resolved
- Control glucose pre- and post-operatively
- Encourage the patient to stop smoking at least 30 days pre-operatively
- Instruct patient to wash with 4% chlorhexidine gluconate (CHG or Hibiclens®) the night before and the morning of surgery. (Directions can be found at www.hopkinsmedicine.org/heic)
- Use appropriate peri-operative antibiotic prophylaxis (see p. 88) that is given prior to, but no more than 1 hour before, skin incision

Intra-operative interventions

- Clean hands with surgical scrub sponge 2–5 minutes and brush nails. For subsequent cases Avagard ® can be used
- Do not remove hair at incision unless necessary for the operation
- Never shave, only use clippers
- Hair removal, if necessary, should take place immediately before surgery
- If CHG wash not done by patient, clean incision site with CHG immediately prior to surgery
- Prepare the surgical site and surrounding area with an approved antiseptic and allow to DRY prior to placing drapes
- Maintain normal core temperature (36.5°C) throughout the procedure
- Control serum blood glucose levels using insulin as necessary
- Use aseptic technique when placing IV devices
- Use aseptic technique when manipulating stopcocks and ports
- Assemble sterile equipment and solutions immediately before use
- Administer 80% O_2 when possible

Post-operative interventions

- Place a sterile dressing (as anatomically possible) 24–48 hours post surgery
- Change dressing using sterile supplies and good hand hygiene
- Control serum blood glucose levels using insulin as necessary

References:
Guidelines for prevention of SSI: Infect Control Hosp Epidemiol 1999;20:247.
Perioperative oxygen: N Engl J Med 2000;242:161.

Bioterrorism

Below are recommendations for treatment, prophylaxis, and infection control for the Category A agents of bioterrorism. Information about other potential agents of bioterrorism can be found on the CDC website at http://www.bt.cdc.gov/index.asp.

Contact HEIC immediately if any of the following agents/diseases are suspected. The microbiology lab should be notified prior to sending specimens (5-6510). **Specimens should not be sent via the pneumatic tube.**

Important phone numbers:
- HEIC Infection Control: 5-8384 (3-3855)
- Microbiology Lab: 5-6510
- Maryland Department of Health and Mental Hygiene, see www.dhmh.state.md.us/labs/html/terrorism.html for on call numbers
- Baltimore City Health Department: 410-396-4436, after hours 410-396-3100
- U.S. Army Medical Research Institute of Infectious Diseases USAMRID: 301-619-4996, hotline 301-619-4027
- CDC Emergency Response Office: 770-488-7100

Agent & infection control	Treatment & prophylaxis
Anthrax **Infection Control** Standard precautions; there is no evidence for person to person transmission of anthrax.	**Treatment** • Ciprofloxacin 400 mg IV Q12H **OR** • Doxycycline 100 mg IV Q12H If inhalational anthrax, ADD Clindamycin 600 mg IV Q8H Patients with meningitis • Vancomycin 22.5 mg/kg IV Q12H PLUS Ciprofloxacin 400 mg IV Q8H PLUS Rifampin 600 mg IV Q24H **Prophylaxis** • Ciprofloxacin 500 mg PO BID x 60 days **OR** • Doxycycline 100 mg PO BID x 60 days Anthrax vaccine may also be recommended by HEIC.
Botulism This is a toxin-mediated disease; there is not a role for antibiotics. **Infection Control** Standard precautions	**Treatment** • Equine antitoxin (acquire from CDC) **Prophylaxis** None

Agent & infection control	Treatment & prophylaxis
Pneumonic plague **Infection Control** Droplet precautions for the first 48 hours of therapy. A private room is required. Movement of patients should be limited to essential medical purposes only, and a mask should be placed on the patient during transport.	**Treatment** • Streptomycin 15 mg/kg (max. 1 g) IM/IV Q12H **OR** • Doxycycline 100 mg IV Q12H Patients with meningitis • Chloramphenicol 25 mg/kg IV Q6H **Prophylaxis** • Doxycycline 100 mg PO BID **OR** • Ciprofloxacin 500 mg PO BID
Smallpox **Infection Control** Maximum + Airborne precautions. A private room is required. Movement of patients should be limited to essential medical purposes only, and a mask should be placed on the patient during transport.	**Treatment** Supportive therapy **Prophylaxis** • Smallpox vaccine should be given (preferably within 4 days of exposure) • Preexposure and postexposure vaccination recommended if > 3 years since last vaccination.
Tularemia **Infection Control** Standard precautions; there is no evidence for person-to-person transmission of tularemia.	**Treatment** • Streptomycin 15 mg/kg (max. 1 g) IM/IV Q12H **OR** • Gentamicin 5 mg/kg IV Q24H **Prophylaxis** • Doxycycline 100 mg PO BID
Viral hemorrhagic fevers **Infection Control** Maximum + Airborne precautions. A private room is required. Movement of patients should be limited to essential medical purposes only, and a mask should be placed on the patient during transport.	**Treatment** • Lassa fever, Rift Valley fever, or either Argentine, Bolivian, Brazilian, or Venezuelan hemorrhagic fever • Ribavirin 30 mg/kg (max. 2 g) IV initial dose, then 16 mg/kg (max. 1 g) IV Q6H x 4 days, then 8 mg/kg (max. 500 mg) IV Q8H x 6 days • Ebola, Marburg, Yellow fever, Omsk hemorrhagic fever, Kyasanur Forest Disease: supportive therapy **Prophylaxis** None

References:
Anthrax: JAMA 2002;287:2236
Botulinum: JAMA 2001;285:1059
Plague: JAMA 2000;283:2281
Smallpox: JAMA 1999;281:2127
Tularemia: JAMA 2001;285:2763
VHF: JAMA 2002;287:2391

Aminoglycoside dosing and monitoring

- Aminoglycosides enhance the efficacy of some antibiotics. Except for urinary tract infections, aminoglycosides should seldom be used alone to treat infections.
- The following dosing guidelines do NOT apply to cystic fibrosis or OB patients.
- Aminoglycosides are known to aggravate the symptoms of myasthenia gravis and should NOT be used in these patients.

Estimation of creatinine clearance (CrCl) by Cockcroft-Gault equation:

$$\text{CrCl} = \frac{(140 - \text{age})\ (\text{weight in kg}^*)}{72\ (\text{serum creatinine}^{**})} \times 0.85\ (\text{if female})$$

* Use Actual Body Weight (ABW) unless patient is obese (≥ 20% over Ideal Body Weight (IBW)).

For obese patients, use **Dosing Body Weight**

(DBW) = [IBW + 0.4 (ABW – IBW)]

IBW female (kg) = (2.3 x inches over 5') + 45.5

IBW male (kg) = (2.3 x inches over 5') + 50

** For patients with low muscle mass (i.e., many patients > 65 yrs.), some advocate using a minimum value of 1 to avoid overestimation of CrCl

Extended interval ("once-daily") aminoglycoside dosing and therapeutic drug monitoring

Extended-interval dosing has become the preferred method of giving aminoglycosides in many cases (see rationale below). However, **patients MUST meet ALL of the following criteria to be eligible for extended-interval dosing:**

- Creatinine clearance **greater than 60 mL/min**
- Stable renal function (creatinine NOT changed by 0.5 mg/dL or 30% in previous 48 hours)
- Patient is NOT pregnant
- Patient does NOT have extensive burns (> 20% BSA) or trauma
- Patient does NOT have ascites, extensive edema, shock, or any other condition where the volume status is unclear
- The aminoglycoside is NOT being used to treat meningitis

If the patient does not meet ALL of the criteria above, traditional aminoglycoside dosing is recommended (see Traditional Aminoglycoside Dosing)

DOSING

- **GENTAMICIN/TOBRAMYCIN:** In most patients, a dose of **5 mg/kg IV once daily** is recommended. Higher doses (7 mg/kg IV once daily) may be required in certain circumstances. Doses should be rounded to the nearest 10 mg.

- **AMIKACIN:** In most patients, a dose of **15–20 mg/kg IV once daily** is recommended. Dose should be rounded to the nearest 50 mg.

THERAPEUTIC DRUG MONITORING (LEVELS)

If the patient meets ANY of the criteria below, a trough level is recommended prior to the 2nd dose. A **trough** level should be obtained immediately before administration of a dose **(i.e., 24 hours after the previous dose was given)**

- Concomitant nephrotoxic medications (i.e., Vancomycin, Cyclosporine, Amphotericin B, etc.)
- Concurrent exposure to contrast media
- Age ≥ 60 years
- Patient is in the ICU
- Other risks for nephrotoxicity (e.g. diabetes, kidney transplant)

Interpretation of GENTAMICIN/TOBRAMYCIN levels:

Trough level	Gentamicin/Tobramycin dosing recommendation
< 1 mcg/mL	Continue current regimen. Repeat trough level weekly
1–1.5 mcg/mL	Accumulation may be occurring. Recheck trough level in 24 hours
> 1.5 mcg/mL	Use traditional dosing method

Interpretation of AMIKACIN levels:

Trough level	Amikacin dosing recommendation
< 4 mcg/mL	Continue current regimen. Repeat trough level weekly
4–6 mcg/mL	Accumulation may be occurring. Recheck trough level in 24 hours
> 6 mcg/mL	Use traditional dosing method

Rationales for extended-interval dosing

- Optimization of peak concentration/MIC ratio
- Allowing for a drug-free period
  - Takes advantage of post-antibiotic effect (PAE) of aminoglycosides
  - May decrease risk of toxicity
  - May lower incidence of adaptive resistance
- Convenience of less frequent administration
- Decreased frequency of drug level monitoring
- At least as efficacious as traditional dosing

Traditional aminoglycoside dosing and therapeutic drug monitoring

DOSING

- **GENTAMICIN/TOBRAMYCIN: a loading dose of at least 2 mg/kg** should be given to all patients, regardless of renal function.
  - Calculate a **maintenance dose** based on CrCl, indication, and *ABW* (unless patient is obese, in which case use *DBW* as defined at the beginning of the section).
  - All doses should be rounded to the **nearest 10 mg**.

	Indication	
CrCl (mL/min)	Pneumonia/sepsis/ *Pseudomonas*/ neutropenic fever	Other Gram-negative infections
> 90	2 mg/kg Q8H	2 mg/kg Q8H
80–89	2 mg/kg Q8H	2 mg/kg Q8H
70–79	2 mg/kg Q8H	1.7 mg/kg Q8H
60–69	2.2 mg/kg Q12H	2 mg/kg Q12H
50–59	2.2 mg/kg Q12H	1.7 mg/kg Q12H
40–49	2 mg/kg Q12H	1.7 mg/kg Q12H
30–39	2.2 mg/kg Q24H	2 mg/kg Q24H
20–29	2 mg/kg Q24H	1.7 mg/kg Q24H
< 20	2.5 mg/kg ONCE*	2 mg/kg ONCE*

* Give one dose, check level in 24 hours, redose when level < 2 mcg/mL

- **AMIKACIN: a loading dose of at least 8 mg/kg** should be given to all patients, regardless of renal function.
  - Calculate a **maintenance dose** based on CrCl, indication, and *ABW* (unless patient is obese, in which case use *DBW* as above).
  - All doses should be rounded to the nearest 50 mg.

	Indication	
CrCl (mL/min)	Pneumonia/sepsis/ *Pseudomonas*/ neutropenic fever	Other Gram-negative infections
> 90	8 mg/kg Q8H	7 mg/kg Q8H
80–89	8 mg/kg Q8H	7 mg/kg Q8H
70–79	8 mg/kg Q8H	6 mg/kg Q8H
60–69	8 mg/kg Q12H	7 mg/kg Q12H
50–59	8 mg/kg Q12H	6 mg/kg Q12H
40–49	7 mg/kg Q12H	6 mg/kg Q12H
30–39	8 mg/kg Q24H	6 mg/kg Q24H
20–29	7 mg/kg Q24H	6 mg/kg Q24H
< 20	10 mg/kg ONCE*	8 mg/kg ONCE*

* Give one dose, check level in 24 hours, redose when level < 10 mcg/mL

THERAPEUTIC DRUG MONITORING (LEVELS)

There is controversy regarding aminoglycoside levels. Some argue that peak levels and estimated creatinine clearance are better predictors of subsequent nephrotoxicity and that trough levels add little useful information, while others believe that high trough levels are predictive of nephrotoxicity. Trough levels, when used in combination with peak levels, are useful in calculating patient-specific dosage adjustments.

When levels should be obtained:

- Peak and trough levels should be obtained around the 3rd dose
  - A **peak** level should be obtained 30 minutes after the end of a 30-minute infusion of the 3rd dose
  - A **trough** level should be obtained immediately before administration of the 3rd dose
- Some advocate peak and trough levels after the 1st dose in patients with serious infections or less predictable volumes of distribution (e.g., patients with diffuse edema, ascites, shock, burns, or pregnant patients). Antibiotic Management input may be of use in these cases (3-9229).
- Levels should be obtained at least once a week. More frequent levels should be considered:
  - After changes in dosing regimen
  - If creatinine changes by 0.5 mg/dL or 30%
  - If there are major changes in the patient's volume status
  - If the patient is not responding

Desired serum concentrations of GENTAMICIN/TOBRAMYCIN

- Peak levels
  - Pneumonia, sepsis, *Pseudomonas*: 8–10 mcg/mL
  - Other Gram-negative infections: 6–8 mcg/mL
- Trough levels
  - < 2 mcg/mL

Desired serum concentrations of AMIKACIN

- Peak levels
  - Pneumonia, sepsis, *Pseudomonas*: 25–35 mcg/mL
  - Other Gram-negative infections: 20–30 mcg/mL
- Trough levels
  - < 10 mcg/mL

A. Aminoglycoside dosing and monitoring

Aminoglycoside dosing and monitoring for Gram-positive synergy

DOSING

- **GENTAMICIN**: 3 mg/kg IV once daily is recommended for treatment of endocarditis with Viridans streptococci or *S. bovis* in patients with normal renal function (CrCl ≥ 60 ml/min).
- **GENTAMICIN:** 1 mg/kg IV Q8H is recommended for treatment of all other Gram-positive endocarditis infections and some cases of severe VRE infections in patients with normal renal function (CrCl ≥ 60 ml/min).

Dosing adjustment for renal insufficiency

CrCl (mL/min)	Dosing
40–59	1 mg/kg Q12H
20–39	1 mg/kg Q24H
< 20	1 mg/kg ONCE*

* Give one dose, check level in 24 hours, redose when level < 1 mcg/mL

NOTE: See infective endocarditis guidelines (p. 47) for duration.

THERAPEUTIC DRUG MONITORING (LEVELS)

- Peak and trough are recommended around the 3rd dose to assure appropriate dosing.

Desired serum concentrations of GENTAMICIN

- Peak levels
  - 3 – 5 mcg/mL
- Trough levels
  - < 1 mcg/mL

Monitoring for toxicity

NEPHROTOXICITY

- Serum creatinine should be measured at least every other day. If creatinine increases by 0.5 mg/dL or 30% from baseline, use traditional dosing.
- Measure serum aminoglycoside levels with traditional dosing
- Some data suggest that lowest level of nephrotoxicity occurs when aminoglycosides are administered during the activity period (e.g. 13:30), therefore afternoon administration is preferred.

OTOTOXICITY

- Consider biweekly clinical screening for ototoxicity
  - Check baseline visual acuity using a Snellen pocket card
  - To screen for ototoxicity, have patient shake head and then re-read card.
  - Concern should be raised if patient loses 2 lines of visual acuity. Consider formal audiology testing.
  - Contact Audiology (5-6153) for help with testing for ototoxicity

References:
Aminoglycoside levels and Gram-negative pneumonia: Am J Med 1984;77:657.
Daily dosing: Antimicrob Agents and Chemother 1995; 39:650.
Daily dosing: Antimicrob Agents and Chemother 1999; 43:1549.
Nephrotoxitiy : Antimicrob Agents and Chemother 2003; 47:1010.
Gram-positive Synergy: Circulation 2005; 111(23):e394-434.
Individualized pharmacokinetic dosing: Crit Care Med 1991;19:1480.

Vancomycin dosing and monitoring

DOSING

1. Estimate creatinine clearance (CrCl) using Cockcroft-Gault equation:

$$\text{CrCl} = \frac{(140 - \text{age})\,(\text{weight in kg})}{72\,(\text{serum creatinine}^*)} \times 0.85 \text{ (if female)}$$

* For patients with low muscle mass (i.e., many patients > 65 yrs), some advocate using a minimum value of 1 to avoid overestimation of CrCl

2. Patients who are seriously ill with complicated infections such as **meningitis, pneumonia, osteomyelitis, endocarditis, and bacteremia** should receive initial loading dose of 25-30 mg/kg, followed by **15-20 mg/kg Q8-12H** assuming normal renal function and using **Actual Body Weight (ABW)**. For other indications see nomogram dosing below.
3. Calculate maintenance dose (using ABW) based on estimated or actual CrCl. See suggested nomogram dosing below.

Note: Younger patients with normal renal function may need higher or more frequent dosing than suggested below.

Weight (kg)	CrCl (mL/min) >60	30–59	15–29	<15 or dialysis, (HD,CVVHD)
<40	Consider ID/Abx Mgmt input (7-4570)			
40–49	750 mg Q12H	750 mg Q24H	750 mg Q48H	1000 mg, then redose by level†
50–59	1000 mg Q12H	1000 mg Q24H	1000 mg Q48H	1000 mg, then redose by level†
60–75	1000 mg Q12H	1000 mg Q24H	1000 mg Q48H	1000 mg, then redose by level†
76–90	1250 mg Q12H	1250 mg Q24H	1250 mg Q48H	1250 mg, then redose by level†
90–110	1500 mg Q12H	1500 mg Q24H	1500 mg Q48H	1500 mg, then redose by level†
> 110	Consider ID/Abx Mgmt input (7-4570)			

†For patients with CrCl <15 mL/min and not receiving hemodialysis redose when random level <15–20 mcg/mL. For patients receiving maintenance hemodialysis, redose after hemodialysis session if pre-hemodialysis level <25 mcg/mL for pneumonia, osteomyelitis, endocarditis or bacteremia. For meningitis, consider redosing patient if pre-hemodialysis level <30 mcg/mL.

THERAPEUTIC DRUG MONITORING (LEVELS)

- **Peak levels** should NOT be obtained.
- **Trough levels** are the most accurate and practical method for monitoring Vancomycin effectiveness and toxicity.

B. Vancomycin dosing and monitoring

Measuring serum Vancomycin levels

- Trough levels should be obtained just prior to the next dose at steady-state conditions (approximately before the 4th dose).
- In patients with ESRD on hemodialysis, it is preferable to obtain a pre-hemodialysis level with the routine laboratory venipuncture on the morning of hemodialysis. In the event a pre-hemodialysis level is not obtained, a post-hemodialysis level may be drawn at least six hours after the dialysis session.
- Trough levels should be considered in patients with any the following circumstances:
  - Receiving aggressive dosing (>1500 mg Q12H) or Q8H interval
  - Serious infections such as meningitis, endocarditis, osteomyelitis, and MRSA pneumonia.
  - Unstable renal function (change in SCr of 0.5 mg/dL or 50% from baseline) or dialysis
  - Concurrent therapy with nephrotoxic agents (e.g. aminoglycosides, Colistin, Amphotericin B)
  - Prolonged courses (>3-5 days) of therapy.
- Frequency of monitoring Vancomycin trough levels:
  - Once-weekly monitoring is recommended for patients with stable renal function who have achieved desired trough levels.
  - More frequent monitoring is recommended for patients who are hemodynamically unstable and/or with changing renal function.

Desired Vancomycin trough levels

- Pneumonia, osteomyelitis, endocarditis, bacteremia: 15-20 mcg/mL
- CNS infections: 20 mcg/mL
- Neutropenic fever, skin and skin-structure infections: 10-15 mcg/mL
- For MRSA infections serum trough concentrations >10 mcg/mL should always be maintained to avoid development of resistance.

Monitoring for Toxicity

- Serum creatinine should be measured at least every other day initially, then weekly if patient's renal function remains stable.
- Limited data suggest a direct causal relationship between nephrotoxicity and higher serum trough concentrations (>15-20 mcg/mL). Monitor Vancomycin trough levels (see above for frequency and indications).
- Formal audiology testing is not recommended for patients receiving Vancomycin, unless signs and symptoms of ototoxicity became apparent.

References:
IDSA/ASHP/SIDP Guidelines therapeutic monitoring of Vancomycin: Am J Health-Syst Pharm. 2009; 66; 82.
ATS/IDSA Guidelines for HAP/VAP: AJRCCM 2005; 171:338.
IDSA Guidelines for Bacterial Meningitis: Clin Infect Dis 2004:39:1267.

Recommendations for monitoring patients receiving long-term antimicrobial therapy

- Long term defined as ≥ 1 week, except for aminoglycosides and Amphotericin B (see below)
- For use once initial dosing and serum levels have been established
- These monitoring recommendations and monitoring for agents not listed should be individualized, based on each patient's clinical features, including general health status, age, underlying conditions and organ dysfunction, concomitant medications, drug treatment history, type of infection, and type and dose of antibiotic

Antimicrobial agent(s)	Test	Frequency	Other
Aminoglycosides (Amikacin, Gentamicin, Tobramycin, Streptomycin)	CBC BUN, Creatinine Aminoglycoside level – ***trough*** (see dosing section page 132)	Weekly Twice weekly Weekly (twice weekly, if increased risk)	Clinical monitoring and patient education for hearing/vestibular dysfunction at each visit (see page 137 for vestibular screening method)
Amphotericin B, AmBisome®	BUN, Creatinine, K, Mg, Phos CBC, AST, ALT	Twice weekly Weekly	
β-lactams (Aztreonam, carbapenems, cephalosporins, penicillins)	CBC, BUN, Creatinine	Weekly	
Oxacillin, Nafcillin, carbapenems	add AST/ALT/bilirubin	Weekly	
Antipseudomonal penicillins	add K	Weekly	
Micafungin	AST/ALT/bilirubin	Weekly	
Colistin	BUN, Creatinine	Weekly (twice weekly, if increased risk)	Clinical monitoring for neurotoxicity (dizziness, paresthesia, vertigo, confusion, visual disturbances, ataxia)
Daptomycin	CBC, BUN, Creatinine , CPK	Weekly	Clinical monitoring for myopathy
Linezolid	CBC	Weekly	Clinical monitoring for peripheral neuropathy and optic neuritis
Rifampin	CBC, AST/ALT/bilirubin	Weekly	**Drug interactions** (monitor start of any new medications)
Voriconazole /Posaconazole	CBC, AST/ALT/ bilirubin	1 – 2 weeks	**Drug interactions** (monitor start of any new medication), visual changes
Vancomycin	Normal renal function: CBC, BUN, Creatinine Vancomycin level – ***trough*** (see dosing section p. 138) Dialysis: Vancomycin level (see dosing section p. 138)	 Weekly Every two weeks, unless change in creatinine (↑50% from baseline) At each dialysis session	

Reference: Practice Guidelines for Outpatient Parenteral Antimicrobial Therapy: Clin Infect Dis 2004; 38:1651.

Oral antimicrobial use in hospitalized patients

When using an agent that is considered to be bioequivalent (no significant difference in rate and extent of absorption of the therapeutic ingredient) via the parenteral and oral route, the oral formulation is preferred if the patient does not have the contraindications listed below.

Contraindications to oral therapy

- NPO (including medications)
- Inability to take other oral medications OR not tolerating a liquid diet/tube feeds
- Hemodynamic instability
- Receiving continuous NG suctioning
- Severe nausea, vomiting, diarrhea, GI obstruction, dysmotility, mucositis
- A malabsorption syndrome
- A concomitant disease state that contraindicates the use of oral medications

NOTE: There are only a limited number of agents that can be used orally for bacteremia or fungemia; these are noted in the table below.

Bioavailability of oral antimicrobials

Antimicrobial	% Oral Absorption
Should NOT be used orally for bacteremia	
Amoxicillin	74 – 90%
Amoxicillin/Clavulanate (Augmentin®)	74 – 90%
Azithromycin*	38 – 83%
Cephalexin	90%
Cefpodoxime*	41 – 50%
Clindamycin	90%
Doxycycline	90 – 100%
Tetracycline	75 – 80%
Can be used orally for bacteremia or fungemia	
Ciprofloxacin†	65 – 85%
Fluconazole	>90%
Linezolid†	100%
Metronidazole	100%
Moxifloxacin†	90%
Trimethoprim/sulfamethoxazole†	85 – 90%
Voriconazole†¶	~96%

* Oral absorption is enhanced in presence of food
† Should not be used for *S. aureus* bacteremia
‡ Oral absorption is decreased in presence of food
¶ Inter-patient variability

Antimicrobial dosing in renal failure

Dosing recommendations can vary according to indication and patient-specific parameters. All dosage adjustments are based on creatinine clearance calculated by Cockcroft-Gault equation.

$$\text{CrCl} = \frac{(140 - \text{age})\,(\text{weight in kg})}{72\,(\text{serum creatinine}^*)} \times 0.85 \text{ (if female)}$$

*For patients with low muscle, some advocate using a minimum of 1 to avoid overestimation of CrCl.

†If patient is on hemodialysis (HD) schedule administration so that patient receives daily dose immediately AFTER dialysis. For assistance with dosage adjustments for patients receiving CVVHD or CVVHDF, please call pharmacy.

Drug	Typical dose (may vary)	CrCl (mL/min)	Dose Adjustment for renal insufficiency
Acyclovir IV	5–10 mg/kg Q8H	>50 25–50 10–24 <10 or HD†	5–10 mg/kg Q8H 5–10 mg/kg Q12H 5–10 mg/kg Q24H 2.5–5 mg/kg Q24H
Acyclovir PO (Genital herpes)	200 mg 5x daily	>10 <10	200 mg 5x daily 200 mg Q12H
Acyclovir PO (Herpes Zoster)	800 mg 5x daily	>25 10–25 <10 or HD†	800 mg 5x daily 800 mg Q8H 800 mg Q12H
Amantadine	100 mg Q12H	>50 30–50 15–29 <15 or HD†	100 mg Q12H 200 mg x 1 day, then 100 mg Q24H 200 mg x 1 day, then 100 mg Q48H 200 mg weekly
Amoxicillin	500–1000 mg Q12H	>30 10–30 <10 or HD†	500–1000 mg Q12H 250–875 mg Q12H 250–875 mg Q24H
Amoxicillin (pneumonia)	1 g Q8H	>30 10–30 <10 or HD†	1g Q8H 1g Q12H 1g Q24H
Amoxicillin/ clavulanate	500–1000 mg Q12H	>30 10–30 <10 or HD†	500–1000 mg Q12H 250–500 mg Q12H 250–500 mg Q24H
Amphotericin B	0.7–1 mg/kg Q24H	–	No dosage adjustment
AmBisome®	3–5 mg/kg Q24H	–	No dosage adjustment
Ampicillin	1–2 g Q4–6H	>50 10–50 <10 or HD†	1–2 g Q4–6H 1–2 g Q6–8H 1–2 g Q8H
Ampicillin/ sulbactam	1.5–3 g Q6H	≥30 15–29 ≤14 or HD†	1.5–3 g Q6H 1.5–3 g Q12H 1.5–3 g Q24H
Azithromycin	250–500 mg Q24H	–	No dosage adjustment
Aztreonam	1–2 g Q8H	≥30 10–29 <10 or HD†	1–2 g Q8H 1–2 g Q12H 1–2 g Q24H

Drug	Typical dose (may vary)	CrCl (mL/min)	Dose Adjustment for renal insufficiency
Cefazolin	1–2 g Q8H	≥35 11–34 <10 HD†	1–2 g Q8H 500 mg–1 g Q12H 500 mg–1 g Q24H 2 g Q HD, if HD in 2 days OR 3g Q HD, if HD in 3 days
Cefepime	1 g Q8	>60 30–60 <29 HD†	1 g Q8H 1 g Q12H 1 g Q24H Load with 1 g, then 500 mg Q24H
Cefepime (Central nervous system infections)	2 g Q8H	>60 30–60 11–29 <11 or HD†	2 g Q8H 2 g Q12H 2 g Q24H 1 g Q24H
Cefotetan	1–2 g Q12H	≥30 10–29 <10 or HD†	1–2 g Q12H 1–2 g Q24H 500 mg Q24H
Cefoxitin	1–2 g Q6H	>50 30–50 10–29 <10 or HD†	1–2 g Q6H 1–2 g Q8–12H 1–2 g Q12–24H 500 mg–1 g Q24H
Cefpodoxime	100–400 mg Q12H	≥30 <30 HD†	100–400 mg Q12H 100–400 mg Q24H 100–400 mg three times/week
Ceftazidime	1–2 g Q8H For *Pseudomonas* 2 g Q8H	>50 30–50 15–29 5–15 HD†	1–2 g Q8H 1–2 g Q12H 1–2 g Q24H 500 mg–1 g Q24H Load with 1 g, then 500 mg Q24H
Ceftriaxone	1–2 g Q24H	–	No dosage adjustment
Ceftriaxone (Central nervous system infections)	2 g Q12H	–	No dosage adjustment
Cephalexin	500 mg PO Q6H	>50 10–50 <10 or HD†	500 mg Q6H 500 mg Q8H 500 mg Q12H
Cidofovir	5 mg/kg Q week for 2 weeks, then every other week	≤55 or Cr>1.5	Not recommended
Ciprofloxacin IV	400 mg Q8–12H	≥30 <30 or HD†	400 mg Q8–12H 400 mg Q24H
Ciprofloxacin PO	250–750 mg Q12H	≥30 <30 or HD†	250–750 mg Q12H 250–500 mg Q24H
Clarithromycin	250–500 mg Q12H	≥30 <30	250–500 mg Q12H 250–500 mg Q24H
Clindamycin	PO: 300 mg Q8H IV: 600 mg Q8H	–	No dosage adjustment
Colistin (Colistimethate)	2.5 mg/kg Q12H	>70 25–70 <25 or HD†	2.5 mg/kg Q12H 1.25 mg/kg Q12H 1.5 mg/kg Q36H
Daptomycin for endocarditis/ bacteremia	6–10 mg/kg Q24H	≥30 <30 HD†	6–10 mg/kg Q24H 6–10 mg/kg Q48H 6–10 mg/kg Q48H
Dicloxacillin	250–500 mg Q6H	–	No dosage adjustment
Doxycycline	100 mg Q12H	–	No dosage adjustment

Drug	Typical dose (may vary)	CrCl (mL/min)	Dose Adjustment for renal insufficiency
Ertapenem	1 g Q24H	≥30 <30 or HD†	1 g Q24H 500 mg Q24H
Ethambutol	15–25 mg/kg Q24H	≥10 <10 HD†	Normal dose Q24H Normal dose Q48H Normal dose QHD session
Fluconazole	200–800 mg Q24H	≥50 <50 or HD†	Normal dose (e.g. 100, 400, 800 mg) Q24H Load w/normal dose, then 50% of normal dose Q24H
Flucytosine (5–FC)	12.5–25 mg/kg Q6H	>40 20–40 10–19 <10 or HD†	12.5–25 mg/kg Q6H 12.5–25 mg/kg Q12H 12.5–25 mg/kg Q24H 12.5–25 mg/kg Q24–48H
Ganciclovir (Induction dose)	5 mg/kg Q12H	≥70 50–69 25–49 10–25 <10 or HD†	5 mg/kg Q12H 2.5 mg/kg Q12H 2.5 mg/kg Q24H 1.25 mg/kg Q24H 1.25 mg/kg three times/week, administer after HD
Ganciclovir (Maintenance dose)	5 mg/kg Q24H	≥70 50–69 25–49 10–25 <10 or HD†	5 mg/kg Q24H 2.5 mg/kg Q24H 1.25 mg/kg Q24H 0.625 mg/kg Q24H 0.625 mg/kg three times/week, administer after HD
Gentamicin	–	–	See section on aminoglycoside dosing
Isoniazide	300 mg Q24H	–	No dosage adjustment
Linezolid	600 mg Q12H	–	No dosage adjustment
Meropenem	1 g Q8H	>51 26–50 10–25 <10 or HD†	1 g Q8H 1 g Q12H 500 mg Q12H 500 mg Q24H
Meropenem (Central nervous system infections)	2 g Q8H	>51 26–50 10–25 <10 or HD†	2 g Q8H 1 g Q8H 1 g Q12H 1 g Q24H
Metronidazole	500 mg Q8H	–	No dosage adjustment
Micafungin	100–150 mg Q24H	–	No dosage adjustment
Moxifloxacin	400 mg Q24H	–	No dosage adjustment
Norfloxacin	400 mg Q12H	≥30 <30 or HD†	400 mg Q12H 400 mg Q24H
Oseltamivir	75 mg Q12–24H	≥30 10–29 <10 or HD†	75 mg Q12–24H 75 mg Q24–48H 30 mg Q every other HD session
Oxacillin	1–2 g Q4–6H	–	No dosage adjustment
Penicillin G	3–4 million units Q4H	≥50 10–50 <10 or HD†	3–4 million units Q4H 1.5 million units Q4H 1.5 million units Q6H
Piperacillin	3–4 g Q6H	>40 20–40 <20 HD†	3 g Q6H (4 g Q6H for *Pseudomonas*) 3 g Q8H (4 g Q8H for *Pseudomonas*) 3 g Q12H (4 g Q12H for *Pseudomonas*) 2 g Q8H

Drug	Typical dose (may vary)	CrCl (mL/min)	Dose Adjustment for renal insufficiency
Piperacillin/ tazobactam	3.375–4.5 g Q6H	>40 20–40 <20 HD†	3.375 g Q6H (4.5 g Q6H for *Pseudomonas*) 2.25 g Q6H (3.375 g Q6H for *Pseudomonas*) 2.25 g Q8H (2.25 g Q6H for *Pseudomonas*) 2.25 g Q12H (2.25 g Q8H for *Pseudomonas*)
Posaconazole	400 mg Q12H	–	No dosage adjustment
Pyrazinamide	15–30 mg/kg Q24H	≥10 <10 HD†	15–30 mg/kg Q24H 12–20 mg/kg Q24H 25–30 mg/kg QHD session
Quinupristin/ dalfopristin	7.5 mg/kg Q8H	–	No dosage adjustment
Rifampin (TB)	600 mg Q24H	–	No dosage adjustment
Rifampin	300 mg Q8–12H	–	No dosage adjustment
Rimantadine	100 mg Q12H	>10 ≤10	100 mg Q12H 100 mg Q24H
Tigecycline	100 mg once, then 50 mg Q12H	–	No dosage adjustment
TMP/SMX (UTIs or cellulitis)	PO: 1–2 DS tab Q12H IV: 160–320 mg Q12H (Dosing is based on TMP component)	≥30 <30	1–2 DS tab Q12 or 160–320 mg IV Q12H 1–2 DS tab Q24H or 160–320 mg IV Q24H
TMP/SMX (PCP or serious systemic infections)	5 mg/kg Q6–8H	≥30 <30 HD†	5 mg/kg Q6–8H 2.5 mg/kg Q6–8H 2.5 mg/kg Q8H
Valacyclovir (Genital herpes)	500–1000 mg Q12H	≥30 10–29 <10 or HD†	500–1000 mg Q12H 500–1000 mg Q24H 500 mg Q24H
Valacyclovir (Herpes Zoster)	1 g Q8H	≥50 30–49 10–29 <10 or HD†	1 g Q8H 1 g Q12H 1 g Q24H 500 mg Q24H
Valganciclovir (Induction dose)	900 mg Q12H	≥60 40–59 25–39 10–24 <10 or HD†	900 mg Q12H 450 mg Q12H 450 mg Q24H 450 mg Q48H Not recommended
Valganciclovir (Maintenance dose)	900 mg Q24H	≥60 40–59 25–39 10–24 <10 or HD†	900 mg Q24H 450 mg Q24H 450 mg Q48H 450 mg twice weekly Not recommended
Vancomycin	–	–	See section on vancomycin dosing
Voriconazole	See Voriconazole guidelines page 20	–	No dosage adjustment is necessary for PO. IV should not be administered to patients with CrCl ≤50 mL/min due to accumulation of the vehicle.

†If patient is on hemodialysis (HD) schedule administration so that patient receives daily dose immediately AFTER dialysis. For assistance with dosage adjustments for patients receiving CVVHD or CVVHDF, please call pharmacy.

Cost of selected antimicrobial agents

Drug	Daily dose*	Cost/day**
Amikacin	1000 mg once daily	$ 5
Amoxicillin	500 mg three times daily	$ 1
Amoxicillin/clavulanate	500 mg three times daily	$ 3
Amoxicillin/clavulanate	875 mg twice daily	$ 2
Ampicillin	2 g every 4 hours	$ 36
Ampicillin/sulbactam	1.5 g every 6 hours	$ 11
Azithromycin PO	500 mg once daily	$ 2
Azithromycin IV	500 mg once daily	$ 7
Aztreonam	1 g every 8 hours	$ 96
Cefazolin	1 g every 8 hours	$ 4
Cefepime	1 g every 8 hours	$ 15
Cefotetan	1 g every 12 hours	$ 17
Cefoxitin	1 g every 6 hours	$ 17
Cefpodoxime	200 mg twice daily	$ 5
Ceftazidime	2 g every 8 hours	$ 20
Ceftriaxone	1 g once daily	$ 2
Cephalexin	500 mg every 6 hours	$ 1
Ciprofloxacin PO	500 mg twice daily	$ 1
Ciprofloxacin IV	400 mg every 12 hours	$ 4
Clarithromycin	500 mg twice daily	$ 2
Clindamycin IV	600 mg every 8 hours	$ 7
Clindamycin PO	300 mg every 8 hours	$ 1
Daptomycin	500 mg once daily	$191
Doxycycline	100 mg twice daily	$ 1
Ertapenem	1 g once daily	$ 52
Fosfomycin	3 g once	$ 36
Gentamicin	80 mg every 8 hours	$ 2
Gentamicin	300 mg once daily	$ 2
Linezolid PO	600 mg twice daily	$134
Linezolid IV	600 mg every 12 hours	$172
Meropenem	1 g every 8 hours	$ 87
Metronidazole PO	500 mg every 8 hours	$ 1
Metronidazole IV	500 mg every 8 hours	$ 5
Minocycline	100 mg twice daily	$ 1
Moxifloxacin PO	400 mg once daily	$ 3
Moxifloxacin IV	400 mg once daily	$ 12
Nitrofurantoin	100 mg twice daily	$ 2
Oxacillin	2 g every 4 hours	$ 82
Penicillin G	2 MU every 4 hours	$ 12
Piperacillin	3 g every 6 hours	$ 37
Piperacillin/tazobactam	3.375 g every 6 hours	$ 84
Quinupristin/dalfopristin	500 mg every 8 hours	$417
Rifampin PO	300 mg every 8 hours	$ 4
Rifampin IV	300 mg every 8 hours	$ 52
Tigecycline	50 mg twice daily	$ 98
Tobramycin IV	120 mg every 8 hours	$ 6
TMP/SMX PO	1 DS tab twice daily	$ 1
TMP/SMX IV	350 mg every 8 hours	$ 19
Vancomycin PO	125 mg four times daily	$ 65
Vancomycin IV	1 g every 12 hours	$ 10

* Estimated, based on a 70 kg patient; may vary according to indication and patient-specific parameters

** Johns Hopkins Hospital acquisition cost, rounded up to nearest $1, updated 05/09

Cost of selected antifungal agents

Drug	Daily dose*	Cost/day**
Amphotericin B	50 mg once daily	$ 10
Liposomal AmB (AmBisome®)	210 mg once daily	$214
Liposomal AmB (AmBisome®)	350 mg once daily	$357
Fluconazole PO	200 mg once daily	$ 1
Fluconazole IV	200 mg once daily	$ 7
Fluconazole IV	400 mg once daily	$ 8
Itraconazole PO (solution)	200 mg once daily	$ 19
Micafungin	100 mg once daily	$ 88
Micafungin	150 mg once daily	$132
Posaconazole PO (suspension)	400 mg twice daily	$100
Voriconazole PO	200 mg twice daily	$ 70
Voriconazole IV	300 mg every 12 hours	$311

* Estimated, based on a 70 kg patient; may vary according to indication and patient-specific parameters

** Johns Hopkins Hospital acquisition cost, rounded up to nearest $1, updated 05/09

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Important Phone Numbers

Antibiotic Approval:	**3-9ABX (3-9229)**
Antibiotic Management Program:	**7-4570**
Infectious Diseases Consults:	**3-8026**
Tucker Service (Transplant ID)	**# 4-0242**
Osler 2 Pharmacy:	**5-6150**
Carnegie 6 Pharmacy:	**5-6505**
Weinberg Pharmacy:	**5-8998**
Microbiology Lab:	**5-6510**
Hospital Epidemiology & Infection Control:	**5-8384**
HEIC Emergency Beeper:	**3-3855**

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