Antimicrobial Guidelines for Prison Populations

Quantum Units Education
Affordable. Dependable. Accredited.

www.quantumunitsed.com

Table of Contents

Tables:

1. Purpose

The purpose of this document is to provide guidance on the appropriate use of antimicrobials, to provide recommendations and standards for the medical management of inmates receiving antimicrobial therapy, and to outline the Federal Bureau of Prisons (BOP) Antimicrobial Stewardship Program.

This document should be utilized in tandem with the BOP *Technical Guidance for the Use of Injectable Medications*, as applicable.

2. Introduction

Antimicrobial resistance is a growing problem in the healthcare and community settings—leading to increased morbidity, mortality, and healthcare costs. The Centers for Disease Control and Prevention (CDC) states that antibiotic resistance is one of the world's most pressing public health problems. Inappropriate antimicrobial prescribing practices are largely responsible for the growth of resistant microbes. Studies have shown antibiotic use is unnecessary or inappropriate in as many as 50% of the cases in the United States. According to one study, antibiotics were prescribed in 68% of acute respiratory tract visits; of those, 80% were unnecessary, according to CDC guidelines. Common prescribing concerns include unnecessary antimicrobials, overuse of broad spectrum antibiotics, ineffective agents, wrong doses, and extended durations of therapy. All of these contribute to the growing resistance problem.

Fast Facts from the CDC*

- Antibiotic overuse contributes to the growing problems of *Clostridium difficile* infection and antibiotic resistance in healthcare facilities.
- Improving antibiotic use through stewardship interventions and programs improves patient outcomes, reduces antimicrobial resistance, and saves money.
- Interventions to improve antibiotic use can be implemented in any healthcare setting, from the smallest to the largest.
- Improving antibiotic use is a both medication-safety and patient-safety issue.

* CDC Get Smart for Healthcare: http://www.cdc.gov/getsmart/healthcare/inpatient-stewardship.html

To combat bacterial resistance and minimize adverse effects related to treatment, many institutions and organizations have developed antimicrobial stewardship programs. Such programs provide healthcare providers with guidance on pathogen identification and selection of appropriate antimicrobial agents, dosage, and the route and duration of therapy. When implemented appropriately, antimicrobial stewardship programs in conjunction with infection control can lead to decreased antimicrobial resistance and reduced healthcare costs.

3. Antimicrobial Stewardship in the BOP

The BOP *Antimicrobial Stewardship Guidance* employs several strategies to ensure appropriate use of antimicrobials. These strategies include:

(1) Education: The BOP educates providers through a variety of means, both locally and nationally, to ensure that antimicrobials are utilized appropriately. Part of this approach is the issuance of Clinical Practice Guidelines on topics such as methicillin-resistant *Staphylococcus aureus* (MRSA), hepatitis B, hepatitis C, and tuberculosis. The use of antimicrobials is also addressed in continuing medical education presentations, drug utilization reviews, and peer reviews, as well as informational presentations given by staff at the local level.

(2) Formulary Management: The BOP utilizes a formulary with varying degrees of restrictions. Medications are either *unrestricted* (e.g., amoxicillin) or *restricted* (e.g., clarithromycin as a second-line agent requiring physician co-sign). Additionally, some medications may be restricted to use for certain diagnoses only.

Depending upon local circumstances, the pharmacy and therapeutics committees in some institutions may choose to place additional restrictions on medications on the BOP National Formulary or to remove certain items from their local formularies.

(3) Prior Approval Programs: All medications not listed on the BOP National Formulary require prior approval via the non-formulary request process. The BOP does not require prior-approval for medications listed on the National Formulary, so long as their use complies with any applicable formulary restrictions.

Similar to the *formulary management* option described above, the pharmacy and therapeutics committees in some institutions require additional approval for the use of certain formulary medications. This approval may include the institution's clinical director or pharmacist, or both. This type of local prior approval is often applied to second-line therapy and may require culture and sensitivity data.

(4) Streamlining: *Streamlining* refers to the practice of converting a patient from broad-spectrum to narrow-spectrum therapy. If a provider starts a patient on empiric treatment with broad-spectrum antimicrobials, he or she should narrow the treatment selection to better meet the patient's specific needs once culture and sensitivity data are available. This may involve changing antibiotics, reducing the number of medications, or discontinuing treatment.

Benefits associated with streamlining include:

- Reduced secondary infections
- Decreased morbidity and mortality
- Minimized antimicrobial resistance
- Minimized toxicity and adverse effects
- Reduced healthcare expenses

4. General Guidance for Diagnosis and Identifying Infection

Before initiating antibiotic therapy, providers should:
(1) Confirm that an infection is in fact present.
(2) Identify the microorganism(s) causing the infection.
(3) Select the most appropriate antimicrobial therapy.

When determining if an infection is present, providers should look for both systemic and local signs of infection. *Systemic signs* of infection include malaise, fever, and chills; whereas, *local signs* of infection vary depending on the location of the infection. For example, skin and soft tissue infections are often characterized by redness, warmth, and purulent discharge. Urinary tract infections may be characterized by lower abdominal pain and burning with urination. Bone infections may present as an open tract in the skin with discharge.

Potential pathogens exist on all body surfaces that are exposed to the environment, including the skin, GI tract, lungs, nasal cavity, vaginal canal, etc. This colonization is normal. In the presence of an infection, understanding which pathogens normally colonize a particular site of infection or entry point (e.g., catheter site for bacteremia, GI tract rupture for intra-abdominal infection, urethra for bladder or kidney infection, etc.) is paramount, so that appropriate empiric antibiotic therapy can be initiated until culture and sensitivity data are available.

Table 1. Common Methods to Confirm the Presence of Infection and Identify the Cause

- **Fever:** A body temperature above 38°C (100.4°F)
- **Elevated white blood cell count:** Normal range = 4,000–10,000/mm^3
- **Physical presentation:**
  - Pain and inflammation—swelling, erythema, tenderness, or purulent drainage
  - Cough and/or congestion
- **Predisposing factors:**
  - Obtain a complete medical history, including underlying disease states.
  - Alterations in normal flora of the host
  - Disruption of natural barriers such as skin and mucus membranes
  - Immunosuppression secondary to malnutrition, underlying disease, hormones, or drugs
- **Other diagnostic tests to consider:**
  - Chest x-ray
  - CT scan
  - Spinal tap
  - Aspiration of abscesses
- **Sample infected body materials and perform cultures/gram stains/sensitivity for those with moderate to severe infections, as well as those requiring IV antibiotics—*before initiating empiric antimicrobial therapy*:**
  - Obtain a blood culture in all acutely ill, febrile patients.
  - If the urinary tract is involved obtain a urine culture for all men, in the context of suspected recurrent infections in women, and whenever, sepsis is suspected for both men and women
  - If diarrhea is present, obtain stool cultures with the presence of fever and hematochezia, for protracted diarrhea, within the context of a diarrheal outbreak, and with a patient history of prior antibiotic use and suspected *C. difficile* infection.
  - If an open wound is present, culture discharge, in accordance with *MRSA Clinical Practice Guidelines*.
- ***Providers should be aware of normal flora/colonizing organisms when evaluating cultures and sensitivities.***

Note: *Gram stain results tell whether pathogen is gram (+) or (–) and may help narrow empiric therapy.*
Note: *Culture results are used to de-escalate/narrow therapy, based on sensitivities.*

Diagnosis of Specific Infections

Upper Respiratory Infections (not otherwise specified)

The diagnosis of non-specific upper respiratory tract infections or acute rhinopharyngitis should be used to denote an acute infection that is typically viral in origin, and in which sinus, pharyngeal, and lower airway symptoms — although frequently present — are not prominent.

Rhinosinusitis

Most cases of acute rhinosinusitis that are diagnosed in ambulatory care are due to uncomplicated viral upper respiratory tract infections. Any one of three clinical presentations is used to help differentiate between acute bacterial and viral rhinosinusitis:

(1) Onset with persistent symptoms lasting ≥ 10 days, without any evidence of clinical improvement.

(2) Onset with severe symptoms or signs of high fever (≥102º F), together with purulent nasal discharge or facial pain, lasting at least 3–4 consecutive days at the beginning of the illness.

(3) Onset with worsening symptoms or signs—characterized by a new onset of fever, headache, or increased nasal discharge—following a typical viral upper respiratory infection that lasted 5-6 days and was initially improving ("double sickening").

➔ *Sinus radiographs are not recommended for diagnosis in routine cases*.

Pharyngitis

The large majority of adults with acute pharyngitis have a self-limiting illness that should be treated with supportive care only. The benefits of antibiotic treatment of adult pharyngitis are limited to those patients with group A streptococcal (GAS) infection. GAS is the etiologic agent in approximately 5–15% of adult cases of pharyngitis.

Clinical features alone are unreliable in differentiating between GAS and viral pharyngitis, except where overt viral features are present (e.g., rhinorrhea, cough, oral ulcers, and/or hoarseness). Because the signs and symptoms of streptococcal and non-streptococcal (usually viral) pharyngitis overlap, diagnosis should be accomplished through laboratory testing with either a throat culture or a rapid antigen detection test (RADT).

Throat cultures are *not* recommended for confirming negative RADT results in adults. Throat cultures may be indicated when investigating outbreaks of GAS infection, as a means of monitoring the development and spread of antibiotic resistance, or when pathogens such as gonococcus are being considered.

Bronchitis

When evaluating adults who have an illness with an acute cough, or with a presumptive diagnosis of uncomplicated acute bronchitis, *the provider should focus on ruling out pneumonia*. In healthy, non-elderly adult patients, pneumonia is uncommon in the absence of vital sign abnormalities or findings of consolidation on lung auscultation. Chest radiographs are not warranted when these objective signs of pneumonia are not present in the patient presenting with acute nasopharyngeal symptoms and cough.

➔ *Chest radiography is only warranted for patients with a cough lasting three weeks or longer, in the absence of other known causes*.

Osteomyelitis

The diagnosis of osteomyelitis is often accomplished using x-ray; however, it is important to note that changes may not appear on x-ray for 10–14 days following an infection. Clinical features include fever, leukocytosis, and erythema/pain/swelling in the area of infection. Bone scans are of limited benefit, since they are non-specific for infection and will show any inflammation that is present. Erythrocyte sedimentation rate and C-reactive protein may be beneficial, but again are non-specific. CT/MRI may also be useful in diagnosis. It is important to follow cultures and sensitivities for the source of infection (i.e., blood, bone biopsy, or aspirate cultures).

Acute osteomyelitis cases have an approximate 80% cure rate; however, chronic osteomyelitis is more difficult to treat due to necrotic bone being a site for continued infection.

Clostridium Difficile Infection (CDI)

According to the CDC, while many types of healthcare-associated infections are on the decline, the incidence of CDI remains at historically high levels. Multiple risk factors have been identified for the development of CDI, including:

- Age greater than 64
- Duration of hospitalization
- Exposure to chemotherapy
- Infection with human immunodeficiency virus
- Gastrointestinal surgery or other manipulation of the GI tract, including tube feeding
- Exposure to antimicrobial agents

The most modifiable risk factor is exposure to antimicrobial agents. Antimicrobial agents disrupt normal GI flora, allowing *C. difficile* to flourish. Both extended exposure and exposure to multiple antimicrobial agents increase the risk for CDI. Minimizing the frequency and duration of antimicrobials, as well as reducing the number of antimicrobial agents prescribed, help to decrease the risk for CDI.

The severity of CDI is categorized as:

- ***Mild to Moderate:*** WBC $\leq$15,000 *and* SrCr < 1.5x baseline
- ***Severe:*** WBC >15,000 *or* SrCr >1.5x baseline
- ***Complicated:*** Hypotension, shock, toxic megacolon, bowel perforation, severe colitis on CT scan

Diagnosis of CDI should be based on a combination of clinical and laboratory findings. Diagnostic stool evaluations should be pursued in patients that have clinically significant diarrhea, usually defined as three or more loose stools per day for at least two days. CDI may also be considered if a patient presents with several loose stools (10 to 15) with fever or nocturnal diarrhea, even if symptoms have been present for as little as one day in duration. Some patients may present with ileus, and diarrhea may be infrequent. The optimal approach for laboratory diagnosis of *C. difficile* is uncertain; however, the current preferred laboratory diagnostic method is via toxin assay. Stool cultures are the most sensitive test, but are not clinically practical due to slow turnaround time (two to three days).

5. Culture and Sensitivity

Culture and sensitivity (C&S) results are used to help direct and streamline therapy. They should be considered for all moderate to severe infections, as well as all infections requiring IV therapy. The optimal time for cultures is prior to the initiation of antimicrobial therapy. If culture results are negative, the provider should re-evaluate the patient's diagnosis and consider discontinuing the antimicrobial. This is particularly true when the culture sample is taken prior to initiating therapy.

➔ *When culturing a tissue that is normally colonized, the resulting growth will include many of the colonizing bacteria, in addition to any pathogens causing an infection. For example, skin/soft tissue is colonized with many different organisms. In this case, a culture would be of little value. Therefore, it is only appropriate to culture purulent discharge from the skin, e.g., a lanced abscess, or fluid that would normally be sterile—such as blood, urine, or cerebrospinal fluid.*

Urinalysis

Urine will often grow organisms when cultured because it passes through tissue that is typically colonized with bacteria. Therefore, a urinary infection should be confirmed by the presence of bacteria and elevated white blood cells in the urinalysis, and by systemic signs of infection.

Indicators of infection on a urinalysis:

- *Turbid/cloudy urine.*
- *Positive leukocyte esterase*, which indicates the presence of white blood cells in the urine.
- *Presence of >10 WBCs.* Upon microscopy, the presence of 10 WBCs per high-power field is equivalent to 100 cells/mm^3 of urine, which is considered the upper limit of normal.
- *Positive nitrite test*, which indicates the presence of a nitrate-reducing microorganism, such as *Escherichia coli* or any other member of the Enterobacteriaceae family.
- *Elevated pH (6.5–8).* This may indicate the presence of organisms that produce the enzyme urease, which catalyzes the hydrolysis of urea into ammonia and carbon dioxide. Some of these organisms include *Staphylococcus saprophyticus, Klebsiella pneumonia,* and *Proteus* species.
- *Presence of ≥10^5 colony forming units (CFU)* of bacteria per milliliter of urine.
  - ➔ *Approximately one-third to one-half of young women with symptomatic lower urinary tract infections have less than 10^5 CFU/ml of urine. Thus, the presence of ≥10^2 CFU/ml should be considered in the context of the patient characteristics and the signs and symptoms.*

Urine Culture

➔ *A urine culture must always be interpreted in the context of a urinalysis and patient symptoms.*

A urine culture is not required for the treatment of women with symptomatic cystitis unless the patient has recurrent urinary tract infections, is immunocompromised, or has other co-morbid complications. A urine culture is always warranted for the evaluation of men presenting with symptoms of cystitis.

Asymptomatic patients with positive urine cultures have either asymptomatic bacteriuria or a contaminated urine specimen. Typically, catheterized patients will become colonized within 48 hours of catheterization. Asymptomatic bacteriuria is generally not treated, with two important exceptions: pregnant women and patients scheduled for genitourinary surgical procedures

Respiratory Cultures

- **Lower Respiratory Tract:** Appropriate specimens for use in identifying pathogens that cause disease of the lower respiratory tract (tracheitis, bronchitis, pneumonia, lung abscess, and empyema) include expectorated and induced sputum, endotracheal tube aspirations, bronchial brushings, washes or alveolar lavages collected during bronchoscopy, and pleural fluid.
- **Upper Respiratory Tract:** Appropriate specimens for use in identifying pathogens that cause upper respiratory tract infections include samples from the nasopharynx, throat, oral ulcerations, and inflammatory material from the nasal sinuses.

➔ *All specimens should be stored under refrigeration until delivered to the laboratory (to inhibit growth of normal flora).* Neisseria gonorrhea *is particularly susceptible to dehydration, so swabs must be inoculated directly to plate media or put into an appropriate transport medium.*

➔ *Rapid antigen detection (RADT) tests for GAS can be utilized to direct treatment of pharyngitis. If an RADT test is utilized, ensure that the test is a CLIA waived variety. RADT tests should only be performed under structured waived testing programs, and each site must have their own CLIA waiver.*

6. Therapy Selection

When selecting therapy, providers should consider: the severity and acuity of the disease, host factors, factors related to the medications used, and the necessity for multiple agents. Depending on severity and acuity, therapy is often begun empirically—directed at organisms that are frequently known to cause the infection in question.

When selecting empiric antibiotic therapy, it is necessary to select an antimicrobial with the following characteristics:

- Spectrum is broad enough to target organisms that are reasonably suspected of causing the infection, yet narrowed to cover only the suspected families of organisms.

  Example: *If a patient is suspected of having an infection caused by a gram-positive organism, empiric therapy should be selected for gram-positive organisms. The therapy should not cover both gram-positive and gram-negative organisms.*
- Least potential for adverse effects
- Greatest ease of administration
- Most cost-effective

Local susceptibility data should always be considered to direct and narrow the therapy. If/when a particular pathogen is isolated as the causative pathogen of the infection, the antibiotic should be switched to the most narrow-spectrum antibiotic that has activity against that pathogen, as defined by the criteria listed above.

Table 2. Common Diagnoses NOT Recommended for Treatment with Antibiotics

- Upper respiratory infections
- Acute rhinosinusitis
- Acute pharyngitis where group A *Streptococcus* is not suspected
- Bronchitis
- If MRSA is suspected, refer to the BOP Clinical Practice Guidelines, *Management of MRSA Infections*, on when to treat.

Specific Diagnoses

Upper Respiratory Infections (URIs) – Not Otherwise Specified

➔ *Antibiotic treatment of nonspecific upper respiratory infections in adults does not enhance illness resolution nor prevent complications, and is therefore not recommended.*

Purulent secretions in the nares and throat (commonly reported and seen in patients with an uncomplicated, upper respiratory tract infection) neither predict bacterial infection nor benefit from antibiotic treatment.

Rhinosinusitis

➔ *Most cases of acute rhinosinusitis are viral in nature and therefore antibiotic treatment is not indicated. Symptomatic treatment and reassurance is the preferred, initial management strategy for these patients.*

Empiric antimicrobial therapy should be initiated as soon as it is determined that clinical presentation matches the definition for acute <u>bacterial</u> rhinosinusitis. Once initiated, treatment should be continued for 5–7 days for uncomplicated cases.

- Amoxicillin/clavulanate is the antimicrobial of choice for acute bacterial rhinosinusitis. Doxycycline or a fluoroquinolone may be used as an alternative for adult patients allergic to penicillin.
- Although routine dosing is usually adequate, some patients should be considered for high-dose amoxicillin/clavulanate. Factors identifying those patients include:
  - Geographic region with high endemic rates of penicillin-nonsusceptible *S. pneumoniae*
  - Severe infection with evidence of systemic toxicity (fever ≥102º F, and threat of suppurative complications)
  - Age >65
  - Antibiotic use within the past month
  - Recent hospitalization

Macrolides are no longer recommended due to high resistance rates in *S. pneumoniae* (~30%). Sulfamethoxazole/trimethoprim is no longer recommended due to high resistance rates in *S. pneumoniae* and *H. influenzae* (~30–40%). Second- and third-generation oral cephalosporins are no longer recommended for empiric monotherapy of acute bacterial rhinosinusitis due to variable rates of resistance among *S. pneumoniae*.

Acute Pharyngitis

Since antibiotic therapy is only beneficial in the 5–15% of pharyngitis cases with GAS infection, antibiotic prescriptions should be limited to those patients who have confirmed acute GAS pharyngitis. The preferred antibiotic for treatment of acute GAS pharyngitis is penicillin or amoxicillin, with sufficient treatment duration to eradicate infection (usually 10 days). First-generation cephalosporins are preferred for penicillin-allergic patients whose allergy is not associated with anaphylaxis. Clindamycin or clarithromycin for 10 days, or azithromycin for 5 days, is recommended in penicillin-allergic patients with anaphylaxis.

➔ *See the algorithm in Appendix 1, Treatment of Pharyngitis.*

All patients with pharyngitis should be offered, or be referred to the commissary for, appropriate doses of analgesics, antipyretics, and other supportive care, in accordance with the BOP National Formulary Part I, Over the Counter Prescribing Criteria Matrix.

Bronchitis

➔ *Routine antibiotic treatment of uncomplicated bronchitis is not recommended, regardless of duration of the cough.*

In the unusual circumstance when pertussis infection is suspected, consult the current CDC guidelines. Patient satisfaction with the care for acute bronchitis is largely reliant on provider-patient communication, rather than on the use or non-use of antibiotics.

Pneumonia

Pneumonia treatment is divided into several basic types:

- **Community-acquired pneumonia (CAP).**
  ➔ *See the algorithm in Appendix 2, Treatment of Community Acquired Pneumonia.*
- **Hospital-acquired pneumonia (HAP).** Occurs at least 48 hours or more after admission, but was not incubating at the time of admission. HAP patients who are intubated should be managed in the same way as those with ventilator-associated pneumonia.
- **Ventilator-associated pneumonia (VAP).** Refers to pneumonia that arises more than 48–72 hours after endotracheal intubation.
- **Healthcare-associated pneumonia (HCAP)**. Includes any patient who was hospitalized in an acute care hospital for two or more days within 90 days of the infection; who resided in a nursing home or long-term care facility; who received recent intravenous antibiotic therapy, chemotherapy, or wound care within 30 days of the current infection; or who attended a hospital or hemodialysis clinic.

The initial treatment of HAP, VAP, and HCAP is consolidated within this guidance—with the assumption that providers will narrow therapy, based on local bacteriologic variability and culture and sensitivity reports.

➔ *See the algorithm in Appendix 3, Treatment of Hospital, Ventilator, and Healthcare Pneumonia.*

➔ *See also Appendix 4, Antibiotics Used in the Treatment of Pneumonia.*

Deep Tissue Infections

Retropharyngeal abscess, intracranial abscess, or other deep tissue infection may compromise the airway, vision, or neurologic function. Patients with evidence of intraorbital or intracranial extension of suppurative infection warrant hospitalization, imaging, and surgical consultation. Antibacterial therapy is often warranted.

Immunocompromised

Special attention is warranted in patients with suboptimal immune defenses, including:

- Patients without a spleen
- HIV infection
- Patients with cancer or those undergoing therapy for cancer
- Dialysis patients
- Those undergoing stem cell or organ transplantation
- Those with congenital immunodeficiency
- Immunosuppressive medications (e.g., chronic steroid therapy)

Patients who have undergone splenectomy have a reduced ability to fight infections caused by encapsulated organisms (e.g., *S. pneumoniae*). Appropriate antimicrobial therapy and close follow-up may be appropriate because a simple URI may quickly progress to a systemic illness in immunocompromised patients. Although the threshold for hospitalization is lowered for these patients, their risks of nosocomial infections must be weighed against the benefits of close monitoring in the inpatient setting.

Osteomyelitis

Osteomyelitis is an infection of the bone, and can be divided into three major categories based on the source of the infection. Infections can be hematogenous, contiguous, or related to a diabetic ulcer or vascular insufficiency.

- **Hematogenous infections** originate in the blood and usually affect the long bones. They are more common in children <16 years old, males, and IV drug users. Risk factors include prematurity, respiratory distress syndrome, puncture wounds, and sickle cell disease. Common pathogens include *S. aureus*, *Streptococci* species, *Salmonella* in sickle cell patients, and *Pseudomonas* following nail puncture injury.
- **Contiguous osteomyelitis** infections occur when the organisms spread directly from a localized area, such as surgery or bone injury. Common pathogens include various *Staphylococci* and gram-negative rods (including *Pseudomonas*).
- **Osteomyelitis associated with diabetic ulcers or vascular insufficiency** could be considered a subcategory of contiguous osteomyelitis. Usual pathogens include anaerobes, *Staphylococci*, *Streptococci* species, and gram-negative rods. These infections are almost always polymicrobial in nature.

Antibiotic treatment of osteomyelitis is usually 4–6 weeks in duration, and surgery often plays an important role in the treatment.

Cellulitis

Non-Purulent Cellulitis Infections – Methicillin-Sensitive *Staphylococcus aureus* (MSSA)

Non-purulent cellulitis infections—at institutions that have surveillance cultures indicating that a Methicillin-Resistant *Staphylococcus aureus* (MRSA) infection is unlikely—can be managed with empiric therapy, as follows:

- Dicloxacillin 500 mg po q6h
- Cephalexin 500 mg po q6h
- Clindamycin 300–450 mg po q6-8h
- Cefazolin 1–2 g IV q8h
- Oxacillin or nafcillin 2 g IV q4h
- Clindamycin 600–900 mg IV q8h

Follow-up after starting empiric therapy should be done after 48–72 hours to assess for clinical improvement. If there is no improvement, resistance or an alternative diagnosis should be considered. If there is clinical improvement, treatment should be continued for 5–10 days.

Cellulitis Infections – MRSA

For cellulitis within an institution where MRSA is suspected, refer to the BOP Clinical Practice Guidelines, *Management of MRSA Infections*.

Cellulitis Infections Associated with Diabetic Ulcers

Cellulitis infections associated with diabetic ulcers should be managed according to severity:

Mild: Cellulitis affecting the superficial tissue, and extending < 2 cm around a diabetic ulcer would be considered mild cellulitis. Initial treatment is as follows:

- Penicillin VK 500 mg po q6h *and* SMX-TMP DS: two tablets po q12h *or* Doxycycline 100 mg po q12h
- Clindamycin 300–450 mg po q6-8h

If there is no clinical improvement after administration of antibiotics, therapy should be changed to match treatment for moderate cellulitis.

Moderate: Moderate cellulitis extends > 2 cm around a diabetic ulcer, and usually affects deeper tissues. Coverage for these infections begins to cover gram-negative rods and anaerobes. Treatment for moderate cellulitis includes:

- SMX-TMP DS 2 tabs po q12h *and* amoxicillin-clavulanate 875/125mg po q12h
- Clindamycin 300-450 mg po q 6-8h *and*
  - Ciprofloxacin 750 mg po q12h *or*
  - Levofloxacin 750 mg po q24h *or*
  - Moxifloxacin 400 mg po q24h

Severe: Cellulitis associated with signs of systemic toxicity is considered severe cellulitis. Usual treatment is with IV vancomycin, in addition to another agent (refer to *Appendix 7* for specific dosing guidance). The second agent should include imipenem 500 mg IV q6h, ertapenum 1 g IV daily, *or* meropenem 1 g IV q8h if the organism is suspected to be an Extended Spectrum Beta-Lactamase producer.

Acne

Acne is a very common condition, affecting 45 million people in the United States, and carries a lifetime prevalence of 85%. In the BOP, treatment of acne is classified as "Limited Medical Value." Treatment of conditions in this category is usually excluded from the scope of services provided. Patients who have cystic acne and who show evidence of, or are at high risk for, permanent scarring may be considered for treatment on a case by case basis. All other patients should be referred to the commissary to purchase appropriate over-the-counter products.

While scarring can be a common clinical manifestation of acne, permanent scarring is characterized by either excessive tissue formation (hypertrophic scars and keloids) or atrophic scars, both of which can be brought about by dermal damage and the longstanding presence of cysts.

Patients who are candidates for acne treatment (have evidence of, or are at high risk for permanent scarring) should be reviewed by the Institution Utilization Review Committee prior to the initiation of therapy.

➔ *Oral antibiotic therapy should be limited to 12–18 weeks when medically indicated. Antibiotics used to treat acne can contribute to the development of antibiotic resistance.*

Clostridium difficile Infection (CDI)

- **Metronidazole:** CDI is treated with metronidazole for initial episodes of mild to moderate infection. Metronidazole may also be used for an initial recurrence, but should not be used for long-term treatment.
- **Vancomycin:** Oral vancomycin is the treatment of choice for initial and subsequent episodes of severe infection. Oral vancomycin should also be utilized for the second or later recurrences.
- **Probiotics:** The use of probiotics is not recommended to prevent or treat CDI.

➔ *Diagnostic* C. *difficile assays should NOT be conducted in asymptomatic patients following the completion of antibiotic therapy, since the persistent detection of the organism is common and not indicative of treatment failure.*

For additional information please see the Society for Healthcare Epidemiology of America – Infectious Disease Society of America joint Clinical Practice Guidelines for *Clostridium difficile*.

Dental Prophylaxis

Infective Endocarditis

Currently, the American Dental Association (ADA) and the American Heart Association (AHA) recommend the use of preventive antibiotics prior to dental procedures that involve manipulation of gingival tissue or the periapical region of the teeth, or perforation of the oral mucosa, for patients with the following conditions:

- Prosthetic cardiac valve or prosthetic material used for cardiac valve repair
- History of infective endocarditis
- Cardiac transplant that develops cardiac valvulopathy

(list of conditions continues on next page)

- The following congenital heart conditions:
  - Unrepaired or incompletely repaired cyanotic congenital heart disease, including those with palliative shunts and conduits.
  - During the first six months after a procedure to completely repair a congenital heart defect with a prosthetic material or device, whether by surgery or catheter intervention.
  - Repaired congenital heart defect with residual defect at the site or adjacent to the site of a prosthetic patch or prosthetic device.

When indicated, antibiotic administration is recommended *prior* to dental treatment; however, if the dose is not administered before the procedure, it may be given to the patient *up to two hours after* the procedure.

➔ *Except for the conditions listed above, all other congenital heart conditions—as well as mitral valve prolapse, rheumatic heart disease, bicuspid valve disease, and calcified aortic stenosis—are no longer recommended for antimicrobial prophylaxis.*

The current prophylactic regimens for prevention of bacterial endocarditis are listed in *Table 3* below. All providers are encouraged to access the AHA and ADA websites for the latest premedication recommendations, including the links found at: http://www.gmda.org/resources/premedication/2007premed.htm.

Table 3. Dental Prophylaxis for Bacterial Endocarditis Prevention (Adult Patients Only)

Scenario	Route	Prophylactic Regimen (Administer ONE of the following medications 30–60 minutes before the procedure.)	
NOT Allergic to Penicillins or Ampicillin	Oral	Amoxicillin	2 grams
	IM*	Ampicillin	2 grams
Allergic to Penicillins or Ampicillin	Oral	Cephalexin	2 grams
		Clindamycin	600 milligrams
		Azithromycin *or* clarithromycin	500 milligrams
	IM*	Cefazolin *or* ceftriaxone**	1 gram
		Clindamycin	600 milligrams

* IM = Intramuscular (use if patient is unable to take oral medication)

** Cephalosporins should not be used in a person with a history of anaphylaxis, angioedema, or urticaria from using penicillins or ampicillin

Adapted from: Table 2 in Wilson W, Taubert KA, Gewitz M, et al. Prevention of infective endocarditis: guidelines from the American Heart Association. *JADA.* 2008;139:3s–24s. Available at http://jada.ada.org/content/139/suppl_1/3S.full.pdf

Dental Prophylaxis for Patients with Prosthetic Joints

Current recommendations for dental prophylaxis for those with prosthetic joints continues to be controversial. The use of prophylaxis is lacking evidence, and the area is defined as a research gap by the Infectious Disease Society of America. (See resources listed in *National Guidelines* section of this document.) Providers should review and decide on the use of prophylaxis on a case-by-case basis.

7. Intravenous to Oral Conversion Guidelines

The ideal route for administration of any medication achieves serum concentrations adequate to produce the desired therapeutic result, without producing undesired effects. In the past, switching a patient to oral (PO) therapy was accomplished after an adequate course of intravenous (IV) therapy. Today, the PO option is often able to achieve therapeutic concentrations and positive outcomes for patients that were once solely managed with IV medications. As a result, many patients are now converted to PO therapy as part of their initial course of treatment.

The IV to PO conversion promotes many positive clinical outcomes, including: increased quality of life, decreased risk of the adverse events associated with IV infusions, decreased administration errors due to the ease of PO administration, and decreased risk of the secondary infections related to IV catheters. Often times, if a patient is in an inpatient bed, conversion of IV medications to PO can hasten their discharge.

In addition to the clinical advantages of switching patients from IV to PO routes, institutions can realize several other benefits, including: decreased costs related to medications (PO formulations are generally less expensive), decreased equipment and supply needs (PO does not require IV sets/pumps), decreased laboratory monitoring, and decreased personnel time for preparation and administration.

The ease of use, safety profile, and ability to achieve therapeutic concentrations makes the oral formulation the ideal route of administration, whenever possible.

Three Types of IV to PO Therapy Conversions

(1) Sequential Therapy

Sequential therapy converts a parenteral medication with an oral counterpart.

- ***Example:*** levofloxacin 500 mg IV *to* levofloxacin 500 mg PO

(2) Switch Therapy

Switch therapy converts a parenteral medication to an oral equivalent within the same class of medication and of the same level of potency. The oral medication, however, is not the same compound and may not have the same pharmacokinetic properties as the parenteral compound.

- ***Example:*** cefazolin 1g IV q12h *to* cephalexin 500 mg PO qid

Table 4. Examples of Medications That Can Be Converted with the *Sequential* or *Switch* Methods

Antibiotics		Antifungals/Antivirals
• Azithromycin	• Ciprofloxacin	• Fluconazole
• Cefuroxime	• Levofloxacin	• Itraconazole
• Clindamycin	• Moxifloxacin	• Voriconazole
• Doxycycline	• Metronidazole	• Acyclovir
• Linezolid	• Sulfamethoxazole/Trimethoprim	• Gancyclovir
Note: *This list is not exhaustive.*		

(3) Step-Down Therapy

Step-down therapy (a) converts a parenteral medication to an oral agent within the *same class* of medication, but where the frequency, dose, and spectrum of activity may not be exactly the same; *or* (b) replaces the parenteral medication with an oral agent that may be from a *different class* of medication.

- ***Example (a) of converting an IV to a PO in the same class:*** ampicillin/sulbactam 3 gram IV every 6 hours can be converted *to* amoxicillin/clavulanate 875mg/125mg PO every 12 hours
- ***Example (b) of replacing an IV with a PO of a different class:*** vancomycin 1g IV q12h *to* Bactrim DS 2 tabs PO bid *or* doxycycline 100mg PO bid

Table 5. Step-Down Therapy Conversion Medication Pairs

IV Medication	Oral Medication	IV Medication	Oral Medication
• ampicillin	• amoxicillin	• ticarcillin/clavulanate	• multiple options
• ampicillin/sulbactam	• amoxicillin/clavulanate	• aztreonam	• ciprofloxacin ***or*** levofloxacin
• piperacillin/tazobactam	• multiple options	• cefazolin	• cephalexin
• cefotaxime ***or*** ceftriaxone	• cefpodoxime ***or*** cefuroxime axetil	• ceftazidime ***or*** cefepime	• ciprofloxacin ***or*** levofloxacin

Notes:
- Confirm culture and susceptibility results before initiation of step-down therapy.
- This list is not exhaustive.

Source: Table 29-1 in Murdaugh LB. *Competence Assessment Tools for Health-System Pharmacies.* Fourth Edition. American Society of Health-System Pharmacists, Inc. Bethesda, Maryland; 2008.

General IV to PO Conversion Considerations

- *Oral medication needs to have known activity against the infection*. Providers should ensure that the cultured pathogen is susceptible to the PO antibiotic. In the absence of a positive culture, the PO medication should empirically cover commonly suspected organisms, based on the condition being treated and local sensitivities.

  Example: Community-acquired pneumonia in a hospitalized immunocompetent patient on a general medical floor is typically caused by *Streptococcus pneumoniae*, *Haemophilus influenzae*, or an atypical organism (*Chlamydophilia pneumoniae*, *Mycoplasma pneumoniae*, or *Legionella*)

- *Oral dosage forms should be provided to the patient in the manner that best improves patient adherence and tolerance to the medication*.

- *Medication should be well-absorbed and demonstrate adequate bioavailability.*

  Note: Although bioavailability is important, it is more important for adequate therapeutic blood levels to be achievable. Most medications are able to achieve these levels unless the patient has a medical condition that would not allow normal absorption to be achieved (see first item below on *gastrointestinal tract functioning*).

- *For osteomyelitis:* Although there is no standard, the literature does support consideration for conversion to oral antibiotics if the patient has a confirmed case of osteomyelitis, the organism is identified, antibiotic susceptibility is determined, oral agent(s) with good bioavailability are selected, and the patient demonstrates good compliance.

Major Criteria to Consider When Selecting Patients for IV to PO Conversion

(1) Gastrointestinal (GI) tract must be intact and functioning: To have a successful IV to PO conversion, it is crucial that the GI tract have the ability to absorb the medication. Factors influencing GI absorption include pH, surface area, permeability, and blood flow. As part of this evaluation, providers may review medication administration records to determine if the patient is receiving other PO medications. Enteral feeding is an absolute contraindication ***only*** if the feeding cannot be interrupted. See *Table 6* below for other considerations.

Table 6. Considerations Concerning the GI Tract and Conversion from IV to PO Therapy

Contraindications to Conversion	Use Conversion with Caution If …
• Continuous or frequent nasogastric (NG) suctioning • Displaying signs and symptoms of shock • Continuous tube feedings that cannot be interrupted and patient requires a medication known to bind to enteral nutrition formulations	• Difficulty swallowing • Loss of consciousness (without feeding tube access) • NPO status • No medications are being administered orally • Severe/persistent nausea or vomiting • GI transit time too short for absorption (malabsorption syndromes, partial or total removal of the stomach, short bowel syndrome) • Active GI bleed (documentation bleeding has stopped) • Documented ileus or GI obstruction

➔ *For additional information on managing IV to PO conversion in the presence of continuous tube feeding, contact a Medical Referral Center (MRC).*

(2) Clinical status must be improving: The clinical signs and symptoms of the condition for which the antibiotic is being prescribed should be improving or resolving in patients before being switched to PO therapy (see *Table 7* below). The patient should be clinically stable, and clinical deterioration should not be anticipated.

Table 7. Signs That Clinical Status is Improving

- In patients with active infections, a febrile or maximum temperature < 100.4° F in past 24 hours,
- White blood cell (WBC) count trending downward[1,2,3].
- In cases where GI bleeding was present, confirmed and documented stoppage of bleeding.

[1] Normalization of WBC indicates the patient's inflammatory response to the infection is waning.

[2] If clinical status is improving, but leukocytosis remains, evaluate the patient's medication profile for other medications that may be causing an increase or sustained high WBC, such as steroids. In this case, a safe conversion to PO therapy can still be made for patients who meet all other criteria for IV to PO conversion.

[3] Neutropenic patients (absolute WBC < 500 cell/mm^3) are usually excluded from IV to PO conversion, although this varies between institutions.

(list of criteria to consider continues on next page)

(3) The patient's condition must not require IV therapy: Oral therapy can be used effectively to treat many different infections; however, certain infections require IV therapy due to the severity or location of the infection. These include:

- Infective endocarditis
- Bacterial meningitis
- Brain abscess
- Orbital cellulitis
- Other CNS infections
- Endophthalmitis
- Patients with numerous antibiotic allergies

Considerations for Converting Specific Medications from IV to PO

Refer to the National BOP Formulary for current formulary status, restrictions, or criteria for individual medications.

Fluoroquinolones:

- ***These medications are excellent candidates for IV to PO conversion.*** Oral formulations have high bioavailability, rapid absorption, and good distribution within the body.
- ***Absorption is affected by concomitant administration with divalent and trivalent cations*** (*examples:* calcium, calcium containing antacids, iron and zinc salts, didanosine, sucralfate). In addition, the absorption and effectiveness of oral fluoroquinolones is decreased in the presence of enteral feedings.

  In order to prevent issues with absorption, manufacturers provide the following instructions:
  - ***Ciprofloxacin:*** Give 2 hours before or 6 hours after any products containing the cations listed above. It should not be given via a feeding tube.
  - ***Levofloxacin:*** Give 2 hours before or 2 hours after any products containing the cations listed above.
  - ***Moxifloxacin:*** Give 4 hours before or 8 hours after any products containing the cations listed above.

Triazole Antifungals:

- ***Fluconazole*** has high bioavailability and is well-absorbed. It is not affected by food or alteration in gastric pH.
- ***Itraconazole*** requires an acidic environment for absorption; therefore, antacids, H_2 antagonists, proton-pump inhibitors, and sucralfate can significantly decrease itraconazole's bioavailability. Manufacturer labeling provides directions for avoiding absorption issues.
  - Itraconazole solution is better absorbed on an empty stomach.
  - Contrary to the solution, itraconazole capsules are better absorbed with food.
- ***Voriconazole*** is best absorbed if given 1 hour before or 1 hour after meals.

➔ ***Both voriconazole and itraconazole IV solutions are contraindicated in renal dysfunction*** *due to possible toxic accumulation of cyclodextran, which is found in both of the IV formulations*.

Vancomycin:

- ***IV use:*** For treatment of gram-positive bacterial infections
- ***PO use:*** *The oral formulation is poorly absorbed* and therefore should only be used to treat *Clostridium difficile* colitis.

➔ ***Do not use vancomycin in IV to PO conversion programs.*** *The IV and PO formulations have different indications*.

Linezolid:

- Linezolid exhibits a weak, non-selective, reversible inhibition of monoamine oxidase (MAO).
- Patients should avoid foods high in tyramine due to an increased risk of serotonin syndrome, leading to a hypertensive emergency. Examples of foods high in tyramine include aged cheeses; cured meats, such as sausage, pepperoni, or salami; soy sauce; and sauerkraut. Improperly stored or spoiled food can also contain tyramine.

IV to PO Conversion Myths

There are many myths associated with IV to PO conversions. New information and studies have disproved many of these myths, such as:

Myth: ***Infectious diseases need IV treatment. Convert to PO sparingly.***
Truth: Newer antimicrobials are available with equivalent IV and oral bioavailability. Literature has shown IV to PO conversion is efficacious, convenient, cost-effective, and safe.

Myth: ***PO antimicrobial must be the same medication or in the same class as the IV treatment.***
Truth: PO needs to cover the same or similar spectrum of activity, have similar tissue penetration, and be effective against the same isolated or suspected organism(s) as the IV. It does not need to be the same medication or in the same class.

8. Multi-Drug Resistant Organisms – Specific Diagnoses

MRSA

See the BOP Clinical Practice Guidelines, *Management of Methicillin-Resistant Staphylococcus aureus (MRSA) Infections*, available at: http://www.bop.gov/news/medresources.jsp

Extended Spectrum Beta Lactamase (ESBL)

Extended Spectrum Beta Lactamase is an enzyme that mediates resistance to third-generation cephalosporins and monobactams. Pathogens known to produce ESBL are gram-negative Enterobacteriaceae, including: *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *Citrobacter freundii*, *Proteus mirabilis*, *Morganella morganii*, and *Enterobacter cloacae*.

If an organism is a confirmed ESBL producer, all penicillins, cephalosporins, and aztreonam should be considered resistant, regardless of other results. Cephamycins (cefotetan and cefoxitin) can still be used, based on individual sensitivities.

Vancomycin Resistant Enterococci (VRE)

Typically, VRE is a hospital-acquired infection caused by *Enterococcus faecium*. It is most often seen in the urine, but can be found in bloodstream infections, as well as wounds associated with catheters and surgical procedures.

Risk factors for VRE include:

- Previous treatment with vancomycin or other antibiotics for extended periods of time
- Hospitalization
- Medical devices/catheters
- Recent surgery
- Immunosuppression
- VRE colonization

9. Communication Strategies

Literature suggests that patient satisfaction is influenced more by communication, than by whether or not the patient receives an antibiotic. The following strategies can be used to validate a patient's illness, and help justify not prescribing antibiotics when they are not clinically indicated.

- ***Choosing terminology*** such as "viral bronchitis," instead of referring to "just a virus" can validate the patient's symptoms. In addition, sharing normal findings of an exam, such as clear lung sounds, reassures patients that the illness may not be as severe as they first thought and helps them be more open to the idea of not receiving an antibiotic.

- ***Offering symptomatic relief*** is another important strategy. Many patients want an antibiotic because they believe it will make them feel better. By suggesting effective symptomatic therapies, providers can offer patients the relief they are seeking.

- ***Providers should discuss side effects of antibiotics***, including adverse events and resistance, and describe what to expect in the days after the initial evaluation. It is important for patients to be aware of what to expect when symptoms change or become more severe, including when it might be appropriate to return for re-evaluation and further treatment.

10. Competencies and Training

Providers who are treating infections need to maintain competence on a variety of subjects in order to provide the best care possible for the patient. When treating patients, providers should be competent in the topics listed below. These competencies may be obtained through a variety of means and should be performed initially and on a regular basis thereafter.

For Physicians/Dentists/MLPs

- Ordering and interpreting culture and sensitivity reports
- Familiarity with BOP Clinical Practice Guidelines, *Management of MRSA Infections*
- Understanding and interpreting antibiograms
- Review of decision flowcharts (algorithms) for various infectious states
- Appropriate dosing of IV antibiotics
- Knowledge of formulary PO antibiotic agents
- Knowledge of formulary IV antibiotic agents
- Timeline for de-escalation of antibiotic therapy
- Awareness of Antibiotic Therapy Guideline Updates
- Understanding the principles of Antibiotic Stewardship
- Knowing the common side effects and adverse events associated with antimicrobials

For Nurses

- Understanding of C&S reports
- Understanding common IV antibiotic dosing frequencies and regimens
- Knowing the signs of improving clinical status that facilitate de-escalation
- Understand the timing of medication dosing and blood sample collection
- Knowing the signs/symptoms of common allergic reactions to frequently used medications
- Awareness of Antibiotic Therapy Guideline Updates
- Understanding the principles of Antibiotic Stewardship
- Knowing the common side effects and adverse events associated with antimicrobials

(Continued on next page)

For Pharmacists

- Interpreting and utilizing C&S reports in evaluating appropriate antibiotic selection
- Understanding and interpreting antibiograms
- Understanding appropriate therapies/flowcharts (algorithms) for locally treatable conditions
- Calculating accurate dosage adjustments based on abnormal renal and liver function tests
- Therapeutic drug monitoring, to include appropriate frequency of lab value collection and understanding of target values
- Appropriate IV to PO dose conversion, to include dose timing and frequency
- Familiarity with BOP Clinical Practice Guidelines, *Management of MRSA Infections*
- Awareness of Antibiotic Therapy Guideline Updates
- Understanding the Principles of Antibiotic Stewardship
- Knowledge of antibiotic pharmacokinetics
- Knowing the common side effects and adverse events associated with antimicrobials

Training Sources/Additional Information

Providers in the BOP may seek assistance from several sources when attempting to optimize antimicrobial therapy including:

- Sanford Guide® to Antimicrobial Therapy
- Pharmacists – Several pharmacists in the BOP have specific Antimicrobial Stewardship training. In addition, MRC pharmacists have broad experience in the area of antimicrobials and can assist with selection, IV to PO conversion, and streamlining.
- MRC reference labs – Staff at these locations have expertise in the area of microbiology and can assist others with culture and sensitivity collections and interpretation.
- CDC – The CDC *Get Smart for Healthcare* website has valuable information on appropriate use of antimicrobials. Available at: *http://www.cdc.gov/getsmart/healthcare/inpatient-stewardship.html*
- American Society of Health-System Pharmacists (ASHP) at *http://www.ashp.org*.
- Infectious disease specialists
- Infectious Disease Society of America (IDSA) at *http://www.idsociety.org/Index.aspx*
- Society of Infectious Disease Pharmacists (SIDP) at *http://www.sidp.org/*
- John's Hopkins Antibiotic Guide online: *www.hopkinsguides.com*
- Nebraska Medical Center Antimicrobial Stewardship Program online: *http://www.nebraskamed.com/careers/education-programs/asp*

National Guidelines

Acute Bacterial Rhinosinusitis

Chow AW, Benninger MS, Brook I, et al. IDSA clinical practice guideline for acute bacterial rhinosinusitis in children and adults. *Clin Infect Dis*. 2012;54(8):1041–1045. Available at: http://cid.oxfordjournals.org/content/54/8/1041

Asymptomatic Bacteremia

Nicolle LE, Bradley S, Colgan R, et al. Infectious Diseases Society of America guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults. *Clin Infect Dis*. 2005;40:643–654. Available at: http://www.idsociety.org/uploadedFiles/IDSA/Guidelines-Patient_Care/PDF_Library/Asymptomatic%20Bacteriuria.pdf

Clostridium difficile

Cohen SH, Gerding DN, Johnson S, et al. Clinical practice guidelines for *Clostridium difficile* infection in adults: 2010 Update by the Society for Healthcare Epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA). *Infect Control Hosp Epidemiol*. 2010;31(5):431–455. Available at: http://www.cdc.gov/HAI/pdfs/cdiff/Cohen-IDSA-SHEA-CDI-guidelines-2010.pdf

Diabetic Foot Infections

Lipsky BA, Berendt AR, Cornia PB, et. al. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. *Clin Infect Dis*. 2012;54(12):132–173. Available at: http://www.idsociety.org/uploadedFiles/IDSA/Guidelines-Patient_Care/PDF_Library/2012%20Diabetic%20Foot%20Infections%20Guideline.pdf

Group A Streptococcal Pharyngitis

Shulman ST, Bisno AL, Clegg HW, et al. Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2012;55(10):e86–e102. Available at: http://cid.oxfordjournals.org/content/55/10/e86.full.pdf+html

Pneumonia

Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. *Am J Respir Crit Care Med*. 2005;171(4):388–416. Available at: http://ajrccm.atsjournals.org/content/171/4/388.full. Accessed August 14, 2011.

Mandell LA, Wunderink RG, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. *Clin Infect Dis*. 2007;44(Suppl 2):S27–72. Available at: http://www.thoracic.org/statements/resources/mtpi/idsaats-cap.pdf. Accessed August 14, 2011.

(list of National Guidelines continued on next page)

National Guidelines *(continued)*

Prevention of Infective Endocarditis

Wilson W, Taubert KA, Gewitz M, et al. Prevention of infective endocarditis: guidelines from the American Heart Association. *JADA*. 2008;139:3s–24s. Available at http://jada.ada.org/content/139/suppl_1/3S.full.pdf

Prevention of Prosthetic Joint Infections for Dental Patients

American Academy of Orthopaedic Surgeons and American Dental Association. *Prevention of Orthopaedic Implant Infection in Patients Undergoing Dental Procedures: Evidence-Based Guideline and Evidence Report*. Rosemont, IL: American Academy of Orthopaedic Surgeons; 2012:1–325. Available at: http://www.aaos.org/research/guidelines/PUDP/PUDP_guideline.pdf

Osmon DR, Berbari EF, Berendt AR, et al. Diagnosis and management of prosthetic joint infection: clinical practice guidelines by the Infectious Diseases Society of America. *Clin Infect Dis*. 2013;56(1):e1–25. Accessed at: http://www.idsociety.org/uploadedFiles/IDSA/Guidelines-Patient_Care/PDF_Library/IDSA%20PJI%20Guideline%20CID%2012%202012.pdf

Vancomycin

Rybak M, Lomaestro B, Rotschafer JC, et al. Therapeutic monitoring of vancomycin in adult patients: a consensus review of the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, and the Society of Infectious Diseases Pharmacists. *American Journal of Health-System Pharmacy*. 2009;66(1):82–98. Available at: http://www.ajhp.org/content/66/1/82.full

References

American Dental Association and American Academy of Orthopaedic Surgeons. Antibiotic prophylaxis for dental patients with total joint replacements. *JADA*. 2003;134:895–899. Available at http://jada.ada.org/content/134/7/895.full.pdf+html

Antibiotic Prophylaxis for Patients after Total Joint Replacement: Information Statement from the American Academy of Orthopaedic Surgeons, 2009. Available at: http://orthodoc.aaos.org/davidgrimmmd/Antibiotic%20Prophylaxis%20for%20Patients%20after%20Total%20Joint%20Replacement.pdf. Accessed November 27, 2012.

Armbrust, A, Capraro GA, Fey PD, et al. *Antimicrobial and Clinical Microbiology Guidebook*. 2nd ed. Omaha, NE: Nebraska Medical Center; 2010. Available at: http://www.nebraskamed.com/careers/education-programs/asp. Accessed September 15, 2011.

Baddour LM. Cellulitis and erysipelas. In: Sexton DJ, Kaplan SL, eds. *UpToDate*. Waltham, MA: UpToDate; 2008. Available at: http://www.uptodate.com/contents/cellulitis-and-erysipelas

Centers for Disease Control and Prevention. Get smart: know when antibiotics work. CDC Web site. Available at: http://www.cdc.gov/getsmart/antibiotic-use/fast-facts.html. Accessed September 14, 2011.

Centers for Disease Control and Prevention. Vancomycin-resistant enterococci (VRE) in healthcare settings. CDC Web site. Available at: http://www.cdc.gov/HAI/organisms/vre/vre.html#a3. Accessed on May 16, 2012.

Fishman N. Antimicrobial stewardship. *Am J Med*. 2006;119(6 Suppl 1):S53–61; discussion S62–70.

Gilbert DN, Moellering RC Jr , Eliopoulos GM, et al, eds. *The Sanford Guide to Antimicrobial Therapy*, 40th ed. Sperryville, VA; 2010.

Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. *Am J Respir Crit Care Med*. 2005;171(4):388–416. Available at: http://ajrccm.atsjournals.org/content/171/4/388.full. Accessed August 14, 2011.

Hall-Flavin, DK. Depression (Major Depression): MAOIs and Diet. Mayo Clinic Web site. Available at: http://www.mayoclinic.com/health/maois/HQ01575. Accessed February 9, 2011.

Hatzenbuehler J, Pulling TJ. Diagnosis and management of osteomyelitis. *Am Fam Physician*. 2011;84(9):1027–1033. Available at: http://www.aafp.org/afp/2011/1101/p1027.html

Kelly CP, LaMont JT. Treatment of *Clostridium difficile* infection in adults. In: Calderwood SB, ed. *UpToDate*. Waltham, MA: UpToDate; 2012. Available at http://www.uptodate.com/contents/treatment-of-clostridium-difficile-infection-in-adults

(References continued on next page)

References *(continued)*

Kuti JL, Le TN, Nightingale CH, Nicolau DP, R Quintiliani. Pharmacoeconomics of a pharmacist-managed program for automatically converting levofloxacin route from IV to oral. *Am J Health Sys Pharm*. 2002;59:2209–2215. Available at: http://www.ajhp.org/content/59/22/2209.full.pdf+html

Lacy CF, Armstrong LL, Goldman MP, et al., eds. *Drug Information Handbook*, *15th ed.* Hudson, OH: Lexi-Comp; 2007.

Lew DP, Waldvogel FA. Osteomyelitis. *Lancet*. 2004;364:369–379.

Lipsky BA, Berendt AR, Deery HG, et al. Diagnosis and treatment of diabetic foot infections. *Clin Infect Dis*. 2004;39:885–910.

Management of Osteomyelitis: Emphasis on Methicillin-Resistant Staphylococcus aureus *(MRSA): Consensus Guidelines from SFGH (San Francisco General Hospital) Orthopedic Surgery, Infectious Diseases, and Infectious Diseases Pharmacy*. Available at: http://clinicalpharmacy.ucsf.edu/idmp/sfgh_specific/osteo_sfgh.htm

Mandell LA, Wunderink RG, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. *Clin Infect Dis*. 2007;44(Suppl 2):S27–72. Available at: http://www.thoracic.org/statements/resources/mtpi/idsaats-cap.pdf. Accessed August 14, 2011.

Martin C, Hoven A. *University Guide to Empiric Antimicrobial Therapy*. Lexington, KY: University of Kentucky; 2004. Available at: http://www.hosp.uky.edu/pharmacy/formulary/criteria/UK_Antimicrobial_Manual.pdf

Murdaugh LB. *Competence Assessment Tools for Health-System Pharmacies*. 4th ed. Bethesda, MD: American Society of Health-System Pharmacists, Inc.; 2008.

Pichichero M. Treatment and prevention of streptococcal tonsilliopharyngitis. In: Sexton DJ, Edwards MS, eds. *UpToDate*. Waltham, MA: UpToDate; 2010. Available at: http://www.uptodate.com/contents/treatment-and-prevention-of-streptococcal-tonsillopharyngitis

Rehm SJ, Sekeres JK, Neuner E, et al. Guidelines for antimicrobial usage, index of tables. *Cleveland Clinic Continuing Medical Education (CME)*. Cleveland Clinic Center for Continuing Education; 2009. Available at: http://www.clevelandclinicmeded.com/medicalpubs/antimicrobial-guidelines

Shulman ST, Bisno AL, Clegg HW, et al. Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2012;55(10):e86–e102. Available at: http://cid.oxfordjournals.org/content/55/10/e86.full.pdf+html

(References continued on next page)

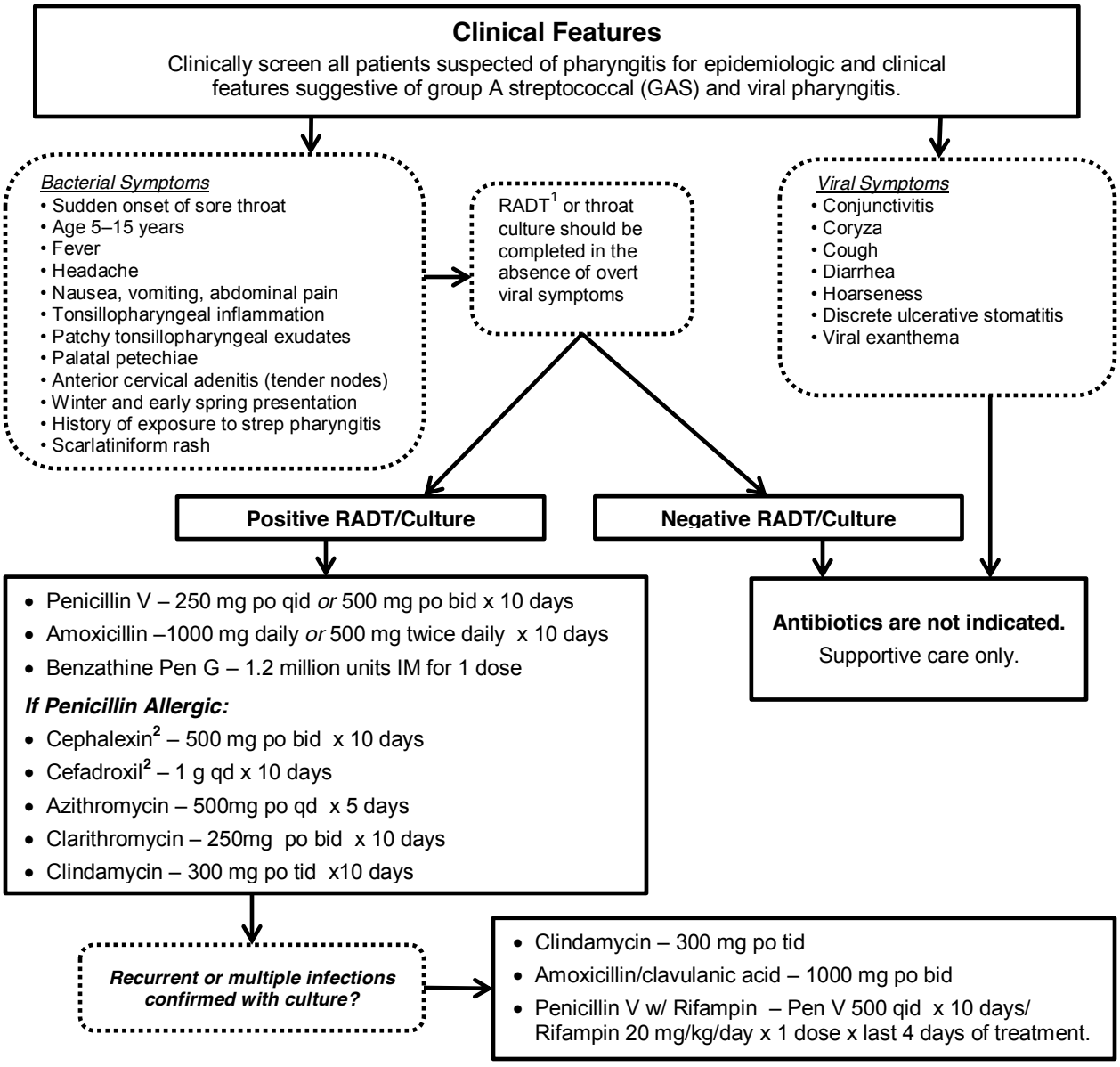
References *(continued)*

Weintrob AC, Sexton DJ. Overview of diabetic infections of the lower extremities. In: Sexton DJ, ed. *UpToDate*. Waltham, MA: UpToDate; 2008. Available at: http://www.uptodate.com/contents/overview-of-diabetic-infections-of-the-lower-extremities

Weller, PF. Vancomycin hypersensitivity. In: Adkinson NF Jr, ed. *UpToDate*. Waltham, MA: UpToDate; 2011. Available at: http://www.uptodate.com/contents/vancomycin-hypersensitivity.

Wynn RL, Meiller TF, Crossley HL. *Drug Information Handbook for Dentistry, 17th ed*. Hudson, OH: Lexi-Comp, Inc.; 2011:1914–1915.

Appendix 1: Treatment of Pharyngitis



Notes:

[1] RADT tests should only be performed under structured waived testing programs, and each site must have their own CLIA waiver.

[2] Cephalexin or cefadroxil are preferred agents for penicillin-allergic patients; however, they are to be avoided in individuals with immediate type hypersensitivity to penicillin.

➔ Usual duration of therapy is 10 days.

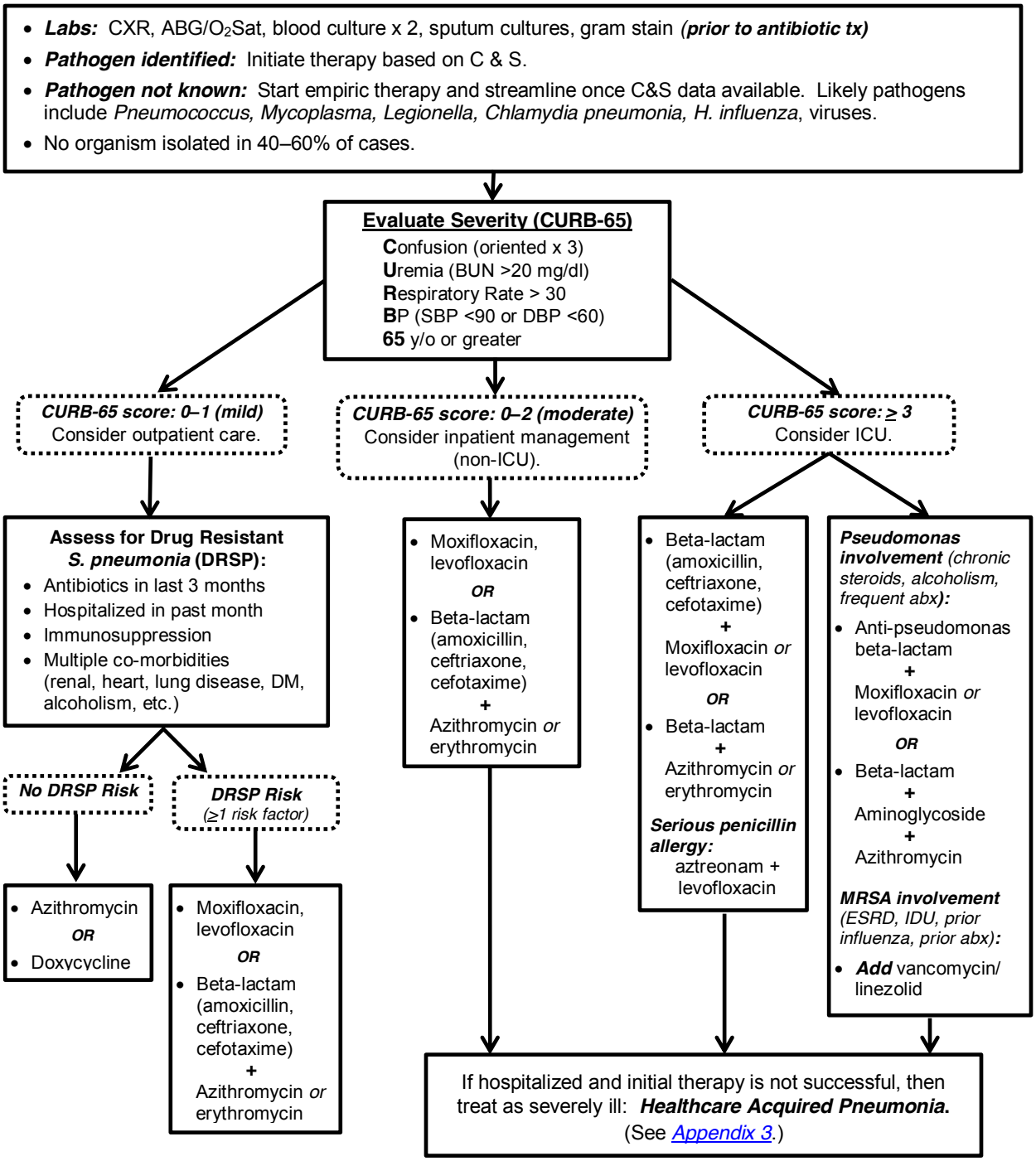
➔ Consider pill line in patients with compliance concerns.

References:

Shulman ST, Bisno AL, Clegg HW, et al. Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by the Infectious Diseases Society of America. *Clin Infect Dis.* 2012;55(10):e86–e102. Available at: http://cid.oxfordjournals.org/content/55/10/e86.full.pdf+html

Pichichero M. Treatment and prevention of streptococcal tonsilliopharyngitis. In: Sexton DJ, Edwards MS, eds. *UpToDate*, 2010. Available at: http://www.uptodate.com/contents/treatment-and-prevention-of-streptococcal-tonsillopharyngitis

Appendix 2: Treatment of Community Acquired Pneumonia



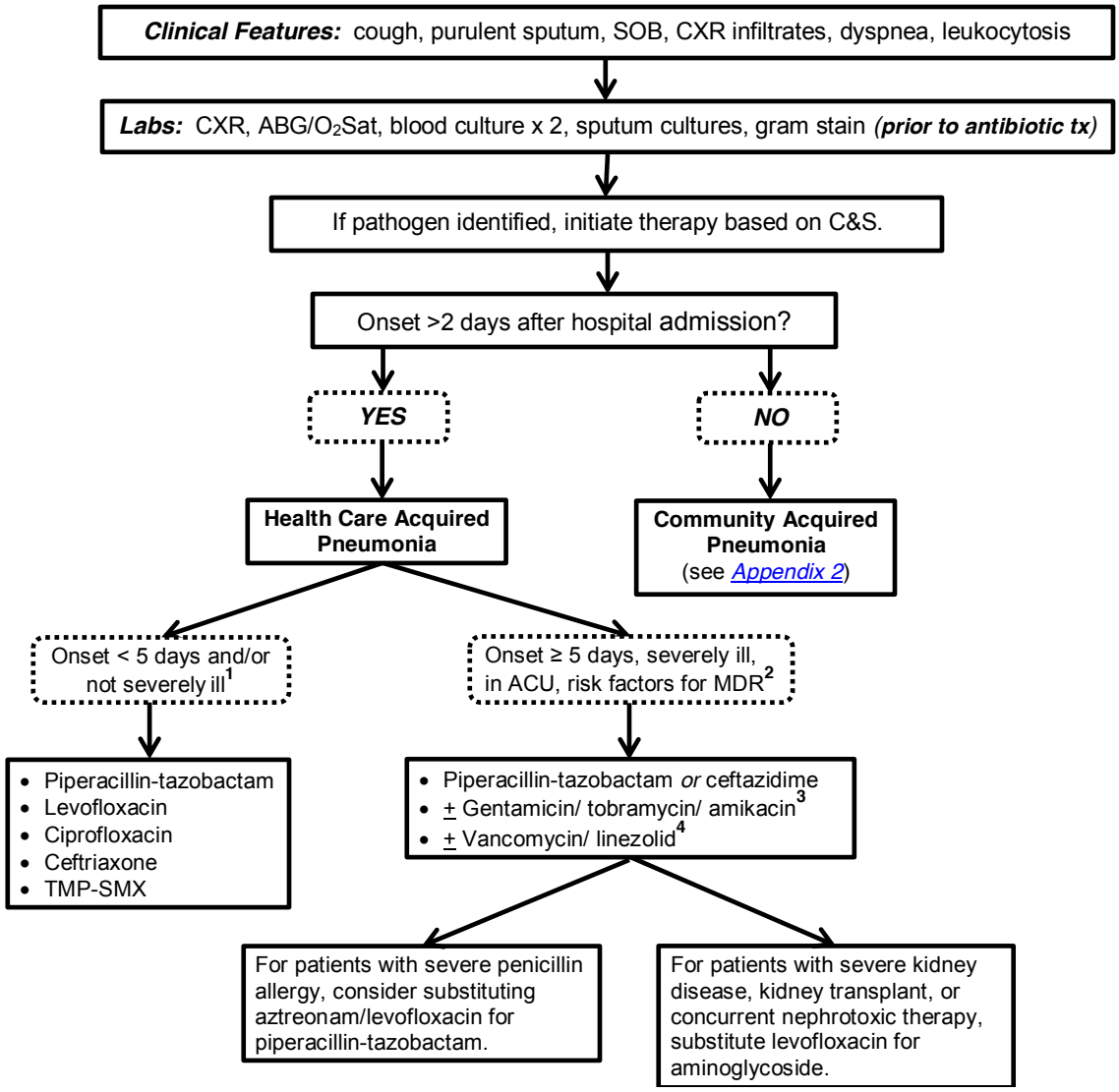
➔ ***Treatment duration is a minimum of 5 days***

➔ ***Patient should be afebrile for 48-72 hours and clinically stable before stopping antibiotics.***

Reference:

Mandell LA, Wunderink RG, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. *Clin Infect Dis*. 2007;44(Suppl 2):S27–S72. Available at: http://www.thoracic.org/statements/resources/mtpi/idsaats-cap.pdf.

Appendix 3: Treatment of Hospital, Ventilator, and Healthcare Acquired Pneumonia



Notes:

[1] **Early onset (<5 days):** Pathogens include *S. pneumoniae*, *H. influenza*, gram-negative bacilli (*E. coli*, *Enterobacter*, *Serratia*, *Klebsiella*), *MSSA*, *Legionella*.

[2] **Late onset (≥5 days):** Pathogens include *Pseudomonas*, *MRSA*, resistant gram-negative bacilli, *Acinetobacter* (use amikacin in combination).

[3] If rare gentamicin resistance occurs, substitute with tobramycin and then amikacin.

[4] Consider linezolid for confirmed MRSA resistant to vancomycin.

- Immunocompromised patients, e.g. HIV, transplant; patients who are recipients of steroids (≥15mg of prednisone qd) or other immunosuppressants may have pneumonia due to PCP, CMV, *Aspergillus, Nocardia,* etc.
- Treatment duration is usually 7–14 days, but if no improvement or slow response, further treatment may be required.
- Anaerobic pleuropulmonary infections may require 6 weeks of therapy.
- For aspiration pneumonia, consider ampicillin-sulbactam ± clindamycin.
- For extended-spectrum beta-lactamases (ESBL) positive pathogens, consider imipenem-cilastin.

Reference:

Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. *Am J Respir Crit Care Med.* 2005;171(4):388–416. Available at: http://ajrccm.atsjournals.org/content/171/4/388.full.

Appendix 4: Antibiotics Used in the Treatment of Pneumonia

Antibiotic Dosage*	Risk Factors for Multidrug Resistant Pathogens
Antipseudomonal cephalosporin: • Ceftazidime 2 gm IV q 8 hours **Other cephalosporins:** • Ceftriaxone 1–2 gm IV q 24 hours **Carbapenems:** • Imipenem-cilastin 500 mg IV q 6 hours ***OR*** 1 gm q 8 hours **Beta-lactam/beta-lactamase inhibitors:** • Piperacillin-tazobactam 3.375 gm IV q 6 hours • Ampicillin-sulbactam 1.5–3 mg IM/IV q 6 hours **Aminoglycosides[1]:** • Gentamicin/ tobramycin ▸ 5-7 mg/kg IV per day (once daily dosing) ▸ 1-1.7 mg/kg q 8 hours (conventional dosing) • Amikacin ▸ 15-18 mg/kg IV per day (once daily dosing) ▸ 5–7.5 mg/kg IV q 8–12 hours (conventional dosing) **Antipseudomonal quinolones:** • Levofloxacin 500–750 mg IV/PO q day • Ciprofloxacin 250–750 mg q 12 hours **MRSA Agents:** • Vancomycin 1 gm IV q 12 hours[2] • Linezolid 600 mg IV/PO q 12 hours **Miscellaneous:** • Aztreonam 1–2 gm IV/IM q 8–12 hours • Azithromycin 500 mg IV/PO q day • Amoxicillin 500–875 mg PO q 12 hours • Doxycycline 100 mg PO/IV q 12 hours • SMX-TMP 1–2 DS tablets q 12 hours **** Doses assume normal renal/hepatic function.***	• Antimicrobial therapy in preceding 90 days • Current hospitalization of 5 days or more • High frequency of antibiotic resistance in the community or in the specific hospital unit • Presence of risk factors for healthcare-associated pneumonia: ▸ Hospitalization for 2 days or more in the preceding 90 days ▸ Residence in a nursing home or extended care facility ▸ Home infusion therapy (including antibiotics) ▸ Chronic dialysis within 30 days ▸ Home wound care ▸ Family member with multidrug-resistant pathogen • Immunosuppressive disease and/or therapy suggesting a variable outcome impact, according to the severity

Notes:
[1] Trough levels for gentamicin and tobramycin generally should be less than 2 µg /mL, and amikacin should be less than 8 µg/mL, but will depend on indication.
[2] Trough levels for vancomycin should be 15–20 µg/mL. (See *Appendix 7, Vancomycin Mon*itoring.)

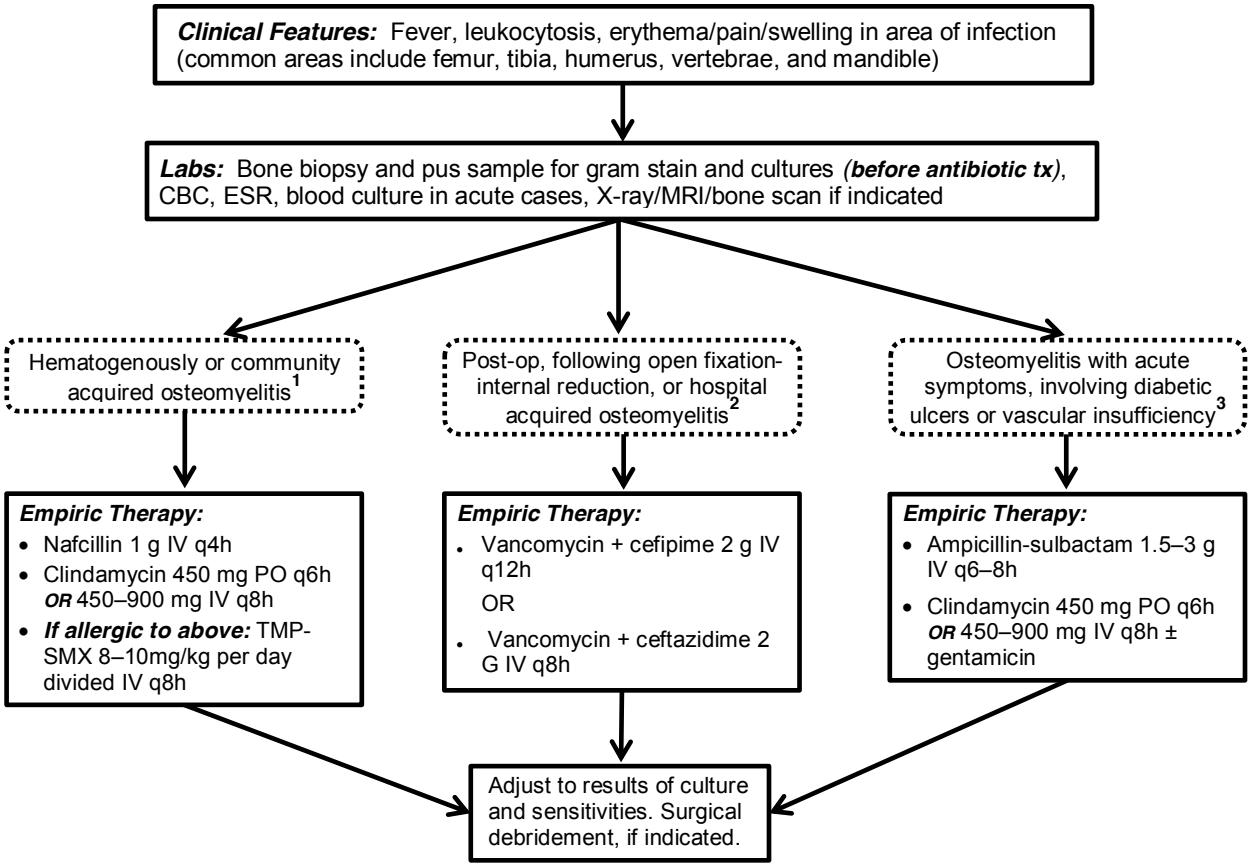
References:

Gilbert DN, Moellering RC Jr , Eliopoulos GM, et al, eds. *The Sanford Guide to Antimicrobial Therapy*, 40th ed. Sperryville, VA; 2010.

Martin C, Hoven A. *University Guide to Empiric Antimicrobial Therapy*. Lexington, KY: University of Kentucky; 2004. Available at: http://www.hosp.uky.edu/pharmacy/formulary/criteria/UK_Antimicrobial_Manual.pdf

Rehm SJ, Sekeres JK, Neuner E, et al. Guidelines for antimicrobial usage, index of tables. *Cleveland Clinic Continuing Medical Education (CME)*. Cleveland Clinic Center for Continuing Education, 2009. Available at: http://www.clevelandclinicmeded.com/medicalpubs/antimicrobial-guidelines

Appendix 5: Treatment of Osteomyelitis



Notes:

[1] Usual pathogens include *S. aureus*, *Streptococci* species, *Salmonella* in sickle cell patients, *Pseudomonas* following nail puncture injury.

[2] Usual pathogens include various forms of *Staphylococci*, gram-negative rods (including *Pseudomonas*).

[3] Usually polymicrobial, including anaerobes, *Staphylococci*, *Streptococci* species, GNR.

➔ ***Usual treatment duration is 4–6 weeks.***

➔ Therapy should start with IV therapy. Conversion to oral antibiotics can be considered if the patient has a confirmed case of osteomyelitis, the organism is identified, antibiotic susceptibility determined, oral agent(s) with good bioavailability is selected, and the patient demonstrates good compliance.

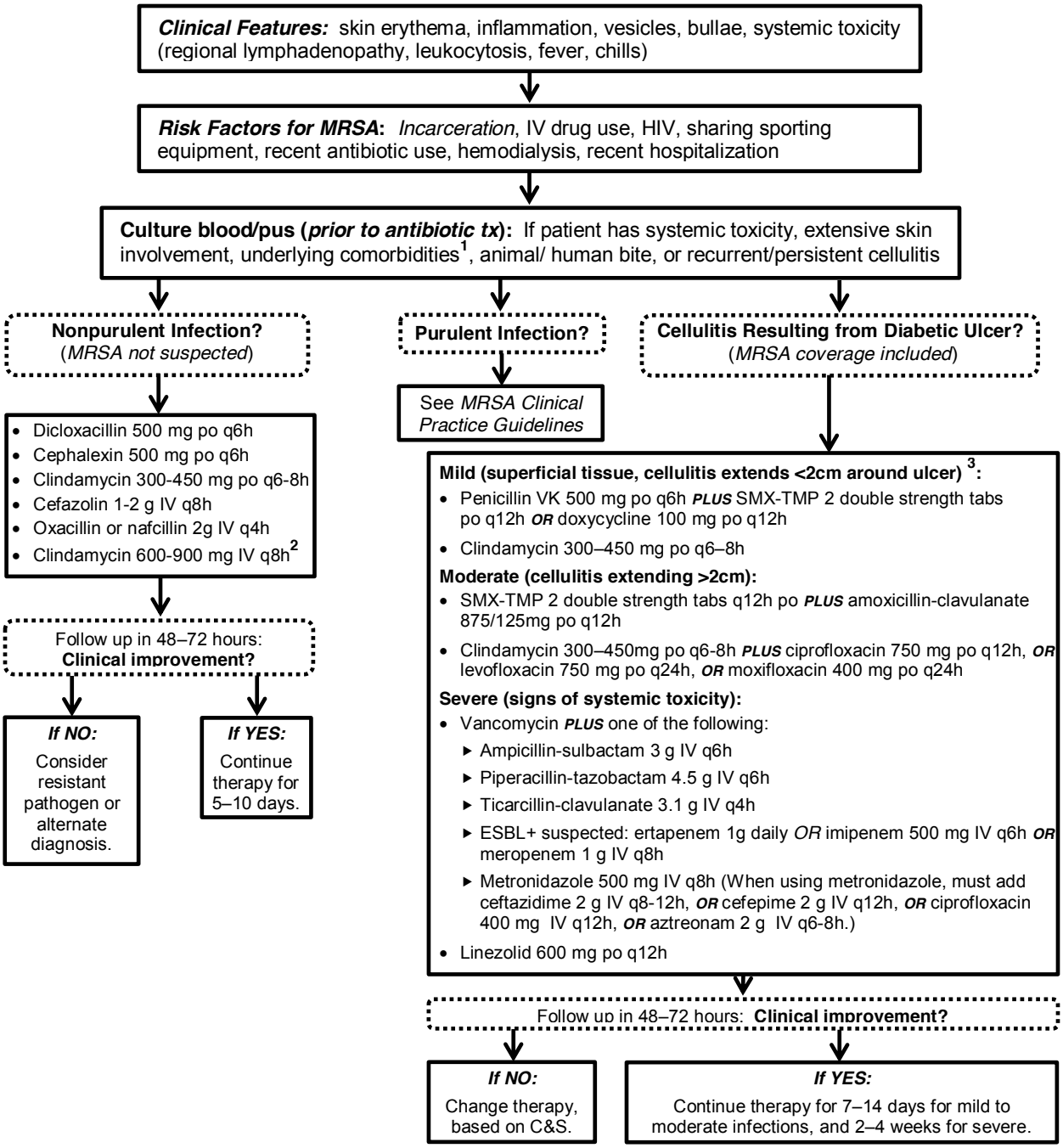
References:

Gilbert DN, Moellering RC Jr , Eliopoulos GM, et al, eds. *The Sanford Guide to Antimicrobial Therapy*, 40th ed. Sperryville, VA; 2010.

Martin C, Hoven A. *University Guide to Empiric Antimicrobial Therapy*. Lexington, KY: University of Kentucky; 2004. Available at: http://www.hosp.uky.edu/pharmacy/formulary/criteria/UK_Antimicrobial_Manual.pdf

Rehm SJ, Sekeres JK, Neuner E, et al. Guidelines for antimicrobial usage, index of tables. *Cleveland Clinic Continuing Medical Education (CME)*. Cleveland Clinic Center for Continuing Education, 2009. Available at: http://www.clevelandclinicmeded.com/medicalpubs/antimicrobial-guidelines

Appendix 6: Treatment of Cellulitis



Notes:

Dosages assume normal renal/hepatic function.

Usual pathogens: S*taphylococci* & beta hemolytic *Streptococci*. For diabetic ulcers, may include gram-negative bacilli & anaerobes.

[1] *Comorbidities:* diabetes, lymphedema, malignancy, neutropenia, immunodeficiency, splenectomy

[2] If known clindamycin resistance is high, consider adding 2nd agent.

[3] If mild infections are unresponsive to therapy, change to moderate treatment to cover gram-negative bacilli and anaerobes.

References:

Baddour LM. Cellulitis and erysipelas. In: Sexton DJ, Kaplan SL, eds. *UpToDate*. Waltham, MA: UpToDate; 2008.

Gilbert DN, Moellering RC Jr, Eliopoulos GM, et al, eds. *The Sanford Guide to Antimicrobial Therapy*, 40th ed. Sperryville, VA; 2010.

Lipsky BA, Berendt AR, Deery HG, et al. Diagnosis and treatment of diabetic foot infections. *Clin Infect Dis*. 2004;39:885–910.

Weintrob AC, Sexton DJ. Overview of diabetic infections of the lower extremities. In: Sexton DJ, ed. *UpToDate*. Waltham, MA: UpToDate; 2008.

Appendix 7: Vancomycin Monitoring

Vancomycin is a glycopeptide antibiotic that emerged in the 1980s as the primary treatment for serious gram-positive infections involving MRSA. For many years, because of concern over the potential for nephrotoxic and ototoxic complications of vancomycin, target serum concentrations have been tightly controlled within a narrow range. However, data analysis indicates that conventional doses of vancomycin have little potential for the development of these complications. In light of this new information, the American Society of Health-System Pharmacists (ASHP), the Infectious Diseases Society of America (IDSA), and the Society of Infectious Disease Pharmacists (SIDP) convened in 2009 to develop a consensus review of vancomycin drug monitoring.

Key points in this review include:

- Vancomycin dosing is based on actual body weight (ABW).
- Vancomycin exhibits bactericidal activity against *S. aureus* and *S. epidermidis*.
- Peak serum concentrations of vancomycin are no longer used to monitor treatment.
- The clinical usefulness of monitoring vancomycin trough concentrations is twofold: trough serum concentrations (1) are the most accurate and practical surrogate marker for Area Under the Curve (AUC), and (2) serve as a useful method to monitor for vancomycin-related nephrotoxicity.

Studies have shown that the strongest predictor of vancomycin nephrotoxicity is the concomitant use of nephrotoxins. There are limited data suggesting a direct causal relationship with specific serum vancomycin concentrations. *Therefore, routinely obtaining more than a single trough concentration is NOT recommended for treatment courses less than 3 to 5 days, or for doses targeting a trough below 15 µg/mL.*

Trough levels should be obtained just prior to the fourth dose, so that the drug has adequate time to reach steady state concentration. Once the trough is drawn—unless the results are immediately known and a provider is available to review and make necessary dosing adjustments—the scheduled dose should be given without delay.

The chart on the following page, "IDSA Vancomycin Drug Monitoring Summary," contains some of the current recommendations for monitoring vancomycin therapy.

Note: "Red Man Syndrome" (RMS) is a reaction that has been associated with the infusion rate of vancomycin. RMS differs from an allergic reaction in that it is not mediated by drug-specific antibodies and it can occur as early as the first dose. To prevent RMS, infusion rates of vancomycin should be given at no higher than 10 mg/min. Patients who have experienced RMS may continue to receive vancomycin; however, the rate of infusion must be decreased.

IDSA Vancomycin Drug Monitoring Summary	
Trough Monitoring	
Criteria for monitoring	*Peak monitoring is NOT recommended.* *Trough Monitoring is recommended for the following:* • Troughs should be obtained just prior to the next dose at steady-state conditions **(just before the 4th dose)**. • Aggressive dosing with a target trough of 15–20 µg/mL • All patients at high risk of nephrotoxicity (e.g., patients receiving concurrent nephrotoxins). • Patients with unstable renal function (deteriorating or significantly improving) • Prolonged courses of therapy (more than five days)
Frequency of monitoring	• Frequent monitoring (more than one trough before the fourth dose) for short courses or for uncomplicated infections *is not recommended*. • All patients on prolonged courses of vancomycin should have at least one steady-state trough concentration obtained no earlier than at steady state **(just before the 4th dose)** and repeated as clinically appropriate. • Once-weekly monitoring is recommended for hemodynamically stable patients on long-term therapy. • More frequent or daily trough monitoring is advisable in patients who are hemodynamically unstable.
Optimal trough concentration for uncomplicated infections	**Minimum trough concentrations should always be maintained above 10 µg/mL to avoid development of resistance.**
Optimal trough concentration for complicated infections (bacteremia, endocarditis, osteomyelitis, meningitis, hospital-acquired pneumonia caused by *S. aureus)*	Trough concentrations of 15–20 µg/mL are recommended to improve penetration, increase the probability of obtaining optimal target serum concentrations, and improve clinical outcomes.
Dosing	
Dosing to achieve optimal trough concentrations	Doses of 15–20 mg/kg (ABW) given every 8–12 hr are recommended for most patients with normal renal function to achieve the suggested serum concentrations, with adjustments as necessary after the trough is obtained.
Loading doses for complicated infections	In seriously ill patients, a loading dose of 25–30 mg/kg (ABW) can be used to facilitate rapid attainment of target trough concentrations
Adverse Events	
Vancomycin-induced toxicity	**Nephrotoxicity:** A minimum of two or three consecutive documented increases in serum creatinine concentrations (defined as an increase of 0.5 mg/dL or a ≥50% increase from baseline, whichever is greater) after several days of therapy. **Ototoxicity:** Monitoring for ototoxicity is necessary when the patient is receiving other ototoxic agents such as aminoglycosides.