WRNMMC
Antimicrobial Stewardship Handbook
2018-2019

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LTC Kurt Schaecher, PhD (Chief, Clinical Microbiology)

Contact information:
- Antimicrobial stewardship program (ASP) clinical pharmacist; pager pin 106-0448 (available 0630-1530 Monday-Friday excluding federal holidays)
- Clinical pharmacist consult number (24/7 availability): main pharmacy 301-295-2121, ICU pharmacy 301-400-3422
- Adult ID on call: 301-538-7900
- Pediatric ID on call: 301-648-0545
- Allergy/Immunology: consult pager 106-3366, clinic phone number 301-295-4511

How to use this handbook:
- The recommendations listed are for **ADULT** patients unless otherwise specified.
- **All doses in the text are for patients with normal renal and hepatic function.**
- This handbook contains guidelines based off of antibiogram data specific to WRNMMC and should not be generalized to other institutions.
- Copies of this handbook **should not** be distributed outside of the WRNMMC institution without permission.
- Recommendations given in this handbook are meant to serve as treatment guidelines. They should **NOT** supplant clinical judgment or Infectious Diseases (ID) consultation when indicated. As with all clinical reference resources, continued research may result in new knowledge and recommendations.
Antimicrobial Stewardship (ASP) Essentris Note

**Purpose:** to serve as communication between the ASP team, patient care teams, and clinical pharmacists. Common interventions recommended by the ASP team address the following: therapeutic drug level monitoring, de-escalation, IV to PO conversion, PK/renal dosing, drug-drug interactions, duration of therapy, redundant antimicrobial coverage, bug-drug mismatch, and recommendation for a formal ID consultation.

ASP team contact information is embedded into the signature block as depicted below. If an ASP recommendation is of an urgent nature, attempts will be made to contact the patient care team directly via pager in addition to placing a note in the EMR. Please ensure updated pager information is located in the EMR ADT Orders.

**ANTIMICROBIAL STEWARDSHIP (ASP) EVALUATION NOTE**

- **Assessment:** 86 yo female with a hx of uncontrolled DM2 currently on IV vancomycin and piperacillin-tazobactam for empiric treatment of hospital acquired pneumonia. Currently on day #3 of Abx therapy. Treatment team has outlined in their progress note a plan for 14 days of therapy.

- **Plan/Recommendation:** Respiratory cultures have resulted as Enterobacter cloacae. Pt with a rapid response to empiric therapy and is afebrile with a normal WBC and no oxygen requirement. No contraindications noted for PO medications. Recommend de-escalation to monotherapy with an oral PO like levofloxacin 250mg PO daily. Recommend consideration for a shorter 7 day course of therapy as per IDSA/ATS guidelines.

- **Signatures:**
  - ID Staff Attending
  - Med ICU Staff Attending
  - Fellow
  - Resident
  - Intern
  - Medical Student
  - ASP/ID Pharmacy Specialist

**Signature:** AyAHe, Hemar CTR 7841  
**Time/Date:** 0936 07Mar2017

The patient's inpatient antimicrobial regimen was reviewed taking into account indication, severity of illness, co-morbid conditions to include kidney and liver function, absorption, and potential drug-drug interactions. When appropriate, the following is addressed with the primary team: de-escalation, change of dosing, change of administration (PO, IV, via NGT or PEJ), or consideration of an alternate antimicrobial regimen based on patient's clinical course, labs, cultures or other supportive studies. Other recommendations may be made based on the clinical situation. When appropriate, a formal inpatient ID consultation will be recommended. ASP cases are discussed with an attending ID physician as appropriate. The ASP recommendation is based only on review of the most recent chart documentation. The patient was not interviewed or examined. This recommendation should not supplant clinical judgment or ID consultation when indicated. For questions regarding this recommendation please contact ID Clinical Pharmacist pager pin 106-0448 (0830-1530 Monday-Friday; excluding Federal Holidays) or on-call ID contact number 301-938-7900 (nights and weekends).

When applicable, these recommendations were also discussed with MICU, SICU or ward Clinical Pharmacist.

ASP signature block contains pertinent contact information.
Note continued

Clinical Pharmacy Specialist
Signature:  
Time/Date:  
Comment:  

Primary Medical Team Response
Comment:  

Signatures
- Staff Attending
- Fellow
- Resident
- Intern
- Medical Student
- Physician Assistant
- Nurse Practitioner
- Other Provider
- ASP Response
- ASP Evaluation

Allergy Information
1
Type:  NONE  
Name:  
Symptoms:  
Onset Date:  
Severity:  
Other Symptom:  
SNOMED Code:  
RxNorm Code:  
Last Modification Date:  
Inactive:  

Antimicrobials
Subjective
Objective

Tubes/lines/Drains
Pharmacy/ASP Metrics (non-printing section)
ASP Workload

Note Time | Type | Topic | Stored At
---|---|---|---
N/A | MultiD Discharge Summary | | 1038 07 Mar 2017
N/A | Anesthesia Eval | | 0656 06 Mar 2017
N/A | Medication Reconciliation | | 2218 02 Mar 2017
N/A | History and Physical | | 1820 03 Mar 2017
0938 07 Mar 2017 | Provider Progress Note | | 1006 07 Mar 2017
0920 07 Mar 2017 | Antimicrobial Stewardship ASP | | 0952 07 Mar 2017
0748 07 Mar 2017 | Consolidated Consult | | 0758 07 Mar 2017
0617 07 Mar 2017 | Consolidated Consult | | 0805 07 Mar 2017
0556 07 Mar 2017 | Consolidated Consult | | 0558 07 Mar 2017

ASP notes will have the “topic” of Antimicrobial Stewardship Clinical Note and will be searchable under Physician Notes.
# Table of Contents

Antimicrobial Restrictions and Obtaining Approval ........................................ 1

Treatment Guidelines

- Acute Rhinosinusitis in Adults and Children ....................................... 2
- Acute Otitis Media in Children ............................................................. 6
- Candidemia (Non-Neutropenic Patients) ............................................. 8
- *Clostridium difficile* Infections ......................................................... 10
- Central Nervous System Infections in Adults ...................................... 13
- Febrile Neutropenia ............................................................................. 17
- Pneumonia in Adults ........................................................................... 19
- Pneumonia in Children ....................................................................... 22
- Intra-abdominal Infections .................................................................. 26
- Asymptomatic Bactiuria ....................................................................... 29
- Candiduria ........................................................................................... 30
- Urinary Tract Infections (UTI) in Women ........................................... 31
- UTI in Men ........................................................................................... 34
- Catheter Associated UTI ...................................................................... 36
- Skin and Soft Tissue Infections .......................................................... 38
- Pre-operative and Pre-procedural Prophylaxis ..................................... 41
- *Staphylococcus aureus* bacteremia .................................................... 46

IV to PO Conversion .................................................................................. 48

Calculating an Estimate of Creatinine Clearance ...................................... 50

Prolonged Infusion of Piperacillin/Tazobactam ....................................... 51

Vancomycin Dosing and Monitoring Guide ......................................... 53

Aminoglycoside Dosing and Monitoring Guide ..................................... 56

Beta-lactam Allergy Assessment .............................................................. 59

Antibiogram ............................................................................................. 61
Restricted Medications Requiring Approval from Infectious Diseases

- In accordance with the WRNMMC ASP Instruction 6015.04.
- Contact adult ID 301-538-7900 or pediatric ID 301-648-0545 for approval.
- Approving ID provider name should be annotated in the medication order comment section.
- Approval is not required for any patient transferred to WRNMMC already receiving one of these antimicrobials. Continued use of the agent will be assessed through the ASP.
- Pharmacy may dispense the first dose of a restricted medication without ID approval if ordered overnight but the ordering team must acquire ID approval the following day.
- Consider obtaining an ID consultation in cases requiring the use of restricted antimicrobials.

Medications requiring approval prior to first dose:

1. Colistimethate injection (pre-approval not required for inhaled colistin preparation)
2. Dalbavancin injection
3. Daptomycin injection
4. Fidaxomicin oral
5. Ganciclovir injection
6. Liposomal amphotericin injection
7. Rifapentine oral
8. Tigecycline injection
9. Valganclovir oral (transplant services have pre-authorized use)
10. All non-formulary antimicrobials to include ceftaroline, ceftazidime-avibactam, ceftolozane-tazobactam, isavuconazole, and tedizolid

Medications requiring approval after 72 hours of use:

1. Carbapenem injection (Imipenem-cilastatin, Meropenem, Ertapenem)
2. Echinocandin injection (Micafungin, Caspofungin, Anidulafungin)
3. Linezolid injection or oral (pre-authorized use in cystic fibrosis patients)
4. Voriconazole injection or oral (hematology-oncology services have pre-authorized use)
5. Posaconazole oral (hematology-oncology services have pre-authorized use)
ACUTE RHINOSINUSITIS

DIAGNOSTIC CONSIDERATIONS

- Acute sinusitis is a clinical diagnosis and most cases do NOT require antibiotic treatment
- There is considerable clinical overlap with typical viral upper respiratory infections (URI)
- Halitosis, fatigue, headache, and decreased appetite are not specific for a bacterial sinusitis
- Plain radiographs or CT are nonspecific and can be abnormal even in asymptomatic patients
- Secondary bacterial infection following a viral URI is uncommon, occurring in 0.5-2% of adult cases and about 6-7% of pediatric cases; rarely presents prior to 7-10 days of symptoms

CRITERIA FOR ANTIBIOTIC THERAPY

- Persistent symptoms lasting ≥10 days without clinical improvement
- Fever (≥102°F) and purulent nasal discharge or facial pain lasting at least 3-4 consecutive days
- Initial improvement following a viral URI followed by clinical worsening (new onset of fever, headache, or increase in nasal discharge)
- Complicated acute sinusitis:
  - Systemic toxicity with fever ≥102°F and threat of suppurative complications
  - Increased risk for penicillin (PCN) resistant strains of Streptococcus pneumoniae. Risk factors include attendance at daycare, age <24 months or > 65 years, recent hospitalization, antibiotic use within the last 30 days, or immunocompromised state

EMPIRIC THERAPY

Typical duration of antibiotic therapy for uncomplicated acute bacterial sinusitis:
- Children 10-14 days
- Adults 5-7 days

Important concepts:
- Fluoroquinolones, azithromycin, and trimethoprim-sulfamethoxazole are NOT first line therapy
- Second and third generation oral cephalosporins to include cefprozil, cefuroxime, cefdinir, cefpodoxime, and cefixime are no longer recommended for empiric monotherapy due to variable rates of resistance among pneumococcal isolates
- Routine empiric coverage for MSSA or MRSA is not recommended
- Consider allergy consult for any patient labeled with a PCN allergy (see page 59)

Adjunctive therapy:
- Intranasal saline irrigation with either physiologic or hypertonic saline may be considered
- Intranasal corticosteroids may be considered in patients with a history of allergic rhinitis
- Topical or oral decongestants and/or antihistamines are not routinely recommended

Consider Infectious Diseases, Otolaryngologist, Allergy consultation:
- Severe infection (persistent fever ≥102°F), orbital edema, impaired function of the extraocular muscles, proptosis, visual disturbance, severe headache, altered mental status, meningeal signs
- Recalcitrant infection with failure to respond to extended courses of antibiotics
- Immunocompromised host
- Multiple medical problems that might compromise response to treatment (e.g. hepatic or renal impairment, hypersensitivity to antibiotics, organ transplant)
- Unusual or resistant pathogens
- Fungal sinusitis or granulomatous disease
- Nosocomial or trauma related infection
- Anatomic defects causing obstruction and requiring surgical intervention
- Multiple recurrent episodes (3-4 episodes per year) suggesting chronic sinusitis
- Chronic sinusitis ± polyps or asthma with recurrent acute bacterial sinusitis exacerbations
- Evaluation of immunotherapy for allergic rhinitis

For WRNMMC use only, page 2
### EMPIRIC REGIMENS IN CHILDREN

<table>
<thead>
<tr>
<th>Indication</th>
<th>First-line Regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial empiric therapy</strong></td>
<td>Amoxicillin-clavulanate 45 mg/kg/day PO ÷ BID</td>
</tr>
<tr>
<td><strong>Alternative for uncomplicated sinusitis:</strong></td>
<td>Amoxicillin 90 mg/kg/day PO ÷ BID WITHOUT clavulanate may be considered for mild to moderate illness in children ≥ 2 years of age who do not attend daycare and have not been treated with antibiotics in the past 30 days</td>
</tr>
<tr>
<td><strong>Complicated sinusitis:</strong></td>
<td>Amoxicillin-clavulanate 90 mg/kg/day PO ÷ BID (use 14:1 amoxicillin to clavulanate formulation)</td>
</tr>
<tr>
<td><strong>Risk for resistance or failed initial therapy</strong></td>
<td>Amoxicillin-clavulanate 90 mg/kg/day PO ÷ BID (use 14:1 amoxicillin to clavulanate formulation)</td>
</tr>
<tr>
<td><strong>Severe infection requiring hospitalization</strong></td>
<td>Clindamycin 30-40 mg/kg/day PO ÷ TID PLUS cefixime 8 mg/kg/day PO ÷ BID OR cefpodoxime 10 mg/kg/day PO ÷ BID</td>
</tr>
<tr>
<td></td>
<td>Levofloxacin 10-20 mg/kg/day PO ÷ q12-24 h</td>
</tr>
</tbody>
</table>

### EMPIRIC REGIMENS IN ADULTS

<table>
<thead>
<tr>
<th>Indication</th>
<th>First-line Regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial empiric therapy</strong></td>
<td>Amoxicillin-clavulanate 875 mg/125 mg PO BID</td>
</tr>
<tr>
<td><strong>Complicated sinusitis:</strong></td>
<td>Amoxicillin-clavulanate 2000 mg/125 mg PO BID</td>
</tr>
<tr>
<td><strong>Risk for resistance or failed initial therapy</strong></td>
<td>Amoxicillin-clavulanate 2000 mg/125 mg PO BID</td>
</tr>
<tr>
<td></td>
<td>Levofoxacin 500 mg PO q24h</td>
</tr>
<tr>
<td></td>
<td>Moxifloxacin 400 mg PO q24h</td>
</tr>
<tr>
<td><strong>Severe infection requiring hospitalization</strong></td>
<td>Ampicillin/sulbactam 1.5-3 gram IV q6 h</td>
</tr>
<tr>
<td></td>
<td>Ceftriaxone 1 gram IV q24h</td>
</tr>
<tr>
<td></td>
<td>Levofoxacin 500 mg PO or IV q24h</td>
</tr>
<tr>
<td></td>
<td>Moxifloxacin 400 mg PO or IV q24h</td>
</tr>
</tbody>
</table>
EMPIRIC REGIMENS FOR THE PCN ALLERGIC PATIENT

**Children:**

**Type 1 hypersensitivity/severe allergy:** Levofloxacin 10-20 mg/kg/day PO ÷ q12-24 h

**Non-type 1 hypersensitivity:** Clindamycin 30-40 mg/kg/day PO ÷ TID **PLUS** cefixime 8 mg/kg/day PO ÷ BID **OR** cefpodoxime 10 mg/kg/day PO ÷ BID

**Adults:**

Doxycycline 100mg PO BID **OR** Levofloxacin 500mg PO q24h **OR** Moxifloxacin 400mg PO q24h

**REFERENCES**

**ALGORITHM FOR THE MANAGEMENT OF ACUTE BACTERIAL RHINOSinusITIS**

**Signs & Symptoms either:**
- Persistent & not improving (≥10 days)
- Severe (≥3-4 days); or
- Worsening after initial improvement

**Severe infection? or Risk for antibiotic resistance?**
- Age <2 or >65 years
- Daycare attendance
- Prior antibiotics within past 30 days
- Prior hospitalization within past 5 days
- Immunocompromised

---

**No**

Initiate first-line therapy

Improvement after 3-5 days

Complete therapy with 5-7 day course

Worsening or no improvement after 3-5 days

Broaden coverage or switch to different antimicrobial class

Worsening or no improvement after 3-5 days

- Refer to specialist
- CT or MRI to investigate noninfectious causes or supplicative complications
- Sinus or meatal cultures for pathogen-specific therapy

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**Yes**

Initiate therapy for complicated sinusitis

Improvement after 3-5 days

Complete therapy with 7-10 day course

Worsening or no improvement after 3-5 days

Complete therapy with 7-10 day course
**ACUTE OTITIS MEDIA (AOM)**

**DIAGNOSTIC AND MANAGEMENT CONSIDERATIONS**

- AOM is a clinical diagnosis often associated with pain and fever, using **one of three** criteria:
  1. Moderate-severe bulging tympanic membrane
  2. Mild bulging, intensely red tympanic membrane with ↓ movement on otoscopy (middle ear effusion)
  3. Acute onset of otorrhea not due to acute otitis externa

- Unilateral AOM with mild symptoms in 6-24 month old patients can initially be observed for self-resolution with close 48-72 hour follow-up without antibiotics, or with "safety net" antibiotics (prescribed but not given unless there is no improvement in 48-72 hours).

- Bilateral or unilateral non-severe AOM in children >24 months may also undergo observation, but treatment should be started in 48-72 hours if worsening.

- Antibiotic therapy of AOM does **NOT** provide symptomatic relief in the first 24 hours, and the mainstay treatments for analgesia are ibuprofen and/or acetaminophen. Ibuprofen should not be given to infants younger than 6 months.

- The number needed to treat (NNT) to achieve improvement in symptoms in AOM is 4-8 depending on how strictly AOM is defined.

- The NNT to prevent mastoiditis in children as a complication of AOM is 4800.

**CRITERIA FOR ANTIBIOTIC THERAPY AND PREVENTION MEASURES**

- **Severe** AOM in children ≥ 6 months [moderate-severe otalgia, >48 hr otalgia, or T 39°C (102.2°F)]

- Non-severe, **bilateral** AOM in children 6-24 months

- If meets criteria for AOM and worsens during a 24-72 hour observation period, or on initial therapy, or for whom a 24-72 hour follow-up appointment cannot be guaranteed.

- Children with underlying conditions that may alter the natural course of AOM should be treated more aggressively and watchful waiting strategy should **NOT** be used, including: the presence of grommets, cleft palate, immune deficiencies, and craniofacial abnormalities.

- Do **NOT** prescribe prophylactic antibiotics to reduce the number of recurrent AOM, but rather offer tympanostomy tubes for those patients with 3 episodes in 6 months or 4 episodes in 1 year with 1 episode in the preceding 6 months.

- All patients should be encouraged to receive their pneumococcal vaccines per ACIP guidelines.

- All patients >6 months without a contraindication should receive their annual influenza vaccine.

- Clinicians should encourage mothers to exclusively breastfeed for at least 6 months given the benefits of reducing AOM in infants and young children.

- For penicillin allergic patients, highly recommend allergy assessment (see page 59)

**EMPIRIC THERAPY**

Typical duration of antibiotic therapy for uncomplicated, acute otitis media:

- Children 6-24 months: **10 days**
- Children >24 months and adults: **5-7 days**
- If ceftriaxone is used, then treatment is for a maximum of **3 days**

**Adjunctive management:**

- If severe AOM, tympanocentesis should only be considered if the provider is skilled in the procedure. If necessary, consider consultation with an otolaryngologist.

- If tympanocentesis or a draining, perforated tympanic membrane reveals multidrug-resistant bacteria, consult infectious diseases.
<table>
<thead>
<tr>
<th>Indication</th>
<th>First-line Regimens (pediatric dosing)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial empiric therapy</strong> (NO amoxicillin in preceding 30 days and NO concurrent purulent conjunctivitis)</td>
<td>Amoxicillin; 80-90 mg/kg/day divided in 2 doses</td>
</tr>
<tr>
<td>For patients who received amoxicillin in preceding 30 days, have concurrent purulent conjunctivitis, OR failed initial therapy with amoxicillin</td>
<td>Amoxicillin-clavulanate; 90 mg/kg/day of amoxicillin + 6.4 mg/kg/day of clavulanate in 2 divided doses [use 14:1 ratio]</td>
</tr>
<tr>
<td><strong>Severe disease or rescue therapy after failure of initial therapy</strong></td>
<td>Amoxicillin-clavulanate; 90 mg/kg/day of amoxicillin + 6.4 mg/kg/day of clavulanate in 2 divided doses [use 14:1 ratio]</td>
</tr>
<tr>
<td></td>
<td>Ceftriaxone; 50 mg/dose IV or IM for 3 days</td>
</tr>
<tr>
<td></td>
<td>Consider tympanocentesis or consult specialist as necessary</td>
</tr>
<tr>
<td><strong>Penicillin-allergic patients</strong></td>
<td>Cefdinir; 14 mg/kg/day divided in 1 or 2 doses</td>
</tr>
<tr>
<td></td>
<td>Cefuroxime; 30mg/kg/day in 2 divided doses</td>
</tr>
<tr>
<td></td>
<td>Cefpodoxime; 10 mg/kg/day in 2 divided doses</td>
</tr>
<tr>
<td></td>
<td>Clindamycin; 30-40 mg/kg/day in 3 divided doses</td>
</tr>
<tr>
<td><strong>Penicillin-allergic patients after failure of initial therapy (severe allergy, consider ID consult)</strong></td>
<td>Ceftriaxone; 50 mg/dose IV or IM for 3 days</td>
</tr>
<tr>
<td></td>
<td>Clindamycin (30-40 mg/kg per day in 3 divided doses) with or without an oral third-generation cephalosporin</td>
</tr>
<tr>
<td></td>
<td>Consider tympanocentesis or consult specialist as necessary</td>
</tr>
</tbody>
</table>

**REFERENCES**


For WRNMMC use only, page 7
CANDIDEMIA IN NON-NEUTROPENIC PATIENT

RISK FACTORS
- Total parenteral nutrition
- Prolonged use of broad-spectrum antibiotics
- Hematologic malignancy
- Bone marrow or solid organ transplant
- Gastrointestinal compromise
- Indwelling central vascular catheters
- Colonization with *Candida* at multiple sites
- Premature neonate
- Corticosteroids

DIAGNOSTIC AND THERAPEUTIC CONSIDERATIONS
- Blood cultures:
  - Yeast in a blood culture should not be considered a contaminant
  - Candida can be isolated in routine blood culture bottles (fungal isolator not required)
  - When a central venous catheter is present, obtain one set simultaneously from each lumen and one set from a peripheral vein site. Paired cultures should be obtained from PICC lines, portacaths, and hemodialysis catheters when applicable.
  - Ensure blood culture bottles are labeled with the corresponding source site
- Remove all invasive intravascular catheters
- Consult Ophthalmology to evaluate for endophthalmitis
- See page 19 for anti-fungal recommendations in neutropenic patients
- Azoles:
  - Among azoles, fluconazole has the highest penetration into the CSF, eye, and urinary tract, and is preferred over other triazoles for empiric treatment of candidemia
  - Avoid fluconazole if *C. glabrata* or *C. krusei* is isolated
  - Avoid use in pregnant women
- Echinocandins:
  - Broader spectrum of activity against *Candida spp.*
  - Poor penetration of the CNS, eye, and urinary tract
- Amphotericin B, liposomal amphotericin (AmBisome):
  - Effective against most *Candida spp.* except for *C. lusitaniae.*
  - Generally, azoles and echinocandins are preferred agents due to Amphotericin B toxicity profile but Amphotericin B is indicated if there are concerns for a metastatic infection.
  - Lipid formulation does not achieve adequate urine concentrations and should be avoided if there is urinary tract involvement.

ANTIFUNGAL THERAPY – IMPORTANT CONCEPTS

Typical duration of antibiotic therapy:
- **14 days** following documented clearance of blood cultures and clinical symptoms
- Persistent candidemia and/or metastatic complications need a longer duration of therapy

Infectious Diseases consultation:
- All pediatric cases
- Persistent candidemia or suboptimal response to therapy
- Suspected metastatic complications (i.e. endophthalmitis, endocarditis, meningitis/encephalitis)
- Isolation of *C. auris*
- AmBisome (liposomal amphotericin) use
EMPIRIC THERAPY: UNSPECIFIED CANDIDEMIA

Hemodynamically stable and **NO** prior azole use within 3 months:

**Fluconazole** 800 mg IV/PO x1 loading dose, then 400 mg IV/PO q24h

Hemodynamically unstable **OR** received prior long-term azole therapy:

**Micafungin** 100 mg IV q24h

DIRECTED THERAPY: SPECIFIED CANDIDEMIA

**Candida albicans:**
**Fluconazole** 800 mg IV/PO x1 loading dose, then 400 mg IV/PO q24h
If Micafungin was started empirically, transition to Fluconazole once patient is stable.

**Candida glabrata:**

**Micafungin** 100 mg IV q24h

Majority of *C. glabrata* isolates demonstrate Fluconazole resistance. Fluconazole can be used if the patient is stable and the isolate is susceptible with MIC ≤ 8mcg/mL. Other azoles such as Voriconazole should not be used in Fluconazole-resistant strains because of a shared mechanism of resistance.

**Candida krusei:**

**Micafungin** 100 mg IV q24h

Fluconazole should **NEVER** be used because of intrinsic resistance. This mechanism of resistance is not shared with Voriconazole, therefore Voriconazole may be considered in susceptible isolates. If AmBisome is used, treat with 5 mg/kg q24h.

**Candida lusitaniae:**

**Fluconazole** 800 mg IV/PO x1 loading dose, then 400 mg IV/PO q24h
If Micafungin was started empirically, transition to Fluconazole once patient is stable. *C. lusitaniae* is resistant to Amphotericin B in approximately 20% of cases.

**Candida parapsilosis:**

**Fluconazole** 800 mg IV/PO x1 loading dose, then 400 mg IV/PO q24h
Fluconazole may be used at standard dosing for susceptible strains. High dose (800 mg IV/PO Q24h) if strain has intermediate resistance. Micafungin 100 mg IV once daily for Fluconazole resistant isolate. However, consider switching to AmBisome if there is poor clinical response. The MICs of echinocandins are higher for *C. parapsilosis* than any other *Candida spp*.

**Candida tropicalis:**

**Fluconazole** 800 mg IV/PO x1 loading dose, then 400 mg IV/PO q24h
Fluconazole may be used at standard dosing for susceptible strains. High dose (800 mg IV/PO q24h) if strain has intermediate resistance. Micafungin 100 mg IV q24h for Fluconazole resistant isolate.

**Candida auris:** Multi-class (azoles, echinocandin, polyene) resistance possible. **Consult ID.**
NEONATES:

- If candidemia is identified, then **must treat empirically for CNS infection until this complication is ruled out.**
- A lumbar puncture is recommended. Imaging (CT or head US) is also recommended as CSF may be unremarkable in 25% of infants with candida meningoencephalitis.
- CT or ultrasound of the GU tract, liver, and spleen should be performed if there is persistent candidemia.
- Lipid formulations of Amphotericin B should be used with caution, particularly if there is urinary tract involvement.

<table>
<thead>
<tr>
<th>Candidemia WITH CNS infection:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphotericin B deoxycholate 1-2 mg/kg per day</td>
</tr>
<tr>
<td>Addition of flucytosine 25 mg/kg/dose q6h should be considered if poor clinical response</td>
</tr>
<tr>
<td>For susceptible strains in stable patients, step-down to fluconazole 12 mg/kg q24h may be considered</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Candidemia WITHOUT CNS infection:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluconazole 12 mg/kg q24h is an alternative to Amphotericin B deoxycholate if susceptible</td>
</tr>
</tbody>
</table>

REFERENCES


CLOSTRIDIUM DIFFICILE INFECTION (CDI)

**DEFINITIONS AND RISK FACTORS**

**Definition of CDI:**
- Three or more unformed stools within 24 hours plus a positive test for toxigenic *C. difficile*
- Colonoscopy suggestive of pseudomembranous colitis (histopathology or visual inspection)
- Rarely CDI may present with ileus and no diarrhea

**Severe CDI:**
- WBC > 15,000
- Serum creatinine > 1.5 x the upper limit of normal (or > 50% from baseline)

**Fulminant CDI:**
- Pancolitis, and/or toxic megacolon
- Ileus
- Hypotension or shock

**Risk factors for CDI:**
- Precedent antibiotic use; risk increases with prolonged exposure
- Any antibiotic can predispose to *C. difficile* colonization; however, fluoroquinolones, clindamycin, and broad-spectrum penicillins and cephalosporins are more commonly implicated
- Proton pump inhibitors and histamine 2 receptor antagonists are associated with increased risk
- Recurrent disease after a complete course of therapy occurs in approximately 25% of patients
DIAGNOSTIC CONSIDERATIONS

- Asymptomatic carriage of \textit{C. difficile} occurs in 20% of hospitalized adults. Recommend against testing unless the patient is clinically symptomatic. At WRNMMC, \textit{C. difficile} PCR on unformed stool is utilized. While highly sensitive (>90% sensitivity), the test cannot distinguish colonization from active infection.
- Prior to testing:
  - Ensure patient has diarrhea defined as ≥ 3 unformed liquid stools/24hr period
  - Discontinue laxatives 24-48 hours prior to see if diarrhea resolves (unless clinically unstable)
  - Restrict to one specimen within 7 days
- Rectal swab can be submitted in cases of ileus
- Test of cure is NOT recommended

ANTIMICROBIAL THERAPY – IMPORTANT CONCEPTS

- STOP ALL ANTIMICROBIAL AGENTS WHENEVER POSSIBLE
- Efficacy of IV metronidazole is poorly established for CDI but is recommended when ileus is present
- There is no efficacy of IV vancomycin for CDI
- Vancomycin solution can be used for patients with a NGT/PEG tube
- Asymptomatic carriage of \textit{C. difficile} should not be treated
- Fidaxomicin can be considered for certain CDI and recurrent CDI cases; requires ID approval for use

Consider Infectious Diseases, Gastroenterology, General Surgery consultation:
- Treatment refractory cases
- Multiple recurrences of CDI
- Consideration for fecal transplant
- To xic megacolon, ileus, perforation

TREATMENT FOR INITIAL EPISODE

Non-Severe CDI:
Metronidazole is no longer recommended

\textbf{Vancomycin} 125mg PO/NGT Q6H for 10 days ($0.77/per cap; $30.80 treatment course, May 2018 formulary cost)

Consideration for oral fidaxomicin use (200mg PO twice a day for 10 days) over vancomycin:
($101.74/per 200mg fidaxomicin tab; $2,034.80 treatment course, May 2018 formulary cost)
- No response to vancomycin
- Patients at increased risk of morbidity and mortality (> 65 years of age, inflammatory bowel disease, transplant recipients, severe immunocompromise)

Severe CDI:

\textbf{Vancomycin} 125mg PO/NGT Q6H for 10 days

\textbf{OR}

\textbf{Fidaxomicin} 200 mg PO twice a day for 10 days

Fulminant CDI:
\textbf{Vancomycin} 500mg PO/NGT Q6H \textbf{PLUS Metronidazole} 500mg IV Q8H
If ileus present \textbf{ADD Vancomycin} 500mg in 100mL normal saline as a retention enema per rectum Q6H
Consider ID and General Surgery consultations
First recurrence:
If standard dose PO vancomycin was used initially, use pulse/taper course:
125 mg orally four times daily for 10-14 days
125 mg orally twice daily for 7 days
125 mg once daily for 7 days
125 mg orally every 2-3 days for 2-8 weeks

OR

Fidaxomicin 200mg PO twice a day for 10 days
($101.74/per 200mg fidaxomicin tab; $2,034.80 treatment course, May 2018 formulary cost)
Consider when vancomycin used for the initial episode and patient is at increased risk of morbidity and mortality (> 65 years of age, inflammatory bowel disease, transplant recipients, severe immunocompromise)

Second recurrence:
Vancomycin PO pulse taper course as above

OR

Fidaxomicin 200mg PO twice a day for 10 days

Consideration for Gastroenterology consult for fecal microbiota transplant in case-by-case basis; especially if fidaxomicin was used for initial and first recurrence episodes

Subsequent recurrences (i.e. 3 prior CDI episodes):
Gastroenterology consult for consideration of fecal microbiota transplant

REFERENCES

1) Clinical Practice Guidelines for Clostridium difficile Infection in Adults and Children: 2017 Update by the Infectious Disease Society of America (IDSA) and Society of Healthcare Epidemiology of America (SHEA). Abstracted May 14, 2018


MENINGITIS AND ENCEPHALITIS IN ADULTS

DEFINITIONS AND RISK FACTORS

Community-Acquired Meningitis:
- Inflammation of the membranes (meninges) surrounding the brain and spinal cord typically presenting with headache, fever and a stiff neck. Most cases are caused by a viral infection, but bacterial and fungal infections are other causes. Risk factors include age (young and elderly), CSF leak, immunocompromise, lack of immunization as well as certain food risks (e.g. for Listeria).

Healthcare-Associated Meningitis and Ventriculitis
- Meningitis and ventriculitis can occur during hospitalization or after hospital discharge associated with invasive procedures, head trauma, or indwelling intracranial devices.

Encephalitis:
- Presence of an inflammatory process of the brain in association with clinical evidence of neurologic dysfunction. Of the pathogens reported to cause encephalitis, the majority are viruses. Risk factors include young and elderly, immunocompromise (both humoral and cellular immune deficits), and insect vector and/or animal contact.

DIAGNOSTIC CONSIDERATIONS

- New headache, fever, evidence of meningeal irritation, seizures and/or worsening mental status are suggestive of ventriculitis or meningitis in the setting of recent trauma or neurosurgery
- New headache, fever, nausea, lethargy and/or change in mental status are suggestive of CSF shunt infection
- In addition to blood cultures, CSF should be sent for cell count with differential, glucose, protein, Gram stain and culture, and BioFire FilmArray® as below
- **BioFire FilmArray® Meningitis/Encephalitis Panel** detects 14 pathogens utilizing a nested multiplex PCR with results in one hour: Escherichia coli, Haemophilus influenzae, Listeria monocytogenes, Neisseria meningitidis, Streptococcus agalactiae, Streptococcus pneumoniae, Cytomegalovirus, Enterovirus, Herpes simplex virus-1 (HSV-1), Herpes simplex virus-2 (HSV-2), Human herpesvirus 6 (HHV-6), Human parechovirus, Varicella zoster virus (VZV), Cryptococcus neoformans/gattii.
- **Indications for head CT prior to lumbar puncture (LP):** history of CNS disease (mass lesion, CVA), new-onset seizure (<1 week), papilledema, altered consciousness, focal neurologic deficit, immunocompromised state (HIV/AIDS, immunosuppressive therapy, transplant patient)
- An opening pressure during a LP should be obtained and documented when feasible

ANTIMICROBIAL THERAPY AND MANAGEMENT – IMPORTANT CONCEPTS

- Antibiotics should be started as soon as possible if bacterial meningitis is a potential diagnosis, ideally within 30 minutes. Do not wait for CT scan or LP results. If LP must be delayed, get blood cultures and start therapy.
- Addition of dexamethasone is recommended in all adult patients with suspected pneumococcal meningitis (note that this will be most adult patients)
- Dexamethasone dose is 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.
- Infectious Diseases consultation should be obtained on all meningitis/encephalitis cases
- Narrow therapy to pathogen-specific antibiotics based on available culture data
- Strongly consider allergy consult to verify reported penicillin allergy (see page 59)
- Antibiotic doses are higher for CNS infections, see below and page 53 for Vancomycin dosing
- Typical duration of antibiotic therapy:
  - S. pneumoniae 10-14 days; N. meningitidis 7 days; Listeria 21 days; H. influenzae 7 days; Gram negative bacilli 21 days
## Empiric Therapy for Meningitis

<table>
<thead>
<tr>
<th>Host</th>
<th>Pathogens</th>
<th>Preferred Antibiotics</th>
<th>Alternative for serious PCN allergy (ID consult recommended)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunocompetent age &lt;50</td>
<td><em>S. pneumo, N. mening, H. influenza</em></td>
<td>Vancomycin <strong>PLUS</strong> Ceftriaxone</td>
<td>Vancomycin <strong>PLUS</strong> Moxifloxacin*</td>
</tr>
<tr>
<td>Immunocompetent age &gt; 50</td>
<td><em>S. pneumo, Listeria, H. influenzae, N. mening, Group B streptococci</em></td>
<td>Vancomycin <strong>PLUS</strong> Ceftriaxone PLUS Ampicillin</td>
<td>Vancomycin <strong>PLUS</strong> Moxifloxacin* PLUS TMP/SMX</td>
</tr>
<tr>
<td>Immuno-compromised†</td>
<td><em>S. pneumo, N. mening, H. influenzae, Listeria, Gram negatives</em></td>
<td>Vancomycin <strong>PLUS</strong> Cefpime <strong>PLUS</strong> Ampicillin</td>
<td>Vancomycin <strong>PLUS</strong> TMP/SMX <strong>PLUS</strong> Ciprofloxacin</td>
</tr>
<tr>
<td>Post-neurosurgery or penetrating head trauma</td>
<td><em>S. pneumo (if CSF leak), H. influenzae, Staphylococci, Gram negative</em></td>
<td>Vancomycin <strong>PLUS</strong> Cefpime OR Meropenem</td>
<td>Vancomycin <strong>PLUS</strong> Ciprofloxacin OR Aztreonam</td>
</tr>
<tr>
<td>Infected shunt</td>
<td><em>S. aureus, coagulase-negative staphylococci, Gram negatives (rare)</em></td>
<td>Vancomycin <strong>PLUS</strong> Cefpime <strong>PLUS</strong> Meropenem</td>
<td>Vancomycin <strong>PLUS</strong> Ciprofloxacin</td>
</tr>
</tbody>
</table>

*Allergy consult for verification of true beta-lactam allergy and possible desensitization
†Immunocompromised is defined as solid organ transplant, BMT in the past year, leukemia undergoing treatment, or neutropenia

### Pathogen-Specific Therapy (ID Consult Recommended)

<table>
<thead>
<tr>
<th>Pathogens</th>
<th>Preferred Antibiotics</th>
<th>Alternatives for serious PCN allergy (Consult allergy for PCN skin testing + desensitization)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>S. pneumo</em> PCN MIC ≤ 0.06 µg/ml AND/OR Ceftriaxone MIC &lt; 0.5 µg/ml</td>
<td>Penicillin <strong>OR</strong> Ceftriaxone</td>
<td>Vancomycin <strong>OR</strong> Moxifloxacin <strong>OR</strong> Linezolid</td>
</tr>
<tr>
<td><em>S. pneumo</em> PCN MIC &gt; 0.1-1 µg/ml AND Ceftriaxone MIC &lt; 1 µg/ml</td>
<td>Ceftriaxone</td>
<td>Moxifloxacin <strong>OR</strong> Linezolid; Consult ID</td>
</tr>
<tr>
<td><em>S. pneumo</em> PCN MIC &gt;1 µg/ml AND Ceftriaxone MIC ≥ 1 µg/ml</td>
<td>Ceftriaxone <strong>PLUS</strong> Vancomycin <strong>PLUS</strong> Rifampin</td>
<td>Moxifloxacin <strong>OR</strong> Linezolid; Consult ID</td>
</tr>
<tr>
<td><em>N. meningitidis</em> PCN susceptible (MIC &lt; 0.1)</td>
<td>Penicillin <strong>OR</strong> Ceftriaxone</td>
<td>Consult ID</td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em></td>
<td>Ampicillin <strong>OR</strong> Ceftriaxone</td>
<td>Ciprofloxacin</td>
</tr>
</tbody>
</table>
Non β-lactamase producer

*Haemophilus influenzae*

| β-lactamase producer | Ceftriaxone | Ciprofloxacin |

*Listeria monocytogenes*

| Ampicillin ± Gentamicin | TMP/SMX |

*P. aeruginosa*

| Cefepime OR Meropenem | Ciprofloxacin PLUS Aztreonam |

*Escherichia coli*

<table>
<thead>
<tr>
<th>Klebsiella pneumoniae</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftriaxone</td>
</tr>
</tbody>
</table>

*Enterobacter spp.*

| Meropenem | Ciprofloxacin OR TMP/SMX (if susceptible) |

*S. aureus-MSSA*

| Nafcillin or Oxacillin* | Vancomycin |

*S. aureus-MRSA*

| Vancomycin* |

Coagulase-negative staphylococci if Oxacillin MIC ≤0.25

| Oxacillin* | Vancomycin |

Coagulase-negative staphylococci if Oxacillin MIC >0.25

| Vancomycin* |

*Enterococcus*

| Ampicillin PLUS Gentamicin | Vancomycin PLUS Gentamicin |

*Candida species*

| Liposomal Amphotericin B |

*Cryptococcus*

| Liposomal Amphotericin B PLUS Flucytosine |

* Consider addition of rifampin if susceptible and prosthetic material is in place

**ENCEPHALITIS**

- Herpes viruses (HSV, VZV) remain the predominant causes of treatable encephalitis
- The **BioFire FilmArray Meningitis/Encephalitis Panel** can detect treatable viruses (HSV, VZV, CMV) in addition to other viral pathogens
- Imaging with MRI with gadolinium is helpful in defining encephalitis and in considering key temporal lobe findings in HSV reactivation
- Remember that *Listeria monocytogenes* can cause both a meningitis as well as a rhomboencephalitis
- Have low threshold to treat if suspect HSV. If left untreated, mortality exceeds 70%.
- Treatment: Acyclovir 10 mg/kg/IV Q8H for 14-21 days; ensure patient is hydrated and infuse slowly to prevent acyclovir induced crystal nephropathy

**ANTIMICROBIAL DOSES FOR CNS INFECTIONS – NORMAL RENAL FUNCTION**
Antibiotics

- Ampicillin: 2 g IV q4h
- Aztreonam: 2 g IV q6h
- Ceftriaxone: 2 g IV q12h
- Cefepime: 2 g IV q8h
- Ciprofloxacin: 400 mg IV q8h
- Moxifloxacin: 400 mg IV q24h
- Meropenem: 2 g IV q8h
- Metronidazole: 500 mg IV q6h
- Oxacillin: 2 g IV q4h
- Penicillin: 4 million units IV q4h
- 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), see page 53
  - Maintain troughs close to 20 mcg/ml

Antifungals

- Amphotericin: 0.7-1 mg/kg IV q24h
- AmBisome: 3-4 mg/kg IV q24h for cryptococcal meningitis
- AmBisome: 5 mg/kg IV q24h for Candidal meningitis
- Fluconazole: 800-1200 mg IV/PO q24h (can give in divided doses)
- Flucytosine: 25 mg/kg PO q6h

Intraventricular antibiotics (ID consult recommended)

- Amikacin: 30 mg q24h
- Gentamicin: 5 mg q24h
- Tobramycin: 5 mg q24h
- Vancomycin: 20 mg q24h

REFERENCES

NEUTROPENIC FEVER

DEFINITIONS

Fever:
- Single temp ≥ 38.3 (101°F)
- Temp ≥ 38.0 (100.4°F) sustained over an hour
- Avoid rectal temperature measurements when neutropenic

Neutropenia:
- Absolute neutrophil count (ANC) < 500 cell/mm³
- ANC expected to fall below 500/mm³ within 48 hours
- For mild neutropenia (ANC < 1000 cell/mm³) or uncertain trajectory, consult Hematology-Oncology

DIAGNOSTIC CONSIDERATIONS

- Do not delay antibiotics while obtaining specimens for culture.
- Blood cultures:
  - Obtain prior to administration of antibiotics if possible.
  - Obtain at least two sets. When a central venous catheter is present, obtain one set simultaneously from each lumen and one set from a peripheral vein site. Paired cultures should be obtained from PICC lines, portacaths, and hemodialysis catheters when applicable.
  - Ensure blood culture bottles are labeled with the corresponding source site.
  - Candida can be isolated in routine blood culture bottles (fungal isolator not required).
- Review past microbiology for known colonization or infections with resistant organisms.
- Culture specimens from other sites of suspected infection as clinically indicated.
- Consider rapid diagnostics such as respiratory biofire (nasopharyngeal swab) when appropriate.
- Strongly consider allergy consult to verify reported penicillin allergy (see page 59)

ANTIMICROBIAL THERAPY – IMPORTANT CONCEPTS

Empiric Antibiotic Therapy:
- High risk patients require hospitalization for IV empiric antibiotic therapy: monotherapy with anti-pseudomonal β-lactam agents such as cefepime, ceftazidime, a carbapenem (meropenem or imipenem-cilastatin), or piperacillin-tazobactam
- Low risk patients (anticipated brief neutropenia and no or few comorbidities) may be candidates for outpatient oral therapy – Hematology-Oncology consult required prior to decision for outpatient management
- Tailor antimicrobials based on culture data and susceptibilities when available

Duration of antibiotic therapy:
- Typically until patient is afebrile and has ANC ≥ 500 cells/mm³
- Consider de-escalation of IV empiric antibiotic therapy to oral prophylactic regimen prior to recovery of ANC IF:
  - Received at least 5 days of broad-spectrum antimicrobial therapy AND
  - Afebrile for 48 consecutive hours AND
  - Stable vital signs AND
  - No identifiable source of infection

Consider Infectious Diseases consultation:
- Staphylococcus aureus bacteremia
- Staphylococcus aureus isolates with vancomycin MIC > 1
- Invasive mold infections
- Patient is clinically unstable and/or has persistent fever despite appropriate broad spectrum anti-bacterial and anti-fungal coverage
- Multi-drug resistant pathogen
WHEN VANCOMYCIN IS INDICATED EMPIRICALLY

Vancomycin is **NOT** a standard part of empirical antibiotic therapy for fever and neutropenia **BUT** should be considered in the following situations:

- Suspected catheter-related bloodstream infection (rigors/fever during infusion or evidence of catheter exit site inflammation) or Gram-positive bacteremia awaiting speciation
- Severe mucositis (especially if receiving fluoroquinolone prophylaxis)
- Skin or soft tissue infection
- Pneumonia documented radiographically
- Severe sepsis or hemodynamic instability
- Known colonization or infection with MRSA

See page 53 for vancomycin dosing guidelines

Consider **Daptomycin 8-10mg/kg Q24H** instead of vancomycin **IF** there is a history of vancomycin resistant *Enterococcus* (VRE) colonization or infection. Daptomycin should not be used for pneumonia. **Linezolid 600 mg IV/PO Q12H** is an alternative. Empiric VRE coverage should be discontinued if cultures are negative for VRE.

EMPIRIC THERAPY: CONSIDER ADDITION OF VANCOMYCIN AS ABOVE

Hemodynamically stable, no sepsis, no known drug resistance, no abdominal findings:

**Ceftazidime** or **Cefepime** 2 grams IV Q8H

Hemodynamically stable, no sepsis **WITH** abdominal findings or suspected abdominal source:

**Piperacillin-tazobactam** 4.5 gm IV Q6H (see page 51 for prolonged infusion protocol)

Consider *C. difficile* stool PCR when appropriate

Hemodynamically stable, no sepsis **WITH** history of drug resistance to above agents and/or ESBL, AmpC:

**Meropenem** 1gram IV Q8H

Non-severe penicillin allergy: challenge with cephalosporin or carbapenem as appropriate; provide antihistamine, steroids and epinephrine PRN at bedside in the event of an immediate IgE-mediated reaction. Consideration for allergy consultation as appropriate.

Severe penicillin allergy (anaphylaxis, bronchospasm or Stevens-Johnson Syndrome). Allergy consult to verify highly recommended. Treat with a regimen that avoids β-lactam drugs as below.

**Aztreonam** 2 gram IV Q8H **AND** **Vancomycin** (loading dose followed by maintenance dose, see page 53 for vancomycin dosing guidelines)

If septic, would add **Gentamicin** 5-7mg/kg IV (see page 56 for dosing guidelines)

If abdominal findings or suspected abdominal source, add **Metronidazole** 500mg IV Q6H

Sepsis without focal findings:

**Piperacillin-tazobactam** 4.5 gm IV Q6H (see page 51 for prolonged infusion protocol) **AND** **Gentamicin** 5-7mg/kg IV

**AND** **Vancomycin** (loading dose followed by maintenance dose, see page 53 for vancomycin dosing guidelines, see page 56 for aminoglycoside dosing guidelines)

**Meropenem** 1 gram IV Q8H in place of piperacillin-tazobactam in cases of known resistance or AmpC/ESBL
ANTI-FUNGALS

Empiric antifungal therapy: persistent fever or new fever after 4-7 days of broad spectrum antibiotics and no identified bacterial infection. Investigation for invasive fungal infections should be initiated (i.e. CT Chest, CT sinus).

If receiving fluconazole prophylaxis or no fungal prophylaxis:

Micafungin 100mg IV Q24H if sinus and/or chest CT NOT suggestive of fungal infection

OR

Voriconazole 6mg/kg IV or PO Q12H x two doses followed by 4mg/kg IV or PO Q12H IF chest CT suggestive of fungal infection

If receiving voriconazole or posaconazole prophylaxis OR sinus CT is suggestive of fungal infection:

AmBisome (liposomal Amphotericin B) 5mg/kg IV Q24H

REFERENCES

5) Outpatient Management of Fever and Neutropenia in Adults Treated for Malignancy: American Society of Clinical Oncology and Infectious Diseases Society of America Clinical Practice Guideline Update. DOI: 10.1200/JCO.2017.77.6211 Journal of Clinical Oncology - published online before print February 20, 2018

PNEUMONIA (PNA) IN ADULTS - INPATIENT

DEFINITIONS AND RISK FACTORS

Community-Acquired Pneumonia (CAP):
• New lung infiltrate plus clinical evidence of infection (fever, purulent sputum, leukocytosis, or hypoxia) not acquired in the hospital setting

Hospital-Acquired Pneumonia (HAP):
• Pneumonia not present at admission and occurring >48 hours after hospital admission

Ventilator-Associated Pneumonia (VAP)
• Pneumonia occurring >48 hours after endotracheal intubation and mechanical ventilation

Risk factors for mortality:
• Requiring ventilator support
• Septic shock
Risk factors for MRSA:
- Prior IV antibiotics (Abx) in the last 90 days
- Hospitalization where > 20% of S. aureus isolates are MRSA or unknown
- Necrotizing PNA with cavitation in the absence of risk factors for aspiration is concerning for possible MRSA PNA especially if there was a preceding influenza-like illness

Risk factors for Pseudomonas and other multi-drug resistant (MDR) pathogens:
- Structural lung disease (bronchiectasis, post-obstruction) or cystic fibrosis (CF)
- Prior IV antibiotics in the last 90 days
- Prolonged hospitalization > 7 days
- Recent mechanical ventilation > 48 hours
- Immunocompromised: solid organ transplant, hematologic malignancy, bone marrow transplant, active chemotherapy, prednisone ≥ 20 mg daily for ≥ 3 weeks
- VAP cases: concomitant septic shock, preceding ARDS, acute renal replacement prior to onset

DIAGNOSTIC CONSIDERATIONS

- Attempt to obtain respiratory and blood cultures prior to antibiotics for patients being admitted to the hospital
- Immunocompetent patients with CAP should have a CXR infiltrate to meet diagnostic criteria
- Consider Biofire Respiratory FilmArray® for atypical PNA or viral PNA
- Consider viral etiology during the respiratory virus season (fever, sore throat, myalgias, rhinorrhea, headache, cough)
- Legionella (detects only serogroup 1 responsible for 70-80% of infections) and Streptococcus pneumoniae urinary antigen testing (specificity 96% and PPV of 88.8-96.5%) should be performed especially for ICU patients

ANTIMICROBIAL THERAPY AND MANAGEMENT – IMPORTANT CONCEPTS

- Strongly consider allergy consult to verify reported penicillin allergy (see page 59)
- Typical duration of antibiotic therapy:
  - 5-7 days
  - 3-5 days for CAP in patients without immunocompromise or structural lung disease with good clinical response to therapy
- Cough and CXR abnormalities may take 4-6 weeks to improve. There is no need to extend antibiotics if the patient is otherwise stable (i.e. no fever).
- Empiric coverage for S. aureus, Pseudomonas and other gram-negative bacilli is recommended for VAP
- Azithromycin and fluoroquinolones have been associated with QT prolongation. Doxycycline 100 mg IV/PO BID can be used for atypical coverage in patients with contraindications to QT prolonging agents.
- Daptomycin is contraindicated in PNA
- Linezolid is an alternative agent to Vancomycin for MRSA pneumonia. Continued use of linezolid > 72 hours requires ID approval (except in CF). Avoid use in patients with concomitant S. aureus bacteremia.
- See page 51 for prolonged infusion of piperacillin-tazobactam protocol
- See page 53 for Vancomycin dosing
- See page 56 for aminoglycoside dosing
- Transition to PO therapy when appropriate (see page 48)
- Narrow therapy to pathogen-specific Abx based on available culture data
- Enterococci and candida species are often isolated from sputum in hospitalized patients. Generally, they should be considered colonizing organisms and should NOT be treated with Abx.
- In general, Abx are not recommended for ventilator-associated tracheobronchitis
- PNA in HIV patients: consider opportunistic infections especially with low CD4 <200 (ie. Tuberculosis, PCP)
Consider Infectious Diseases consultation:

- *Staphylococcus aureus* bacteremia
- *Staphylococcus aureus* isolates with vancomycin MIC > 1
- Patient is clinically unstable and/or has persistent fever despite appropriate broad spectrum Abx
- Multi-drug resistant pathogen
- Mycobacteria or fungal etiologies

**CAP EMPIRIC THERAPY IN ADULTS REQUIRING HOSPITALIZATION**

**Non-ICU:**

**Ceftriaxone** 1 gram IV Q24H + **Azithromycin** 500mg IV/PO Q24H  
Atypical coverage can be discontinued after receiving 1.5grams of Azithromycin (ie. 500mg IV/PO Q24H x 3 days)

Beta-lactam allergy: **Moxifloxacin** 400mg IV/PO Q24H

**ICU:**

**Ceftriaxone** 1 gram IV Q24H + **Azithromycin** 500mg IV/PO Q24H  
Atypical coverage can be discontinued after receiving 1.5grams of Azithromycin (ie. 500mg IV/PO Q24H x 3 days)

Beta-lactam allergy: **Moxifloxacin** 400mg IV/PO Q24H

**Risk factors for MRSA or increased mortality:**
ADD **Vancomycin** IV (see page 53 for dosing)

**Risk factors for Pseudomonas, MDR pathogens, or increased mortality:**

**Cefepime** 2 grams IV Q8H + **Levofloxacin*** 750mg IV/PO Q24H

Alternative:

**Piperacillin-tazobactam** 4.5 gram IV Q6H + **Levofloxacin*** 750mg IV/PO Q24H

Beta-lactam allergy: **Levofloxacin** 750mg IV/PO Q24H + **Aztreonam** 2gram IV Q8H

Narrow coverage if cultures are negative for *Pseudomonas* at 48 hours

*WRNMMC Pseudomonal isolates have >20% resistance to fluoroquinolones, utilization would be for concomitant atypical coverage over empiric double coverage against *Pseudomonas*.

**HAP/VAP EMPIRIC THERAPY IN ADULTS**

**Cefepime** 2 grams IV Q8H (Alternative: **Piperacillin-tazobactam** 4.5 gram IV Q6H)

**PLUS** **Vancomycin** IV (see page 53 for dosing)

If risk factors for MDR *Pseudomonas* or increased mortality: ADD **Amikacin** IV 15-20mg/kg to the above (see page 56 for aminoglycoside dosing and monitoring)

Beta-lactam allergy: **Levofloxacin** 750mg IV/PO Q24H + **Amikacin** IV 15-20mg/kg (see page 56 for aminoglycoside dosing and monitoring) + **Vancomycin** IV (see page 53 for dosing guidelines)

At risk for, or ESBL organism isolated: **Meropenem** 1gram IV Q8H; can consider **Ertapenem** 1gram IV Q24H if no risk for *Pseudomonas*
DE-ESCALATION OR STEP-DOWN THERAPY

As guided by culture and susceptibilities whenever possible

Step down therapy may not be appropriate if no sputum culture was obtained or poor quality sample, antibiotics were given prior to sputum culture, or high-risk for MDR. A course of atypical coverage should be completed if indicated.

No culture data and clinically improving:
Cefpodoxime 200mg PO BID or Amoxicillin/clavulanate 875mg PO BID
Beta-lactam allergy: Moxifloxacin 400mg PO Q24H

ASPIRATION

Aspiration event ≠ Aspiration PNA

Most aspiration events result in chemical pneumonitis and do not require antibiotic treatment

Patients often have fever, leukocytosis, and infiltrates for the first 48 hours post aspiration

Prophylactic antibiotics ARE NOT recommended for patients at increased risk for aspiration

Indications for antibiotic treatment: continued symptoms for 48 hours after aspiration

REFERENCES


COMMUNITY ACQUIRED PNEUMONIA (CAP) - CHILDREN

INTRODUCTION AND PREVENTION

These guidelines are for healthy children >3 months of age. These recommendations are NOT applicable for infants < 90 days, immunocompromised children, children receiving home mechanical ventilation, or children with chronic conditions or underlying lung disease (e.g. cystic fibrosis).

- Pneumococcal 13-valent conjugate vaccine series, Haemophilus influenzae type B vaccine series, and pertussis vaccine (DTaP) series should be given to reduce risk of CAP.
- Pertussis vaccine booster (Tdap) should be given at age 11.
- Children ≥ 6 months of age should receive the annual influenza vaccine.
- Parents and caretakers of infants <6 months of age, including pregnant women, should receive the influenza vaccine and pertussis vaccine (Tdap) to protect their infants from potential exposure.
DIAGNOSTIC CONSIDERATIONS

- **Complete blood count (CBC)** should be obtained in moderate to severe pneumonia.
- **Blood cultures** are recommended only in those requiring hospitalization for moderate to severe pneumonia, particularly ones complicated by pleural effusion, empyema, or lung abscess.
- **Biofire Respiratory FilmArray®** should be obtained. A positive test for a respiratory virus, such as RSV or influenza, may decrease the need for antibiotics or additional diagnostic studies. A positive test for *Mycoplasma* can justify the use of macrolide monotherapy.
- If the FilmArray® is not available, alternatives include rapid influenza and/or RSV antigen immunoassays (although these have suboptimal sensitivity) or respiratory viral culture for influenza, RSV, adenovirus, and parainfluenza viruses (take several days to result). Commercial tests for *Mycoplasma* do not offer adequate sensitivity and specificity in a clinically relevant time frame.
- **CXR** is not necessary to confirm suspected CAP in patients well enough for outpatient treatment. Posteroanterior and lateral CXRs should be obtained in patients with suspected or documented hypoxemia or with significant respiratory distress.
- **Sputum samples** for culture and Gram stain should be obtained in hospitalized children with productive cough who can cooperate with the collection (usually > 10 years old).
- **Tracheal aspirates** for culture and Gram stain should be obtained at time of initial endotracheal tube placement in those children requiring mechanical ventilation.
- **Pulse oximetry** should be performed in all children with pneumonia and suspected hypoxemia.

CONSIDERATIONS FOR HOSPITALIZATION

- Moderate to severe pneumonia
- Respiratory distress as manifested by:
  - RR >50 for age 2-12 months
  - RR >40 for age 1-5
  - RR >20 for age > 5 years
  - Presence of dyspnea, retractions, grunting, nasal flaring, apnea, altered mental status, or POx <90%
- Infants less than 3-6 months of age
- Concern for inability of parents to carefully observe child at home, comply with recommended oral antibiotic regimen, or return for follow-up
- Inability to tolerate PO fluids and medications

CONSIDERATION FOR PICU ADMISSION

- Need for CPAP, BiPAP or endotracheal intubation
- PEWS score ≥ 6
- Impending respiratory failure, sustained tachycardia, hypotension, or need for inotropic support
- Pulse oximetry < 92% on inspired oxygen of ≥ 0.50
- Altered mental status from hypercarbia or hypoxemia

EMPIRIC THERAPY

- Antibiotic therapy is not necessary if positive for RSV, influenza, or other respiratory viruses in the absence of clinical, laboratory, or radiographic findings that suggest bacterial co-infection.
- If influenza is detected and the child has had ≤48 hours of symptoms, antiviral therapy (e.g. oseltamivir x5 days) is appropriate.

**Duration of therapy:**
- With the exception of **5 days** of azithromycin to treat a suspected **atypical pneumonia**, **10 days** of total antibiotics (i.e. 10 days of PO or 10 days of IV+PO) is recommended for uncomplicated CAP.
- Patients with concomitant bacteremia, moderate to large pleural effusions, and/or empyema may require longer treatment courses and a Pediatric Infectious Diseases consult should be strongly considered.
<table>
<thead>
<tr>
<th>Indication</th>
<th>First-line Regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>OUTPATIENT</strong>&lt;br&gt;Previously healthy and appropriately immunized infants and children with mild-moderate CAP</td>
<td><strong>Amoxicillin</strong>: 90 mg/kg/day divided in 2 doses PO  &lt;br&gt;Max of 3 grams/day  &lt;br&gt;<em>Streptococcus pneumoniae</em> is the most common cause  &lt;br&gt;<em>Avoid azithromycin monotherapy in children &lt; 5 years old. Up to 40% of pneumococcal isolates in the community are resistant to macrolides.</em></td>
</tr>
<tr>
<td><strong>OUTPATIENT</strong>&lt;br&gt;School-aged children (≥5 years) and adolescents who have findings compatible with atypical pathogens</td>
<td><strong>Azithromycin</strong>: 10mg/kg PO once daily on day 1  &lt;br&gt;followed by 5 mg/kg once daily on days 2-5  &lt;br&gt;Max of 500 mg on day 1, followed by 250 mg on days 2-5  &lt;br&gt;Pathogens include <em>Mycoplasma pneumoniae</em> and <em>Chlamydophila pneumoniae</em>. <em>Legionella</em> is rare in children. Atypical pneumonia is usually associated with milder disease, subacute presentation, low-grade fever, pharyngitis, and lower WBC. Classic finding on CXR is multifocal, peribronchial interstitial infiltrates, although presentations vary.</td>
</tr>
<tr>
<td><strong>INPATIENT</strong>&lt;br&gt;Immunized with <em>Haemophilus influenzae</em> type B (Hib) and pneumococcal (Prevnar-13®) vaccines</td>
<td><strong>Ampicillin</strong>: 150-200 mg/kg/day IV ÷ q6h; with initial dose of 50 mg/kg  &lt;br&gt;Max dose 12 grams/day in children &lt;12, adolescent/adult max dose 14 grams/day  &lt;br&gt;<em>Vancomycin</em> (40-60 mg/kg/day IV ÷ q6-8h, with initial dose of 20 mg/kg) <strong>should be added if</strong> clinical, laboratory, or imaging characteristics are consistent with MRSA infection, or there is severe respiratory illness requiring PICU admission</td>
</tr>
<tr>
<td><strong>INPATIENT</strong>&lt;br&gt;NOT fully immunized with <em>Haemophilus influenzae</em> type B (Hib) and pneumococcal (Prevnar-13®) vaccines, OR those with life-threatening infection to include empyema</td>
<td><strong>Ceftriaxone</strong>: 50-100 mg/kg/day ÷ q12-24h, initial dose of 50 mg/kg  &lt;br&gt;<em>Vancomycin</em> (40-60 mg/kg/day IV ÷ q6-8h, with initial dose of 20 mg/kg) <strong>should be added if</strong> clinical, laboratory, or imaging characteristics are consistent with MRSA infection, or there is severe respiratory illness requiring PICU admission</td>
</tr>
<tr>
<td><strong>INPATIENT</strong>&lt;br&gt;Patients with significant concern for atypical pathogen including <em>M. pneumoniae</em> or <em>C. pneumoniae</em></td>
<td><strong>Azithromycin</strong>: 10mg/kg IV/PO once daily on day 1  &lt;br&gt;followed by 5 mg/kg once daily on days 2-5  &lt;br&gt;can be added <strong>in addition to</strong> a β-lactam antibiotic</td>
</tr>
<tr>
<td>Indication</td>
<td>First-line Regimens</td>
</tr>
<tr>
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</tr>
<tr>
<td>Penicillin-allergic patients</td>
<td><strong>Non-serious reactions to Amoxicillin:</strong></td>
</tr>
</tbody>
</table>
| **Allergy assessment is highly recommended (see page 59)** | 1) Trial of **Amoxicillin** under medical observation **OR**  
2) Trial of cephalosporin under medical observation:  
**Cefpodoxime** (Vantin®): 10 mg/kg/day PO ÷ BID; Max of 400 mg per day  
**OR**  
**Cefuroxime** (Ceftin®): 30 mg/kg/day PO ÷ BID; Max of 1 gram per day  
**OR**  
**Cefprozil** (Cefzil®): 30 mg/kg/day PO ÷ BID; Max of 1 gram per day  
**Serious allergy, history of anaphylaxis:**                                                                                                                                 |
|                                  | 1) **Levofloxacin**: 16-20 mg/kg/day IV/PO ÷ BID for children 6 months to 5 years  
8-10 mg/kg/day IV/PO once daily for children 5-16 years  
Max daily dose of 750 mg  
**OR**  
2) **Linezolid**: 30 mg/kg/day IV/PO ÷ TID for children <5 years  
20 mg/kg/day IV/PO ÷ BID for children 5-11 years  
600 mg IV/PO BID for children ≥ 12 years  
Max of 600 mg per dose  
**OR**  
3) **Clindamycin**: 30-40 mg/kg/day IV ÷ TID; Max of 4.8 grams per day  
20-30 mg/kg/day PO ÷ TID; Max of 1.8 grams per day                                                                                                                                 |

**REFERENCES**
INTRA-ABDOMINAL INFECTIONS

CONSIDERATIONS

- For the treatment of *C. difficile*, see page 10
- Strongly consider allergy consult to verify reported penicillin allergy (see page 59)
- Carbapenems should be reserved for patients with known or increased risk for ESBL isolates
- Lack of source control: defined as on-going contamination or continued undrained source
- Empiric therapy should be tailored to culture results whenever possible

BILIARY TRACT CHOLECYSTITIS AND CHOLANGITIS – IMPORTANT CONCEPTS

- Blood cultures should be obtained to help guide therapy if positive
- Cultures should be obtained from bile or stents removed at endoscopic retrograde cholangiopancreatography (ERCP) or percutaneous transhepatic cholangiography (PTC) to guide antimicrobial therapy
- Most commonly isolated organisms: *E. coli, Klebsiella* spp., *Proteus* spp.
- Anaerobes (including *Bacterioides* spp) are less common in uncomplicated community-acquired infections and should be considered in patients with biliary manipulation or serious infection
- Pseudomonas should be considered in serious infections or patients who have undergone prior procedures or have been exposed to broad-spectrum Abx
- In severely ill patients with cholangitis and complicated cholecystitis, adequate biliary drainage is crucial as antibiotics will not enter bile in presence of an obstruction
- Empiric coverage of enterococci is usually not needed in mild/moderate disease
- Infection with yeast is rare; empiric antifungal coverage is generally not warranted. Treat only if yeast is recovered from biliary cultures.

Typical duration of antibiotic therapy:

- **Uncomplicated cholecystitis**: treat only until obstruction is relieved. Post-procedure Abx are not indicated if the obstruction is successfully relieved (by surgery, ERCP, or percutaneous drain).
- Patients undergoing cholecystectomy for acute cholecystitis should have antimicrobial therapy discontinued within 24 hours unless there is evidence of infection outside the wall of the gallbladder.
- **Complicated cholecystitis**: 4 days, unless adequate source control is not achieved
- **Biliary sepsis**: 4-7 days, unless adequate source control not achieved

DIVERTICULITIS – IMPORTANT CONCEPTS

- **Acute diverticulitis**: inflammation of diverticulum generally due to microperforation
- **Simple/uncomplicated**: acute disease without an associated complication (bowel obstruction, abscess, fistula, or perforation)
- **Complicated diverticulitis**: acute disease with at least one complication as above
- Antimicrobial treatment for acute uncomplicated diverticulitis may not accelerate recovery or prevent complications/recurrence.
- CT imaging is preferred to assess for complications and need for drainage in severe disease.
- Almost all infections are polymicrobial. Most commonly isolated organisms: *E. coli, K. pneumoniae, Enterobacter* spp., *Proteus* spp., and anaerobes (including *Bacterioides* spp., *Prevotella* spp., *Peptostreptococci* spp.)

Typical duration of antibiotic therapy:

- **4-5 days**, unless adequate source control not achieved
**PANCREATITIS – IMPORTANT CONCEPTS**

- CT with contrast or MRI of the pancreas should be reserved for patients with unclear clinical diagnosis or who fail to clinically improve within the first 48-72 hours after admission.
- Infected pancreatic necrosis is defined by CT imaging with gas in the pancreas and/or percutaneous or surgical specimens with organisms evident on Gram stain or culture.
- The majority of infections are monomicrobial – *E. coli, Pseudomonas, Klebsiella, Enterococcus*. Use of Abx with poor pancreatic penetration should be avoided (aminoglycosides, first-generation cephalosporins, ampicillin).
- **Routine use of prophylactic antibiotics in severe acute pancreatitis and/or sterile necrosis has no effect on morbidity and mortality and is NOT recommended.**
- Infected necrosis should be considered in patients with pancreatic or extra-pancreatic necrosis who fail to improve after 7-10 days of hospitalization (peak incidence is in the 3rd week of disease).
- Infection develops in 30-50% of patients with documented necrosis on CT imaging or at time of surgery.

**Typical duration of antibiotic therapy:**

- Infected pancreatic necrosis: continue antibiotics for **14 days after source control obtained**

**PERITONITIS – IMPORTANT CONCEPTS**

- **Primary peritonitis/spontaneous bacterial peritonitis (SBP):** spontaneous infection of the peritoneal cavity, usually associated with liver disease and ascites
- **Secondary peritonitis:** infection of the peritoneal cavity due to spillage of organisms into the peritoneum, usually associated with GI perforation
- The diagnosis of SBP is based on neutrophil count in ascitic fluid of > 250/mm³.
- Ascitic fluid cultures and blood cultures should be performed in all patients with suspected SBP.
- Most common organisms: Enterobacteriaceae (esp *E. coli, K. pneumoniae*), *S. pneumoniae*, enterococci, and anaerobes (esp for small bowel and colonic perforations).
- Polymicrobial infections should prompt suspicion for GI perforation.
- Patients with suspected secondary bacterial peritonitis should undergo CT imaging.
- Consider repeat paracentesis after 48 hours of therapy and changing antibiotics if ascitic fluid PMNs has not dropped by 25% after 48 hours and/or patient not clinically responding.
- Treatment of enterococci remains controversial, but should be considered in critically ill or immunosuppressed or when it is dominant organism isolated in peritoneal culture.
- **Empiric antifungal therapy indicated for:** esophageal perforation, immunosuppression, prolonged antacid or antibiotic therapy, prolonged hospitalization, persistent GI leak. Definitive therapy indicated when cultured in blood or recovered from peritoneal culture in critically ill or immunosuppressed patients. See page 8 for Candida treatment recommendations.
- All patients with cirrhosis and upper GI bleed should receive SBP prophylaxis for 7 days. After an episode of SBP, lifelong prophylaxis is warranted to prevent future episodes.
- Post-operative antibiotics for appendicitis are not necessary in absence of peritonitis, abscess, or gangrene.
- **Antibiotics are only adjunctive to source control**

**Typical duration of antibiotic therapy:**

- Primary SBP: **5 days**
- Secondary peritonitis:
  - Uncomplicated: **24-48 hours**
  - Complicated: **4 days** unless adequate source control not achieved
EMPIRIC THERAPY

Community-acquired infections, mild-to-moderate severity (without prior biliary procedures AND who are not severely ill):

**Ceftriaxone** 1-2 gram IV Q24H

If severe PCN allergy: **Aztreonam** 2gram IV Q8H

**ADD** anaerobic coverage with **Metronidazole** 500mg IV Q8H for infections involving proximal perforation in the presence of obstruction or ileus, distal small bowel, appendix, and colon.

Hospital-acquired infections OR community-acquired infections of high severity (prior biliary procedures, bilio-enteric anastomosis of any severity, advanced age, immunocompromised, or severely ill):

**Piperacillin-tazobactam** 3.375gram IV Q6H (if Pseudomonas strongly suspected, increase to 4.5gram IV q6h), see page 51 for prolonged infusion protocol

**OR**

**Cefepime** 2gram IV Q8H **PLUS** **Metronidazole** 500mg IV Q8H

**ADD** **Vancomycin** for severe sepsis (see page 53 for dosing recommendations)

If severe PCN allergy: **Aztreonam** 2gram IV Q8H **PLUS** **Metronidazole** 500mg IV Q8H ± **Vancomycin** (see page 53 for dosing recommendations) for Gram positive coverage or severe sepsis

If isolated on cultures, Candida spp. should be treated in patients with hospital-acquired infections or severe community-acquired infections (see page 8 for treatment recommendations).

REFERENCES

ASYMPTOMATIC BACTERIURI A (ASB)

DEFINITION AND IMPORTANT CONCEPTS

- Defined as positive urine culture WITHOUT signs or symptoms of UTI (dysuria, urgency, increased frequency, suprapubic pain, fever, flank pain)
- Foul smelling or cloudy urine alone is NOT diagnostic of a UTI
- Women with dysuria and the presence of vaginal discharge/odor, pruritus, dyspareunia, and absence of urinary frequency or urgency should prompt consideration of vaginitis
- Routine urine cultures in asymptomatic patients is NOT recommended
  - Diabetics, elderly, catheterized patients, and patients with spinal cord injuries should NOT be screened or treated for asymptomatic bacteriuria
- Antibiotics DO NOT decrease asymptomatic bacteriuria or prevent subsequent development of UTI
- Pyuria accompanying asymptomatic bacteriuria is NOT an indication for treatment
- Prevalence of asymptomatic bacteriuria is high and increases with advancing age
  - 1-5% of pre-menopausal women
  - 3-9% of post-menopausal women
  - 40-50% of long-term care residents
  - 9-27% of women with diabetes
- **Patients admitted for another reason are commonly over treated for UTI.** For example, a patient admitted with a congestive heart failure exacerbation or pneumonia is unlikely to have a coexisting urinary tract infection. If the patient does not have symptoms of a UTI, antibiotics should not be started for a “dirty urine” or the antibiotics should be stopped as soon as possible when it is recognized they do not have a UTI.
- Signs and symptoms for UTI are difficult to assess in patients who are unable to talk or present with mental status changes. There are multiple causes of mental status change. Antibiotics can cause a multitude of side effects (e.g. toxicity, drug interactions, allergic reactions, *C. difficile*, promote drug resistance). If the patient has no other signs of infection (fever, leukocytosis, hemodynamic instability), it may be reasonable to conduct a work up, address issues like dehydration or metabolic derangements, and re-evaluate for improvement before starting empiric antimicrobials for possible UTI in these cases. Clinical judgment is warranted to determine if antibiotics are ultimately indicated.
- Multiple studies have looked at the negative impact of inappropriate treatment of ASB

INDICATIONS FOR TREATMENT

- **NO TREATMENT IS INDICATED** unless they fall into one of the following categories:
  - Pregnant female
  - Post kidney transplant (especially within 3 months from transplant)
  - Patient undergoing urologic procedure (kidney, bladder, or prostate gland)

REFERENCES

**CANDIDURIA IN ADULTS**

**DISCLAIMER**
- The following recommendations **DO NOT** apply to febrile neutropenic patients or very low birth weight infants

**ASYMPTOMATIC CANDIDURIA:**
- Common in catheterized patients receiving antibiotics and usually represents colonization, not infection
- **Removal of predisposing factors like indwelling urinary catheters is recommended when feasible**
- Antifungal treatment is **NOT** indicated, except for those at high-risk for dissemination
  - **High-risk** = neutropenic patients, very low birth weight infants, and patients who are to undergo urologic procedures

**Asymptomatic candiduria undergoing urologic procedures:**
- **Fluconazole** 400mg PO daily (6mg/kg) for several days before and after the procedure
- **AmB deoxycholate** 0.3-0.6 mg/kg daily is an alternate therapy

**CANDIDA CYSTITIS, PYELONEPHRITIS, AND UTI ASSOCIATED WITH FUNGAL BALL**
- **Elimination of urinary tract obstruction and exchange/removal of nephrostomy tubes or stents is recommended when feasible**
- Lipid formulations of amphotericin (AmB), echinocandins (micafungin, caspofungin), voriconazole, itraconazole, and posaconazole do **NOT** achieve adequate urinary concentrations for UTI treatment.
- Candida pyelonephritis is usually secondary to hematogenous spread except for patients with renal transplant or abnormalities of the urogenital tract. Echinocandins do penetrate into renal tissue and may remain appropriate for pyelonephritis of hematogenous origin.
- **Infectious Diseases consultation is recommended in low birth weight infants, pregnant women, immunosuppressed patients, drug resistant Candida isolates, or if AmB is required**
- AmB is the treatment of choice for invasive candidiasis in pregnant women

**Symptomatic Candida Cystitis:**
- For fluconazole susceptible organisms, **Fluconazole** 200mg PO daily (3 mg/kg) for 14 days
- For *Candida glabrata* resistant to fluconazole, **AmB deoxycholate** 0.3-0.6 mg/kg IV daily for 1-7 days **OR** **Flucytosine** 25 mg/kg PO 4 times daily for 7-10 days
- For *Candida krusei*, **AmB deoxycholate** 0.3-0.6 mg/kg IV daily for 1-7 days

**Ascending Candida pyelonephritis:**
- Fluconazole susceptible organisms: **Fluconazole** 200-400 mg (3-6 mg/kg) PO daily for 2 weeks
- Fluconazole-resistant *C. glabrata*: **AmB deoxycholate** 0.3-0.6 mg/kg IV daily with or without **Flucytosine** 25 mg/kg PO 4 times daily. Oral monotherapy with **Flucytosine** 25 mg/kg 4 times daily for 2 weeks may also be considered.
- Fluconazole resistant *C. krusei*, **AmB deoxycholate** 0.3-0.6 mg/kg IV daily for 1-7 days is recommended

**For Candida UTI associated with fungus balls:**
- Antifungal treatment is the same as noted above for Candida cystitis and pyelonephritis, and **surgical intervention** is strongly recommended. Nephrostomy tubes may be irrigated with **AmB deoxycholate** 25-50 mg in 200-500ml sterile water.

**REFERENCES**
URINARY TRACT INFECTION (UTI) - WOMEN

DEFINITIONS AND RISK FACTORS

Asymptomatic bacteriuria: does NOT require treatment in the majority of cases (see page 29)

Acute cystitis:
- Signs and symptoms to include dysuria, urgency, increased urinary frequency, suprapubic pain
- AND pyuria (>10 WBC/hpf)
- AND positive urine culture ≥ 100,000 CFU/mL

Acute pyelonephritis:
- Signs and symptoms to include fever, chills, flank pain, costo-vertebral angle tenderness, nausea, and vomiting
- May have evidence of upper tract infection: leukocytosis, WBC casts, imaging abnormalities
- AND pyuria (>10 WBC/hpf)
- AND positive urine culture ≥ 100,000 CFU/mL

Complicated infection: risk factors which increase the risk of treatment failure
- Abnormal GU anatomy, obstruction, presence of indwelling catheter/stent/nephrostomy tube, pregnancy, poorly controlled diabetes, hospital-acquired infection, acute kidney injury or chronic kidney disease, renal transplantation, other immunocompromising condition
- Acute complicated pyelonephritis can include progression of upper tract infection to emphysematous pyelonephritis, corticomedullary or perinephric abscess, or papillary necrosis

DIAGNOSTIC CONSIDERATIONS

- Urine cultures (UCx) should ONLY be obtained when a significant suspicion for a UTI exists based on symptoms
- UCx should be interpreted taking into account the results of the urinalysis (UA) AND patient symptoms
- Epithelial cells on a UA indicates contamination and corresponding UCx results should NOT be considered reliable
- Indications for UCx:
  - Patient has signs and symptoms of a UTI
  - Patients who cannot provide a history (intubated, demented) and have sepsis or other indications of infection without another source identified
- UCx NOT recommended:
  - Change in urine color, odor, or turbidity
  - Patients lacking S/Sx of UTI
  - Fever workup in a patient who can reliably provide a history as to whether he/she has S/Sx of a UTI
  - Pre-operatively except in urologic surgery where mucosal bleeding is anticipated
  - When a urinary catheter is placed or changed
  - At admission to the hospital unless there is concern for UTI
  - After treatment of UTI to document cure (unless pregnant or will undergo urologic procedure as above)
- Presence of bacteria in the urine represents one of the following and requires clinical correlation between UA/UCx findings AND history/exam:
  - Specimen contamination
  - Asymptomatic bacteriuria (see page 29)
  - UTI
- 3 or more organisms in a UCx suggests contamination and a new specimen should be obtained if UTI is still suspected
- Women with dysuria and the presence of vaginal discharge/odor, pruritus, dyspareunia, and absence of urinary frequency or urgency should prompt consideration of vaginitis
- The absence of pyuria is a strong indicator that UTI is unlikely
- Pyuria alone without clinical S/Sx of UTI is NOT an indication for treatment
• In suspected UTI, a **urine Gram stain** can be ordered in addition to UA/UCx which can give early diagnostic information to assist in guiding empiric therapy (GPC like *Enterococcus* species vs. GNR organisms)

• **Staphylococcus aureus in the urine** without recent catheterization or instrumentation is concerning for the possibility of systemic infection and/or hematogenous seeding

• If an appropriate antimicrobial for an upper tract infection is used but symptoms do not abate, imaging should be obtained to rule out complications (stone, obstruction, abscess, etc)

**ANTIMICROBIAL THERAPY AND MANAGEMENT – IMPORTANT CONCEPTS**

• 75-95% of uncomplicated cystitis and pyelonephritis in women is caused by *E. coli*

• Review prior urine culture data to help guide empiric therapy

• **Narrow therapy to pathogen-specific antibiotics based on available culture data**

• **Infectious Diseases consultation** should be considered for multi-drug resistant organisms

• Strongly consider allergy consult to verify reported penicillin allergy (see page 59)

• **Nitrofurantoin should be avoided in CrCl < 30ml/min**

• Nitrofurantoin and fosfomycin should be avoided in any upper tract or invasive disease (pyelonephritis or urosepsis)

• Oral beta-lactams should be avoided in cases of concomitant bacteremia due to inadequate blood concentrations

• **Carbapenem use > 72 hours requires ID approval, reserved for ESBL and MDRO organisms**

• If UCx results as enterococcal species, therapy should be adjusted based on susceptibility
  - If susceptible, amoxicillin 500mg PO Q8H or ampicillin 2gram IV Q6H is recommended

• **Typical duration of antibiotic therapy:**
  - **Uncomplicated acute cystitis:** single-dose up to 5 days depending on agent used
  - **Uncomplicated acute pyelonephritis:** 5-14 days depending on agent used
  - **Complicated UTI:** optimal duration is not known and should be tailored to co-morbid conditions, severity of illness, and rapidity of response to treatment, generally 5-14 days

**WRNMMC INPATIENT URINARY ISOLATES**

<table>
<thead>
<tr>
<th>Top Gram Negative Organisms</th>
<th>% patients</th>
<th>Amikacin</th>
<th>Amoxicillin</th>
<th>Amoxicillin clavulante</th>
<th>Ampicillin</th>
<th>Cefotaxime</th>
<th>Ceftriaxone</th>
<th>Ceftazidime</th>
<th>Ciprofloxacin</th>
<th>Gentamicin</th>
<th>Imipenem</th>
<th>Levofloxacin</th>
<th>Meropenem</th>
<th>Nitrofurantoin</th>
<th>Piperacilina/ Ticarcilina</th>
<th>Tobramycin/ Amikacin</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Escherichia coli</em></td>
<td>116</td>
<td>100%</td>
<td>86%</td>
<td>50%</td>
<td>96%</td>
<td>88%</td>
<td>88%</td>
<td>87%</td>
<td>64%</td>
<td>100%</td>
<td>80%</td>
<td>80%</td>
<td>65%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td>55</td>
<td>98%</td>
<td>60%</td>
<td>69%</td>
<td>60%</td>
<td>60%</td>
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<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>32</td>
<td>100%</td>
<td>97%</td>
<td>97%</td>
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</tbody>
</table>

#patients: first isolate per patient included in the analysis for each organism

Fosfomycin susceptibility (2017 data):
- *E. coli* (non-ESBL) = 98% (n=477)
- *E. coli* (ESBL) = 97% (n=31)
Acute uncomplicated cystitis in women

Fluoroquinolones (FQs) are **NOT** first line therapy; additionally inpatient *E. coli* isolates have > 30% FQ resistance

**First-line regimen:**
Nitrofurantoin 100mg PO BID x 5 days

OR

Fosfomycin 3gram PO x 1 dose

**Alternatives:**
Trimethoprim-sulfamethoxazole (TMP/SMX) DS 160/800 mg one tab PO BID x 3 days
**Should be used with caution prior to culture results as resistance >20% for inpatient *E. coli* urinary isolates

Beta-lactams (e.g. amoxicillin-clavulanate, cefpodoxime, cefdinir, cefaclor, cephalixin) PO for 3-7 days should be used with caution as they have less clinical efficacy than first line regimens and TMP/SMX

FQs (ciprofloxacin 250mg PO BID OR levofloxacin 250mg once daily) x 3 days have propensity for collateral damage and should only be considered an alternative for acute uncomplicated cystitis

Acute uncomplicated pyelonephritis in women

**First-line regimen:**
Ceftriaxone 1gram IV Q24H

OR

Ciprofloxacin 400mg IV Q12H OR Levofloxacin 750mg IV Q24H
Ciprofloxacin 500mg PO BID x 7 days or Levofloxacin 750mg PO Q24H x 5days is appropriate if tolerating PO and not requiring hospitalization
** FQs should be used with caution prior to culture results as resistance >30% for inpatient *E. coli* urinary isolates

**Oral step-down therapy when patient is stable and if organism is susceptible** (see page 48 for IV to PO conversion)

**Alternatives:**
TMP/SMX DS 160/800mg one tab PO BID x 14 days if susceptible
Beta-lactams PO x 10-14 days are less effective than other agents

Severe beta-lactam allergy and unable to use non-beta lactam above: Aztreonam 1gram IV Q8H

Severely ill or hemodynamically unstable:
Cefepime 2gram IV Q12H (2gram Q8H if *Pseudomonas* suspected) OR
Piperacillin-tazobactam 3.375 gram IV Q6H (4.5gram Q6H if *Pseudomonas* suspected) OR
Meropenem 500mg IV Q8H (1gram Q8H if *Pseudomonas* suspected) OR
Gentamicin IV (see page 56 for dosing)
Complicated UTI in women

* Regimen depends on previous antimicrobial use, results of any recent urine cultures, and current urine Gram stain
* Lower risk for MDRO: Ceftriaxone OR FQ can be considered
* Higher risk for MDRO: Cefepime, Piperacillin-Tazobactam, Carbapenem, or Gentamicin can be considered
* Nitrofurantoin, fosfomycin, and TMP/SMX can be used for cystitis if isolate is susceptible
* For pyelonephritis, treatment can be completed with FQ or TMP/SMX oral therapy if susceptible
* Severe beta-lactam allergy and unable to use one of the above non-beta lactams: Aztreonam 2gram IV Q8H

REFERENCES


URINARY TRACT INFECTION (UTI) - MEN

DEFINITIONS AND RISK FACTORS

See above on page 31

- It has been conventional to consider UTI in men as complicated, however, acute uncomplicated UTIs can occur especially in men who participate in insertive anal intercourse and those patients that lack circumcision.
- Dysuria, urinary frequency and urgency, and pyuria can also be seen with acute bacterial prostatitis. The presence of fever, chills, malaise, myalgias, pelvic or perineal pain, or obstructive symptoms such as dribbling and hesitancy (due to acute urinary retention) in a man with symptoms of cystitis suggests acute bacterial prostatitis.

DIAGNOSTIC CONSIDERATIONS

See above on page 31

- UTI in men in the absence of obstructive pathology or urologic abnormalities (BPH, stones, strictures) is uncommon
- Urethritis and sexually transmitted infections should be considered in sexually active males
- Men with recurrent cystitis should undergo evaluation for prostatitis

ANTIMICROBIAL THERAPY AND MANAGEMENT – IMPORTANT CONCEPTS

See above on page 32

- See above page 32 for WRNMMC inpatient urinary isolate susceptibilities
- As involvement of the prostate is common, antimicrobials with good prostatic tissue penetration are recommended
- If UCx results as enterococcal species, therapy should be adjusted based on susceptibility
  - If susceptible, amoxicillin 500mg PO Q8H or ampicillin 2gram IV Q6H is recommended
- Typical duration of antibiotic therapy:
  - Optimal duration is unknown and should be tailored to co-morbid conditions, severity of illness, and rapidity of response to treatment, generally 5-14 days
  - Shorter course (5-7 days) in cystitis without S/Sx of severe pyelonephritis or prostatitis is likely sufficient2-4
EMPIRIC THERAPY

Acute cystitis in men

**TMP/SMX DS 160/800mg one tab PO BID**

**OR**

**Ciprofloxacin 500mg PO BID OR Levofloxacin 750mg PO Q24H**

Acute pyelonephritis in men

**First-line regimen:**

**Ceftriaxone 1gram IV Q24H**

**OR**

**Ciprofloxacin 400mg IV Q12H OR Levofloxacin 750mg IV Q24H**

Oral step-down therapy to FQ or TMP/SMX when patient is stable and if organism is susceptible (see page 48 for IV to PO conversion)

**Severe beta-lactam allergy and unable to use non-beta lactam above:** **Aztreonam 2 gram IV Q8H**

**Severely ill, hemodynamically unstable, or increased risk for drug resistant organism:**

**Cefepime 2gram IV Q12H (2gram Q8H if Pseudomonas suspected) OR**

**Piperacillin-tazobactam 3.375 gram IV Q6H (4.5gram Q6H if Pseudomonas suspected) OR**

**Meropenem 500mg IV Q8H (1gram Q8H if Pseudomonas suspected)**

REFERENCES


http://uroweb.org/guideline/urological-infections/

For WRNMMC use only, page 35
CATHETER ASSOCIATED UTI (CA-UTI)

DEFINITIONS AND RISK FACTORS

- **Asymptomatic bacteriuria (ASB):** does **NOT** require treatment in the majority of cases (see page 29)
- **CAUTI:** presence of indwelling urethral, suprapubic or intermittent catheterization within previous 48 hours **AND**
  - S/Sx of UTI with no other identified source of infection (fever with no other source, suprapubic or flank pain)
  - **AND** pyuria
  - **AND** positive UCx ≥ 1,000 CFU/ml
- Pyuria alone ≠ CAUTI
- **Bacteriuria alone ≠ CAUTI;** incidence of bacteriuria associated with an indwelling catheter is 3-8% per day and by one month, nearly 100% of patients will be bacteriuric. **Remove catheter whenever possible!**

DIAGNOSTIC CONSIDERATIONS

- **Specimen collection:**
  - Ideally, catheter should be removed and midstream urine sample collected from a spontaneous void
  - If catheter is still indicated, urine sample should be drawn from the catheter port using aseptic technique, **NOT** from the urine collection bag
  - **In patients with long term catheters (≥ 2 weeks), replace catheter before collecting a specimen**
  - Urine should be collected **before** antibiotics are started
- Presence of odorous or cloudy urine alone should **NOT** be used to differentiate CA-ASB from CA-UTI or as an indication for urine culture or antimicrobial therapy

ANTIMICROBIAL THERAPY AND MANAGEMENT – IMPORTANT CONCEPTS

- If a catheter is still indicated in setting of CAUTI, **replace the catheter** especially if it has been in place ≥ 2 weeks
- Screening for and treatment of CA-ASB is **NOT** recommended except in pregnant women and patients undergoing urologic procedures where mucosal bleeding is anticipated
- Prophylactic antibiotics at the time of catheter removal or replacement is **NOT** recommended
- Prophylactic antibiotics for patients with short-term or long-term catheterization, including those undergoing surgical procedures, to reduce CA-ASB or CA-UTI is **NOT** routinely recommended
- See above page 32 for WRNMMC inpatient urinary isolate susceptibilities
- Review prior urine culture data to help guide empiric therapy
- **Narrow therapy to pathogen-specific antibiotics based on available culture data**
- If UCx results as **enterococcal species**, therapy should be adjusted based on susceptibility
  - **If susceptible, amoxicillin 500mg PO Q8H or ampicillin 2gram IV Q6H is recommended**
- **Typical duration of antibiotic therapy:**
  - Female patient ≤ 65 yrs with lower tract infection: 3 days
  - Prompt resolution of symptoms: 7 days; 5 day regimen can be considered if not severely ill and FQ is used
  - Delayed response: 10-14 days

For WRNMMC use only, page 36
EMPIRIC THERAPY

**Ceftriaxone** 1gram IV Q24H

OR

**Ciprofloxacin** 500mg PO (400mg IV) BID OR **Levofloxacin** 750mg PO/IV Q24H

OR

**TMP/SMX** 160/800mg (double strength tab) PO BID if isolate is susceptible

**Severely ill, hemodynamically unstable, or increased risk for drug resistant organism:**

Cefepime 2gram IV Q12H (2gram Q8H if *Pseudomonas* suspected) OR
Piperacillin-tazobactam 3.375 gram IV Q6H (4.5gram Q6H if *Pseudomonas* suspected) OR
Meropenem 500mg IV Q8H (1gram Q8H if *Pseudomonas* suspected)

**Severe beta-lactam allergy and unable to use non-beta lactam above:** **Aztreonam** 2 gram IV Q8H
Highly recommend Allergy consult (see page 59)

REFERENCES

SKIN AND SOFT TISSUE INFECTION (SSTI)

DEFINITIONS AND RISK FACTORS

Mild SSTI:
- Non-purulent: typical cellulitis/erysipelas with no focus of purulence, no systemic symptoms
- Purulent: incision and drainage (I/D) is indicated, no systemic symptoms

Moderate to Severe SSTI:
- Rapid progression, failed I/D plus oral antibiotics, or systemic signs of infection such as temperature >38°C, hypotension, tachycardia (heart rate >90 bpm), tachypnea (respiratory rate >24) or abnormal white blood cell count (>12,000 or <400 cells/μL), or immunocompromised
- Clinical signs of deeper infection: bullae, skin sloughing, hypotension, or evidence of organ dysfunction; necrotizing fasciitis (ID and General Surgery consultations recommended)

Risk factors for MRSA:
- Precedent antibiotic use (within 3 months); risk increases with prolonged exposure
- Recent hospitalization (risk is higher with prolonged stays > 2 weeks)
- Prior colonization or infection with MRSA
- Nursing home or long term care facility
- IV drug abuse

DIAGNOSTIC CONSIDERATIONS

- Purulent material from an I/D should be sent for Gram stain and culture (tissue or pus collected in a syringe or container is preferred over swabs). **If swabs are sent, at least 2 are needed to perform Gram stain and culture.**
- **Avoid superficial cultures of non-debrided wounds or ulcers.**
- Cellulitis is uncommonly bilateral, consider chronic stasis/venous insufficiency with skin changes.

ANTIMICROBIAL THERAPY AND MANAGEMENT – IMPORTANT CONCEPTS

- **Strongly consider allergy consult to verify reported penicillin allergy** (see page 59)
- **Elevation of the affected extremity is a priority**
- **Tinea pedis can increase risk for cellulitis and should be treated if present**
- Resolution of erythema can take days especially with lymphedema
- **Typical duration of antibiotic therapy:**
  - 5-7 days for mild-moderate SSTI
  - Diabetic foot infection depends on clinical response, blood supply, and need for surgical intervention
- Diabetic foot ulcer management is multi-disciplinary: consider podiatry, orthopedics, vascular, and wound care consultations as appropriate along with optimal medical management of the diabetes
- Animal bites: preferred treatment with Amoxicillin/clavulanate 875 mg PO BID or Ampicillin/sulbactam 1.5-3gram IV Q6H. Assess need for tetanus immunization and rabies prophylaxis.
- **Clindamycin susceptibility for MRSA isolates is 43% for inpatients and 52% for outpatients** (Antibiogram page 61)
- Monotherapy with fluoroquinolones for *S. aureus* infections is **NOT** recommended
- Daptomycin and Dalbavancin require ID approval for use
- Continued use of linezolid > 72 hours requires ID approval
- Narrow therapy based on available culture data

Consider Infectious Diseases consultation:
- Necrotizing fasciitis
- Non-response to empiric therapy
- Concerns for atypical pathogens (mycobacteria, fungal)
- Suspected osteomyelitis

For WRNMMC use only, page 38
SSTI EMPIRIC THERAPY IN ADULTS

Non-purulent: cellulitis, erysipelas; predominantly caused by beta-hemolytic streptococci

**Mild:**
Dicloxacillin 500mg PO Q6H **OR** Cephalexin 500mg PO Q6H  
Beta-lactam allergy: Clindamycin 300-450mg PO Q6-8H

**Moderate:**
Cefazolin IV 1gram Q8H **OR** Ceftriaxone IV 1 gram Q24H  
Beta-lactam allergy: Clindamycin IV 600-900mg Q8H

**Severe:**
Consider emergent surgical and ID consultations  
Vancomycin IV (see page 53 for dosing) **PLUS** Piperacillin/tazobactam IV 4.5 gram Q6H  
**ADD** Clindamycin IV 900mg Q8H if necrotizing process is suspected

Beta-lactam allergy: Vancomycin IV **PLUS** Ciprofloxacin IV 400mg Q8H  
**ADD** Clindamycin IV 900mg Q8H if necrotizing process is suspected

Purulent: abscess, furuncle, carbuncle; usually caused by *S. aureus* (MSSA and MRSA)
I/D is the primary treatment and culture of purulence should be performed when possible  
Avoid Clindamycin use for empiric MRSA coverage (Clindamycin susceptibility for MRSA is 43% for inpatients and 52% for outpatients) (see Antibiogram page 61)

**Mild:**
I/D only  
Consider antibiotics: immunocompromised state or significant co-morbid conditions, large abscess > 2 cm, multiple abscesses, abscess located in an area difficult to drain (face, genitalia); adjacent joint, prosthetic material, or hardware

**Moderate:**
Trimethoprim/sulfamethoxazole DS 1-2 tablets PO BID **OR** Doxycycline 100mg PO BID  
MSSA isolated from cultures: Cephalexin 500mg PO Q6H **OR** Dicloxacillin 500mg PO Q6H

**Severe:**
Vancomycin IV (see page 53 for dosing)  
Alternative: Daptomycin IV 4mg/kg Q24H  
MSSA isolated from cultures: Cefazolin 1 gram IV Q8H **OR** Nafcillin 2 gram IV Q4H
**DIABETIC FOOT INFECTION**

**Non-infected:** no purulence or signs of inflammation (erythema, pain, tenderness, warmth, induration)

No antibiotics indicated, optimize wound care

**Mild:** Purulence and ≥1 signs of inflammation and cellulitis (if present) ≤2cm around the ulcer; limited to skin or superficial subcutaneous tissue

Oral options:
- Amoxicillin-clavulanate 875 mg PO BID OR Cephalexin 500mg PO QID
- Beta-lactam allergy: Clindamycin 300-450 mg PO TID

IV options:
- Cefazolin 1gram IV Q8H OR Nafcillin 2 gram IV Q4H OR Ampicillin/sulbactam 1.5-3 gram IV Q6H
- Beta-lactam allergy: Clindamycin 600 mg IV Q8H

**Moderate:** Same as mild **PLUS** at least one of the following: >2cm cellulitis, lymphangitic streaking, spread beneath the superficial fascia, deep tissue abscess, gangrene, involvement of muscle-tendon-joint-bone

- Ampicillin/sulbactam 1.5-3gram IV Q6H **OR** Ertapenem 1gram IV Q24H **OR** Ceftriaxone 1gram Q24H **PLUS** Metronidazole 500 mg IV/PO TID
- **ADD** Vancomycin if patient has risk factors for MRSA
- Beta-lactam allergy:
  - Ciprofloxacin 500 mg PO BID or 400 mg IV Q12H
  - **PLUS** Metronidazole 500 mg IV/PO TID
  - **PLUS** Vancomycin IV (see page 53 for dosing)

**Severe:** Any of the above **PLUS** systemic toxicity or metabolic instability

- Piperacilin/tazobactam 4.5 gram IV Q6H **PLUS** Vancomycin IV (see page 53 for dosing)

**OR**

- Cefepime 2 gram IV Q8H **PLUS** Metronidazole 500 mg IV Q8H **PLUS** Vancomycin IV

- Beta-lactam allergy:
  - Ciprofloxacin 400mg IV Q8H **OR** Aztreonam 2 gram IV Q8H
  - **PLUS** Metronidazole 500mg IV Q8H
  - **PLUS** Vancomycin IV

- **ADD** Clindamycin IV 900mg Q8H if necrotizing process is suspected

**REFERENCES**

1) Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections. *Clin Infect Dis* 2014;59(2);e10-52.
**PRE-OPERATIVE AND PRE-PROCEDURAL PROPHYLAXIS**

**IMPORTANT CONCEPTS**

- **Dosing:**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Usual Dose#</th>
<th>Redosing during procedure*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefazolin</td>
<td>&lt; 120kg: 2gram</td>
<td>Q4h (Q2h for cardiac surgery)</td>
</tr>
<tr>
<td></td>
<td>≥ 120 kg: 3gram</td>
<td></td>
</tr>
<tr>
<td>Cefotetan</td>
<td>&lt; 120kg: 2gram</td>
<td>Q6h</td>
</tr>
<tr>
<td></td>
<td>≥ 120 kg: 3gram</td>
<td></td>
</tr>
<tr>
<td>Clindamycin</td>
<td>900 mg</td>
<td>Q6h</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>400 mg</td>
<td>None</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>5 mg/kg^</td>
<td>None</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>500 mg</td>
<td>None</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>15 mg/kg</td>
<td>None</td>
</tr>
</tbody>
</table>

* Redosing in the operating room is recommended at an interval of approximately two times the half-life of the agent in patients with normal renal function. Recommended redosing intervals marked as “none” are based on typical case length; for unusually long procedures, redosing may be needed.

^ Gentamicin should be given as a single dose of 5 mg/kg to maximize tissue penetration and minimize toxicity. Use actual body weight unless patient is 20% over ideal body weight. In this case, dosing weight should be used (see page 56).

# Dose adjustments may be indicated for patients with a BMI > 30

- **Timing:**
  - The timing of administration is critical.
  - Antimicrobials should be started within 60 minutes of the surgical incision.
  - Vancomycin and fluoroquinolones should be started 60-120 minutes before the initial incision because of the prolonged infusion times required for these drugs.

- **Post-Procedure doses:**
  - Post-procedure doses for the majority of cases are NOT needed.
  - Postoperative duration of antimicrobial prophylaxis should be limited to less than 24 hours, regardless of the presence of indwelling catheters or drains.¹ There are no data to support continuation of prophylaxis after wound closure even if indwelling drains and intravascular catheters have not yet been removed.

- **Prophylaxis for patients already on antibiotics:**
  - For antibiotics other than vancomycin: hold standing dose until 1 hour before incision.
  - For vancomycin: Re-dose a full dose if 8 hours or more have passed since the last dose. Or give a half dose if fewer than 8 hours have passed since prior dose in a patient with normal renal function.

**RECOMMENDED REGIMENS BASED ON PROCEDURE**

- Recommendations provided do not apply to infants < 1 year of age
- Recommendations are for patients with no relevant microbiology data that would suggest resistant organisms
- **Highly recommend that patients with a reported PCN allergy be referred for evaluation** (see page 59)
  - Patients with a reported PCN allergy have a 50% increased odds of surgical site infection attributable to receipt of second-line perioperative antibiotics²
**Cardiac surgery & Thoracic surgery**

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Prophylaxis Recommendation</th>
<th>PCN allergy / alternate regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median sternotomy</td>
<td>Cefazolin</td>
<td>Vancomycin</td>
</tr>
<tr>
<td>Median sternotomy with MRSA colonization or prior VAD*</td>
<td>Cefazolin <strong>PLUS</strong> Vancomycin</td>
<td>Vancomycin</td>
</tr>
<tr>
<td>Pacemaker or ICD insertion</td>
<td>Cefazolin</td>
<td>Clindamycin OR Vancomycin</td>
</tr>
<tr>
<td>Pacemaker or ICD insertion with MRSA colonization/infection</td>
<td>Cefazolin <strong>PLUS</strong> Vancomycin</td>
<td>N/A</td>
</tr>
<tr>
<td>Lobectomy, pneumonectomy, lung resection, thoracotomy, VATS</td>
<td>Cefazolin</td>
<td>Clindamycin</td>
</tr>
<tr>
<td>Thoracic surgery with esophageal approach</td>
<td>Cefotetan</td>
<td>Clindamycin</td>
</tr>
</tbody>
</table>

*Ventricular assist device

**General surgery**

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Prophylaxis Recommendation</th>
<th>PCN allergy / alternate regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedures involving entry into lumen of upper GI tract, gastric bypass procedures, pancreaticoduodenectomy, highly selective vagotomy, Nissan fundoplication</td>
<td>Cefotetan</td>
<td>Clindamycin +/- Gentamicin</td>
</tr>
<tr>
<td>Biliary tract procedures (i.e. cholecystectomy, choledochoenterostomy)</td>
<td>Cefotetan</td>
<td>Clindamycin +/- Gentamicin</td>
</tr>
<tr>
<td>Hepatectomy</td>
<td>Cefotetan</td>
<td>Clindamycin +/- Gentamicin</td>
</tr>
<tr>
<td>Whipple procedure or pancreatectomy</td>
<td>Cefotetan</td>
<td>Clindamycin PLUS Ciprofloxacin</td>
</tr>
<tr>
<td>Small bowel procedures</td>
<td>Cefotetan</td>
<td>Clindamycin PLUS Gentamicin</td>
</tr>
<tr>
<td>PEG</td>
<td>Cefazolin OR Cefotetan</td>
<td>Clindamycin +/- Gentamicin</td>
</tr>
<tr>
<td>Appendectomy</td>
<td>Cefotetan</td>
<td>Clindamycin PLUS Gentamicin</td>
</tr>
<tr>
<td>Colorectal procedures, penetrating abdominal trauma</td>
<td>Cefotetan</td>
<td>Clindamycin PLUS Gentamicin</td>
</tr>
<tr>
<td>Inguinal hernia repair</td>
<td>Cefazolin</td>
<td>Clindamycin</td>
</tr>
<tr>
<td>Complicated, emergent or repeat inguinal hernia repair</td>
<td>Cefotetan</td>
<td>Clindamycin +/- Gentamicin</td>
</tr>
<tr>
<td>Mastectomy</td>
<td>Prophylaxis not recommended</td>
<td>Prophylaxis not recommended</td>
</tr>
<tr>
<td>Mastectomy with LND*</td>
<td>Cefazolin</td>
<td>Clindamycin PLUS Gentamicin</td>
</tr>
</tbody>
</table>

*Lymph node dissection

**Gynecologic surgery**

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Prophylaxis Recommendation</th>
<th>PCN allergy/ alternate regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cesarean delivery procedures</td>
<td>Cefazolin*</td>
<td>Clindamycin PLUS Gentamicin</td>
</tr>
<tr>
<td>Hysterectomy (vaginal or abdominal)</td>
<td>Cefazolin OR Cefotetan</td>
<td>Clindamycin PLUS Gentamicin</td>
</tr>
<tr>
<td>Oncology procedures</td>
<td>Cefotetan</td>
<td>Clindamycin PLUS Gentamicin</td>
</tr>
<tr>
<td>Repair of cystocele or rectocele</td>
<td>Cefazolin</td>
<td>Clindamycin</td>
</tr>
</tbody>
</table>

*For non-elective C-section, also give azithromycin 500mg IV single dose (NEJM 2016; 375:123)
### Head and Neck surgery

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Prophylaxis Recommendation</th>
<th>PCN allergy/ alternate regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parotidectomy, thyroidectomy, tonsillectomy</td>
<td>Prophylaxis not recommended</td>
<td>Prophylaxis not recommended</td>
</tr>
<tr>
<td>Reconstructive procedure with prosthesis placement</td>
<td>Cefazolin</td>
<td>Clindamycin</td>
</tr>
<tr>
<td>Adenoidectomy, rhinoplasty, tumor-debulking, or mandibular fracture repair</td>
<td>Cefotetan OR Clindamycin</td>
<td>Clindamycin</td>
</tr>
<tr>
<td>Major neck dissection</td>
<td>Cefazolin</td>
<td>Clindamycin</td>
</tr>
</tbody>
</table>

### Neurosurgery

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Prophylaxis Recommendation</th>
<th>PCN allergy/ alternate regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Craniotomy, CSF-shunting procedures, implantation of intrathecal pumps</td>
<td>Cefazolin</td>
<td>Clindamycin</td>
</tr>
<tr>
<td>Laminectomy</td>
<td>Cefazolin</td>
<td>Clindamycin</td>
</tr>
<tr>
<td>Spinal fusion</td>
<td>Cefazolin</td>
<td>Clindamycin OR Vancomycin</td>
</tr>
<tr>
<td>Spinal fusion with MRSA colonization/infection</td>
<td>Cefazolin PLUS vancomycin</td>
<td>Vancomycin</td>
</tr>
<tr>
<td>Transsphenoidal procedures</td>
<td>Ceftriaxone</td>
<td>Moxifloxacin 400mg</td>
</tr>
</tbody>
</table>

### Orthopedic surgery

<table>
<thead>
<tr>
<th>Procedure*</th>
<th>Prophylaxis Recommendation</th>
<th>PCN allergy/ alternate regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clean operations involving hand, knee, or foot, arthroscopy</td>
<td>Prophylaxis not recommended</td>
<td>Prophylaxis not recommended</td>
</tr>
<tr>
<td>Total joint replacement</td>
<td>Cefazolin</td>
<td>Clindamycin</td>
</tr>
<tr>
<td>Total joint replacement with MRSA colonization/infection</td>
<td>Cefazolin PLUS vancomycin</td>
<td>Vancomycin</td>
</tr>
<tr>
<td>Open reduction of fracture/internal fixation</td>
<td>Cefazolin</td>
<td>Clindamycin OR Vancomycin</td>
</tr>
<tr>
<td>Lower limb amputation</td>
<td>Cefotetan</td>
<td>Clindamycin PLUS Gentamicin</td>
</tr>
</tbody>
</table>

*Spinal fusion, laminectomy – see above under Neurosurgical procedures
### Plastic surgery

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Prophylaxis Recommendation</th>
<th>PCN allergy / alternate regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clean with risk factors or clean-contaminated</td>
<td>Cefazolin</td>
<td>Clindamycin</td>
</tr>
<tr>
<td>Tissue expander insertion/implants/all flaps</td>
<td>Cefazolin</td>
<td>Clindamycin</td>
</tr>
<tr>
<td>Rhinoplasty</td>
<td>No prophylaxis OR Cefazolin</td>
<td>No prophylaxis OR Clindamycin</td>
</tr>
</tbody>
</table>

### Transplant surgery

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Prophylaxis Recommendation</th>
<th>PCN allergy / alternate regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal transplant/adult live donor</td>
<td>Cefazolin</td>
<td>Clindamycin</td>
</tr>
<tr>
<td>Liver transplant</td>
<td>Cefotetan</td>
<td>Clindamycin PLUS Ciprofloxacin</td>
</tr>
</tbody>
</table>

### Urologic surgery/procedures

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Prophylaxis Recommendation</th>
<th>PCN allergy / alternate regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transrectal prostate biopsy</td>
<td>Ciprofloxacin *</td>
<td>Ciprofloxacin OR Gentamicin</td>
</tr>
<tr>
<td>Transurethral surgery (ie TURP, TURBT, ureteroscopy, cystourethoscopy)</td>
<td>Cefazolin</td>
<td>Gentamicin</td>
</tr>
<tr>
<td>Lithotripsy</td>
<td>Cefazolin</td>
<td>Gentamicin</td>
</tr>
<tr>
<td>Nephrectomy or radical prostatectomy</td>
<td>Cefazolin</td>
<td>Clindamycin</td>
</tr>
<tr>
<td>Radical cystectomy, ileal conduit, cystoprostatectomy, or anterior exenteration</td>
<td>Cefotetan</td>
<td>Clindamycin PLUS Gentamicin</td>
</tr>
<tr>
<td>Penile or other prostheses</td>
<td>(Cefazolin OR Vancomycin) PLUS Gentamicin</td>
<td>(Clindamycin OR Vancomycin) PLUS Gentamicin</td>
</tr>
</tbody>
</table>

*Oral Ciprofloxacin 500mg PO Q12H prior to biopsy and repeat 12 hours after first dose can be used. Otherwise, post-procedure antibiotic courses are not recommended. If the patient is at high risk for colonization with fluoroquinolone resistant or multi-drug resistant organisms contact Infectious Diseases.

### Vascular surgery

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Prophylaxis Recommendation</th>
<th>PCN allergy / alternate regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carotid and brachiocephalic procedures without prosthetic grafts</td>
<td>Prophylaxis not recommended</td>
<td>Prophylaxis not recommended</td>
</tr>
<tr>
<td>Upper extremity procedures with prosthetic grafts and lower extremity procedures</td>
<td>Cefazolin</td>
<td>Clindamycin OR Vancomycin</td>
</tr>
<tr>
<td>Abdominal aorta procedure or groin incision</td>
<td>Cefotetan</td>
<td>Vancomycin PLUS Gentamicin</td>
</tr>
</tbody>
</table>
## Interventional Radiology procedures

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Prophylaxis Recommendation</th>
<th>PCN allergy/ alternate regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biliary/GI; chemo embolization/percutaneous liver ablation (hx of biliary surgery), cecostomy</td>
<td>Cefotetan</td>
<td>Clindamycin PLUS Gentamicin</td>
</tr>
<tr>
<td>Chemo embolization; fibroid/uterine artery embolization; percutaneous liver/renal/lung ablation; vascular malformation ablation</td>
<td>Prophylaxis not recommended</td>
<td>Prophylaxis not recommended</td>
</tr>
<tr>
<td>Lymphangiogram/embolization</td>
<td>Cefazolin</td>
<td>Clindamycin</td>
</tr>
<tr>
<td>Placement of tunneled catheters</td>
<td>Prophylaxis not recommended</td>
<td>Prophylaxis not recommended</td>
</tr>
<tr>
<td>Placement of implantable access device (ie Mediport)</td>
<td>Cefazolin</td>
<td>Clindamycin</td>
</tr>
</tbody>
</table>

### REFERENCES

STAPHYLOCOCCUS AUREUS BACTEREMIA (SAB)

DEFINITIONS AND RISK FACTORS

The following abbreviations will be used:
Methicillin-Susceptible Staphylococcus aureus (MSSA)
Methicillin-Resistant Staphylococcus aureus (MRSA)
Blood culture (BCx)

Uncomplicated SAB: must meet **ALL** of the following
- Exclusion of endocarditis
- No evidence of metastatic infection
- No implanted prostheses
- Negative follow-up blood cultures obtained 48-72 hours after initial set
- Resolution of fever within 72 h of initiating effective therapy
- Not immunosuppressed or neutropenic
- Removal of any indwelling catheter or prosthetic material

Complicated SAB:
- Those who do not meet all criteria for uncomplicated SAB

DIAGNOSTIC CONSIDERATIONS

- *Staphylococcus aureus* should **never** be treated as a BCx sample contaminant
- All patients with SAB should be evaluated for a potential source of infection
- At WRNMMC, a positive BCx will be processed with the FilmArray® Blood Culture Identification Panel (BCID)
  - Within approximately an hour, SAB should be further characterized as MSSA or MRSA
  - Therapy should be tailored as soon as possible in the setting of monomicrobial bacteremia
  - **MSSA treatment with vancomycin is associated with increased mortality risk compared to beta-lactam**
- Baseline EKG should be obtained for patients with high grade SAB, a new block is concerning for ring abscess
- Echocardiography is recommended for **ALL** patients with SAB
  - TTE should be performed first, if negative TEE should be pursued unless contraindicated
  - It may be reasonable to forgo TEE in circumstances where all of the following conditions have been met:
    - Nosocomial acquisition of bacteremia
    - Rapid clearance of BCx (sterile follow-up BCx w/in 4 days of the initial positive BCx)
    - No permanent intracardiac device
    - No hemodialysis dependence
    - No clinical signs of endocarditis or secondary foci of infection/metastatic seeding
    - Focus of infection removed promptly (if present)
    - Defervescence within 72 hours of initial positive BCx

ANTIMICROBIAL THERAPY AND MANAGEMENT – IMPORTANT CONCEPTS

- **Infectious Diseases (ID) consultation should be obtained for all SAB cases**
  - Involvement of ID has been associated with improved adherence to standards of care, better use of diagnostic imaging, increased diagnosis of metastatic disease, longer treatment duration, fewer relapses, lower readmission rates and decreased mortality
  - An alternative to vancomycin should be used in MRSA isolates with a vancomycin MIC > 2 mcg/mL
- SAB should **NOT** be treated with PO therapy
- Repeat BCx should be obtained to document clearance (48-72 hours after initial positive)
- Control the source:
  - Remove infected catheters and prosthetic devices. Retention is associated with prolonged bacteremia, treatment failure, significant ↑ in SAB relapse and death.
  - Evaluate for metastatic infection (endocarditis, osteomyelitis, septic arthritis, abscess, etc)
  - Abscesses should be drained
It is not uncommon for SAB to persist for several days (3-5 days) after the initiation of appropriate antibiotic therapy and defervescence of the patient.

- Metastatic foci and complications become more frequent in bacteremia lasting >3 days.
- Failure to clear the bacteremia should prompt evaluation for metastatic foci of infection.

**Typical duration of antibiotic therapy:**

- Minimum treatment duration is 14 days with length of therapy determined by type of SAB.
  
  - **Uncomplicated SAB:** 14 days from negative BCx
  
  - **Complicated SAB:** specific duration dependent on complications (prolonged bacteremia vs. endocarditis vs. osteomyelitis vs. retained prosthesis, etc.)

**THERAPY**

**Empiric SAB therapy: Vancomycin** loading dose followed by maintenance dose (see page 53 for dosing)

**MRSA**

**First-line regimen:**

*Vancomycin* loading dose followed by maintenance dose (see page 53 for dosing)

**Alternative:**

*Daptomycin* 6mg/kg IV Q24H (requires ID approval; a higher dose 8-10mg/kg may be recommended in certain cases)

Avoid with concomitant pneumonia

**MSSA**

**First-line regimen:**

*Nafcillin* 2gram IV Q4H OR 12 gram IV continuous infusion after a 2gram IV loading dose

**Alternative:**

*Cefazolin* 2gram IV Q8H

**Severe beta-lactam allergy:** *Vancomycin* loading dose followed by maintenance dose (see page 53 for dosing)

Strongly consider allergy consult to verify reported penicillin allergy (see page 59)

**REFERENCES**


6) Impact of Infectious Disease Consultation on Quality of Care, Mortality, and Length of Stay in Staphylococcus aureus Bacteremia: Results From a Large Multicenter Cohort Study. Clin Infect Dis. 2015 May;60(10):1451-61.


IV TO PO CONVERSION

BACKGROUND

Intravenous (IV) to oral (PO) therapy interchange programs are often used in hospital settings to promote cost-effective utilization of medications. Studies have also shown that appropriate conversion from IV to PO antimicrobial therapy can decrease the length of hospitalization without adversely affecting patient outcome and may also improve patient care by reducing the risk of intravascular catheter infection due to shorter line dwell times and less endoluminal contamination. Additional benefits of IV to PO conversion include greater patient comfort, decreased nursing needs, and easier ambulation.

PATIENT ELIGIBILITY CRITERIA

- Overall clinical improvement
- Tolerating diet, tube feedings, and/or other oral medications via oral route, NG-tube, G-tube, or PEG
- Afebrile for at least 24 hours
- WBC within normal limit or trending towards normal range
- Hemodynamically stable

CONTRAINDICATIONS

- May not be appropriate in certain serious infections:
  - Septicemia, meningitis, endocarditis, endovascular infections, intracranial abscess, osteomyelitis, prosthetic implant/hardware infection, gram positive bacteremia, neutropenia (ANC<1000), necrotizing fasciitis
- Active NPO order
- Gastric suction
- Not tolerating a diet or tube feeds (i.e. nausea, vomiting, severe diarrhea with > 5 liquid stools/day, GI obstruction, dysmotility or ileus, grade III or IV mucositis, swallowing disorder)
- Malabsorption disorder
- Active GI bleed
- Active gut graft-vs-host disease
- Hemodynamic instability
## INTRAVENOUS TO ORAL CONVERSION TABLE

Listed antimicrobials have > 80% bioavailability when given PO

<table>
<thead>
<tr>
<th>IV</th>
<th>PO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azithromycin 250 mg/500 mg IV q24h</td>
<td>Azithromycin 250 mg/500 mg PO q24h</td>
</tr>
<tr>
<td>Ciprofloxacin 200 mg IV q12h</td>
<td>Ciprofloxacin 250 mg PO q12h</td>
</tr>
<tr>
<td>Ciprofloxacin 400 mg IV q12h</td>
<td>Ciprofloxacin 500 mg PO q12h</td>
</tr>
<tr>
<td>Ciprofloxacin 400 mg IV q8h</td>
<td>Ciprofloxacin 750 mg PO q12h</td>
</tr>
<tr>
<td>Clindamycin 600 mg IV q8h</td>
<td>Clindamycin 300 mg PO q6h</td>
</tr>
<tr>
<td>Clindamycin 900 mg IV q8h</td>
<td>Clindamycin 300-450 mg PO q8h</td>
</tr>
<tr>
<td></td>
<td>Clindamycin 450 mg PO q6-8h (MRSA)</td>
</tr>
<tr>
<td>Doxycycline 100 mg IV q12h</td>
<td>Doxycycline 100 mg PO q12h</td>
</tr>
<tr>
<td>Fluconazole 100mg /200mg/400mg IV q24h</td>
<td>Fluconazole 100 mg /200 mg/400 mg PO q24h</td>
</tr>
<tr>
<td>Levofoxacin 250 mg IV q24h</td>
<td>Levofoxacin 250 mg PO q24h</td>
</tr>
<tr>
<td>Levofoxacin 500 mg IV q24h</td>
<td>Levofoxacin 500 mg PO q24h</td>
</tr>
<tr>
<td>Levofoxacin 750 mg IV q24h</td>
<td>Levofoxacin 750 mg PO q24h</td>
</tr>
<tr>
<td>Linezolid 600 mg IV q12h</td>
<td>Linezolid 600 mg PO q12h</td>
</tr>
<tr>
<td>Metronidazole 250 mg/500mg IV q8h</td>
<td>Metronidazole 250 mg/500 mg PO q8h</td>
</tr>
<tr>
<td>Moxifloxacin 400 mg IV q24h</td>
<td>Moxifloxacin 400 mg PO q24h</td>
</tr>
<tr>
<td>Rifampin 300 mg/600 mg IV q12h/q24h</td>
<td>Rifampin 300 mg/600 mg PO q12h/q24h</td>
</tr>
</tbody>
</table>
| Voriconazole 3-4 mg/kg IV q12h (loading dose 6 mg/kg IV q12h x 1 day) | Initial loading dose (<40kg): 200 mg PO q12h x 1 day
|                              | Initial loading dose (>40kg): 400 mg PO q12h x 1 day
|                              | Voriconazole 3-4 mg/kg PO q12h maintenance doses rounded as follows:
|                              | Voriconazole 100 mg PO q12h (<40kg)
|                              | Voriconazole 200 mg PO q12h (>40kg)
|                              | Voriconazole 300 mg PO q12h (>40kg, severe disease) |
| TMP-SMX IV q6-12h             | TMP-SMX equivalent TMP dose PO q6-12h   |

MRSA; Methicillin resistant *Staphylococcus aureus*

TMP-SMX; trimethoprim-sulfamethoxazole

## REFERENCES

ESTIMATE OF CREATININE CLEARANCE

ADULTS - COCKCROFT-GAULT EQUATION

\[
\text{CrCl (mL/min)} = \frac{(140 – \text{age}) \times \text{IBW} \times 0.85}{72 \times \text{Ser}}
\]

Scr = serum creatinine concentration (mg/dL); if > 65 years old and Scr < 1 mg/dL, round up to 1.0
Age = years
IBW = ideal body weight (kg)
IBW male = 50kg + (2.3 x inches > 5 feet)
IBW female = 45.5kg + (2.3 x inches > 5 feet)

NOTE:
**Actual body weight (ABW) is the patient’s weight as measured on the scale
**If ABW is less than the ideal body weight, use ABW to calculate the CrCl
**For obese patients, use adjusted body weight (AjBW) to calculate CrCl
Obese: BMI >30 or actual body weight > 20% of IBW
AjBW = IBW + 0.4 (ABW – IBW)


PEDIATRIC GFR CALCULATOR

Utilize the pediatric GFR calculator at the following link or QR code:

PROLONGED INFUSION OF PIPERACILLIN-TAZOBACTAM

BACKGROUND

Dose optimization is an essential component for clinical success in the treatment of serious infections as well as preventing the emergence of resistance. Recent literature supports prolonged/extended infusion times of beta-lactam antibiotics as a way to maximize the time-dependent bactericidal activity and improve the probability of target attainment. For beta-lactams, in vitro and animal studies have demonstrated that the best predictor of bacterial killing is the time duration which the free drug concentration exceeds the MIC of the organism ($t_{\text{T>MIC}}$).

DEFINITIONS, ADMINISTRATION, CONTRAINDICATIONS

- Intermittent infusion: infusion lasting 30-60 minutes
- Extended (or prolonged) infusion: infusion lasting 4 hours
- Nurse infuses piperacillin-tazobactam over 4 hours piggy-backed on its own dedicated line, or run parallel with patient’s maintenance IV fluid via Y-site if indicated
- Prepare in a larger volume of 200-250mL. The line must be cleared with a compatible solution after infusion to avoid up to 40% drug loss in the infusion dead-space.
- Reference Lexi-comp or Micromedex for IV compatibility info. Call pharmacy with additional questions.
- Contraindications:
  - Pediatric population (less than 18 years old)
  - Medication scheduling and/or drug compatibility conflicts that cannot be resolved without placing additional lines
  - Patients with other medical intervention (e.g. physical therapy) that cannot be performed adequately during the IV infusion AND administration times cannot be modified to accommodate the intervention
  - Patients who are on a prolonged course of antibiotics (e.g. osteomyelitis), are clinically improving, AND the organism has an MIC ≤4
  - Note: There is no data demonstrating improved outcomes using extended-infusion in intermittent hemodialysis/peritoneal dialysis populations. Use of extended-infusion is optional in these patients.

Clinical Implications of extended infusion dosing: Extended infusion 3.375g IV Q8h (over 4 hours) vs intermittent infusion 3.375g IV Q6H (over 30 min)

Lodise TP et al. Clinical Infectious Diseases 2007; 44:357–63
DOSING RECOMMENDATIONS FOR PIPERACILLIN-TAZOBACTAM

First dose should be a one-time 30 minute bolus to avoid delays in patient care. Maintenance doses can then be extended-infusions started 4 hours later or as below.

In select cases, more intensive piperacillin-tazobactam dosing may be warranted, e.g. sepsis, critically ill patients with severe or deep seated infections, infections with MIC > 16 mg/L, obesity with weight > 120kg or BMI >40, CrCl > 120 ml/min, or enhanced drug clearance such as those with cystic fibrosis: consider doses of 4.5g Q8H (infused over 4 hours) or Q6H. Call pharmacy in these cases.

<table>
<thead>
<tr>
<th>Renal function</th>
<th>CrCl &gt;40 mL/min</th>
<th>CrCl 20-40 mL/min</th>
<th>CrCl &lt;20 mL/min</th>
<th>IHD, PD</th>
<th>CRRT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intermittent Dosing (30-min infusion)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General</td>
<td>3.375 gram IV Q6H</td>
<td>2.25 gram IV Q6H</td>
<td>2.25 gram IV Q8H</td>
<td>2.25 gram IV Q12H</td>
<td>3.375 gram IV Q6H</td>
</tr>
<tr>
<td>Pseudomonas/nosocomial PNA/CF</td>
<td>4.5 gram IV Q6H</td>
<td>3.375 gram IV Q6H</td>
<td>2.25 gram IV Q6H</td>
<td>2.25 gram IV Q8H</td>
<td></td>
</tr>
<tr>
<td><strong>Extended-infusion Dosing (4-hour infusion)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General, Pseudomonas, nosocomial PNA, CF</td>
<td>3.375 gram IV Q8H (4.5 gram IV Q8H in select populations described above)</td>
<td>3.375 gram IV Q12H</td>
<td>3.375 gram IV Q8H</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

IHD= intermittent dialysis, PD = peritoneal dialysis, PNA = pneumonia, CF = cystic fibrosis
CRRT = continuous renal replacement therapy (includes CVVH, CVVHD, CVVHDF

REFERENCES

This protocol was adapted from the Stanford Health Care Extended-Infusion Piperacillin/Tazobactam (Zosyn®) Protocol with permission

For WRNMMC use only, page 53

VANCOMYCIN DOSING AND MONITORING - ADULTS

BACKGROUND – LOADING DOSE

Why use a loading dose:
A single loading dose of 25 mg/kg (based on actual body weight, see page 50) can be used to facilitate rapid attainment of target trough serum vancomycin concentration.

Indications for a loading dose:
Serious infections to include severe sepsis or shock, meningitis, endocarditis, MRSA bacteremia

VANCOMYCIN DOSING CONSIDERATIONS

- The following recommendations are for isolates with a vancomycin minimum inhibitory concentration (MIC) ≤2 mcg/mL
- Consult ID for MRSA isolates with a vancomycin MIC > 2 mcg/mL; an alternative to vancomycin should be used in these cases
- An individual’s age, comorbid conditions, weight fluctuations due to ascites or third spacing, and fluid overload should be considered. Patients may warrant lower dosing in these cases.

- Dosing should be based on actual body weight (ABW) including obese patients (see page 50)
  - Max initial dose = 2,500 mg
  - Standard Rate of Administration: 1,000 mg over 60 minutes (500mg over 30 min)
  - Max peripheral IV concentration: 5 mg/mL, max central line concentration: 10 mg/mL
  - Round doses to nearest 250 mg

LOADING DOSING RECOMMENDATIONS

Consider a lower dose for renal replacement therapy/hemodialysis (20mg/kg)

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Loading Dose (mg)</th>
<th>Infusion Rate (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-39</td>
<td>750</td>
<td>60</td>
</tr>
<tr>
<td>40-49</td>
<td>1,000</td>
<td>60</td>
</tr>
<tr>
<td>50-59</td>
<td>1,250</td>
<td>90</td>
</tr>
<tr>
<td>60-69</td>
<td>1,500</td>
<td>90</td>
</tr>
<tr>
<td>70-85</td>
<td>1,750</td>
<td>120</td>
</tr>
<tr>
<td>86-120</td>
<td>2,000</td>
<td>120</td>
</tr>
<tr>
<td>≥ 120</td>
<td>2,500</td>
<td>120-150</td>
</tr>
</tbody>
</table>
A vancomycin trough should be obtained no earlier than at steady state (30 min prior to the 4th dose). Once the target trough level is achieved, once-weekly trough monitoring is recommended with stable renal function. More frequent monitoring is recommended with changing renal function.

A target trough level of 15-20mcg/mL is recommended for serious infections to include catheter-associated bacteremia, S. aureus bacteremia, pneumonia, CNS infection, deep-seated or sequestered infection (e.g. abscess), endocarditis, osteomyelitis/prosthetic joint infections, febrile neutropenia cases, or sepsis. For skin and soft tissue infections without sepsis or UTI, the target trough is 10-15 mcg/mL.

Minimum serum trough concentrations > 10mcg/mL should be maintained to avoid development of resistance

Caution should be used when exceeding 2,000 mg per dose or > 4,000 mg in a 24 hour period due to concerns for increased nephrotoxicity

Patients with CrCl > 70 may require Q8H dosing based on trough levels

**Adult patients: use standard order set labeled “Vancomycin Adult Initial Dosing Order Set”**

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>CrCl (mL/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Based on ABW</strong></td>
<td>&lt;60</td>
</tr>
<tr>
<td>&lt;40</td>
<td>Consult Pharmacy</td>
</tr>
<tr>
<td>40-60</td>
<td>750mg Q12H</td>
</tr>
<tr>
<td>60-75</td>
<td>1000mg Q12H</td>
</tr>
<tr>
<td>75-90</td>
<td>1250mg Q12H</td>
</tr>
<tr>
<td>90-110</td>
<td>1500mg Q12H</td>
</tr>
<tr>
<td>110-125</td>
<td>1750mg Q12H</td>
</tr>
<tr>
<td>125-140</td>
<td>2000mg Q12H</td>
</tr>
<tr>
<td>&gt; 140</td>
<td>Consult Pharmacy</td>
</tr>
</tbody>
</table>

* For patients with CrCl <30, obtain random vancomycin level with AM labs to allow for dosing adjustments

** For patients with CrCl <15 and not receiving HD, redose when random level is <15-20 mcg/mL
Vancomycin dosing in patients on thrice weekly HD via high-flux membranes

For serious infections, a loading dose of 25mg/kg IV can be considered, otherwise use a loading dose of 20mg/kg

Loading dose should be followed by:
Weight < 70kg: 500mg QHD
Weight ≥ 70kg: 750mg QHD

In patients with ESRD on hemodialysis (HD), **pre-HD levels are preferable**. If a pre-HD is not able to be obtained, a post-HD level may be drawn six hours after the session has ended (to account for redistribution).

Once pre-dialysis level is within target range, a pre-dialysis level can be checked once a week or more frequently at the discretion of the provider. Highly recommend coordination with Nephrology or patient’s dialysis center.

Longer intervals between sessions (e.g. 72H rather than 48H, such as over a weekend) may result in lower pre-dialysis levels. A higher dose (e.g. increased by 250mg) at the last dialysis session prior to the longer interval is warranted.

**Consult with Nephrology regarding peritoneal dialysis or low-flux membrane HD**

<table>
<thead>
<tr>
<th>Level prior to 3rd dialysis session:</th>
<th>Recommended adjustment:</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;15 mcg/mL</td>
<td>Increase dose by 250-500mg</td>
</tr>
<tr>
<td>15-25 mcg/mL</td>
<td>No change</td>
</tr>
<tr>
<td>≥ 26 mcg/mL</td>
<td>Hold vancomycin for one dose, followed by resuming 500mg post HD</td>
</tr>
</tbody>
</table>

REFERENCES


**AMINOGLYCOSIDE DOSING AND MONITORING**

**DOsing Considerations – Gram Negative Infections**

Ideal body weight (IBW) in kg should be used
- IBW male = 50kg + (2.3 x inches > 5 feet)
- IBW female = 45.5kg + (2.3 x inches > 5 feet)

For patients < 20% IBW, use Actual Body Weight (ABW) (i.e. if ABW/IBW<1.2)
For patients ≥ 20% over IBW, use Dosing Body Weight (DBW) (i.e. if ABW/IBW>1.2)
DBW = IBW + 0.4 (ABW – IBW)

Use the Cockcroft-Gault equation to estimate creatinine clearance (CrCl): see page 50
If patient’s renal function is declining, this equation may overestimate CrCl

**Patient-specific dosing**, previously referred to as “conventional or traditional dosing,” typically utilizes smaller doses with more frequent administration

**Extended-interval dosing**, also sometimes referred to as “once-daily” administration, utilizes higher dose and less frequent AG administration. AGs are concentration dependent antibiotics, meaning that as AG concentration increases, the rate and extent of bacterial killing increases. Optimum bactericidal activity for the AGs is achieved when the exposure concentration is approximately 8 to 10 times the MIC.

**Exclusion Criteria for High-Dose Extended Interval Therapy**:  
- Renal insufficiency (CrCl <30 mL/min or rapidly declining renal function)  
- Pregnancy  
- Synergy for gram-positive infections  
- Ascites  
- Burns (>20%)  
- Endocarditis

* If high-dose extended interval therapy is used in a cystic fibrosis patient; Pulmonology, Infectious Diseases, or a clinical PharmD experienced in treating this patient population should be consulted.

**Below Dosing is for Serious Gram-Negative Sepsis/Infections** (not applicable for synergistic dosing or for urinary tract infections which use lower doses)

**Empiric Initial Dosing – Gentamicin and Tobramycin**

<table>
<thead>
<tr>
<th>CrCl (mL/min)</th>
<th>Loading Dose</th>
<th>Extended-interval **</th>
<th>Patient-specific/conventional</th>
</tr>
</thead>
<tbody>
<tr>
<td>N/A</td>
<td>2-2.5mg/kg x 1</td>
<td>1.7mg/kg Q8H</td>
<td></td>
</tr>
<tr>
<td>&gt;60</td>
<td>5-7mg/kg IV Q24H</td>
<td>1.7mg/kg Q12H</td>
<td></td>
</tr>
<tr>
<td>40-59</td>
<td>5-7mg/kg IV Q36H</td>
<td>1.7mg/kg Q24H</td>
<td></td>
</tr>
<tr>
<td>30-39</td>
<td>5-7mg/kg IV Q48H</td>
<td>1.7mg/kg Q48H</td>
<td></td>
</tr>
<tr>
<td>20-29</td>
<td>5-7mg/kg IV Q48H</td>
<td>1.7mg/kg Q48H</td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>Not recommended</td>
<td>2mg/kg load, then dose by level</td>
<td></td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>Not recommended</td>
<td>Call pharmacy</td>
<td></td>
</tr>
<tr>
<td>CRRT</td>
<td>Not recommended</td>
<td>Call pharmacy</td>
<td></td>
</tr>
</tbody>
</table>

**See Hartford and/or Urban Craig nomogram for monitoring of once-daily dosing regimens**
Use 7 mg/kg for gram-negative sepsis, other serious gram-negative infections, critically ill patients or suspicion for higher MICs. Round dose to nearest 10mg for gentamicin/tobramycin.
EMPIRIC INITIAL DOSING – AMIKACIN

<table>
<thead>
<tr>
<th>CrCl (mL/min)</th>
<th>Extended-interval **</th>
<th>Patient-specific/conventional</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loading Dose</td>
<td>N/A</td>
<td>7.5mg/kg x 1</td>
</tr>
<tr>
<td>&gt;60</td>
<td>15-20mg/kg IV Q24H</td>
<td>5-7.5mg/kg Q8H</td>
</tr>
<tr>
<td>40-59</td>
<td>15mg/kg IV Q36H</td>
<td>5-7.5mg/kg Q12H</td>
</tr>
<tr>
<td>30-39</td>
<td>15mg/kg IV Q48H</td>
<td>5-7.5mg/kg Q24H</td>
</tr>
<tr>
<td>20-29</td>
<td>15mg/kg IV Q48H</td>
<td>5-7.5mg/kg Q48H</td>
</tr>
<tr>
<td>&lt;20</td>
<td>Not recommended</td>
<td>5mg/kg load, then dose by level</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>Not recommended</td>
<td>Call pharmacy</td>
</tr>
<tr>
<td>CRRT</td>
<td>Not recommended</td>
<td>Call pharmacy</td>
</tr>
</tbody>
</table>

**See Hartford nomogram below for monitoring of once-daily dosing regimens**

**Round dose to nearest 50mg for amikacin. Suggested max dose of amikacin is 1500mg.**

MONITORING – HARTFORD NOMOGRAM FOR EXTENDED-INTERVAL DOSING

**Initial level testing:** obtain a random level at **10 hours** (acceptable range 6-14 hours) **after the first dose**
- Gentamicin/tobramycin 7 mg/kg dosing: plot the random level on the Hartford Nomogram below to determine the recommended dosing interval
- Amikacin 15 mg/kg dosing: divide the serum random level by 2 then plot on the Hartford Nomogram
- Amikacin 20 mg/kg dosing: divide the serum random level by 3 then plot on the Hartford Nomogram
For WRNMMC use only, page 58

MONITORING – URBAN CRAIG NOMOGRAM FOR EXTENDED-INTERVAL DOSING

Applicable for gentamicin/tobramycin 5 mg/kg/dose

**Initial level testing:** single level drawn 8-12 hours after the first dose, plot on below nomogram

![Nomogram](image)

**PEAK AND TROUGH LEVELS**

**Extended-interval dosing:**
- Maintenance trough levels should be monitored at least weekly unless there are acute changes in renal function. A trough is obtained 30-60 minutes prior to a dose.
  - Routine monitoring of peaks is not required unless the patient is having fluctuations in renal function or is failing extended interval dosing
- Goal trough: gentamicin/tobramycin: < 1mcg/mL, amikacin < 4mcg/mL
- Goal peak: gentamicin/tobramycin: 16-20mcg/mL, amikacin 40-60mcg/mL

**Patient-specific (conventional dosing):**
- Peak is obtained 30 minutes after a 30-minute infusion of the 3rd or 4th dose
- Trough is measured 30-60 minutes before the 3rd or 4th dose
- Maintenance peak/trough levels should be monitored at least once weekly
- Goal trough: gentamicin/tobramycin <1-2mcg/mL, amikacin < 10mcg/mL
- Goal peak: gentamicin/tobramycin: 8-10mcg/mL (goal may be higher in MDR organisms), amikacin 20-35 mcg/mL (may be higher in MDR organisms)

Aminoglycosides (AG) can cause **nephrotoxicity** and **ototoxicity**. Renal function should be closely monitored. If continued on AG therapy screening for ototoxicity via audiology should be performed on a routine basis.

**REFERENCES**

BETA-LACTAM ALLERGY ASSESSMENT

BACKGROUND

- 8-10% of the general population and up to 20% of inpatients report a beta-lactam allergy
- 90% have negative skin testing and nearly 99% can be cleared of their reported allergy
- Even with prior IgE-mediated reactions, 80% will lose their specific sensitization after 10 years
- Beta-lactam allergy significantly impacts patient care with antimicrobial regimens deviating from first-line therapy in up to 38% of patients, lengthier hospitalizations, and increased incidence of MRSA, VRE, and C. difficile

FORMS OF REACTIONS

- **Anticipated side effects.** Side effects known to be associated with use of beta-lactam antibiotics (e.g. nausea, diarrhea).
- **Immediate (Type I or IgE-mediated) reactions.** Typically occur earlier in a treatment course and often shortly after a dose is administered, but not longer than a few hours afterwards. Symptoms may include mild reactions such as urticaria, to more significant or life-threatening reactions with bronchoconstriction, hypotension, and/or laryngeal edema. This is the form best assessed by skin testing and oral challenge.
- **Delayed (Type IV or T cell mediated) reactions.** These include the classic amoxicillin rash noted in up to 10% of children (but with only a 4% recurrence rate in one large study) after 72 hours of treatment, but classically on day 7 or 8 and consisting of a maculopapular or macular rash that often lasts several days. There is NO mucosal involvement.
- **Other immune mediated reactions.** Serum sickness, interstitial nephritis, thrombocytopenia, hepatitis, drug rash with eosinophilia and systemic symptoms (DRESS). Not amenable to testing, challenge, or desensitization.
- **Stevens-Johnson Syndrome (SJS).** Exfoliative dermatitis that is accompanied by mucosal involvement. Contraindication for testing, challenge, or desensitization.

EVALUATION CONSIDERATIONS

- **Brief, focused history:**
  - At what age did the reaction occur?
  - How long after starting the antibiotic course did symptoms occur?
  - What symptoms were present (cutaneous, respiratory, cardiovascular) and did the patient require hospitalization or emergency procedures such as intubation?
  - If a rash occurred, what did the rash look like? Was it pruritic? How long after stopping the antibiotic did the rash persist?
  - Was there any mucosal involvement?
  - Since the reaction, has a beta-lactam been prescribed and if so, what happened?

- **IF...**
  - The patient had anticipated side effects such as isolated diarrhea following a course of a beta-lactam, this is inconsistent with an IgE-mediated reaction and beta-lactam antibiotics may be prescribed.
  - The patient has tolerated a beta-lactam since the initial reaction or has been tested and passed a beta-lactam challenge, the patient is at no greater risk than the general population for an IgE-mediated reaction, beta-lactam antibiotics may be prescribed.
  - The patient had cutaneous only symptoms that were delayed in onset, had no associated mucosal involvement, and took several days to clear, contact Allergy/Immunology (see consult flow chart below). This is most consistent with a delayed-type reaction.
  - The patient had mucosal involvement, history suggestive of or diagnosis of DRESS, SJS, interstitial nephritis, or serum sickness, testing, challenge, and desensitization are contraindicated and an alternate agent should be pursued.
  - The patient had symptoms suggestive of a possible IgE-mediated or immediate type reaction, consult Allergy/Immunology (see consult flow chart below).
**IMPORTANT CONCEPTS**

- **Cephalosporins:**
  - True cross reactivity amongst the core penams (i.e. amoxicillin, penicillin, etc) and cephalosporins is 2-3%, approximately the risk of the general population for a reaction to an antibiotic agent.
  - Consider an Allergy/Immunology consult (see consult flow chart below).

- **Other Notes:**
  - Meropenem and ertapenem are suspected to have low cross-reactivity with the core penams (penicillin, amoxicillin, etc). An Allergy/Immunology consult can be obtained, but providers can also consider a challenge dose of 10% of the total treatment dose followed by 30 minutes of observation, then administration of the remaining 90% of the dose and additional 60 minutes of observation. Rescue medications such as epinephrine should be available.
  - Aztreonam cross-reactivity is limited to ceftazadime.

---

**Allergy/Immunology consult pager:** 301-633-0528 (2nd call: 106-3366)

**Allergy/Immunology clinic:** 301-295-4511/4510

**Essentris Order:** in order menu “Allergy Penicillin Consult”
## Antibiogram 2017 - WRNMNC
### Outpatient Overall

| Top 15 Gram Negative Organisms | # patients | Amikacin | Aztreonam/ceftazidime | Ampicillin/sulbactam | Aztreonam | Cefazolin | Cefepime | Cefotaxime | Ceftiraxone | Ciprofloxacin | Ertapenem | Gentamicin | Imipenem | Levofloxacin | Meropenem | Nalidixic acid | Piperacillin/Tazobactam | Tobramycin | Trimethoprim/Sulfamethoxazole |
|--------------------------------|------------|----------|------------------------|----------------------|------------|-----------|----------|-----------|------------|--------------|------------|-----------|----------|-----------|----------|-------------|-----------|----------------|-------------------------|-----------|-----------------------------|
| Escherichia coli               | 1129       | 100%     | 85%                    | 59%                  | 75%        | 95%       | 91%      | 86%       | 94%        | 94%          | 84%        | 100%      | 94%      | 100%       | 63%       | 100%         | 99%          | 96%           | 82%                  | 78%         |
| Klebsiella pneumoniae          | 239        | 100%     | 92%                    | 0%                   | 89%        | 97%       | 76%      | 94%       | 95%        | 96%          | 64%        | 99%       | 97%      | 95%        | 93%       | 100%         | 100%         | 43%           | 64%                  | 96%         |
| Pseudomonas aeruginosa         | 122        | 100%     | 94%                    | 0%                   | 83%        | 99%       | 98%      | 6%        | 85%        | 84%          | 80%        | 89%       | 0%       | 93%        | 91%       | 0%           | 0%          | 93%           | 91%                  | 0%          |
| Proteus mirabilis              | 111        | 100%     | 94%                    | 0%                   | 83%        | 100%      | 99%      | 59%       | 97%        | 97%          | 84%        | 98%       | 94%      | 0%         | 98%        | 93%          | 85%          | 88%           | 0%                    |
| Klebsiella oxytoca             | 28         | 100%     | 96%                    | 0%                   | 83%        | 100%      | 68%      | 22%       | 100%       | 100%         | 66%        | 83%       | 100%     | 80%        | 88%        | 88%          | 88%          | 88%           | 88%                  |
| Citrobacter koseri             | 30         | 100%     | 100%                   | 0%                   | 100%       | 100%      | 100%     | 100%      | 100%       | 100%         | 100%       | 100%      | 100%     | 100%       | 100%      | 100%         | 100%         | 100%          | 100%                 |
| Enterobacter aerogenes         | 42         | 100%     | 100%                   | 0%                   | 100%       | 100%      | 100%     | 100%      | 100%       | 100%         | 100%       | 100%      | 100%     | 100%       | 100%      | 100%         | 100%         | 100%          | 100%                 |
| Enterobacter cloacae           | 41         | 100%     | 100%                   | 0%                   | 100%       | 100%      | 100%     | 100%      | 100%       | 100%         | 100%       | 100%      | 100%     | 100%       | 100%      | 100%         | 100%         | 100%          | 100%                 |
| Serratia marcescens            | 22         | 100%     | 100%                   | 0%                   | 100%       | 100%      | 100%     | 100%      | 100%       | 100%         | 100%       | 100%      | 100%     | 100%       | 100%      | 100%         | 100%         | 100%          | 100%                 |
| Citrobacter freundii           | 24         | 100%     | 100%                   | 0%                   | 100%       | 100%      | 100%     | 100%      | 100%       | 100%         | 100%       | 100%      | 100%     | 100%       | 100%      | 100%         | 100%         | 100%          | 100%                 |

Top numbers indicate % susceptible
Bottom numbers indicate number of isolates tested for antibiotic analysis for each organism

Data source: NMCPHC HL7 formatted CHCS Microbiology database
Prepared by the Epidata Center Department Navy and Marine Corps Public Health

Data generated with fewer than 30 isolates results in less statistical significance for estimates of % susceptibility. Statistically significant decrease relative to 2016 (p < 0.05). Chi square
<table>
<thead>
<tr>
<th>Gram Positive Organisms of Interest</th>
<th># patients</th>
<th>Ampicillin</th>
<th>Ceftriaxone</th>
<th>Ceftriaxone meningitis</th>
<th>Clindamycin</th>
<th>Doxycycline</th>
<th>Erythromycin</th>
<th>Linezolid</th>
<th>Oxacillin</th>
<th>Penicillin G</th>
<th>Penicillin meningitis</th>
<th>Tetracycline</th>
<th>Trimethoprim/sulfamethoxazole</th>
<th>Vancomycin</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>305</td>
<td>68%</td>
<td>98%</td>
<td>54%</td>
<td>100%</td>
<td>80%</td>
<td>1%</td>
<td>93%</td>
<td>96%</td>
<td>100%</td>
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<td>96%</td>
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<td>MRSA</td>
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<td>52%</td>
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<td>15%</td>
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<td>0%</td>
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<td>93%</td>
<td>97%</td>
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<tr>
<td>Coagulase negative staphylococci</td>
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<td><em>Enterococcus faecium</em></td>
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<td>Vancomycin Resistant Enterococcus</td>
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<td>Streptococcus pneumoniae</td>
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<td>100%</td>
<td>10%</td>
<td>10%</td>
<td>8</td>
<td>10%</td>
<td></td>
</tr>
</tbody>
</table>

^ MRSA: methicillin-resistant *Staphylococcus aureus* (oxacillin resistant)
^ MSSA: methicillin-susceptible *Staphylococcus aureus* (oxacillin susceptible)
Top numbers indicate % susceptible.
Bottom numbers indicate number of isolates tested for antibiotic.
Data source: NMCPHC HL7 formatted CHCS Microbiology database.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center and MAJ Jonathan D’Ambrozzo.
### Inpatient Overall

#### Top Gram Negative Organisms

<table>
<thead>
<tr>
<th>Organism</th>
<th># patients</th>
<th>Amikacin</th>
<th>Ampicillin</th>
<th>Ampicillin/Clavulanate</th>
<th>Aztreonam</th>
<th>Cefazolin</th>
<th>Cefepine</th>
<th>Cefotaxime</th>
<th>Ceftriaxone</th>
<th>Ciprofloxacin</th>
<th>Erup tupen</th>
<th>Gentamicin</th>
<th>Imipenem</th>
<th>Levofoxacin</th>
<th>Meropenem</th>
<th>Piperacillin/ Tazobactam</th>
<th>Tetracycline</th>
<th>Trimethoprim/ Sulfaemethoxazole</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Escherichia coli</strong></td>
<td>186</td>
<td>100%</td>
<td>101%</td>
<td>101%</td>
<td>101%</td>
<td>101%</td>
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<td>101%</td>
<td>101%</td>
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</tr>
<tr>
<td><strong>Klebsiella pneumoniae</strong></td>
<td>100</td>
<td>98%</td>
<td>90%</td>
<td>R</td>
<td>101%</td>
<td>101%</td>
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<td>101%</td>
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</tr>
<tr>
<td><strong>Pseudomonas aeruginosa</strong></td>
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<td>R</td>
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<td><strong>Proteus mirabilis</strong></td>
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<td>88%</td>
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<td>100%</td>
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</tr>
<tr>
<td><strong>Stenotrophomonas maltophilia</strong></td>
<td>10</td>
<td>100%</td>
<td>R</td>
<td>R</td>
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</tr>
<tr>
<td><strong>Serratia marcescens</strong></td>
<td>13</td>
<td>100%</td>
<td>R</td>
<td>R</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
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<td>100%</td>
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<td>100%</td>
</tr>
<tr>
<td><strong>Klebsiella oxytoca</strong></td>
<td>22</td>
<td>100%</td>
<td>R</td>
<td>R</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
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</tr>
<tr>
<td><strong>Morganella morganii</strong></td>
<td>6</td>
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<td>R</td>
<td>R</td>
<td>100%</td>
<td>100%</td>
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</tr>
<tr>
<td><strong>Citrobacter freundii</strong></td>
<td>7</td>
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<td>R</td>
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<td>100%</td>
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</tr>
<tr>
<td><strong>Citrobacter koseri</strong></td>
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<td>100%</td>
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</tr>
</tbody>
</table>

Top numbers indicate % susceptible.
Bottom numbers indicate number of isolates tested for antibiotic.
Data source: NMCPHMC HL7 formatted CHCS Microbiology database.
Data generated with fewer than 30 isolates results in less statistical significance for estimates of % susceptibility. Statistically significant decrease relative to 2016 (p < 0.05), Chi square.
## Antibiogram 2017 - WRNMMC
### Inpatient Overall

<table>
<thead>
<tr>
<th>Gram Positive Organisms of Interest</th>
<th># patients</th>
<th>Ampicillin</th>
<th>Ceftriaxone</th>
<th>Ceftriaxone meningitis</th>
<th>Chloramphenicol</th>
<th>Doxycycline</th>
<th>Erythromycin</th>
<th>Linezolid</th>
<th>Oxacillin</th>
<th>Penicillin G</th>
<th>Penicillin meningitis</th>
<th>Tetracycline</th>
<th>Trimethoprim/sulfamethoxazole</th>
<th>Vancomycin</th>
</tr>
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<tbody>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>141</td>
<td>81%</td>
<td>96%</td>
<td>45%</td>
<td>100%</td>
<td>68%</td>
<td>12%</td>
<td>97%</td>
<td>94%</td>
<td>100%</td>
<td>158</td>
<td>158</td>
<td>158</td>
<td>158</td>
</tr>
<tr>
<td>MRSA ^</td>
<td>46</td>
<td>43%</td>
<td>99%</td>
<td>2%</td>
<td>100%</td>
<td>0%</td>
<td>91%</td>
<td>93%</td>
<td>100%</td>
<td>100%</td>
<td>58</td>
<td>58</td>
<td>58</td>
<td>58</td>
</tr>
<tr>
<td>MSSA ~</td>
<td>93</td>
<td>99%</td>
<td>97%</td>
<td>79%</td>
<td>100%</td>
<td>20%</td>
<td>92%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>96</td>
<td>96</td>
<td>96</td>
<td>96</td>
</tr>
<tr>
<td>Coagulase negative staphylococci</td>
<td>3</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>33%</td>
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<td>50%</td>
<td>100%</td>
<td>100%</td>
<td>96</td>
<td>96</td>
<td>96</td>
<td>96</td>
</tr>
<tr>
<td><em>Enterococcus faecalis</em></td>
<td>74</td>
<td>99%</td>
<td>95%</td>
<td>45%</td>
<td>18%</td>
<td>100%</td>
<td>24%</td>
<td>100%</td>
<td>79%</td>
<td>25%</td>
<td>96</td>
<td>96</td>
<td>79</td>
<td>79</td>
</tr>
<tr>
<td><em>Enterococcus faecium</em></td>
<td>20</td>
<td>10%</td>
<td>90%</td>
<td>10%</td>
<td>95%</td>
<td>20%</td>
<td>20%</td>
<td>20%</td>
<td>20%</td>
<td>20%</td>
<td>10%</td>
<td>10%</td>
<td>10%</td>
<td>10%</td>
</tr>
<tr>
<td>Vancomycin Resistant Enterococcus</td>
<td>16</td>
<td>0%</td>
<td>15%</td>
<td>0%</td>
<td>15%</td>
<td>0%</td>
<td>15%</td>
<td>0%</td>
<td>15%</td>
<td>0%</td>
<td>15%</td>
<td>15%</td>
<td>15%</td>
<td>15%</td>
</tr>
</tbody>
</table>

* MRSA: methicillin-resistant *Staphylococcus aureus* (oxacillin resistant)
~ MSSA: methicillin-susceptible *Staphylococcus aureus* (oxacillin susceptible)
Top numbers: indicate % susceptible.
Bottom numbers: indicate number of isolates tested for antibiotic.
Data source: NMCFHC HL7 formatted CHCS Microbiology database.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center on 01-29-18 and MAJ D’Ambrozzo 03-10-18.

# patients: Patients included in the analysis for each organism.
Data generated with fewer than 30 isolates results in less statistical significance for estimates of % susceptibility. Statistically significant decreases relative to 2015 ($p < 0.05$), Chi square.