MICHIGAN MEDICINE
UNIVERSITY OF MICHIGAN

GUIDELINES FOR TREATMENT OF BONE AND JOINT INFECTIONS IN ADULTS

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Revision History:
02/2021: Added fungi, mycobacteria, and Actinomyces comment
03/2021: Updated vancomycin dosing & hyperlinks
09/2021: Updated vancomycin infusion reaction terminology

Hematogenous Osteomyelitis			
Clinical Setting	**Empiric Therapy**	**Duration**	**Comments**
Usually associated with: • Patients under age 17 years or over 50 years (recommendations intended for adults only) • IV drug use • Other risk for bacteremia e.g., central line, dialysis, sickle cell disease, urethral catheterization, UTI Bacterial Etiology: • *S. aureus* • 30% Gram negative bacilli (consider if fresh water exposure, recent broad spectrum antibiotics in the prior 90 days, recent >2 days hospitalized in prior 90 days, or hemodynamic instability) • *Salmonella* in sickle cell disease • *Serratia* and *Pseudomonas spp*. in IVDU	Consider holding antibiotics until deep tissue cultures can be obtained in hemodynamically stable patients Preferred: **Vancomycin*** IV (see nomogram) If known MSSA colonization or infection: **Cefazolin*** 2 g IV q8h Alternative for vancomycin allergy (not vancomycin infusion reaction**): **Daptomycin*** 6 mg/kg IV daily If Sickle Cell disease: **Vancomycin*** IV (see nomogram) + **Ceftriaxone** 2 g IV daily If IVDU or other Gram negative risk (see bacterial etiology): **Vancomycin*** IV (see nomogram) + **Piperacillin-tazobactam** 4.5 g IV q6h Alternative for patient with mild penicillin allergy: **Vancomycin*** IV (see nomogram) + **Cefepime** 2 g IV q8h Alternative for patients with life-threatening penicillin allergy: **Vancomycin*** IV (see nomogram) **+ Aztreonam** 2 g IV q8h	4-6 weeks	Approximately 45% of *S. aureus* at UMHS are MRSA, so initial treatment to cover MRSA is warranted. De-escalate to a beta-lactam if methicillin-susceptible *S. aureus* (MSSA) is identified. Infectious Diseases Consultation recommended. **Daptomycin** requires prior approval. Baseline CK followed by weekly CK should be measured in patients placed on **daptomycin** due to increased risk of rhabdomyolysis. Increased dose of **daptomycin** may be indicated with documented MRSA bacteremia. Infections due to fungi, mycobacteria, or *Actinomyces* require longer durations of therapy – consult appropriate national guidelines for guidance.

* Adjust dose based on renal function; vancomycin dose may require adjustment for select organisms or patients
Target vancomycin AUC 400-600 mcg*hr/mL

Vertebral Osteomyelitis			
Clinical Setting	**Empiric Therapy**	**Duration**	**Comments**
Usually hematogenous source Persons at risk: • Age >60 years • IVDU • Urinary tract infections Bacterial Etiology: • *S. aureus* • Occ. Coagulase negative *staphylococcus* • Enteric Gram negatives • *Pseudomonas* in IVDU or water exposure	Consider holding antibiotics until deep tissue cultures can be obtained in hemodynamically stable patients Preferred: **Vancomycin*** IV (see nomogram) + **Ceftriaxone** 2 g IV q12h If known MSSA colonization or infection: **Oxacillin** 2 g IV q4h Alternative for suspected or documented Pseudomonal infection (see bacterial etiology): **Vancomycin*** IV (see nomogram) + **Cefepime*** 2 g IV q8h Alternative for severe penicillin allergy: **Vancomycin*** IV (see nomogram) **+ Aztreonam*** 2 g IV q6h Alternative for vancomycin allergy or intolerance (not vancomycin infusion reaction**): **Linezolid** 600 mg PO/IV q12h + other antibiotic as indicated above	Minimum 6 weeks	Evaluation for epidural infection is critical. See full Vertebral Osteomyelitis FGP Guideline Infectious Diseases consultation strongly recommended. Step down therapy to oral antibiotic usually indicated after 6 weeks of therapy. Approximately 45% of *S. aureus* at UMHS are MRSA, so initial treatment to cover MRSA is warranted. De-escalate to a beta-lactam if *methicillin-susceptible S. aureus (MSSA)* is identified. **Cefazolin** may replace **oxacillin**, if no epidural extension of infection is present. **Linezolid** requires prior approval. Baseline CBCP and weekly CBCP are recommended with **linezolid** therapy due to risk of cytopenia, especially thrombocytopenia; alternative therapy should be considered in patients with thrombocytopenia. **Linezolid** should be used with caution in patients on medications with serotonergic activity, e.g., SSRI and MAOI. See SSRI & Linezolid Education. **Daptomycin** may replace **linezolid** if no epidural extension of infection is present. Empiric dosing takes into account epidural abscess with possible CNS extension. Infections due to fungi, mycobacteria, or *Actinomyces* require longer durations of therapy – consult appropriate national guidelines for guidance.

* Adjust dose based on renal function; vancomycin dose may require adjustment for select organisms or patients
Target vancomycin AUC 400-600 mcg*hr/mL

Septic Arthritis			
Clinical Setting	**Empiric Therapy**	**Duration**	**Comments**
Usually associated with: • Age >80 years • Diabetes mellitus • Rheumatoid arthritis • Prosthetic joint • Recent joint surgery • Skin infection • IV drug abuse • Alcoholism • Prior intra-articular steroid injection Bacterial Etiology: • *S. aureus* • Streptococcal species, including *S. pneumoniae* • Gram negative bacilli associated with trauma, intravenous drug users, older adults, and in association with underlying immunosuppression. • *N. gonorrhea* in oligoarthritis, (particularly young, sexually active), associated tenosynovitis, vesicular pustules, late complement deficiency, negative synovial fluid culture and Gram stain	Consider holding antibiotics until deep tissue cultures can be obtained in hemodynamically stable patients Preferred: **Vancomycin*** IV (see nomogram) If known MSSA colonization or infection: **Cefazolin*** 2 g IV q8h Alternative for vancomycin allergy (not vancomycin infusion reaction**): **Linezolid** 600 mg PO/IV q12h OR **Daptomycin*** 6 mg/kg IV daily If risk for gonorrhea: **Vancomycin*** IV (see nomogram) + **Ceftriaxone** 1 g IV daily + **Azithromycin** 1 g PO in a single dose If risk for Gram negative bacilli (see bacterial etiology): **Vancomycin*** IV (see nomogram) **+ Piperacillin-tazobactam*** 4.5 g IV q6h	2-4 weeks For *S. aureus*: minimum 4 weeks For *N. gonorrhea*: After 24-48h of ceftriaxone with substantial clinical improvement, transition to oral stepdown therapy to complete total of at least 7 days	Approximately 45% of *S. aureus* at UMHS are MRSA, so initial treatment to cover MRSA is warranted. De-escalate to a beta-lactam if *methicillin-susceptible S. aureus (MSSA)* is identified. Consult Orthopedic surgery for joint drainage. ID consultation recommended. **Linezolid** and **daptomycin** require prior approval. Baseline CBCP and weekly CBCP are recommended with **linezolid** therapy due to risk of cytopenia, especially thrombocytopenia; alternative therapy should be considered in patients with thrombocytopenia. **Linezolid** should be used with caution in patients on medications with serotonergic activity, e.g., SSRI and MAOI. See SSRI & Linezolid Education. Baseline CK followed by weekly CK should be measured in patients placed on **Daptomycin** due to increased risk of rhabdomyolysis. Infections due to fungi, mycobacteria, or *Actinomyces* require longer durations of therapy – consult appropriate national guidelines for guidance.

* Adjust dose based on renal function; vancomycin dose may require adjustment for select organisms or patients
Target vancomycin AUC 400-600 mcg*hr/mL

Pelvic Osteomyelitis Associated with Chronic Decubitus Ulcers			
Clinical Setting	**Empiric Therapy**	**Duration**	**Comments**
Acute osteomyelitis associated with contiguous spread from pressure ulcer Bacterial Etiology: Mixed infections due to *Staphylococcus sp., Streptococcus sp.* and enteric organisms	Consider holding antibiotics until deep tissue cultures can be obtained in hemodynamically stable patients Preferred: **Vancomycin*** IV (see nomogram) **+ Piperacillin-tazobactam*** 4.5 g IV q6h Alternative for patients with penicillin allergy: Mild allergy (rash) **Vancomycin*** IV (see nomogram) **+ Cefepime*** 2 g IV q8h **+ Metronidazole** 500 mg PO/IV q8h Anaphylaxis: **Vancomycin*** IV (see nomogram) **+ Aztreonam*** 2 g IV q8h **+ Metronidazole** 500 mg PO/IV q8h Alternatives for vancomycin intolerance (not vancomycin infusion reaction**) or allergy: **Daptomycin*** 6 mg/kg IV daily + other antibiotic as indicated above.	6-8 weeks of therapy depending on response	Infectious Disease consultation recommended. Surgical debridement of overlying ulcer with deep tissue or bone biopsy is an important component of management. Tailor therapy based on culture data. Treatment should be modified to cover previously isolated pathogens with recurrent or relapse of the same site. **Daptomycin** requires prior approval. Baseline CK followed by weekly CK should be followed in patients placed on **daptomycin** due to increased risk of rhabdomyolysis. Infections due to fungi, mycobacteria, or *Actinomyces* require longer durations of therapy – consult appropriate national guidelines for guidance.

* Adjust dose based on renal function; vancomycin dose may require adjustment for select organisms or patients
Target vancomycin AUC 400-600 mcg*hr/mL

Diabetic Foot Ulcers with Osteomyelitis			
Clinical Setting	**Empiric Therapy**	**Duration**	**Comments**
Acute osteomyelitis with recent ulcer • Staphylococcus spp (esp *S. aureus*) • Streptococcus spp • *Corynebacterium* and other skin flora	Consider holding antibiotics until deep tissue cultures can be obtained in hemodynamically stable patients Preferred: **Vancomycin*** IV (see nomogram) Alternatives for Vancomycin intolerance (not vancomycin infusion reaction**) or allergy: **Daptomycin*** 6 mg/kg IV daily OR **Linezolid** 600 mg PO/IV q12h	6-8 weeks of therapy depending on response	Infectious Disease consultation recommended. Surgical debridement of overlying ulcer with deep tissue or bone biopsy is an important component of management. Tailor therapy based on culture data. Treatment should be modified to cover previously isolated pathogens with recurrent or relapse of the same site. **Linezolid** and **daptomycin** require prior approval. Baseline CBCP and weekly CBCP are recommended with **linezolid** therapy due to risk of cytopenia, especially thrombocytopenia; alternative therapy should be considered in patients with thrombocytopenia. **Linezolid** should be used with caution in patients on medications with serotonergic activity, e.g., SSRI and MAOI. See SSRI & Linezolid Education. Baseline CK followed by weekly CK should be followed in patients placed on **daptomycin** due to increased risk of rhabdomyolysis. Infections due to fungi, mycobacteria, or *Actinomyces* require longer durations of therapy – consult appropriate national guidelines for guidance.
Risk for Gram negative bacillus infection: • Chronic ulcer with osteomyelitis • Osteomyelitis with fresh water exposure • recent broad spectrum antibiotics in the prior 90 days • recent >2 days hospitalized in prior 90 days hemodynamic instability Bacterial etiology • Staphylococcus spp (esp *S. aureus*) • Streptococcus spp • Enterobacteraciae • Obligate anaerobes • Rarely *Pseudomonas*	Preferred if risk for Gram negative: **Vancomycin*** IV (see nomogram) + **Piperacillin-tazobactam*** 4.5 g IV q6h Alternative for patients with penicillin allergy Mild allergy (rash) **Vancomycin*** IV (see nomogram) + **Cefepime*** 2 g IV q8h + **Metronidazole** 500 mg PO/IV q8h Anaphylaxis **Vancomycin*** IV (see nomogram) + **Aztreonam*** 2 g IV q8h + **Metronidazole** 500 mg PO/IV q8h Alternatives for Vancomycin intolerance (not vancomycin infusion reaction**) or allergy **Daptomycin*** 6mg/kg IV daily OR **Linezolid** 600mg PO/IV q12h + other antibiotic as indicated above.		

* Adjust dose based on renal function; vancomycin dose may require adjustment for select organisms or patients
Target vancomycin AUC 400-600 mcg*hr/mL

Prosthetic Joint infections			
Clinical Setting	**Empiric Therapy**	**Duration**	**Comments**
Higher risk associated: • Prior arthroplasty • RA • Periorperative infections • Prior joint infections • Prolonged surgery • High BMI • Postoperative bleeding • DM • Advanced age Bacterial Etiology: Early onset: <3 months after surgery • *S. aureus* • Aerobic Gram negative bacilli • Anaerobes • Mixed infections Delayed onset: 3-24 months after surgery • Coagulase negative staphylococcus • Enterococcus • Propionibacterium Late onset: >24 months after surgery • *S. aureus* • Beta-hemolytic streptococci • Aerobic Gram negative bacilli	Consider holding antibiotics until deep tissue cultures can be obtained in hemodynamically stable patients *Early (<3 mo) and Late (>24 mo) Onset* Preferred: **Vancomycin*** IV (see nomogram) + **Piperacillin-tazobactam** 4.5 g IV q6h Alternative for Suspected or Documented Gram negative Infection: **Vancomycin*** IV (see nomogram) + **Cefepime*** 2 g IV q8h Alternative for Severe Penicillin Allergy: **Vancomycin*** IV (see nomogram) **+ Aztreonam*** 2 g IV q8h Alternative for Vancomycin Allergy or Intolerance (not vancomycin infusion reaction**): **Daptomycin*** 6 mg/kg IV daily + other antibiotic as indicated above *Delayed (3-24 mo) Onset* Preferred: **Vancomycin*** IV (see nomogram) Alternatives for Vancomycin intolerance (not vancomycin infusion reaction**) or allergy: **Daptomycin*** 6 mg/kg IV daily OR **Linezolid** 600 mg PO/IV q12h	4-6 weeks Oral antimicrobial suppression indicated in some cases of retained hardware	Infectious Diseases consultation strongly recommended. Approximately 45% of *S. aureus* at UMHS are MRSA, so initial treatment to cover MRSA is warranted. De-escalate to a beta-lactam if methicillin-susceptible *S. aureus* (MSSA) is identified. **Linezolid** and **daptomycin** require prior approval. Baseline CBCP and weekly CBCP are recommended with **linezolid** therapy due to risk of cytopenia, especially thrombocytopenia; alternative therapy should be considered in patients with thrombocytopenia. **Linezolid** should be used with caution in patients on medications with serotonergic activity, e.g., SSRI and MAOI. See SSRI & Linezolid Education. Baseline CK followed by weekly CK should be followed in patients placed on **daptomycin** due to increased risk of rhabdomyolysis. Infections due to fungi, mycobacteria, or *Actinomyces* require longer durations of therapy – consult appropriate national guidelines for guidance.

*Adjust dose based on renal function; vancomycin dose may require adjustment for select organisms or patients
Target vancomycin AUC 400-600 mcg*hr/mL

Osteomyelitis following Trauma and/or Orthopedic Procedures			
Clinical Setting	**Empiric Therapy**	**Duration**	**Comments**
Associated with contaminated open fractures or surgical treatment of closed fractures Bacterial Etiology: Most common • *S. aureus* • Coagulase negative staphylococcus • Enteric Gram negative bacilli Less common • *Enterococcus sp.* • *Acinetobacter* • *Pseudomonas sp.* • Anaerobes	Consider holding antibiotics until deep tissue cultures can be obtained in hemodynamically stable patients Preferred: **Vancomycin*** IV (see nomogram) **+ Piperacillin-tazobactam*** 4.5 g IV q6h Alternative for Vancomycin Allergy or Intolerance (not vancomycin infusion reaction**): **Daptomycin*** 6 mg/kg IV daily OR **Linezolid** 600 mg IV q12h **+** other antibiotic as indicated above. Alternative for Penicillin Allergy (non-anaphylaxis): **Vancomycin*** IV (see nomogram) + **Cefepime*** 2 g IV q8h Alternative for Severe Penicillin Allergy: **Vancomycin*** (see nomogram) **+ Aztreonam** * 2 g IV q8h	6 weeks Oral suppression indicated in some cases of retained hardware	Infectious Diseases consult strongly recommended. Approximately 45% of *S. aureus* at UMHS are MRSA, so initial treatment to cover MRSA is warranted. De-escalate to a beta-lactam if *methicillin-susceptible S. aureus (MSSA)* is identified. **Linezolid** and **daptomycin** require prior approval. **Linezolid** should be used with caution in patients on medications with serotonergic activity, e.g., SSRI and MAOI. See SSRI & Linezolid Education. Baseline CBCP and weekly CBCP are recommended with **linezolid** therapy due to risk of cytopenia, especially thrombocytopenia; alternative therapy should be considered in patients with thrombocytopenia. Baseline CK followed by weekly CK should be followed in patients placed on **daptomycin** due to increased risk of rhabdomyolysis. Infections due to fungi, mycobacteria, or *Actinomyces* require longer durations of therapy – consult appropriate national guidelines for guidance.

* Adjust dose based on renal function; vancomycin dose may require adjustment for select organisms or patients
Target vancomycin AUC 400-600 mcg*hr/mL
** For vancomycin infusion reactions, vancomycin infusion should be slowed to >2 hr

References:

1. Lipsky BA, Berendt RA, Cornia PB, etal. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. Clin Infect Dis 2012;54(12):132-173.
2. Berbari EF, Kanj SS, Kowalski TJ, etal. 2015 Infectious Diseases Society of America (IDSA) clinical practice guidelines for the diagnosis and treatment of native vertebral osteomyelitis in adults. Clin Infect Dis 2015;61(6):e26-46.
3. Osmon Dr, Berbari EF, Berendt, etal. Diagnosis and management of prosthetic joint infection: clinical practice guidelines by the Infectious Diseases Society of America. Clin Infect Dis 2013;56(1);e1-25.
4. Zimmerli W, Trampuz A, Ochsner PE. Prosthetic joint infections. N Engl J Med 2004;351:1645.