C.S. MOTT CHILDREN'S HOSPITAL
MICHIGAN MEDICINE

SUSPECTED PEDIATRIC ACUTE BONE AND JOINT INFECTIONS UNIVERSITY OF MICHIGAN CLINICAL PRACTICE GUIDELINE

I. OVERVIEW: Bone and joint infections are relatively common invasive bacterial infections in children and adolescents. These infections can develop via hematogenous spread, via direct spread from adjacent soft tissue infection, or as a result of trauma or surgery. In the pediatric population, these infections typically present with symptoms of fever, refusal to walk or move an extremity, or localized tenderness and inflammatory changes over a bone or joint. The most common causative organisms in pediatric patients include *Staphylococcus aureus*, *Streptococcus pyogenes*, and *Streptococcus pneumoniae*. In patients < 4 years, *Kingella kingae* is also common. Appropriate surgical management and antibiotic therapy for these infections is important due to the relative difficulty of antibiotic penetration into bone and joint tissue. Although treatable, improperly managed bone and joint infections can result in significant morbidity and even death.

II. PURPOSE: The purpose of this document is to provide guidance to all medical providers in the emergency department or on an inpatient service who are caring for a pediatric patient with a suspected acute bone or joint infection. Consultants may also benefit from this document. Current practices are variable based on provider, and it is the hope that this guideline will also help to standardize the care of these patients.

III. SCOPE: This guideline includes management of non-neonatal pediatric patients (from 90 days to 17 years of age) who are evaluated in the emergency department or admitted to the hospital for an acute presentation of a suspected hematogenous (not associated with trauma or surgery) bone or joint infection. The guideline includes recommendations for diagnostic work-up, antibiotic therapy, and other aspects of management in the emergency department, on the inpatient floor, and at the time of patient discharge. This guideline also does not pertain to patients with chronic bone or joint infections, or infections complicated by the presence of hardware. In those instances, it is best to discuss management directly with the on-call Pediatric Infectious Diseases team.

IV. DEFINITIONS:

- Acute hematogenous osteomyelitis (AHO): Infection within a bone, generally accompanied by a host inflammatory response, that is diagnosed within 4 weeks of symptom onset in a previously uninfected bone.
- Acute bacterial arthritis (ABA): Bacterial infection of synovial fluid of a joint, with associated signs of acute inflammation.

V. GUIDELINE:

Emergency Department evaluation

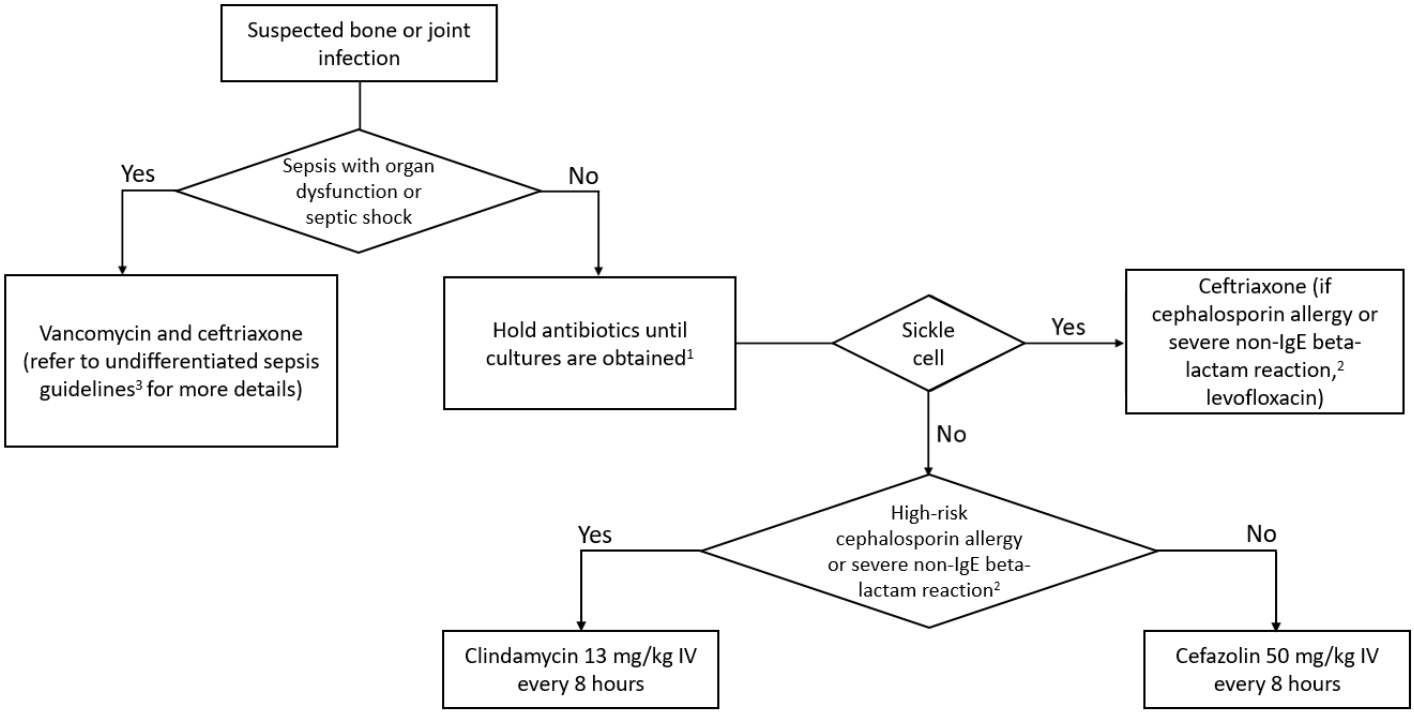
- **Initial evaluation:**
  - Obtain sexual history in adolescents with ABA, to assess risk of *Neisseria gonorrhoeae.*
  - Lab work: CBC with differential, ESR, CRP, blood culture.
    - Consider Lyme serology in children with large joint ABA (particularly the knee) who are well-appearing, have lower CRP/ESR, and have potential for exposure to *Ixodes scapularis* (black-legged ticks or deer ticks) in a Lyme endemic region (which includes Washtenaw County).
  - Imaging (preferably obtained before orthopedic surgery consult):
    - X-rays: Obtain to evaluate for radiographic signs of infection and rule out fracture or other pathology. X-rays may be normal in early AHO and cannot be used to rule out infection.
    - Ultrasound: Obtain if needed to evaluate for joint effusion, and/or other pathology.
  - Additional imaging studies should be obtained on an individual basis as guided by consultants, based on the history of present illness.

- **Surgical management:**
  - Orthopedic surgery should be consulted to evaluate for the need for further imaging (such as MRI) and/or acute surgical intervention.

        - AHO: Bone, fluid, and/or soft tissue specimens should be sent for Gram stain, aerobic and anaerobic culture, and pathology.
        - ABA: Joint fluid should be obtained via arthrocentesis or in the OR (at the discretion of orthopedic surgery). Hip or shoulder ABA may benefit from more invasive procedures up front due to increased risk of avascular necrosis. As much synovial fluid should be collected as possible and should be sent for cell count with differential, Gram stain, and culture. The Microbiology lab will hold any residual fluid in case additional studies are later recommended.
            - If Gram stain and cultures are negative and patient is < 4 years of age, consider sending residual joint fluid for "*Kingella kingae* by PCR" (minimum volume 0.5 mL).
            - If Gram stain and cultures are negative and diagnosis of Lyme arthritis is in question despite positive Lyme serology results, consider sending residual joint fluid for Lyme PCR (sendout to Mayo, test ID LYMPV, minimum volume 0.5 mL).
    - In the case of suspected AHO where orthopedic surgery has decided against acute surgical intervention, pediatric Interventional Radiology (IR) should be contacted to discuss an IR-guided bone biopsy to be sent for Gram stain, aerobic and anaerobic culture, and pathology.
        - Biopsy is recommended when feasible, but the decision to proceed with biopsy may be influenced by patient-specific factors such as location of infection, risks of procedure or sedation, available blood culture results, and duration of any prior antimicrobial therapy.
        - The yield of cultures obtained within 24 to 48 hours after initiation of antibiotic therapy is similar to that of cultures obtained prior to antibiotics.

- **Admission:**
    - Pediatric orthopedic surgery will determine whether the patient will be better served on the orthopedic service or a general pediatric service with an orthopedic surgery consult.

- **Empiric antibiotics:** Please call Pediatric Infectious Diseases to discuss prior to starting antibiotics, unless patient is in sepsis with organ dysfunction or septic shock.



[1]Including both blood and bone or joint cultures. Hold antibiotics for no longer than 48-72 hours. If uncomfortable holding antibiotics, please call Pediatric Infectious Diseases to discuss prior to starting.

[2]High-risk allergy is defined by angioedema, respiratory/cardiovascular symptoms, or anaphylaxis. Also avoid use for severe non-IgE mediated allergy to any beta-lactam antibiotic. See BETA-LACTAM ALLERGY EVALUATION, ANTIBIOTIC SELECTION, AND BETA-LACTAM ALLERGY EVALUATION SERVICE CONSULTATION IN PATIENTS WITH A REPORTED ALLERGY for more information.
[3]EMPIRIC ANTIBIOTIC GUIDELINES FOR UNDIFFERENTIATED SEPSIS WITH ORGAN DYSFUNCTION OR SHOCK IN PATIENTS ON PEDIATRIC SERVICES (EXCLUDING NICU).

Inpatient management

- **Consults:**
  - If not already done, consult Pediatric Infectious Diseases.
  - Orthopedic surgery will continue to follow the patient on the floor if there is highly suspected or confirmed AHO or ABA, even if there is no initial need for surgical intervention.

- **Targeted antibiotics:**
  - After culture results are available, antibiotics should be adjusted to target the appropriate organism (see Table I).
    - For patients with additional antibiotic allergies, resistant organisms, and/or other difficulties selecting appropriate antibiotics, please discuss with Pediatric Infectious Diseases.

- **Repeat laboratory studies:**
  - While hospitalized, inflammatory markers should be obtained every 24-48 hours until clear improvement noted.
  - If blood culture is positive, it should be repeated daily until negative for 48 hours.

- **Repeat imaging:**
  - If blood cultures are persistently positive, and/or patient is still febrile, and/or exam is not significantly improving after > 48 hours of appropriate therapy, consider repeat imaging in conjunction with consultant recommendations.

Discharge planning

- **Criteria for oral step-down therapy and discharge:**
  - Oral therapy and discharge can be considered when following criteria are met:
    - Afebrile
    - Negative blood cultures ≥ 48 hours
    - Tolerating PO
    - Substantial clinical improvement with near return to normal function
    - Improving inflammatory markers
  - See Table I for specific recommendations for oral step-down therapy.

- **Outpatient follow-up:**
  - In most cases, patients will receive a minimum 10-day course of antibiotics for ABA and a minimum 3-week course of antibiotics for AHO.
    - The Pediatric Infectious Diseases team will typically arrange follow-up near the end of the minimum treatment course.
    - In general, antibiotic prescriptions should be written with sufficient supply to last at least through the first Pediatric Infectious Diseases follow-up appointment.
    - Treatment courses will be extended as needed at the discretion of the Pediatric Infectious Diseases physicians during follow-up clinic appointments.

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Table I. Targeted antibiotics for treatment of bone and joint infections

Organism	IV therapy	Oral step-down therapy	Dosing Recommendations
***Staphylococcus aureus* (MSSA) or culture negative**	First line[1]: **Cefazolin**[2] Allergy[3] alternative, without bacteremia: **Clindamycin** Allergy[3] alternative, with bacteremia: **Vancomycin**[2]	First line[1]: **Cephalexin**[2] Allergy[3] alternative: **Clindamycin** OR **TMP-SMX**[2,4] (preferred if culture negative)	**Amoxicillin**: 33 mg/kg/dose PO q8h (max: 1000 mg/dose) **Amoxicillin-clavulanate**: 33 mg amoxicillin/kg/dose PO q8h of the 600-42.9 mg/5 mL concentration (max: 1000 mg/dose) **Ampicillin:** 50 mg/kg/dose IV q6h (max: 2000 mg/dose) **Cefazolin:** 50 mg/kg/dose IV q8h (max: 2000 mg/dose) **Ceftriaxone:** 100 mg/kg/dose IV once, then 50 mg/kg/dose IV q12h (max: 2000 mg/dose) **Cefuroxime:** 50 mg/kg/dose IV q8h (max: 1500 mg/dose) **Cephalexin:** 37.5 mg/kg/dose PO 4 times daily (max: 1000 mg/dose) **Clindamycin:** 13 mg/kg/dose IV/PO q8h (max: 900 mg/dose IV, 600 mg/dose PO) **Levofloxacin:** < 5 years: 10 mg/kg/dose IV/PO q12h (max: 375 mg/dose IV/PO) ≥ 5 years: 10 mg/kg/dose IV/PO q24h (max: 750 mg/dose IV/PO) **TMP-SMX**[4]**:** 6 mg TMP/kg/dose IV/PO q12h (max: 320 mg TMP/dose) **Vancomycin:** Pediatric vancomycin dosing guidelines
***Staphylococcus aureus* (MRSA)**	First line[1], without bacteremia: **Clindamycin** With bacteremia: **Vancomycin**[2]	First line[1]: **Clindamycin** Clindamycin resistance: **TMP-SMX**[2,4]	
Streptococcus pneumoniae*, group A or B *Streptococcus	First line[1]: **Ampicillin**[2] Allergy[3] alternative: **Clindamycin**	First line[1]: **Amoxicillin**[2] Allergy[3] alternative: **Clindamycin**	
Kingella kingae	First line[1]: **Ampicillin**[2] Allergy[3] alternative: **Cefuroxime** OR **TMP-SMX**[2,4]	Beta-lactamase negative or unknown: **Amoxicillin**[2] Beta-lactamase positive: **Amoxicillin-clavulanate**[2] Allergy[3] alternative: **TMP-SMX**[2,4]	
Other	Discuss with Pediatric Infectious Diseases		

[1]Recommendations assume organism is susceptible to listed agent. If organism is resistant, move to the next recommended agent or discuss with Pediatric Infectious Diseases.

[2]Renal adjustment may be necessary. See Antimicrobial dosing recommendations for pediatric patients.

[3]Discuss with Pediatric Infectious Diseases and refer to BETA-LACTAM ALLERGY EVALUATION, ANTIBIOTIC SELECTION, AND BETA-LACTAM ALLERGY EVALUATION SERVICE CONSULTATION IN PATIENTS WITH A REPORTED ALLERGY for more information.

[4]TMP-SMX = Trimethoprim-sulfamethoxazole.

Authors:
Elizabeth Lloyd, MD (Pediatric Infectious Diseases)
Alison Tribble, MD (Pediatric Infectious Diseases, Antimicrobial Stewardship)
Karen Davidge, PharmD (Pharmacy, Antimicrobial Stewardship)
Kristin Klein, PharmD (Pharmacy, Antimicrobial Stewardship)
Nicholas Dillman, PharmD (Pharmacy, Antimicrobial Stewardship)

Consultants:
Noelle Whyte, MD (Pediatric Orthopedic Surgery)
Frances Farley, MD (Pediatric Orthopedic Surgery)
Michele Carney, MD (Pediatric Emergency Medicine)
Brittany Allen, MD (Pediatric Hospitalist)
Ravi Srinivasa, MD (Interventional Radiology)

Key References:

1) Caird M, et al. Factors distinguishing septic arthritis from transient synovitis of the hip in children. J Bone Joint Surg Am. 2006 Jun;88(6):1251-7.
2) Keren R, et al. Comparative effectiveness of intravenous vs oral antibiotics for postdischarge treatment of acute osteomyelitis in children. JAMA Pediatr. 2015 Feb;169(2):120-8.
3) Peltola H, et al. Short- versus long-term antimicrobial treatment for acute hematogenous osteomyelitis of childhood: prospective, randomized trial on 131 culture-positive cases. Pedatr Infect Dis J 2010;29:1123-8.
4) Woods CR, Bradley JS, Chatterjee A, et al. Clinical Practice Guideline by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America: 2021 Guideline on Diagnosis and Management of Acute Hematogenous Osteomyelitis in Pediatrics. J Pediatric Infect Dis Soc. 2021 Sep 23;10(8):801-844. doi: 10.1093/jpids/piab027. PMID: 34350458.
5) Woods CR, Bradley JS, Chatterjee A, Kronman MP, Arnold SR, Robinson J, Copley LA, Arrieta A, Fowler SL, Harrison C, Eppes SC, Creech CB, Stadler LP, Shah SS, Mazur LJ, Carrillo-Marquez MA, Allen CH, Lavergne V. Clinical Practice Guideline by the Pediatric Infectious Diseases Society (PIDS) and the Infectious Diseases Society of America (IDSA): 2023 Guideline on Diagnosis and Management of Acute Bacterial Arthritis in Pediatrics. J Pediatric Infect Dis Soc. 2023 Nov 6:piad089. doi: 10.1093/jpids/piad089. Epub ahead of print. PMID: 37941444.
6) McDaniel LM, Fiawoo S, Tamma PD, Same RG. Trimethoprim-Sulfamethoxazole for Pediatric Osteoarticular Infections. J Pediatric Infect Dis Soc. 2023 Oct 28;12(10):534-539. doi: 10.1093/jpids/piad076. PMID: 37757866.
7) Peltola H, Paakkonen M, Kallio P, Kallio MJ, Osteomyelitis-Septic Arthritis Study G. Prospective, randomized trial of 10 days versus 30 days of antimicrobial treatment, including a short-term course of parenteral therapy, for childhood septic arthritis. Clinical Infectious Diseases 2009; 48(9): 1201-10.

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