Guidelines for the Evaluation and Management of Pediatric Acute Hematogenous Osteomyelitis and Acute Bacterial Arthritis

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I. Basic Principles

a. For a list of abbreviations, please see Appendix 1.
b. Acute bacterial arthritis (ABA) refers to a bacterial infection of synovial fluid with signs of acute inflammation. This was previously known as septic arthritis. It is also referred to colloquially as a "septic joint". To be in concordance with the most recent PIDS/IDSA update, this guideline will use the term ABA.[1]
c. Acute hematogenous osteomyelitis (AHO) is defined as an infection of the bone and marrow that is diagnosed within 4 weeks of symptom onset. It is most often caused by inoculation of bacteria that reach the bone through hematogenous spread.[2–4]
d. Pathophysiology
    i. ABA: Most commonly occurs following translocation of a pathogen into joint synovial fluid from the bloodstream. It can also occur from direct inoculation (trauma or procedural).[1]
    ii. AHO: Occurs when bacteria enter and proliferate in bone and bone marrow. Bacteria can reach bone matrices via hematogenous spread, direct inoculation through trauma or a procedure, or spread of infection from an adjacent joint or soft tissue.[2,5,6]

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e. Presenting symptoms typically include fever, difficulty or inability to bear weight, tenderness, erythema and decreased movement of the affected area. Physical exam often shows visible swelling, erythema, warmth, and tenderness to palpation of the affected area in addition to decreased range of motion (ROM) and difficulty or inability to bear weight.[7]
f. Initial laboratory workup is targeted at looking for evidence of inflammation and infection, while also evaluating for other causes (fractures, malignancy) through basic imaging (x-rays and ultrasound [US]).
g. The most common microbes are *Staphylococcus aureus* and *Streptococcus pyogenes* (Group A streptococcus, GAS). In children ages 6 months to 4 years, *Kingella kingae* is another important causative organism.
    i. Nationally, the most common causative organism is *S. aureus,* which is responsible for approximately 60% of all AHO cases in children. This is followed by group A streptococcus and *Kingella kingae*.[3,5,6]
h. Treatment consists of antibiotic treatment and supportive care. In ABA, debridement of the joint is important to prevent further damage. AHO can be managed medically but some cases require surgical intervention (to be determined by Orthopedics). The antibiotic regimen is ideally guided by a culture of the infected area.[8] If a culture cannot be obtained or if the culture finalizes with no growth, antibiotics are chosen based on the most likely pathogen and the antibiotic with the most favorable side effect profile.[1,2]
    i. For ABA, the sample for culture is usually synovial fluid obtained by arthrocentesis. This procedure is both diagnostic and therapeutic. Arthrocentesis can be performed by Orthopedic Surgery, MSK IR, Radiology, or a PEM provider with fluoroscopic or US guidance.
    ii. For AHO, a bone sample for culture can be obtained from a surgical procedure with Orthopedic Surgery or a bone biopsy by MSK IR.
i. With timely diagnosis and intervention if needed along with appropriate antibiotic treatment, many of these patients recover without long-term health issues or physical limitations. In one study that evaluated outcomes in pediatric ABA and AHO, 73% of patients had no long-term sequelae of the infection.[9]

II. Inclusions / Exclusions

a. This guideline is intended to aid in the evaluation and management of patients aged 6 months to 18 years old with suspected osteomyelitis and/or acute bacterial arthritis of the extremities.
    i. This refers to bones and joints in the arms and legs.
    ii. This guideline can be applied to patients with recurrent infectious osteomyelitis.
b. This guideline excludes patients with the following conditions or characteristics:
    i. Any osteomyelitis or acute bacterial arthritis not involving the extremities (vertebrae, scapula, rib, skull)
    ii. Penetrating trauma
    iii. Prior orthopedic hardware
    iv. Immunocompromised
    v. Sickle cell disease
    vi. Orbital cellulitis
    vii. Decubitus ulcers
    viii. Necrotizing fasciitis
    ix. Chronic osteomyelitis

III. **Diagnosis**

a. Laboratory evaluation[5]

i. Complete blood count (CBC) – Evaluates for evidence of inflammation and infection including leukocytosis and thrombocytosis.

ii. Blood culture – Can provide information about the causative organism if positive. Blood culture should be obtained prior to initiation of empiric antibiotics, though as described below, most patients should have antibiotics held prior to obtaining tissue/fluid specimens.

iii. C-reactive protein (CRP) – Evaluates for evidence of inflammation and can be used to assess response to treatment.[10] Orthopedic Surgery may also use the maximum CRP value to make decisions about the need for operative interventions. CRP is expected to rise following invasive procedures. If a CRP is planned to be trended, it should be ordered no more frequently than every 72 hours (half-life of 19 hours[11]).

iv. Additional labs such as CMP or lactate can be obtained based on provider preference or if clinically indicated.

b. Imaging

i. X-rays of the affected area are appropriate as initial evaluation. These can identify other causes of presenting symptoms such as fracture or malignancy. They can also show evidence of joint involvement, effusion, soft tissue swelling, or bone infection (though this is usually after the infection has been present for 10-14 days). However, a normal x-ray does not exclude ABA or AHO.[5,6,12]

ii. US of the affected joint should be considered to evaluate for a joint effusion if the x-ray is suggestive. Consideration of US as an initial imaging step is reasonable if the history and physical suggest acute bacterial arthritis.

iii. Magnetic resonance imaging (MRI) is the next appropriate imaging study following x-rays and US (if performed). MRI with contrast is the preferred imaging for AHO and is superior to CT scan and bone scan. In cases of ABA, MRI is helpful in determining if there is a concomitant osteomyelitis as patients with both conditions are at increased risk of complications.[12–14]

1. Contrast-enhanced MRIs are the most sensitive imaging modality for osteomyelitis and therefore are the preferred type of imaging if this diagnosis is being considered.[15] For contrast-enhanced scans, patients must have an IV and often need sedation due to scan length and the need for the patient to be still. This is recommended in patients where there is no clear surgical plan to help with diagnostic clarity.
2. There is a rapid sequence MRI for MSK infections that is non-contrast. Patients do not need to have an IV and generally do not need sedation due to the short scan time. This **only** is recommended in patients where Orthopedic Surgery is planning an operative intervention to aid in surgical planning. It is not sensitive for excluding adjacent bone infections and should not be used as a diagnostic imaging study. This can only be ordered by the Orthopedic Surgery team.[16]
3. The MRI can be completed either while the patient is in the ED or after admission depending on MRI availability and coordination if sedation is needed.

c. Investigations not recommended
    i. Labs: erythrocyte sedimentation rate (ESR), procalcitonin, Lyme disease serologies*
        1. In acute infection, ESR both rises and falls more slowly than CRP. Additionally, it may continue to rise during the initial treatment phase. While it was included in the original Kocher criteria for ABA, its utility has been lessened by more recent literature showing low specificity and sensitivity. The use of ESR is not recommended by national guidelines as its added value when used in combination with CRP is expected to be negligible.[1,2,10,17,18]
        2. Lyme disease is not endemic to our surrounding area. Lyme disease serologies are unlikely to be of benefit in patients with suspected ABA unless the patient has traveled to a Lyme-endemic area*.
    ii. Imaging: computed tomography (CT), bone scan
d. Consulting teams
    i. Consult Orthopedic Surgery if concern for acute bacterial arthritis or acute hematogenous osteomyelitis.
    ii. Consult Pediatric Infectious Disease as a non-urgent consult after admission if concerned for ABA or AHO. This is to aid in the selection of antibiotics, determination of treatment duration, and follow up after discharge.
    iii. Consult MSK IR if there is a need for a bone biopsy in cases of osteomyelitis. This often occurs later in the hospitalization after the Orthopedics and ID teams have consulted.
e. If the diagnostic workup is not consistent with ABA or AHO, please leave this pathway and consider other diagnoses. These can include transient synovitis, trauma, malignancy, post-infectious arthritis, and rheumatologic causes (e.g., juvenile idiopathic arthritis).

IV. Antibiotics

a. Make decision about need for empiric antibiotics.[1,2]
    i. If the patient is ill-appearing, has hemodynamic changes or the infection has rapidly progressed, it is reasonable to start empiric antibiotics. Blood culture should be collected prior to antibiotic administration.
    ii. If the patient is well-appearing and hemodynamically stable, admit without antibiotics until further studies can be completed (MRI, bone/tissue/fluid culture). This helps to optimize the yield of any tissue/fluid cultures.
b. Antibiotic selection and common pathogens
    i. Common pathogens: *S. aureus* (methicillin-susceptible *S. aureus* [MSSA], methicillin-resistant *S. aureus* [MRSA]), GAS, *Kingella kingae* (6 months to 4 years)[1,2,5]
    ii. Initial antibiotics
        1. Acute Bacterial Arthritis
            a. If patient is well appearing, start IV cefazolin.
            or
            b. If patient is ill- or toxic-appearing, start IV vancomycin.
            or
            c. If there are Gram negatives identified on the Gram stain, start IV ceftriaxone.

2. Acute Hematogenous Osteomyelitis
    a. If patient is well appearing, start IV cefazolin.
    or
    b. If patient is ill- or toxic-appearing, start IV vancomycin.
3. Note on MRSA
    a. If patient has a personal history of MRSA infection, it is reasonable to look at previous susceptibilities and select an empiric antibiotic accordingly. If the susceptibilities are not available for review and the patient is well appearing, it is reasonable to start IV cefazolin. This is recommended because up to one-third of cases of ABA and AHO can be culture-negative, and initial therapy active against MRSA can complicate the ultimate transition to oral antibiotics.
4. If patient is presenting with recurrent osteomyelitis, antibiotic selection can be made based on prior susceptibilities and discussion with ID team.

V. Tissue Sampling

a. Acute Bacterial Arthritis
    i. If an effusion is identified on imaging, an arthrocentesis should be performed as both a diagnostic and therapeutic step in management.
    ii. Lab studies on joint aspirate: cell count with differential, Gram stain, aerobic/anaerobic culture, *Kingella kingae* PCR (for patients up to 4 years old without another causative organism identified).
        1. Arthrocentesis can be performed by Orthopedic Surgery, MSK IR, Radiology, or a PEM provider.
        2. MSK IR to perform if Orthopedics is unsuccessful, or if the joint is the shoulder or hip.
        3. Radiology can perform hip aspirations during weekday business hours. If Radiology does not have availability or if it is after hours, these will be performed by MSK IR.
        4. For Radiology and MSK IR contact and logistics information, see ED guideline titled "Hip Aspiration Process for ED Patients" in the EU Guidelines folder on Box.
    iii. Arthrocentesis may require sedation; this should be arranged as needed by the primary team.

b. Acute Hematogenous Osteomyelitis
    i. The benefits of obtaining a tissue sample in cases of suspected osteomyelitis are that it can help guide antibiotic selection and provide additional diagnostic clarity.[2,8]
    ii. Tissue sampling should first be discussed with the Orthopedic Surgery and ID teams.
        1. If Orthopedic Surgery is already planning on taking the patient to the OR, a tissue sample can be obtained at the same time.
        2. Orthopedic Surgery generally treats subperiosteal abscesses or loculated fluid collections with surgical decompression/debridement.
    iii. If Orthopedic Surgery is not planning on any operative intervention, and if recommended by consulting teams, consult **MSK IR** for a bone biopsy provided no causative organism has been identified via non-invasive methods (e.g., blood culture).
    iv. Lab studies on tissue sample: Gram stain, aerobic/anaerobic culture, surgical pathology, *Kingella kingae* PCR (for patients up to 4 years old without another causative organism identified, if not already sent on another specimen).

c. Unnecessary lab studies for both ABA and AHO
    i. Mycology and AFB cultures. In immunocompetent hosts without antecedent trauma, the yield of these studies is exceptionally low. The rare instances where these tests may be useful likely fall under the exclusion criteria for this guideline.
d. Ordering *Kingella kingae* testing
    i. *Kingella kingae* PCR is not currently orderable in Epic. A dedicated order will be created as part of ongoing quality improvement work, but for now the workflow outlined below should be utilized.
    ii. Miscellaneous Lab Test order
    iii. Name of test to be performed: "Kingella PCR, test ID KKRP, send to Mayo"
    iv. Specimen type/source: either synovial fluid or tissue
    v. Collection details:
        1. If synovial fluid, a 0.5mL sample of fluid should be sent in a lavender top EDTA tube.
        2. If tissue, the sample should be sent in a sterile container.

VI. Inpatient Care and Monitoring of Response to Treatment

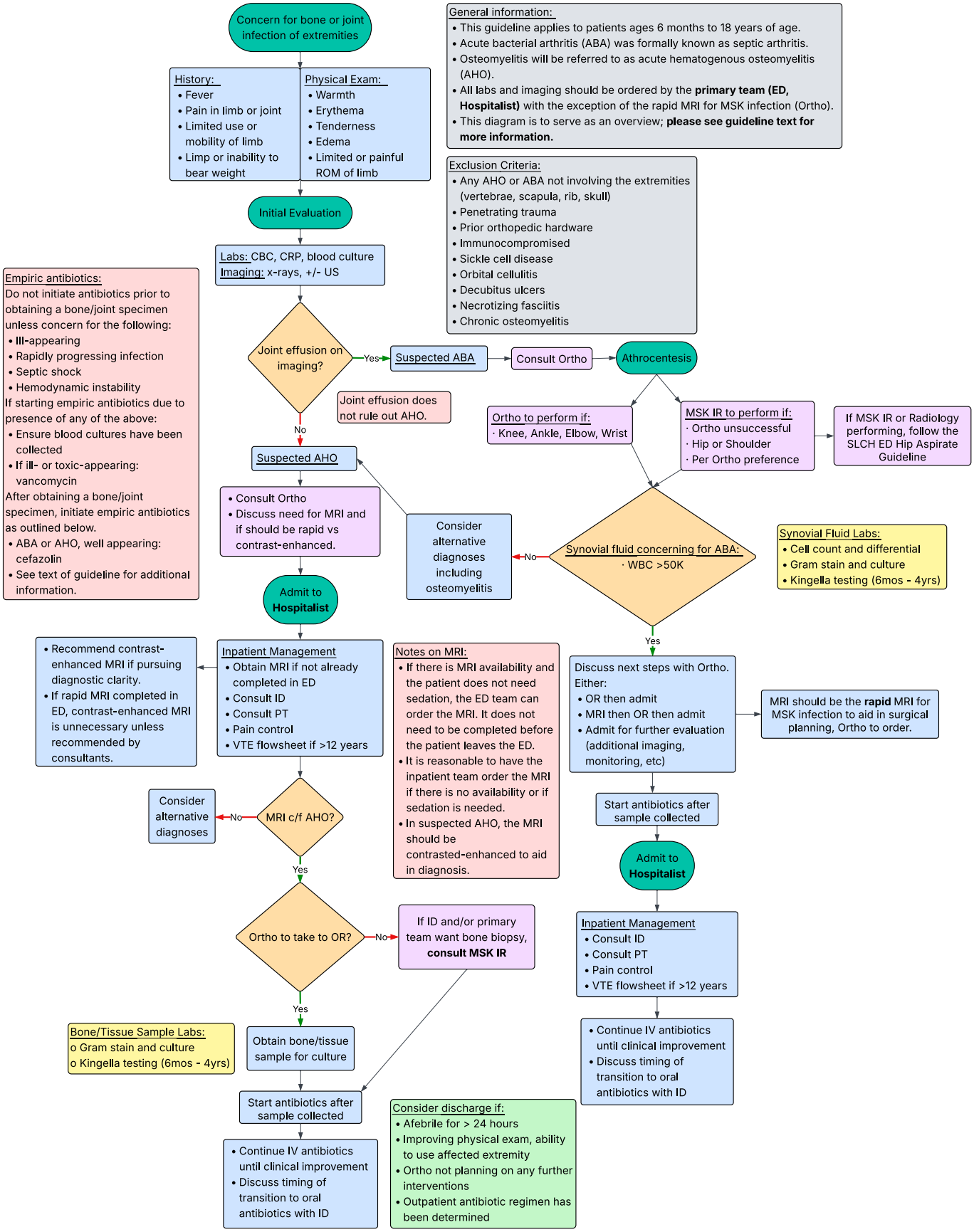
a. If there is concern for ABA or AHO, these patients should be admitted to a H**ospitalist** team for further evaluation.
b. Inpatient care considerations
    i. Consider a Physical Therapy (PT) consult to help with mobility.
    ii. Pain control: consider scheduling acetaminophen and/or ibuprofen and having an option for breakthrough pain (i.e. oxycodone).
        1. It can be helpful to plan for a dose of pain medication just before a PT session or an exam with Orthopedic Surgery.
c. Venous thromboembolism (VTE) risk
    i. Orthopedic surgery, immobilization, acute inflammation, and/or bacteremia are all risk factors for VTE. Patients with MSK infection can have one or all of these and are at increased risk for VTE.[19]
    ii. If the patient is >12 years of age, fill out the VTE flowsheet in Epic and follow the recommendations.
    iii. If the patient is critically ill, consider prophylactic anticoagulation and a Hematology consult.
d. Monitoring of treatment response[20]
    i. Labs
        1. Consider repeating a CRP 72 hours after initial CRP and at least 48 hours after any operative intervention, if recommended by the consulting ID service. A rapid decline in CRP or reduction of CRP of ≥50% within 3-5 days following initiation of antibiotics may be consistent with uncomplicated osteomyelitis and suggest transition to oral antibiotics is appropriate.
        2. Most patients will be transitioned to oral antibiotics with clinical improvement. For patients who will continue intravenous antibiotics for >1 week, obtain a CBC with differential and CMP at least weekly to monitor for antibiotic toxicities.
        3. If an ESR was obtained as part of the initial evaluation, it should not be repeated while inpatient as it takes >7 days to observe a meaningful change in value.
    ii. Fever curve
    iii. Frequent examinations of affected area with attention to appearance (erythema, edema, and skin condition), active and passive range of motion, pulses, and pain/tenderness.

e. Inadequate treatment response – if any of the below are identified, consider discussion with ID and Orthopedic Surgery.
    i. Continued or worsening fever curve
    ii. Continued pain, worsening exam findings (increased edema, erythema, tenderness)
        1. Worsening exam findings with extreme edema, cool and pale skin, and lack of pulses should raise concern for compartment syndrome and warrant emergent action.
    iii. No improvement or worsening of CRP
    iv. Persistent positive blood cultures (defined as ≥3 days of bacteremia)

VII. Disposition and Care After Discharge

a. Consider discharge if the following criteria are met:
    i. Improving or resolved fevers
    ii. Improving pain, erythema, edema, ability to use affected extremity or bear weight
    iii. Orthopedic Surgery not planning on any further interventions
    iv. All drains have been removed
    v. Outpatient antibiotic regimen has been determined
b. Selection of oral antibiotics
    i. In studies evaluating oral transition for patients with AHO, the median duration of IV therapy is about 4 days; shorter durations of IV therapy for patients who are otherwise meeting discharge criteria may also be appropriate.
    ii. Oral antibiotics should be selected based on documented microbiologic results whenever possible.
    iii. For patients without positive microbiologic results, oral antibiotics should be selected to maintain a similar spectrum of coverage to what the patient received intravenously. For most patients, who receive cefazolin empirically, this will be an oral first-generation cephalosporin (e.g., cephalexin, cefadroxil). Doses of oral antibiotics used for the treatment of osteoarticular infections are typically higher than what is used for other infections. Discuss antibiotic dosing with ID and/or pharmacy prior to writing a prescription.
    iv. The typical duration of antibiotics is 10-14 days for ABA or 21-28 days for AHO.
c. Follow up
    i. These patients will have ID clinic follow up to continue monitoring response to antibiotics. ID will arrange.
    ii. If Orthopedic Surgery performed a procedure, the patient will have Orthopedics clinic follow up. Orthopedics will arrange; ideally ID and Orthopedics will coordinate appointments.
d. Other considerations
    i. Discuss with PT before discharge regarding any home health medical equipment needs (walker, crutches, etc.).

VIII. Figure: Overview of Guideline



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Appendix 1: Abbreviations

a. ABA = acute bacterial arthritis
b. AHO = acute hematogenous osteomyelitis
c. CBC = complete blood count
d. CRP = C-reactive protein
e. CT = computed tomography
f. ESR = erythrocyte sedimentation rate
g. GAS = Group A streptococcus
h. MRSA = methicillin-resistant *Staphylococcus aureus*
i. MSSA = methicillin-susceptible *Staphylococcus aureus*
j. MRI = magnetic resonance imaging
k. MSK IR = musculoskeletal interventional radiology
l. ROM = range of motion
m. US = ultrasound
n. VTE = venous thromboembolism