TEXAS CHILDREN'S HOSPITAL
EVIDENCE-BASED OUTCOMES CENTER
Acute Hematogenous Osteomyelitis (AHO) and/or Septic Arthritis
Evidence-Based Guideline

Definition: Acute hematogenous osteomyelitis (AHO) is inflammation of the bone and bone marrow caused by an infectious organism that reaches the bone through the bloodstream; it is considered acute if a diagnosis is made within 2-4 weeks of symptom onset. [1]
Septic arthritis is the infection of the joint, which can be caused by bacteria, fungi, mycobacteria, or viruses.

Pathophysiology: AHO is the most common form of osteomyelitis found in children; it occurs as the result of an infection that spread through the bloodstream. The pathophysiology and epidemiology of osteomyelitis are greatly influenced by the anatomy of the bone in pediatric patients. [2-4]
The blood supply to the bone (nutrient artery) divides into a tortuous capillary bed that joins sinusoidal veins before entering the bone marrow of the metaphysis. The slow movement of blood and lack of a reticuloendothelial lining make it easy for bacteria to seed the bone and grow rapidly. [2,4] The bacterial growth leads to cellulitis in the bone marrow which then causes an inflammatory response. [4] The inflammatory response leads to the accumulation of leukocytes which produces an exudate that causes pressure and necrosis of the bone. The most common causative organisms *Staphylococcus aureus* and *Kingella kingae*. [1]
Septic arthritis may occur in isolation or concurrently with AHO. Microorganisms can enter the joint space by hematogenous spread, direct inoculation, or extension of a contiguous focus of infection (e.g., osteomyelitis). [5]

Epidemiology: Acute hematogenous osteomyelitis occurs more commonly in children than in adults. Although any bone can be affected, AHO occurs primarily in the long bones, most commonly the femur or tibia. [3]
Bacterial arthritis occurs more commonly in childhood than during other periods of life. [5] The hip and knee are the joints most frequently involved.

Inclusion Criteria
- Age ≥6 months
- Healthy children without underlying conditions (e.g., spina bifida, sickle cell disease, immunodeficiency)

Exclusion Criteria
- Age <6 months
- Ill/Toxic appearance
- Contiguous osteomyelitis (next to a decubitus ulcer)
- Penetrating trauma
- Chronic osteomyelitis
- Immunocompromised patients
- Known rheumatologic disease
- History of a recent orthopedic procedure
- Prosthesis of the affected joint
- Bleeding disorder

Differential Diagnosis
Fracture
Myositis
Discitis
Cellulitis
Slipped capital femoral epiphysis (SCFE)
Legg calve perthes (LCP)
Juvenile idiopathic arthritis (JIA)
Reactive arthritis
Post-infectious arthritis
Bone tumor (e.g., Ewing's sarcoma, osteosarcoma)
Leukemia (e.g., acute lymphoblastic, acute myeloid)
Hemearthrosis (e.g., bleeding disorder)
Spondylolisthesis
Spondylolysis

Diagnostic Evaluation
Clinicians should immediately refer to the Septic Shock guideline and intervene rapidly if patient has toxic appearance, ill appearance, altered mental status, and/or compromised perfusion with abnormal vital signs.

Table 1. Vital Sign Changes of Sepsis [6]

Age	Heart Rate	Resp Rate	Systolic BP	Temp (°C)
0d - 1m	>205	>60	<60	<36 or >38
>1m - 3m	>205	>60	<70	<36 or >38
>3m - 1y	>190	>60	<70	<36 or >38.5
>1y - 2y	>190	>40	<70 + (age in yr x 2)	<36 or >38.5
>2y - 4y	>140	>40	<70 + (age in yr x 2)	<36 or >38.5
>4y - 6y	>140	>34	<70 + (age in yr x 2)	<36 or >38.5
>6y - 10y	>140	>30	<70 + (age in yr x 2)	<36 or >38.5
>10y - 13y	>100	>30	<90	<36 or >38.5
>13y	>100	>20	<90	<36 or >38.5

Table 2. Signs and Symptoms of Shock [6]

	Sign and/or Symptom
Peripheral Pulses	Decreased or weak Bounding
Capillary refill	≥ 3 sec Flash (< 1 sec)
Skin	Mottled, cool Flushed, ruddy, erythroderma (other than face) Petechiae below the nipple, any purpura
Mental status	Decreased, irritability, confusion inappropriate crying or drowsiness, poor interaction with parents, lethargy, diminished arousability, obtunded

History: Assess for
- Favoring an extremity/Limp
- Limp deformity
- Patient/Family skin and soft tissue infection (SSTI)
- Fever
- Trauma
- Bone Pain
- Cellulitis
- Duration of symptoms
- Pain with diaper changes (non-toilet trained children)

Physical Examination

Erythema
- Warmth
- Swelling
- Point tenderness
- Gait refusal
- Restricted movement
- Failure to bear weight
- Metaphyseal pain
- Fever

Laboratory Tests

Obtain a blood culture, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and complete blood cell count (CBC).
Obtain a BUN/Creatinine for antibiotic monitoring parameters.

Diagnostic Imaging Studies

Obtain a radiograph to rule out fracture or malignancy.
Obtain an ultrasound to rule out joint effusion of the hip.
Consider obtaining magnetic resonance imaging (MRI) for diagnostic and surgical interventions.

Critical Points of Evidence*

TCH Evidence-Based Recommendations

Evidence Supports

- Obtain a blood culture in patients with suspected AHO and/or septic arthritis. [7-16] – Strong recommendation, low quality evidence
  Remarks: According to a sample of TCH patients [12], the median time to positivity of a blood culture was 16.3 hours (IQR 12.5-19.5 hours).
- Initiate IV antibiotics after drawing a blood culture if suspicion of AHO and/or septic arthritis. [8,12,14,16,17] – Strong recommendation, low quality evidence
- For suspected AHO not requiring surgery, if blood and body fluid cultures remain negative at 24 hours, obtain an IR-performed bone biopsy with culture as soon as possible to maximize yield. [7,12,14,16,18] – Strong recommendation, low quality evidence
- Utilize MRI for diagnostic imaging and surgical interventions for patients with suspected AHO and/or suspected septic arthritis of the hip with a Kocher score of 2-4 or suspected septic arthritis of a non-hip joint. [13,19-31] – Strong recommendation, low quality evidence
- Administer short-term parenteral antibiotics followed by oral therapy for uncomplicated, confirmed AHO and/or septic arthritis. Criteria for transition to oral therapy include: afebrile, clinical improvement (e.g., weight-bearing, ambulating), source control (e.g., adequate surgical drainage), clearance of bacteremia (≥2 negative blood cultures), ability to take oral antibiotics, improving CRP, no evidence of endovascular disease (if evaluation is warranted), organism sensitive to age-appropriate oral antibiotics. [18,32-45] – Strong recommendation, low quality evidence
- Use scheduled acetaminophen or ibuprofen for patients with AHO and/or septic arthritis and mild pain (pain scores ≤4). [46-49] – Strong recommendation, low quality evidence
  Remarks: Scheduled acetaminophen and ibuprofen are equally effective for pain control. Ketorolac and ibuprofen *should not* be given concurrently. In a patient with AHO and/or septic arthritis, strongly consider administering an anti-inflammatory agent.
- Use ibuprofen, acetaminophen, or oxycodone for patients with AHO and/or septic arthritis and moderate pain (pain scores >4). [46-49] – Strong recommendation, low quality evidence
  Remarks: Scheduled acetaminophen and ibuprofen are equally effective for pain control. Ibuprofen alone or acetaminophen alone may not result in adequate analgesia for patients with moderate pain. Ketorolac and ibuprofen *should not* be given concurrently. In a patient with AHO and/or septic arthritis, strongly consider administering an anti-inflammatory agent.
- Use IV ketorolac perioperatively (≤5 days duration) in patients with AHO and/or septic arthritis and moderate pain (pain scores >4). [50-56] – Strong recommendation, low quality evidence
  Remarks: Ketorolac and ibuprofen *should not* be given concurrently.
- Children with clinical features concerning for septic hip arthritis should have a diagnostic evaluation (i.e., needle aspiration, arthroscopy, or arthrotomy of the hip joint) if the patient has an elevated laboratory marker (WBC >12X10^3/µL, ESR >40 mm/h, or CRP >2 mg/dL [20 mg/L]), an effusion, and a Kocher score of 2-4 (1 point for each of the following: non weight bearing, ESR >40 mm/h, fever, WBC >12X10^3/µL). [13,57-70] – Strong recommendation, low quality evidence
- Children with clinical features concerning for septic hip or shoulder arthritis should undergo a diagnostic and/or therapeutic evaluation as soon as possible given the known sequelae of delayed treatment. [71-74] – Strong recommendation, very low quality evidence
- Consult Orthopedics if the joint aspiration is purulent, turbid, or positive for any of the following findings: WBC >50X10^3 µL, neutrophil >90%, positive gram stain. [75] – Strong recommendation, very low quality evidence
  Remarks: The absence of purulent/turbid fluid does not rule out an infection.

Evidence Against

- Do not *routinely* obtain a post-surgical MRI. Consider a post-surgical MRI if persistent, worsening, or new clinical findings. [22,76] – Strong recommendation, very low quality evidence

Evidence Lacking/Inconclusive

- Utilize ESR, CRP, and CBC, in conjunction with other diagnostic studies, to establish a diagnosis of AHO and/or septic arthritis. [13,57-70] – Strong recommendation, very low quality evidence
  Remarks: Patients without an elevated ESR, CRP, or CBC are not likely to have AHO and/or septic arthritis; the value of these laboratory tests lies in their negative predictive value. In patients with an elevated ESR, CRP, or CBC, further tests to diagnose AHO and/or septic arthritis are warranted.
- Consider additional analgesia for patients with AHO and/or septic arthritis and moderate pain (pain scores >4) who are receiving ibuprofen, acetaminophen, or oxycodone. [46-49] – Weak recommendation, very low quality evidence
  Remarks: Ibuprofen alone or acetaminophen alone may not result in adequate analgesia for patients with moderate pain. Ketorolac and ibuprofen *should not* be given concurrently. In a patient with AHO and septic arthritis, strongly consider administering an anti-inflammatory agent.

- Use IV morphine in conjunction with acetaminophen or ibuprofen for patients with AHO and/or septic arthritis and severe pain (pain scores >7). [77,78] – Strong recommendation, very low quality evidence
  Remarks: Ibuprofen alone or acetaminophen alone may not result in adequate analgesia for patients with severe pain. IV morphine provides faster pain relief than oral morphine or oxycodone.
- No evidence found regarding the use of procalcitonin as a diagnostic adjunct for children with suspected AHO and/or septic arthritis. – Unable to make a recommendation
- Currently, there is not enough evidence to support an evidence-based recommendation for the use of percutaneous aspiration as a first-line treatment option for septic arthritis. The team recommends continued research in this area to further understand the significance of utilization in pediatric septic arthritis. [65,71,79-82] – Unable to make a recommendation

*NOTE: The references cited represent the entire body of evidence reviewed to make each recommendation.

Condition-Specific Elements of Clinical Management

Treatment Recommendations

We recommend Vancomycin (15 mg/kg/dose, q6 to q8 hours) for the initial therapy for children with moderate to severe bone and joint infections. For severe infections, we recommend the addition of Cefazolin (25-33mg/kg/dose [100 mg/kg/DAYdivided every 6 to 8 hours]) or Nafcillin (37.5-50 mg/kg/dose q6 hours).
In children less than 3 to 5 years of age, we recommend the addition of Cefazolin (25-33mg/kg/dose [100 mg/kg/DAYdivided every 6 to 8 hours]) or Nafcillin (37.5-50 mg/kg/dose q6 hours) to cover for *Kingella kingae*. *Kingella kingae* infections are more common in children under the age of 3 but can also occur in children up to the age 5.
Clindamycin (13 mg/kg/dose q8 hours) may be considered for the treatment of bone and joint infections in children with mild disease caused by *Staphylococcus aureus,* but recent TCH data suggest clindamycin resistance rates of up to 30% for invasive staphylococcal disease.

Antibiotic Recommendations

In Houston, children with suspected musculoskeletal infections should be empirically treated to cover *S. aureus*. *S. aureus* is responsible for the overwhelming majority of skin and soft tissue infections seen at TCH. About 30% of *S. aureus* osteomyelitis infections at TCH are MRSA. Local surveillance data from the Infectious Disease laboratory reports that for community *S. aureus* isolates at TCH, 16% are clindamycin-resistant.

Bone Biopsy/Initiation of Antibiotics

Antibiotics should be initiated immediately if there is suspicion of AHO and/or septic arthritis. For suspected AHO not requiring surgery, if blood and body fluid cultures remain negative at 24 hours, obtain a bone biopsy as soon as possible to maximize yield.

Duration of Antibiotic Therapy

The duration of treatment for osteomyelitis can range from 3 to 12 weeks, with most patients requiring treatment for 4 to 6 weeks. Typically, the duration of treatment for septic arthritis is 3 weeks. Treatment duration is dependent on the extent of the disease, causative organism, and inflammatory markers.

Admission Criteria

- Suspected AHO
- Suspected Septic Arthritis of the hip or shoulder

Discharge Criteria

- Clinical improvement (e.g., improved range of movement, pain controlled, weight-bearing, ambulating)
- Source control (e.g., adequate surgical drainage)
- Appropriate mental status for age
- Tolerating PO and able to take oral antibiotics
- Appropriate support system (e.g., PMD, caregivers)
- Afebrile
- Improving CRP
- Home care/transfer arranged
- Home Health orders for PICC placed, if needed
- Clearance of bacteremia (≥2 negative blood cultures) Baseline “monitoring labs” obtained
- Follow-up visits scheduled (e.g., PMR, Infectious Disease, PT, Ortho)
- Plan of care for antibiotics
- No evidence of endovascular disease, if evaluation is warranted
- Organism sensitive to age-appropriate oral antibiotics

Consults/Referrals

Consult Orthopedic Surgery for patients with complicated osteomyelitis requiring drainage or debridement.
Consult Orthopedic Surgery for patients with suspected septic arthritis of the hip and a Kocher score of 2-4.
Consult Interventional Radiology for bone biopsy, PICC line Placement, or joint aspiration of the hip.
Consult Infectious Disease as soon as there is concern for AHO and/or septic arthritis of the hip.
Consult Physical Therapy for concern regarding range of motion and gait training, following surgical intervention.
Request to see Child Life for coping techniques, procedural teaching, and psychosocial support

Follow-Up Care

Follow-up care is recommended for all children hospitalized with AHO and septic arthritis.
For a child who is not following the expected clinical course, consider complications, such as an alternative or ineffective antibiotic treatment due to lack of antibiotic coverage or resistance patterns.

Measures

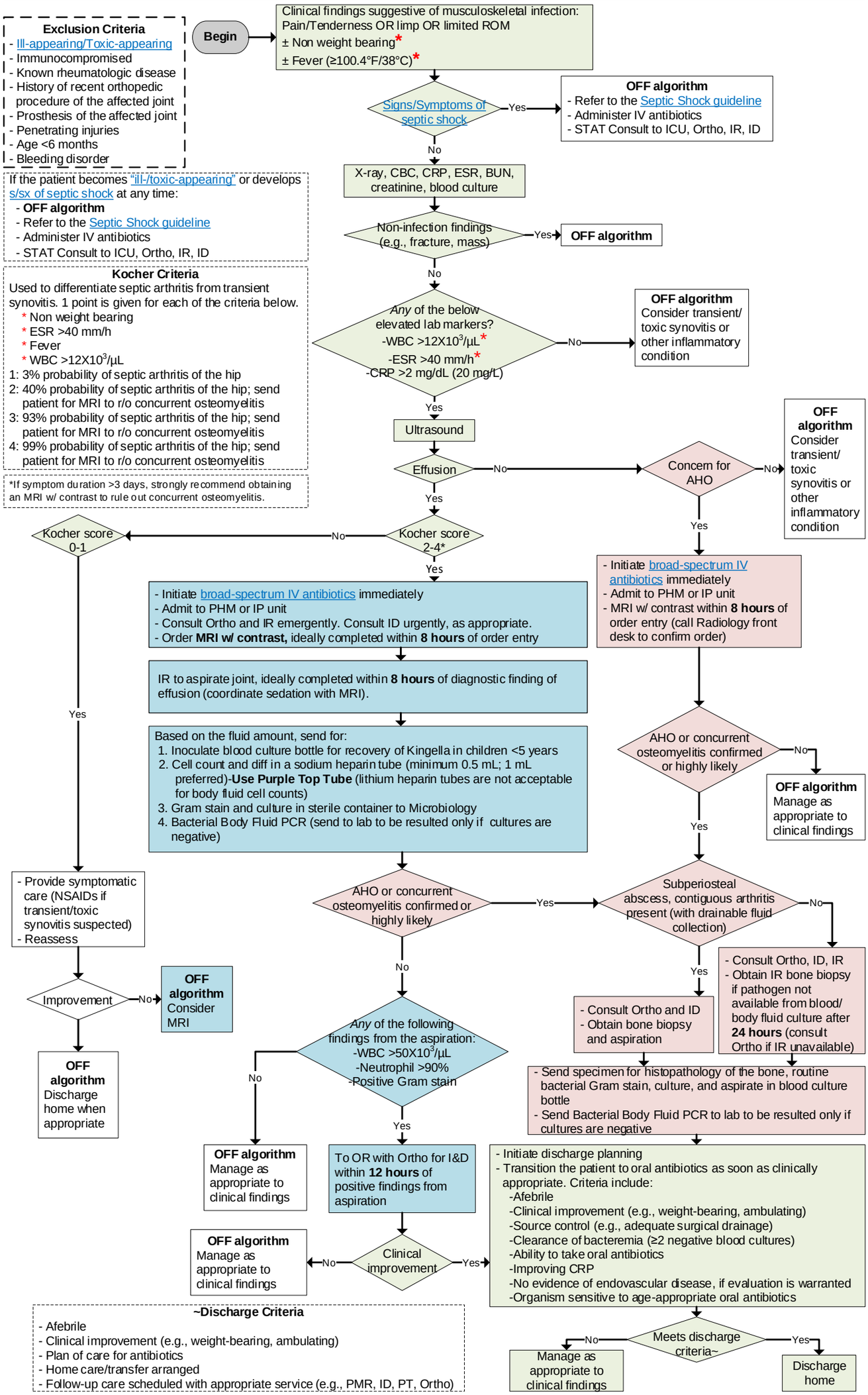
Process

- Time to obtain MRI from order entry
- Time to hip joint aspiration from IR consult order
- Time to first dose of antibiotics

Outcome

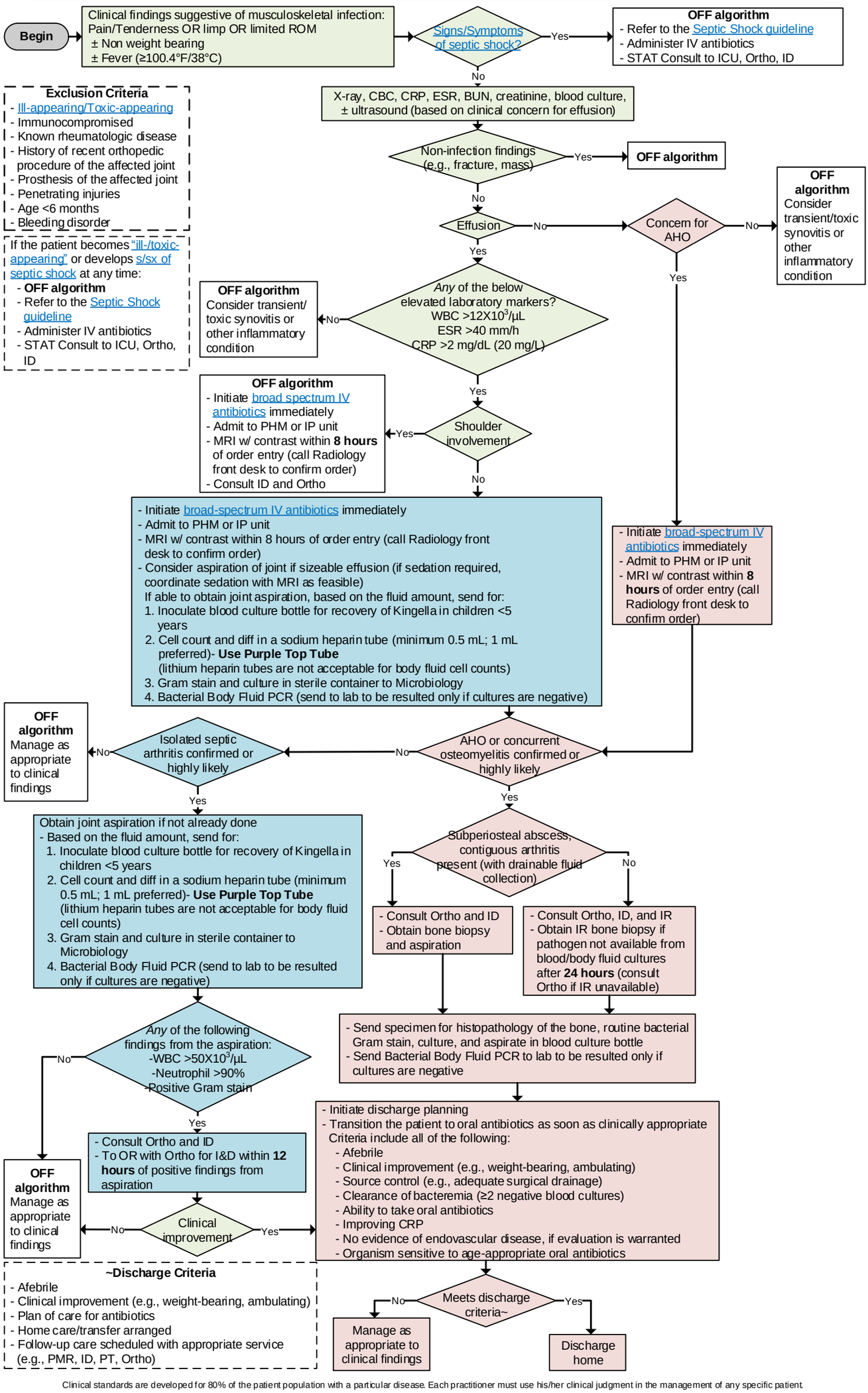
- Length of stay (e.g., inpatient, observation)

TCH Evidence-Based Outcomes Center
Clinical Algorithm for Suspected Acute Hematogenous Osteomyelitis (AHO) and/or Septic Arthritis of the HIP



Clinical standards are developed for 80% of the patient population with a particular disease. Each practitioner must use his/her clinical judgment in the management of any specific patient.

TCH Evidence-Based Outcomes Center
Clinical Algorithm for Suspected Acute Hematogenous Osteomyelitis (AHO) and/or Septic Arthritis of the NON-HIP (See separate algorithm for hips)



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Clinical Standards Preparation

This clinical standard was prepared by the Evidence-Based Outcomes Center (EBOC) team in collaboration with content experts at Texas Children's Hospital. Development of this clinical standard supports the TCH Quality and Patient Safety Program initiative to promote clinical standards and outcomes that build a culture of quality and safety within the organization.

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No relevant financial or intellectual conflicts to report.

Development Process

This clinical standard was developed using the process outlined in the EBOC Manual. The literature appraisal documents the following steps:

1. Review Preparation
   - PICO questions established
   - Evidence search confirmed with content experts
2. Review of Existing External Guidelines
   - Cincinnati Children's Hospital Treatment of Acute Hematogenous Osteomyelitis Best Evidence Statement (BESt; 2011)
3. Literature Review of Relevant Evidence
   - Searched: PubMed, Cochrane, Google
4. Critically Analyze the Evidence
   - 9 randomized controlled trials and 64 nonrandomized studies
5. Summarize the Evidence
   - Materials used in the development of the clinical standard, literature appraisal, and any order sets are maintained in a Musculoskeletal Infections evidence-based review manual within EBOC.

Evaluating the Quality of the Evidence

Published clinical guidelines were evaluated for this review using the **AGREE II** criteria. The summary of these guidelines are included in the literature appraisal. AGREE II criteria evaluate Guideline Scope and Purpose, Stakeholder Involvement, Rigor of Development, Clarity and Presentation, Applicability, and Editorial Independence using a 4-point Likert scale. The higher the score, the more comprehensive the guideline.
This clinical standard specifically summarizes the evidence *in support of* or *against* specific interventions and identifies where evidence is *lacking/inconclusive*. The following categories describe how research findings provide support for treatment interventions.
"Evidence Supports" provides evidence to support an intervention
"Evidence Against" provides evidence against an intervention.
"Evidence Lacking/Inconclusive" indicates there is insufficient evidence to support or refute an intervention and no conclusion can be drawn *from the evidence.*
The **GRADE** criteria were utilized to evaluate the body of evidence used to make practice recommendations. The table below defines how the quality of the evidence is rated and how a strong versus weak recommendation is established. The literature appraisal reflects the critical points of evidence.

Recommendation	
STRONG	Desirable effects clearly outweigh undesirable effects or vice versa
WEAK	Desirable effects closely balanced with undesirable effects
Quality	**Type of Evidence**
High	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies
Moderate	Evidence from RCTs with important limitations (e.g., inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies
Low	Evidence for at least 1 critical outcome from observational studies, RCTs with serious flaws or indirect evidence
Very Low	Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence

Recommendations

Practice recommendations were directed by the existing evidence and consensus amongst the content experts. Patient and family preferences were included when possible. The Content Expert Team and EBOC team remain aware of the controversies in the diagnosis/management of musculoskeletal infections in children. When evidence is lacking, options in care are provided in the clinical standard and the accompanying order sets (if applicable).

Approval Process

Clinical standards are reviewed and approved by hospital committees as deemed appropriate for its intended use. Clinical standards are reviewed as necessary within EBOC at Texas Children's Hospital. Content Expert Teams are involved with every review and update.

Disclaimer

Practice recommendations are based upon the evidence available at the time the clinical standard was developed. Clinical standards (guidelines, summaries, or pathways) do not set out the standard of care and are not intended to be used to dictate a course of care. Each physician/practitioner must use his or her independent judgment in the management of any specific patient and is responsible, in consultation with the patient and/or the patient's family, to make the ultimate judgment regarding care.

Version History

Date	Comments
Mar 2012	AHO guideline originally completed
Nov 2015	SA evidence summary originally completed
Jul 2016	AHO guideline updated
Sep 2018	SA evidence summary updated
Nov 2019	Merged the AHO guideline and the SA evidence summary. Reaffirmed/Updated practice recommendations and updated the algorithms.
Nov 2020	Updated Cefazolin dosing recommendations for infants and children.
Jan 2021	Updated Hip Algorithm- Care coordination
Sept 2021	Signs and Symptoms of Shock Table Revised
Feb 2024	Removed EC Joint Aspiration Care Coordination algorithm from Hip Algorithm.