ACUTE HEMATOGENOUS OSTEOMYELITIS AND PYOGENIC ARTHRITIS GUIDELINE

Definition:

Osteomyelitis is inflammation of the bone and bone marrow generally caused by a bacterial infection. The most common form in childhood is acute hematogenous osteomyelitis (AHO), which is infection of the bone of less than two weeks duration spread hematogenously. [1]

Incidence:

The incidence of acute hematogenous osteomyelitis is approximately 60/100,000 cases, accounting for one percent of pediatric hospitalizations. The risk is higher in younger children, with 50% of cases identified in children younger than five years of age. [7] Boys are affected about twice as often as girls. [2,3] The majority of cases are limited to a single anatomic site.

Etiology:

Acute hematogenous osteomyelitis typically arises in the metaphysis of long tubular bones, with approximately two-thirds of all cases involving the femur, tibia or humerus. While a variety of bacterial pathogens may be involved, *Staphylococcus aureus* is the pre-eminent pathogen and is responsible for 70–90% of acute hematogenous osteomyelitis infections in children. Other etiological agents, in no particular order, include *Streptococcus pyogenes, Streptococcus pneumoniae, Group B streptococci, coagulase-negative staphylococci, Kingella kingae*, enteric Gram-negative bacilli and anaerobic bacteria. [1,4-5]

Diagnosis:

The diagnosis of osteomyelitis depends primarily on clinical findings. Patients most commonly complain of pain at the affected site that may be associated with noted erythema, warmth, or edema. Symptoms may be present for days to weeks and often are associated with fever. Diagnostic imaging and laboratory results can assist with the diagnosis. Plain radiographs of the affected region are most helpful in narrowing the differential as they may not show significant changes early in AHO. Magnetic resonance imaging (MRI) is the most accurate modality, with high sensitivity and specificity, even in early disease. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are important non-specific inflammatory markers that can be followed during treatment to assess clinical response. Blood cultures are positive in approximately 50% of patients with AHO and should be drawn prior to initiating therapy. [7]

Clinical features suggestive of bone infection:

- Constitutional symptoms (irritability, decreased appetite or activity), with or without fever
- Focal symptoms and signs of inflammation (pain, erythema, swelling, and tenderness)
- Limitation of function (limp, limited use of an extremity)
- Elevation of ESR and/or CRP levels

Differential Diagnosis:

- Transient synovitis
- Reactive arthritis
- Legg-Calve´-Perthes disease
- Pyogenic arthritis
- Malignancy
- Chronic Osteomyelitis
- Trauma
- Fracture
- Sickle Cell Disease
- Juvenile idiopathic arthritis
- Slipped capital femoral epiphysis

Guideline Inclusion Criteria: [14-19]

- Physical exam and/or history suggestive of acute hematogenous osteomyelitis or septic joint.
- Less than 14 days of signs and symptoms
- Previously healthy children ages 6 months to 18 years of age.

Guideline Exclusion Criteria: [8,14-15]

- Evidence of sepsis or hemodynamic instability
- Contiguous osteomyelitis: penetrating trauma or fracture

Complicated or difficult to treat osteomyelitis

- Multifocal
- Chronic
- Head, face, or orbital involvement
- Presence of orthopedic device or prosthesis
- Post-operative wound
- Presence of an indwelling vascular catheter

History of the following disease states:

- Bone or cartilage disorder
- Congenital or acquired bone disease
- Congenital or acquired immunodeficiency
- Type I or II diabetes
- Sickle cell disease
- Chronic sinusitis
- Sacroiliitis
- Fasciitis
- Synovitis
- Arthropathy

Transition to Management off Pathway

- Culture is negative
- Culture is positive for bacterial etiology other than methicillin-sensitive *Staphylococcus aureus* (MSSA) or *Kingella kingae*
- Culture is positive for methicillin-resistant *Staphylococcus aureus* (MSRA)
- Culture was positive for MSSA or *Kingella kingae* and patient does not meet criteria for oral step-down therapy in <5 days of start of focused antibiotic therapy.

Diagnostic Evaluation:

History: Assess for

- Bone pain for several days
- Restricted use of the involved limb
- Minor trauma coincident with bacteremia
- Fever

Physical Examination: Assess for

- Constitutional symptoms of infection that are consistent with osteomyelitis, with or without fever
- Signs of localized inflammation of bone, including redness, swelling, point tenderness, and/or loss of function.
- Warmth, swelling, and point tenderness of the involved site.

Critical Points of Evidence

Evidence Supports

Early transition to oral antimicrobial therapy (≤5 days) compared to prolonged intravenous antimicrobial therapy for duration of treatment. [9, 14-17, 20-24]

Use of a combination of laboratory tests to confirm likelihood of diagnosis: blood culture, CRP, and ESR.

Use of MRI as the preferred imaging study for diagnosis. [5-6,20]

Use of molecular diagnostics (i.e. polymerase chain reaction) to determine the etiology when obtained cultures are negative (specifically for *Kingella kingae*).

Empiric antimicrobial therapy that includes an agent directed against MRSA. [7,11,25-26]

Evidence Lacking/Inconclusive

The quantitative CRP measurement to best measure clinical response and guide decisions regarding transition from intravenous to oral antimicrobial therapy.

Optimal duration of intravenous antimicrobial therapy prior to transition to oral antimicrobial therapy.

Optimal duration of combined intravenous and oral antimicrobial therapy for complete clinical cure/resolution.

Evidence Against

Routine use of MRI to assess for clinical cure/improvement

Practice Recommendations

Laboratory Testing

An initial diagnostic evaluation should be ordered prior to start of antibiotic therapy; CRP and ESR can be followed to track resolution of the illness. [7]
(Strong recommendation, Moderate quality evidence.)

Cultures are critical to focus antimicrobial therapy, blood cultures and aspirate should be performed prior to the initiation of antimicrobial therapy if the patient is stable. [11]
(Strong recommendation, Moderate quality evidence.)

Polymerase chain reaction (PCR) tests for *Staphylococcus aureus* and *kingella kingae* should be ordered if culture is negative.
(Strong recommendation, low quality evidence)

Imaging
Plain film radiograph should be ordered for the affected region; critical for excluding differential diagnosis such as fracture or malignancy. [33]
(Strong recommendation, Moderate quality evidence.)

MRI is the modality of choice when imaging other than plain radiography to establish the diagnosis of osteomyelitis or to delineate the location and extent of bone involvement. [5-6,20,33-36]
(Strong recommendation, High quality evidence.)

Antibiotic Therapy
Empiric antimicrobial therapy that includes an agent directed against MRSA should be started early and after cultures have been obtained.
(Strong recommendation, moderate quality evidence)

Following a short intravenous antimicrobial therapy (≤5 days) the patient should be transitioned to oral antibiotics.
(Strong recommendation, Moderate quality evidence.)

Clinical Management
(for full recommendations see attached pathway and addendums)

Laboratory Assessment:
Diagnostic: *(See Addendum 3 for Diagnostic Test algorithm)*
Initial test prior to antibiotic therapy should include [8-12]:
- Complete Blood Count (CBC) with differential
- Comprehensive Metabolic Panel (CMP)
- Erythrocyte Sedimentation Rate (ESR)
- C - reactive protein (CRP)
- Blood culture minimum of one set

CRP test should be repeated every 48 hours to evaluate response to antimicrobial therapy. Surgery may cause an increase in CRP level of patients and should be accounted for when evaluating patient response to antimicrobial therapy

Fluid/tissue sample should be collected for diagnostic if aspiration is indicated.

Antibiotics should be withheld until cultures are obtained unless patient condition warrants administration.

Imaging Assessment:
Magnetic Resonance Imaging:
(See MRI Block Time Algorithm)
MRI has been found to be extremely sensitive 97% and specific 92% in helping to diagnose hematogenous osteomyelitis infections. [36]

Orthopedic should be consulted prior to MRI to coordinate aspiration procedure if indicated.

MRI orders should include the following information:
- Priority: **STAT**
- Reason for exam: OSTEO-ORTHO PROTOCOL
- Call reporting to: **MD name**
- Phone number: **MD telephone number**

Antibiotics:
(See Addendum 2 for dose guidelines)
Empiric antibiotic therapy should be started prior to identification of specific etiologic agent: [6-7,14,18-20,27,25,33]
- patients less than 4 years of age should receive clindamycin and ceftriaxone
- patients 4 years of age or older should receive clindamycin and cefazolin

(Strong recommendation, moderate quality evidence)

Focused antibiotic therapy based on etiologic agent and Susceptibilities: [6-7,19-20,27,36]
- MSSA – Oxacillin
- Kingella kingae – Ceftriaxone

(Strong recommendation, moderate quality evidence)

Antibiotic oral therapy transition:
(See Addendum 2 for dose guidelines)
The following criteria must be met in less than 5 days to transition to oral antibiotics: [7,9-11,14-18,23]
- Confirmed diagnosis of uncomplicated osteomyelitis
- Clinical improvement of signs and symptoms
- Afebrile for at least 48 hrs
- CRP decreased from 50% of initial CRP
- Received at least 72 hrs of IV antibiotics

(Strong recommendation, Moderate quality evidence.)

Oral antibiotic therapy options based on etiologic agent: [6-7,14,18-20,27,31,36]
- MSSA – Cephalexin
- Kingella kingae – Amoxicillin/Clavulanate

(Strong recommendation, Moderate quality evidence.)

Additional antimicrobial therapy options: [6-7,20,27-29,36]
(REQUIRES INFECTIOUS DISEASES APPROVAL, See Addendum 2 for recommendations)

Discharge Criteria
- Patient is afebrile for 24 hours with clinical improvement in symptoms and physical exam
- Patient has tolerated one dose of oral antibiotics identical to the planned home regimen in the hospital
- Scheduled follow-up with the primary pediatrician, infectious disease, and orthopedics is arranged.
- Antibiotic prescription is filled and delivered prior to discharge or easily accessible by parents immediately after discharge to avoid missed dose

(Strong recommendation, low quality evidence)

Consults/Referrals:

- Orthopedic consultation early to evaluate need for additional imaging and if aspiration is necessary.
- Infectious Diseases consultation early for diagnostic and antibiotic guidance.
    - Certain antimicrobial therapy options require approval from Infectious Diseases.

Outcome Measures

See addendum 4.

Addendums

- DCMC Acute Hematogenous Osteomyelitis Antibiotic Dosing and Recommendations
- DCMC Acute Hematogenous Osteomyelitis Diagnostic Testing ordering form and information
- DCMC Acute Hematogenous Osteomyelitis Scorecard

ACUTE HEMATOGENOUS OSTEOMYELITIS PATHWAY

EVIDENCE-BASED OUTCOME CENTER

INCLUSION CRITERIA

- Physical exam and/or history consistent with ACUTE hematogenous osteomyelitis or septic joint
- Less than 14 days of signs and symptoms
- Previously healthy children ages 6 months to 18 years of age

EXCLUSION CRITERIA

- Evidence of sepsis or hemodynamic instability
- Contiguous osteomyelitis: penetrating trauma or fracture
- Complicated or difficult to treat osteomyelitis
  - Multifocal
  - Chronic
  - Head, face, or orbital involvement
  - Presence of orthopedic device or prosthesis
  - Post-operative wound

History of the following disease states:

- Bone or cartilage disorder
- Congenital or acquired bone disease
- Congenital or acquired immunodeficiency
- Type I or II diabetes
- Sickle cell disease
- Chronic sinusitis
- Sacroiliitis
- Fasciitis
- Synovitis
- Arthropathy

RECOMMENDED INITIAL DIAGNOSTIC EVALUATION

Labs:
CBC w/diff
BMP
CMP
ESR
CRP
Blood Culture

Imaging:
Order plain film of affected region

Consult Orthopedics to evaluate need for additional imaging and aspiration

High clinical suspicion?

- No → **Manage OFF-Pathway**
- Yes →

Immediate Aspiration/ I&D
Addendum 3 for specimen requirements

- Yes → Coordinate w/Anesthesia & Orthopedics
- No → MRI indicated Addendum 1

MRI indicated Addendum 1 → Yes

- Age ≥ 3 → "Fast" MRI Rapid Sequence Protocol
- Age < 3 → Sedatation Osteo Protocol

"Fast" MRI Rapid Sequence Protocol → Failed → Sedatation Osteo Protocol

Images consistent with Acute Osteo/Septic Joint?

- Yes → Aspiration Consult w/ Anesthesia & Orthopedics Addendum 3 for specimen requirements
- No → **Manage OFF-Pathway**

Aspiration Consult w/ Anesthesia & Orthopedics Addendum 3 for specimen requirements → START EMPIRIC ANTIBIOTIC THERAPY (See Addendum 2 for antibiotic dosing)

ID Consultation

Age < 4 years	Age ≥ 4 years
Clindamycin + Ceftriaxone	Clindamycin + Cefazolin

Inpatient Care

1. MRSA/MRSA nasal swab
2. CRP every 48 hrs.
3. Focus antibiotic therapy based on CR results (Addendum 2)

Meets Criteria for oral step-down therapy?

- Confirmed diagnosis of acute hematogenous osteomyelitis
- Clinical improvement of signs and symptoms
- Afebrile for at least 24 hrs
- CRP decreased 50% from initial CRP
- Received at least 72 hrs of IV antibiotics

- No → **Manage OFF-Pathway**
  - Shared decision-making: ID/Ortho/PCRS
  - develop plan of care for antibiotic selection, route, and duration of therapy
  - Treatment plan discussed with family, care team agreement/discussion
- YES →

DISCHARGE CRITERIA

- Afebrile for 24 hours with clinical improvement in symptoms and physical exam.
- Tolerated one dose of oral antibiotics identical to the planned home regimen in the hospital.
- Scheduled follow-up with the primary pediatrician, infectious disease, and orthopedics.
- Antibiotic prescription is filled and delivered prior to discharge or easily accessible by parents immediately after discharge

ADDENDUM 1: Rapid Osteo Protocol

RAPID SEQUENCE ("FAST") NON-SEDATED MRI *WITHOUT* CONTRAST

- "Fast" imaging reduces time in scanner from 45+ min to under 7 min
- When possible, non-sedated MRI's can be attempted the afternoon/ evening of patient presentation (without anesthesia on standby)

Order a MRI with the following information:

- **Priority: STAT**
- **Reason for exam: RAPID OSTEO PROTOCOL**
- **Order Without Contrast**
- **Call reporting to: Please list call back name/number**
  - **1st Option: Pedi Ortho PA**
  - **2nd Option: PCRS attending on-call**
- **Phone number: MD telephone number**

SEDATION OSTEO PROTOCOL

INCLUSION CRITERIA: All Children aged < 3 or Failed Rapid Protocol

Order a MRI with the following information:

- **Priority: STAT**
- **Reason for exam: SEDATION OSTEO PROTOCOL**
- **MRI/ or block time @07:00AM may be used if approved by Ortho team**
- **Call reporting to: MD name**
- **Phone number: MD telephone number**

Place NPO orders per anesthesia guidelines

ADDENDUM 2

DCMC ACUTE HEMATOGENOUS OSTEOMYELITIS ANTIBIOTIC DOSING AND RECOMMENDATIONS

EMPIRIC ANTIBIOTIC THERAPY		
Age < 4 years Potential pathogens: *S. aureus* *S. pyogenes* *S. pneumoniae* *Kingella kingae*	Clindamycin 40 mg/kg/day IV divided every 6 hours + Ceftriaxone 100 mg/kg/day IV every 24 hours	Maximum dose: 600 mg/dose, 2400 mg/day May consider every 8 hour dosing for home therapy only Recommended monitoring: CBC
		Maximum dose: 2000 mg/dose, 4000 mg/day May consider 100 mg/kg/day IV divided every 12 hours for patients > 20 kg or those requiring >2000 mg/dose Recommended monitoring: CBC +/- CMP
Age ≥ 4 years Potential pathogens: *S. aureus* *S. pyogenes*	Clindamycin 40 mg/kg/day IV divided every 6 hours + Cefazolin 150 mg/kg/day IV divided every 8 hours	See above 900 mg/dose, 2700 mg/day reserved for patients with severe disease and/or patients that are obese
FOCUSED ANTIBIOTIC THERAPY		
MSSA *Intravenous Therapy*	Oxacillin 200 mg/kg/day IV divided every 4 to 6 hours *(consider continuous infusion)*	Maximum dose: 2000 mg/dose, 12 gram/day May consider continuous infusion for home therapy Recommended monitoring: CBC & CMP
MSSA *Oral Therapy*	Cephalexin 150 mg/kg/day PO divided every 6 hours	Maximum dose: 1000 mg/dose, 4000 mg/day Renal dosage adjustment if CrCl < 10 mL/min May consider every 8 hour dosing for home therapy only Recommended monitoring: CBC +/- CMP
Kingella kingae *Intravenous Therapy*	Ceftriaxone 100 mg/kg/day IV every 24 hours	See above
Kingella kingae *Oral Therapy*	Amoxicillin/clavulanate 90 mg/kg/day PO divided every 12 hours *(dosed based on amoxicillin component)*	Maximum dose: 4000 mg amoxicillin component/day Renal dosage adjustment if CrCl < 30 mL/min Recommend monitoring: CBC & CMP

Additional Antimicrobial Therapy Options which Require Infectious Diseases Approval for Use	
Clindamycin 30 mg/kg/day PO divided every 6 hours	Maximum dose: 600 mg/dose, 1800 mg/day May consider every 8 hours dosing for home therapy only Recommended monitoring: CBC
Sulfamethoxazole-trimethoprim 15-20 mg/kg/day PO divided every 6 to 12 hours *(dosed based on trimethoprim component)*	Maximum dose: 960 mg trimethoprim component/day Renal dosage adjustment if CrCl < 30 mL/min Recommended monitoring: CBC & CMP
Linezolid (less than 12 years old) 30 mg/kg/day IV/PO divided every 8 hours Linezolid (greater than or equal to 12 years old) 20 mg/kg/day IV/PO divided every 12 hours	Maximum dose: 600 mg/dose, 1200 mg/day Recommended monitoring: CBC & CMP

ADDENDUM 3

DCMC ACUTE HEMATOGENOUS OSTEOMYELITIS DIAGNOSTIC TESTING RECOMMENDATIONS

Fluid Specimens

Order the following labs in Compass:

1) Routine culture → Select specimen type → Select body site → Select collection method or source
2) Miscellaneous lab testing → Enter specimen type: ***other: see description*** and enter sample location → Enter order comment: Hold tissue/fluid in lab for possible PCR testing. Store frozen with no additives
3) Cell ct w/ diff joint fluid

**Providers may choose to order additional or alternative tests based on the clinical scenario*

During/after the procedure do the following (order of priority):

1) Inoculate x 1 AEROBIC blood culture bottle with a minimum of 0.5 mL fluid
    a. To be sent for routine culture
2) Place remaining fluid in a sterile specimen container
    a. To be held for possible PCR testing OR sent for additional tests
3) Send laboratory test down time form with the following information:
    a. Miscellaneous lab testing
    b. Specimen type: ***other: see description*** and enter sample location
    c. Write in "Hold tissue/fluid in lab for possible PCR testing. Store frozen with no additives"

If < 1.5 mL fluid then,

1) Send sterile specimen container to be held for possible PCR testing
    a. 0.5 mL required for each PCR test (Kingella kingae, S. aureus)

If ≥ 1.5 mL fluid then,

1) Send sterile specimen container for cell count with differential
    a. 0.5 mL required
2) Hold remaining fluid for possible PCR testing
    a. 0.5 mL required for each PCR test (Kingella kingae, S. aureus)

Tissue Specimens

Order the following labs in Compass:

1) Tissue culture w/ smear → Select specimen type → Select body site → Select collection method or source
2) Miscellaneous lab testing → Enter specimen type: tissue → Enter order comment: Hold tissue/fluid in lab for possible PCR testing. Store frozen with no additives

**Providers may choose to order additional or alternative tests based on the clinical scenario*

During/after the procedure do the following (order of priority):

1) Place tissue sample in sterile specimen container
2) Send laboratory test down time form with the following information:
    a. Miscellaneous lab testing
    b. Specimen type: tissue
    c. Write in "Hold tissue/fluid in lab for possible PCR testing. Store frozen with no additives"

If tissue sample size ≤ 1 x 1 mm

1) Send sterile specimen container for tissue culture w/ smear

If tissue sample size > 1 x 1 mm

1) Send sterile specimen container for tissue culture w/ smear
2) Hold remaining tissue for possible PCR testing

A 1 x 1 mm sized tissue sample required for each PCR test (*Kingella kingae*, *S. aureus*)

ADDENDUM 4

DCMC ACUTE HEMATOGENOUS OSTEOMYELITIS SCORECARD

Type of Measure	Domain	Measure Definition	Donabedian Classification	IOM Domain(s)
Care Process Team	Efficiency in Diagnosis	Utilization of MRI block schedule with Ortho Procedures	Process	Effective, Efficient, Equitable, Safe
		Utilization of laboratory tests: Kingella kingae PCR, S. aureus PCR, CRP, Cell count w/ differential, WBC, & ESR	Process	Effective, Efficient, Equitable, Safe
		Time to culture	Process	Effective, Efficient, Equitable, Safe, Timely
		Site of positive culture	Process	Effective, Efficient, Equitable, Safe
	Medications	Length of IV antimicrobial therapy	Outcome	Effective, Efficient, Equitable, Safe
		Length of PO antimicrobial therapy	Outcome	Effective, Efficient, Equitable, Safe
	Patient Experience	Number of times under sedation/received sedation.	Process	Effective, Efficient, Equitable, Safe
Avoidable Events	Hospitalizations	Rate of readmission to hospital within 30 days	Outcome	Effective, Efficient, Safe
	Infection	Rate of PICC line complications	Outcome	Effective, Efficient, Safe
Throughput		Average Length of Stay	Outcome	Care Coordination, Effective, Efficient, Safe, Timely
Financial		Average Total Cost of Care	Outcome	Effective, Efficient

OSTEO PROTOCOL LAB ORDERS

Hematology x 87037

Ordering Physician: _____

Collector's Username: _____
Date: _____ Time: _____

Patient Label

☐ **Fluid Specimen** **or** ☐ **Tissue Specimen**

Body site: _____

Send in Lavender 2ml or 0.5ml (bullet) tube, depending on volume of specimen

___ **Cell Count with Diff Body Fluid ---------- send STAT / ROUTINE**
with a callback to Surgery OR #_____ x _____

Prioritize Culture Request based on amount of fluid

Send remaining specimen in SYRINGE with sterile syringe cap to lab.

Note: Gram Stain (smear) included with Aerobic/Anaerobic Culture. Bare minimal for both Aerobic/Anaerobic total of 0.5ml

___ **Aerobic Culture (0.5ml)**

___ **Anaerobic Culture (0.5ml)**

___ **Misc lab Testing --- Hold fluid/tissue in lab for possible PCR testing. Store frozen with no additives. Each organism for PCR requires (0.5ml)**

Optional Tests:

___ **Fungal Culture(0.5ml)**

___ **AFB Culture (1.0ml)**

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2022 Revision: The osteomyelitis EBOC workgroup has made an update to the imaging piece of the osteomyelitis/septic joint protocol based on our review of current literature/expert opinion.

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