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Acute Hematogenous Osteomyelitis

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Objectives After completing this article, readers should be able to:

1. Describe the pathophysiology of acute hematogenous osteomyelitis.
2. Correlate most common infectious causes of osteomyelitis with the age of the patient.
3. Recognize the typical clinical manifestations of acute hematogenous osteomyelitis.
4. Explain the appropriate use of ancillary information obtained by laboratory determinations and imaging studies to establish the diagnosis of acute hematogenous osteomyelitis.
5. Discuss the medical and surgical principles of management in the treatment of acute hematogenous osteomyelitis.

Pathophysiology

The most common type of osteomyelitis, an infection of bone, that occurs in children is acute hematogenous osteomyelitis. Infection initially is established in the metaphyseal region of tubular bones, beginning as a metaphysitis following seeding by bacteria. The appendicular skeleton is the most common site of osteomyelitis. The lower extremity, especially the femur, is involved more often than the upper extremity, where the humerus is most likely to be infected. The pelvic bones or clavicles are less likely to be involved than the long bones of the extremities. The most common bone involved in acute hematogenous osteomyelitis in children is the femur. The axial skeleton is less likely to be the site of acute hematogenous osteomyelitis. Manifestations of osteomyelitis involving the axial skeleton are most commonly discitis, vertebral osteomyelitis, and infection involving the ribs and cranial bones.

In most cases, the preceding bacteremia leading to acute hematogenous osteomyelitis is cryptic and asymptomatic, although osteomyelitis can be a focal complication of clinically symptomatic bacteremia and even overt sepsis. The nidus of infection begins in the valveless sinusoidal loops of the venules at their reflection at the epiphysis and is attributed to slow and nonlaminar blood flow through this vascular bed. Colonization often is promoted by antecedent inconsequential trauma that causes a metaphyseal hematoma. Once an abscess is established, inflammatory recruitment of adjacent areas occurs by direct extension, usually tracing along the path of least resistance.

In neonatal osteomyelitis, infection can breach the epiphyseal growth plate through vascular channels that are present until secondary ossification centers form and the vessels atrophy. Because such atrophy is not complete until the second year after birth, epiphysitis and septic arthritis of the adjacent joint frequently complicate neonatal osteomyelitis. As the skeleton matures and the growth plate becomes avascular, the residual structure becomes durable and relatively impermeable to infectious breaches.

In older children, the metaphyseal infection of acute hematogenous osteomyelitis generally tracks parallel to the long axis of the growth plate, extending until infection ruptures through cancellous bone into the subperiosteal space. Pus and inflammatory debris may accumulate within the subperiosteal space, causing the periosteum to separate from the diaphysis of the bone, resulting in formation of a periosteal abscess. Periosteal elevation can become apparent radiographically when osteomyelitis has been untreated for several weeks. When the capsular insertion of joint synovium is distal to the epiphyseal growth plate, rupture into the periosteal space can occur within the intra-articular space.
resulting in a concomitant septic arthritis. Septic arthritis involving the hip and shoulder caused by the extension of osteomyelitis of the proximal femur and proximal humerus, respectively, occurs more frequently than does septic arthritis in other sites.

Osteomyelitis can result from penetrating trauma with direct inoculation of bacteria into bone, local spread into bone from a contiguous area of infection (skin or soft-tissue infection), infection due to vascular insufficiency such as a diabetic foot infection, infection occurring in a child who has an underlying neurovascular disease such as Charcot-Marie-Tooth disease or sickle hemoglobinopathy, or an orthotic prosthesis that becomes secondarily infected.

**Microbiology**

**Staphylococcus aureus** is and always has been the most common cause of acute hematogenous osteomyelitis in all age groups. (1) This predominance is even more pronounced since the incidence of hemoinvasive infections due to *Haemophilus influenzae* type b and *Streptococcus pneumoniae* has been reduced following implementation of universal childhood immunization against these pathogens. *S aureus* has selected virulence factors that enhance pathogenicity for osteomyelitis, including adhesions allowing attachment to bony matrix and catalytic and proteolytic enzymes that allow compromise of the integrity of local structures and host immunity, promoting extension of infection into contiguous tissues. Most strains of methicillin-resistant *S aureus* demonstrating the community-acquired pattern of antibacterial susceptibility also have additional virulence factors, such as Panton-Valentine leukocidin, which causes tissue necrosis and effectively defends the microbe against phagocytic engulfment and intracellular killing. Osteomyelitis due to methicillin-resistant *S aureus* seems to be a more severely symptomatic infection that has a greater risk for significant host morbidity than does osteomyelitis due to methicillin-susceptible *S aureus*. (2)

Less common causes of acute hematogenous osteomyelitis include *S pyogenes* and *Kingella kingae*. For children born with hemoglobin SS or SC disease, *Salmonella* are important causes of osteomyelitis. The risk in this specific population is several hundredfold greater than for children who do not have an underlying sickle hemoglobinopathy, although in some series, osteomyelitis due to *S aureus* still accounted for the greater number of cases. (3)

The potential bacterial agents causing neonatal osteomyelitis are more varied than those that cause osteomyelitis in older children. In addition to the previously discussed bacteria, *S agalactiae*, coagulase-negative staphylococci, and *Enterobacteriaceae* such as *Escherichia coli*, *Klebsiella pneumoniae*, *Serratia marcescens*, and *Citrobacter* are found.

*Pseudomonas aeruginosa* is an important cause of osteochondritis of the tarsal and metatarsal bones of the foot that results from penetrating trauma, especially as a result of stepping on a protruding nail. Infection following penetrating injury through the sole of a tennis shoe has traditionally identified this type of footwear as an important cofactor for this form of skeletal infection. Whether the bacteria have a predilection for the innersole and lining of tennis shoes or because the soft sole allows the nail to penetrate into the foot more readily is not clear.

Rarely, childhood osteomyelitis can be due to fungal pathogens. *Coccidioides immitis* is the most significant fungal pathogen, in that the organism is capable of causing skeletal infection in apparently immunologically normal hosts. *Histoplasma capsulatum* also has been reported to have caused osteomyelitis, but less frequently than *C immitis*. Most often, *Histoplasma* infection is restricted to a host who has an underlying cell-mediated immunodeficiency.

Discitis is an inflammatory process involving the discs that separate the vertebral bodies of the spinal column and most commonly occurs in toddlers and young children. The cause is less clear than that proposed for acute hematogenous osteomyelitis of the long bones; approximately 50% of cases appear to be due to sterile inflammation. Of the infectious causes, *S aureus* is the most common agent and is believed to become established by prior bacteremia and incidental trauma.

Vertebral osteomyelitis is less common than is discitis and occurs more commonly in older children and adolescents. Vertebral osteomyelitis can be caused by seeding of the vascular vertebral body through prior bacteremia, especially if the bacteremia is either prolonged and sustained or is intermittent but frequent. In addition to *S aureus*, vertebral osteomyelitis can be caused by pathogens not commonly observed in osteomyelitis involving an extremity. Vertebral osteomyelitis due to *Brucella* arises from bacteremia, often prolonged, that has resulted from previous and often ongoing consumption of contaminated meat or dairy products. Vertebral osteomyelitis specifically due to *P aeruginosa* has been associated with intravenous drug abuse. In contrast to osteomyelitis due to *Brucella* and *P aeruginosa*, vertebral osteomyelitis due...
to *C. immitis*, *H. capsulatum*, and *Mycobacterium tuberculosis* most commonly arises from a previous pulmonary focus that extends directly or through lymphatic drainage. However, vertebral osteomyelitis caused by any three of these latter pathogens in children is uncommon.

**Clinical Presentations**

Acute hematogenous osteomyelitis has two distinct presentations. The first scenario is the acutely ill, febrile child who has systemic inflammatory symptoms and signs typical of septicemia, with additional focal findings of skeletal infection. The second common clinical picture involves the child who may be afebrile or have low-grade fever and demonstrates a more gradual progression of symptoms and signs localized to the area of bony infection and manifested as pain and tenderness at the site of infection that may worsen with movement and weight-bearing. A concomitant loss of function due to bone pain that worsens when mechanical activity obligates movement or compressive torque of the infected structure is a common aspect of this presentation.

Because most cases of acute hematogenous osteomyelitis involve the ends of long bones, the area of maximum tenderness and pain with pressure coincides with the area of metaphyseal infection and can be suggested by history and demonstrated by physical examination. Innervation of bone is restricted largely to the periosteaum and does not allow the discrete point tenderness that generally is associated with skin or soft-tissue infection, but repeated examination or activities that involve the infected bone consistently elicit pain localized to the immediate area. Overall, the hallmark of osteomyelitis, regardless of the presence of fever or systemic inflammatory signs, is localized pain and diminished function.

Neonatal osteomyelitis is more likely associated with septic arthritis of the joint adjacent to the metaphyseal infection due to the vascularity of the epiphyseal growth plate and, thus, may present with symptoms and signs associated with the joint infection: localized tenderness, swelling of the synovial capsule, a position of comfort that maximizes intra-articular volume, pain and reduced range of motion with passive manipulation of the infected extremity, and pseudoparesis due to a reluctance to move the affected limb. Neonatal osteomyelitis, especially that occurring within the first postnatal month, is also more likely to be multifocal than is osteomyelitis occurring in older children and presents more often as septicemia in a critically ill patient.

Discitis and vertebral osteomyelitis present most commonly as back pain with localized tenderness at the area of involvement. The pain can be exacerbated by loading the vertebral column through sitting, standing, or walking. In most cases, the child is afebrile at the time medical attention is sought for the pain or loss of function, but a solicited history often can reveal an antecedent febrile illness or prior episode of trauma involving the back. Parents also may observe that the child seems most comfortable lying supine or being held and that any motion that provokes truncal movement elicits cries of pain.

Pelvic osteomyelitis is difficult to diagnose, and compared with osteomyelitis involving a long bone, diagnosis frequently is delayed. (4) The ilium is involved most frequently, pain most commonly is referred to adjacent structures, especially the hip or soft tissues of the thigh or buttocks, and the pain may be associated with a limp. When the sacroiliac joint is involved, compression of the pelvis by bilateral simultaneous inward pressure applied to the iliac crests can exacerbate pain localizing to the sacroiliac, as can maneuvers that cause pelvic torque, such as flexion, abduction, and external rotation of the hip. The best diagnostic tool for pelvic osteomyelitis is a high degree of suspicion on the part of the examiner. The child who presents with pain involving the hip, anterior or posterior thigh, or lower abdomen that is exacerbated and associated with reduced function with pelvic motion, weight-bearing, or walking, and in whom other causes of pain have been excluded should be suspected of having pelvic osteomyelitis until the condition can be excluded by imagining studies.

**Diagnosis**

The ancillary evaluations most helpful in establishing the diagnosis of osteomyelitis are serum markers of inflammation, specifically, the complete blood count, C-reactive protein concentration, and erythrocyte sedimentation rate. Most children who have acute hematogenous osteomyelitis have a peripheral leukocytosis at presentation, with the total leukocyte count modestly elevated to values of 12 to 16 × 10^9/L (12 to 15 × 10^9/L), although an increased number of immature polymorphonuclear leukocyte forms may not be present. Established osteomyelitis generally is associated with an elevated erythrocyte sedimentation rate ranging from 30 to 50 mm/hour. The most important acute-phase reactant of the serum inflammatory proteins contributing to the erythrocyte sedimentation rate is fibrinogen, which has a circulatory life of approximately 4 days. Hence, the erythrocyte sedimentation rate often is normal or only
modestly elevated during the first days of acute hematogenous osteomyelitis and may not rise appreciably until the infection has been present for approximately 1 week.

Use of serum C-reactive protein concentrations to evaluate a patient for possible osteomyelitis has garnered favor because this acute-phase reactant has a serum circulation life of approximately 1 day and tends to become elevated sooner than does the erythrocyte sedimentation rate in the early stage of acute hematogenous osteomyelitis. Conversely, the C-reactive protein concentration declines to normal values more rapidly than does the erythrocyte sedimentation rate following institution of appropriate therapy. Serial determinations of C-reactive protein concentrations have been proposed as a predictor of outcome (5) because higher concentrations present beyond the third day of therapy retrospectively identified patients more likely to have a complicated treatment course. Prospective serial determinations may lack the precision to be useful in predicting outcomes for individual patients.

Neither an elevated erythrocyte sedimentation rate nor C-reactive protein concentration is specifically diagnostic for osteomyelitis due to the nonspecific nature of acute-phase reactants. Both of these determinations must be interpreted in the context of a child who has symptoms and signs consistent with osteomyelitis.

Imaging studies are a useful adjunct in establishing the diagnosis of acute hematogenous osteomyelitis. Radiographic evaluation generally is the initial imaging evaluation due to its ease of acquisition and ability to evaluate for other bony conditions, such as fractures. However, the radiographic abnormalities associated most commonly with osteomyelitis are not apparent until the infection has been established for a minimum of 10 to 14 days. That period of time is required for demineralization caused by inflammatory osteoclastic activity associated with infection to become visible (Fig. 1). Triphasic radioisotope scanning with $^{99m}$technetium is more sensitive in detecting acute osteomyelitis earlier than is radiography (6) and has high accuracy in identifying osteomyelitis present for at least 3 days. Scintigraphic scanning may yield falsely negative results during the first 3 days of infection in children (7) and may provide false-negative results in neonates who have osteomyelitis even longer than 3 days.

Computed tomography scan can be useful, especially in revealing bony structures and when metallic orthotic prosthetic devices are present. However, magnetic resonance imaging (MRI) has the capacity to diagnose acute hematogenous osteomyelitis early, especially by identifying marrow edema that is apparent in the early phases of metaphyseal infection before other imaging modalities are diagnostic (Fig. 2). MRI provides unmatched imaging of soft tissues adjacent to infected bone for the presence of edema or pus, has the best capacity to distinguish discitis from vertebral osteomyelitis, (8) and facilitates detection of pelvic osteomyelitis when abscesses requiring drainage are present. For pelvic osteomyelitis specifically, $^{99m}$technetium scanning can establish the diagnosis reliably, but MRI can define pelvic soft-tissue structures when the differential diagnosis is not limited to pelvic osteomyelitis but also might include intra-abdominal or upper leg and hip disease.

The definitive diagnosis of osteomyelitis can be established by aspiration of the metaphysis or subperiosteal pus for identification of the infecting pathogen. Aspirated specimens can be obtained by identifying the point of maximum

Figure 1. Radiographic image depicting long-bone regions (left labels) and bony changes (right labels) due to *Staphylococcus aureus* osteomyelitis occurring in the distal right humerus of a 12-month-old infant.
tenderness, by imaging guidance, or by surgical intervention, especially when an abscess has been identified. Surgical drainage can serve as both a diagnostic and therapeutic intervention. Aspirated specimens should be sent for Gram stain and bacterial culture, with susceptibility testing of recovered isolates. A syringe containing aspirated purulent material from which air has been purged serves as an appropriate method to transport specimens for culture and is preferred to specimens obtained by swabbing because yield is directly influenced by specimen volume. In addition to plating on nutrient solid media, injecting a portion of the specimen into a blood culture bottle can increase the probability of recovering the pathogen.

Management

The appropriate management of osteomyelitis requires the combined efforts of the orthopedic surgeon to collect specimens that establish the cause of osteomyelitis and to provide drainage and debridement of the acute infection when an abscess is present (9) and the pediatrician to supervise antibiotic therapy and monitor the clinical response.

After specimens have been obtained, empiric treatment with a broad-spectrum regimen of parenteral therapy is warranted; selection of the appropriate agents is predicated on the most probable cause based on the patient’s age, clinical presentation, and site of infection, as well as local antibacterial susceptibility patterns. Few antibacterial agents are specifically approved by the United States Food and Drug Administration for the treatment of osteomyelitis in infants and children; rather, published research, treatment experience, and consensus opinion and recommendations have guided therapeutic choices.

Empiric therapy directed against *S aureus* is the cornerstone of antimicrobial treatment and should employ agents likely to be effective, as predicted by susceptibility patterns provided by local health systems or agencies. In those regions where methicillin-resistant *S aureus* has not emerged as a problem, use of semisynthetic penicillins, such as oxacillin or nafcillin, or a first-generation cephalosporin, such as cefazolin, is appropriate. When methicillin resistance is assumed due to established susceptibility patterns, empiric use of vancomycin or clindamycin is appropriate, with clindamycin preferred because of its more favorable pharmacokinetics and bone penetration. If local susceptibility patterns have identified significant clindamycin resistance in *S aureus* isolates, empiric treatment with vancomycin is warranted. Newer parenteral agents, such as daptomycin or linezolid, may be appropriate alternatives and may become preferred to vancomycin. However, lack of substantial treatment experience in childhood osteomyelitis limits unequivocal recommendation at this time.

Empiric antimicrobial therapy for neonatal osteomyelitis necessitates a regimen with an antimicrobial spectrum broader than for childhood osteomyelitis due to the increased probability of gram-negative bacillary infection. Empiric treatment for osteomyelitis due to *S aureus*...
using agents appropriate for the anticipated susceptibility of the bacterium is indicated. In addition, use of a third-generation cephalosporin or extended-spectrum penicillin with predicted activity against Enterobacteriaceae and Pseudomonas, such as cefepime or piperacillin-tazobactam, respectively, should be administered until the infectious agent is established. Beta-lactam antibiotics are preferred to aminoglycosides in the treatment of gram-negative bacillary infestations in infants because of their enhanced effectiveness in treating sepsis in neonates and due to more favorable overall pharmacokinetics for treatment of skeletal infections.

Once the putative pathogen has been identified by obtaining the appropriate cultures and antibacterial susceptibility has been established for the isolate, changing to specific antimicrobial treatment and transitioning from parenteral to oral therapy is appropriate. (10) The time to transition from parenteral to oral therapy should be based on clinical and laboratory criteria indicative of an initial therapeutic response, should not be obligated to fulfill an arbitrary prescribed parenteral treatment duration, and usually can occur early in treatment without detriment to the patient or ultimate clinical outcome. (11)

Criteria directing the transition to oral therapy include identification of an oral agent active against the pathogen based on susceptibility testing, clinical improvement that indicates response to initial parenteral therapy, likelihood that the patient can take and retain an orally administered agent, and anticipated discharge from hospital. For osteomyelitis due to methicillin-susceptible *S. aureus,* an oral cephalosporin such as cephalexin is appropriate; dicloxacillin should be avoided due to unpalatability. For osteomyelitis due to methicillin-resistant *S. aureus,* clindamycin is an appropriate oral agent, although unpalatability can be a factor when using the liquid formulation. Inadequate experience with trimethoprim-sulfamethoxazole in childhood osteomyelitis limits endorsement of its use. Linezolid or levofloxacin may be the best choice as individual circumstances dictate, but experience with these agents in treatment of childhood osteomyelitis is more limited than for beta-lactam antibacterials and clindamycin. Thus, the rationale for use and potential adverse effects should be coherently and completely disclosed.

Due to diminished penetration into bone, orally administered beta-lactam antimicrobials generally must be administered in higher-than-traditional doses (approximately two to four times greater) to achieve inhibitory concentrations at the site of infection. Due to the need for such higher oral doses of beta-lactam antimicrobials, methodologies to assess antimicrobial effectiveness in vivo have been advocated. The method used most commonly to predict success of oral therapy is to obtain serum specimens at times predicted to correlate with “peak” and “trough” drug concentrations, which is approximately 45 to 60 minutes following oral administration and within 30 minutes of the next scheduled oral dose, respectively.

Achieving a serum bactericidal concentration of at least 1:8 dilution at predicted peak serum drug concentration has been used most commonly as the value to predict likely therapeutic success of oral therapy. A trough serum bactericidal concentration of at least 1:2 also has been shown to predict therapeutic success and may be more predictive of successful outcome, (12) but this determination is not used as commonly as serum bactericidal concentration determined at peak concentration.

An advantage of clindamycin is that the drug accumulates in phagocytes and tissues, so cumulative drug concentrations exceed serum drug concentrations. For this reason, use of a standard traditional dosing regimen is likely to be effective in treatment of acute hematogenous osteomyelitis.

The duration of treatment for acute hematogenous osteomyelitis due to *S. aureus* historically has ranged from 4 to 6 weeks. More recent experience, however, has demonstrated that compliant oral therapy with an appropriate agent for 3 to 4 weeks is associated with therapeutic success for most patients. This shorter regimen is now the recommended antibiotic treatment for uncomplicated acute hematogenous osteomyelitis due to *S. aureus* in most children. (13)(14)

Oral therapy is inappropriate when no effective oral agent exists or if the patient cannot tolerate an oral antibiotic. Placement of a venous catheter to provide outpatient therapy with a parenteral agent can be an alternative to oral therapy, but cost and potential complications of the vascular access device are important considerations.

The most important task in monitoring response to therapy is to ensure and reinforce compliance with the prescribed regimen. Treatment end-points are recovery of pain-free functionality and resolution of local and systemic symptoms and signs of infection. Ancillary measurements of therapeutic response include resolution of peripheral leukocytosis and diminution of serum inflammatory markers to normal values, especially the C-reactive protein concentration. Although radiographic resolution also can be used as an indication of therapeutic success, delayed resolution of radiographic abnormalities and postinfectious sequelae despite successful anti-infective treatment and clinical resolution preclude use of radiography as a timely predictor of treatment response.
Summary

• Based on strong research evidence and clinical experience, most cases of acute hematogenous osteomyelitis begin as an infection in the metaphysis of a long bone that progresses by local extension and potentially can rupture into an adjacent joint or subperiosteal space, especially if appropriate treatment is delayed. The most common infectious agent causing acute hematogenous osteomyelitis in childhood is S. aureus. Osteomyelitis in neonates has a more varied etiology that, in addition to S. aureus, includes S. agalactiae and the Enterobacteriaceae. (1)(2)(3)

• Based on strong research evidence and clinical experience, the clinical presentation of osteomyelitis is primarily focal pain at the site of infection and reduced function of the involved limb or structure due to exacerbation of pain with activity. Most patients are also febrile and have modest peripheral leukocytosis and elevated serum acute inflammatory phase reactants, especially C-reactive protein, at presentation. The diagnosis is confirmed definitively by recovery of the pathogen through aspiration of the metaphyseal or subperiosteal infection or by recovery of the organism from blood cultures obtained from a patient who has symptoms, signs, laboratory findings, and imaging modalities consistent with skeletal infection. (1)(5)

• Based on some research experience as well as consensus, the diagnosis of osteomyelitis can be supported by imaging studies, with triphasic 99mTc technetium scanning and MRI being the preferred modalities due to increased precision in the diagnosis of acute osteomyelitis in the early phase of disease, especially when the infection occurs in the pelvis, vertebrae, or intervertebral disc space. (4)(6)(7)(8)

• Based on strong research evidence as well as consensus, anti-infective therapy for osteomyelitis is determined by isolate recovery and identification, antimicrobial susceptibility testing in vitro, and prescription of an antibiotic regimen likely to deliver therapeutic concentrations to the site of infection, as predicted by testing in vivo. Transition from parenteral to oral antibacterial therapy, when clinically allowed, is appropriate, and serum bactericidal concentrations determined against the patient’s isolate can be used as a predictor of probable success of orally administered anti-infective therapy. (9)(10)(11)(12)

• Based on some research evidence as well as consensus, the duration of antimicrobial treatment of acute hematogenous osteomyelitis is generally 3 to 4 weeks and should continue until resolution of local and systemic inflammatory symptoms and signs, recovery of painless function of the affected area, and diminution of serum markers of acute inflammation, specifically C-reactive protein, to normal values. (13)(14)

References

9. Which of the following statements regarding the pathophysiology of osteomyelitis is true?
   A. Children who have hemoglobin SS disease are at increased risk of osteomyelitis from *Pseudomonas*.
   B. Concomitant septic arthritis occurs most commonly in neonates.
   C. Discitis is seen most commonly in the adolescent population.
   D. Osteomyelitis in children occurs most commonly as a direct extension from infected soft-tissue structures.
   E. Vertebral osteomyelitis is seen most commonly in infants and toddlers.

10. In which of the following bones is hematogenous osteomyelitis most likely to occur?
    A. Clavicle.
    B. Femur.
    C. Humerus.
    D. Ischium.
    E. Tibia.

11. You are evaluating a 7-year-old boy who has had fever and right thigh pain for the past 2 days. Findings on his physical examination are unremarkable, with full range of motion of the hips and knees, but he complains of point tenderness in the area of the right anterior distal femur. He walks with a slight limp favoring the right leg. You suspect acute osteomyelitis. Which of the following is the best test to confirm your diagnosis at this time?
    A. Anteroposterior radiographs of the leg.
    B. Blood culture.
    C. Erythrocyte sedimentation rate.
    D. Magnetic resonance imaging of the leg.
    E. Technetium scan.

12. A 2-week-old girl is brought to your office because she has not moved her left arm for the past day. Her mother reports subjective fevers for 1 day. She was born at term with no complications. Maternal laboratory tests, including group B *Streptococcus* screening, yielded negative results. The well-appearing infant has a temperature of 38.3°C, but other vital signs are normal. She cries with movement of her left arm and appears to have decreased range of motion in her left shoulder. There is no erythema or bruising. You decide to hospitalize her for the evaluation and treatment of possible osteomyelitis. Which of the following is the best antibiotic regimen to start at this time?
    A. Ampicillin and gentamicin.
    B. Cefazolin and vancomycin.
    C. Cefepime and clindamycin.
    D. Gentamicin and vancomycin.
    E. Metronidazole and cefotaxime.
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