

# Bone and Joint Infections in Children

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Bone and joint infections are a significant cause of morbidity in infants and young children. Although many principles regarding pathogenesis, diagnosis, and treatment of infection have remained constant over the years, other aspects of this important pediatric diagnosis are continuing to evolve. This article reviews current information regarding pathogenesis, epidemiology, and microbiology of pediatric bone and joint infections and the clinical presentation, diagnosis, and treatment of these infections.

## **Osteomyelitis**

Osteomyelitis is inflammation of the bone caused by infection with bacterial or fungal organisms. Osteomyelitis often is categorized into three different types: (1) acute hematogenous osteomyelitis; (2) osteomyelitis secondary to contiguous spread of infection after trauma, puncture wounds, surgery, or joint replacement; and (3) osteomyelitis secondary to vascular insufficiency [1]. Acute hematogenous osteomyelitis is seen most often in children. Osteomyelitis caused by contiguous spread of infection is less common in children, and infection secondary to vascular insufficiency is rare in children.

### *Pathogenesis*

Acute hematogenous osteomyelitis results from symptomatic or asymptomatic bacteremia. Because of its rich vascular supply, the metaphysis of the bone is most often involved. The infecting organism travels to metaphyseal capillary

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loops, where it replicates and causes local inflammation. As the bacteria replicate, they travel through vascular tunnels and adhere to cartilaginous matrix. *Staphylococcus aureus* is the most common cause of infection perhaps because of its capacity to express bacterial adhesions that promote attachment to extracellular bone matrix. This organism also is able to evade host defenses, attack host cells, and colonize bone persistently [1].

The bony metaphyses of children younger than 18 months are vascularized by the transphyseal vessels. Because these vessels enter the epiphysis and ultimately the joint space, young children are believed to have a higher risk of joint space infection complicating osteomyelitis. One clinical study found the incidence of adjacent joint involvement to be the same, however, in children older than 18 months compared with children younger than 18 months [2]. The authors speculated that some cases of joint involvement could be due to subperiosteal spread of infection into the joint space or that an adjacent site of osteomyelitis may predispose an adjacent joint to hematogenous seeding.

Animal models show that bone infection is more likely after bacteremic animals sustain trauma to the affected area. These animal models may explain why a history of trauma is elicited in approximately 30% children before onset of symptoms [3]. Contiguous osteomyelitis in children is seen in the setting of trauma; animal bites; puncture wounds; and direct extension of infection from an infected sinus, mastoid bone, or dental abscess.

### *Epidemiology*

The exact incidence of childhood osteomyelitis in the United States is unknown. Other countries report a decrease in the diagnosis in recent years [4]. Approximately 50% of cases of osteomyelitis occur in the first 5 years of life. Boys are more likely than girls to be affected. The long bones of the lower extremities are most often involved, although any bone may be affected.

### *Microbiology*

The type of infecting organism depends on the age of the child and underlying medical problem (Table 1). *S. aureus* is the most common cause of osteomyelitis in all age groups, accounting for 70% to 90% of infections. Infection caused by methicillin-resistant *S. aureus* (MRSA) is becoming an increasingly common problem. One group of investigators identified 59 patients with musculoskeletal infections caused by *S. aureus* over a 2-year period at their center. More than half of the patients described were infected with community-acquired MRSA (CA-MRSA) [5].

In addition to *S. aureus*, young infants may develop osteomyelitis caused by *Streptococcus agalactiae* or enteric gram-negative bacteria. Organisms other than *S. aureus* causing infection in older children include *Streptococcus pyogenes*,

Table 1  
Usual infectious causes of pediatric osteomyelitis and pyogenic arthritis

Age	Organism
Infants 0–2 mo	<i>Staphylococcus aureus</i> <i>Streptococcus agalactiae</i> Gram-negative enteric bacteria <i>Candida</i>
≤5 y	<i>S. aureus</i> <i>Streptococcus pyogenes</i> <i>Streptococcus pneumoniae</i> <i>Kingella kingae</i> <i>Haemophilus influenzae</i> type b (if child not completely immunized with conjugate Hib vaccine)
>5 y	<i>S. aureus</i> <i>S. pyogenes</i>
Adolescent	<i>Neisseria gonorrhoeae</i>

*Streptococcus pneumoniae*, and *Kingella kingae* [6]. *S. pyogenes* causes approximately 10% of cases of acute hematogenous osteomyelitis with a peak incidence of disease in preschool-age and early school-age children [7]. Children with *S. pyogenes* osteomyelitis often have a recent history of varicella infection and present with higher fever and white blood cell (WBC) counts compared with children infected with *S. aureus*.

Children with osteomyelitis caused by *S. pneumoniae* are younger than children infected with *S. aureus* and *S. pyogenes*. They are more likely to have joint involvement [8]. The proportion of bone infections caused by *S. pneumoniae* is relatively small (approximately 1–4%); the impact of heptavalent pneumococcal conjugate vaccine on the incidence of osteomyelitis is limited.

*K. kingae* is reported as a pathogen with increasing frequency [9]. A cluster of bone and joint infections caused by *K. kingae* at a daycare center underscores the importance of this organism in children with musculoskeletal infections [10]. *K. kingae* is a fastidious gram-negative coccobacillary bacterium found in normal respiratory flora. Infection with this organism often is preceded by an upper respiratory tract infection or stomatitis; disrupted respiratory mucosa may facilitate invasion and hematogenous dissemination.

There has been a substantial decrease in musculoskeletal infections secondary to *Haemophilus influenzae* type b (Hib) as a result of an effective immunization program against this pathogen. Hib infection is rare in a completely immunized child, although other serotypes are reported to cause bone and joint infections.

Puncture wounds to the foot may result in osteomyelitis caused by mixed flora, including *Pseudomonas*, *S. aureus*, enteric gram-negative bacteria, and anaerobes. The source of bacteria is usually from moist colonized soles of tennis shoes. A series of cases describes osteomyelitis of the metatarsals occurring as a result of toothpick puncture injuries. The organisms isolated included skin and environmental organisms; others have reported infection with mouth organisms as a result of toothpick injuries [11].

Anaerobes are a rare cause of pyogenic osteomyelitis in healthy children. Predominant organisms are *Bacteroides*, *Fusobacterium*, *Clostridium*, and *Peptostreptococcus*. Anaerobic osteomyelitis can occur as the result of a bite, chronic sinusitis, mastoiditis, or dental infection.

Organisms causing bone infection in children with sickle cell disease include *Salmonella* and *S. aureus* and less commonly *Escherichia coli*, Hib, *Shigella*, and *S. pneumoniae*. Unusual causes of osteomyelitis include infection with *Mycobacterium*, *Bartonella*, *Coxiella burnetii*, or fungi (Table 2). The specific etiology of osteomyelitis is not determined in many cases; nonetheless, resolution after empirical therapy for *S. aureus* is usual [12].

### Clinical manifestations

Most children with acute hematogenous osteomyelitis are symptomatic for less than 2 weeks. Symptoms include complaints of acute, persistent, and increasing pain over the affected bone. Osteomyelitis in an infant may present as irritability or reluctance to move the affected limb. Fever is usually present. Swelling or redness of the soft tissue over the affected bone may be seen. In one study, patients with culture-positive osteomyelitis were more likely than patients

Table 2  
Other microbiologic causes of bone or joint infection in children

Risk Factors	Organism
<b>Osteomyelitis</b>	
Exposure to farm animals	<i>Coxiella burnetii</i>
Kitten exposure	<i>Bartonella</i>
Travel/contact	<i>Mycobacterium tuberculosis</i>
Sinusitis/mastoiditis/dental abscess	Anaerobes
Puncture wound foot	<i>Pseudomonas</i> , <i>Staphylococcus aureus</i>
Sickle cell disease	<i>Salmonella</i> , <i>S. aureus</i>
Travel or residence in endemic area ± immunosuppression	<i>Coccidioides immitis</i> <i>Blastomyces dermatitidis</i> <i>Histoplasma capsulatum</i> <i>Cryptococcus neoformans</i>
Chronic granulomatous disease	<i>Aspergillus</i> , <i>S. aureus</i> , <i>Serratia</i>
<b>Arthritis</b>	
Tick exposure in an endemic area	<i>Borrelia burgdorferi</i>
Travel/contact	<i>M. tuberculosis</i>
Rat exposure	<i>Streptobacillus moniliformis</i> <i>Spirillum minus</i>
Viral infection	Rubella, parvovirus B19, varicella zoster, hepatitis B
Travel or residence in an endemic area ± immunosuppression	<i>C. immitis</i> <i>B. dermatitidis</i> <i>H. capsulatum</i> <i>C. neoformans</i>
Newborn with intravascular line	<i>Candida</i>

with culture-negative osteomyelitis to have a history of antecedent trauma, changes in skin overlying the bone, associated cellulites, or high fever [12].

Pelvic osteomyelitis is reported in 1% to 11% of all cases of acute hematogenous osteomyelitis and typically affects older children [13]. Symptoms include hip, buttock, low back, or abdominal pain. Fever may be absent. Findings on physical examination include tenderness of the pelvic bones, pain with hip movement, decreased range of motion at the hip, and refusal or inability to bear weight. Any bone in the pelvis may be involved, but the ilium tends to be affected most often, presumably because of its rich blood supply. Symptoms and findings frequently are nonspecific and poorly localized and often are attributed to other diagnoses, such as pyogenic arthritis of the hip or appendicitis. Establishing the correct diagnosis often is delayed.

Osteomyelitis in a neonate is an uncommon but serious infection. It often results from hematogenous spread of microorganisms in patients with indwelling venous catheters. Presenting signs and symptoms include fever, irritability, refusal to move the affected limb, and redness and swelling over the affected area. Diagnosis may be delayed because of nonspecific signs of illness. Infection involving multiple bones and contiguous joints and soft tissue is common.

The differential diagnosis of bone pain in children includes trauma, malignancy, and bone infarction in patients with sickle cell disease. Differentiation between bone infection and infarction in a child with sickle cell anemia is difficult because in both cases the acute onset of fever and bone pain is common. In addition, a patient may have infarction that predisposes to infection.

Chronic recurrent multifocal osteomyelitis is a poorly understood inflammatory illness characterized by recurrent bone pain and fever. Girls are predominantly affected and have radiologic evidence of multiple, often symmetric bone lesions involving primarily the long bones and clavicles. Associated findings include psoriasis vulgaris and palmoplantar pustulosis.

### *Diagnosis*

The diagnosis of osteomyelitis depends primarily on clinical findings and corroborative laboratory and radiographic results. The WBC count may be normal or increased. Erythrocyte sedimentation rate (ESR) is elevated in 80% to 90% of cases, and C-reactive protein (CRP) is elevated in 98% of cases. ESR generally peaks 3 to 5 days after admission, and CRP peaks within 48 hours of admission. CRP typically returns to normal 7 to 10 days after appropriate therapy. ESR may remain elevated for 3 or 4 weeks, even with appropriate therapy [14]. Patients who require surgical incision and drainage procedures may have prolonged time to normalization of ESR or CRP [15].

Every attempt should be made to establish a microbiologic diagnosis. A bacteriologic diagnosis can be made in 50% to 80% of cases if blood and bone cultures are obtained. In the case of culture-negative osteomyelitis that is not responding as expected to empirical therapy, a bone biopsy specimen should be

obtained for histopathologic staining and for culture for bacteria, mycobacteria, and fungi. Inoculation of bone or abscess material directly into an aerobic blood culture bottle facilitates isolation of *K. kingae*. Cultures for *K. kingae* and other fastidious organisms may need to be incubated longer than usual laboratory protocol [6].

Plain films show soft tissue swelling in the first few days of illness. Periosteal and lytic changes in the bone generally are not seen until substantial bone destruction has occurred, usually 10 to 21 days after onset of symptoms. In some cases of proven bacterial osteomyelitis, bone changes are never seen on plain film, presumably because prompt diagnosis and treatment prevented extensive bone destruction.

The sensitivity of skeletal scintigraphy, using technetium-labeled methylene diphosphonate isotope, is 80% to 100%. Radionuclide bone scans usually are positive within 48 to 72 hours of onset of symptoms. In some cases of osteomyelitis, vascular supply to the bone is compromised, with decreased uptake of technetium to the affected area, resulting in a "cold scan." Some experts prefer bone scan as the initial study in the evaluation of suspected uncomplicated osteomyelitis of the long bones. It is less expensive than MR imaging, sedation of the child is generally not necessary, and it is particularly useful when multifocal osteomyelitis is suspected or the exact location of infection is not obvious on physical examination [16,17]. Radionuclide scans may be positive in other illnesses that result in increased osteoblastic activity, including malignancy, trauma, cellulitis, postsurgery, and arthritis.

MR imaging gives excellent resolution of bone and soft tissue. It is particularly useful for visualizing soft tissue abscess associated with osteomyelitis, bone marrow edema, and bone destruction. Contrast enhancement with gadolinium is used to look for areas of abscess formation [18]. If pelvic or vertebral body osteomyelitis is suspected, MR imaging is the imaging study of choice. MR imaging gives better spatial resolution than bone scan and is preferred if a surgical procedure to diagnose or drain an abscess is necessary. Limitations of MR imaging include the need for sedation in younger children, high cost, and inability to assess easily whether other bones are affected.

Differentiating bone infarction versus infection can be difficult in a child with sickle cell disease. In both situations, children present with fever and bone pain and have elevated inflammatory markers. Biopsy and culture of affected bone is often necessary to establish the diagnosis. Some authors have used the pattern of MR imaging contrast enhancement to distinguish acute medullary bone infarction from osteomyelitis [19].

### *Treatment*

Successful treatment of osteomyelitis depends on the appropriate selection and administration of antibiotic therapy and surgical intervention as needed. Empirical selection of antibiotics depends on the age of the child and the clinical

Table 3  
Empirical parenteral antibiotic therapy for pediatric bone and joint infections\*

Infants 0–2 mo	Nafcillin* plus cefotaxime
Children ≤5 years <sup>†</sup>	Nafcillin* plus cefotaxime or ceftriaxone or Cefuroxime
Children >5 y	Nafcillin* or cefazolin* <sup>‡</sup>

\* If MRSA is a concern (if local rates of MRSA are >5–10%), use intravenous vancomycin or clindamycin as empirical therapy.

<sup>†</sup> Children who have been completely immunized against *Haemophilus influenzae* type b do not require antibiotic coverage for *H. influenzae* type b.

<sup>‡</sup> Use ceftriaxone if *Neisseria gonorrhoeae* a consideration.

situation (Table 3). Infants 0 to 2 months old with osteomyelitis should be treated with antibiotics that have excellent coverage against *S. aureus*, *S. agalactiae*, and enteric gram-negative bacteria.

Children 2 months to 5 years old should be treated empirically with antibiotics active against *S. aureus*, *S. pneumoniae*, *S. pyogenes*, *K. kingae*, and Hib (if not completely immunized with Hib vaccine). The American Academy of Pediatrics Committee on Infectious Diseases defines complete immunization for Hib as having had at least one dose of conjugate Hib vaccine at 15 months of age or older, two doses between 12 and 14 months of age, or a complete primary series when younger than 12 months with a booster dose at 12 months of age or older [20]. *K. kingae* generally is susceptible to most  $\beta$ -lactam antibiotics, including second-generation and third-generation cephalosporins. It often is resistant to clindamycin, and resistance to clotrimazole is reported [6].

When culture results are available, antibiotic therapy is modified depending on the organism and the susceptibility pattern. If no organism is isolated, but the patient is improving, initial empirical coverage is continued. If the patient is not improving, further diagnostic testing should be considered, including bone biopsy for histopathology and culture if not previously obtained or imaging studies to rule out areas of infection that may require surgical drainage or débridement.

Infection caused by MRSA is increasingly common in many communities. Many isolates of CA-MRSA are susceptible to clindamycin. Isolates of *S. aureus* that are erythromycin resistant and clindamycin susceptible should be evaluated for the presence of inducible macrolide-lincosamide-streptogramin B (MLS<sub>B</sub>) resistance. This evaluation is done by means of a “D” test, performed by many hospital laboratories. Although some children treated with clindamycin for an infection with MRSA of the MLS<sub>B</sub> phenotype clear their infection, it is recommended that in the setting of serious infection, clindamycin should not be used if this phenotype is identified [21].

Alternative drugs to consider for treatment of osteomyelitis caused by MRSA include intravenous vancomycin, trimethoprim-sulfamethoxazole, and linezolid. Bone and joint infections caused by MRSA should be managed in consultation

with an expert in infectious disease. Empirical use of these antibiotics before organism identification and susceptibility testing depends on severity of illness and incidence of MRSA in the community.

In an open-label, noncomparative, nonrandomized, compassionate use study, linezolid was used to treat serious infections caused by resistant gram-positive bacteria. Microbiologic cure for the cases of osteomyelitis caused by MRSA was 72% [22]. Most patients in this study were adults. Side effects of linezolid include gastrointestinal symptoms and rash. Long-term use of linezolid has been associated with neutropenia, anemia, thrombocytopenia, and optic and peripheral neuropathies. Cases of lactic acidosis also have been reported with linezolid use. Linezolid was not effective in at least one animal study of experimental chronic *S. aureus* osteomyelitis [23].

The decision to change from parenteral to oral therapy depends on the availability of an appropriate oral antibiotic, the child's ability to take the medication by mouth, reliable caregivers, and the ability of the family to comply with frequent follow-up. Generally, oral therapy is begun when the child is afebrile, symptoms and signs of infection are resolving, and CRP is returning to normal. The availability of percutaneous central venous catheters has made home intravenous therapy of bone and joint infections an increasingly popular option. The prolonged presence of a central venous catheter increases the risk of infectious complications, including exit site infections and catheter-associated bacteremia [24]. Intravenous therapy should not be unduly prolonged after the child has shown significant improvement.

Sequential intravenous to oral therapy is proven to be effective and safe, provided that close follow-up of the patient is ensured. The dose of oral antibiotic is generally two to three times the usual dose for children if a  $\beta$ -lactam antibiotic, such as dicloxacillin or cephalexin, is used. The usual recommended oral doses of clindamycin, trimethoprim-sulfamethoxazole, fluoroquinolone antibiotics, and linezolid can be used because of the excellent bioavailability of these drugs (Table 4). Vancomycin always must be given intravenously.

Duration of therapy depends on extent of infection, clinical response, and presence of underlying risk factors. In general, 3 to 6 weeks of antibiotic therapy is given depending on the clinical response [14,25]. There is good evidence that treatment for less than 3 weeks results in an unacceptably high rate of relapse. Chronic infection is reported in 19% of children treated for less than 3 weeks compared with 2% in children treated longer than 3 weeks [26].

Table 4  
Doses of oral antibiotics used for bone and joint infections

Antibiotic	Dose(mg/kg/d)	Interval
Cephalexin	100	q6-8h
Dicloxacillin	100	q6h
Clindamycin	30	q6-8h

### *Prognosis*

Most children who receive appropriate therapy for osteomyelitis have no long-term sequelae. Recurrence of infection occurs in approximately 5% of cases. Risk factors for development of complications include delay in diagnosis, short duration of therapy, and young age at the time of initial illness. The reported incidence of sequelae in neonates with osteomyelitis ranges from 6% to 50%. Permanent abnormalities include disturbance in bone growth, limb-length discrepancies, arthritis, abnormal gait, and pathologic fractures.

There does not seem to be a significant difference in outcome for bone infections caused by MRSA compared with infections caused by methicillin-susceptible *S. aureus*. Children infected with MRSA tend to have longer duration of fever and prolonged hospitalization, however. Patients with complicated clinical courses, including patients with associated deep vein thrombosis, were found in one study more likely to be infected with MRSA with genes encoding for the Panton-Valentine leukocidin (PVL1) [5]. This strain of MRSA causes severe inflammatory lesions after intradermal injection in laboratory animals and has been associated with a poor prognosis in patients with pneumonia.

Chronic osteomyelitis develops in less than 5% of children after acute hematogenous infection. It is observed more frequently after contiguous osteomyelitis. Bone necrosis occurs as a result of chronic inflammation and vascular compromise. Extensive fibrosis eventually results. Signs and symptoms of chronic osteomyelitis vary from chronic vague symptoms of swelling, pain, or intermittent drainage of the affected bone to acute exacerbations of fever, swelling, or redness over the bone. Effective management of chronic osteomyelitis usually requires surgical and medical management, with prolonged courses of antibiotics [27].

### **Pyogenic arthritis**

Infection of the joint space in children usually is a complication of bacteremia. Viruses, fungal organisms, and *Mycobacterium tuberculosis* are uncommon causes of joint space infection (see Table 2). Children also may develop reactive arthritis as a consequence of bacterial infection elsewhere in the body.

### *Pathogenesis*

Pyogenic arthritis usually occurs as a result of infection of the vascular synovium by means of hematogenous dissemination of bacteria. An acute inflammatory response follows, resulting in migration of polymorphonuclear WBCs, production of proteolytic enzymes, and cytokine secretion by chondrocytes. Degradation of articular cartilage begins 8 hours after onset of infection [28].

In children younger than 18 months of age, pyogenic arthritis can result from extension of a metaphyseal bone infection through transphyseal blood vessels.

The growth plate, the epiphysis, and eventually the joint space may be infected. Infection of the proximal femur and humerus often involves the hip and shoulder joints because the proximal metaphysis of each of these bones is intracapsular.

### *Epidemiology*

Most cases of pyogenic arthritis occur in children 3 years old or younger. Cases are more frequent in boys. The joints of the lower extremities (hips, knees) are most often affected.

### *Microbiology*

*S. aureus* is the most common cause of pyogenic arthritis in all age groups, and infection with CA-MRSA is becoming more common. Infants younger than 2 months of age also may have infection caused by *S. agalactiae*, *Neisseria gonorrhoeae*, and gram-negative enteric bacteria. Arthritis caused by *Candida* also is seen in the neonatal age group. *S. aureus*, *S. pyogenes*, *S. pneumoniae*, and *K. kingae* are predominant organisms in the 2-month to 5-year age range. Children older than 5 years are most likely to have arthritis caused by *S. aureus* and *S. pyogenes*. *N. gonorrhoeae* arthritis occurs in sexually active adolescents.

Before universal immunization of children with a conjugate Hib vaccine, Hib was a common cause of pyogenic arthritis in children younger than 5 years. Infection with Hib is now rare in immunized children. Arthritis caused by *K. kingae* has replaced Hib as the most common gram-negative arthritis in the child 2 months to 5 years old [6].

*S. pneumoniae* is reported to cause approximately 6% to 20% of all cases of pyogenic arthritis [29,30]. The impact of the recently licensed heptavalent pneumococcal vaccine on pneumococcal pyogenic arthritis is still being evaluated [31]. The vaccine confers immunity to the seven pneumococcal serotypes most frequently associated with invasive disease in children, but is not immunogenic against all serotypes. A surveillance study involving 157,471 children over a 3-year period after the vaccine was licensed revealed a significant decrease in the number of cases of invasive pneumococcal disease caused by serotypes in the vaccine or closely related to the serotypes in the vaccine [32]. There was no significant change in the incidence of disease caused by other serotypes. The types of invasive disease reported were primarily bacteremia and pneumonia. Because the incidence of pneumococcal arthritis after bacteremia is only about 0.6% [29], a significant decrease in the number of cases of pneumococcal bacteremia is likely to result in only a small reduction in cases of pyogenic arthritis.

Other causes of arthritis should be suspected on the basis of exposure history (see Table 2). *Borrelia burgdorferi* causes Lyme disease in endemic areas. Arthralgia is seen in early disseminated Lyme disease. Weeks to months after the initial infection, children may develop pauciarticular arthritis of the large joints, particularly the knees [33]. *N. gonorrhoeae* infection should be considered in a sexually active adolescent with joint infection. Hematogenous spread of the

Table 5  
Infectious causes of reactive arthritis

Site of infection	Organism
Gastrointestinal tract	<i>Salmonella</i> <i>Shigella</i> <i>Campylobacter</i> <i>Yersinia enterocolitica</i>
Genitourinary tract	<i>Chlamydia trachomatis</i> <i>Neisseria gonorrhoeae</i> *
Other	<i>Streptococcus pyogenes</i> * <i>Neisseria meningitidis</i> *

\* These organisms also may infect the joint space directly.

organism can involve skin and joints (arthritis-dermatitis syndrome). The arthritis associated with *N. gonorrhoeae* also may be reactive in nature. Reactive arthritis is defined as inflammation of a joint after infection at some other site. Organisms that are associated with reactive arthritis are listed in [Table 5](#).

### *Clinical manifestations*

Trauma or upper respiratory tract infection often precedes joint symptoms. Symptoms of pyogenic arthritis include acute onset of joint pain, fever, irritability, and limp. Pain associated with pyogenic arthritis of the hip may be referred to the groin, thigh, or knee. Findings on physical examination include redness, swelling, and warmth over the affected joint. The child complains of pain with movement of the joint and restricted range of motion. Patients should be evaluated for signs of pharyngitis, rash, heart murmur, hepatosplenomegaly, and evidence of other joint or bone involvement.

### *Differential diagnosis*

The most common cause of hip pain in childhood is transient synovitis. Transient synovitis predominates in children 5 to 10 years old. The child generally has low-grade fever or is afebrile. Pain is usually unilateral, but may be bilateral in some cases. Pain ranges from mild to severe enough to wake the child up at night. Physical examination generally reveals a non-ill-appearing child with decreased range of motion of the hip joint.

Other causes of joint pain and swelling include reactive arthritis, juvenile rheumatoid arthritis, trauma, and malignancy. Legg-Calvé-Perthes disease is an idiopathic avascular necrosis of the capital femoral epiphysis and may cause mild pain and limp in boys (mean age 7 years). Slipped capital femoral epiphysis is the most common hip disorder of adolescents; symptoms may include abnormal gait, pain, and abnormal range of motion of the hip joint.

## Diagnosis

Diagnosis of pyogenic arthritis must be made promptly to prevent damage to the articular cartilage. Every attempt should be made to establish a microbiologic diagnosis. Blood and joint fluid should be obtained for aerobic and anaerobic cultures. Joint fluid should be inoculated directly into blood culture bottles to enhance identification of fastidious organisms such as *K. kingae*. Gram stain and cell count also should be performed on joint fluid. A WBC count of 50,000/mm<sup>3</sup> or greater with a predominance of polymorphonuclear cells is consistent with bacterial infection, but also is seen sometimes with rheumatologic disease. The peripheral WBC count, ESR, and CRP are generally elevated, although occasionally CRP is normal, especially with infection caused by *K. kingae*. If *N. gonorrhoeae* is suspected, cultures of joint fluid, blood, pharynx, skin lesion, cervix, urethra, vagina, and rectum should be obtained and inoculated onto special media. *N. gonorrhoeae* also can be detected by nucleic acid amplification techniques using urine, urethral, cervical, or vaginal specimens. A throat culture for *S. pyogenes* should be sent if the patient has signs or symptoms of pharyngitis. Antibody titers to antistreptolysin O and anti-DNase B also may be useful to diagnose infection with *S. pyogenes*. Lyme disease serology (including Western blot) is used to diagnose Lyme arthritis in a patient with the appropriate exposure history. Plain radiographs of adjacent bone are useful in evaluating for other causes of joint pain and swelling, including trauma, malignancy, and osteomyelitis.

The prompt diagnosis of pyogenic arthritis of the hip is important to prevent serious permanent long-term sequelae. Untreated infection of the hip can result in vascular compromise and ischemic necrosis of the femoral head. Differentiation between pyogenic arthritis and transient synovitis of the hip is challenging. Several studies have shown that a combination of clinical and laboratory features can assist in differentiating these diagnoses (Table 6). Kocher et al [34] found that

Table 6  
Differentiation of pyogenic arthritis from transient synovitis of the hip

Study	Predictors analyzed	No. predictors present (+): Predictive probability of pyogenic arthritis (%)*
Kocher et al [34]	History of fever	4 +: 99.8%
	Non-weight bearing	3 +: 93–95.2%
	ESR $\geq$ 40 mm/h	2 +: 33.8–62.2%
	WBC $>$ 12,000/mm <sup>3</sup>	1 +: 2.1–5.3%
		0 +: 0.1%
Jung et al [36]	Body temperature $>$ 37°C	5 +: 99.1%
	ESR $>$ 20 mm/h	4 +: 84.8–97.3%
	CRP $>$ 1 mg/dL	3 +: 24.3–77.2%
	WBC $>$ 11,000/mm <sup>3</sup>	2 +: 4.3–22.7%
	Increased hip joint space $>$ 2 mm	1 +: 0.3–9.9%
	0 +: 0.1%	

\* Exact predictive probability depends on which multivariate predictor was positive.

if a child with hip pain had all four diagnostic variables of fever, refusal to walk, elevated ESR ( $\geq 40$  mm/h) and elevated WBC count ( $>12,000/\text{mm}^3$ ), the probability of pyogenic arthritis was greater than 99%.

Kocher's criteria have been applied retrospectively to patients with a known diagnosis of pyogenic arthritis. In one study, the predictive probability of presence of fever, refusal to walk, and elevated ESR and WBC count was found to be considerably less reliable (60%) in predicting pyogenic arthritis [35]. Of patients within the group defined as having proven or presumed septic arthritis who had positive cultures, however, 35% were diagnosed with infection with coagulase-negative staphylococci. This organism is not a usual cause of pediatric pyogenic arthritis and is more often considered a contaminant. This study underscores, however, the fact that the validity of clinical prediction algorithms may vary among studies.

Other investigators have used similar methods in an attempt to differentiate pyogenic arthritis and transient synovitis. Jung et al [36] evaluated children with hip pain using fever ( $>37^\circ\text{C}$ ), ESR ( $>20$  mm/h), CRP ( $>1$  mg/dL), WBC count ( $>11,000/\text{mm}^3$ ), and plain radiographs to determine if there was widening of the joint space ( $>2$  mm) to predict the presence of pyogenic arthritis. If four or five of these criteria were present, the child had a high likelihood (predictive probability  $>99.1\%$ ) of septic arthritis and was a candidate for joint aspiration.

Although most clinicians use fever and elevated inflammatory markers to guide their management of children with hip pain, there is considerable overlap in the clinical and laboratory findings in children with pyogenic arthritis and transient synovitis [37]. Close follow-up of patients in whom the diagnosis is unclear is crucial. Plain radiographs are obtained to rule out fracture, malignancy, or osteomyelitis as the cause of pain. Ultrasound is useful in determining whether fluid is present in the hip joint and is used to guide joint aspiration. Ultrasound cannot differentiate infected from noninfected fluid.

### Management

The successful management of pyogenic arthritis depends on timely decompression of the joint space and institution of appropriate antibiotic therapy. Children with pyogenic arthritis should be managed in collaboration with an orthopedic surgeon experienced in the treatment of pediatric bone and joint infections. Aspiration of the affected joint usually is performed for diagnostic and therapeutic purposes. In the case of hip and shoulder joint infections, prompt surgical drainage of infected joint fluid usually is required. The initial choice of empirical antibiotic therapy (see Table 3) depends on the age of the child, clinical presentation, and local patterns of antibiotic resistance. In general, infants younger than 2 months old are treated with nafcillin and a third-generation cephalosporin to cover *S. aureus* and enteric gram-negative bacteria. Older children should receive antibiotic therapy active against *S. aureus*, *S. pyogenes*, and *K. kingae*. If *N. gonorrhoeae* is suspected, ceftriaxone should be used. Clindamycin is an appropriate antibiotic for most gram-positive bacteria, in-

cluding some strains of CA-MRSA. It is not active, however, against *K. kingae*. If MRSA is suspected, vancomycin should be used empirically until culture and susceptibility results are available. If cultures are positive for MRSA, clindamycin is an appropriate drug if the isolate is susceptible, and there is no evidence of the  $MLS_B$  phenotype (see the section on osteomyelitis). Intra-articular injection of antibiotics is not appropriate. Most antibiotics achieve high synovial fluid concentrations, and the antibiotic may cause a chemical synovitis when directly injected into the joint. As with osteomyelitis, a child should be treated with intravenous antibiotics until there is significant clinical improvement, inflammatory markers are returning to normal, and the child's oral intake is normal. The doses of oral antibiotics used are the same as doses used to treat osteomyelitis (Table 4).

Some centers have found the use of guidelines helpful in standardizing care of uncomplicated cases of pyogenic arthritis. Use of short courses of intravenous therapy (3–4 days) followed by the appropriate oral antibiotic decreased the duration of hospitalization at one center [38]. Compared with patients who were treated before implementation of guidelines, there was no increase in the risk of adverse outcomes in patients followed a minimum of 1 year. Although clinical guidelines may be useful as a framework for evaluation and treatment of pyogenic arthritis, strict guidelines are not appropriate for children with underlying risk factors for severe disease or for children not responding to initial therapy.

The duration of therapy for uncomplicated pyogenic arthritis depends on the response to therapy and the suspected organism [39]. Generally, infections with *S. pneumoniae*, *K. kingae*, Hib, and *N. gonorrhoeae* are treated for 2 to 3 weeks. Infections caused by *S. aureus* or gram-negative enteric bacteria are treated 3 to 4 weeks.

### Prognosis

Complications of pyogenic arthritis include abnormal bone growth, limp, unstable articulation of the affected joint, and decreased range of motion. Complications are reported in approximately 10% to 25% of all cases. Risk factors for sequelae include delay in time to diagnosis of more than 4 or 5 days, onset of disease in infancy, infection with *S. aureus* or gram-negative bacteria, and infection of adjacent bone. In one study from Costa Rica, a 4-day course of dexamethasone given with appropriate antimicrobial and surgical therapy decreased the duration of symptoms and long-term joint dysfunction. [40]. Further studies are needed to confirm the benefits and risks of this treatment approach.

### Summary

The numbers of bone and joint infections resulting from vaccine-preventable infections, such as Hib and *S. pneumoniae*, have decreased in recent years. *S. aureus* remains an important cause of pyogenic arthritis and osteomyelitis, and

the prevalence of CA-MRSA is increasing. Transition from intravenous to oral antibiotic therapy remains the treatment of choice for uncomplicated pediatric bone and joint infections if the family is reliable and close follow-up can be ensured.

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