Current Approach to the Evaluation and Management of Septic Arthritis

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Abstract: Septic arthritis is an emergent condition caused by bacterial infection of a joint space. The most common etiology is hematogenous spread from bacteria, but it can also occur from direct inoculation from bites, injection injuries, cellulitis, abscesses, or local trauma. Septic arthritis occurs most frequently in the lower extremities, with the hips and knees serving as the most common locations. The most sensitive findings include pain with motion of the joint, limited range of motion, tenderness of the joint, new joint swelling, and new effusion. Laboratory testing and imaging can support the diagnosis, but the criterion standard is diagnostic arthrocentesis. Treatment involves intravenous antibiotics and joint decompression.

Key Words: arthritis, infection, septic joint

TARGET AUDIENCE

This CME activity is intended for all practitioners who care for pediatric patients presenting with possible septic arthritis, which may include general pediatricians, pediatric emergency physicians, general emergency physicians, sports medicine physicians, and orthopedic surgeons.

LEARNING OBJECTIVES

After completion of this article, the reader should be better able to:

1. Describe the signs and symptoms of pediatric septic arthritis.
2. Assess the laboratory and imaging tests that can be utilized to facilitate the diagnosis.
3. Explain the management strategies for pediatric septic arthritis.

Joint pain is a common presentation to the emergency department and can have a wide range of etiologies ranging from benign to life-threatening. One of the most dangerous causes is septic arthritis. Bacterial septic arthritis has been suggested to account for up to 6.5% of all childhood arthritis cases.1 The overall incidence of septic arthritis has been estimated at 4 to 10 cases per 100,000 children.2,3

Risk factors for the development of septic arthritis include young age (ie, aged <3 years), male sex, preceding trauma, immunocompromised state, respiratory distress syndrome, and history of umbilical cord catheterization.1,4-6 Septic arthritis most commonly affects the lower extremities, primarily involving the knee, hip, and ankle joints.5,3 While the hip and knee each account for approximately one-third of all pediatric septic joint infections, the knee is the most frequent overall location in young infants and neonates.3,7,8 Interestingly, up to 20% of septic arthritis cases may be polyarticular, although this is most common in immunocompromised patients.7,9,10 Importantly, among pediatric patients with septic arthritis, 10% to 13% of children will have a concomitant osteomyelitis, and 9% to 11% of children will develop bacteremia or sepsis.1,11

Septic arthritis is important to diagnose and rapidly treat in order to prevent long-term disability. Therefore, it is essential for providers to understand the historical features, physical examination findings, diagnostic testing, and management options in order to provide optimal care for these patients.

Anatomy and Pathophysiology

The most common cause of septic arthritis is hematogenous spread of bacteria from concomitant bacteremia, whereas a much smaller proportion of cases are due to direct inoculation from bites, injection injuries, cellulitis, abscesses, or local trauma.3,7,10,12 Because the cells of the joint lining lack a basement membrane, the joint space is particularly vulnerable to bacteremic seeding.7,13 Neonates and children younger than 18 months are at the highest risk because of significantly increased vascularity at the physeal plate, allowing for easy translocation of bacteria.4,5

Several factors play a role in the evolving epidemiology of pediatric septic arthritis, including improvements in vaccinations, antibiotics, and the changing prevalence of bacteria.1,13 The causative agent often varies depending on the geographical location and age group.8,10,13,14 One study from India found that the majority of cases were caused by methicillin-sensitive Staphylococcus aureus (MSSA; 53%), followed by Escherichia coli (18%), and Klebsiella pneumoniae (13%).15 Whereas a study of neonates at a hospital in the United States isolated higher rates of group B streptococcus, Streptococcus pneumoniae, Haemophilus influenzae, Salmonella enterica, and Candida albicans.16 However, the most frequent organism isolated from the joints of children and adolescents remains S. aureus, with a steady rise in the incidence of community-acquired methicillin-resistant S. aureus (MRSA) strains.15,16 These organisms usually gain access to the bloodstream through small breaks in the skin or mucous membranes, whereas septic arthritis from gram-negative species is more likely to arise from bacteremia following injection drug use or damage to the lining of the genitourinary or gastrointestinal tracts.7,17,18

Once the bacteria have entered the joint space, they adhere to the synovium and cause damage through several mechanisms, including direct damage from the bacterial toxins and from the host's inflammatory response.7 The joint cartilage is also susceptible to ischemic injury as it is avascular and dependent on the synovium for oxygen and nutrients.7 Excessive pressure from the purulent joint fluid accumulation can decrease blood flow to the synovium, further worsening the joint damage.7

History and Physical Examination

Patients may present with a myriad of symptoms, including fever, joint pain, refusal to walk, or limited range of motion in
the affected joint. The most sensitive findings include pain with motion of the joint, limited range of motion, tenderness of the joint, new joint swelling, and new effusion. However, swelling, tenderness, and effusions may be more difficult to detect in deeper joints (eg, hip, shoulder, sacroiliac). Although commonly described, fever is found in only 34% to 54% of patients, and axial load pain is seen in only 36% of cases. Several comorbidities increase the likelihood of septic arthritis. For example, diabetes mellitus and rheumatoid arthritis significantly increase the risk of septic arthritis due to immunosuppression, existing joint damage, and a higher propensity for skin infections, which can lead to direct inoculation of the joint.

Unfortunately, younger children and neonates often have a delay in diagnosis because they present in a more atypical fashion and may not be able to provide a reliable history or examination. This age group may present with more subtle signs, such as irritability, poor feeding, local warmth, mild joint pain, or pseudoparalysis. Risk factors in this population include prolonged hospital or neonatal intensive care unit stays with multiple peripheral or central intravenous lines, anemia, human immunodeficiency virus infection, low birth weight, and prematurity.

### Diagnostic Testing

While blood tests are often obtained, they are inadequate to exclude the diagnosis of septic arthritis. The serum white blood cell (WBC) may be elevated, but the sensitivity ranges from 42% to 90% with a positive likelihood ratio of only 1.4 to 1.7.12,17,18,24-27 The erythrocyte sedimentation rate (ESR) differs based on the threshold value that is selected, ranging from a sensitivity of 66% for 15 mm/h to 97% for 30 mm/h. C-reactive protein (CRP) greater than 10 mg/dL has a sensitivity of 87% to 91%. Unfortunately, both CRP and ESR are poorly specific with values ranging from 11% to 49%. Procalcitonin has been found to have a much higher specificity, ranging from 94% to 100%. While promising, more data are needed on the diagnostic accuracy of procalcitonin prior to routine use. Blood cultures should be obtained in all patients with suspected septic arthritis, as they can help identify the etiologic agent if the synovial fluid culture is negative. Importantly, up to 14% of patients with negative synovial fluid cultures will have positive blood cultures.

Radiographs are often obtained of the affected joints and may demonstrate soft tissue swelling or a joint effusion. Ultrasound, computed tomography, and magnetic resonance imaging may be more accurate for identifying the effusion but are unable to confirm or exclude the diagnosis of septic arthritis. Ultrasound has the added benefit of identifying the optimal site for aspiration and providing real-time guidance during the procedure.

The criterion standard for diagnosing septic arthritis is aspiration of the synovial fluid. Synovial fluid analysis can also help with determining alternate etiologies for the joint effusion, including hemorrhrosis, gout, pseudogout, and other forms of inflammatory arthritis (Table 1).

While a synovial WBC greater than 50 × 10^9/L is concerning for septic arthritis, a synovial WBC greater than 100 × 10^9/L is highly specific for the diagnosis. Importantly, an elevated synovial WBC can be found with other inflammatory causes of arthritis (eg, gout, pseudogout). Additionally, one study found that up to half of all patients with culture-proven septic arthritis had a synovial WBC of less than 28 × 10^9/L. Synovial polymorphonuclear leukocytes (PMNs) are also typically elevated in septic arthritis but are only 60% sensitive and 78% specific when the synovial PMNs are greater than 90%. Therefore, while synovial WBC or PMNs can suggest the diagnosis, they are insufficiently accurate to confirm or exclude the diagnosis in isolation.

Lyme arthritis can present a challenge to clinicians practicing in Lyme-endemic areas, as patients can present with an isolated monoarticular arthritis, and synovial fluid findings often overlap those of septic arthritis. The following features are more suggestive of septic arthritis in these populations: age younger than 2 years, involvement of a nonknee joint, fever, refusal to bear weight, pain with short arc motion, elevated peripheral WBC count, elevated ESR, elevated CRP, and a significantly elevated synovial WBC count (>100 × 10^9/L). However, given the significant overlap in features, it is advisable to also obtain Lyme serology (ie, immunoglobulins M and G) in endemic areas when there is suspicion of Lyme arthritis.

Other diagnostic studies, such as glucose, protein, lactate, and crystal analysis, may also be helpful; however, the single most important study to obtain is a Gram stain and culture. This is particularly important with neonates and younger infants, in whom the total synovial fluid may not be sufficient to run all of the available tests. While the Gram stain can be used to suggest the diagnosis, it should not be relied upon to exclude septic arthritis in isolation, as studies have found that the sensitivity is only 29% to 65%, while the specificity is 80% to 100%. Synovial fluid cultures will identify the underlying pathogen in more than 80% of cases. False-negatives can occur due to a variety of reasons, including presentation very early in the clinical course, obtaining a sample after antibiotics are given, inadequate fluid sample, arthrocentesis of a nearby incorrect joint space or bursa, and poor plating technique. In these cases, the diagnosis is often made based on a combination of clinical and laboratory results or operative findings. To decrease the likelihood of a false-negative culture, larger amounts of synovial fluid should be collected when possible, and samples intended for culture should be placed in blood culture bottles.

### Management

The management of pediatric septic arthritis includes intravenous antibiotics and joint decompression with irrigation. Antibiotic

### TABLE 1. Synovial Fluid Findings in Monoarticular Arthritis

<table>
<thead>
<tr>
<th>Synovial Fluid Measure</th>
<th>Normal Fluid</th>
<th>Noninflammatory</th>
<th>Hemorrhagic</th>
<th>Inflammatory</th>
<th>Septic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Color</td>
<td>Clear</td>
<td>Yellow</td>
<td>Red</td>
<td>Yellow</td>
<td>Yellow/green</td>
</tr>
<tr>
<td>Clarity</td>
<td>Transparent</td>
<td>Transparent</td>
<td>Bloody</td>
<td>Translucent-opaque</td>
<td>Opaque</td>
</tr>
<tr>
<td>Viscosity</td>
<td>High</td>
<td>High</td>
<td>Variable</td>
<td>Low</td>
<td>Variable</td>
</tr>
<tr>
<td>WBCs</td>
<td>&lt;2 × 10^9/L</td>
<td>&lt;2 × 10^9/L</td>
<td>&lt;2 × 10^9/L</td>
<td>2–100 × 10^9/L</td>
<td>10–100 × 10^9/L</td>
</tr>
<tr>
<td>Percentage of PMNs</td>
<td>&lt;25%</td>
<td>&lt;25%</td>
<td>50%–75%</td>
<td>&gt;50%</td>
<td>&gt;75%–80%</td>
</tr>
<tr>
<td>Culture result</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Usually positive</td>
</tr>
</tbody>
</table>
therapy is initiated empirically to cover the suspected organism based on age, vaccination status, and underlying comorbidities.\textsuperscript{45,50} Historically, \textit{H. influenza} was a common cause of septic arthritis and osteomyelitis.\textsuperscript{51} However, with the widespread prevalence of vaccination against \textit{H. influenza}, infections have declined dramatically.\textsuperscript{51} The underlying causes can vary significantly by age group. For example, the primary causes of septic arthritis in neonates are group B streptococcus, \textit{S. aureus}, and gram-negative organisms.\textsuperscript{52–54} Therefore, first-line treatment usually consists of oxacillin or cefotaxime plus gentamicin.\textsuperscript{52–54} In older children, pathogens include MSSA, \textit{Streptococcus pyogenes}, and \textit{Kingella kingae}.\textsuperscript{52} As a result, antibiotic coverage for this group includes either an antistaphylococcal penicillin (eg, oxacillin, nafcillin) or a first-generation cephalosporin.\textsuperscript{52} \textit{Staphylococcus aureus}, including both MSSA and MRSA, remains the most common overall cause of septic arthritis in all age groups, but the proportion of resistant organisms has increased over the past 2 decades.\textsuperscript{55–57} In a retrospective study of confirmed osteomyelitis or septic arthritis, rates of MRSA rose from 11.8\% in 2001–2002 to 34.8\% in 2009–2010.\textsuperscript{15} Consequently, it has been recommended to provide empiric coverage for MRSA if local MRSA rates are higher than 10\% or the patient has MRSA risk factors (eg, recent hospitalization, injection drug use, immunocompromise).\textsuperscript{4,5,15,54} Vancomycin is considered first-line for MRSA coverage, whereas linezolid, clindamycin, and daptomycin are alternatives that may provide adequate coverage depending on local resistance patterns.\textsuperscript{54,58–63} Importantly, \textit{K. kingae} is often resistant to vancomycin and clindamycin, so a penicillin or cephalosporin should also be given pending culture results.\textsuperscript{64} Special consideration should be paid to patients with sickle cell disease as they are at higher risk of infection from \textit{Salmonella} species.\textsuperscript{65,66} Treatment for these patients should include a third-generation cephalosporin (eg, cefotaxime, ceftriaxone) or a fluoroquinolone (eg, ciprofloxacin).\textsuperscript{65,67} Additionally, if Lyme arthritis is on the differential, providers should include an agent that is active against 	extit{Borrelia burgdorferi} (ie, doxycycline, amoxicillin with probenecid, or ceftriaxone) while awaiting serologic results.\textsuperscript{68} Classically, intravenous antibiotics for septic arthritis have been continuously given for 4 to 6 weeks.\textsuperscript{69} However, recent studies have demonstrated that shorter durations of therapy are noninferior, while also having a lower rate of adverse effects.\textsuperscript{70,71} One prospective study of pediatric patients found that 86\% of patients were able to transition to oral antibiotics by day 5.\textsuperscript{71} In this study, a persistently elevated CRP was the most common finding associated with the need for continued parenteral therapy.\textsuperscript{71} Another study found that patients could safely be transitioned to oral antibiotics when the CRP levels dropped below 2 mg/dL.\textsuperscript{66,72} If CRP testing is not readily available, current literature supports transitioning to oral antibiotics within 5 days in uncomplicated cases.\textsuperscript{70,71,74–78} Ten total days of oral therapy is typically sufficient for treatment of uncomplicated septic arthritis, although this should be extended to 20 days if there is concomitant osteomyelitis.\textsuperscript{64,73} Several studies have suggested a potential short-term benefit to glucocorticoid therapy; however, long-term results have been inconclusive.\textsuperscript{64,79–81} These studies have found that patients treated with dexamethasone had a shorter duration of fever, fewer local inflammatory signs, less pain, lower levels of acute phase reactants, shorter duration of parenteral antibiotics, and a shorter hospital length of stay.\textsuperscript{79–81} Most studies used a dose of 0.15 mg/kg of dexamethasone given every 6 hours for 4 days.\textsuperscript{79–81} However, it is important to discuss the use of this agent with the orthopedic surgery and infectious disease team prior to initiation.

Rapid joint decompression is another important component of therapy to reduce the risk of subsequent complications.\textsuperscript{82} Joint decompression can include either open arthrotomy or serial needle aspirations. The type and number of repeat procedures vary, depending on the severity of illness, patient age, and involved joint.\textsuperscript{83} The literature remains controversial regarding whether to pursue open arthrotomy or needle aspiration. However, several studies have found that needle aspiration with irrigation is associated with similar outcomes and a shorter length of hospital stay when compared with open arthrotomy.\textsuperscript{82–86} While needle aspiration has similar outcomes in many joints, open arthrotomy is usually preferred in the hip due to the potential for worse outcomes in this area.\textsuperscript{82,83} However, one recent study suggested that if the patient had symptoms for less than 5 days and is otherwise healthy, repeated needle joint aspirations may be as effective as arthrotomy in this location.\textsuperscript{57}

### Complications

Potential complications from septic arthritis include osteomyelitis, bacteremia, and sepsis, as well as direct joint damage.\textsuperscript{64,88} Destruction of the surrounding cartilage and bone can also result in growth disturbance, joint dislocation, premature degenerative arthritis, and loss of joint function.\textsuperscript{88} The rate of complications is highest in neonates and those with delayed diagnoses.\textsuperscript{89,91–93} Neonates may not manifest growth deformities for years and should be followed through skeletal maturity.\textsuperscript{92,95} Deformities and bone length discrepancies are usually tolerated better in the upper extremities than the lower extremities.\textsuperscript{96} Septic arthritis caused by MRSA infections is associated with an increased risk of subperiosteal abscesses, as well as higher rates of septic shock, longer hospital stays, more surgical interventions, and a higher risk of long-term sequelae.\textsuperscript{57,88}

### Disposition

All cases of septic arthritis require admission and the initiation of intravenous antibiotics. An orthopedic surgeon should be consulted as soon as septic arthritis is suspected. Patients may additionally benefit from an infectious disease consult, although this is less urgent. Patients with septic arthritis should be followed after discharge to monitor for long-term complications.

### CONCLUSIONS

Septic arthritis is an emergent condition caused by bacterial infection of a joint space. This review article discusses the pathophysiology, historical features, physical examination findings, diagnostic strategies, and treatment for this dangerous condition. Knowledge of these aspects can assist providers in effectively identifying and managing this important condition.

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