Septic Arthritis

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Introduction and Epidemiology

Osteoarticular infections are a source of significant morbidity within the pediatric population. Expeditious diagnosis and multidisciplinary management are of paramount importance in an effort to mitigate complications and disability. Pediatric osteoarticular infections manifest as osteomyelitis and septic arthritis. Septic arthritis is defined as an acute infection of the synovial joints leading to inflammation and destruction of the affected joint structures, cartilage, and potential for extension to the metaphysis leading to secondary osteomyelitis in some joints. Therefore, mitigation of these complications is predicated upon judicious diagnosis, expeditious operative intervention, and antibiotic administration.

The literature provides a variable incidence of pediatric septic arthritis, which ranges from 4 to 12 per 100,000 [1–8]. The vast majority of these studies are retrospective case-control series with relatively small sample sizes [1–8] which may explain the wide variation in reported incidences. In contrast, Safdieh et al. reported epidemiologic data from a nationwide inpatient database analysis by querying hospital billing and diagnosis coding [6]. The authors demonstrated an incidence of 5.2 per 100,000 for septic arthritis [6]. This was similar to another inpatient database analysis that demonstrated a septic arthritis incidence of 4.2 per 100,000 [5]. The majority of studies suggest a static trend in the incidence of pediatric septic arthritis over time [1–8]. In resource-poor regions, the incidence of septic arthritis has been reported to be higher up to 20 per 100,000 [9].

Several risk factors and demographic associations have been noted in the literature. Okubo et al. demonstrated that pediatric septic arthritis was more prevalent among children who are male, white or black, and between ages 0 and 4 years [5]. In addition, low socioeconomic status seems to be associated with an increased prevalence of septic arthritis [5]. Furthermore, older children (10–14 years of age) were associated with increased rate of complications and sequelae such as osteomyelitis and bacteremia/septicemia

[5]. The vast majority of septic arthritis cases involve the hip, knee, and ankles, although septic arthritis can be manifested in any synovial joint. Other risk factors for septic arthritis include immunodeficiency syndromes, sickle cell disease, prematurity, respiratory distress syndrome, and low birth weight [10].

Lyme disease is also a common entity that can cause infectious arthritis in pediatric patients. Lyme disease is classically a multisystem tick-borne disease caused by the spirochete, *Borrelia burgdorferi*, and is particularly common in the northeastern region of the United States. Lyme disease is noted to be the most common tick-borne disease in the United States [11]. It is associated with a bimodal age distribution among pediatric patients from ages 5–9 years and adults from ages 55–59 years [11]. According to the Centers for Disease Control and Prevention (CDC), the geographic distribution of high incidence areas with Lyme disease appears to be expanding and, therefore, should be a more prominent differential diagnosis alongside septic arthritis [11].

Pathology and Microbiology

Primary septic arthritis is most commonly the result of hematogenous spread. Local inoculation can also occur from joint penetration and trauma. An array of inflammatory biochemical processes is elicited following bacterial joint infection. Intra-articular bacteria release toxins that trigger a cytokine cascade from the synovial tissue. The resulting inflammatory acute phase response attracts leukocytes which produce a viscous cycle of cytokine-induced damaged via the release of collagenases and peptidases that can lead to cartilage damage within 8 hours of infection [12–16]. This aggressive response represents an orthopedic surgical emergency and can be quelled with expeditious source control via surgical intervention and antibiotic administration.

Secondarily, septic arthritis can occur from bacterial translocation from an adjacent source. The synovial joint capsule of the shoulders, elbows, hips, and ankles also contain the metaph-

ysis. In these joints, extra-cortical extension of a metaphyseal osteomyelitis can seed the capsular joint space. Conversely, primary septic arthritis can cause a metaphyseal osteomyelitis via spread through the transphyseal network of vessels. This latter mode of metaphyseal spread is more common during the first 18 months of age [17]. Merlini et al. reviewed contrast-enhanced MRI studies and demonstrated that the transphyseal network of vessels can potentiate translocation of bacteria and cause concomitant hip osteomyelitis and septic arthritis in patients less than 18 months of age, which was a previous hypothesis proposed by Alderson et al.'s animal model study [17, 18].

Across all age groups, *Staphylococcus aureus* is the most commonly found bacterial cause of septic arthritis, with increasing rates of community-acquired *methicillin-resistant Staphylococcus aureus* (MRSA) [17] (Figs. 12.1 and 12.2). MRSA genotypes with two genes, *Panton-Valentine leukocidin (pvl)* and *fibronectin-binding factor (fnbB)*, produce an aggressive form of septic arthritis [19]. MRSA genotypes that stem from an USA300 clone often carry both of these genes. Carrillo-Marquez et al. demonstrated that MRSA-USA300 is the predominant MRSA genotype that causes septic arthritis in children – 81% of MRSA infections [20]. This genotype is associated with longer duration of fever, higher incidence of bacteremia, osteomyelitis, thrombophlebitis, pulmonary embolism, and longer hospital stay [19, 20]. The severity of infection associated with MRSA-USA300 is linked to the gene products of *pvl and fnbB*. *Pvl* cytotoxin fenestrates the leukocyte cell membrane and instigates cell lysis, which releases more cytokines and fuels the inflammatory viscous cycle. This is aided by the function of *fnbB*, which encodes proteins that facilitate enhanced bacterial invasion, adhesion, and biofilm formation [19, 20].

Certain pediatric populations are associated with other types of bacterial septic arthritis (Table 12.1). Namely, in infants, Group B Streptococcus is prevalent and is a common cause of many osteoarticular infections [21, 22]. *Neisseria gonorrhoeae* must be considered in sexual assault victims or in sexually active adolescents presenting with signs of septic arthritis. In addition, *Kingella kingae* is increasingly found in culture and polymerase chain reaction (PCR) analysis in septic arthritis cases in children younger than 4 years of age [23, 24]. Furthermore, *Salmonella* associated septic arthritis is more frequent in countries such as Zambia, Kenya, and Malawi

Fig. 12.1 Bacterial causes of osteoarticular infection [17]

Most Common Bacteria Identified in Osteoarticular Infections by Tissue Culture
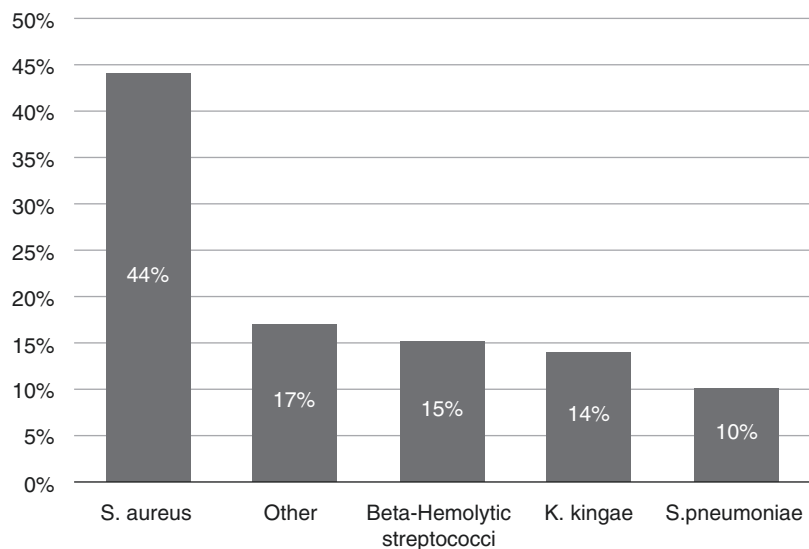
where there is a higher prevalence of sickle cell disease and malaria [9].

The pathophysiology of Lyme arthritis has been extensively studied. Arthritis is the most

Fig. 12.2 This illustration depicts a three-dimensional (3D) computer-generated image of a group of methicillin-resistant *Staphylococcus aureus* (MRSA) bacteria, which were arranged in a cluster. ID # 19059, Center for Disease Control USA 2013/Antibiotic Resistance Coordination and Strategy Unit/Courtesy Jennifer Oosthuizen - Medical Illustrator. (With permission)

prominent feature of Lyme disease [11]. Following a deer tick bite, *B. burgdorferi* modifies surface lipoproteins that promote infection to the synovial tissue and facilitate inflammation of the joint [25] (Fig. 12.3a, b). Acutely, arthritis results from synovial inflammation, preponderance of neutrophils, immune complex accumulation, and cytokine release [25]. Several host genetic factors have been studied that may predispose and facilitate progressive and refractory arthritis [26]. Following antibiotic treatment for acute Lyme arthritis, some patients can have recurrent polyarticular disease. Steere et al. have elucidated three main theories for this phenomenon: T-cell epitope mimicry, persistent or recurrent infection, and bystander activation (persistent immune reactivity despite eradication of *B. burg-*

Table 12.1 Other causative organisms of septic arthritis

Organism	Circumstance
Group B streptococcus	Infants
Neisseria gonorrhoeae	Sexual abuse victims, sexually active adolescents
Salmonella typhi	Sickle cell disease or trait
Kingella kingae	Young children below 4 years of age
Pseudomonas aeruginosa	Penetrating foot trauma
Pasteurella sp.	Animal bite
Haemophilus influenzae	Unimmunized patient
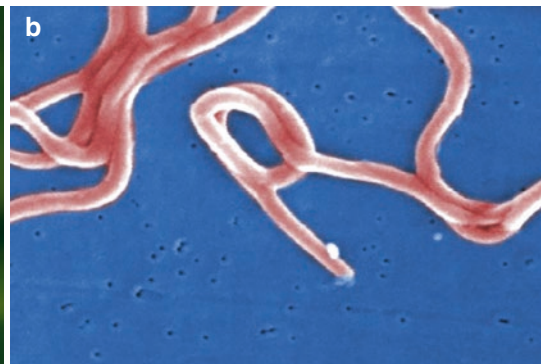
Fig. 12.3 (**a**) Photograph showing the blacklegged tick, *Ixodes pacificus*, known vector for the zoonotic spirochetal bacteria, *Borrelia burgdorferi*, which is the pathogen responsible for causing Lyme disease. ID # 7663/ Center for Disease Control USA 2005/Courtesy James Gathany; William L. Nicholson, Ph.D. (With permission).

(**b**) This digitally colorized scanning electron microscopic (SEM) image depicts a grouping of gram-negative, anaerobic, *Borrelia burgdorferi* bacteria, which had been derived from a pure culture. ID # 13176/Center for Disease Control USA 2011/Claudia Molins/Courtesy: Janice Haney Carr. (With permission)

dorferi) [25]. Even after antibiotic treatment, *B. burgdorferi* can remain intracellular and be detected with culture and PCR testing [27, 28].

Clinical Presentation and Examination

Septic arthritis is most commonly a monoarticular disease characterized by acute onset of pain, swelling, and joint immobility (pseudoparalysis). In general, fever is also reported. Initially, each patient must be assessed for associated life-threatening systemic conditions. Patients with fever, tachycardia, tachypnea, and hypotension should be investigated for sepsis. In addition, patients with nuchal rigidity should be concomitantly evaluated for meningitis. Similarly, auscultation of the heart and lungs may prompt evaluation for pneumonia, if there are abnormal breath sounds, or infectious endocarditis, if a cardiac murmur is present.

Initial diagnosis of septic arthritis in the emergency department is difficult. Vardiabasis et al. demonstrated that the initial emergency department diagnosis of septic arthritis was consistent only 42% of the time with the final definitive diagnosis [29]. This is particularly true in younger children who are non-ambulatory and/or non-verbal. Infants can have general malaise, distress, and pain upon moving the affected joint. Infants may not have fever or other systemic signs of infection. In the young child, diagnosis is also difficult as they can have distress with diaper changes, refusal to eat, and persistent crying. Patients of ambulatory age may refuse to bear weight and favor the contralateral extremity.

On examination, the affected joint may have swelling, effusion, warmth, and erythema (Fig. 12.4). Any attempt with short arc range of motion will produce pain and distress. In cases with septic hip arthritis, the child will present with pain and limp. In addition, capsular accumulation of fluid or abscess will prompt the child to place the hip joint in flexion, abduction, and external rotation in an effort to maximize intracapsular volume and limit stretching of the joint capsule, which triggers pain. In some instances,

Fig. 12.4 A 10-year-old male who presented with a warm, swollen, erythematous, and painful left knee with an obvious effusion. Topical analgesia cream applied before knee joint arthrocentesis

hip pain can be referred to the knee – which may be the chief presenting complaint. This is due to nerve innervation of the hip joint by articular branches of the obturator nerve that refer pain to the dermatomal distribution along the anteromedial thigh via cutaneous nerve branches. If increased intracapsular pressure causes a capsular tear, fluid collections can develop in the surrounding musculature, and hip joint instability should be considered.

In addition to septic arthritis, Lyme disease is an important consideration in a child who presents with joint pain and limp, particularly in endemic regions. It must be noted that Lyme can present many months after the initial tick bite and pain can be recurrent [30]. The Centers for Disease Control has provided criteria for clinical case definition along with laboratory diagnostic criteria (Table 12.2) [11]. Aiyer et al. reported on the distribution of joint involvement in patients with Lyme disease and demonstrated that the knee is most commonly involved

Table 12.2 CDC clinical and diagnostic criteria for Lyme disease [1]

Clinical case criteria
Erythema migrans, or
One advanced manifestation, as defined below, and laboratory confirmation of infection
Recurrent, brief attacks (lasting weeks or months) of objective joint swelling in one or a few joints, sometimes followed by chronic arthritis in one or a few joints
Manifestations not considered criteria for diagnosis include chronic progressive arthritis, not preceded by brief attacks, and chronic symmetrical polyarthritis
Arthralgia, myalgia, or fibromyalgia syndromes alone are not criteria for musculoskeletal involvement
Laboratory criteria
Positive culture for *B. burgdorferi* from clinical specimen, or
Demonstration of diagnostic levels of IgM and IgG antibodies to the spirochetes in serum
Two-tier testing interpreted using established criteria, where:
Positive IgM is sufficient only when B30 days from system onset
Positive IgG is sufficient at any point during illness
Single-tier IgG immunoblot seropositivity using established criteria, or
CSF antibody positive for *B. burgdorferi* by enzyme immunoassay (EIA) or immunofluorescence assay (IFA), when the titer is higher than it was in serum

[1] Information adapted from CDC [11] and table adapted from Aiyer et al. [31]

Distribution of Joint Involement in Lyme Arthritis
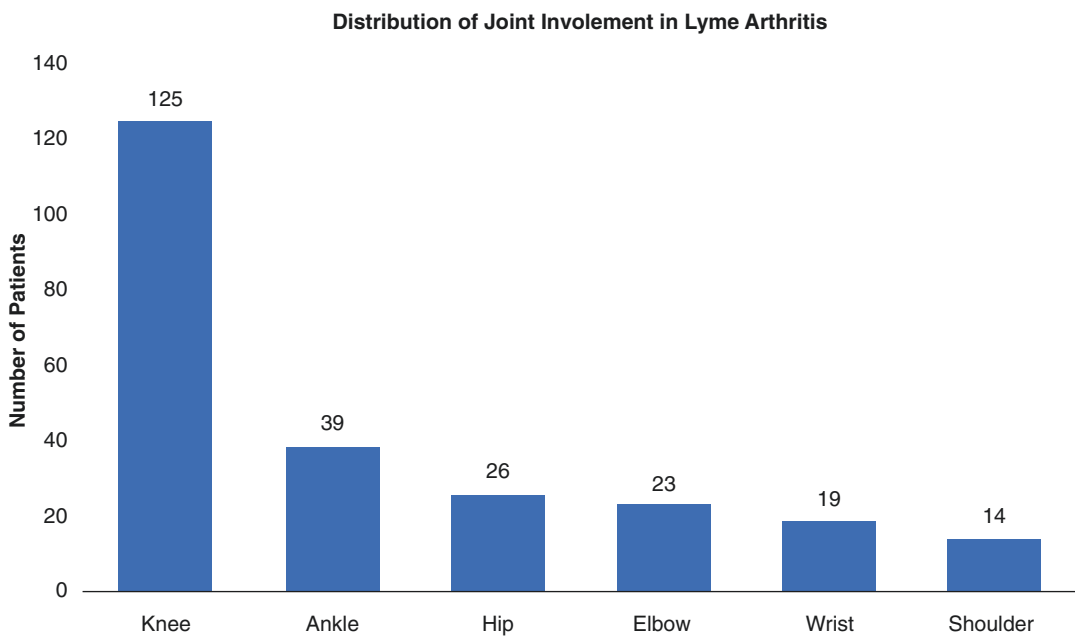
Fig. 12.5 Adapted from case series from Aiyer et al. [31] Distribution of joints involved with Lyme arthritis in 155 patients

in vast majority of cases, followed by the ankle (Fig. 12.5) [31]. Steere et al. demonstrated that 80% of patients diagnosed with Lyme disease had arthritis of some degree [32]. Symptoms were migratory and were noted, on average, 2 weeks after the onset of erythema migrans [32] (Fig. 12.6). This was associated with recurrent fatigue which lasted as long as 6 years [32]. The relapsing and remitting nature of these symptoms can distinguish Lyme from that of septic arthritis.

Fig. 12.6 This clinical photograph depicts the pathogno-monic erythematous rash in the pattern of a bull's-eye, referred to as erythema migrans. The rash manifested at the site of a tick bite, signifies a case of Lyme disease, caused by the bacterium *Borrelia burgdorferi*, and trans-mitted to humans, by the bite of infected blacklegged ticks. ID # 9875 / Center for Disease Control 2007/ James Gathany / Courtesy: James Gathany. (With permission)

Investigations and Differential Diagnosis

Septic arthritis is a clinical diagnosis with labora-tory and imaging studies utilized in an adjunctive fashion in an effort to corroborate a high pre-test probability.

Laboratory Studies

In addition to a white blood cell (WBC) count and polymorphonuclear cell-type predominance (left-shift) on the peripheral complete blood count (CBC) study, serum inflammatory markers are elevated in the setting of septic arthritis. Most

Table 12.3 Kocher criteria [42]

Non-weight-bearing on affected side
Erythrocyte sedimentation rate >40 mm/hr
Fever >38.5 °C (101.3 °F)
White blood cell count >12,000 cells/mm^3

centers test for acute phase reactants such as C-reactive protein (CRP) and the erythrocyte sedimentation rate (ESR). The standard values for the ESR are dependent upon the testing labo-ratory and generally peak at 3–5 days within the onset of infection and normalize within 7–10 days after treatment (up to 4–6 weeks). An elevated CRP signifies an acute inflammatory response and peaks within 48 hours of onset of the infection and starts declining within 6 hours of treatment initiation. Pääkkönen et al. demonstrated that if both studies remain normal after a 3-day hospital stay, then septic arthritis is a low probability [33]. However, CRP elevation may not be apparent in some circumstances, particularly in *K. kingae* infections. Basmaci et al. demonstrated that in 10% of septic arthritis cases with *S. aureus* or *K. kingae*, the CRP was less than 10 mg/L [34]. Similarly, Ceroni et al. developed a diagnostic laboratory criterion to differentiate *K. kingae* septic arthritis from that of *S. aureus* [35]. The authors demonstrated that the CRP was consis-tently decreased in the setting of *K. kingae* infec-tions [35]. CRP is not acutely elevated in cases of osteomyelitis or other chronic infections.

Many diagnostic algorithms have been devel-oped to aid in the diagnosis of septic arthritis and distinguish this entity from transient synovitis [36–42]. The Kocher criteria was originally described to differentiate hip septic arthritis from transient synovitis of the hip (Table 12.3) [42]. The positive predictive probability was <0.2% for zero variables, 3% for one variable, 40% for two vari-ables, 93.1% for 3 variables, and 99.6% for four variables. When applied to other patient popula-tions, the Kocher criteria demonstrated diminished but good diagnostic positive predictive probabili-ties [41]. This criterion has been broadly applied to diagnose infections of other joints [42]. Other investigators have studied the utility of CRP and its role within diagnostic algorithms for septic arthritis [36–40]. Caird et al. performed a prospec-

tive randomized controlled trial to distinguish pediatric septic arthritis from transient synovitis of the hip and demonstrated that CRP >20 mg/L was a strong independent risk factor and the second-best predictor of septic arthritis [38]. This prospective trial reaffirmed the role of CRP in the diagnostic armamentarium for septic arthritis, as published by previous retrospective literature [36, 37]. CRP can also be utilized to trend the patient's clinical response to antibiotic treatment and need for additional surgical intervention.

In addition to inflammatory markers, blood cultures should also be drawn prior to the administration of antibiotics to rule out bacteremia.

Imaging

Plain radiographs should be obtained as an initial test for patients who present with joint pain, inability to bear weight, and weakness. Plain radiographs serve to rule out trauma and neoplastic bone or soft tissue disorders. In the setting of septic arthritis, plain radiographs can demonstrate signs of joint space expansion with fluid, i.e., effusion, fat pad signs, or medial joint space widening in the setting of hip or shoulder septic arthritis [40]. The role of plain radiography in the setting of septic arthritis is to rule out other co-existing pathology such as fracture or subacute-chronic osteomyelitis.

Ultrasound has become widely adopted and utilized to diagnose joint effusions in a child suspected of septic arthritis. Most centers have become reliant upon ultrasound to diagnose deep joint effusions such as in the hip or shoulder as a prerequisite to joint aspiration [43]. Ultrasound is expeditious, readily available, and without radiation. In addition, in infants, ultrasound is a reliable imaging modality to assess the status of deep joint structures, such as the cartilaginous ossific nucleus, which cannot be visualized on radiographs in infants. If both hips are imaged, a difference in joint fluid volume >5 mm compared with the contralateral side is considered an indication for aspiration [44] (Fig. 12.7). Ultrasound
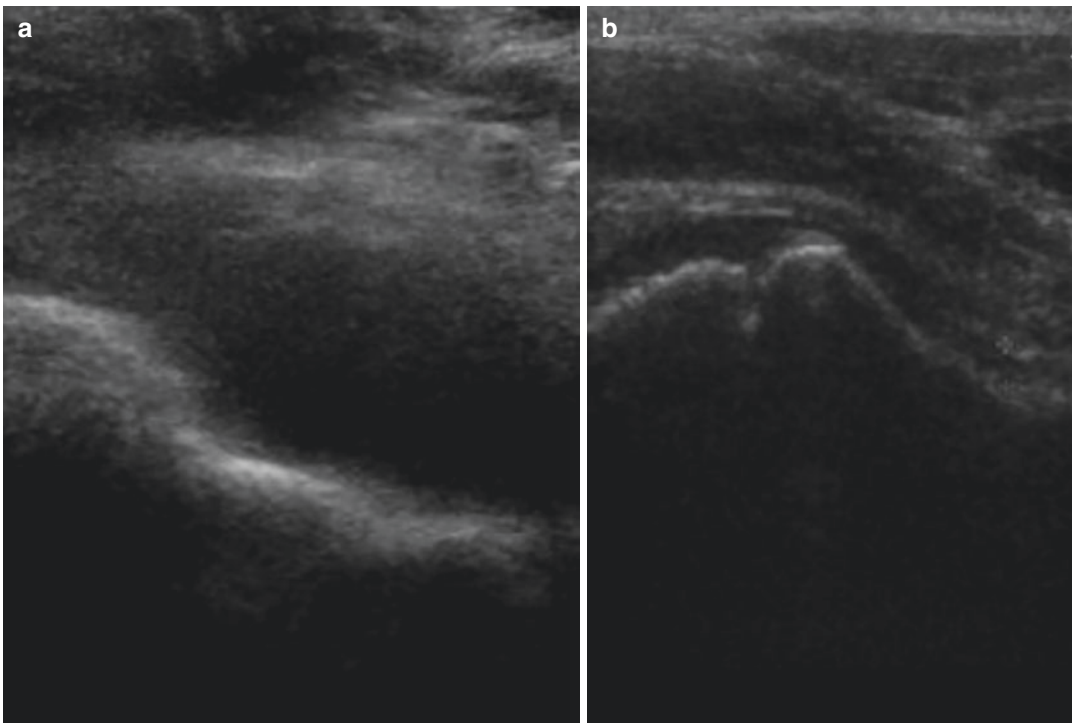
Fig. 12.7 Ultrasound of pediatric hip. (**a**) is long ultrasound cut of the hip with a large effusion. (**b**) is example of normal hip ultrasound
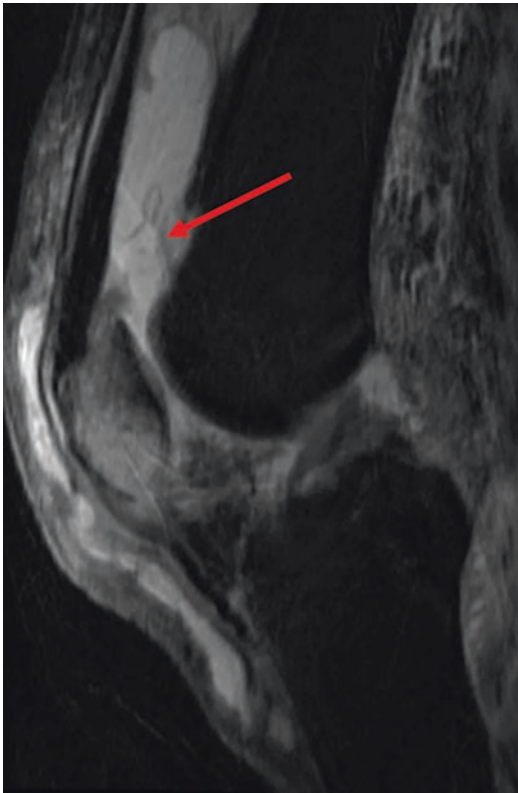
Fig. 12.8 MRI sagittal T2 image of patient with large joint effusion in setting of knee septic arthritis

is associated with a 5% false-negative rate and is suggested to be less reliable in patients with symptoms less than 24-hours or those with polyarticular involvement [45]. A negative ultrasound considerably lowers the probability of septic arthritis [46]. However, adjacent infections such as osteomyelitis and intramuscular infections must be ruled out with magnetic resonance imaging (MRI) if clinical suspicion for an osteoarticular infection is high [46]. In the setting of positive ultrasound findings, along with concerning clinical and laboratory studies, arthrocentesis is warranted. It should be noted that an ultrasound cannot differentiate fluid density between joint purulence and sterile effusions, as seen in the setting of inflammatory arthropathies.

To characterize the full extent of an osteoarticular infection, an MRI is an extremely valuable and indispensable tool (Fig. 12.8). MRI can also be utilized if there is a diagnostic quandary with equivocal ultrasound or laboratory results with high clinical suspicion and pre-test probability. Furthermore, an MRI is effective at identifying concomitant unsuspected adjacent osteoarticular infections [47, 48]. Monsalve et al. reviewed MRI studies of patients with septic arthritis of which 68% had concomitant unsuspected osteomyelitis [47]. As such, some authors have recommended routine MRI studies in patients suspected of septic arthritis in an effort to detect these related adjacent infections [47, 49]. However, other authors have expressed caution and developed algorithms to ensure appropriate use of cross-sectional imaging [50]. Rosenfeld et al. demonstrated that age above 3.6 years, CRP >13.8 mg/L, duration of symptoms >3 days, platelets <314 × 10 cells/μL, and ANC >8.6 × 10 cells/μL were risk factors for adjacent infection in the setting of pediatric septic arthritis [50]. Patients with three or more of these risk factors were associated with an 80% positive predictive value for adjacent osteoarticular infection [50].

In the setting of Lyme disease, Ecklund et al. identified three characteristic MRI findings – myositis, adenopathy, and lack of subcutaneous edema. These findings along with a consistent clinical picture of Lyme arthritis may prevent unnecessary surgical intervention [51].

Arthrocentesis

If the clinical picture and the serum laboratory and radiology studies are concerning for septic arthritis, the next best step in diagnosis is a joint aspiration. The sample should be obtained prior to the initiation of antibiotics. In most cases, aspiration of a superficial joint, such as the knee or elbow, can be performed at bedside with relative ease and accuracy with proper pain control for the child. For deep joints, such as the hip, an ultrasound-assisted arthrocentesis is often helpful and necessary. The joint aspirate sample should be sent to the laboratory expeditiously to evaluate, at a minimum, for gram stain/culture and synovial fluid cell count with differential. If an ultrasound-guided arthrocentesis fails to yield synovial fluid for laboratory analysis, a surgical

arthrocentesis is recommended in the operating room under anesthesia. This sample should be sent for immediate analysis to aid in surgical decision-making.

The role of gram stain has been questioned. In a systematic review of the English literature, Kang et al. demonstrated that gram stain alone is only positive for approximately 30% of cases, which increased when the tissue was also cultured [10, 52]. Furthermore, Bram et al. demonstrated that gram stain is a poor screening tool for the detection of septic arthritis and the sensitivity further drops for the detection of gram-negative organisms [52]. As such, a negative gram stain must be taken into clinical context and further work-up must be performed if suspicion for septic arthritis remains high.

PCR studies of synovial fluid or tissue can expedite the identification of the causal organism and is an area of further research [53]. PCR studies are of particular utility if antibiotics were initiated prior to joint fluid aspiration, in which case, gram staining and culture become less worthwhile. In addition, PCR studies for the detection of *K. kingae* have garnered increased attention and practice [54]. In endemic regions, Lyme titer and PCR should also be obtained.

Synovial fluid total nucleated cell count $\geq 50,000/mm^3$ with increased percentage of polymorphonuclear cells (>90%) is classically associated with septic arthritis [55]. Margaretten et al. demonstrated the likelihood ratios for septic arthritis as a function of synovial fluid total nucleated cell count (Table 12.4) [55]. For counts $\geq 50,000/mm^3$, the likelihood ratio for septic arthritis is 2.9 (confidence interval (CI), 2.5–3.4)

Table 12.4 Synovial WBC count stratified by likelihood for septic arthritis [55]

Synovial WBC count	Likelihood ratio for septic arthritis	95% confidence interval for likelihood ratio
<25,000/μL	0.32	0.23–0.43
≥25,000/μL	2.9	2.5–3.4
≥50,000/μL	7.7	5.7–11.0
≥100,000/μL	28.0	12.0–66.0

Adapted from Margaretten et al. [55]

[55]. Despite these findings, the evidence for diagnostic cell count thresholds remains debated and the clinical picture must be given greater weight [56]. For example, Heyworth et al. demonstrated that hip septic arthritis was associated with synovial fluid cell counts of 25,000 to 75,000/mm^3 [56]. In 17% of their cases, the synovial fluid WBC values were <50,000/mm^3 [56].

Lyme Arthritis

Lyme arthritis and inflammatory arthritis may be polyarticular and migratory and accompany dermatologic findings. Titers for Lyme must be obtained if the patient resides in endemic areas and if the clinical suspicion is high. The CDC provides a diagnostic laboratory algorithm for Lyme disease (Fig. 12.9) [11]. A modified two-stage serologic test is utilized [57]. The initial ELISA or immunofluorescence assay is confirmed with a Western blot analysis. Negative IgG titers rule out Lyme disease [57]. PCR testing of Lyme from synovial fluid has a sensitivity of 80–85%; however, active infection is difficult to determine as the PCR can detect DNA from past infection with persistent *B. burgdorferi* genetic material [57]. In addition, there is no agreed upon threshold for synovial fluid total nucleated cell counts that define Lyme arthritis. Some authors have noted an average of 25,000 cells/mm^3 but can be up to 100,000 cells/ [3, 58].

Differential Diagnosis

Trauma, neoplastic processes, and other osteoarticular infections must be considered in patients who present with joint pain consistent with septic arthritis. For hip pain specifically, Legg-Calve-Perthes disease, slipped capital femoral epiphysis, transient synovitis, osteomyelitis, and local intramuscular abscess can mimic signs of septic arthritis. Furthermore, conditions such as cellulitis, inflammatory arthritis, and hemarthroses must be assessed. To rule out adjacent

CDC Modified Two-Tiered Testing for Lyme Disease

Initial Test   **Confirmatory Test**
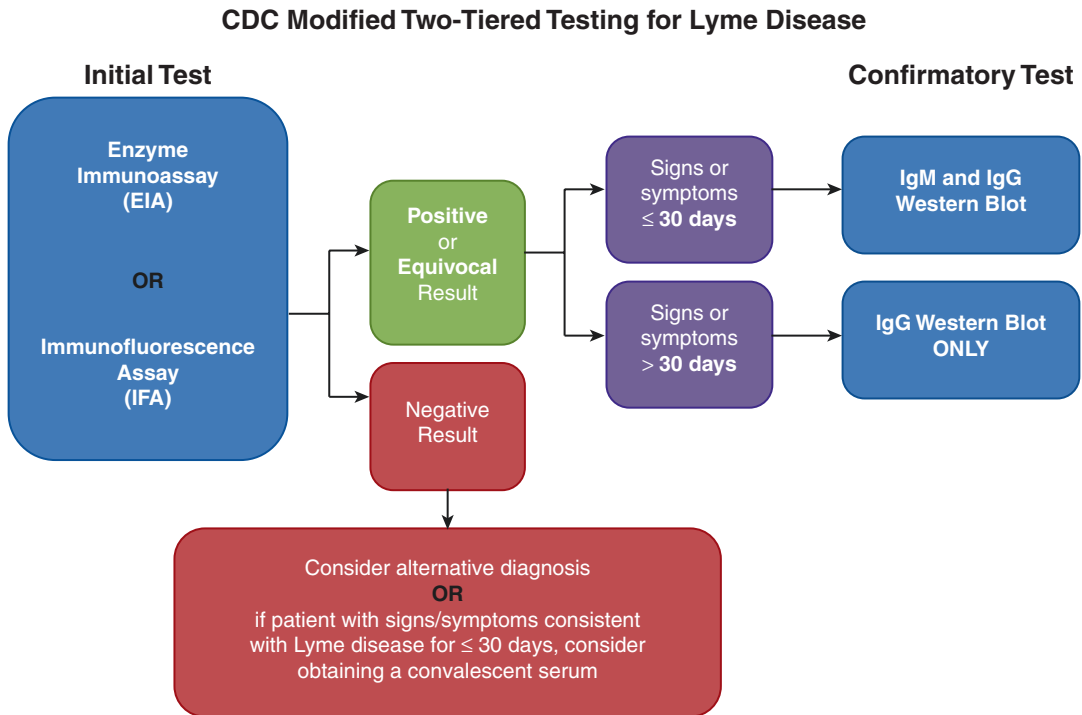
Fig. 12.9 The CDC recommended modified two-step diagnostic process for Lyme disease

osteomyelitis in the hip, some authors have recommended ilium and femoral neck bone marrow aspiration during surgical intervention, particularly if the MRI is equivocal [59]. Transient synovitis typically follows a history of an upper respiratory tract infection and is less likely to present with high fever and chills.

Clinical diagnostic rules, such as the Kocher criteria, have been developed and validated to help distinguish septic arthritis from other similar processes such as transient synovitis [42]. In addition, the range of the synovial fluid total nucleated cell count can be indicative of the disease process. In a systematic review of the literature with meta-analysis, Cruz et al. stratified synovial fluid cell counts with 95% confidence intervals (CI) as 5644–15,388 cells/mm^3 for transient synovitis, 47,533–64,242 cells/mm^3 for Lyme arthritis, and 105,432–260,214 cells/mm^3 for septic arthritis [60].

Bockenstedt et al. provide an excellent comparison of various types of arthritis seen pediatric patients (Table 12.5).

Treatment

After establishing a diagnosis of septic arthritis, treatment is twofold and is optimized with multidisciplinary management and coordination with general pediatrics, orthopedic surgery, and infectious disease specialists. Adequate source control of the infection with joint irrigation and debridement is paramount. In addition, determination of the causal organism and subsequent antibiotic sensitivity is necessary for definitive antibiotic treatment. Prior to this, empiric antibiotics should be prescribed based upon evidence-based recommendations with regard to the most causal organism, patient's age, microbiome of the region, and the patient's clinical state. Typically, antibiotics should be held until a synovial fluid or tissue culture is obtained in an effort to tailor antibiotics to the causal bacteria – except in situations of sepsis and hemodynamic instability, where empiric broad spectrum antibiotics may be life-saving and should not be delayed.

Table 12.5 Comparison of common arthritides in pediatric patients [58]

	Lyme arthritis	Bacterial septic arthritis	Gonococcal arthritis	Reactive arthritis	Oligoarticular juvenile inflammatory arthritis	Rheumatoid arthritis
Onset	Intermediate, months (average 6 months) after rash	Acute (days–2 weeks)	Acute, within 1 month of initial infection	Acute, 2–4 weeks post initial viral infection	Insidious	Insidious
Arthritis features	Oligoarticular, especially knee; may be migratory (<5 joints)	Usually monoarticular	Usually monoarticular	Oligoarticular, lower limb, especially knee	Oligoarticular, lower limb	Classically symmetric, polyarticular pain, stiffness
Systemic signs/symptoms at arthritis onset	50% with antecedent migratory arthralgia; fatigue; occasionally fever	Fever in 60%	Migratory polyarthralgia, often fever, rash, tenosynovitis	Enthesitis, extra-articular features	Unusual	Fatigue
ESR/CRP	Usually modest elevation, but occasionally normal or very elevated	Usually elevated	Usually elevated	Marked elevation in acute phase	Usually elevated	Usually elevated
Synovial fluid cell count (white blood cells/mm^3)	500–>100,000 (average 25,000) 75% PMNs	2000–>100,000 >90% PMNs	15,000–>100,000 >90% PMNs	2000–64,000 variable PMNs	2000–50,000 (ave 20,000) 60% PMNs	2000–50,000 (mean 15,000) variable PMNs
Synovial fluid culture	Negative	Positive in 70–90%	Positive in <50%	Negative	Negative	Negative
Synovial fluid PCR for bacterial DNA	Positive	Data not available	Positive	Negative	Negative	Negative

Adapted from Bockenstedt et al. [58]

Medical Intervention

Optimal empiric antibiotic selection for pediatric septic arthritis is predicated mainly upon the age of the patient, the patient's immunization status (*H. influenza*), and the prevalence rate of MRSA in the local population. Regions with MRSA prevalence ≥10%, ICU patients, or immunocompromised hosts should be treated empirically for MRSA [61]. It should be noted that if vancomycin and gentamycin are prescribed, a target trough level must be monitored regularly and the antibiotic dosing be adjusted accordingly. In addition, the patient's blood cell counts and hepatorenal function must be monitored in the setting of antibiotic therapy to assess for toxicity.

The empiric antibiotic treatment plan for children less than 3 months of age is typically vancomycin and gentamicin combination therapy [62, 63]. This regimen will cover MRSA, Group B Streptococcus, and gram-negative pathogens. The optimal dosing, frequency, and monitoring can vary, and a multidisciplinary dosing protocol should be discussed with infectious disease specialists and pharmacy. For older children, a first-generation cephalosporin is generally prescribed – or vancomycin if there is high rate of community-acquired MRSA. It is important to note that cephalosporins also covers *K. kingae*, whereas vancomycin does not. As such, if both MRSA and *K. kingae* are prevalent, a cephalosporin should be added along with vancomycin [24]. This is similar for *N. gonorrhoeae* as well along with the alternative, doxycycline. Following synovial fluid or tissue culture and antibiotic sensitivity, the antibiotics should be tailored appropriately.

The duration of antibiotic treatment is dependent upon how the patient performs clinically. In most cases, a short course of intravenous antibiotic treatment followed by 3 weeks of oral therapy is sufficient for septic arthritis [64]. Complicated septic arthritis may warrant longer intravenous antibiotic treatment. Several studies have assessed the optimal time to switch from intravenous to oral therapy [65–69]. Chou et al. demonstrated good clinical outcomes when oral antibiotics were initiated when a 50% reduction in CRP is observed with intravenous antibiotics [67]. Arnold et al. recommended that a CRP less than 2 mg/DL is an indicator of stopping antibiotic treatment [65]. Ultimately, the patient's clinical picture will dictate optimal transition time and duration of treatment. The expedited switch to oral therapy is a departure from historic practices of keeping patients on intravenous antibiotics for several weeks, as similar outcomes were noted with both regimens alongside lesser complication profile with oral therapy [68, 69].

In addition to antibiotics, the role of corticosteroids has been assessed as an adjunctive method to reduce morbidity [70, 71]. Farrow et al. performed a systematic review and meta-analysis of both human and animal model trials in the setting of septic arthritis and demonstrated an overall consensus with regard to a reduction in duration of symptoms and inflammatory markers with corticosteroid therapy [70]. In addition, in the animal model data, corticosteroid plus antibiotic therapy was associated with a protective effect on cartilage. These findings were similar to another meta-analysis reported by Qin et al. [71]

For Lyme disease, adequate antibiotic therapy at the time of diagnosis is associated with good outcomes and can mitigate the risk for recurrent migratory arthritis [72]. Lyme arthritis is treated with antibiotics, and surgical intervention is typically not needed. It should be noted, as above, that persistent joint inflammation may be seen for several weeks or months after treatment. Clinical guidelines from the Infectious Diseases Society of America recommend 28 days of one of several oral antibiotics, typically doxycycline or a cephalosporin such as cefuroxime [73]. Dosing, need for intravenous antibiotics, and additional duration of therapy should be evaluated by infectious disease specialists [73].

Surgical Intervention

Septic arthritis represents a true orthopedic surgical urgency for which an irrigation and debridement of the infected joint is the cornerstone of treatment. After diagnosis and imaging to characterize the extent of infection, surgical intervention should be performed expeditiously. In the setting of hemodynamic instability, emergent surgical intervention is necessary for source control.

The type of surgical intervention, either an open arthrotomy or arthroscopic decompression, should be based upon surgeon comfort and the patient's clinical status. Arthroscopic procedures can be performed in nearly all large joints, including the hip in young patients [74, 75]. Arthroscopic hip decompression with irrigation and debridement is typically performed utilizing lateral portals although medial portal arthroscopy has been theoretically proposed [76]. Open hip arthrotomy is more commonly performed. This is achieved utilizing a direct anterior or modified anterolateral approach. Care must be taken to avoid neurovascular structures, maintain perfusion to the hip, and avoid damage to chondral surfaces.

Arthroscopic knee irrigation and debridement is popular and performed readily by most trained orthopedic surgeons. Compared to open arthrotomy, arthroscopic knee decompression is associated with less need for repeat procedures, earlier knee range of motion, and weight-bearing [77]. In addition, arthroscopic knee irrigation and debridement can be performed if a repeat procedure is indicated. In the setting of a septic knee, the risk for revision decompression is associated with bacteremia, older children, and those with late presentation [77–79]. Revision surgery is indicated if the inflammatory markers do not improve after postoperative day two, continued wound drainage, or if the patient is clinically deteriorating.

Following surgical treatment, antibiotics should be prescribed with consultation from infectious disease specialists as detailed above. Surgical follow-up should be maintained for at least a year.

Complications

Timely diagnosis, surgical decompression, and antibiotics are typically associated with favorable outcomes for septic arthritis. However, late presentation, misdiagnosis, or delay in treatment can lead to significant morbidity and even mortality. Modern data from developed regions suggest that the 1-year rate of clinical dysfunction is 10%, compared with greater than 50% in resource-poor settings and historical data [80–82]. Advancements in diagnostic capabilities, testing,

imaging, and care delivery were touted as reasons for this difference [81]. Misdiagnosis is associated with delay to arthrotomy as many culture-negative cases were attributed to juvenile inflammatory arthritis or other pathology that did not necessitate antibiotics or surgical intervention [80, 82]. In the study by Howard-Jones et al., limb-length discrepancy, hip instability, reduced range of motion, and recurrence of septic arthritis were the complications noted at 1 year [81].

Complications associated with septic arthritis of the lower extremity include limp, decreased range of motion, osteonecrosis of the femoral head in the hip or femoral condyle of the knee, limb-length discrepancy, hip instability, osteomyelitis, destruction of the epiphyseal plate, progressive ankylosis, chondral injury leading to early arthritis, and ankylosis leading to long term gait abnormalities [83–85]. Complications in the upper extremity include limb-length discrepancy, angular deformity, pain, and loss of motion. Prematurity and greater severity of illness is correlated with increased rate of long-term sequelae [80, 84]. For the hip specifically, classification systems have been reported in an effort to guide treatment [86–89]. Choi et al. proposed a modified radiographic classification based upon findings of Hunka et al. and proposed treatment regimens for each category [87–89].

Reconstructive options for deformity associated with sequelae of septic arthritis varied and complex. Goals should be aimed to optimize joint range of motion, pain control, and clinical function. Spiegel et al. proposed several treatment options for various sequelae of septic arthritis [90]. Leg length discrepancies can be addressed with epiphysiodesis, guided growth, osteotomies, or soft tissue releases. Hip instability can benefit from open reduction, pelvic support osteotomy, or arthroplasty depending upon the degree of arthritis. Contracture and loss of motion will often necessitate soft tissue releases. In the hip, abductor insufficiency from greater trochanter growth arrest may benefit from greater trochanteric transfer, pelvic support osteotomy, or hip arthrodesis [90]. Each treatment must be tailored to the patient's functional demands, cultural expectations, and resources available to the surgeon and caretakers.

In an effort to minimize variation in care, clinical practice guidelines have been established at various institutions to prevent delay and optimize outcomes for pediatric patients with suspected septic arthritis [91–93]. Standard order sheets that reflect multidisciplinary consensus opinions have been established [91–93]. Kocher et al. demonstrated that the utilization of a clinical guideline at their institution was associated with lower follow-up inflammatory markers, radiation from imaging, presumptive drainage rate along with faster time to discharge, transition to oral antibiotic therapy, and greater compliance of recommended antibiotic therapy [93]. As such, adoption of institution-specific multidisciplinary clinical care guidelines can provide efficiency and optimize outcomes in the setting of pediatric septic arthritis.

Conclusion

Septic arthritis demands a multidisciplinary approach for diagnosis and management (Box 12.1). It is a diagnostic challenge and remains a true orthopedic surgical emergency. Timely diagnosis, surgical decompression, and antibiotic administration are crucial to optimize outcomes. Rates of complication and long-term sequelae from septic arthritis have diminished due to advancements in diagnostic capabilities, broad recognition, and heighted awareness among various providers. However, long-term morbidity, need for additional surgeries, and disability pose a significant challenge and is a realm of significant research and improvement.

> **Box 12.1 Key Learning Points**
> 1. Septic arthritis is a true orthopedic emergency.
> 2. A multidisciplinary approach is key for diagnosis and management.
> 3. Early diagnosis, surgical decompression, and antibiotics are essential for good outcome.
> 4. Delayed diagnosis and inappropriate and inadequate treatment are associated with long-term sequela.

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