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Evaluation and Management of Septic Arthritis and its Mimics in the Emergency Department

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Septic arthritis is a dangerous medical condition associated with significant morbidity and mortality. However, the differential diagnosis can be broad with conditions that mimic this disease and require different evaluation and treatment. This narrative review presents the emergency medicine evaluation and management, as well as important medical conditions that may mimic this disease. Septic arthritis commonly presents with monoarticular joint pain with erythema, warmth, swelling, and pain on palpation and movement. Fever is present in many patients, though most are low grade. Blood testing and imaging may assist with the diagnosis, but the gold standard is joint aspiration. Management includes intravenous antibiotics and orthopedic surgery consult for operative management vs. serial aspirations. Clinicians should consider mimics, such as abscess, avascular necrosis, cellulitis, crystal-induced arthropathies, Lyme disease, malignancy, osteomyelitis, reactive arthritis, rheumatoid arthritis, and transient synovitis. While monoarticular arthritis can be due to septic arthritis, other medical and surgical conditions present similarly and require different management. It is essential for the emergency clinician to be aware how to diagnose and treat these mimics. [West J Emerg Med. 2019;20(2)331-341.]

INTRODUCTION

Monoarticular arthritis is a common presentation to the emergency department (ED) and major cause of disability in the United States. Monoarticular arthritis has a wide range of potential etiologies, ranging from benign to life-threatening. One of the most concerning causes in a patient with monoarticular arthritis is septic arthritis. The prevalence of septic arthritis among ED patients with monoarticular arthritis varies significantly between studies; however, an incidence of 4-60 cases per 100,000 population per year is suggested in the literature.¹⁻⁶ Based on the literature, higher rates of septic arthritis are present in immunocompromised patients and those with prosthetic joints, where disease incidence increases to 70 cases per 100,000 patients annually.⁷⁻¹³ Septic arthritis possesses a bimodal incidence, with peaks in both childhood and adults over the age of 55 years.⁴⁻⁹

Septic arthritis consists of a bacterial infection of the joint space that is associated with rapid joint destruction

within days if not adequately treated. Mortality rates can be significant, ranging from 3-25%.^{3,5-7} Despite the severity of illness, septic arthritis may be subtle, with many patients lacking the classic signs, symptoms, or laboratory findings.⁸⁻¹⁰ There are also a large number of conditions that may mimic septic arthritis, further confounding the diagnosis.

METHODS

We searched PubMed and Google Scholar for articles using the keywords “septic arthritis,” “monoarthritis,” “synovial fluid,” “diagnosis,” “treatment,” and “emergency.” Restricting the literature search to studies published in English, we found an initial 258 articles. We reviewed all relevant articles and decided by consensus which studies to include for the narrative review, focusing on articles investigating ED patients, studies evaluating synovial fluid results, and studies investigating septic arthritis diagnosis or management. A total of 133 articles were selected for inclusion in this review. We did not conduct

a systematic review or meta-analysis, but rather a narrative review evaluating the emergency medicine investigation and management of septic arthritis and its mimics.

DISCUSSION

Septic arthritis typically affects one joint but may be polyarticular in up to 20% of cases (most commonly in immunocompromised patients).^{10,14,15} The most frequently affected joint is the knee, followed by the hip, shoulder, and elbow.⁸⁻¹¹ Septic arthritis results from bacteremia in 70% of cases due to the absence of a protective basement membrane within the joint lining.^{8-11,15-29} This provides easy passage of bacteria into the synovial fluid. Other causes include direct inoculation from trauma or a medical procedure and contiguous spread from osteomyelitis, an abscess, cellulitis, or septic bursitis.^{8-11,15-18}

Organisms

The majority of cases are due to Gram-positive organisms (e.g., *Staphylococcus aureus*), with approximately 15% being due to Gram-negative organisms (Table 1).¹⁵⁻²⁵

The incidence of methicillin-resistant *S. aureus* (MRSA)-related septic arthritis is increasing.²⁰ *Neisseria gonorrhoeae* is another common cause in younger adults; these patients can present with migratory polyarthritis, pustular rash, urethritis, and tenosynovitis.^{8-11,15,17} Polymicrobial infections (e.g., *Pantoea agglomerans* and *Nocardia asteroides*) typically occur after penetrating trauma, such as bite wounds, or with organic foreign material.^{6-10,18-25} Small breaks in the skin and mucous membranes provide entry points for Gram-positive bacteria, while Gram-negative infections result from injection drug use, gastrointestinal sources, or urinary tract mucosal injury.^{8-11,15-28} Once bacteria are present within the normally sterile synovial fluid, the body sends immune cells to the site of infection.^{8-11,15,26,27} The combination of bacteria within the joint capsule, the host inflammatory response, and tissue ischemia can result in significant joint damage.^{10,26,27}

History and Examination

Obtaining an accurate history and assessment of risk factors can provide important clues to the diagnosis. A careful evaluation for risk factors can significantly change

Table 1. Common organisms causing septic arthritis.^{6-11,15-26}

Bacteria (frequency)	Clinical characteristics
Staphylococci (56%)	
Methicillin-sensitive <i>Staphylococcus aureus</i> (42%)	All: skin breakdown, cellulitis over the site (46% of cases), prosthetic joint, recent operation on joint, damaged joint
Methicillin-resistant <i>Staphylococcus aureus</i> (10-50%)	All: high mortality (7-18%) and joint function loss (27-46%)
Coagulase-negative staphylococci (3%)	
Streptococci (16%)	
<i>Streptococcus viridans</i> (1%)	All: splenic dysfunction, post splenectomy, diabetes, cirrhosis
<i>Streptococcus pneumoniae</i> (1%)	All: associated with high frequency of bacteremia (66%) and polyarticular disease (32%)
Unspecified/other streptococci (14%)	All: high mortality (19%), but good functional outcomes in those that survive
Gram-negative rods (15%)	
<i>Pseudomonas aeruginosa</i> (6%)	All: Immunocompromised status, gastrointestinal disorder or infection, injection drug use, elderly
<i>Escherichia coli</i> (3%)	Enteric Gram-negative rods: Urinary tract infection found in 50% of patients
Proteus species (1%)	All: 5% mortality
Klebsiella species (1%)	
Others (4%)	
Other (12%)	
Polymicrobial (5%)	All: immunocompromised status, travel or residence in an endemic area, gastrointestinal disorder or infection
Anaerobes (0.6%)	
<i>Mycobacterium tuberculosis</i> (1.8%)	<i>Neisseria</i> : increases with high-risk sexual activity; 75% occur in women, 72% are polyarticular, 32% have urinary symptoms, recovered from joint fluid in < 50% of cases
<i>Neisseria gonorrhoeae</i> (1.2%)	Tuberculosis: indolent course with gradually progressive joint pain and swelling, symptoms often occur for > 1 year before the diagnosis; only 50% of patients have chest radiograph with active tuberculosis
Brucella (1-11%)	Brucella: more common in immigrants to the United States, typically occurs in regions with unvaccinated livestock and unpasteurized dairy; 54% have sacroiliac joint involvement
Miscellaneous (4%)	

a provider's pretest probability of septic arthritis.^{8,9} Table 2 provides sensitivity, specificity, positive likelihood ratio (+LR), and negative likelihood ratio (-LR) for various history and examination findings.⁸ Of note, this table combines values from several meta-analyses.^{8,9} Several of the findings were not available for pooling of data due to heterogeneity and unreliable methodology of included studies. The most common risk factor is preexisting joint disease or damage; however, this is present in less than half of patients with septic arthritis.^{6-8,10} Other risk factors are typically related to the route of the infection, including hematogenous (e.g., injection drug use), direct inoculation (e.g., trauma or recent procedure), or contiguous spread (e.g., abscess).^{8-10,18}

While each risk factor in isolation has only a modest impact on the likelihood of septic arthritis, the overall risk rises as the number of risk factors increases.⁸⁻¹⁰ Many patients with septic arthritis possess several risk factors.^{6-11,15,16} For example, patients with rheumatoid arthritis are at an

increased risk for septic arthritis due to joint damage, poor skin condition, and immunosuppression.^{26,29} Rheumatoid arthritis complicated by septic arthritis is associated with poor outcomes including high morbidity and mortality.^{10,29,30} Interestingly, one study found that approximately 22% of all patients with culture-proven septic arthritis had no associated risk factors or underlying joint disease.³⁰ This can be partly explained due to septic arthritis from *N. gonorrhoeae* in young patients with otherwise normal joints, though most cases of septic arthritis were due to *S. aureus*.³⁰

Patients traditionally present with a constellation of signs and symptoms including joint pain, tenderness to palpation, swelling, erythema, warmth, and painful or limited range of motion.^{8,9,17} The most common symptom is joint pain, which is found in 85% of patients.^{8,9} Joint swelling occurs in 78% of cases,^{8,9} while joint tenderness has been suggested to be 100% sensitive.^{6,7,15,17} Fever $\geq 39^{\circ}\text{C}$ occurs in up to 58% of patients, and the absence of fever should not be relied upon

Table 2. History and examination findings in septic arthritis.*^{8,9}

Finding	Sensitivity	Specificity	-LR (95% CI)	+LR (95% CI)
History				
Age > 80 years	18.9	94.6	0.86 (0.70-0.96)	3.5 (1.7-6.4)
Rheumatoid arthritis	67.6	72.5	0.45 (0.27-0.67)	2.5 (1.9-2.9)
Diabetes	10.8	96.0	0.93 (0.79-1.0)	2.7 (1.1-6.2)
Joint surgery (< 3 months)	24.0	96.5	0.78 (0.63-0.90)	6.9 (3.7-11.6)
Hip or knee prosthesis	35.1	88.6	0.73 (0.55-0.88)	3.1 (1.9-4.5)
Skin infection, no prosthesis	32.4	88.4	0.76 (0.58-0.91)	2.8 (1.7-4.2)
Skin infection and prosthesis	24.3	98.4	0.77 (0.62-0.88)	15.0 (8.0-26.0)
HIV	75.0	38.8	0.64 (0.23-1.37)	1.2 (0.76-1.5)
Joint pain	85.0	-	-	-
New joint swelling	77.0	-	-	-
Rigors	16.0-21.0	-	-	-
Fever, subjective	44.0-97.0	-	-	-
Diaphoresis	31.0	-	-	-
Physical examination				
Limited motion	92.0	-	-	-
Pain with motion	100	-	-	-
Pain with axial loading	36.0	-	-	-
Tender to palpation	68.0-100	-	-	-
Swelling	45.0-92.0	-	-	-
Joint effusion	92.0	-	-	-
Erythema	13.0-64.0	-	-	-
Increased heat on palpation	18.0-92.0	-	-	-
Fever > 37.5°C	34.0-90.0	-	-	-

-LR, negative likelihood ratio; +LR, positive likelihood ratio; CI, confidence interval; HIV, human immunodeficiency virus.

*Remaining numbers represented by hyphens could not be calculated due to heterogeneity and unreliable methodology.^{8,9}

to exclude the diagnosis; however, up to 90% of patients have been shown to have a low-grade fever ($\geq 37.5^{\circ}\text{C}$).^{8,9} Joint pain that is sudden in onset is more suggestive of intrinsic joint pathology, such as septic arthritis.^{8-10,17,18} A joint with painful and limited active and passive range of motion is suggestive of intra-articular infection.^{8,9}

Laboratory Testing

Serum blood tests are inadequate to rule out septic arthritis. Synovial fluid is the gold standard test for making the diagnosis of septic arthritis. While a complete blood cell count, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) are often obtained, the results of these tests will not sufficiently lower the post-test probability to influence the decision to obtain synovial fluid.^{8-10,17,18} The serum white blood cell (WBC) count may be elevated above $10 \times 10^9/\text{liters (L)}$, but the sensitivity ranges from 42-90% with +LR of only 1.4 (95% confidence interval [CI] [1.1-1.8]).^{8,9,31-36} The sensitivity of ESR differs based upon the specific cut-off value that is selected, with a sensitivity of 66% for 15 mm/hr to > than 90% for 30 mm/hr.^{7-10,30,35-37} One meta-analysis suggests a +LR of 1.3 (95% CI [1.1-1.8]) for ESR > 30 mm/hr.⁹ CRP > 10 mg/L also has a sensitivity approaching 90%; however, a level of 100 mg/L has a poor +LR of 1.6 (95% CI [1.1-2.5]).^{8,9,35} While procalcitonin demonstrates promise, at this time it requires further study before routine use.^{8,10,17,18,38,39} Blood cultures should be obtained in patients with septic arthritis, as they can help identify the source if the synovial fluid culture is negative. Blood cultures will be positive in over one-third of all patients, and 14% of patients with negative synovial fluid cultures will have positive blood cultures.^{6,10,15,17,18}

Imaging

Radiographs are typically obtained of the affected joint and may demonstrate soft tissue swelling or a joint effusion.^{10,40,41} Later stages of septic arthritis may reveal chronic bony changes and calcium deposits.¹⁰ Advanced imaging, including computed tomography and magnetic resonance imaging, possesses greater sensitivity and specificity than plain radiographs, though it is of low utility for the acute diagnosis.^{10,40-42} Ultrasound may provide assistance in determining the presence of intra-articular effusion and locating the site of optimal aspiration.^{10,26,43,44}

Synovial Fluid

Synovial fluid is the gold standard for excluding septic arthritis in patients with high clinical suspicion. Results of the aspiration also assist with determining the etiology of joint effusion (Table 3). However, some of these findings may overlap between categories.^{8,17,18,45} The numbers from this table have been obtained from several meta-analyses and are provided here in one location.

A synovial white blood cell count (sWBC) $\geq 50 \times 10^9/\text{L}$ is concerning for septic arthritis (Table 3).^{8,9,17,18} Moreover,

the likelihood of septic arthritis increases as the sWBC rises, with levels $\geq 100 \times 10^9/\text{L}$ demonstrating an aggregate +LR of 13.2 (95% CI [3.6-51.1]).⁸⁻¹⁰ While the sWBC values can affect the likelihood of septic arthritis, it is important to consider that the patient's immune status may affect these findings, resulting in low sWBC counts in patients with significant immunocompromised status.^{8,9,45} A sWBC $\geq 50 \times 10^9/\text{L}$ (or 50,000 cells/mm³) may also be found in several other inflammatory conditions (e.g., gout, pseudogout).^{8-10,17,18,32} Additionally, nearly half of patients with culture-proven septic arthritis may have sWBC counts $\leq 28,000$ cells/mm³, even in cases due to *S. aureus*, with *N. gonorrhoeae* accounting for 5% of all cases.^{8-10,17,18,32} Synovial polymorphonuclear cells (sPMN) can also be significantly elevated in cases of septic arthritis.^{8,9,15} Unfortunately, this test does not significantly alter probability of septic arthritis, with a +LR of 2.7 (95% CI [2.1-3.5]) when the sPMN is > 90% and a -LR of 0.34 when the sPMN is < 90%.^{8,9}

Other diagnostic assessments include synovial Gram stain, culture, protein, lactate dehydrogenase (LDH), glucose, and lactate.^{8-10,15,17,18} Synovial culture is the single most important test and should be ordered on all patients from whom synovial fluid is collected. Synovial fluid will demonstrate growth in approximately 80% of all cases of nongonococcal septic arthritis.⁸⁻¹⁰ The remaining 20% of negative cultures may demonstrate no growth for a variety of reasons including small number of bacteria present within the joint space, obtaining a sample after initiation of antibiotics, mistaken diagnosis of septic arthritis, poor sampling technique, or poor plating technique.^{8-10,17,18,45} To decrease the likelihood of false negative synovial cultures, larger amounts of synovial fluid should be collected and placed in blood culture bottles. Synovial Gram stain sensitivity ranges from 29-65% in cases of Gram-positive septic arthritis; however, this decreases to 40-50% in Gram-negative cases and 25% in gonococcal cases.^{15-18,45-53}

Synovial protein and glucose do not significantly change the likelihood of septic arthritis.^{8,9} One study found that a synovial lactic dehydrogenase less than 250 U/L may exclude the diagnosis of septic arthritis, but further studies are needed.^{8,53} The presence of crystals does not rule out septic arthritis.^{8,10,17,18,45,54} Synovial lactate has been suggested to have the best diagnostic accuracy of all synovial fluid markers in septic arthritis. Levels above 10 mmol/L demonstrate a +LR > 20.^{8,51,55-57} Of note, it is important that the laboratory be able to differentiate D-lactate, produced by bacteria, from L-lactate, produced by humans.^{8,57} Therefore, this may not be feasible at all institutions.

Management

Rapid diagnosis and treatment reduce the risk of significant morbidity and mortality.^{10,17,18,58,59} Risk factors associated with increased risk of joint destruction include age > 65 years, diabetes, and beta-hemolytic streptococci infection, while risk factors for mortality include age > 65 years, confusion at time of initial presentation,

Table 3. Categories of synovial fluid findings in monoarticular arthritis.

Synovial fluid measure	Normal fluid	Noninflammatory	Hemorrhagic	Inflammatory	Septic
Color	Clear	Yellow	Red	Yellow	Yellow/green
Clarity	Transparent	Transparent	Bloody	Translucent-opaque	Opaque
Viscosity	High	High	Variable	Low	Variable
White blood cells	< 2 x 10 ⁹ /L	< 2 x 10 ⁹ /L	< 2 x 10 ⁹ /L	2-100 x 10 ⁹ /L	10-100 x 10 ⁹ /L
Percentage of PMNs	< 25%	< 25%	50-75%	> 50%	> 75-80%
Culture result	Negative	Negative	Negative	Negative	Usually positive
<u>Synovial result</u>		<u>+LR (95% CI)</u>		<u>-LR (95% CI)</u>	
sWBC > 100 x 10 ⁹ /L		13.2 (3.6-51.1)		0.83 (0.80-0.89)	
sWBC > 50 x 10 ⁹ /L		4.7 (2.5-8.5)		0.52 (0.38-0.72)	
sWBC 25-50 x 10 ⁹ /L		3.2 (2.3-4.4)		0.35 (0.23-0.50)	
sPMN > 90%		2.7 (2.1-3.5)		0.51 (0.39-0.65)	
sLactate > 10 mmol/L		> 20*		0.14-0.45*	

PMNs, polymorphonuclear neutrophil; sWBC, synovial white blood cell count; sPMN, synovial polymorphonuclear cell count; sLactate, synovial lactate; CI, confidence interval; +LR, positive likelihood ratio; -LR, negative likelihood ratio; L, liter.

*Unable to pool results to obtain accurate 95% confidence intervals.

and polyarticular involvement.^{30,59-61} Components of management include early recognition and treatment, with 1) joint aspiration, 2) antibiotics, and 3) orthopedic surgery consultation for possible operative management.^{10,17,18,58,59}

Due to the potential for rapid joint destruction, broad-spectrum antibiotics are often needed.^{17,18,58,59} In patients with strong concern for septic arthritis or in those who are critically ill, both Gram-negative and MRSA coverage is recommended with a combination of cefepime or an antipseudomonal beta-lactam agent and vancomycin, respectively.^{17,18,58,59} If the patient is allergic to vancomycin, daptomycin, clindamycin, or linezolid may be utilized instead.^{17,18,58,59} Once the specific organism is determined, antibiotic therapy should be narrowed. There is currently no role for intra-articular antibiotics or intra-articular corticosteroids for these patients in the ED setting.^{10,58}

While many patients may be managed with antibiotics alone, it is important to involve orthopedic surgery, as some patients may require arthroscopy, serial arthrocentesis, or arthrotomy in addition to the antibiotics.^{10,17,18,58,59}

Arthrocentesis removes bacteria and toxins, decompresses the joint space, and improves blood flow, which may improve recovery.^{10,17,18,58,59} Arthrocentesis is typically repeated on a daily basis until cultures are negative and effusions resolve.^{10,17,18,58,59} In cases that fail to respond to serial arthrocentesis, soft tissue infections that extend outside of the joint or involvement of the hip joint, surgical drainage is often indicated.^{1,58,59} Septic arthritis involving the shoulder may be managed with surgical or radiologically-guided techniques.^{10,58-60} Some joints, such as the sternoclavicular joint, do not respond well to antibiotics alone.⁵⁸⁻⁶⁴ In these cases, cardiothoracic surgical consultation is recommended.⁵⁸⁻⁶⁴

Joint Aspiration

Most joint aspirations are within the purview of the emergency physician.^{10,58,59} While it is traditionally recommended to avoid aspirating through a site with overlying cellulitis, one recent review suggested there was no harm from aspirating through cellulitis, with the only direct definitive contraindication an underlying abscess.⁶⁵ Additionally, anticoagulation is a relative contraindication, but should be weighed against the much higher risk associated with missing a case of septic arthritis.⁶⁶ Prosthetic joints should be discussed with orthopedic surgery prior to aspiration.⁶⁷ If unable to obtain fluid on the initial aspiration, several techniques may be used to increase the likelihood of success. Using a larger gauge needle and a smaller syringe can improve the ability to obtain fluid by generating a greater pressure difference.⁶⁸ Additionally, compression of the contralateral side of the joint with gentle rotation of the needle while aspirating will be of benefit.⁶⁸ Finally, ultrasound should be considered for arthrocentesis, as it locates the area with maximal fluid, while avoiding vascular structures and tendons.

Special Considerations

Gout

Gout can predispose patients to septic arthritis due to chronic joint damage.^{8,10,54,69} Patients with a first instance of an erythematous, swollen, painful joint and those with atypical presentations of their usual gout should undergo joint aspiration. Joint fluid in gout traditionally demonstrates uric acid, or calcium pyrophosphate crystals in pseudogout; however, it is important to note that these crystals do not exclude concomitant septic arthritis, as the pathologies may coexist in up to 5% of cases.^{54,69} Patients with gout and septic

arthritis often demonstrate sWBC counts $> 50 \times 10^9/L$;^{54,70} however, up to 10% of patients may demonstrate sWBC $< 6 \times 10^9/L$.⁷⁰ Patients with concern for possible septic arthritis should undergo joint aspiration, antibiotics, orthopedic consultation, and admission.^{17,18,69,70}

Human Immunodeficiency Virus (HIV)

Patients with human immunodeficiency virus and acquired immunodeficiency syndrome are predisposed to a variety of orthopedic conditions, including infections and vascular infarctions due to a chronic immunocompromised and inflammatory state.^{8,10,71-73} In this population, septic arthritis is most commonly associated with MRSA, though tuberculosis and fungal species have also been identified.⁷¹⁻⁷³ Patients may not be able to produce a normal immune response to septic arthritis, resulting in lower sWBC levels.⁷¹⁻⁷³ Patients with either new or chronic joint pain with effusion should undergo aspiration given the high risk of opportunistic infections.

Prosthetic Joint

Prosthetic joint infection (PJI) occurs most commonly within the first two years after surgery, with a rate of 1-2% for hip and knee arthroplasties and 1% with shoulder arthroplasty.^{67,74-77} Unlike native joints, prosthetic joints do not contain cartilage and are not at risk of cartilage destruction.^{67,77} Acute infections (i.e., $<$ six weeks from operation) should receive urgent antibiotics to preserve the prosthesis, while more chronic infections (i.e., $>$ six weeks from operation) may be treated with less urgency.⁶⁷ Chronic infection is more common than acute postoperative and acute hematogenous infection in these patients.^{78,79} Risk factors for PJI include longer procedural time, postoperative wound drainage, obesity, malnutrition, diabetes, anticoagulants, tobacco use, heavy alcohol use, poor hygiene, prior surgery at the same site, and bacterial colonization.⁷⁹⁻⁸⁴ *S. aureus* is the most common organism, followed by *S. epidermidis* and *Pseudomonas* due to the production of a protective bacterial biofilm.⁸⁴⁻⁸⁶

Signs and symptoms depend upon the patient's immune response and whether the infection is acute or chronic.⁶⁷ Acute infections typically present with a new effusion, erythema, and warmth combined with general symptoms of fever and malaise, while chronic infections may present with more subtle signs of pain over time without significant external evidence of infection.^{67,76,87} Findings may also include an open wound, sinus tract, or abscess.^{67,76,88,89} If there is concern for a PJI, the physician should obtain serum laboratory testing (i.e., WBC, ESR, CRP) and perform a joint fluid aspiration in consultation with the patient's orthopedic surgeon.^{67,88-90} Cultures from a draining wound are not recommended due to risk of skin flora contamination.^{67,76} Diagnostic criteria are shown in Table 4.^{67,76}

Table 4. Musculoskeletal Infection Society definition of periprosthetic joint infection.^{67,76}

Two positive periprosthetic cultures with phenotypically-identified organisms
Or
A sinus tract communicating with the joint
Or
Three of the following minor criteria:
Elevated CRP and ESR
Elevated sWBC or positive leukocyte esterase strip
Elevated synovial neutrophil percentage
Positive histologic analysis of periprosthetic tissue
A single positive culture result

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; sWBC, synovial white blood cell count.

Importantly, the specific thresholds for septic arthritis differ compared to native joints. For acute PJI, thresholds of sWBC $10 \times 10^9/L$ and sPMN $> 90\%$ are recommended.⁹⁰⁻⁹² For chronic PJI, sWBC $3 \times 10^9/L$ and sPMN $> 80\%$ are recommended.^{74,75,88,89} One publication recommended joint aspiration for a CRP > 100 mg/L for acute infection.⁶⁷ Revision surgery and antibiotics are usually required. However, compared with native joint infections, these are typically not needed emergently.^{67,76} If patients present with fever and an acute onset of symptoms, blood cultures should be obtained and antibiotics administered in the ED.^{67,76} Otherwise, antibiotics may be withheld until the case is discussed with the orthopedic surgeon.^{67,76}

Hemophilia

Hemarthrosis is a common presentation among patients with hemophilia A and B.⁹³⁻⁹⁷ This is a hallmark of more severe hemophilia and is associated with chronic disability and reduced quality of life.⁹³⁻⁹⁶ Hemarthrosis can result in chronic joint damage and increases the risk of septic arthritis at a rate of 15-40 times that of the general population.⁹³⁻⁹⁶ Patients with hemophilia who have joint pain, swelling, or erythema should be asked about prior hemarthroses, factor levels, prophylactic medications, and recent factor administration. In most patients, joint aspiration should be avoided in the setting of hemarthrosis.^{97,98} However, if the patient presents with severe pain, fever, joint erythema, or swelling in the absence of trauma and septic arthritis is suspected, aspiration of synovial fluid is important.⁹³⁻⁹⁶ Aspiration of hemarthrosis may improve pain and rehabilitation in patients with rapid intra-articular accumulation of blood, although this is controversial.^{97,98} Before conducting aspiration of suspected hemarthrosis,

emergency physicians should discuss the aspiration with hematology and orthopedics, specifically addressing possible factor replacement prior to joint aspiration.^{97,98}

Mimics

A significant number of conditions may mimic the presentation of septic arthritis, creating difficulty in diagnosis. Knowledge of these conditions and their presentation, diagnosis, and management may improve patient outcomes. Table 5 demonstrates these conditions, and Appendix 1 lists these mimics with evaluation and management recommendations.

CONCLUSION

Septic arthritis is a potentially deadly condition that unfortunately does not always present classically. The red, hot, swollen joint mandates consideration of septic arthritis. No physical examination finding can rule out the condition, and serum blood tests should not be used to exclude septic arthritis. Diagnostic aspiration is required, with the sample sent for synovial WBC, Gram stain, culture, and lactate. Synovial lactate and culture are the best laboratory tests, as some patients can present with normal synovial WBC and Gram stain. Management requires orthopedic surgery consultation and antibiotics. There are a significant number of mimics of septic arthritis, including abscess, cellulitis, gout, rheumatoid arthritis, osteomyelitis, malignancy, Lyme disease, and avascular necrosis. A focused history and examination, along with dedicated diagnostic evaluation, can assist in differentiating these conditions.

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Table 5. Septic arthritis mimics.

Abscess
Avascular necrosis
Cellulitis
Crystal-induced arthropathy
Lyme disease
Malignancy
Osteomyelitis
Reactive arthritis
Rheumatoid arthritis
Transient synovitis

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REFERENCES

- Centers for Disease Control and Prevention (CDC). Prevalence of doctor-diagnosed arthritis and arthritis-attributable activity limitation — United States, 2007-2009. *MMWR Morb Mortal Wkly Rep.* 2010;59(39):1261-5.
- Cisternas MG, Yelin EH, Foreman AJ, et al. Trends in medical care expenditures of US adults with arthritis and other rheumatic conditions 1997 to 2005. *J Rheumatol.* 2009;36(11):2531-8.
- Gupta MN, Sturrock RD, Field M. A prospective 2-year study of 75 patients with adult-onset septic arthritis. *Rheumatology (Oxford).* 2001;40(1):24-30.
- Geirsson AJ, Statkevicius S, Vikingsson A. Septic arthritis in Iceland 1990-2002; increasing incidence due to iatrogenic infections. *Ann Rheum Dis.* 2008;67(5):638-43.
- Dubost JJ, Soubrier M, De Champs C, et al. No changes in the distribution of organisms responsible for septic arthritis over a 20 year period. *Ann Rheum Dis.* 2002;61(3):267-9.
- Kaandorp CJ, Dinant HJ, van de Laar MA, et al. Incidence and sources of native and prosthetic joint infection: a community based prospective survey. *Ann Rheum Dis.* 1997;56(8):470-5.
- Cooper C, Cawley MI. Bacterial arthritis in an English health district: a 10-year review. *Ann Rheum Dis.* 1986;45(6):458-63.
- Carpenter CR, Schuur JD, Everett WW, et al. Evidence-based diagnostics: adult septic arthritis. *Acad Emerg Med.* 2011;18(8):781-96.
- Margaretten ME, Kohlwes J, Moore D. Does this adult patient have septic arthritis? *JAMA.* 2007;297(13):1478-88.
- Ross JJ. Septic arthritis of native joints. *Infect Dis Clin N Am.* 2017;31(2):203-18.
- Kaandorp CJ, Van Schaardenburg D, Krijnen P, et al. Risk factors for septic arthritis in patients with joint disease. a prospective study. *Arthritis Rheum.* 1995;38(12):1819-25.
- Morgan DS, Fisher D, Merianos A, et al. An 18 year clinical review of septic arthritis from tropical Australia. *Epidemiol Infect.*

- 1996;117(3):423-8.
13. Gavet F, Tournadre A, Soubrier M, et al. Septic arthritis in patients aged 80 and older: a comparison with younger adults. *J Am Geriatr Soc.* 2005;53(7):1210-3.
 14. Dubost JJ, Fis I, Denis P, et al. Polyarticular septic arthritis. *Medicine (Baltimore).* 1993;72(5):296-310.
 15. Goldenberg DL, Reed JI. Bacterial arthritis. *N Engl J Med.* 1985;312(12):764-71.
 16. Ross JJ, Shamsuddin H. Sternoclavicular septic arthritis: review of 180 cases. *Medicine (Baltimore).* 2004;83(3):139-48.
 17. Mathews CJ, Coakley G. Septic arthritis: current diagnostic and therapeutic algorithm. *Curr Opin Rheumatol.* 2008;20(4):457-62.
 18. Goldenberg DL, Cohen AS. Acute infectious arthritis. A review of patients with nongonococcal joint infections (with emphasis on therapy and prognosis). *Am J Med.* 1976;60(3):369-77.
 19. Daynes J, Roth MF, Zekaj M, et al. Adult native septic arthritis in an inner city hospital: effects on length of stay. *Orthopedics.* 2016;39(4):e674-9.
 20. Frazee BW, Fee C, Lambert L. How common is MRSA in adult septic arthritis? *Ann Emerg Med.* 2009;54(5):695-700.
 21. Helito CP, Noffs GG, Pecora JR, et al. Epidemiology of septic arthritis of the knee at Hospital das Clinicas, Universidade de Sao Paulo. *Braz J Infect Dis.* 2014;18(1):28-33.
 22. Chao CM, Lai CC, Hsueh PR. Bacteriology of septic arthritis at a regional hospital in southern Taiwan. *J Microbiol Immunol Infect.* 2013;46(3):241-2.
 23. Dubost JJ, Couderc M, Tatar Z, et al. Three-decade trend in the distribution of organisms causing septic arthritis in native joints. *Joint Bone Spine.* 2014;81(5):438-40.
 24. Clerc O, Prod'hom G, Greub G, et al. Adult native septic arthritis: a review of 10 years of experience and lessons for empirical antibiotic therapy. *J Antimicrob Chemother.* 2011;66(5):1168-73.
 25. Robinson DB, El-Gabalawy HS. (2008). Evaluation of the Patient: A. History and Physical Examination. In: Klippel JH, Stone JH, Crofford LJ, et al, eds. *Primer on the Rheumatic Diseases.* New York, NY: Springer-Verlag.
 26. Shirliff ME, Mader JT. Acute septic arthritis. *Clin Microbiol Rev.* 2002;15(4):527-44.
 27. Stevens CR, Williams RB, Farrell AJ, et al. Hypoxia and inflammatory synovitis: observations and speculation. *Ann Rheum Dis.* 1991;50(2):124-32.
 28. Nolla JM, Gomez-Vaquero C, Corbella X, et al. Group B streptococcus (*Streptococcus agalactiae*) pyogenic arthritis in nonpregnant adults. *Medicine (Baltimore).* 2003;82(2):119-27.
 29. Gardner GC, Weisman MH. Pyarthrosis in patients with rheumatoid arthritis: a report of 13 cases and a review of the literature from the past 40 years. *Am J Med.* 1990;88(5):503-11.
 30. Weston VC, Jones AC, Bradbury N, et al. Clinical features and outcome of septic arthritis in a single UK health district 1982-1991. *Ann Rheum Dis.* 1999;58(4):214-9.
 31. Deesomchok U, Tumrasvin T. Clinical study of culture-proven cases of non-gonococcal arthritis. *J Med Assoc Thai.* 1990;73(11):615-23.
 32. McCutchan HJ, Fisher RC. Synovial leukocytosis in infectious arthritis. *Clin Orthop Relat Res.* 1990;257:226-30.
 33. Schlapbach P, Ambord C, Blochlinger AM, et al. Bacterial arthritis: Are fever, rigors, leucocytosis and blood cultures of diagnostic value? *Clin Rheumatol.* 1990;9(1):69-72.
 34. Jeng GW, Wang CR, Liu ST, et al. Measurement of synovial tumor necrosis factor-alpha in diagnosing emergency patients with bacterial arthritis. *Am J Emerg Med.* 1997;15(7):626-9.
 35. Li SF, Henderson J, Dickman E, et al. Laboratory tests in adults with monoarticular arthritis: can they rule out a septic joint. *Acad Emerg Med.* 2004;11(3):276-80.
 36. Li SF, Cassidy C, Chang C, et al. Diagnostic utility of laboratory tests in septic arthritis. *Emerg Med J.* 2007;24(2):75-7.
 37. Ernst AA, Weiss SJ, Tracy LA, et al. Usefulness of CRP and ESR in predicting septic joints. *South Med J.* 2010;103(6):522-6.
 38. Martinot M, Sordet C, Soubrier M, et al. Diagnostic value of serum and synovial procalcitonin in acute arthritis: a prospective study of 42 patients. *Clin Exp Rheumatol.* 2005;23(3):303-10.
 39. Söderquist B, Jones I, Fredlund H, et al. Bacterial or crystal-associated arthritis? Discriminating ability of serum inflammatory markers. *Scand J Infect Dis.* 1998;30(6):591-6.
 40. Coakley G, Mathews C, Field M, et al. BSR & BHPR, BOA, RCGP and BSAC guidelines for management of the hot swollen joint in adults. *Rheumatology.* 2006;45(8):1039-41.
 41. Butalia S, Palda VA, Sargeant RJ, et al. Does this patient with diabetes have osteomyelitis of the lower extremity? *JAMA.* 2008;299(7):806-13.
 42. Nawaz A, Torigian DA, Siegelman ES, et al. Diagnostic performance of FDG-PET, MRI, and plain film radiography (PFR) for the diagnosis of osteomyelitis in the diabetic foot. *Mol Imaging Biol.* 2010;12(3):335-42.
 43. Zieger MM, Dörr U, Schulz RD. Ultrasonography of hip joint effusions. *Skeletal Radiol.* 1987;16(8):607-11.
 44. Valley VT, Stahmer SA. Targeted musculoarticular sonography in the detection of joint effusions. *Acad Emerg Med.* 2001;8(4):361-7.
 45. Fye KH. Arthrocentesis, synovial fluid analysis, and synovial biopsy. In: Klippel JH, Stone JH, Crofford LEJ, et al, eds. *Primer on the Rheumatic Diseases.* (13th ed.). Atlanta: Arthritis Foundation; 2007.
 46. Goldenberg DL, Brandt KD, Cathcart ES, et al. Acute arthritis due to gram negative bacilli: a clinical characterization. *Medicine (Baltimore).* 1974;53(3):197-208.
 47. Bayer AS, Chow AW, Louie JS, et al. Gram-negative bacillary septic arthritis: clinical, radiographic, therapeutic, and prognostic features. *Semin Arthritis Rheum.* 1977;7(2):123-32.
 48. Newman ED, Davis DE, Harrington TM. Septic arthritis due to gram-negative bacilli: older patients with good outcome. *J Rheumatol.* 1988;15(4):659-62.
 49. Argen RJ, Wilson CH, Wood P. Suppurative arthritis. *Arch Intern*

- Med.* 1966;117(5):661–6.
50. Rosenthal J, Bole GG, Robinson WD. Acute nongonococcal infectious arthritis. Evaluation of risk factors, therapy, and outcome. *Arthritis Rheum.* 1980;23(8):889–97.
 51. Riordan T, Doyle D, Tabaqchali S. Synovial fluid lactic acid measurement in the diagnosis and management of septic arthritis. *J Clin Pathol.* 1982;35(4):390–4.
 52. Faraj AA, Omonbude OD, Godwin P. Gram staining in the diagnosis of acute septic arthritis. *Acta Orthop Belg.* 2002;68(4):388–91.
 53. Schmerling RH, Delbanco TL, Tosteson AN, et al. Synovial fluid tests: what should be ordered? *JAMA.* 1990; 264(8):1009–14.
 54. Yu KH, Luo SF, Liou LB, et al. Concomitant septic and gouty arthritis—an analysis of 30 cases. *Rheumatology (Oxford).* 2003;42(9):1062–6.
 55. Brook I, Reza MJ, Bricknell KS, et al. Synovial fluid lactic acid. A diagnostic aid in septic arthritis. *Arthritis Rheum.* 1978;21(7):774–9.
 56. Mossman SS, Coleman JM, Gow PJ. Synovial fluid lactic acid in septic arthritis. *N Z Med J.* 1981;93(678):115–7.
 57. Gratacós J, Vila J, Moyá F, et al. D-lactic acid in synovial fluid. A rapid diagnostic test for bacterial synovitis. *J Rheumatol.* 1995;22(8):1504–8.
 58. Sharff KA, Richards EP, Townes JM. Clinical management of septic arthritis. *Curr Rheumatol Rep.* 2013;15(6):332.
 59. Liu C, Bayer A, Cosgrove SE, et al. Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant *Staphylococcus aureus* infections in adults and children. *Clin Infect Dis.* 2011;52(3):285–92.
 60. Hunter JG, Gross JM, Dahl JD, et al. Risk factors for failure of a single surgical debridement in adults with acute septic arthritis. *J Bone Joint Surg Am.* 2015;97(7):558–64.
 61. Pioro MH, Mandell BF. Septic arthritis. *Rheum Dis Clin North Am.* 1997;23(2):239–58.
 62. Smith JW, Piercy EA. Infectious arthritis. *Clin Infect Dis.* 1995;20(2):225–30.
 63. Song HK, Guy TS, Kaiser LR, et al. Current presentation and optimal surgical management of sternoclavicular joint infection. *Ann Thorac Surg.* 2002;73(2):427–31.
 64. Kachala SS, D'Souza DM, Teixeira-Johnson L, et al. Surgical management of sternoclavicular joint infections. *Ann Thorac Surg.* 2016;101(6):2155–60.
 65. Dooley DP. Aspiration of the possibly septic joint through potential cellulitis: just do it! *J Emerg Med.* 2002;23(2):210.
 66. Ahmed I, Gertner E. Safety of arthrocentesis and joint injection in patients receiving anticoagulation at therapeutic levels. *Am J Med.* 2012;125(3):265–9.
 67. Luthringer TA, Fillingham YA, Okroi K, et al. Periprosthetic joint infection after hip and knee arthroplasty: a review for emergency care providers. *Ann Emerg Med.* 2016;68(3):324–34.
 68. Roberts WN. Primer: pitfalls of aspiration and injection. *Nat Clin Prac Rheumatol.* 2007;3(8):464–72.
 69. Papanicolas LE, Hakendorf P, Gordon DL. Concomitant septic arthritis in crystal monoarthritis. *J Rheumatol.* 2012;39(1):157–60.
 70. Shah K, Spear J, Nathanson LA, et al. Does the presence of crystal arthritis rule out septic arthritis? *J Emerg Med.* 2007;32(1):23–6.
 71. Takhar SS, Hendey GW. Orthopedic illnesses in patients with HIV. *Emerg Med Clin North Am.* 2010;28(2):335–42.
 72. Ho G. (2008). Infectious disorders: septic arthritis. Klippel JH, ed. *Primer on the Rheumatic Diseases.* Atlanta, GA: Arthritis Foundation.
 73. Calabrese LH, Kirchner E, Shrestha R. Rheumatic complications of human immunodeficiency virus infection in the era of highly active antiretroviral therapy: emergence of a new syndrome of immune reconstitution and changing patterns of disease. *Semin Arthritis Rheum.* 2005;35(3):166–74.
 74. Bedair H, Ting N, Jacovides C, et al. The Mark Coventry Award: diagnosis of early postoperative TKA infection using synovial fluid analysis. *Clin Orthop Relat Res.* 2011;469(1):34–40.
 75. Yi PH, Cross MB, Moric M, et al. The 2013 Frank Stinchfield Award: diagnosis of infection in the early postoperative period after total hip arthroplasty. *Clin Orthop Relat Res.* 2014;472(2):424–9.
 76. Osmon DR, Berbari EF, Berendt AR, et al. Diagnosis and management of prosthetic joint infection: clinical practice guidelines by the Infectious Diseases Society of America. *Clin Infect Dis.* 2013;56(1):e1–25.
 77. Bremell T, Abdelnour A, Tarkowski A. Histopathological and serological progression of experimental *Staphylococcus aureus* arthritis. *Infect Immun.* 1992;60(7):2976–85.
 78. Pulido L, Ghanem E, Joshi A, et al. Periprosthetic joint infection: the incidence, timing, and predisposing factors. *Clin Orthop Relat Res.* 2008;466(7):1710–5.
 79. Matar WY, Jafari SM, Restrepo C, et al. Preventing infection in total joint arthroplasty. *J Bone Jt Surg Am.* 2010;92(Suppl 2):36–46.
 80. Peel TN, Dowsey MM, Daffy JR, et al. Risk factors for prosthetic hip and knee infections according to arthroplasty site. *J Hosp Infect.* 2011;79(2):129–33.
 81. Zhu Y, Zhang F, Chen W, et al. Risk factors for periprosthetic joint infection after total joint arthroplasty: a systematic review and meta-analysis. *J Hosp Infect.* 2015;89(2):82–9.
 82. Marmor S, Kerroumi Y. Patient-specific risk factors for infection in arthroplasty procedure. *Orthop Traumatol Surg Res.* 2016;102(1 Suppl):S113–9.
 83. Martin CT, Pugely AJ, Gao Y, et al. Incidence and risk factors for early wound complications after spinal arthrodesis in children: analysis of 30-day follow-up data from the ACS-NSQIP. *Spine (Phila Pa 1976).* 2014;39(18):1463–70.
 84. Muszanska AK, Nejadnik MR, Chen Y, et al. Bacterial adhesion forces with substratum surfaces and the susceptibility of biofilms to antibiotics. *Antimicrob Agents Chemother.* 2012;56(9):4961–4.
 85. Anguita-Alonso P, Hanssen AD, Patel R. Prosthetic joint infection. *Expert Rev Anti Infect Ther.* 2005;3(5):797–804.

86. Salgado CD, Dash S, Cantey JR, et al. Higher risk of failure of methicillin-resistant *Staphylococcus aureus* prosthetic joint infections. *Clin Orthop Relat Res*. 2007;461:48–53.
87. Sendi P, Banderet F, Graber P, et al. Clinical comparison between exogenous and haematogenous periprosthetic joint infections caused by *Staphylococcus aureus*. *Clin Microbiol Infect*. 2011;17(7):1098–100.
88. Zmistowski B, Valle CD, Bauer TW, et al. Diagnosis of periprosthetic joint infection. *J Orthop Res*. 2014;32(Suppl 1):S98–107.
89. Parvizi J, Zmistowski B, Berbari EF, et al. New definition for periprosthetic joint infection: from the workgroup of the Musculoskeletal Infection Society. *Clin Orthop Relat Res*. 2011;469(11):2992–4.
90. Greidanus NV, Masri BA, Garbuz DS, et al. Use of erythrocyte sedimentation rate and C-reactive protein level to diagnose infection before revision total knee arthroplasty: a prospective evaluation. *J Bone Jt Surg Am*. 2007;89(7):1409–16.
91. Schinsky MF, Della Valle CJ, Sporer SM, et al. Perioperative testing for joint infection in patients undergoing revision total hip arthroplasty. *J Bone Joint Surg Am*. 2008;90(9):1869–75.
92. Ghanem E, Antoci V Jr, Pulido L, et al. The use of receiver operating characteristics analysis in determining erythrocyte sedimentation rate and C-reactive protein levels in diagnosing periprosthetic infection prior to revision total hip arthroplasty. *Int J Infect Dis*. 2009;13(6):e444–9.
93. Ashrani AA, Key NS, Soucie JM, et al. Septic arthritis in males with haemophilia. *Haemophilia*. 2008;14(3):494–503.
94. Lidgren L. Orthopaedic infections in patients with rheumatoid arthritis. *Scand J Rheumatol*. 1973;2(2):92–6.
95. Gristina AG, Rovere GD, Shoji H. Spontaneous septic arthritis complicating rheumatoid arthritis. *J Bone Joint Surg Am*. 1974;56(6):1180–4.
96. Mitchell WS, Brooks PM, Stevenson RD, et al. Septic arthritis in patients with rheumatoid disease: a still underdiagnosed complication. *J Rheumatol*. 1976;3(2):124–33.
97. Rodriguez-Merchan EC, Jimenez-Yuste V, Aznar JA, et al. Joint protection in haemophilia. *Haemophilia*. 2011;17(Suppl 2):1–23.
98. Simpson ML, Valentino LA. Management of joint bleeding in hemophilia. *Expert Rev Hematol*. 2012;5(4):459–68.
99. Moran GJ, Krishnadasan A, Gorwitz RJ, et al. Methicillin-resistant *S. aureus* infections among patients in the emergency department. *N Engl J Med*. 2006;355(7):666–74.
100. Taira BR, Singer AJ, Thode HC Jr, et al. National epidemiology of cutaneous abscesses: 1996 to 2005. *Am J Emerg Med*. 2009;27(3):289–92.
101. Gottlieb M, Schmitz G, Grock A, et al. What to do after you cut: recommendations for abscess management in the emergency setting. *Ann Emerg Med*. 2018;71(1):31–3.
102. Singer AJ, Talan DA. Management of skin abscesses in the era of methicillin-resistant *Staphylococcus aureus*. *N Engl J Med*. 2014;370(11):1039–47.
103. Gottlieb M, Peksa GD. Comparison of the loop technique with incision and drainage for soft tissue abscesses: A systematic review and meta-analysis. *Am J Emerg Med*. 2018;36(1):128–33.
104. Gottlieb M, DeMott JM, Hallock M, et al (In press). Systemic antibiotics for the treatment of skin and soft tissue abscesses: a systematic review and meta-analysis. *Ann Emerg Med*. doi: 10.1016/j.annemergmed.2018.02.011.
105. Mankin HJ. Nontraumatic necrosis of bone (osteonecrosis). *N Engl J Med*. 1992;326(22):1473–9.
106. Moya-Angeler J, Gianakos AL, Villa JC, et al. Current concepts on osteonecrosis of the femoral head. *World J Orthop*. 2015;6(8):590–601.
107. Zalavras CG, Lieberman JR. Osteonecrosis of the femoral head: evaluation and treatment. *J Am Acad Orthop Surg*. 2014;22(7):455–64.
108. Raff AB, Kroshinsky D. Cellulitis: a review. *JAMA*. 2016;316(3):325–37.
109. Blumberg G, Long B, Koefman A. Clinical mimics: an emergency medicine-focused review of cellulitis mimics. *J Emerg Med*. 2017;53(4):475–84.
110. Pallin DJ, Binder WD, Allen MB, et al. Clinical trial: comparative effectiveness of cephalexin plus trimethoprim-sulfamethoxazole versus cephalexin alone for treatment of uncomplicated cellulitis: a randomized controlled trial. *Clin Infect Dis*. 2013;56(12):1754–62.
111. Moran GJ, Krishnadasan A, Mower WR, et al. Effect of cephalexin plus trimethoprim-sulfamethoxazole vs cephalexin alone on clinical cure of uncomplicated cellulitis: a randomized clinical trial. *JAMA*. 2017;317(20):2088–96.
112. Dalbeth N, Merriman TR, Stamp LK. Gout. *Lancet*. 2016;388(10055):2039–52.
113. Ragab G, Elshahaly M, Bardin T. Gout: An old disease in new perspective - A review. *J Adv Res*. 2017;8(5):495–511.
114. Li EK. Gout: a review of its aetiology and treatment. *Hong Kong Med J*. 2004;10(4):261–70.
115. Wilson L, Saseen JJ. Gouty arthritis: a review of acute management and prevention. *Pharmacotherapy*. 2016;36(8):906–22.
116. Perez-Ruiz F, Dalbeth N, Bardin T. A review of uric acid, crystal deposition disease, and gout. *Adv Ther*. 2015;32(1):31–41.
117. Bratton RL, Whiteside JW, Hovan MJ, et al. Diagnosis and treatment of Lyme disease. *Mayo Clin Proc*. 2008;83(5):566–71.
118. Murray TS, Shapiro ED. Lyme disease. *Clin Lab Med*. 2010;30(1):311–28.
119. Biesiada G, Czepiel J, Leśniak MR, et al. Lyme disease: review. *Arch Med Sci*. 2012;8(6):978–82.
120. Durfee RA, Mohammed M, Luu HH. Review of osteosarcoma and current management. *Rheumatol Ther*. 2016;3(2):221–43.
121. Taran SJ, Taran R, Malipatil NB. Pediatric osteosarcoma: an updated review. *Indian J Med Paediatr Oncol*. 2017;38(1):33–43.
122. Hatzenbuehler J, Pulling TJ. Diagnosis and management of osteomyelitis. *Am Fam Physician*. 2011;84(9):1027–33.
123. Chiappini E, Mastrangelo G, Lazzeri S. A case of acute osteomyelitis: an update on diagnosis and treatment. *Int J Environ*

- Res Public Health*. 2016;13(6).
124. Birt MC, Anderson DW, Bruce Toby E, et al. Osteomyelitis: recent advances in pathophysiology and therapeutic strategies. *J Orthop*. 2016;14(1):45-52.
125. Castellazzi L, Mantero M, Esposito S. Update on the management of pediatric acute osteomyelitis and septic arthritis. *Int J Mol Sci*. 2016;17(6).
126. Kim PS, Klausmeier TL, Orr DP. Reactive arthritis: a review. *J Adolesc Health*. 2009;44(4):309-15.
127. Selmi C, Gershwin ME. Diagnosis and classification of reactive arthritis. *Autoimmun Rev*. 2014;13(4-5):546-9.
128. Schmitt SK. Reactive arthritis. *Infect Dis Clin North Am*. 2017;31(2):265-77.
129. Scott DL, Wolfe F, Huizinga TW. Rheumatoid arthritis. *Lancet*. 2010;376(9746):1094-108.
130. Wasserman AM. Diagnosis and management of rheumatoid arthritis. *Am Fam Physician*. 2011;84(11):1245-52.
131. Smolen JS, Aletaha D, McInnes IB. Rheumatoid arthritis. *Lancet*. 2016;388(10055):2023-38.
132. Nouri A, Walmsley D, Pruszczynski B, et al. Transient synovitis of the hip: a comprehensive review. *J Pediatr Orthop B*. 2014;23(1):32-6.
133. Cook PC. Transient synovitis, septic hip, and Legg-Calvé-Perthes disease: an approach to the correct diagnosis. *Pediatr Clin North Am*. 2014;61(6):1109-18.