Skin and Soft Tissue Infections
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February 26, 2019

Learning Objectives

- To learn the normal functions of the integument
- To identify the importance of various layers of the skin
- To recognize common superficial skin infections on clinical evaluation
- To appreciate severe skin and soft tissue infections as life-threatening
- To use epidemiologic clues in the patient history to modify the microbiologic differential diagnosis

Normal Skin Function

Intact skin provides one of the first defenses against infection. The integument also protects against environmental insults including ultraviolet radiation, chemicals, mechanical injury, and dessication while helping to regulate temperature and produce vitamin D. Sensory organs located in the skin layers provide the body with information about temperature, position and vibration, and pain. Immunologic surveillance to both resident and foreign antigens occurs in the integumentary system. The skin is also an important window into the rest of the body as systemic illness is often reflected by involvement of the skin.

The epidermis is the thin outermost layer of skin. It has five layers (stratum corneum, stratum lucidum, stratum granulosum, stratum spinosum, stratum basale) which all contain keratinocyte cells; Langerhans cells are also found in the stratum spinosum layer and melanocytes reside is the stratum basale. The epidermis is responsible for the barrier function of the integument, keeping microbes, including both resident skin flora as well as pathogens encountered in the environment, out of the body. The thick, dense layers of keratinized cells form a physical barrier which is relatively waterproof. Langerhans cells perform skin immunosurveillance among other functions, and melanocytes filter ultraviolet rays from the sun in addition to providing skin with its pigment.

The dermis has a papillary layer and a reticular layer and contains fibroelastic tissue (collagen and elastin). Sweat glands and pilosebaceous glands are housed in the dermis. These glands are responsible for the production of free fatty acids and lactic and amino acids which are excreted in a thin layer on the skin’s surface to produce an acidic environment which has antimicrobial properties (normal skin flora is not affected, however). The dermis is also critical to wound healing as connective tissue is produced here and supports and protects the blood vessels, nerves, and lymphatics that are present. Nerve endings sense pain, temperature, and pressure.

The hypodermis is a layer of fat tissue that provides both insulation and mechanical protection as well as stores energy.

Infection Pathogenesis
The vast majority of skin and soft tissue infections occur due to breaches in the normal integrity of the skin. This breach could be mild such as a scratch or severe such as a deep laceration from trauma. Puncture wounds, burns, surgical incisions, and ulcerations also provide portals of entry both for resident skin flora as well as additional pathogens encountered in the environment.

**Microbiology**

The most common organisms that cause skin and soft tissue infections are *Staphylococcus* and *Streptococcus* species, specifically *Staphylococcus aureus* and beta-hemolytic streptococci such as S. pyogenes which can be resident flora of the skin. Nonpurulent skin and soft tissue infections tend to be more associated with streptococcal infections with a smaller but important group due to *S. aureus*. Purulent skin and soft-tissue infections, on the other hand, are highly associated with *S. aureus* including MRSA (methicillin-resistant *Staphylococcus aureus*).

**Methicillin-resistant Staphylococcus aureus (MRSA) genetics**

Methicillin (a semi-synthetic beta-lactamase resistant penicillin) was initially introduced in 1959. Staphylococcus aureus with methicillin resistance was first noted in 1961; these strains were found to carry a mobile genetic element staphylococcal cassette chromosome *mec* (SCCmec). SCCmec contains among other elements, the *mecA* gene which produces an altered penicillin binding protein (PBP2a) that has a decreased affinity for binding to beta-lactam antibiotics meaning that the bacterial cells can continue to divide, even in the presence of the antibiotic. Different SCCmec are carried by hospital-associated and community-associated strains. Hospital-associated MRSA tends to contain either SCC I,II,or III while community-associated MRSA strains more often contain SCC IV or V.

The **Panton-Valentine-Leukocidin** (PVL) toxin is a cytotoxin that destroys white blood cells and causes tissue necrosis. The gene encoding PVL is often carried on the SCC IV and V that are seen in community-associated MRSA strains and is thought to be responsible for some of the virulence associated with these skin and soft tissue infections and necrotizing pneumonias that may occur in otherwise healthy individuals.

**Antimicrobial coverage**

When reliable good quality culture results are available, antibiotic therapy should be tailored to the organisms isolated. Most skin and soft tissue infections are caused by streptococci and staphylococci and this should be used to guide empiric therapy. More severe infections and infections in certain vulnerable populations often require broader treatment empirically.

Antimicrobials with anti-streptococcal activity include: penicillin VK (oral), cephalexin (oral), penicillin (IV), cefazolin (IV), clindamycin (oral and IV).
Antimicrobials with anti-staphylococcal activity against MSSA (methicillin-susceptible \textit{S. aureus}) include cephalexin (oral), dicloxacillin (oral), trimethoprim-sulfamethoxazole (oral), doxycycline (oral), clindamycin (oral or IV), nafcillin (IV), and cefazolin (IV).

Antimicrobials with anti-staphylococcal activity against MRSA (methicillin-resistant \textit{S. aureus}) include doxycycline (oral), trimethoprim-sulfamethoxazole (oral), clindamycin (oral or IV), vancomycin (IV), daptomycin (IV), linezolid (oral or IV), ceftaroline (IV).

The above lists are not all-inclusive and not all listed agents have the same likelihood of being effective against all strains of the bacteria.

**Epidemiology, Clinical Presentation, Diagnosis, and Treatment of Skin and Soft Tissue Infections**

Impetigo and ecthyma are crusted infectious lesions of the skin. **Impetigo** is a localized purulent infection limited to the epidermis which can be primary (bacteria invade normal skin) or secondary (superinfection of compromised skin secondary to trauma, eczema, etc). \textit{Staphylococcus aureus} and beta-hemolytic streptococci such as \textit{Streptococcus pyogenes} are the most frequent causes of non-bullous disease. Impetigo tends to occur in young children (ages 2-5) on the face and extremities and is transmissible person-to-person. Non-bullous lesions start as papules that progress to vesicles and pustules with eventual rupture with resultant honey-colored crusting. Systemic symptoms are uncommon. Bullous manifestations are often due to exfoliative toxin A production by \textit{S. aureus}. **Ecthyma** extends more deeply into the epidermis and dermis resulting in ulceration and, in some cases, bacteremia. Culture of the exudates is recommended, but empiric treatment covering \textit{S. aureus} and streptococci is also reasonable in classic cases. Mild limited impetigo can be treated with topical mupirocin therapy; impetigo cases with multiple lesions or associated with an outbreak and all cases of ecthyma should receive systemic antibiotic therapy. Post-streptococcal glomerulonephritis is a possible complication when group A streptococcus is involved.

Cellulitis and erysipelas are diffuse superficial spreading skin infections that are not associated with purulence (non-purulent skin and soft tissue infections). **Erysipelas** involves the upper dermis and superficial lymphatics, classically on the face. **Cellulitis** involves the deeper dermis and subcutaneous fat. Bacteria (including those that are normal skin commensals) enter through breaks in the skin including due to trauma, preexisting ulceration, etc. Predisposing conditions include edema, primary skin conditions (i.e. psoriatic plaque), immunosuppression, and other infections (varicella, tinea). The skin appears erythematous (rubor), edematous (tumor), tender (dolor), and warm (calor) and the process can rapidly spread. Erysipelas manifestations tend to be well-circumscribed. Inflammation of the lymphatics (lymphangitis) and regional lymphadenopathy may also be present. Systemic manifestations such as fever, chills, tachycardia, and hypotension are variably present. Most infections are felt to be due to streptococci (group A streptococci and other beta-hemolytic strep) with a smaller number due to \textit{S. aureus}. Gram negative cellulitis is uncommon but may be seen in patients with diabetes or immunocompromise. Obtaining a microbiologic diagnosis occurs infrequently in these cases and treatment is generally empiric.
Purulent skin and soft tissue infections include cutaneous abscesses, furuncles, carbuncles, and inflamed epidermoid cysts. A **cutaneous abscess** is a purulent collection in the dermis and subcutaneous tissues. A **furuncle** (also called a boil) is an infection of the hair follicle that ruptures into the subcutaneous tissue to form an abscess. A **carbuncle** is infection of multiple contiguous hair follicles. **Epidermoid cysts** contain cheesy keratinous material that causes inflammation (rather than infection) when the cysts ruptures into the dermis. There is an erythematous raised area or nodule present that may be fluctuant and is tender and warm often with a pustule on top. *S. aureus* is responsible for the majority of cases; others may be polymicrobial and may involve resident flora. The cornerstone of treatment for these purulent skin and soft tissue infections is incision and drainage; systemic antibiotics are used as adjunctive therapy in those with systemic infection, immunocompromise, poor response to surgical therapy, etc. Culture of the purulent material drained at the time of the procedure is recommended; when indicated, antimicrobial therapy is ideally culture-driven. Empiric therapy when necessary should minimally cover *S. aureus*.

**Pyomyositis** is a collection of localized pus in an individual muscle group. The vast majority of infection is due to *S. aureus* which hematogenously seeds an area after local trauma or intense use. Possible underlying predisposing conditions include Human Immunodeficiency Virus infection (HIV) and diabetes. The clinical presentation usually includes fever, localized muscle pain, and swelling; systemic toxicity is less common. Diagnosis is most readily made on MRI scan. Treatment includes drainage along with antibiotics directed at isolates recovered from culture; empiric therapy should include coverage for methicillin-resistant *Staphylococcus aureus* (MRSA).

Necrotizing skin and soft tissue infections spread deeper than their more superficial counterparts to involve the fascia (necrotizing fasciitis) and/or muscle (myonecrosis/gas gangrene) and predisposing conditions (diabetes, venous stasis, immunocompromise, injection drug use) are often present. **Necrotizing fasciitis** involves spread of infection along the superficial fascial plane, involving all layers of the skin and subcutaneous tissue above. When the infectious process occurs in the scrotum and perineal area, it is called **Fournier’s gangrene**. Single pathogens that can cause necrotizing infections include *S. pyogenes*, *S. aureus*, *Aeromonas*, Clostridial species, and *Vibrio vulnificus*; other infections are often polymicrobial including contribution from anaerobic bacteria. **Myonecrosis/gas gangrene** is classically associated with Clostridial infections and may be associated with trauma (contiguous spread from a traumatic wound with vascular compromise—*C. perfringens*) or spontaneous (hematogenous spread from the GI tract from a malignant lesion or in a neutropenic patient e.g.—*C. septicum*). Streptococci can also cause necrotizing infection involving the muscle; usually with less tissue gas production that is classically seen with Clostridial infections. Spread of necrotizing infections can be rapid and associated with systemic toxicity and organ failure; these severe infections are frequently limb- and life-threatening. Signs and symptoms can include pain out of proportion to exam, bullous lesions, crepitus, necrotic tissue (gangrene), hard (woody) edema, high fever, altered mentation, and organ failure, although the presentation can be subtler. There is also a failure to respond to typical therapy that would be expected to treat a more superficial infection. The mainstay of treatment is emergent surgical debridement; broad-spectrum antibiotics should be instituted as adjunctive therapy pending tissue and blood cultures. In group A streptococcal infections and clostridial infections, clindamycin is used adjuncitively to suppress toxin production.
**Streptococcal toxic shock syndrome** occurs when group A streptococcus results in an invasive infection with the early onset of hypotension and organ failure. The bacteria likely enter from the skin, vaginal mucosa, or oropharynx with the last resulting in a transient bacteremia which then seeds a distant site. Necrotizing fasciitis and myonecrosis are commonly associated, but not universal. Patients present with nonspecific fevers, chills, malaise, myalgias, gastrointestinal symptoms, and pain at the necrotizing infection site, if present. This later progresses to septic shock, end organ damage including renal failure, and progressive pain at the localized site of infection as pyrogenic streptococcal exotoxins (A and B) and M protein fragments from the bacteria act as super antigens mediating massive cytokine release. *S. pyogenes* is isolated from normally sterile sites (blood, deep tissue, muscle). Treatment includes emergent surgical debridement of any deep infection and penicillin combined with clindamycin, the latter of which suppresses bacterial toxin production among other mechanisms of action.

**Staphylococcal Toxic Shock Syndrome** was initially identified in the late 1970s. One early cluster of cases was noted in menstruating women using highly absorbent tampons. Some of these products were pulled from the market with a subsequent decline in infections; however, menstrual-related cases still occur and tampon use remains a risk factor. Nonmenstrual case risk factors include post-surgical and post-partum wound infections, trauma, burn injury, skin infections, and respiratory superinfection in the setting of influenza. Production of toxic shock syndrome toxin-1 (TSST-1), an exotoxin, is responsible for disease pathogenesis in the majority menstrual-associated cases and a smaller number of nonmenstrual cases. Other enterotoxins mediate the non-TSST-1 cases. Each of these toxins produces similar clinical manifestations including shock, erythroderma, and multisystem organ failure. The rash starts as macular or simply diffuse erythema and develops into a maculopapular rash that later desquamates (peels). The white blood cell count characteristically shows a left shift to more immature cells and anemia and thrombocytopenia are common early on. Although *S. aureus* may be isolated from the primary infection site, isolation from the blood is not common as this is a toxin-mediated disease. Treatment involves removing any foreign bodies (including tampons present), surgical debridement of any abscesses/infected tissue as appropriate and antistaphylococcal antibiotics. Clindamycin should be used with another appropriate antistaphylococcal antibiotic (depending on if the organism is MSSA or MRSA) to suppress toxin production.

**Microbiology of Soft Tissue Infections in Specific Epidemiologic Settings**

Bite wounds, in addition to providing a portal of entry for common skin flora such as Staphylococci and Streptococci present on the subject who is bitten, are also associated with a risk of oral pathogen transmission from the person or animal performing the biting. Human oral flora commonly seen in bite wounds includes *Eikenella corrodens, Fusobacterium, Peptostreptococcus, Prevotella*, and *Porphyromonas*. These can also be transmitted from a punch to the mouth (closed fist injury) when the recipient’s teeth cause lacerations or breaks in the skin of the hand of the puncher. Dog bites are often associated with bacteria including *Capnocytophaga canimorsus* and *Pasteurella multocida*. *Capnocytophaga* can cause bacteremia and sepsis especially in patients with asplenia, alcohol abuse, and chronic liver disease. Cat bites can also transmit *Pasteurella* as well as *Bartonella henselae*. Therapy for infected bite wounds should include coverage of both aerobic and anaerobic bacteria such as amoxicillin-clavulanate. Animal bite wounds should prompt tetanus toxoid vaccination if not given within the last ten years.
When trauma occurs in the setting of an aquatic environment, the risk of infection with organisms such as *Aeromonas* species, *Edwardsiella tarda*, *Erysipelothrix rhusiopathiae*, *Vibrio vulnificus*, and *Mycobacterium marinum* increases. Aquatic animals such as leeches can also transmit *Aeromonas* infection when used as medicinal therapy as *Aeromonas* is part of the normal foregut flora of the leech. Patients with underlying comorbidities including liver disease and malignancy are at increased risk for disseminated and life-threatening infections with these organisms, especially *Aeromonas*, *Vibrio*, and *Edwardsiella*. *M. marinum* and *E. rhusiopathiae* tend to have more indolent courses.

Diabetic patients commonly develop lower extremity soft tissue ulcers that can become infected. Predisposing factors include neuropathy because the initial breakdown in the skin goes unrecognized and peripheral arterial disease resulting in tissue ischemia. Not all ulcers are infected; infections that do occur are often polymicrobial. In addition to staphylococci and beta-hemolytic streptococci (including group B streptococci) that are common pathogens, gram negative organisms such as *Pseudomonas aeruginosa* are seen with increased frequency.

Patients who are significantly immunosuppressed (i.e. prolonged neutropenia, solid organ transplant), in addition to infections with common pathogens like *S. aureus* and beta-hemolytic streptococci, are also at risk for infections with gram-negative pathogens and fungi. In these cases, a microbiologic diagnosis is often critical due to the widened differential diagnosis. Burn injury patients are often found to be colonized and/or infected with *P. aeruginosa*.

References


Robbins Pathologic Basis of Human Disease (Kummar, Abbas, Aster) 10th ed, Chapters 9 and 24


Bone and Joint Infections
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February 26, 2019

Learning Objectives

- Understand the pathogenesis of osteomyelitis
- Identify risk factors predisposing to osteomyelitis
• Compare and contrast the clinical presentation of acute vs chronic osteomyelitis
• Understand the indications for surgical and medical management of osteomyelitis
• Understand the pathophysiology of septic arthritis
• Compare and contrast the management of both native and prosthetic septic joints

Pathogenesis of Osteomyelitis

Microorganisms can reach the bone by one of three routes:

Hematogenous spread occurs when bacteria enter the blood from a distant focus of infection and seed the bone. Most osteomyelitis in children is hematogenous in origin affecting the long bones of the extremities; in adults, hematogenous spread accounts for about 20% of bone infections, mostly involving vertebral bones, the clavicle and pelvis, and less commonly, the long bones of the extremities. Seeding of implanted devices such as joint arthroplasties can also occur. Vertebral osteomyelitis seeded from a primary tuberculosis infection or a prosthetic knee infection secondary to a MRSA central line-associated blood stream infection are examples of hematogenous spread. Once bacteria enter the blood, they target bones with a rich blood supply. In children, bacteria initially target the metaphysis; sluggish flow in the sinusoidal veins of the metaphyseal vascular loops may aid in bacterial deposition here. Inflammation results in cellulitis and abscess formation in the bone marrow which, due to increased intramedullary pressure, later spreads to the cortical bone and ruptures through or lifts the periosteum. Bone necrosis is common due to disrupted blood flow, and a sequestrum, or separated piece of dead bone, can form. New bone later forms under the elevated periosteum and is termed the involucrum. Spread of the infection to the epiphysis and into the joint space is also not uncommon in children. In adults, the diaphysis is the initial site of infection which can spread to the rest of the medullary canal. Subperiosteal spread is rare as the periosteum of adult bones is more adherent. As a result, massive bone devitalization is rare; soft tissue abscesses are more likely.

Extension from a contiguous site of infection occurs when the tissue or organs adjacent to the bone are initially infected and the infection later moves to the bone which is often devitalized; examples of this type of infection include sacral osteomyelitis associated with a sacral decubitus ulcer and osteomyelitis of the foot secondary to an infected diabetic foot ulcer. Direct inoculation occurs when a microorganism is traumatically or surgically introduced into the bone such as an open fracture after a motorcycle accident, a human or animal bite, or a vertebral bone infection after laminectomy surgery.

Microbiology

Osteomyelitis is most commonly caused by bacteria with a much smaller number of cases attributable to mycobacteria; fungal infections are much less common and tend to occur in immunocompromised individuals. When infection occurs by hematogenous spread, a single organism is usually implicated. Polymicrobial infections are more likely to occur when there is extension from a contiguous source or direct inoculation such as from an open fracture or a surgical site infection. *Staphylococcus aureus* is responsible for most culture-positive cases. Coagulase-negative *staphylococcus*, streptococci, gram negative rods, and enterococci are also commonly seen. Sickle cell disease is associated with osteomyelitis due to *Salmonella* species. Puncture wounds through a shoe should prompt consideration...
for infection with *Pseudomonas aeruginosa*. Exposure to tuberculosis should be explored in a patient with vertebral osteomyelitis without another obvious etiology, especially if there is a more subacute onset.

**Risk Factors for Osteomyelitis**

For hematogenous infections, risk factors include any element that increases the risk for bacteremia such as established infection at a site remote from the bone, the presence of an indwelling central line or cardiac device, receipt of hemodialysis, or intravenous drug use. In children, chronic granulomatous disease and hemoglobinopathies such as sickle cell disease increase the risk of hematogenous osteomyelitis. Extension from a contiguous site is more likely when bone is already devitalized (i.e. poor blood supply) and is commonly seen in patients with diabetes mellitus, decubitus ulcers, and peripheral artery disease leading to ischemia. Trauma, a history of recent surgery, or a human or animal bite may be seen with direct inoculation injuries that subsequently become infected. The presence of foreign bodies increases the risk of infection with any pathogenesis mechanism as the contaminating bacteria are often more difficult or impossible to clear due to the formation of biofilms. *Mycobacterium tuberculosis* infection can disseminate to the bone in 1-3% of cases; vertebral bones and long bones are the most commonly affected.

**Pathologic changes**

The acute phase is characterized by bacterial proliferation and neutrophilic inflammation prior to sequestrum development. The inflammation spreads via cortical canals to the periosteum forming a subperiosteal abscess; if this ruptures, a soft tissue abscess is formed and can spread to the skin or track into the joint space. The chronic phase is characterized by marrow fibrosis, the presence of a sequestrum (necrotic separated bone), and a lymphocytic and plasma cell infiltrate. Later inflammatory cells release cytokines resulting in bone resorption, fibrosis, and, in some cases, a shell of new reactive bone formation called the involucrum. Sinus tracts are also common in chronic infection. In mycobacterial osteomyelitis, caseating granulomas with bone destruction are characteristic.

**Clinical Presentation**

Fever, chills, and malaise are variably present in cases of hematogenous osteomyelitis; in some instances the only symptom is localized pain. Imaging subsequently ordered for evaluation of the pain may lead to the diagnosis. Acute osteomyelitis extended from a contiguous site of infection is often suspected when the original infection site fails to heal such as a diabetic foot ulcer that is enlarging, has increased or purulent drainage, or probes to the bone. Fever and other systemic symptoms may be present depending on the degree of adjacent infection. Direct inoculation infections may manifest as nonunion of the fracture site or poor healing of the surgical incision with sinus tract formation. Tuberculous osteomyelitis most commonly affects the spine and presents with low-grade fever, sweats, weight loss, and localized pain. Concurrent mycobacterial infection at other locations can occur but is uncommon other than in immunocompromised individuals.
Persistent (chronic) infection is more likely with longer duration of infection, suboptimal antibiotic therapy for acute osteomyelitis, poor source control (i.e. remaining necrotic tissue or a foreign body present), and immunosuppression. Chronic infections may present as a chronic non-healing ulceration or a sinus tract with periodic drainage and exacerbations of soft tissue swelling and erythema. Systemic symptoms are absent in most cases; however, occasionally chronic infections can result in flares with resultant bacteremia, endocarditis, and/or sepsis. Noninfectious complications of chronic osteomyelitis include pathologic bone fractures, amyloidosis from chronic long-standing inflammation, and squamous cell carcinoma of sinus tracts.

Diagnosis in all instances is similar. Laboratory tests such as a white blood cell count, erythrocyte sedimentation rate, and c-reactive protein may be variably elevated but are nonspecific. A diabetic foot ulcer that probes to bone has a high likelihood of underlying osteomyelitis and further evaluation to prove osteomyelitis is generally unnecessary. Imaging showing a lytic bony destructive lesion with surrounding sclerosis is consistent with osteomyelitis. An x-ray may show changes if the onset is at least a few weeks prior, but magnetic resonance imaging (MRI) is the most sensitive diagnostic modality. CT scan is an alternative if an MRI is not feasible; a triple phase bone scan can also be obtained but lacks sensitivity and specificity. Microbiologic etiology may be suggested in cases where bacteremia is identified, especially in the case of S. aureus bacteremia. A bone biopsy with culture provides a definitive diagnosis and allows targeting of antimicrobial therapy. Cultures from superficial wounds or sinus tracts have a poor correlation with bone cultures unless S. aureus is isolated; for this reason, wound cultures are generally avoided, especially if a bone biopsy is feasible.

Surgical debridement should be performed if there is a drainable fluid collection or significant necrotic tissue. Prolonged antibiotic therapy (minimum of 6 weeks) is indicated unless the entire focus of infection is surgically removed; in most cases, this is delivered intravenously. Ideally, antibiotic therapy is delayed pending culture acquisition unless the patient is systemically ill or has significant surrounding skin and soft tissue infection.

**Epidemiology and Pathogenesis of Infectious Arthritis**

Risk factors for infection include advanced age, intravenous drug or alcohol use, diabetes mellitus, the presence of a joint prosthesis, recent joint surgery or intraarticular injection (i.e. with steroids), overlying skin infection, and underlying joint disease (i.e. crystal arthropathy, rheumatoid arthritis, osteoarthritis). Some patients will not have any identifiable risk factors, however. Risk factors for disseminated gonococcal infection (DGI) include recent menstruation, pregnancy or the post-partum state, and terminal complement deficiencies.

Spread of infection to the joint can occur from hematogenous seeding, direct inoculation due to trauma or procedure, or contiguous spread of infection in the adjacent soft tissue or bone. Most pyogenic arthritis is monomicrobial and involves hematogenous spread to a single joint. Synovial tissue lacks a basement membrane so that bacteria easily enter the joint space and inflammatory cells follow. The synovium becomes inflamed causing hyperplasia of the membrane cells. Destruction of cartilage can occur due to cytokine and protease release as well as pressure necrosis from large effusions. Infections can involve both native and prosthetic joints. DGI usually starts as asymptomatic mucosal infection
which is unrecognized and disseminates via bacteremia. Inflammatory mechanisms other than direct microbial invasion may be responsible for the arthritis and other clinical manifestations of DGI. The arthritis seen in Lyme disease is likely immune-mediated.

**Microbiology**

Most joint infections are due to bacteria. *Staphylococcus aureus* is the most common organism isolated from native joint septic arthritis in adults and older children; it is also represented disproportionately in rheumatoid arthritis patients. Streptococcal species are also common. *Neisseria gonorrhoeae* is an important etiology in sexually active adolescents and younger adults. *Haemophilus influenzae* predominates in very young children. *Salmonella* has a predilection for individuals with sickle cell disease. Gram negative rods are more common in the elderly, immunocompromised, and those with intravenous drug use as a risk factor. Polymicrobial infections are generally the result of extension from a bowel infection or penetrating trauma into the joint. *Borrelia burgdorferi*, the causative agent of Lyme disease, can cause monoarthritis of the knee or oligoarticular arthritis in the late disseminated stage of illness. Early prosthetic joint infections are most often due to *S. aureus* with a percentage attributed to gram negative rods. Coagulase-negative staphylococci (CONS) predominate in delayed-onset prosthetic joint infections which tend to be more indolent. Late-onset prosthetic joint infections are generally due to hematogenous seeding with a virulent organism such as *S. aureus*, gram-negative rods, or beta-hemolytic streptococci. Fungal and mycobacterial infections are rare and more commonly seen in immunocompromised patients. Viral infections generally result in polyarthritis associated with an acute systemic illness.

**Clinical Presentation**

Acute suppurative arthritis usually presents with the sudden onset of a painful, swollen, warm joint often with fever. Movement of the joint is generally painful and restricted. There is often a joint effusion on exam and there may be overlying erythema. Only one joint is involved in most cases; the knee is most common. The axial skeletal joints are more commonly affected in injection drug users.

Disseminated gonococcal infection occurs more commonly in women, especially with menstruation and pregnancy. The triad of dermatitis, tenosynovitis, and migratory polyarthritis is classic. Skin lesions can be macules, papules, or pustules and are painless. The hands and wrists are most commonly affected by tenosynovitis. Arthritis is more common than a frankly septic joint although the latter can also occur and generally involves the knee.

Fungal and mycobacterial infections tend to be more indolent in nature.

**Diagnosis**

The serum white blood cell count, erythrocyte sedimentation rate (ESR), and c-reactive protein (CRP) are often elevated although these are nonspecific. Blood cultures may be helpful if there is ongoing bacteremia; in many cases, the joint may have been seeded by transient bacteremia and blood cultures may be negative. Imaging including x-rays, computed tomography (CT) scans, and magnetic resonance
imaging scans (MRIs) may show soft tissue edema and joint effusion early on with later loss of joint space and joint erosion and destruction. Arthrocentesis, or aspiration of fluid from the joint, is critical to making the diagnosis and guiding therapy. Synovial fluid typically reveals an elevated white blood cell count (greater than 50,000 in a native joint with a predominance of polymorphonuclear cells; much lower levels of inflammation can be seen in a prosthetic joint infection) and, ideally, growth of the responsible organism to guide therapy. If gonococcal disease is suspected, in addition to joint culture on special media, it is recommended to also perform PCR of the synovial fluid as well as mucosal sites (cervical, urine) as the bacterial gram stain and culture are often negative. Serology for Lyme disease should be obtained if the clinical presentation and epidemiologic exposures are suggestive.

**Treatment**

Urgent treatment is critical to prevent joint destruction, as this may be irreversible. Drainage either by serial aspiration or surgical washout is indicated. Larger joints and prosthetic joints generally require surgical washout as do those infections not responsive to more conservative drainage techniques. Empiric intravenous antibiotic therapy generally consists of vancomycin +/- ceftriaxone in patients with a risk of gram negative infections. Therapy should be tailored to the gram stain and culture. Antibiotic therapy is given for 3-4 weeks in native joint septic arthritis; the first few weeks, and in many cases the entire course, is given intravenously depending on the clinical circumstances. Prosthetic joint infections, on the other hand, generally require removal of the prosthesis with more prolonged therapy (a minimum of 6 weeks of intravenous therapy) depending on the surgical procedure performed. If the prosthesis is unable to be removed, chronic suppressive therapy may be necessary to keep the infection under control; cure is unlikely in these cases due to the persistence of the bacteria in biofilms associated with the prosthesis.

**References**


Robbins Pathologic Basis of Human Disease (Kumar, Abbas, Aster) 10th ed, Chapters 9 and 21.