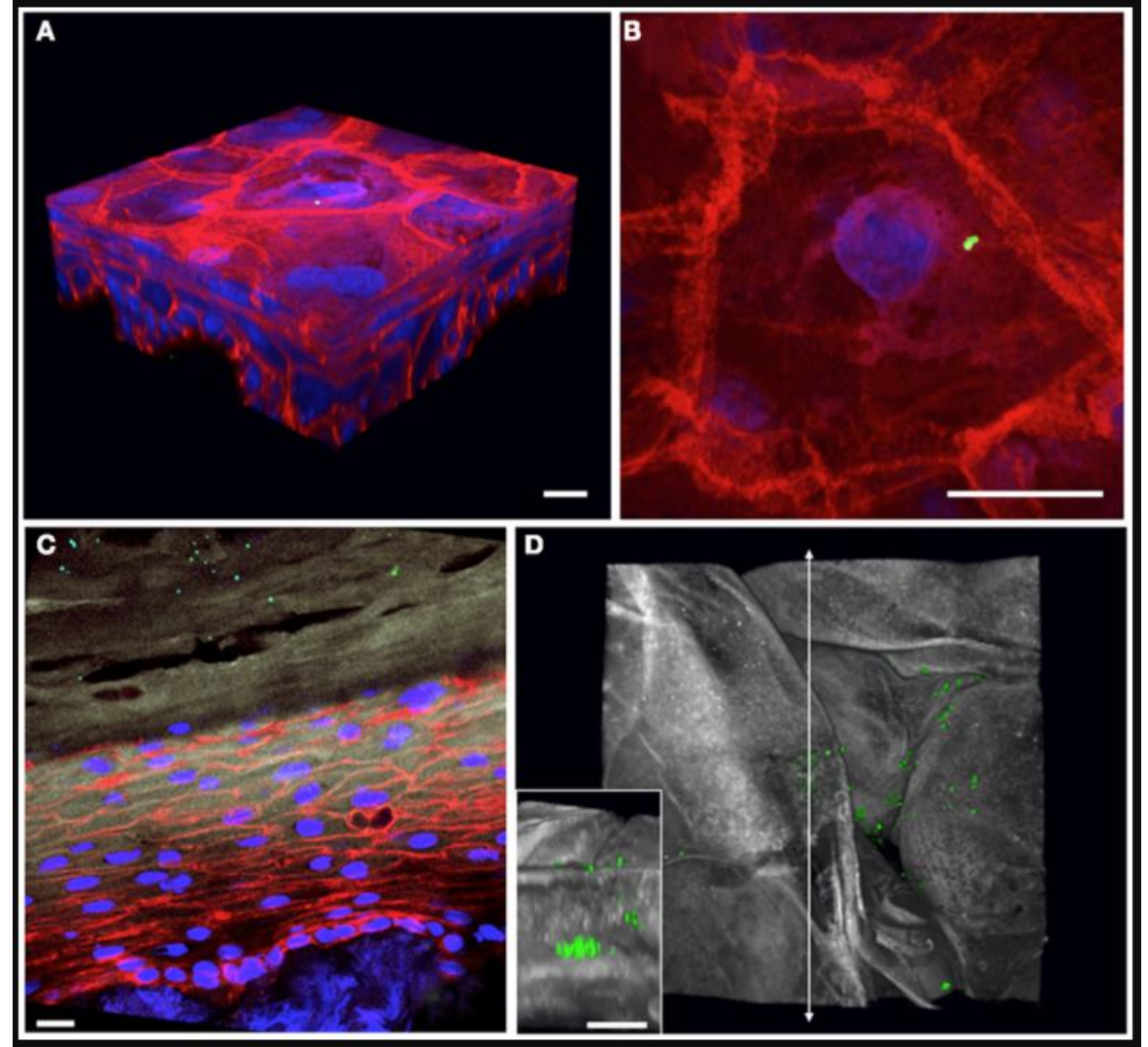


Musculoskeletal System Microbiology

Anas Abu-Humaidan
M.D. Ph.D.



Osteomyelitis and septic arthritis

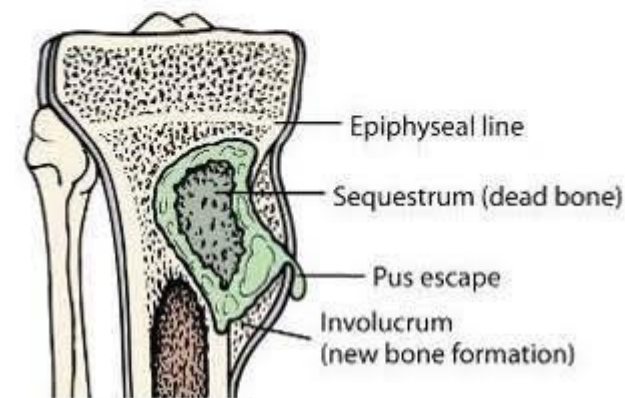
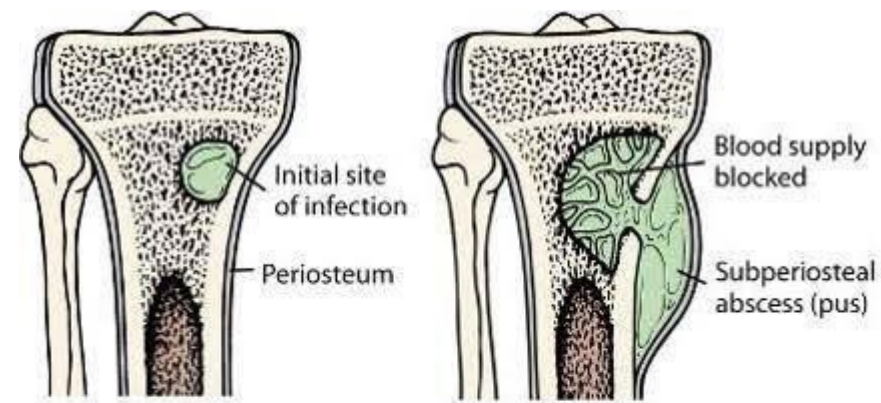
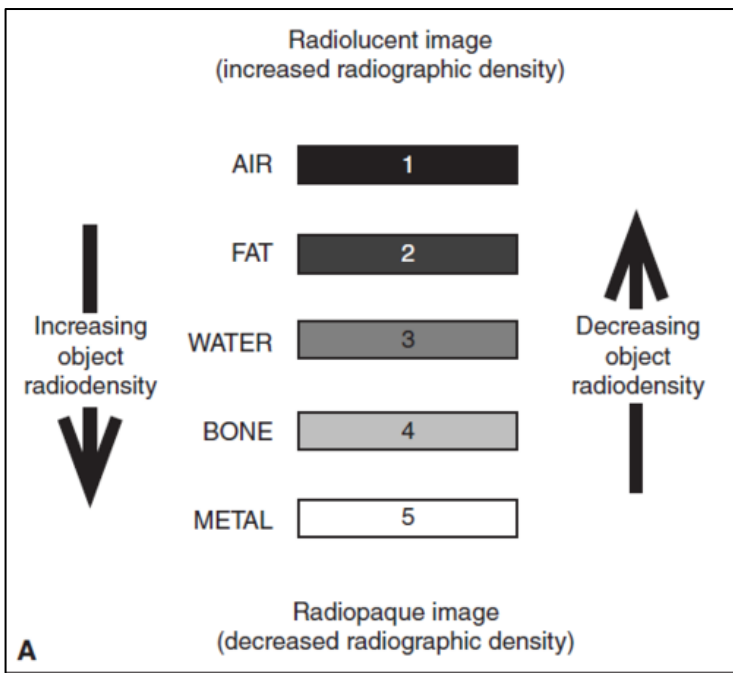
Overview

In this lecture we will discuss:

- Osteomyelitis
- Septic arthritis
- Animal bites

- **Osteomyelitis** is an infection involving bone. Osteomyelitis may be classified based on the mechanism of infection (**hematogenous** versus **nonhematogenous**) and the duration of illness (**acute** versus **chronic**).
- **Acute osteomyelitis** evolves **over several days to weeks** and can progress to a chronic infection.
- The hallmark of **chronic osteomyelitis** is the **presence of dead bone (sequestrum)**. Other common features of chronic osteomyelitis include **involucrum** (reactive bony encasement of the sequestrum), local **bone loss**, and, if there is extension through cortical bone, sinus tracts.
- **Nonhematogenous** osteomyelitis can occur as a result of contiguous spread of infection to bone from adjacent soft tissues and joints or via direct inoculation of infection into the bone (as a result of trauma or surgery).
- **Hematogenous** osteomyelitis is caused by microorganisms that seed the bone in the setting of bacteremia

Osteomyelitis/ Introduction



[Osteomyelitis. In: StatPearls. Copyright © StatPearls Publishing LLC. 2022. All rights reserved.]

Sequestra are usually present; they form as a result of bone ischemia and necrosis in the context of blood vessel compression due to elevated medullary pressure associated with bone marrow inflammation. Sequestra can be seen radiographically. The presence of a sinus tract is pathognomonic of chronic osteomyelitis.

Osteomyelitis/ NONHEMATOGENOUS OSTEOMYELITIS

- Among younger adults, **nonhematogenous osteomyelitis occurs most commonly in the setting of trauma** and related surgery. Among older adults, nonhematogenous osteomyelitis occurs most commonly as a result of contiguous **spread of infection to bone from adjacent** soft tissues and joints.
- Risk factors for nonhematogenous osteomyelitis include poorly healing soft tissue wounds (including decubitus ulcers), presence of orthopedic hardware, diabetes, peripheral vascular disease, and peripheral neuropathy.
- Nonhematogenous osteomyelitis may be **polymicrobial or monomicrobial**. **Staphylococcus aureus** (including methicillin-resistant *S. aureus*), coagulase-negative staphylococci, and aerobic gram-negative bacilli are the most common organisms.

Osteomyelitis/ HEMATOGENOUS OSTEOMYELITIS

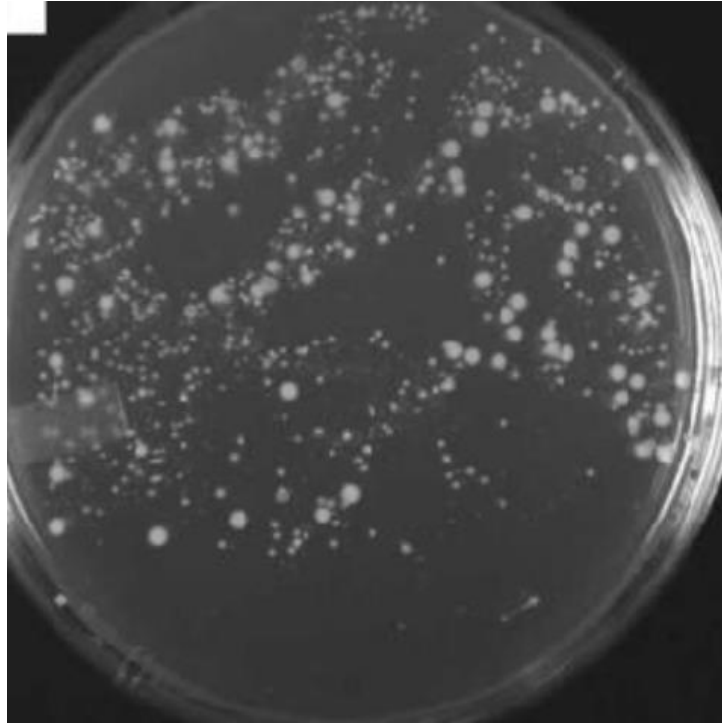
- Hematogenous osteomyelitis **is the most common form of osteomyelitis in infants and children.**
- In adults, **vertebral osteomyelitis** is the most common form of hematogenous osteomyelitis. Most cases occur **in patients >50 years.**
- Hematogenous osteomyelitis is usually **monomicrobial; S. aureus** is by far the most commonly isolated organism. **Aerobic gram-negative rods** are identified in up to 30 percent of cases.
- **Tuberculous osteomyelitis** usually occurs from reactivation of tuberculous bacilli lodged in bone during the **mycobacteremia** occurring at the time of the primary infection.

Osteomyelitis/ PATHOGENESIS

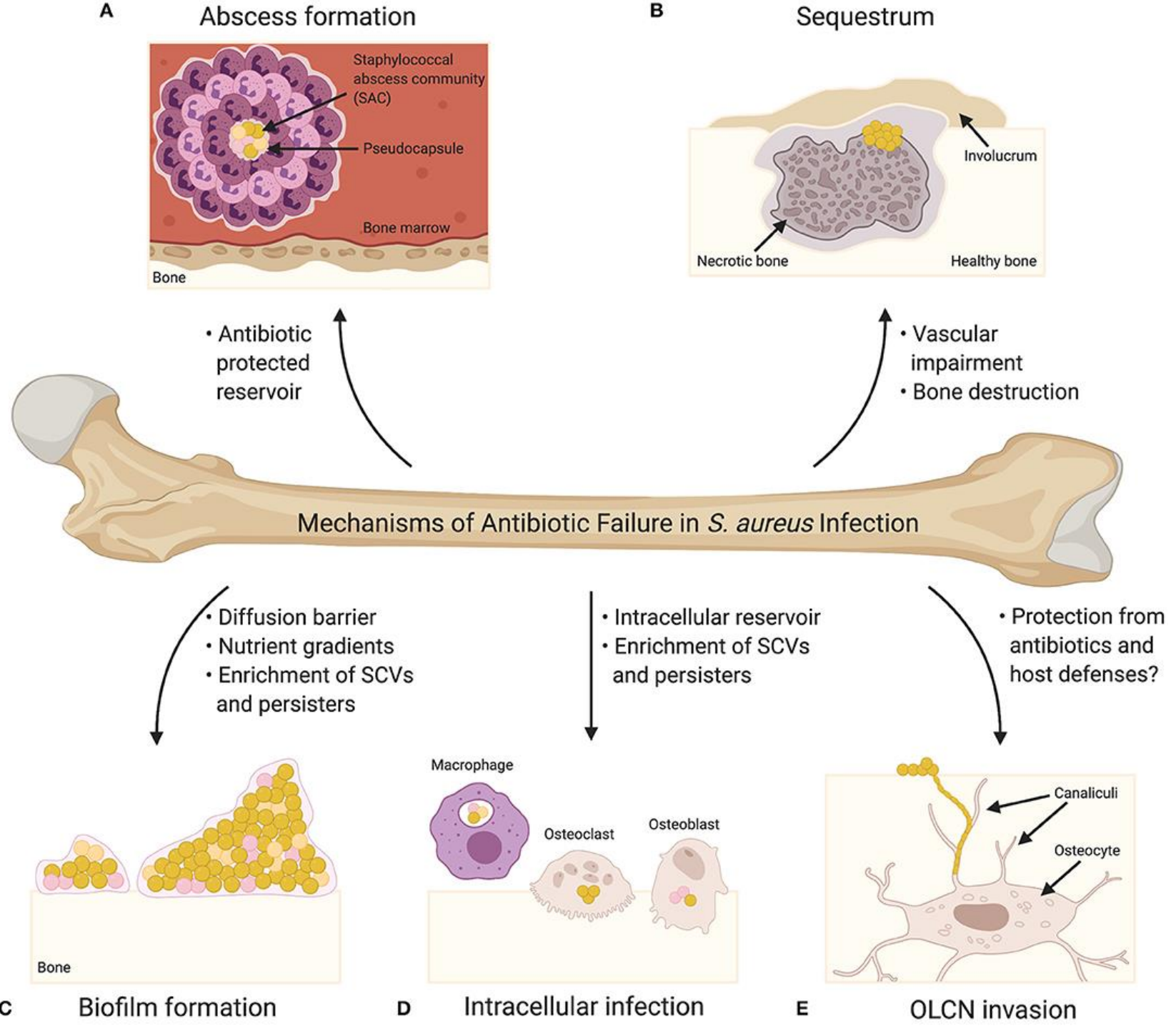
- Normal bone is highly resistant to infection. Osteomyelitis develops when there is a **large inoculation of organisms, presence of bone damage**, and/or presence of hardware or other **foreign material**.
- The pathogenesis of osteomyelitis is multifactorial and poorly understood; important factors include the virulence of the infecting organism(s), the host immune status, and the bone vascularity.

- Bacteria have a number of virulence determinants that may contribute to development of osteomyelitis.
- **Adherence** appears to play a central role in the early stages of *S. aureus*-induced osteomyelitis or arthritis. *S. aureus* adheres to a number of components of bone matrix including fibrinogen, fibronectin, laminin, collagen, bone sialoglycoprotein, and clumping factor A.
- ***S. aureus* can survive intracellularly in cultured osteoblasts.** Persistence of intracellular pathogens within osteoblasts may also be an important factor in the pathogenesis of osteomyelitis. When digested by osteoblasts, *S. aureus* undergoes phenotypic alteration, which renders it **more resistant to the action of antimicrobials**. This may explain in part the high relapse rate of osteomyelitis treated with antimicrobials for a short duration

Osteomyelitis/ PATHOGENESIS



small colony variants



Osteomyelitis/ Clinical manifestations

- Clinical manifestations of hematogenous osteomyelitis **mirror those of nonhematogenous osteomyelitis.**
- **Acute osteomyelitis** typically presents with gradual onset of symptoms **over several days.** Patients usually present with a **dull pain at the involved site, with or without movement.** **Local findings** (tenderness, warmth, erythema, and swelling) and **systemic symptoms** (fever, rigors) may also be present. Patients with osteomyelitis involving the hip, vertebrae, or pelvis tend to manifest few signs or symptoms other than pain.
- **Chronic osteomyelitis** may manifest as **pain, erythema, or swelling,** sometimes in association with a **draining sinus tract;** fever is usually absent. Chronic osteomyelitis may also present **with intermittent flares** of pain and swelling. The presence of a sinus tract is **pathognomonic** of chronic osteomyelitis.

Osteomyelitis/ Clinical approach and diagnosis

- In general, the diagnosis of osteomyelitis is established via **culture obtained from biopsy of the involved bone**. A diagnosis of osteomyelitis may be inferred in the following circumstances:
- Clinical and **radiographic findings typical of osteomyelitis** and **positive blood cultures with a likely pathogen** (such as *Staphylococcus aureus*); in such cases, bone biopsy is not required but may be useful, particularly if subsequent therapeutic debridement is needed.
- **Bone histopathology consistent with osteomyelitis in the absence of positive culture data** (particularly in the setting of recent antibiotic administration).
- Suggestive clinical and typical radiographic findings and **persistently elevated inflammatory markers**, in circumstances with no positive culture data and a biopsy is not feasible.

Osteomyelitis/ management

- Findings of osteomyelitis on **radiographic imaging** should prompt **bone biopsy** for culture and histology **to confirm the diagnosis and to guide antimicrobial therapy**, unless blood cultures are positive for a likely pathogen (such as *S. aureus*, a gram-negative enteric rod, or *Pseudomonas aeruginosa*).
- Patients with negative Gram stain and culture results should be treated with an antimicrobial regimen with activity against the common causes of vertebral osteomyelitis, including **staphylococci, streptococci, and gram-negative bacilli.**

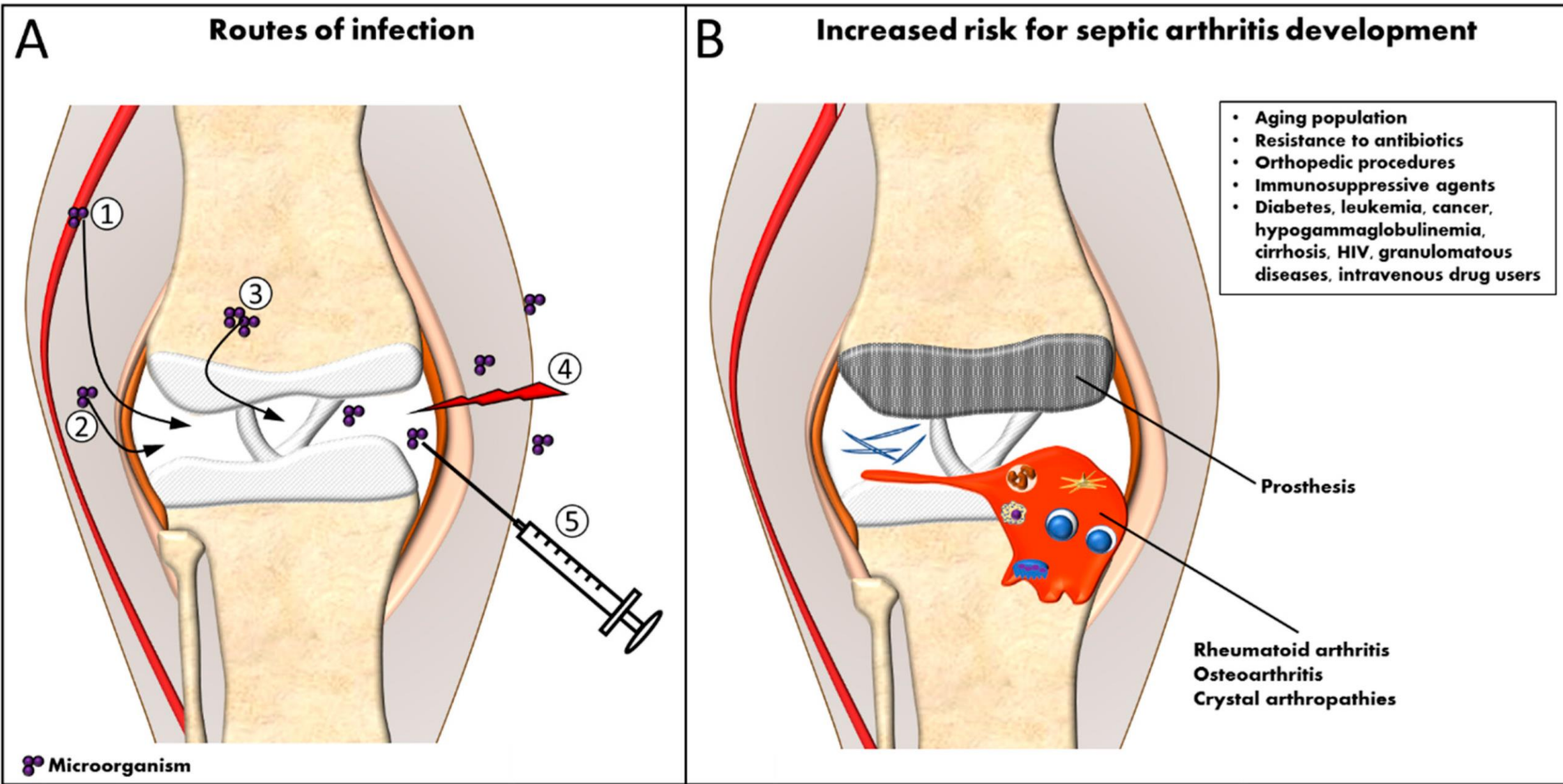
Complications of osteomyelitis include:

- Sinus tract formation
- Contiguous soft tissue infection
- Abscess
- Septic arthritis
- Systemic infection
- Bony deformity and Fracture
- Malignancy

Septic arthritis / overview

- Septic arthritis is synonymous with an **infection in a joint**. Septic arthritis is usually caused by **bacteria** but can also be caused by other microorganisms. Septic arthritis due to bacterial infection is often a destructive form of acute arthritis
- Most commonly, septic arthritis arises via **hematogenous seeding**. Bacteremia is more likely to localize in a joint with **pre-existing arthritis** (such as rheumatoid arthritis, osteoarthritis, gout, pseudogout, Charcot arthropathy), particularly if associated with synovitis.
- Septic arthritis develops as a result **of hematogenous seeding**, direct inoculation of bacteria into the joint, or contiguous spread from an adjacent soft tissue or bone infection.
- Septic arthritis is **usually monomicrobial**. **S. aureus** (including methicillin-resistant S. aureus) is the most common cause of septic arthritis in adults. Other gram-positive organisms such as streptococci are also important potential causes of septic arthritis

Septic arthritis / overview



Septic arthritis / CLINICAL MANIFESTATIONS

- Patients with septic arthritis usually present acutely with a **single swollen and painful joint** (ie, **monoarticular arthritis**). Joint pain, swelling, warmth, and restricted movement occur in 80 percent of patients with septic arthritis. Most patients with septic arthritis are **febrile**; however, older patients with septic arthritis may be afebrile.
- **The knee is involved in more than 50 percent of cases**; wrists, ankles, and hips are also affected commonly



Septic arthritis / DIAGNOSIS

- The diagnosis of septic arthritis should be suspected in patients with acute onset of at least one swollen, painful joint, with or without relevant risk factors
- The **diagnosis of septic arthritis is made based on synovial fluid analysis and culture.**
- In addition, **blood cultures** and, when indicated, **radiographs**, ultrasound, or imaging studies of the involved joint should be obtained.
- Collection of synovial fluid and blood cultures should be performed **prior to administration of antibiotics**. If synovial fluid cannot be obtained with closed needle aspiration, the joint should be aspirated under radiographic guidance.



Septic arthritis / DIAGNOSIS

Organism	Clinical clues
<i>Staphylococcus aureus</i>	Healthy adults, skin breakdown, previously damaged joint (eg, rheumatoid arthritis), prosthetic joint
Streptococcal species	Healthy adults, splenic dysfunction
<i>Neisseria gonorrhoeae</i>	Healthy adults (particularly young, sexually active), associated tenosynovitis, vesicular pustules, late complement deficiency, negative synovial fluid culture and Gram stain
Aerobic gram-negative bacteria	Immunocompromised hosts, gastrointestinal infection
Anaerobic gram-negative bacteria	Immunocompromised hosts, gastrointestinal infection
Brucellosis	Zoonosis
Mycobacterial species	Immunocompromised hosts, travel to or residence in an endemic area
Fungal species (<i>Candida</i> species, sporotrichosis, <i>Cryptococcus</i> , blastomycosis, coccidioidomycosis)	Immunocompromised hosts
Spirochete (<i>Borellia burgdorferi</i>)	Exposure to ticks, antecedent rash, knee joint involvement
<i>Mycoplasma hominis</i>	Immunocompromised hosts with prior urinary tract manipulation

Refer to separate UpToDate topic for discussion of viral causes of arthritis.



Many tickborne diseases can have similar signs and symptoms. If you have been bitten by a tick and develop the symptoms below within a few weeks, a health care provider should evaluate the following before deciding on a course of treatment:

- Your symptoms
- The [geographic region](#) in which you were bitten
- Diagnostic tests, if indicated by the symptoms and the region where you were bitten

The most common symptoms of tick-related illnesses are:

- **Fever/chills:** With all tickborne diseases, patients can experience fever at varying degrees and time of onset.
- **Aches and pains:** Tickborne disease symptoms include headache, fatigue, and muscle aches. With Lyme disease you may also experience joint pain. The severity and time of onset of these symptoms can depend on the disease and the patient's personal tolerance level.
- **Rash:** [Lyme disease](#), [southern tick-associated rash illness \(STARI\)](#), [Rocky Mountain spotted fever \(RMSF\)](#), [ehrlichiosis](#), and [tularemia](#) can result in distinctive rashes:

Septic arthritis / TREATMENT

- Management of acute bacterial arthritis consists of joint drainage and antibiotic therapy.
- Approaches to joint drainage for management of septic arthritis in adults include needle aspiration, arthroscopic drainage, or arthrotomy.
- The initial choice of empiric antimicrobial therapy should cover the most likely pathogens; If the initial Gram stain of synovial fluid **demonstrates gram-positive cocci**, empiric treatment with **vancomycin**. If the initial Gram stain of synovial fluid demonstrates **gram-negative bacilli**, treatment should be guided by risk for **Pseudomonas infection**.
- In one study including 121 adults with septic arthritis, **a poor joint outcome (as defined by the need for amputation, arthrodesis, prosthetic surgery, or severe functional deterioration) occurred in one-third of the patients**; adverse prognostic factors included **older age** and **pre-existing joint disease**.

Animal bites (dogs, cats, and other animals): Evaluation and management

- **Dog bites** account for approximately **90 percent of animal bites** and occur most often in children. Cat bites account for approximately 10 percent of animal bite wounds and happen most often in adult women. Infections are **much more common after cat bites (up to 50 percent of wounds) than dog bites**.
- In children, dog bites usually involve the head and neck; in adolescents and adults, dog bites usually involve the extremities. Dog bites may be associated with a range of injuries, from minor to major wounds. **Cat bites usually occur on the extremities and tend to penetrate deeply, with higher risk of deep infection** (abscess, septic arthritis, osteomyelitis, tenosynovitis, bacteremia, or necrotizing soft tissue infection) **than dog bites**.



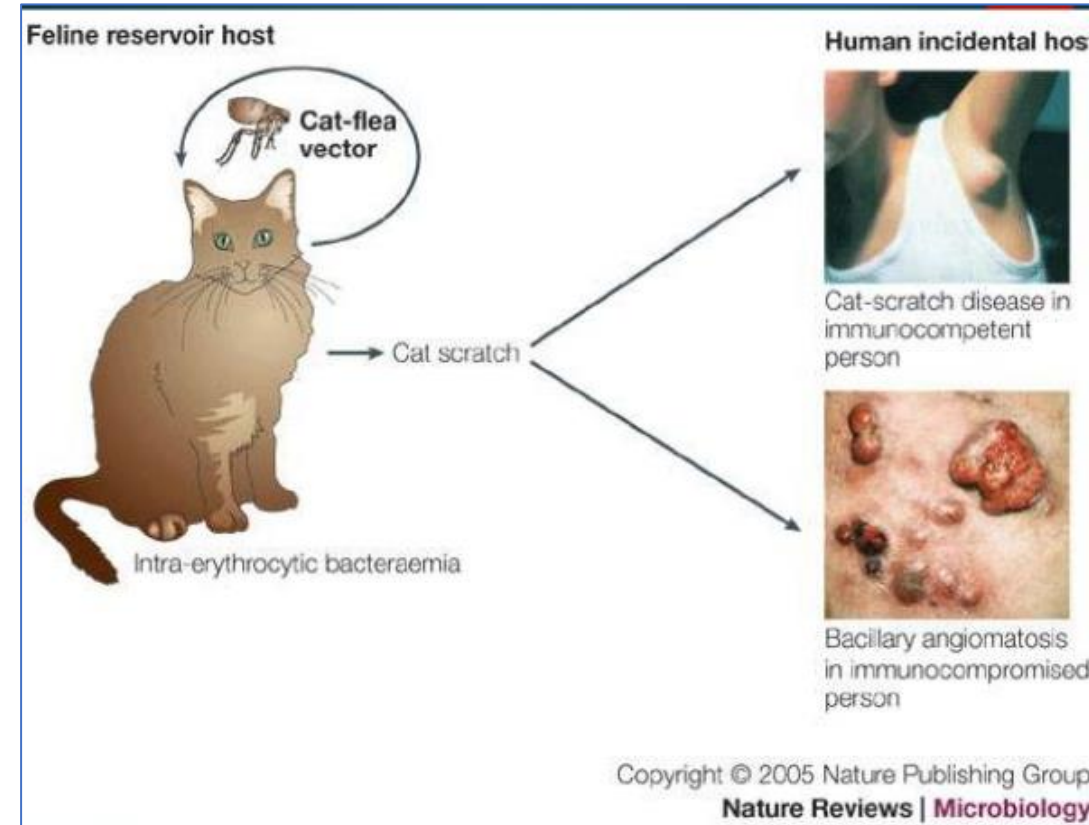
Animal bites (dogs, cats, and other animals): Evaluation and management

- The physical examination should ensure that the patient is **hemodynamically stable** and should **assess for injuries to adjacent structures**, especially for bites with deep puncture wounds on the head, neck, trunk, or close to joints. Bite wounds should be evaluated carefully for foreign material, and a neurovascular assessment should be performed in areas distal to the wound.
- Bite wound infection may be superficial (eg, **cellulitis**, with or without **abscess**) or deep (**abscess, septic arthritis, osteomyelitis**, tenosynovitis, or **necrotizing soft tissue infection**).
- Clinical manifestations of superficial infection include **fever, erythema, swelling, and warmth, purulent drainage**, and/or **lymphangitis**. An associated **superficial abscess** may present as a tender, erythematous, fluctuant nodule.

Bartonella

- *Bartonella* are **gram-negative, coccobacillary** or bacillary rods with **fastidious** growth requirements, requiring prolonged incubation (2 to 6 weeks). usually **facultative intracellular bacteria**.
- Bartonella species are **transmitted by vectors** such as ticks, fleas, sand flies, and mosquitoes
- *B. henselae* is responsible for a disease acquired after exposure to cats (e.g., scratches, bites, contact with the contaminated feces of cat fleas): **cat-scratch disease**, 1–3 weeks after inoculation.
- Symptoms typically include a **non-painful bump or blister at the site of injury** and painful and **swollen lymph nodes**

Introduction to Microbiology and Immunology



Animal bites (dogs, cats, and other animals): Evaluation and management

- Relevant pathogens in the setting of animal bite wounds include the **oral flora of the biting animal** and **human skin flora** (such as staphylococci and streptococci).
- **Pasteurella** species are isolated from 50 percent of dog bite wounds and 75 percent of cat bite wounds.
- **Capnocytophaga canimorsus** can cause bacteremia and fatal sepsis after animal bites, especially in patients with asplenia, alcoholism, or underlying hepatic disease.
- **B. henselae** may be transmitted via the bite of an infected cat; other forms of transmission include **cat scratches**, flea exposure, and contact with cat saliva via broken skin or mucosal surfaces. The incubation period for B. henselae infection is 7 to 14 days.
- **Anaerobes** – Anaerobes isolated from dog and cat bite wounds include Bacteroides species, fusobacteria, Porphyromonas species, Prevotella species.
- The average bite wound culture yields five types of bacterial isolates. **Mixed aerobic and anaerobic bacteria** are observed in 60 percent of cases; **skin flora** are isolated in about 40 percent of cases

Further reading:

- Nonvertebral osteomyelitis in adults: Clinical manifestations and diagnosis
https://ezlibrary.ju.edu.jo:2119/contents/nonvertebral-osteomyelitis-in-adults-clinical-manifestations-and-diagnosis?search=osteomyelitis&topicRef=7660&source=see_link

- Pathogenesis of osteomyelitis
https://ezlibrary.ju.edu.jo:2119/contents/pathogenesis-of-osteomyelitis?search=osteomyelitis&source=search_result&selectedTitle=8~150&usage_type=default&display_rank=7

Septic arthritis:

https://ezlibrary.ju.edu.jo:2119/contents/septic-arthritis-in-adults?search=septic%20arthritis&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1