MSS

MICROBIOLOGY

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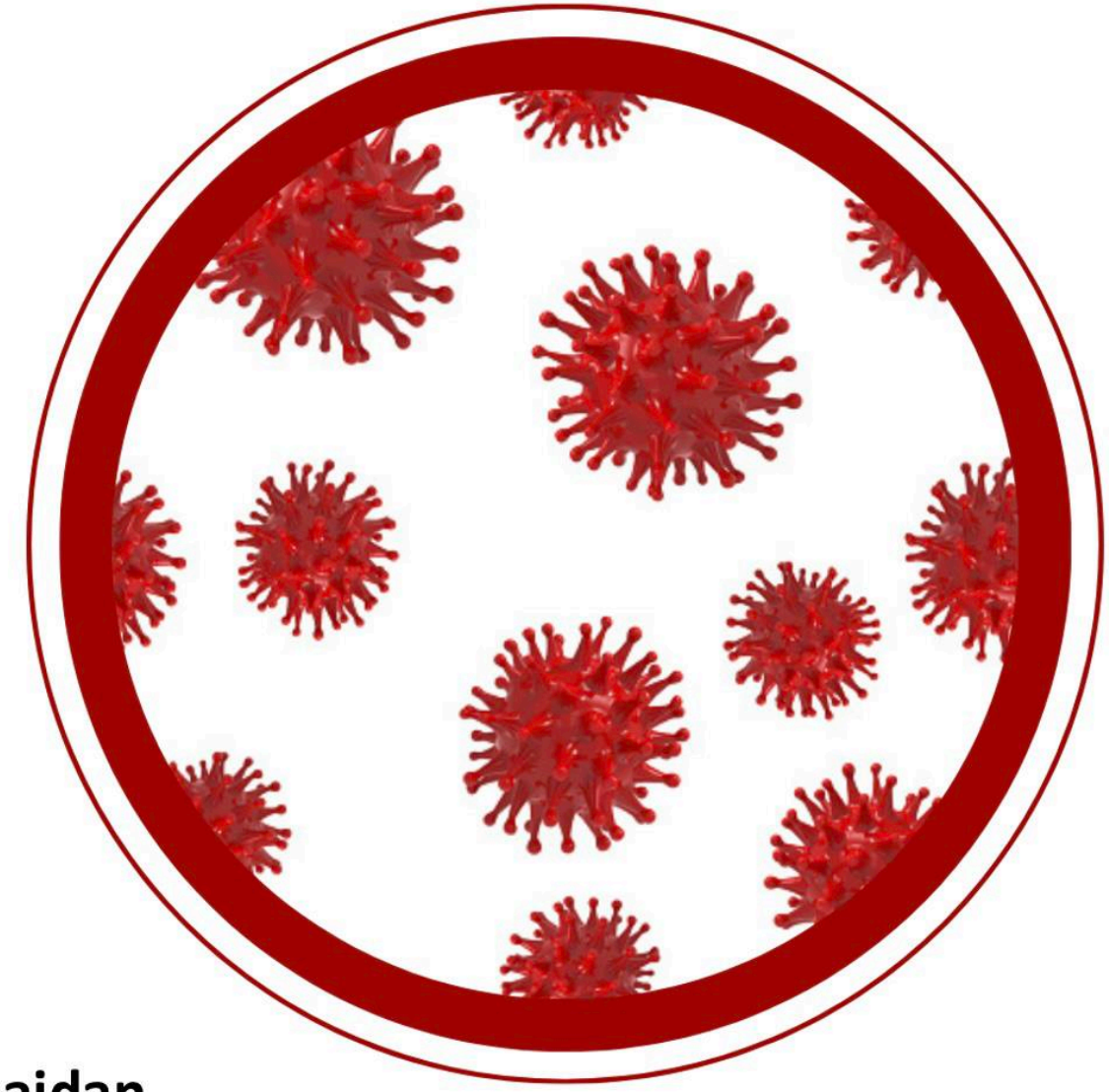

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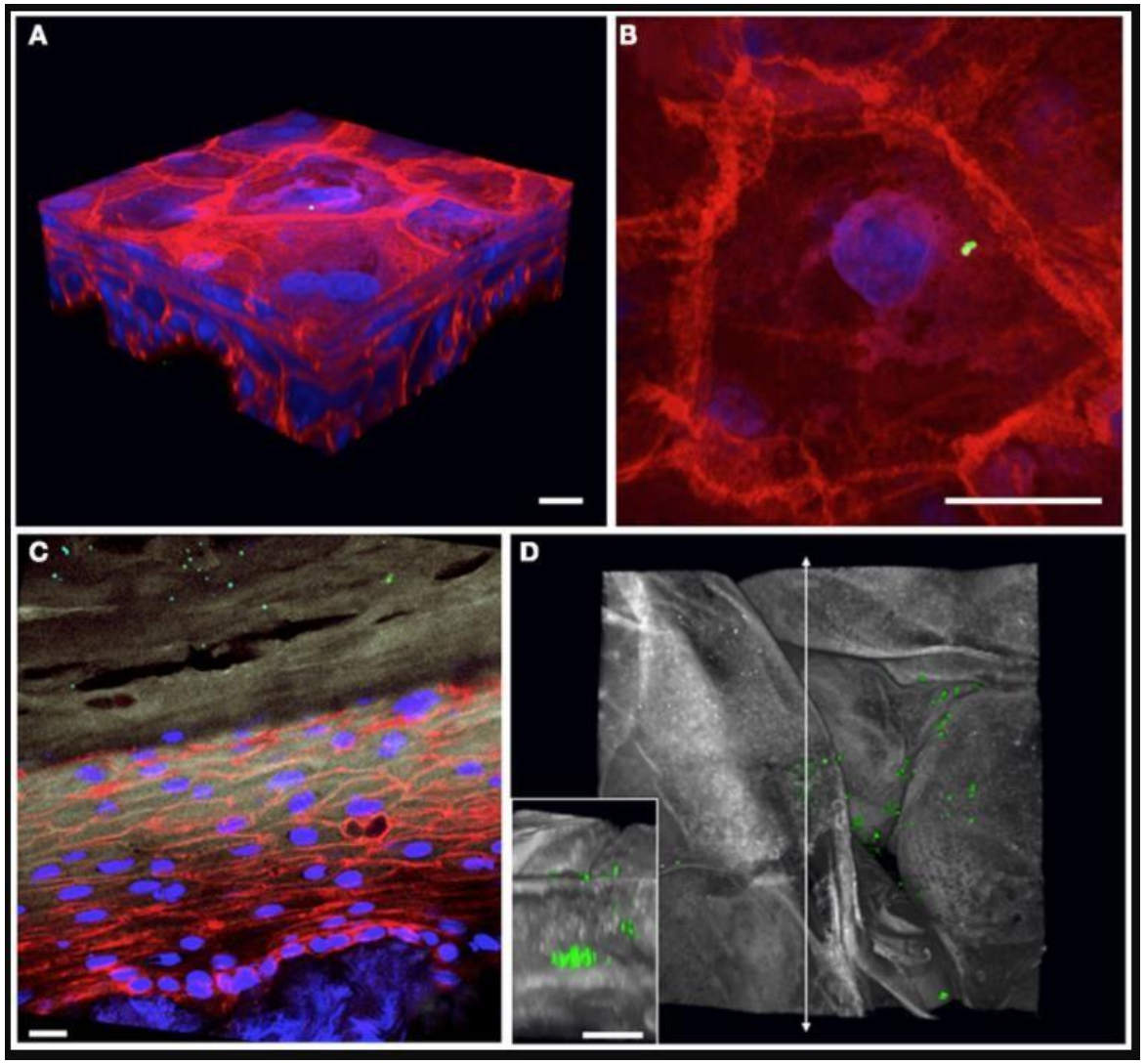


Osteomyelitis and septic arthritis

Overview

In this lecture we will discuss:

- Osteomyelitis
- Septic arthritis
- Animal bites

Osteomyelitis/ Introduction

- **Osteomyelitis** is an infection involving bone. Osteomyelitis may be classified based on the mechanism of infection (**hematogenous** **most probably in children** versus **nonhematogenous** **in older individuals, but if it spreads hematogenously it most commonly causes vertebral osteomyelitis specially in those above 50**) and the duration of illness(**acute** versus **chronic**).
- **In non hematogenous the bacteria can reach the bone in many ways one of them in diabetic food ulcers so diabetic patient are at risk, and in vascular problems and neuropathic problems can also predispose ulcers that can reach the bone and after surgery or implantation of something the pathogen can attach to it and affect the adjacent bone.or trauma and wounds that can lead to deep infection and reach the bone as well.**

- **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.

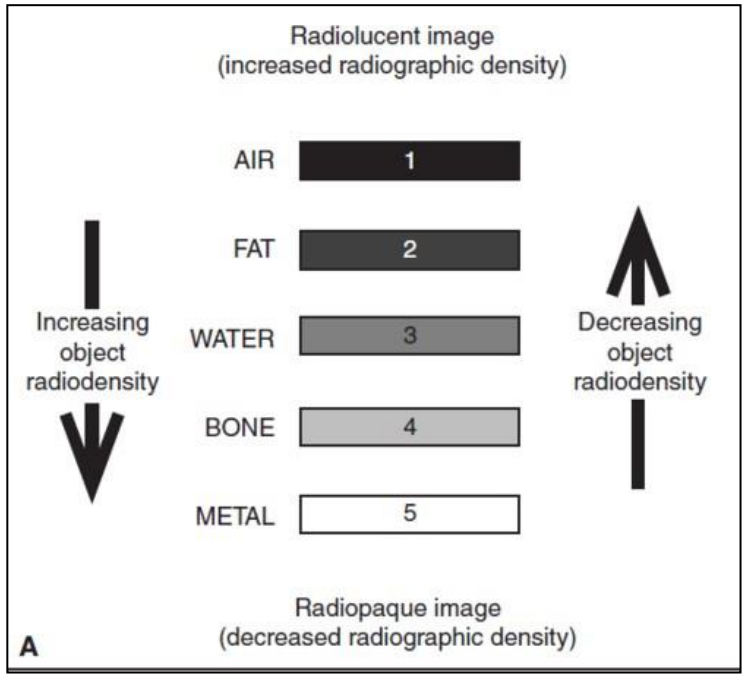
Osteomyelitis/ Introduction

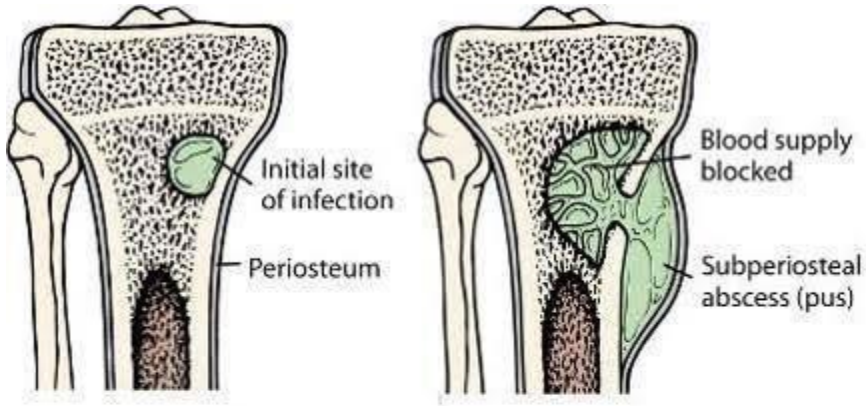
- **Nonhematogenous** osteomyelitis can occur as a result of contiguous spread of infection to bone from adjacent soft tissues and joints or via direct inoculation of infection into the bone (as a result of trauma or surgery).

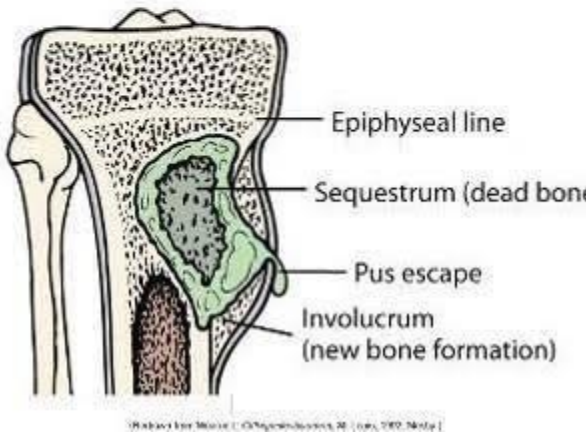
- **Hematogenous** osteomyelitis is caused by microorganisms that seed the bone in the setting of bacteremia

Radiographic images are quite important to see what happens in the bone, for example when the process is acute there is little tissue necrosis within the bone, but when inflammation and edema is continuous within the bone there will be compromise in the blood supply make necrotic tissue which is sequestra and new baby bone formation which called involucrum .so the bone convert into necrotic and almost liquid like tissue the radiodensity of it decrease and become like water and fat. And because of the pressure inside the bone there will be a sinus opening to the outside where pus can escape.

Osteomyelitis/ Introduction







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.

infection can spread to nearby structures mainly the joints and it is one of causes of septic arthritis

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** in diabetics food infection the deeper it's the higher the possibility that is polymicrobial ,**or monomicrobial**. **Staphylococcusaureus** (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** **it's very rare but if it happens it usually affects the vertebrae** usually occurs from reactivation of tuberculous bacilli lodged inbone during the **mycobacteremia** occurring at the time of the primary infection. So of a patient come with pain in vertebrae you must ask If there is a history of exposure to animal (how the mycobacteria transmitted) and to check if there is a limitation of movement or nerve damage or radiculopathy (injury or damage to nerve roots in the area where they leave the spine) and asking About things that predispose to mycobacterium reactivation such

- as immunosuppressants and if there is symptoms related to pulmonary TB.

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** staphylococcus aureus is very good at adhering appears to play a central role in the early stages of S. aureus-induced osteomyelitor arthritis. S. aureus adheres to a number of components of bone matrix including fibrinogen, fibronectin, laminin, collagen, bone sialoglycoprotein, and clumping factor A.

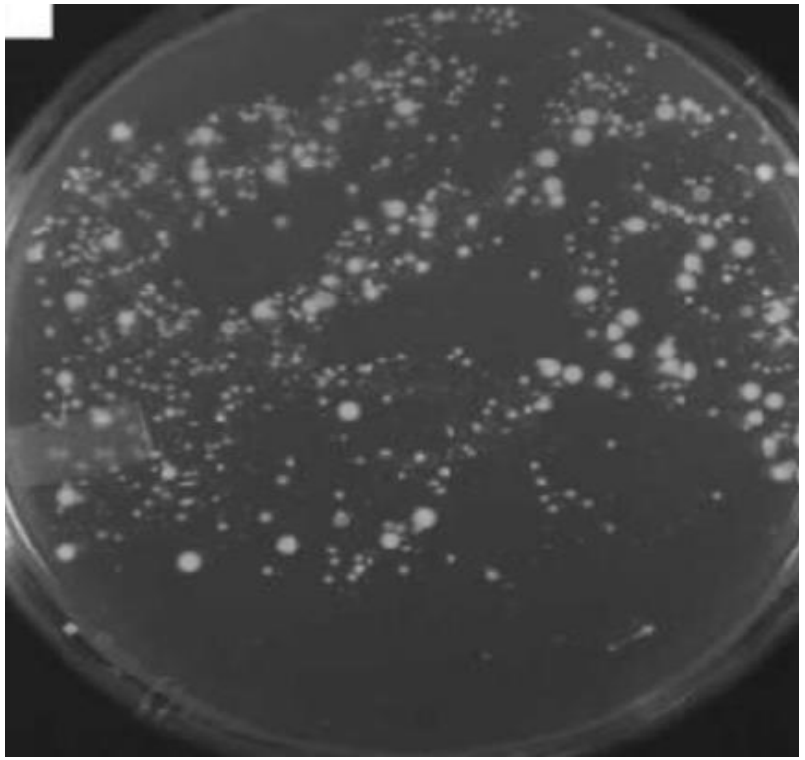
- ***S. aureus*** **can survive intracellularly in cultured osteoblasts.** Persistence of intracellular pathogens within osteoblasts may also be an important factor in the pathogenesis of osteomyelitis. When digested by osteoblasts, *S. aureus* undergoes phenotypic alteration, which renders it **more 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

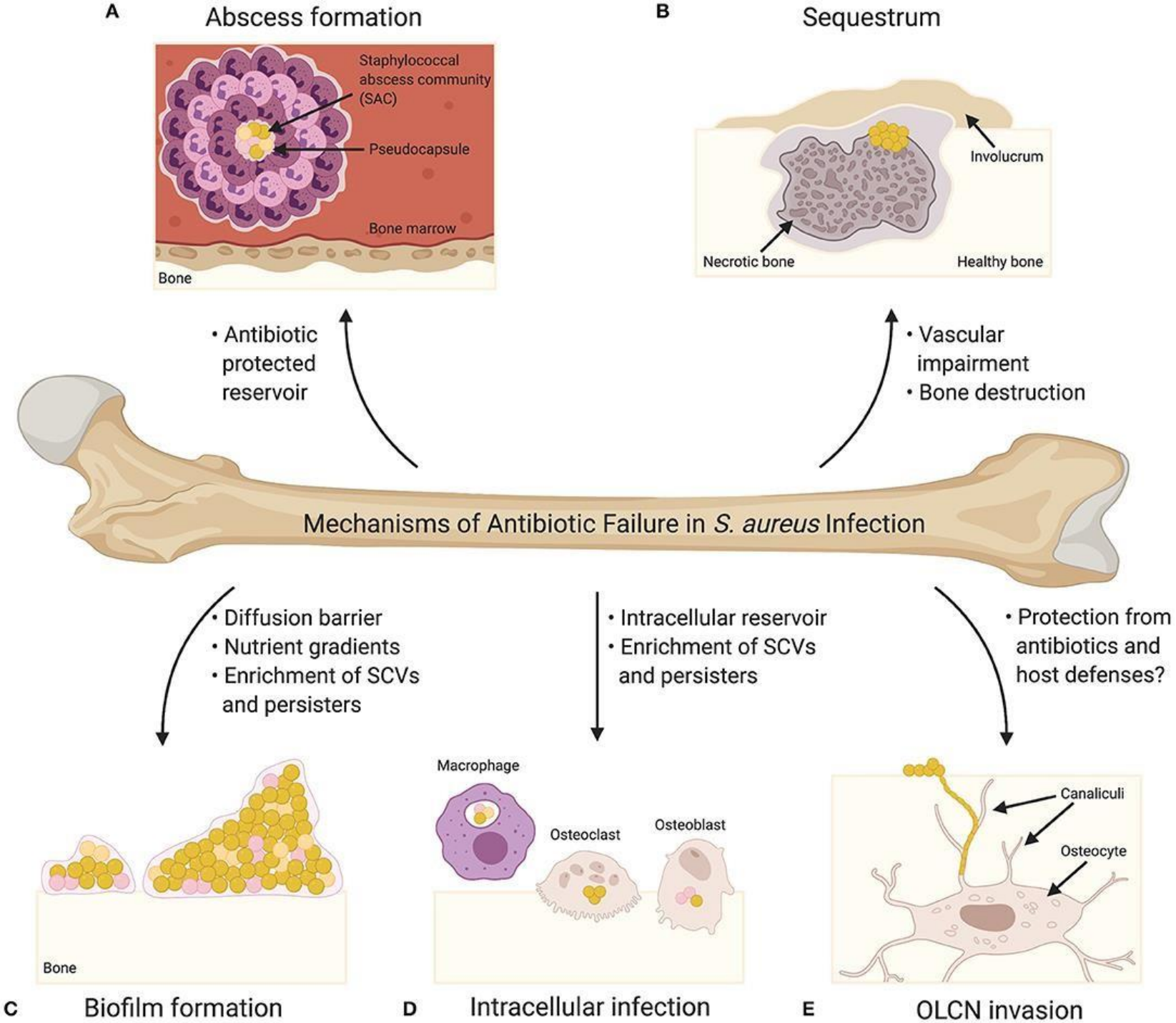
- In certain experiment we incubate staphylococcus aureus from a clinical isolate (from a patient) and we put it with keratinocytes (skin cell) and after 3 hours we check how many bacteria is found inside the cell and get rid of bacteria outside the cell and maintain the intracellular bacteria by using an antibiotic that doesn't penetrate inside inside the cell such as gentamicin and kill most of staphylococcus aureus outside the cell.only about 2% enter the cell that's indicate that is staphylococcus aureus is an extracellular pathogen, but there is a certain amount of them enter inside the cell and they think that it has a relation with antibiotic resistance and to immune system in general because sometimes when bacteria inter inside the cell it is change into different phenotype and changes the proteins that it produce specially if this process takes long time and when they lyse the the keratinocytes they find that it has colonies but not the usual colonies but instead colony that is pinpoint and they are different in size also from the usual colonies. And after researching they found that there is a variant in staphylococcus aureus called small colony variant that is associated with chronic infection and resistant to antibiotics. And after subculture these colonies they reverted back to normal size colony.so seemingly there is a selective pressure when they are in the cell that are exposed to antibiotics makes them change there size but if it gone they switched

back to normal form that is meanly because of certain genes that is activated transcribed and translate to produce new proteins that help it to survive in the new environment and probably they aren't metabolically active as outside the cell they don't replicate as much as outside the cell (they become dormant).

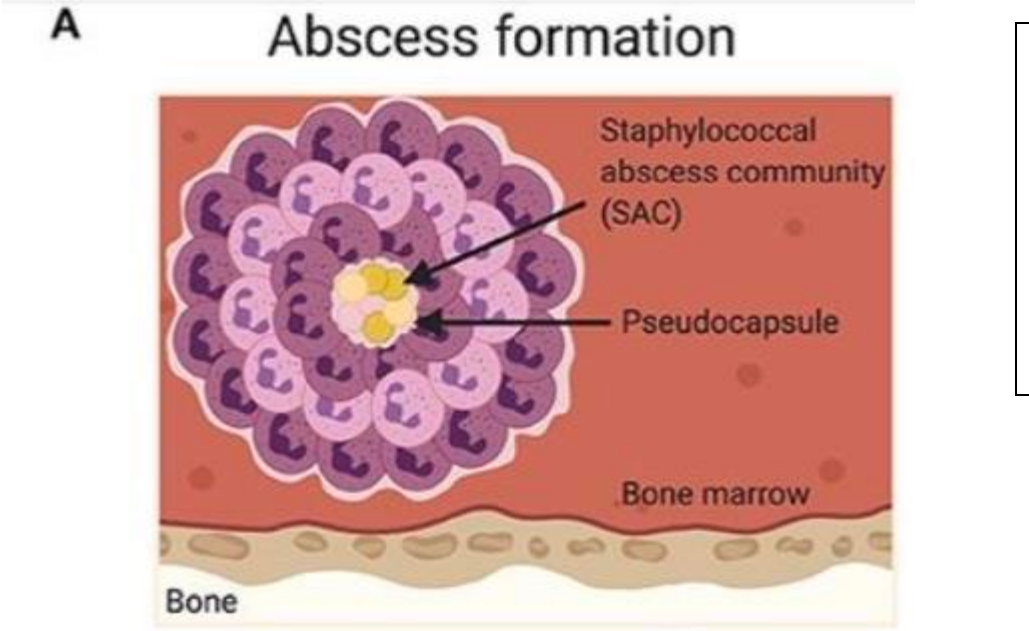
Osteomyelitis/ PATHOGENESIS



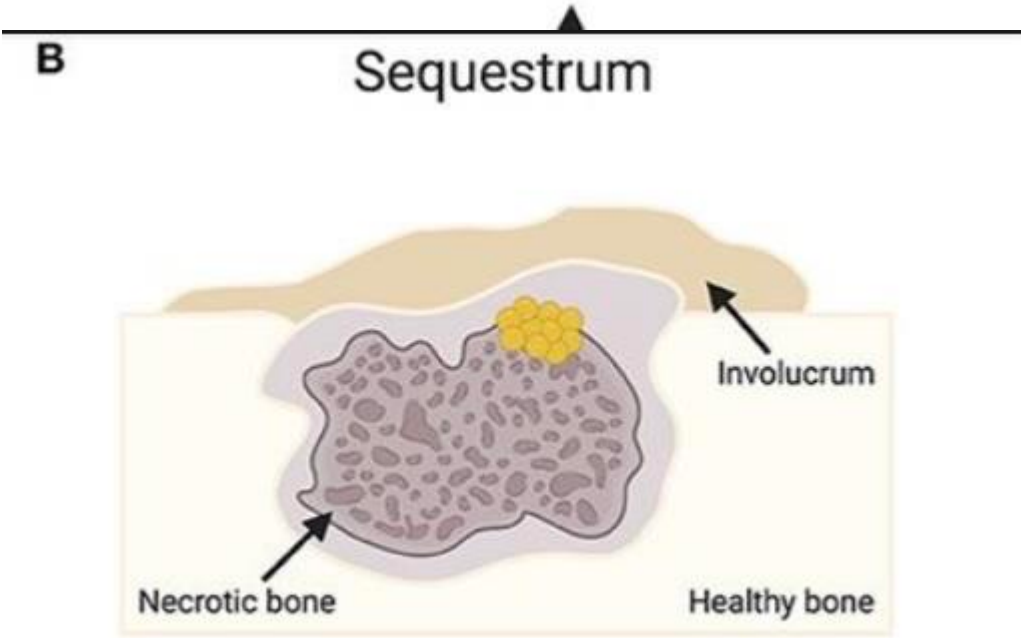
small colony variants



Osteomyelitis/ PATHOGENESIS

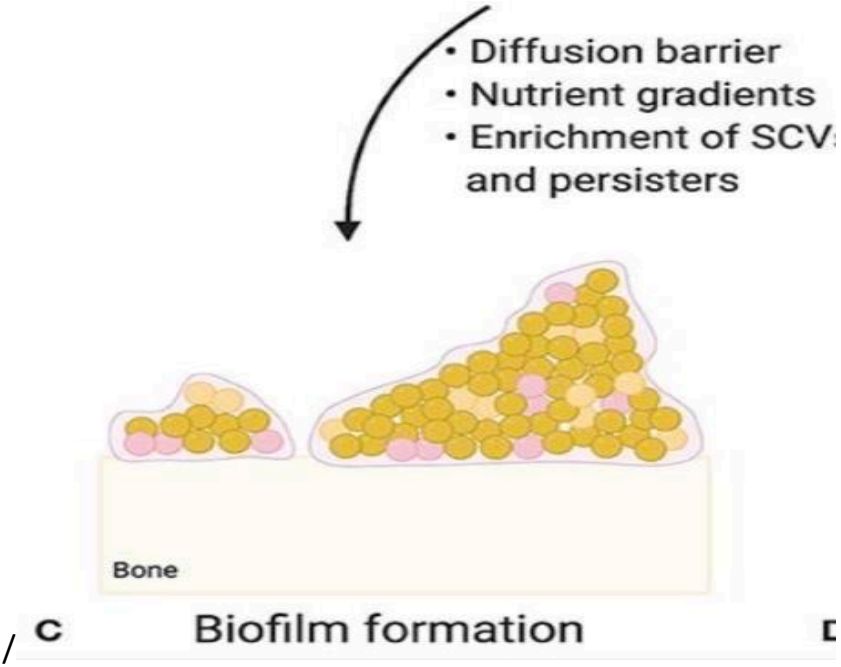


Staphylococcus aureus can form abscess anywhere (bone or brain) and if there is an abscess in the body it is usually due to staphylococcus aureus. And this one of things that makes it difficult to be treated because the antibiotics and the immune mechanisms will not reach it.

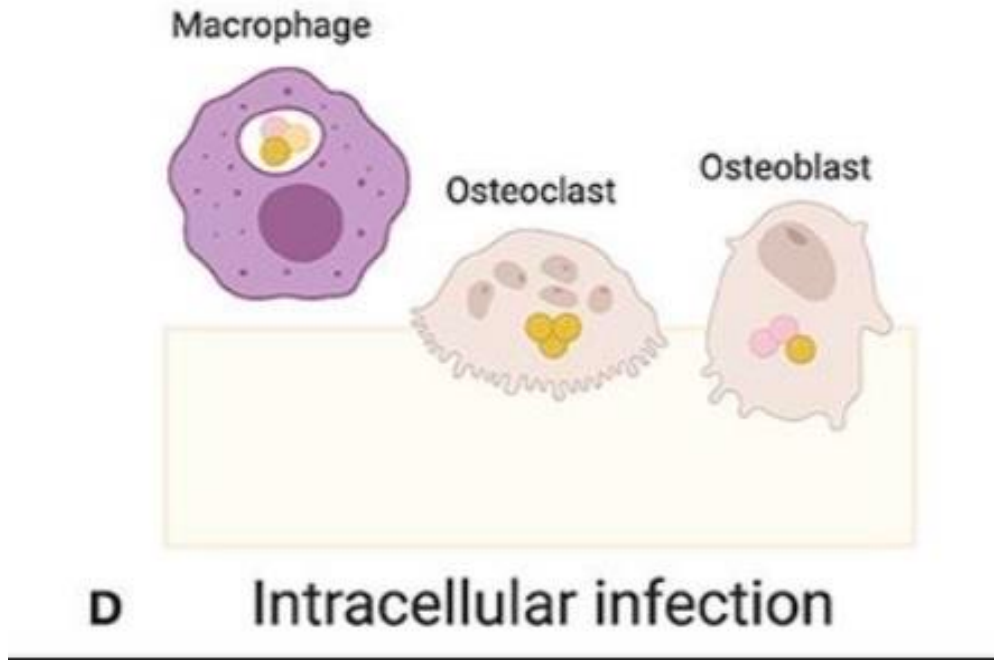


Another reason why it is difficult to be treated is formation of sequestrum which has a compromised blood supply and that is why antibiotics doesn't reach it also

Osteomyelitis/ PATHOGENESIS

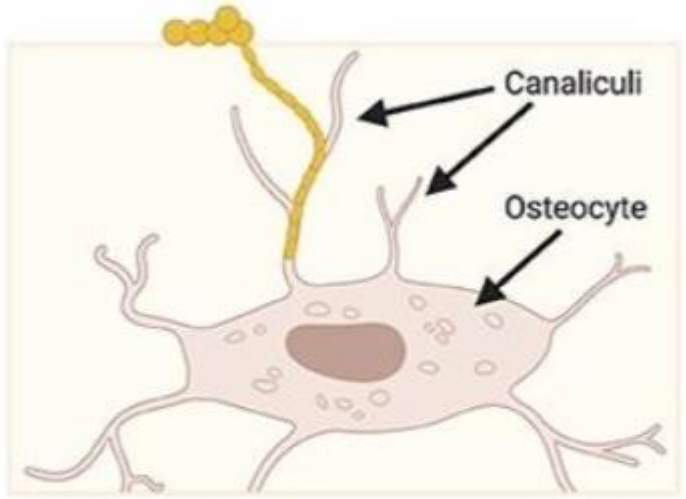


And the formation of biofilm makes the antibiotic also difficult to penetrate Biofilms may act as diffusion barriers for antibiotics, thereby reducing the penetrance of antibiotics toward the deeper layers of the



intracellular survival within osteoblast and osteoclast make it more difficult to treat

Osteomyelitis/ PATHOGENESIS



E OLCN invasion

Osteocytes, the major cell type embedded within the bone matrix, reside in structures known as lacunae, and connect to one another via a three-dimensional network of channels known as canaliculi. Colonization of the osteocyte lacuno-canalicular network (OLCN) is believed to promote chronicity of S. aureus osteomyelitis as the antibiotic concentrations needed for bacterial eradication may not be possible to achieve within the infected OLCN. Bacteria within the OLCN might also be protected from the host response. The doctor did not talk about it.

Survival of staphylococcus aureus can related to recurrent skin infection. For example those patients who have atopic dermatitis and eczema have recurrent staphylococcus aureus colonization because of inflammation of skin and they think that it can also survive inside the keratinocytes

- lClinical manifestations of hematogenous osteomyelitis **mirror those of nonhematogenousosteomyelitis.**

- **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(it produce pus)**; 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.

- In general, the diagnosis of osteomyelitis is established via **culture obtained from biopsy of the involved bone**(and examine it under the microscope this is the definitive diagnosis). 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** in hematogenous spread and it could be enough (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/ managment

- 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 continuous inflammation and chronic infection often lead to cancer

Septic arthritis / overview

- Septic arthritis (it is called septic to differentiate it from other causes of arthritis such as rheumatoid arthritis which is autoimmune ,or metabolic such as gout and also osteoarthritis which is associated with age) and this doesn't mean that is associated with sepsis but just to tell us that is exposed by infection. 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.

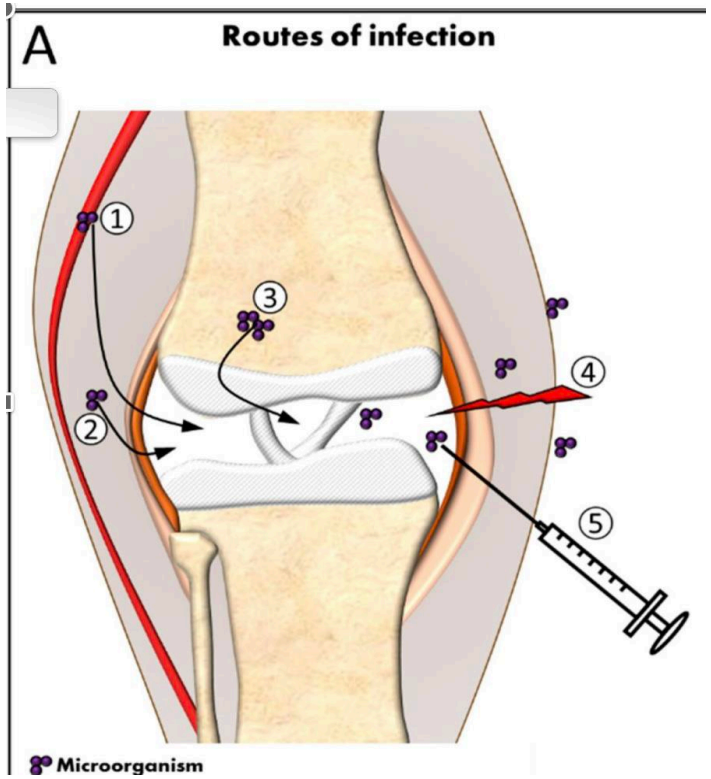
- Septic arthritis develops as a result **of hematogenous seeding**, direct inoculation of bacteria into the joint, or contiguous spread from an adjacent soft tissue or bone infection.

-

- Septic arthritis is **usually monomicrobial. S. aureus** (including methicillin-resistant S. aureus) i

Septic arthritis / overview

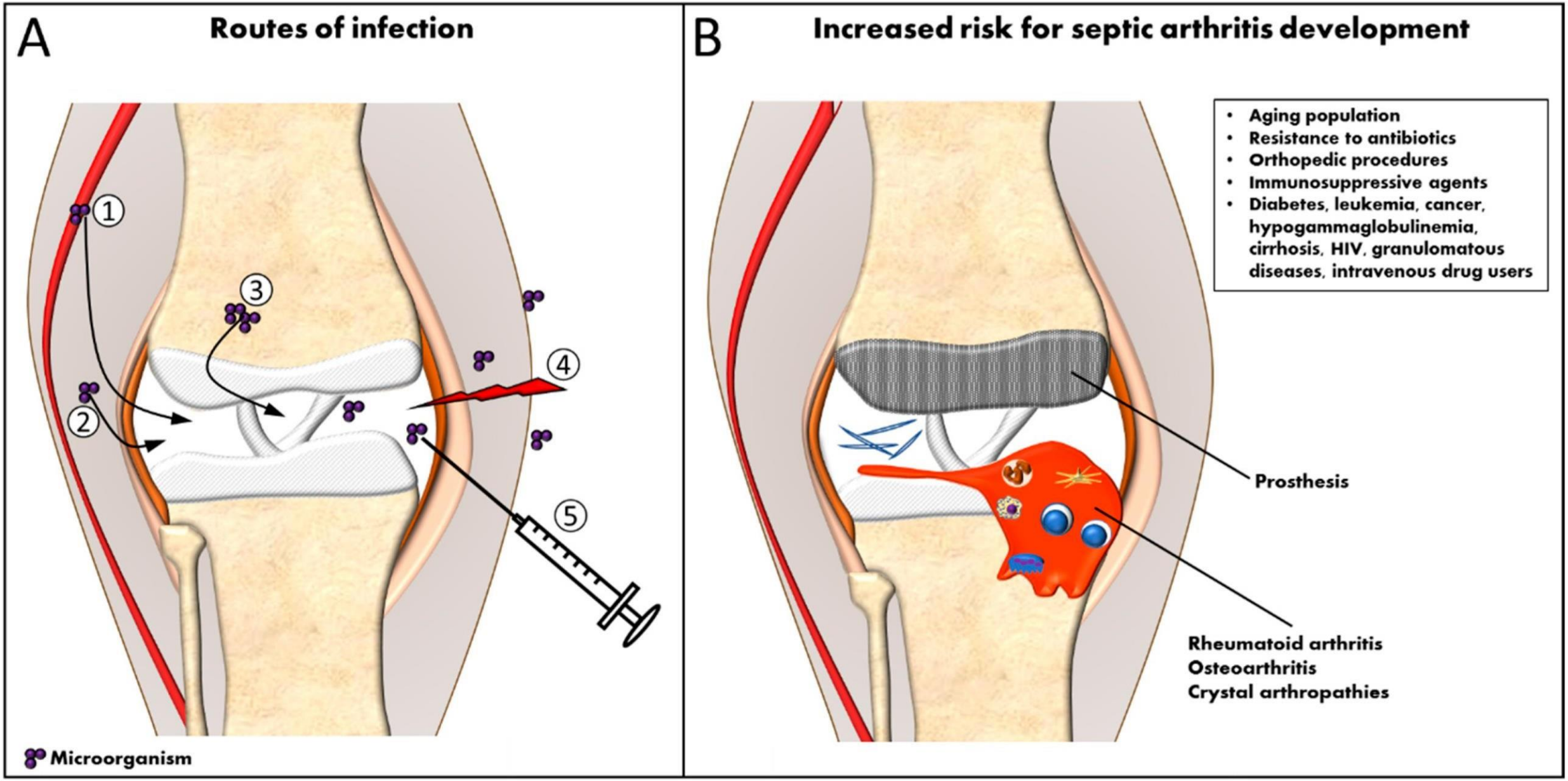
the most common cause of septic arthritis in adults. Other gram-positive organisms such as streptococci are also important potential causes of septic arthritis.



1.the primary source is hematogenous
2.sometimes it is from nearby tissue infection such as in soft tissue infection
3.or from the bone such as in osteomyelitis spreading to the joint
4.or through trauma that penetrates all the covering layer and directly infects the joint
5.iatrogenic during treatment of a patient that have joint problem if you don't follow proper aseptic techniques you may spread bacteria into the joint while you do it

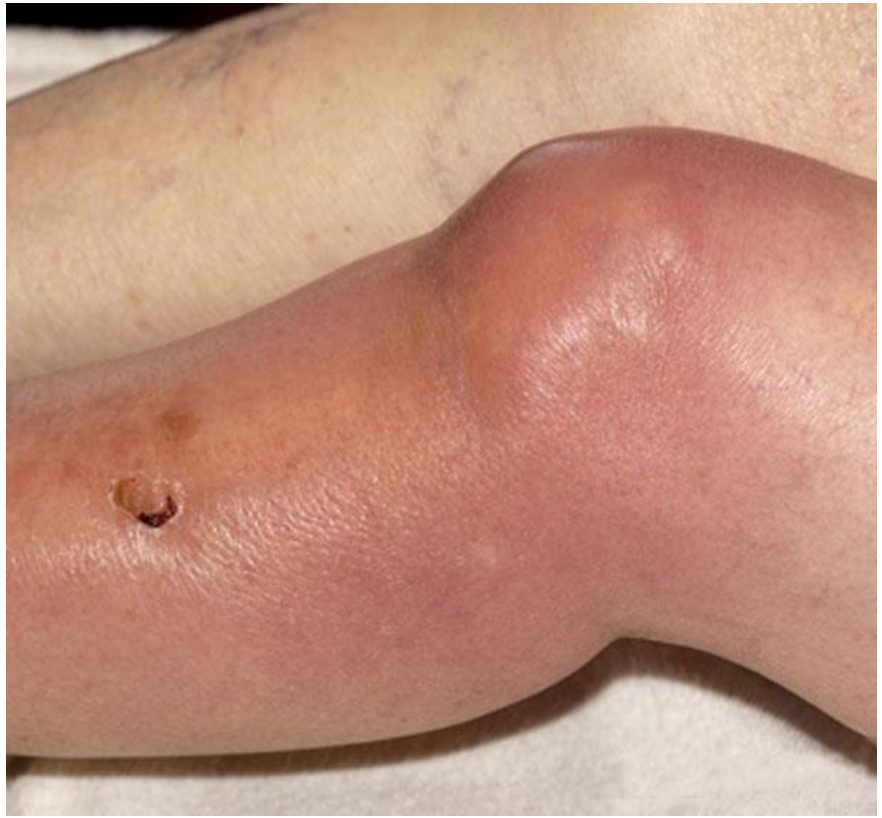
It's not common in adults and children but in elderly and patients that have problems in their joints (osteoarthritis or gout or in patients who have implants in the joints).

Septic arthritis / overview



- 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

In this picture the doctor is not wearing gloves and this may lead to the spread of bacteria from his hand to the joint



- 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** make gram stain **then culture**.
- In addition, **blood cultures** especially if the patient was tired 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

If the synovial fluid contains gram positive, catalase positive and coagulase positive it is staphylococcus aureus and it is the most common cause.
But if it is gram positive catalase negative it is streptococcus pneumoniae especially in patients who remove the spleen
In sexually active patients who have synovial fluid with gram negative diplococcus it is neisseria gonorrhoeae especially because it is asymptomatic in females so infection could be present for a while and the patient does not know and then spread through the blood
Or if the patient was exposure to ticks it is mainly borellia burgdorferi. Which cause Lyme disease that causes rash and pain in joints.

Septic arthritis / DIAGNOSIS

Organism	Clinical clues
Staphylococcus aureus	Healthy adults, skin breakdown, previously damaged joint (eg, rheumatoid arthritis), prosthetic joint
Streptococcal species	Healthy adults, splenic dysfunction
Neisseria gonorrhoeae	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 (*Candida* species, sporotrichosis, *Cryptococcus*, blastomycosis, coccidioidomycosis)	Immunocompromised hosts
Spirochete (*Borellia burgdorferi*)	Exposure to ticks, antecedent rash, knee joint involvement
Mycoplasma hominis	Immunocompromised hosts with prior urinary tract manipulation

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

Graphic 57688 Version 10.0

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:

- 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

Animal bites is considered one of the unique scenarios for bone and soft tissue infections just like the diabetic food.

- **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**(meaning that patient could be losing blood so the doctor priority is to stop bleeding and make sure that his pressure and respiratory rate and other things is ok and then start managing the wound in terms of infection)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 areasdistal 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.

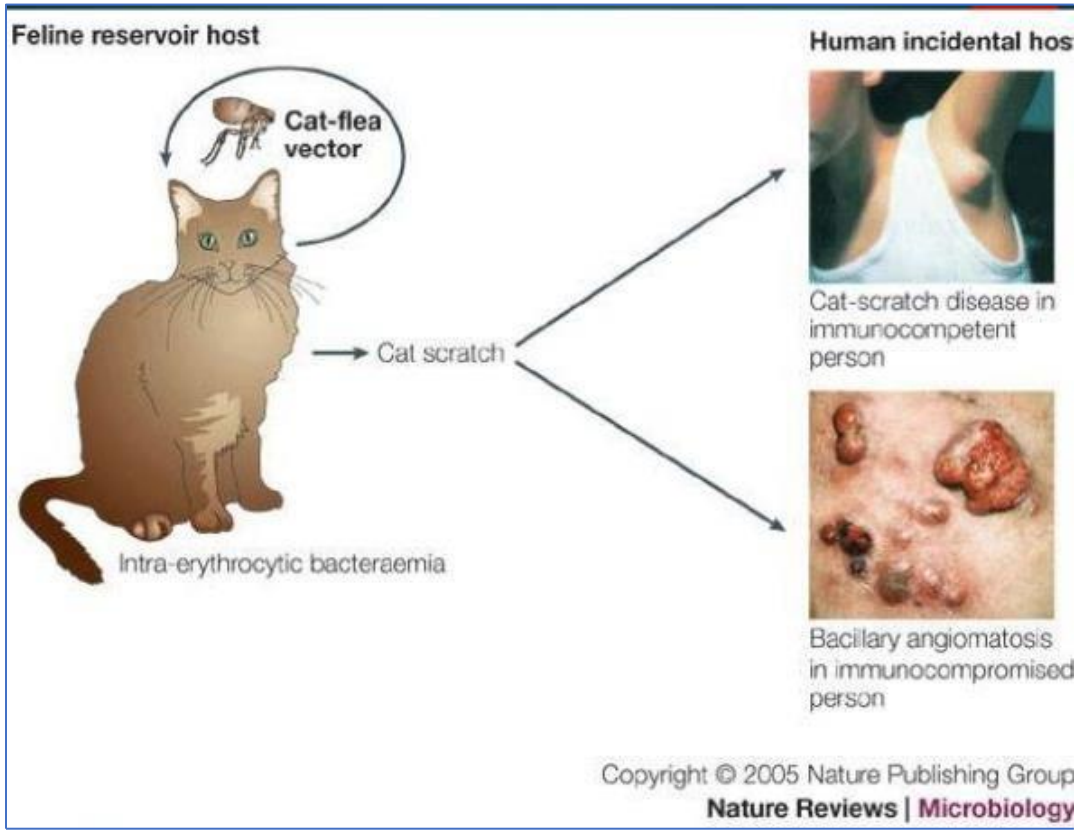
Bartonella

- *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**



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. It is not a risk disease unless the patient is immunocompromised. They are isolated from 50% from dog bites and 50% from cat bites so you should keep it in mind
- **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:

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