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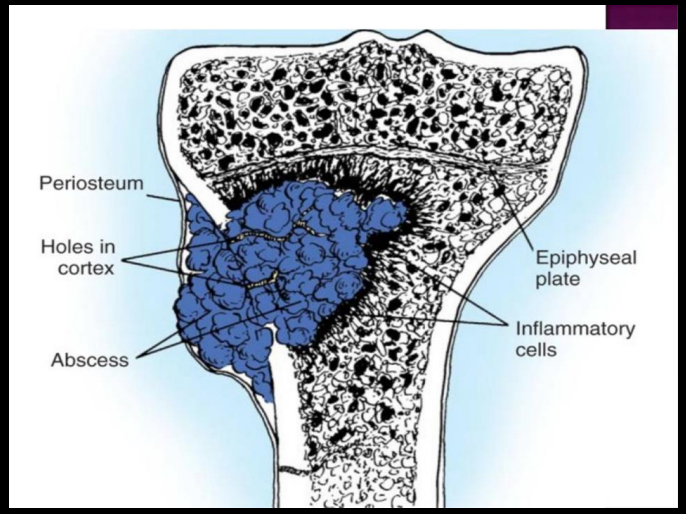


- Predispoding Factors for osteomyelitis

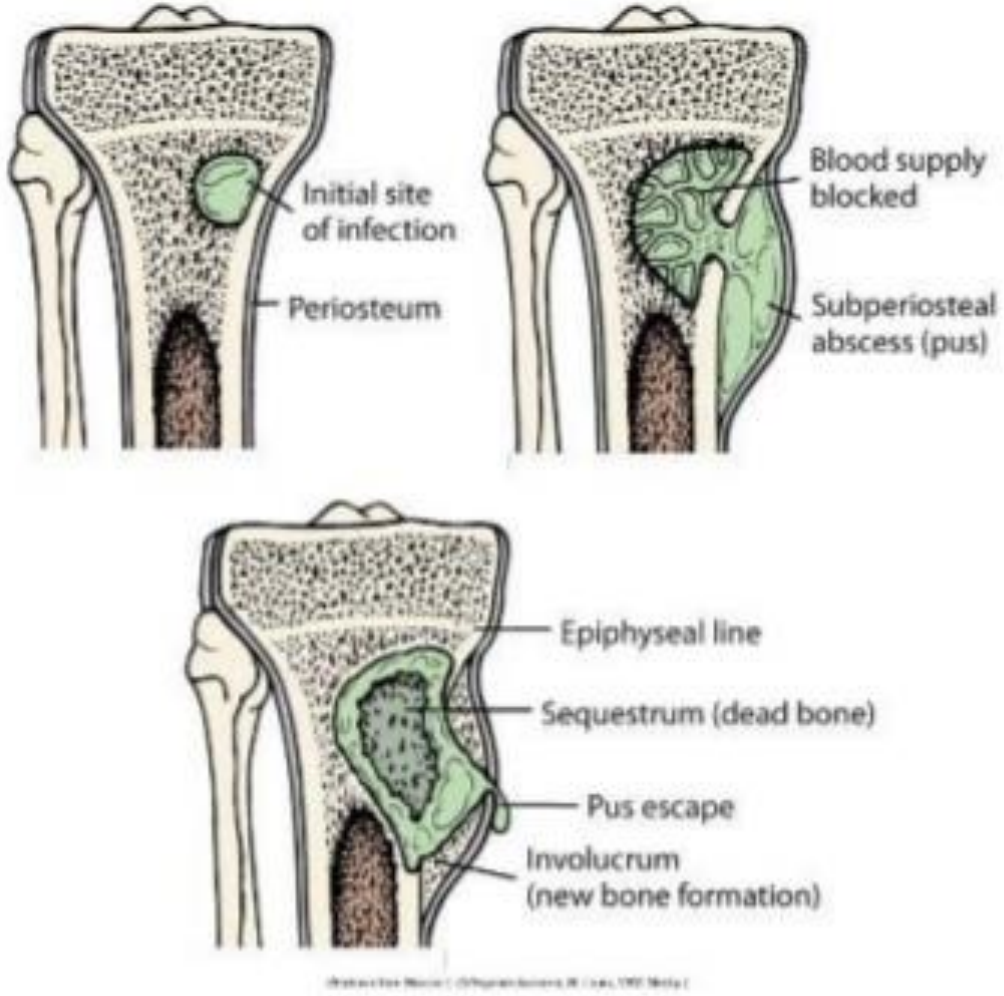
Osteomyelitis

- Nelaton (1834) : coined osteomyelitis
- The root words *osteon* (bone) and *myelo* (marrow) are combined with *itis* (inflammation) to define the clinical state in which bone is infected with microorganisms.

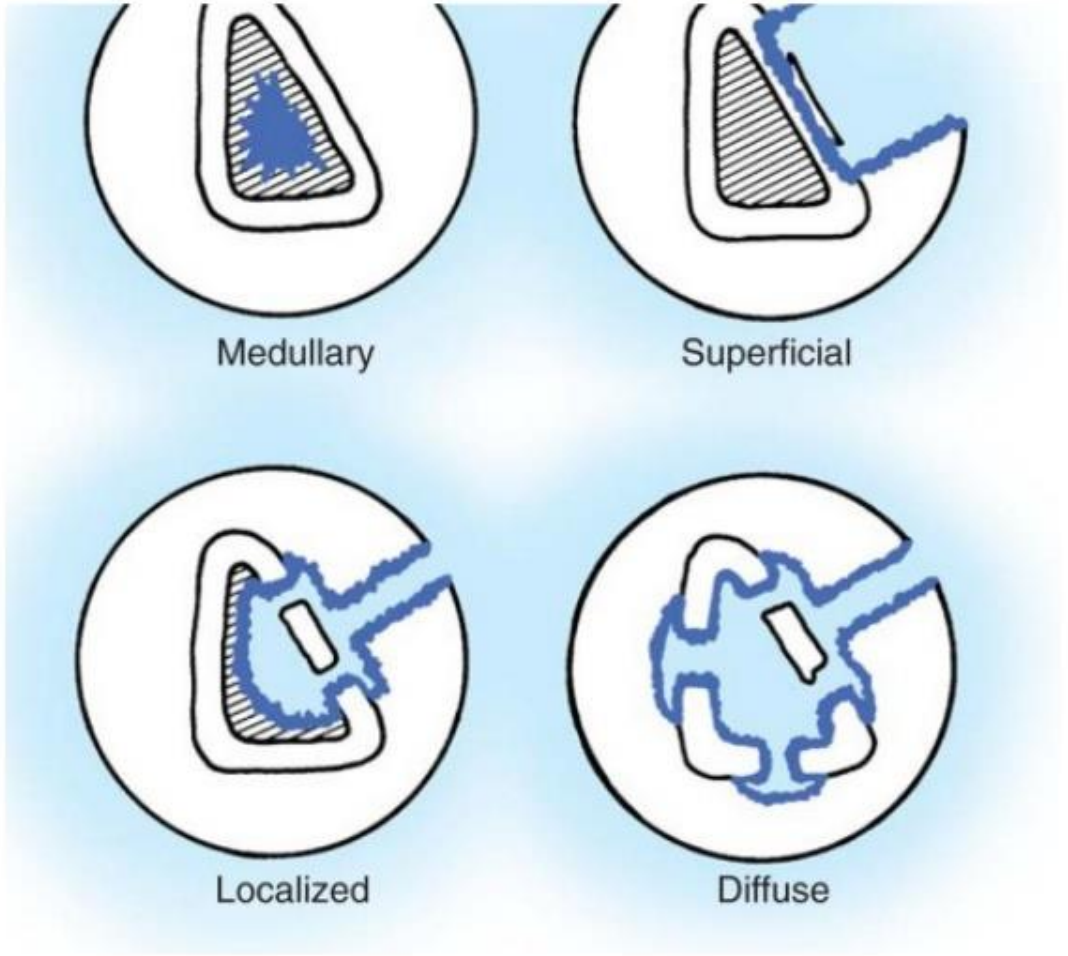
What is osteomyelitis?

- **Osteomyelitis** is a progressive infection of bone or bone marrow, and Surrounding soft tissue usually caused by **pyogenic bacteria**.
- (most common in staphylococcus aureus)
- It can be usefully subclassified on the basis of the causative organism, the route, duration and anatomic location of the infection.
- Infection is more common in the long bones and vertebras, but it can affect any bone in the body.

Development of Osteomyelitis



ANATOMICAL CLASSIFICATION



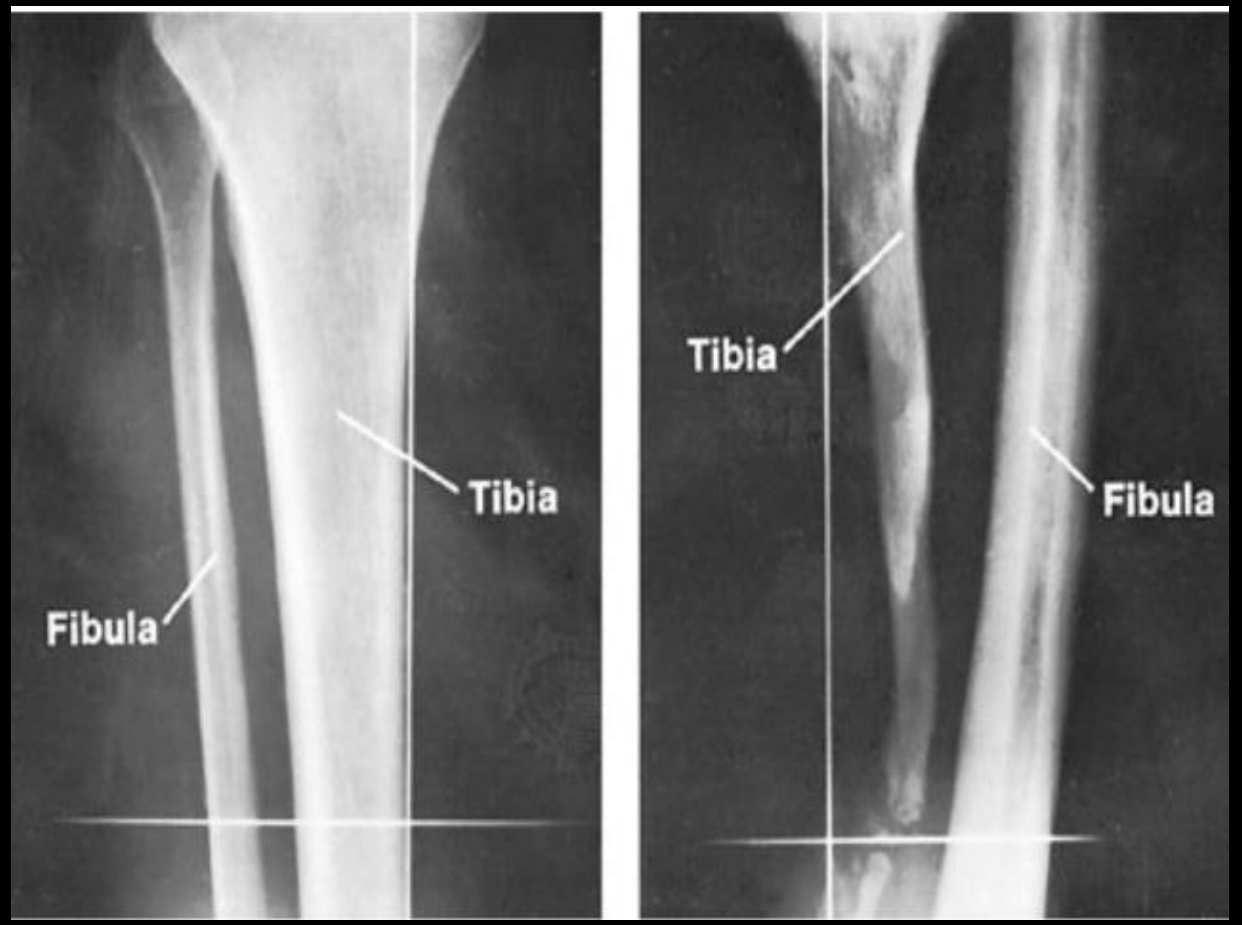
How Common Is Osteomyelitis?

- Chronic osteomyelitis occurs in about 2 in 10,000 adults.
- Children have the acute form of the disease more often than adults do, at a rate of about 1 in 5,000

Classification of Osteomyelitis

- **Pathogenesis**
  - Hematogenous (most common cause in kids)
    - In children: tubular bones
    - In adults: spine, pelvis and small bones
  - Spread from adjacent soft tissue infection
    - Ex: ulcers, diabetic foot ulcers
  - Direct inoculation
    - Ex: Trauma or surgery
- **Chronicity**
  - Acute
  - Subacute
  - Chronic

Progression to subacute or chronic disease depends on timing of dx and tx, comorbid conditions, immune status etc.


Tibia
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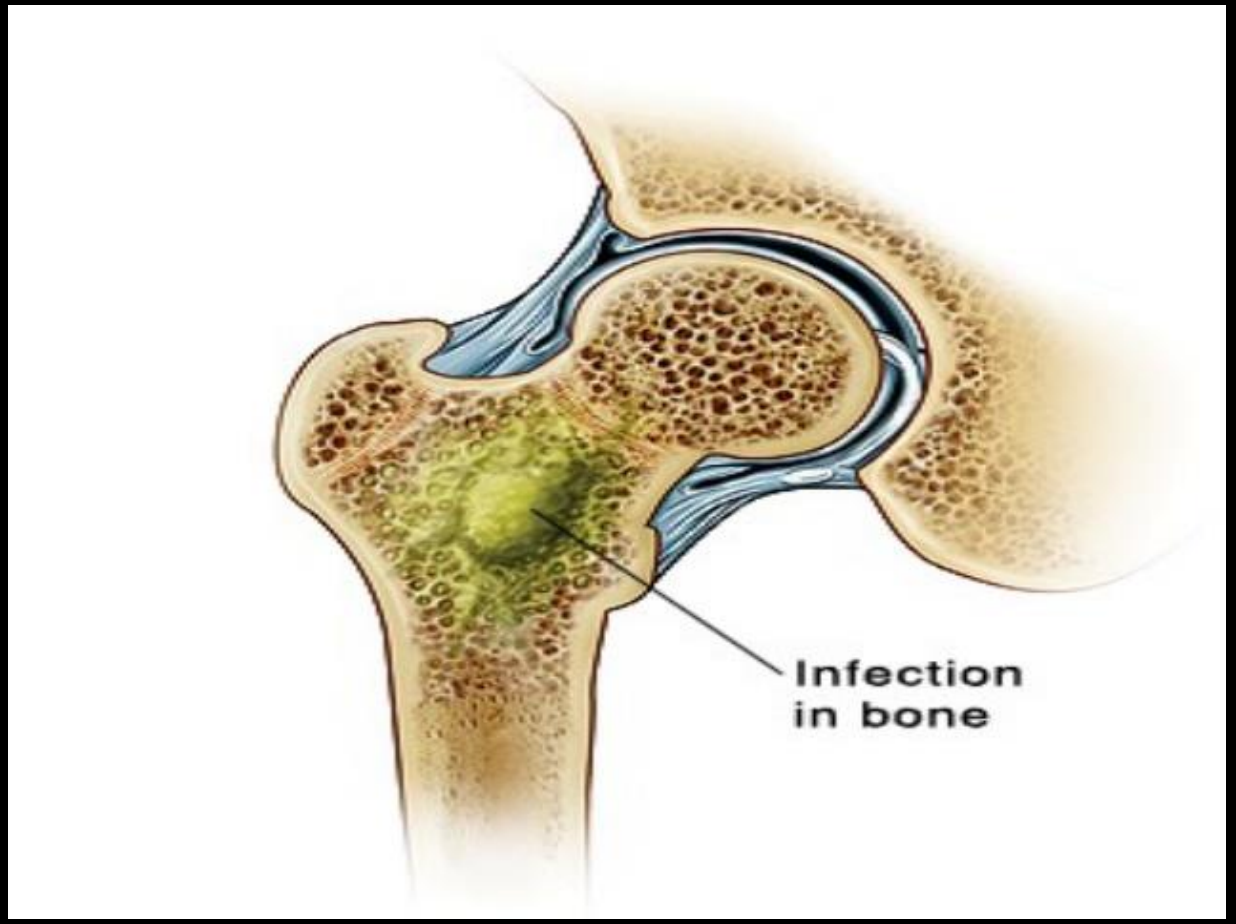
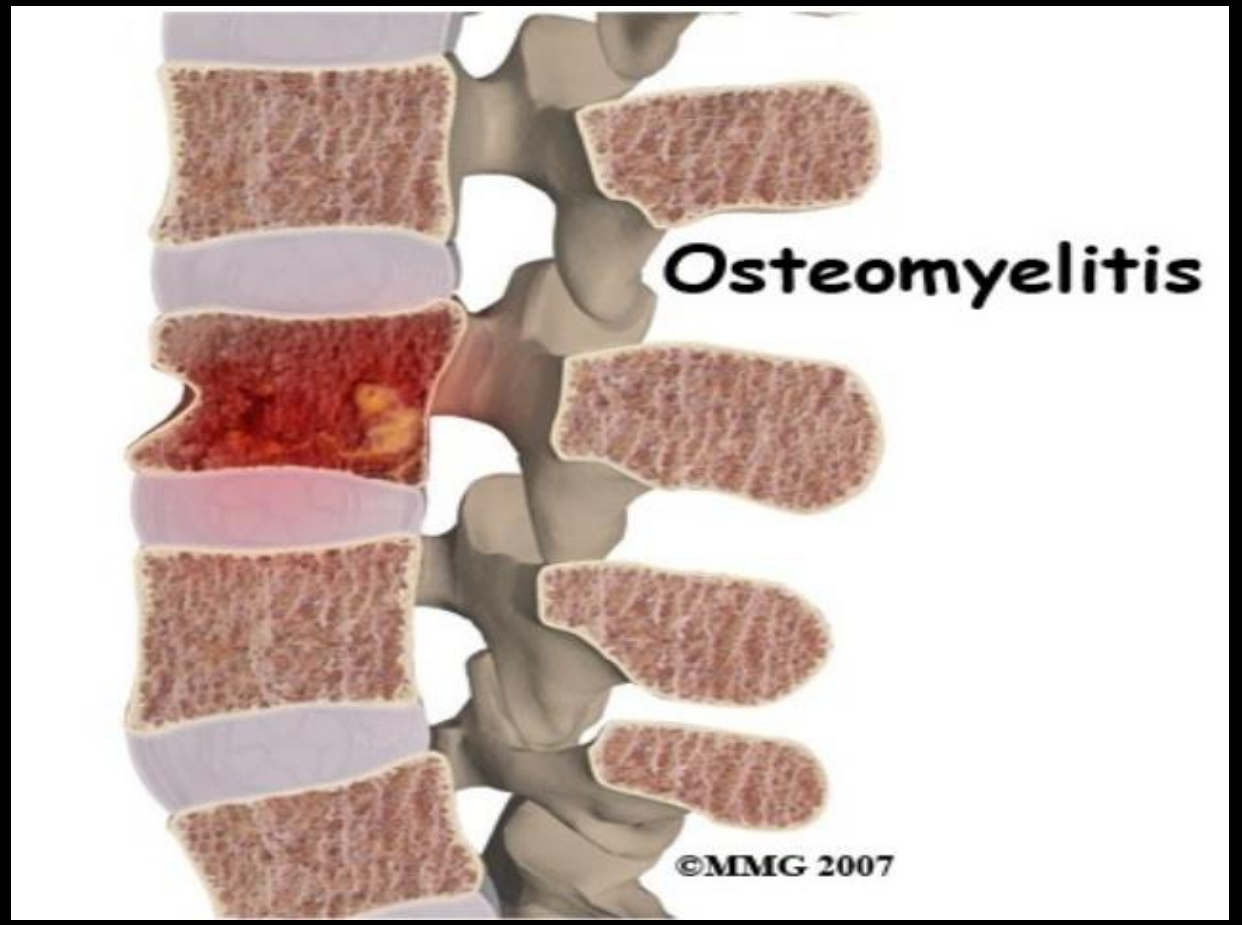

Infection
in bone


Osteomyelitis
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Acute Osteo

- Begins with marrow edema, cellular infiltration and vascular engorgement
- May progress to necrosis and abscess formation
- Spread within the intramedullary cavity → extension through cortex by Havers and Volkman's canals → subperiosteal space → periosteum → soft tissues
- Rupture of joint space → septic arthritis

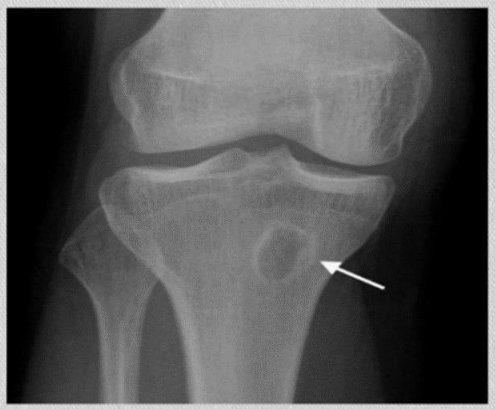
Sub-Acute Osteo

- Occurs in abnormal bone or after inadequate antibiotics
- Localized pyogenic process
- Commonly appears as a well-defined osteolytic metaphyseal lesion (Brodie's abscess) with a sclerotic margin that fades peripherally (fuzzy sclerotic margin)
- S. aureus is most common pathogen

Chronic Osteo

- Occurs after inadequate tx or in pts with altered immunity
- Distinguishing feature is necrotic bone surrounded by granulation tissue
- Interruption of blood supply → necrosis → devitalized bone fragments (sequestra)
- A thick sheath of new periosteal bone can develop around the sequestra (involucrum)
- Fistula tract formation
- Sharp interface between normal and diseased marrow

- Most common sites of indirect entry in children
  - Distal femur
  - Proximal tibia
  - Humerus
  - Radius
- Most common sites of indirect entry in adults are Vascular-rich bone sites
  - Pelvis
  - Tibia
  - Vertebrae



Pathophysiology of Osteomyelitis

- Generally, microorganisms may infect bone through one or more of three basic methods:
- 1. Via the bloodstream.
- 2. Penetrating (trauma).
- 3. Internal fixation of fractures.

PATHOPHYSIOLOGY

Microorganisms enter bone (Phagocytosis).

↓

Phagocyte contains the infection

↓

Release enzymes

↓

Lyse bone

PATHOPHYSIOLOGY

- Bacteria escape host defenses by:

- ✓Adhering tightly to damage bone
- ✓Persisting in osteoblasts
- ✓Protective polysaccharide-rich biofilm

PATHOPHYSIOLOGY

Pus spreads into vascular channels

↓

Raising intraosseous pressure

↓

Impairing blood flow

↓

Chronic ischemic necrosis

↓

Separation of large devascularized fragment

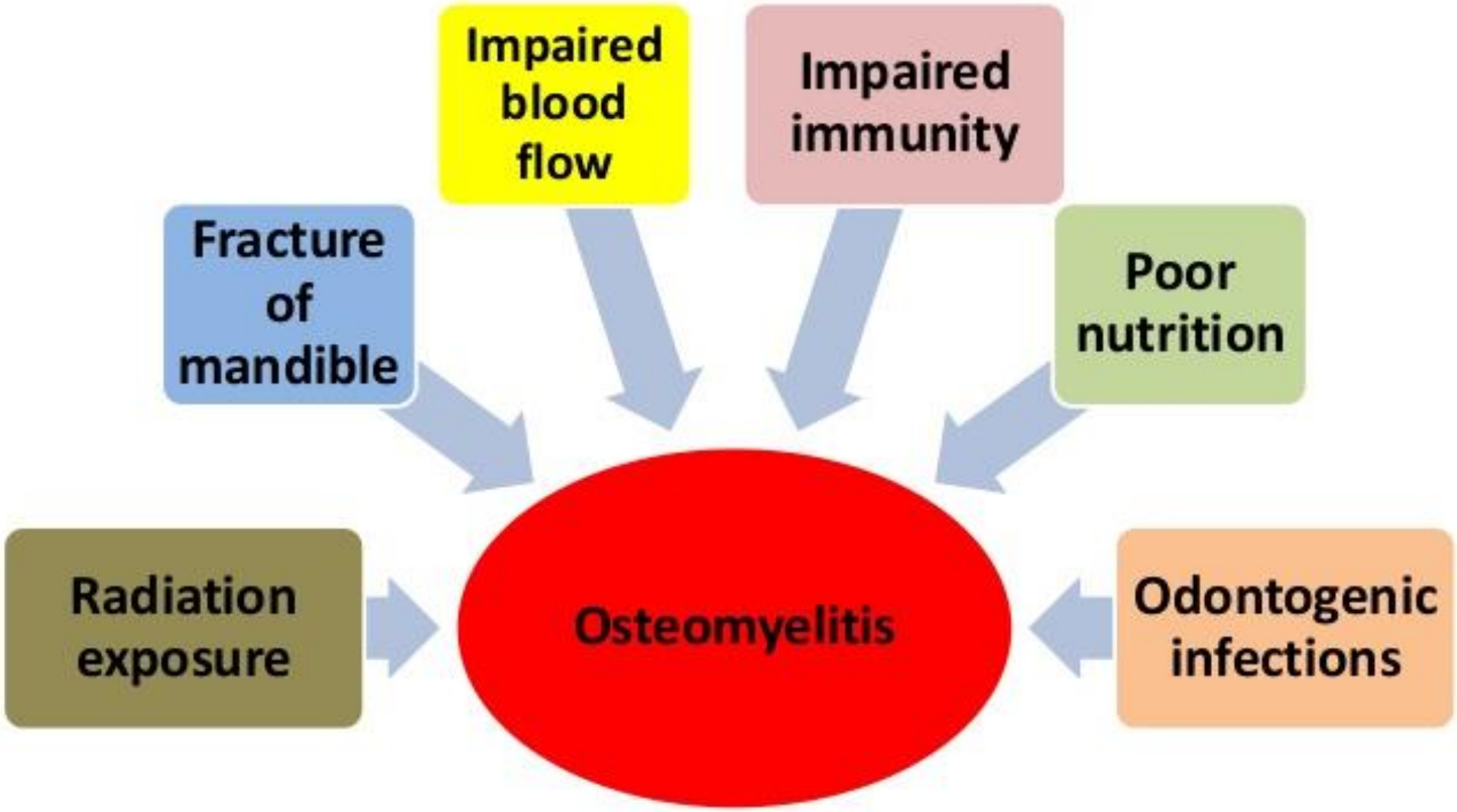
(Sequestra)

New bone formation

(involucrum)

Often, the body will try to create new bone around the area of necrosis.

Predisposing factors



Pathogenesis:

- *Host Factors*

TABLE II Systemic or Local Factors That Affect Immune Surveillance, Metabolism, and Local Vascularity

Systemic (Bs)	Local (Bl)
Malnutrition	Chronic lymphedema
Renal, hepatic failure	Venous stasis
Diabetes mellitus	Major vessel compromise
Chronic hypoxia	Arteritis
Immune disease	Extensive scarring
Malignancy	Radiation fibrosis
Extremes of age	Small vessel disease
Immunosuppression or immune deficiency	Neuropathy
Asplenia	
HIV/AIDS	
Ethanol and/or tobacco abuse	

Risk factors

An approach that is useful in classifying the risk factors for the development of acute osteomyelitis is the same as one commonly employed to discuss the mechanisms responsible for pathogenesis:

- hematogenous dissemination,
- direct inoculation, and
- contiguous spread from an adjacent area of soft tissue infection

Acute hematogenous osteomyelitis is predominantly a disease of children.

Factors that favor the development of acute bone infection are those that predispose to bacteremia.

These include

- indwelling intravascular catheters,
- distant foci of infection, and
- intravenous drug abuse

- The distant sites of focal infection that are most commonly associated with acute osteomyelitis include
- the skin as well as
- urinary and respiratory tracts.

- Two patient groups with an usual susceptibility to acute skeletal infections are those with sickle cell anemia and chronic granulomatous disease.

The second major mechanism for the development of acute osteomyelitis is by direct inoculation.

Injuries due to penetrating bites and puncture wounds of the food may serve to infect bone directly.

Diagnostic procedures (lumbar puncture, fetal monitoring electrodes, suprapubic aspiration, and heel sticks) may result inadvertently in the inoculation of a neighboring osseous structure.

Surgical procedures such as internal fixation of long bone fractures and skeletal traction may cause an infection of the bone.

Osteomyelitis may develop as a consequence of contiguous spread of infection from adjacent soft tissue, particularly if vascular insufficiency complicates the clinical picture.

Infection of the mandible, maxilla, and frontal or mastoid bones may result from persistent or neglected infection of the teeth, paranasal sinuses, or middle ear cavity, respectively.

The major risk factor for chronic infection of bone is inadequate or delayed management of acute osteomyelitis or completely unrecognized bone infection

Why are dialysis patients more susceptible to infections?

1. Impaired host immunity

2. Bacterial virulence and adherence properties

3. Dialysis procedure

Impaired host immunity

•Impaired neutrophil function:

Impaired neutrophil chemotaxis, phagocytic capacity, oxidative metabolism, and intracellular bacterial killing, as well as dysregulated apoptosis have been demonstrated.

•Several uremic retention solutes can affect neutrophil function adversely.

•These include parathyroid hormone, p-cresol, polyamines, aminoguanidine products, and complement factor D.

•In addition, repeated exposure of neutrophils to bio-incompatible, complement-activating dialyzer membranes can lead to transient leukopenia, increased expression of adhesion molecules, degranulation, and release of proteolytic enzymes.

•These interactions might lead to decreased responsiveness to subsequent stimuli, such as bacteremia.

Impaired host immunity

•Alterations in cell-mediated immunity:

Other abnormalities involve cell-mediated immunity due to alterations in T-lymphocyte function.

These include lymphopenia, impaired delayed skin reactivity, dysregulated cytokine synthesis, and impaired macrophage Fc receptor function.

Alterations in B-lymphocyte function affect humoral immunity and result in decreased immunoglobulin levels and a diminished antibody response to microbial antigens.

Impaired host immunity

Iron overload:

Several in vitro and clinical studies have linked iron overload to an increased risk of bacterial infections in HD patients.

Iron overload has been associated with reduced phagocytic function and impaired bacterial killing.

Increased availability of free iron can also stimulate bacterial growth and enhance virulence properties.

Therefore, it has been proposed that increased use of parenteral iron preparations may contribute to the incidence of bacterial infections.

Impaired host immunity

Uremia causes a state of acquired immune deficiency

Bacterial virulence and adherence properties

- Virulence genes:

Under conditions of high bacterial density, bacteria produce extracellular polysaccharides which interact with transcriptional activators leading to increased expression of virulence genes.

These virulence genes facilitate bacterial survival and promote resistance to killing by neutrophils as well as the bactericidal or bacteriostatic effects of antimicrobial agents.

Bacterial virulence and adherence properties

Bacterial biofilm:

These extracellular polysaccharides also form a “slime” or biofilm in the presence of foreign surfaces such as central venous catheters.

The biofilm renders the bacteria less susceptible to antimicrobial agents as it constitutes a barrier between the antimicrobial agent and the bacterial cell wall.

Biofilm formation can potentiate the pathogenicity of skin bacterial flora such as coagulase-negative staphylococci.

Bacterial virulence and adherence properties

Adherence properties of bacteria:

S. aureus commonly adheres to host proteins such as fibronectin commonly present on catheters.

Other bacteria, such as coagulase-negative staphylococci directly adhere to polymer surface.

Catheters made of polyvinylchloride or polyethylene are less resistant to the adherence of bacteria compared with catheters made of polytetrafluoroethylene, silicone elastomer, or polyurethane.

Dialysis procedure

- Access Related
- Equipment
- Dialyzer Reuse

Dialysis procedure

- Access Related

The access site is related to well over 50% of bacteremias in hemodialysis patients. The incidence of bacteremia is far greater in patients with tunneled, cuffed, double-lumen catheters than among those with fistulas or synthetic AV grafts. Following improvements in design, the frequency of catheter-related bacteremia is significantly less in patients with tunneled versus non-tunneled catheters.

Peri-catheter thrombus increases the risk of infection

Heparin use to preserve catheter patency induces biofilm formation and increased incidence of catheter-related blood stream infection as compared to r-TPA.

Use of Buttonhole technique: The buttonhole technique to cannulate AV fistulae has gained popularity over the last decade in the United States. However, increased fistula infection rates have been reported with use of this technique, particularly in patients who self-cannulate their fistulas.

Dialysis procedureEquipment

- Water supply
- Surface water as opposed to ground water contains higher levels of endotoxin, bacteria and other organisms. Disinfectants such as chlorine chloramines reduce the numbers but do not eliminate bacteria in municipal water.

- Water treatment.
- The Association for the Advancement of Medical Instrumentation (AAMI) has published guidelines for the chemical and bacteriologic quality of water used to prepare dialysis fluid.

Some components of the water treatment system may allow amplification of water bacteria. For example, ion exchangers such as water softeners and deionizers do not remove endotoxins or bacteria and may provide sites for significant bacterial multiplication.

•Equipment Water

•Distribution

Defects in the delivery system of water following treatment to the dialysis machine may result in bacterial proliferation.

These include length and diameter of the distribution pipes, material the pipes are made of and inadequate cleansing and disinfection of storage tanks.

These factors may lead to the formation of bacterial biofilms in the distribution system.

- Dialyzer Reuse.

When there is a breakdown in the procedures that are to be followed during the reprocessing of dialyzers, pyrogenic reactions or overt bacterial infections can occur.

Pathophysiology of Osteomyelitis in Diabetic Patients Bone and joint infections have been classified

into three groups:

hematogenous osteomyelitis,

direct infections resulting from traumatic inoculation of bacteria or from local spread of infection from a contiguous source,

and infections in patients with diabetes who have neuropathic and vascular complications

Waldvogel et all

The pathophysiology of infection in the diabetic foot is complex and often creates a conundrum for the physician.

Vascular disease, immunopathy, and neuropathy place the diabetic population at substantial risk.

The incidence of vascular disease is at least four times more prevalent in the diabetic patient than in individuals without the disease, and it increases with the patient's age and duration of diabetes

In this patient group, a predilection for occlusion of the tibial and peroneal arteries between the knee and the ankle exists.

The dorsalis pedis foot arteries are usually spared.

Occlusive “small vessel disease” is a misnomer; microvascular “dysfunction” exists due to endothelial injury and thickening of the capillary basement membranes and supports an aggressive approach to foot revascularization in ischemic patients.

Diabetics have a higher predilection for developing serious infections due to secondary immunodeficiency disease

Recent data implicate neuropathy, not vasculopathy, as the most important contributing factor to these infections.

More than 80% of diabetics with pedal disease have some form of diabetic neuropathy

In general, the pathogenesis of neuropathy is ascribed to abnormalities in sorbitol pathways

Three types of neuropathy are seen in the diabetic population:

- sensory,
- motor, and
- autonomic.

Sensory neuropathy decreases sensation to trauma and thermal injury, leading to ulceration.

Motor neuropathy causes muscular atrophy, weakness, and paresis resulting in deformity and anterior displacement of the plantar fat pads.

Changes in the intrinsic muscles lead to the classic “intrinsic-minus” foot.

Autonomic neuropathy leads to dry, cracked skin caused by a decrease in sweating, as well as callus.

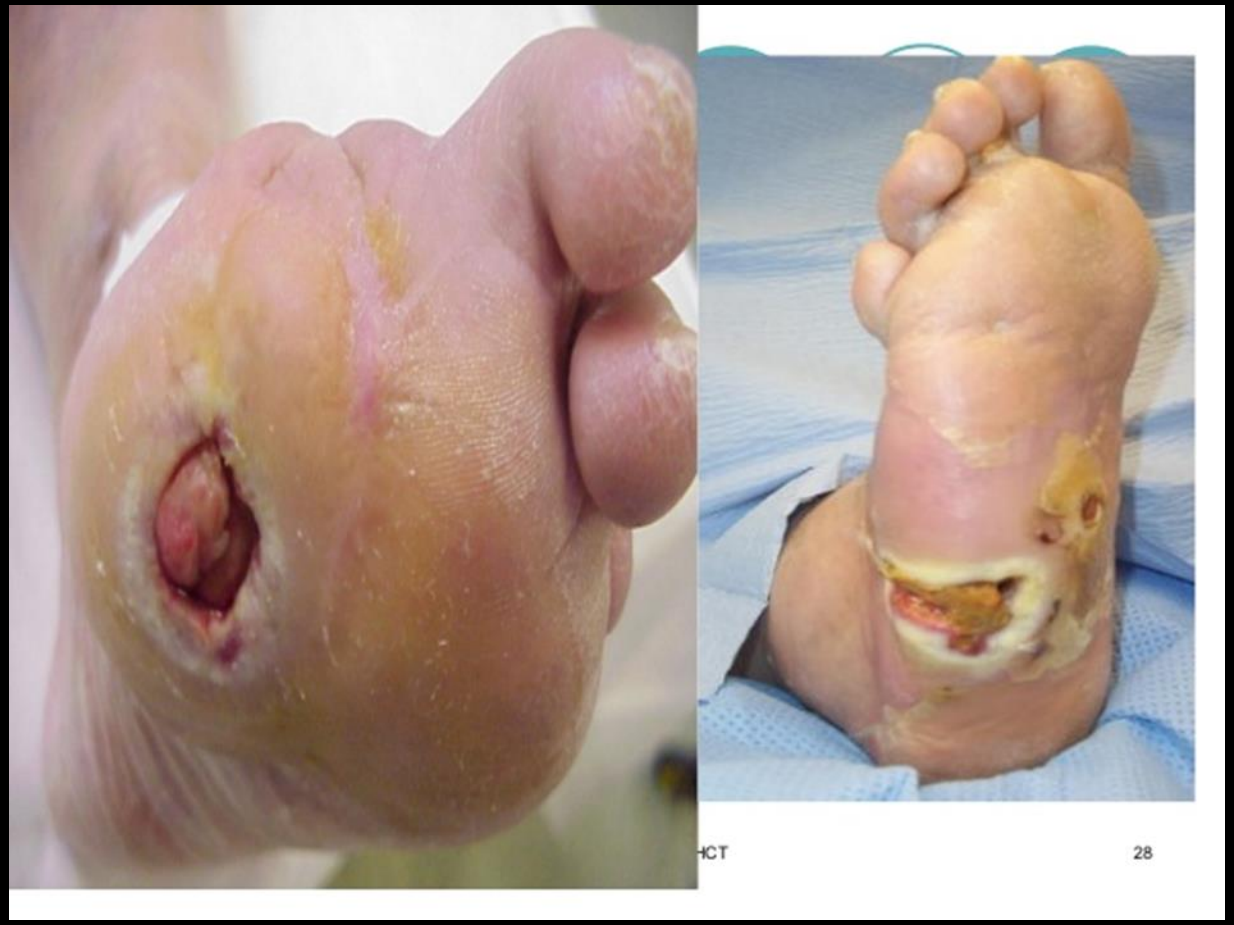
Callus is also associated with sensory neuropathy and biomechanical factors.

The repetitive traumas of walking and increased shear stress create apparent thinning of the skin at the metatarsal heads and the heel.

Thinning of the skin typically refers to the subcutaneous tissue, but also can occur in any structure that contains collagen.

Clearly, these neurological manifestations increase the susceptibility to infection.

Once infection is present in the soft tissues, a contiguous extension to bone (osteomyelitis) can result



- Malnutrition and Infection

Malnutrition increases risk of infection.

PEM is a common cause of secondary immune deficiency and susceptibility to infection in humans.

This causal relationship is further supported by animal studies.

This immunodeficiency represents a key factor in susceptibility to infections and has therefore been termed

nutritionally acquired immunodeficiency syndrome

- In severely malnourished patients, both acquired immunity—i.e., lymphocyte functions—as well as innate host defense mechanisms—i.e., macrophages and granulocytes—are affected.

- Diminished immune functions render undernourished patients more susceptible to infections, notably those by opportunistic pathogens

Joint complications have been a well recognized finding in patients with primary immunodeficiencies for many years

In humoral immunodeficiencies such as common variable immunodeficiency and X-linked agammaglobulinemia, bacterial organisms are the most common causes of infectious arthritis, but mycoplasmas and ureaplasmas are also of particular importance

Table 1
Organisms common in osteoarticular infections in immunodeficient patients

Antibody deficiencies	*Staphylococcus aureus*[a]
X-linked agammaglobulinemia	*Streptococcus pneumoniae*[a]
Common variable immune deficiency	*Haemophilus influenzae*[a]
IgG subclass defects	*Mycoplasma*[a]
	Ureaplasma[a]
	Echovirus[a]
Chronic granulomatous disease	*Staphylococcus aureus*
	Aspergillus[a]
	Burkholderia spp
	Serratia spp[a]
	Candida spp
	Salmonella
	Escherichia coli
Interleukin-1 receptor-associated kinase-4 deficiency	*Staphylococcus aureus*
	Streptococcus pneumoniae[a]

For somewhat unclear reasons,

- the majority of infectious complications that involve the joints in immune deficiency are due to defects of antibody production.
- Humoral immunity is characterized by antibody production against a variety of extracellular microbes that is necessary for their neutralization and elimination.

- Although patients with primary antibody deficiencies are most susceptible to recurrent infections of the sinopulmonary tract, other infections also occur, including meningitis, osteomyelitis, cellulitis, conjunctivitis, hepatitis, and gastroenteritis

- Compared with other congenital immune defects,

bone and joint infections are seen more commonly in patients with

- common variable immunodeficiency (CVID) and
- X-linked agammaglobulinemia (XLA)

Ethanol abused and osteomyelitis

Excessive alcohol consumption predisposes the host to wide range of infections particularly pulmonary infection.

In maxillofacial region osteomyelitis of mandible is reported as complication after routine dental extraction in alcoholics.

An overwhelming amount of evidence from human and animal studies in-vivo and vitro suggest that
alcohol is a potent modulator of immune system at various levels

- Impaired host defense after alcohol consumption

appears to be linked to a combination of :

a) Decreased inflammatory response

b) Altered cytokine production

c) Abnormal reactive oxygen intermediate generation

Cellular immunity particularly antigen specific immune response is impaired by both acute and chronic alcohol use.

In chronic alcoholics vitamin deficiency, malnutrition and advance liver cirrhosis can also contribute to some immune abnormalities

In chronic alcoholic there is defective chemotactic activity due to serum inhibitors.

Defective chemotaxis may explain increased susceptibility to infections.

In addition, in patients with chronic alcoholic hepatitis and cirrhosis there is defective serum bactericidal activity and neutrophil function abnormalities.


Ευχαριστώ για την προσοχή σας
THE END