MICROBIOLOGY OF BONE AND JOINT INFECTIONS

1. The RED color for the important points.
2. The GREEN color for the points in which the doctor said but didn't write in the slides.
3. The BLUE color for explanation only.
4. The ORANGE color is for VERY IMPORTANT points.

► Bone & joint infections may exist separately or together.
► both are more common in infants and children.
► Usually caused by blood borne spread, but can result from local trauma or spread from contiguous soft tissue infection.
► often associated with foreign body at the primary wound site.
► if not treated lead to devastating effect.
► The most common organism (generally) is **Staphylococcus aureus**. (Very important!)

Acute Osteomyelitis

Acute infection of the bone and bone marrow (usually less than 3 weeks). The pathogen may reach the bone through:

1. Hematogenous route. (spread from the blood infection; bacteremia or septicemia)
2. Contiguous soft tissue focus (post operative infection, contaminated open fracture, soft tissue infection, puncture wounds).
3. In association with peripheral vascular disease (diabetes mellitus ,severe atherosclerosis, vasculitis)

❖ It might be of short duration (2days) for hematogenous spread or it may last for several weeks if secondary contiguous infection wound persist

◘ **Etiology, Epidemiology & Risk Factors:**

► Infants: **S.aureus**, group B streptococci, E.coli.
► Children: **S.aureus**, group A streptococci, H.influenzae type B, children from 3 months to 3 years are susceptible, hip vaccine is very effective against it. H. Inf. Can go to the joint, bone, epiglottis and meninges.
► Adults: Hematogenous cases less common, but may occur due to reactivation of a quiescent focus of infection from infancy or childhood. Most cases due to **S.aureus** (may be accompanied by septic arthritis)

◘ **Site of infection:** Metaphysis of long bones (femur, tibia, humerus)
Vertebral Osteomyelitis can occur in adults secondary to a Urinary Tract Infection or prostatitis.

◘ The Candida fungal infection is not a common cause of osteomyelitis but it can be seen in patients having infected central venous catheters

◘ **What are the bacteria that cause osteomyelitis due to contiguous infection of the nearby tissue? (Related to primary focus)**
It can be gram positive cocci: Staph or strept, Gram negative bacilli: E.coli, anaerobes: bacteroides or poly-microbial (more than one organism)

◘ **Special clinical situations:**

1. Coagulas -negative staphylococci, Propionebacterium (normal flora), and S.aureus in foreign body infections (eg.Prosthesis).

2. **Salmonella in sickle cell patients.**
3. Eikenella, Pasturella multocida in human/ animal bites.
4. Enterobacteriacea and Pseudomonas in nosocomial (hospitals) infections and IV drug use.
5. Mycobacterium Tuberculosis (MTB) in AIDS patients

◘ **Patient Presentation:**

- Systemic manifestations occur in less than 50% of patients.
- Acute onset of bone pain and fever with rigors and diaphoresis.
- Symptoms usually of less than 3 weeks duration
- Local signs: soft tissue swelling, erythema (redness), warmth, point tenderness, percussion tenderness over the vertebral body & limited mobility of the involved extremity (five cardinal signs).

◘ **Differential diagnosis:**

- Primary and metastatic bone malignancies.
- Trauma.
- Acute rheumatic arthritis.
- Hemarthrosis.
- Ewing sarcoma.
- Vertebral compression fracture.

◘ **Diagnosis:**

- Blood culture
- Blood culture or aspiration of overlying abscess if blood cultures are negative
- Leucocytosis may or may not occur
- Erythrocyte sedimentation rate (ESR) elevated, but could be normal as well.

The golden standard for the diagnosis of any bacterial infection is the isolation of the causative organism.

◘ **Imaging:**

1. X-ray. (evidence may not be shown in early disease)
2. MRI (highly sensitive & specific): preferred for vertebral osteomyelitis
3. CT scan used as alternative of MRI.(shows early evidence; within 3 days of onset)
4. Technetium bone scans.

◘ **Treatment and Management:**

1. **Appropriate antimicrobial therapy:** (2-4) weeks parenteral (by injections) followed by oral therapy for a total of 6 weeks.
    a. **MSSA [methicillin sensitive staph aureus]:** Nafcillin followed by oral Flocloxacillin (better absorbed), Dicloxacillin or Clindamycin, fucidic acid.
    b. **MRSA [methicillin resistant staph aureus]:** Vancomycin followed by Clindamycin, Linezolid, or TMP-SMX.
    c. Polymicrobial infection: Ampicillin-Sulbactam, Piperacillin-Tazobactam or Quinolone with Metronidazole.
    d. Staphylococcus epidermidis: Vancomycin
    e. Other gram negative bacilli: Quinolones
    f. Anaerobes: Metronidazole or Clindamycin
2. **Surgery:** for neurological complications, paravertebral abscess & hip joint involvement.

◘ **Prognosis & Complications:**

- Early diagnosis and antibiotic treatment produce optimal results.
- Inadequate therapy results in relapse and chronic disease.
- **Complications:** septicemia, metastatic abscesses, septic arthritis, chronic osteomyelitis, loss of limb ,or paravertebral abscess.

- Monthly ESR for 3 months and at 6 months useful to document treatment.
- Cases due to contiguous source more difficult to eradicate. Relapse common (50%), surgery indicated.

Chronic Osteomyelitis

- A chronic infection of the bone and bone marrow usually secondary to inadequately treated or relapse of acute Osteomyelitis. Most infections are secondary to a contiguous focus (e.g. contaminated open fracture) or peripheral vascular disease.
- Management difficult, prognosis poor.
- Infection may not completely cure.
- Brucella and TB are contagious (hematogenous).
- May recur many years, decades, after initial episode.
- chronic infection due hematological spread is rare.
- TB and fungal Osteomyelitis clinically have indolent "chronic" course and maybe seen in Immunocompromised pt..

◘ General risk factors:

- Penetrating trauma
- Prosthetic devices
- Animal bites
- IV drug use

◘ Host risk factors:

- Peripheral vascular disease
- Peripheral neuropathy
- Sickle cell disease, diabetes mellitus & immunocompromised states.

Extent of disease and outcome depends on general nutritional status of involved tissues, degree of bone necrosis, virulence of pathogen.

- **Most common organism:** Staphylococcus aureus.
- **Other microorganisms:** S.epidermidis,enterococci,streptococci,Enterobactericae,Pseudomonas, Acinetobacter spp., anaerobes (Bacteroides, anaerobic streptococci, Clostridium)
- **Polymicrobial infection common:** with decubitus ulcers and diabetic foot infections.
- **MTB osteomyelitis primarily results from hematogenous spread from lung foci or as an extension from a caseating lymph bone (50% in spine, it resembles Brucella Osteomyelitis).** (Very Important!)
- Hematogenous osteomyelitis due to fungi eg. Candida spp., Histoplasma capsulatum, Aspergillus spp. and other fungi may occur.
- In Saudi Arabia, the most common diseases are MTB osteomyelitis and Brucella osteomyelitis.

◘ Patient presentation:

- Sinus tract, persistent wound drainage or a chronic non-healing ulcer are common presentations.
- Overlying skin may be scarred and adherent to the involved bone.
- Acute symptoms and systemic manifestations are uncommon.
- Local signs may be absent except during acute exacerbation.

◘ Diagnosis:

- Blood culture not very helpful- because bacteremia is rare.
- WBC normal, ESR elevated but not specific.

- Radiologic changes complicated by the presence of bony abnormalities
- MRI helpful for diagnosis and evaluation of extent of disease.
- Wound/sinus culture is not reliable because it is usually contaminated by skin flora
- The definite microbiological diagnosis is by culture of bone biopsy

◘ **Treatment:**

- Extensive surgical debridement with antibiotic therapy. Parenteral antibiotics for 3-6 weeks followed by long term oral suppressive therapy.
- MSSA: Cloxacillin
- MRSA and S.epidermidis: Vancomycin then oral Clindamycin
- TB treatment: 4 Drugs: INH, RIF, Pyrazinamide and Ethambutol(We will study them in the Respiratory block).
- Brucella is treated with Tetracycline and Rifampicin for 2-3 months.

Arthritis

Infectious Arthritis is inflammation of the joint space secondary to infection. Generally monoarthritis (affects a single joint) and result in suppurative inflammation. Poltarthritis is rare (affects more than one joint).

- Hematogenous seeding of joint is most common. (hematogenous : spread by blood)
- Pain, swelling, limitation of movement common symptoms (similar to Osteomyelitis).
- Diagnosis by **Arthrocentesis** to obtain synovial fluid for analysis, this synovial fluid is used to do Gram stain, culture, sensitivity test and blood culture. **(Using a syringe to collect synovial fluid from a joint capsule.)**
- Drainage (via arthrocentesis) and antimicrobial therapy important management. (antibiotics alone are not enough, drainage is a must)

◘ **Gonococcal arthritis: most common cause in young, sexually active** adults caused by Neisseria gonorrheae leads to disseminated infection secondary to urethritis/cervicitis. Initially present with polyarthralgia, tenosynovitis, fever,skin lesions. If untreated leads to suppurative monoarthritis.

Patient presentation:

1. **Early disease**: fever, rash, tenosynovitis (especially of hands, wrists), polyarthralgia resulting from non-suppurative arthritis.
2. **Late disease**: monoarticular, suppurative arthritis.

◘ **Nongonococcal arthritis:** occurs in older adults. It results from the introduction of organisms into joint space as a result of bacteremia or fungemia from infection at other body sites.

- Occasionally results from direct trauma, procedures (arthroscopy) or from contiguous soft tissue infection.
- **S.aureus is most common cause.** Other organisms: streptococci and aerobic Gram negative bacilli.
- In sickle cell disease and like osteomyelitis it is caused by salmonella species.
- In children less than 3 -4 years invasive Haemophilus influenzae causes arthritis and osteomyelitis.
- Chronic arthritis may be due to MTB, Brucella or fungi.
- Lyme disease in endemic areas like in USA and Scandinavia, it's uncommon in KSA.

Risk factors:

Age, diabetes, immunosuppression, IV drug use, CV catheters, prior joint damage (rheumatoid arthritis) or procedure (arthroscopy), and History of sexually transmitted diseases.

Patient presentation:

Monoarthicular suppurative arthritis (knee, wrist most common), fever, pain, limitation of joint movement, swollen and tender joint, joint effusion, limited range of movement.

Sternoclavecular or Sacroilliac joint pain present in IV drug users (commonly ***P.aeruginosa***).

Immunocommpromized hosts: disseminated **fungal** or **mycobacterial** disease may present as septic arthritis.

◘ Differential Diagnosis:

- Crystal –induced arthritis (gout, pseudogout)
- **Noninfectious inflammatory arthritis (acute rheumatoid arthritis) (**Immunological arthritis**)**
- Reactive arthritis (Reiter syndrome, acute rheumatic fever)
- Trauma
- Viral arthritis (Parvovirus B19, Hepatitis B virus).

◘ Diagnosis of Infectious Arthritis:

Use History and examination to exclude systemic illness. Note history of tick exposure in endemic areas (to exclude lime disease)

✓ Arthrocentesis should be done as soon as possible:

1. Synovial fluid is cloudy and purulent. (not clear)
2. Leukocyte count generally very high (> 50,000/mm3, with > 75 % **PMN**). [**Polymorphonuclear neutrophil]**
3. Gram stain and culture are positive in >90% of cases.
4. Exclude crystal deposition arthritis or noninfectious inflammatory arthritis.

✓ Blood cultures indicated

✓ If gonococcal infection suspected, take specimen from cervix, urethra, rectum & pharynx for culture or DNA testing for N.gonorrheae.

✓ Urine may be used for DNA testing also.

✓ Culture of joint fluid, skin lesions.

◘ Treatment and Management:

- Arthrocentesis with drainage of infected synovial fluid. (THIS IS A MUST)
- Repeated therapeutic arthrocentesis often needed
- Occassionally, arthroscopic or surgical drainage/debridement. (the medical removal of a patient's dead, damaged, or infected tissue)
- Antimicrobial therapy should be directed at suspected suspected and susceptibility results:
  - **Gonococcal arthritis**: IV Ceftriaxone (or Ciprofloxacin or Ofloxacin) then switch to oral Quinolone or Cefixime for 7-10 days.
  - **Nongonococcal infectiuos arthritis**: depends on cause.

- Gonococcal arthritis has an excellent outcome

- Nongonococcal arthritis: can result in scarring with limitation of movement, ambulation is affected in 50% of cases.
- Risk factors for long –term adverse **sequellae** include: **(pathological conditions resulting from a disease, injury, or other trauma.)**

Age, prior rheumatoid arthritis, poly-articular joint involvement, hip or shoulder involvement, virulent pathogens and delayed initiation or response to therapy.

TABLE FINDINGS IN SYNOVIAL FLUID IN VARIOUS FORMS OF ARTHRITIS

Laboratory Test	Normal	Septic Bacterial Arthritis	Trauma, Degenerative Joint Disease	Rheumatic Arthritis Gout
Clarity and color	Clear	Opaque, yellow to green	Clear, yellow	Translucent or opalescent
Viscosity	High	Variable	High	Low
White blood cells/mm³	<200	25,000-100,000	200-2000	2000-20,000
Polymorphonuclear cells (%)	<25	>75	25-50	≥50
Glucose level (relative to ıeous blood glucose level)	Nearly equal	<25%	Nearly equal	50+80%

Just now that in arthritis, WBC count is very high, PMN count is very high.
But read the whole thing just in case…

◘ **Infections of Joint Prosthesis** (prosthesis: artificial)

- 1-5% of total joint replacement.
- Most infections occur within 5 years of joint replacement.
- Often caused by skin flora e.g. staphylococci.
- Diagnostic aspiration of joint fluid necessary.
- Result in significant morbidity and health care costs.
- Successful outcomes results from multidisciplinary approach. (Meaning: a lot of people work on patient's case; doctors, physiotherapists, nutritionists…)

◘**Etiology and Epidemiology**:

- Results from contamination during surgery or post op. wound infection adjacent to the prosthesis.
- Factors delay healing (hematoma, ischemia)
- Occasionally result from bacteremia
- Prosthesis & bone cement predispose to infection
- Occurs at the prosthesis-bone interface

- Bacteria adhere to biomaterials and develop a biofilm that protect them from host defenses and antimicrobial agents.
- Mostly caused by coagulase negative staph. Or *S.aureus*.
- Occasional pathogens: streptococci, enterococci ,and anaerobes

◘ **Risk factors**:

— History of superficial wound infection, post-surgical complications, underlying illness, any source of bacteremia.

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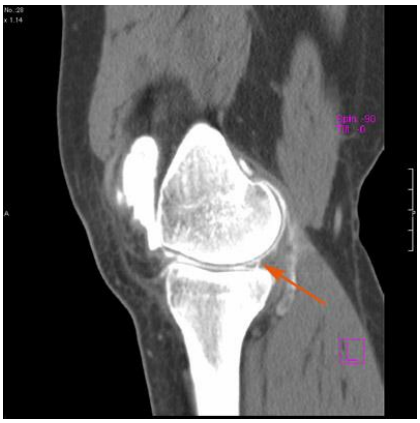
◘ **Differential diagnosis**:

- Aseptic loosening or dislocation of prosthetic joint.
- Prosthetic debris induced Synovitis and hemarthrosis. (synovitis: inflammation of the synovial membrane., hemarthrosis: is a bleeding into joint spaces).

◘ **Diagnosis of Prosthetic Arthritis**:

- Aspiration & surgical exploration to obtain specimen for culture & sensitivity testing & histopathology.
- Skin flora regarded as pathogens if isolated from multiple deep tissue cultures.
- Plain X-ray may not be helpful.
- Arthrography may help define sinus tracts.
- Bone scan not specific for infection.
- Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) may be high.



Arthrography

◘ **Treatment & Management**:

- Surgical debridement and prolonged antimicrobial therapy.
- Surgery: removal of prosthesis.
- Antibiotic –impregnated cement during re-implantation. (Prostheses are anchored with bone cement. The bone cement –which is a binder-fills the free space between the prosthesis and the bone after removing both of them, we drown them in antibiotics, then put them back)
- Antimicrobial for 6 weeks:
    - Begin empiric IV antibiotic to cover MRSA and Gram negative rods (Vancomycin+ Cefepime, Ciprofloxacin,or Aminoglycoside)
    - Chronic therapy with oral drug if removal of prosthesis not possible.