MED437
KING SAUD UNIVERSITY

PATHOLOGY
TEAM 437

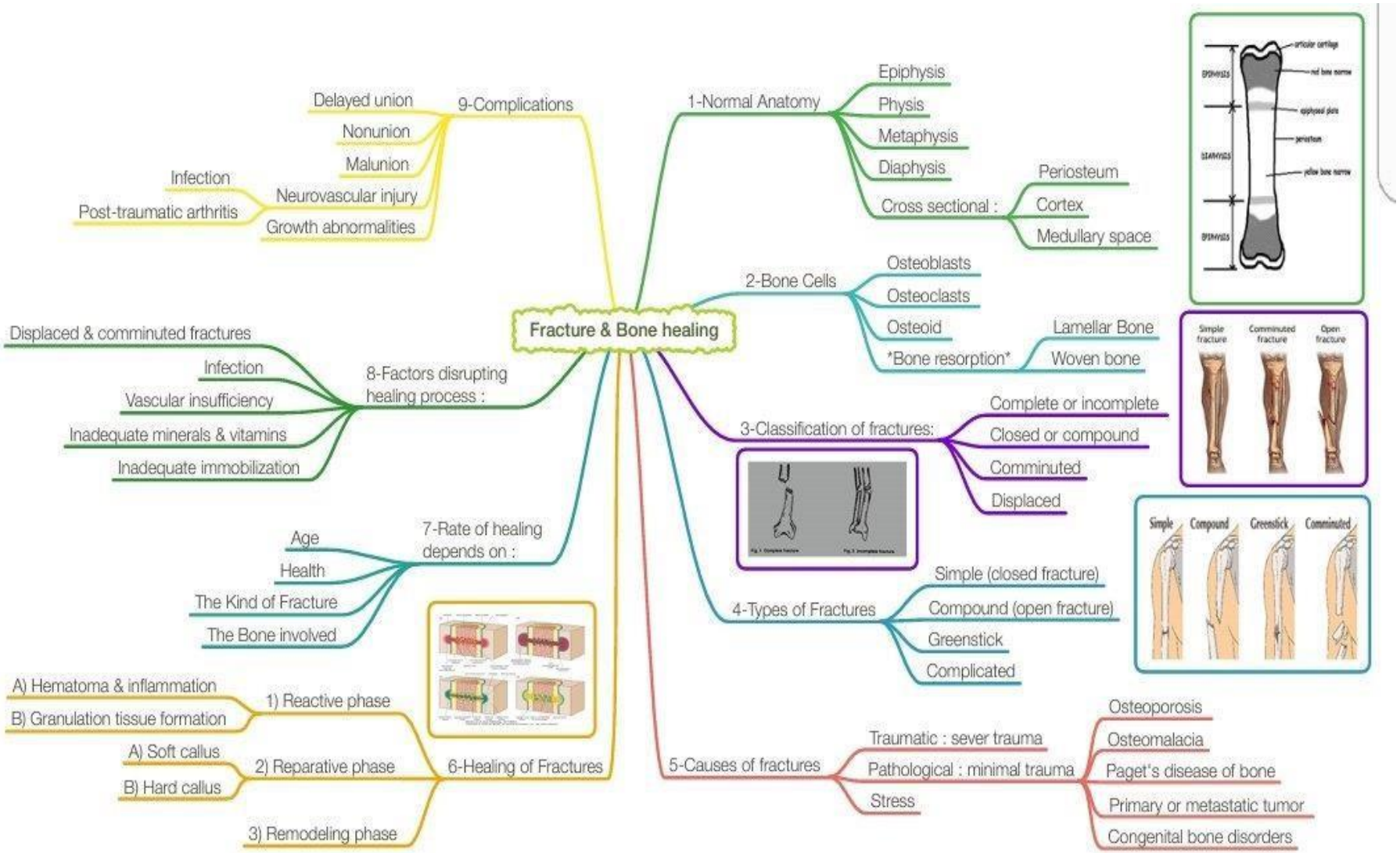
Pathology

teamwork 437

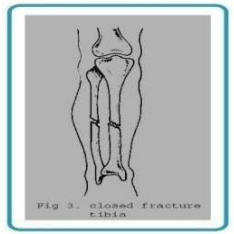
Mind maps

قد يكون السطر الذي حرم عيناك النوم ليلتي ، شفاءً لدائي ازرق العليل ليالٍ طوال ..

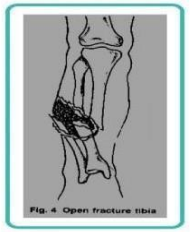
Lecture 1 :


Fracture & Bone healing
1-Normal Anatomy
Epiphysis
Physis
Metaphysis
Diaphysis
Cross sectional :
Periosteum
Cortex
Medullary space
articular cartilage
red bone marrow
epiphyseal plate
periosteum
yellow bone marrow
EPIPHYSIS
DIAPHYSIS
EPIPHYSIS
2-Bone Cells
Osteoblasts
Osteoclasts
Osteoid
Bone resorption
Lamellar Bone
Woven bone
3-Classification of fractures:
Complete or incomplete
Closed or compound
Comminuted
Displaced
Simple fracture
Comminuted fracture
Open fracture
4-Types of Fractures
Simple (closed fracture)
Compound (open fracture)
Greenstick
Complicated
Simple
Compound
Greenstick
Comminuted
5-Causes of fractures
Traumatic : sever trauma
Pathological : minimal trauma
Stress
Osteoporosis
Osteomalacia
Paget's disease of bone
Primary or metastatic tumor
Congenital bone disorders
6-Healing of Fractures
1) Reactive phase
A) Hematoma & inflammation
B) Granulation tissue formation
2) Reparative phase
A) Soft callus
B) Hard callus
3) Remodeling phase
7-Rate of healing depends on :
Age
Health
The Kind of Fracture
The Bone involved
8-Factors disrupting healing process :
Displaced & comminuted fractures
Infection
Vascular insufficiency
Inadequate minerals & vitamins
Inadequate immobilization
9-Complications
Delayed union
Nonunion
Malunion
Infection
Neurovascular injury
Post-traumatic arthritis
Growth abnormalities

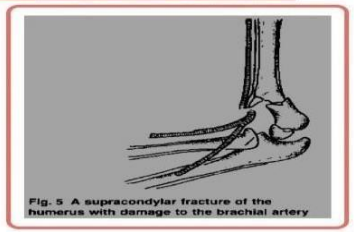
Types of bone fractures



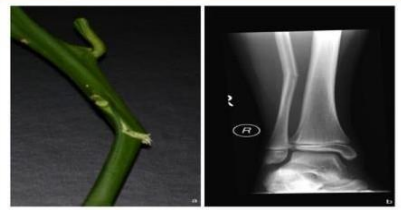
- **Simple (closed fracture)**
  - Overlying tissue is **intact**.
  - Does **NOT** communicate with external environment.
- **Compound (open fracture)**
  - **Extend** into the overlying skin.
  - **Communicate** with external environment.



- **Complicated fracture**
  - Associated with **damage** to nerves, vessels or internal organs.

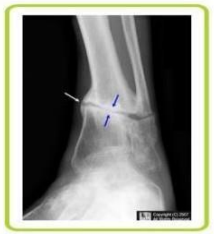


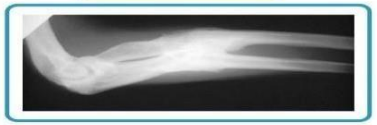
- **Greenstick fracture**



Complications

- **Delayed union** — A fracture that **takes longer** to heal than expected
- **Nonunion** — A fracture that **fails to heal** in a reasonable amount of time.
- **Malunion** — A fracture that **does not heal in normal alignment**
- **Neurovascular injury**
  - **Infection** — Open fracture can be infected
  - **Post-traumatic arthritis** — Fracture that extend into the joints
- **Growth abnormalities** — A fracture in the open physis or **growth plate in child**, can cause problems.





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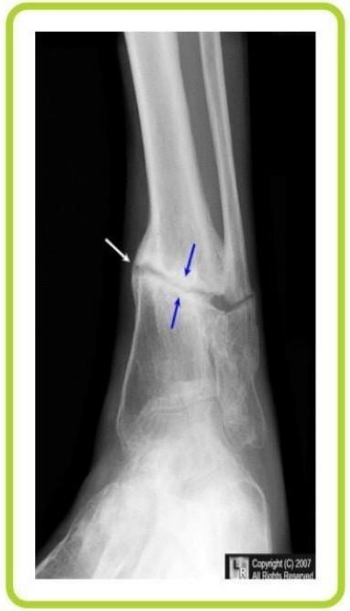
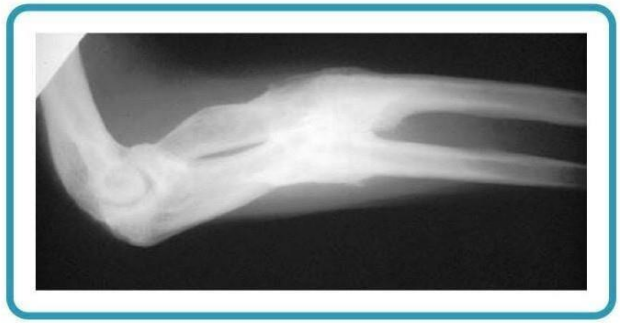
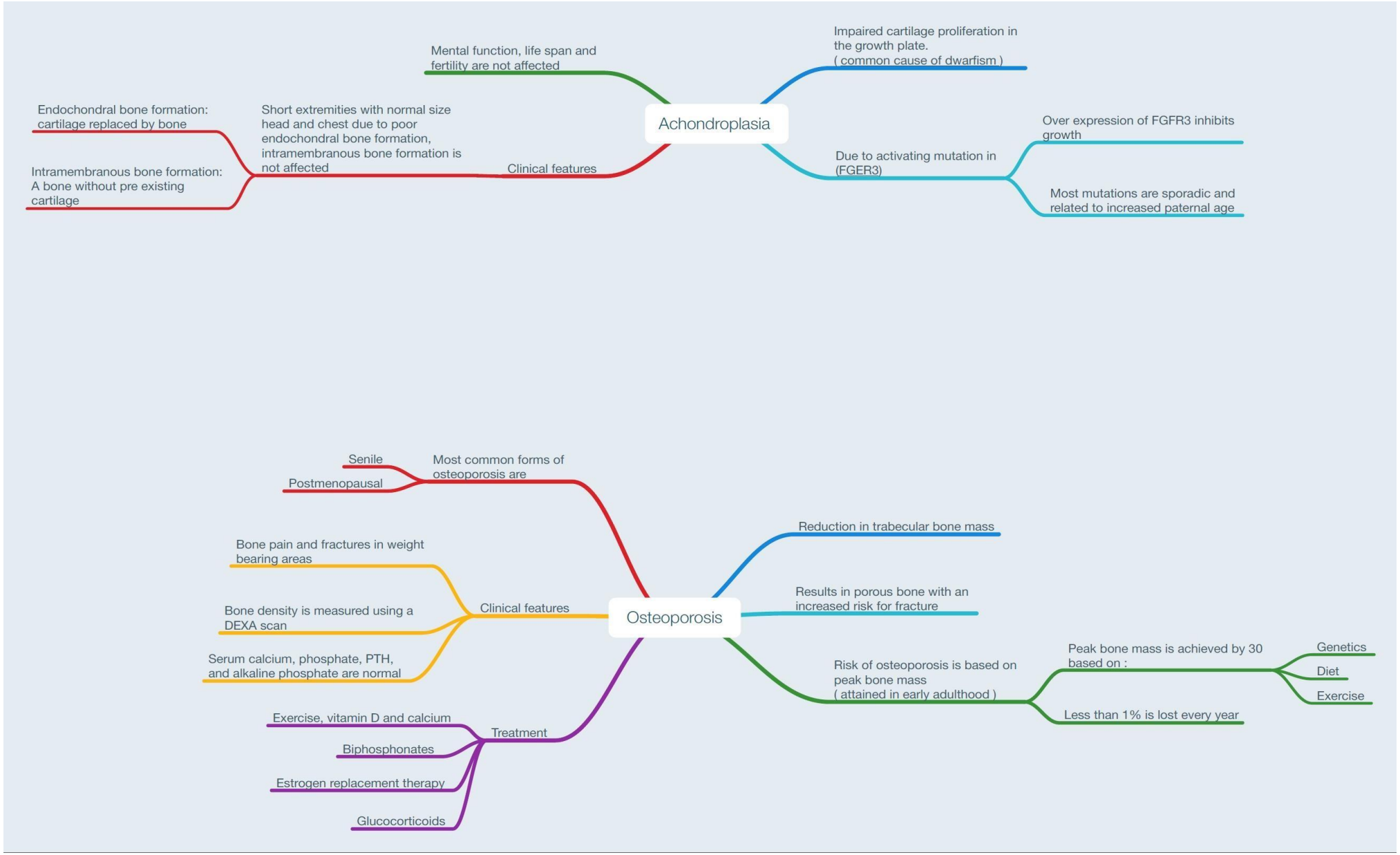


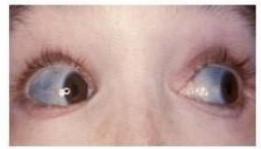


Lecture 2 :

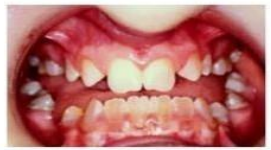

Achondroplasia
Impaired cartilage proliferation in the growth plate.
(common cause of dwarfism)
Due to activating mutation in (FGER3)
Over expression of FGFR3 inhibits growth
Most mutations are sporadic and related to increased paternal age
Clinical features
Mental function, life span and fertility are not affected
Short extremities with normal size head and chest due to poor endochondral bone formation, intramembranous bone formation is not affected
Endochondral bone formation: cartilage replaced by bone
Intramembranous bone formation: A bone without pre existing cartilage
Osteoporosis
Reduction in trabecular bone mass
Results in porous bone with an increased risk for fracture
Risk of osteoporosis is based on peak bone mass (attained in early adulthood)
Peak bone mass is achieved by 30 based on :
Genetics
Diet
Exercise
Less than 1% is lost every year
Most common forms of osteoporosis are
Senile
Postmenopausal
Clinical features
Bone pain and fractures in weight bearing areas
Bone density is measured using a DEXA scan
Serum calcium, phosphate, PTH, and alkaline phosphate are normal
Treatment
Exercise, vitamin D and calcium
Biphosphonates
Estrogen replacement therapy
Glucocorticoids

Osteogenesis Imperfecta

- Also called **Brittle Bone Disease**.
- rare **Congenital** bone disease.
  - Types
    - Type 1: **Autosomal dominant**
    - Type 2: **Autosomal recessive**
  - Genes
    - **COLIA1** : on chromosome **17**
    - **COLIA2** : on chromosome **7**
- Defect in the synthesis of **type1 collagen**
  - Abnormalities in the structure of the protein collagen 1.
  - Amino acids chains **alpha 1 & alpha 2** are defected.
- Clinical features
  - Abnormal bone
  - Blue sclera



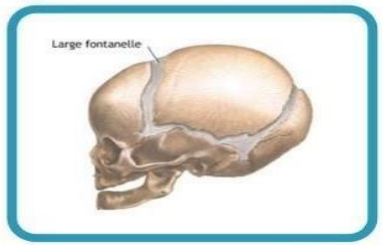
    - Blue pigment of the **choroid layer from behind**.
  - Teeth deformities

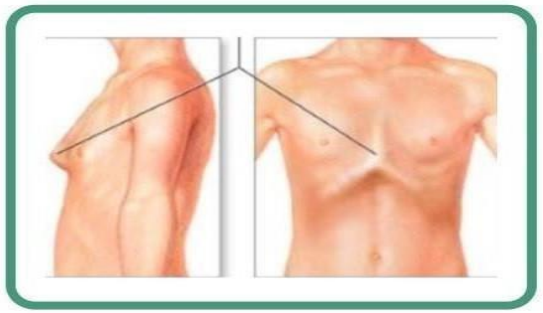


  - Hearing loss
    - Conductive defect in the **middle & inner ear bone**.

Osteomalacia / Rickets

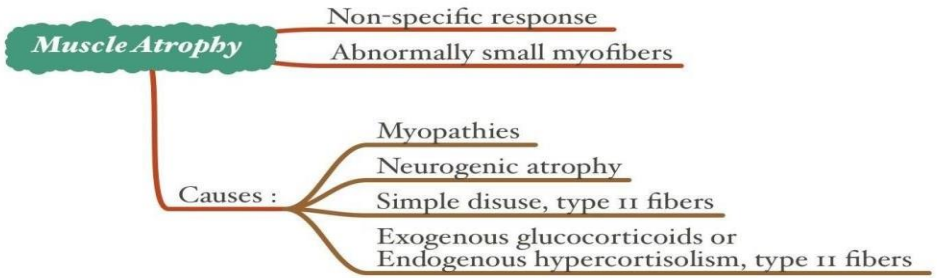
- **Acquired disease**
- **Inadequate mineralization**
  - **Normal bone collagen**
  - **Vitamin D deficiency**
  - **Low Calcium level**
- Depending on age it called :
  - **Rickets : In children**
    - Disorder interferes with deposition of bone in the growth plates
  - **Osteomalacia : In adults**
    - The bone formed during remodeling is undermineralized
- Clinical features
  - Delayed closure of fontanelles
  - Frontal bossing
  - Rachitic rosary
  - Pigeon chest
  - Bowing of the leg

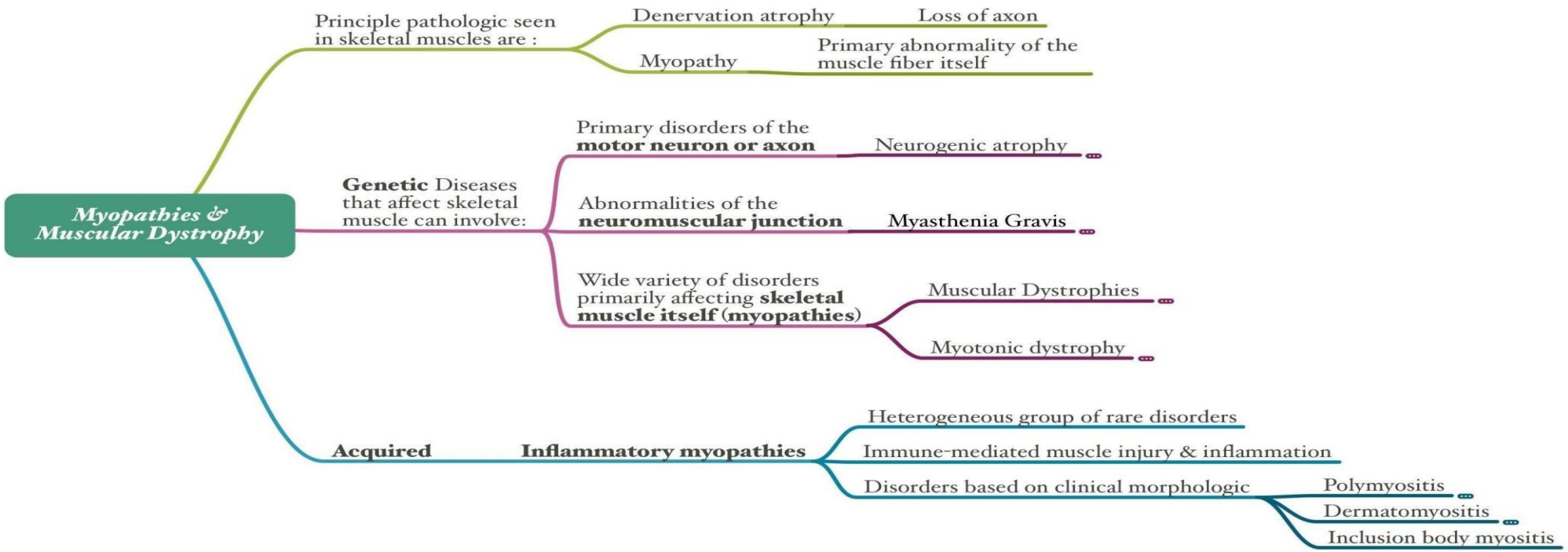




	Etiology	Pathogenesis	Clinical features	
Osteogenesis Imperfecta	Congenital Type1: autosomal dominant. Type2: autosomal recessive. COLIA1: on chromosome 17. COLIA2: on chromosome 7.	• Defect in the synthesis of type I collagen. • Amino acids chains alpha 1 and alpha 2 in the structure of collagen (type 1) are defected.	1. Abnormal bone 2. Blue sclera 3. Teeth deformities 4. Hearing loss	
Achondroplasia	Congenital • Autosomal dominant trait but many cases arise from spontaneous mutation. • Mutation on gene that is located on the short arm of chromosome 4, fragment 16.3 which is called (FGFR3).	• Failure of cartilage cell proliferation at the epiphysial plates of the long bones.	1. Short proximal extremities. 2. Enlarged head with bulging forehead. 3. Depression of the root of the nose. 4. bowing of the legs and neck. General health, intelligence, or reproductive status are not affected, and life expectancy is normal.	
Osteoporosis	Acquired • characterized by reduced bone mass. • It may be localized or may involve the entire skeleton	• Occur when the balance between bone formation and resorption tilts in favor of resorption. • the greater the peak bone mass, the greater the delay in onset of osteoporosis.	Diagnosis - Plain X ray - DXA scan - Biopsy	Prognosis - Osteoporosis is rarely lethal. - Patients have an increased mortality rate due to the complications of fracture.
Osteomalacia And Rickets	Acquired • Inadequate mineralization. • vitamin D deficiency. • Calcium levels are low.	• Rickets disorder in children, interferes with the deposition of bone in the growth plates. • Osteomalacia is the adult, the bone formed during remodeling is undermineralized.	1. Delayed fontanelle closure. 2. Rachitic rosary. 3. Pigeon chest. 4. Bowing of the leg.	

Lecture 3 :


Muscle Atrophy
Non-specific response
Abnormally small myofibers
Causes :
Myopathies
Neurogenic atrophy
Simple disuse, type II fibers
Exogenous glucocorticoids or
Endogenous hypercortisolism, type II fibers

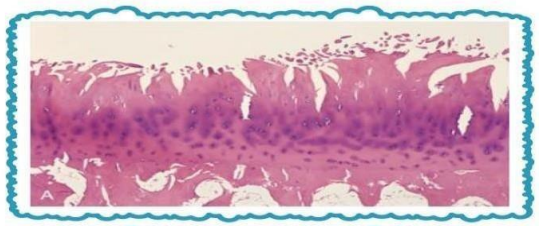

Myopathies &
Muscular Dystrophy
Principle pathologic seen
in skeletal muscles are :
Denervation atrophy
Loss of axon
Myopathy
Primary abnormality of the
muscle fiber itself
Genetic Diseases
that affect skeletal
muscle can involve:
Primary disorders of the
motor neuron or axon
Neurogenic atrophy
Abnormalities of the
neuromuscular junction
Myasthenia Gravis
Wide variety of disorders
primarily affecting skeletal
muscle itself (myopathies)
Muscular Dystrophies
Myotonic dystrophy
Acquired
Inflammatory myopathies
Heterogeneous group of rare disorders
Immune-mediated muscle injury & inflammation
Disorders based on clinical morphologic
Polymyositis
Dermatomyositis
Inclusion body myositis

	Etiology	Pathogenesis	Clinical features
Neurogenic atrophy	**Genetic** disease affects the motor neuron • Involve both fibers types (1,2). • Clustering of myofiber into small groups.	1. Loss of single neuron 2. Re-enervation 3. Grouped atrophy	
Myasthenia gravis	**Genetic** disorder affect the neuromuscular junction Caused by autoantibodies that block the function of post synaptic Ach receptors which results in degradation & depletion of receptors.		1. Ptosis or diplopia due to weakness in the 4 5 extraocular muscles. 2. Repetitive use of muscles make the weakness mor severe. 3. More commonly seen in women. **4. Effective treatment:** cholinesterase inhibitory drugs, immunosupperssion.
Muscular dystrophies	• **Genetic** disorder in muscle itself. • Degenerative disorder characterized by muscle wasting & replacement of skeletal muscle by adipose tissue. • Due to mutations of dystrophin gene.	• Duchenne muscular dystrophy (DMD) : deletion of dystrophin. • Becker muscular dystrophy (BMD) : mutated dystrophin protein of smaller size. • Present in childhood.	DMD : 1. Proximal muscle weakness at 1 year of age, progress to involve distal muscles. 2. Death results from cardiac or respiratory failure, myocardium is commonly involved. BMD 1. Results in milder disease 2. cardiac involvement can be the dominant.
Myotonic dystrophy	• **Sustained involuntary contraction** of a group of muscles, is the cardinal symptom in this disease.	• Mutations in the gene that encodes the dystrophia myotonica protein kinase (**DMPK**). • Present in late childhood**.**	1. Stiffness & difficulty in releasing the grip. 2. Weakness of the hand intrinsic muscles & wrist extensor. 3. Atrophy of muscles of the face and ptosis. 4. Cataracts & Dementia.
Polymyositis	**Acquired** Uncommon inflammatory disease.	• Affect and seen mainly in adults.	1. Symmetrical proximal muscles weakness. 2. Lack of cutaneous involvement. 3. Inflammatory involvement of heart, lungs and blood vessels.
atomyo itis	**Unknown etiology – Acquired**. Inflammatory disorder of the skin and		1. Skin rash. 2. Muscle weakness. 3. Dysphagia.

Lecture 4 :

Osteoarthritis

- *Definition*
  - Degenerative joint disease
  - The most common joint disease
  - Characterized by the progressive degeneration of articular cartilage in weight-bearing joints
- *Types*
  - Primary
    - Appears insidiously with age
    - Without apparent initiating cause
    - Affect only a few joints
  - Secondary
    - Predisposing condition
      - Previous traumatic injur
      - Developmental deformity
      - Underlying systemic disease
        - Diabetes
        - Hemochromatosis
        - Marked obesity
    - Affects young
    - Involve one or several predisposed joints
    - Less than 5% of cases
- *Pathogenesis*
  - Articular cartilage bears the brunt of the degenerative changes in osteoarthritis
  - Chondrocyte function is affected by a variety of influences
    - Mechanical stresses
    - Aging
    - Genetic factors
  - Imbalance results in degeneration and loss of matrix
    - Expression
    - Activity
    - Signaling of cytokines & growth factors
- *Common sites*
  - Spine
  - Hip (More in men)
  - Hand (More in women)
  - Knee (More in women)
  - Foot
- *Morphology*
  - Fibrillation & cracking of the matrix
  - Full-thickness portions of the cartilage are lost (**bone eburnation**)
  - Small fractures, forming loose bodies (**joint mice**)
  - Formation of fibrous walled **cysts**
  - Mushroom-shaped **osteophytes** (bony outgrowths)
- *Clinical features*
  - Characteristic symptoms & signs
  - Aching pain
  - Morning stiffness
  - Crepitus
  - Limitation in range of movement
  - Heberden nodes (in women usually)
- *Prognosis*
  - Slowly progressive
  - With time, significant joint deformity can occur
- *Treatment*
  - Based on symptoms
  - Joint replacement in sever cases



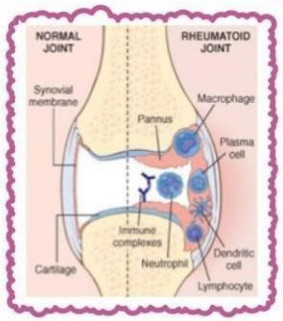
Rheumatoid Arthritis

Definition
- Systemic chronic inflammatory autoimmune disease
- Principally attacking the joints.
- Cause a nonsuppurative proliferative synovitis
- Common condition, it's 3-5 times More in women
- No age is immune, the peak incidence is in the 2nd to 4th decades of life

Pathogenesis
- Pathologic changes are caused by cytokine-mediated inflammation, with $CD4+$ T cells
- Patients also produce antibodies against cyclic citrullinated peptides (CCPs) "diagnostic marker"
- Genetic factors 50% : HLA-DRB1 locus
- Environmental factors : activate T or B cells
- 80% of patient have serum IgM & autoantibodies binds to Fc portions of their own IgG
- Autoantibodies are called **rheumatoid factor**

Laboratory findings
- Rheumatoid factor (non sensitive or specific)
- Anti-CCP (most specific)
- ESR & C-reactive protein

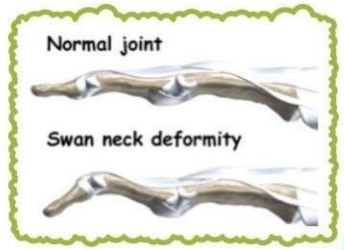
Pathologic features
- Synovial cell hyperplasia and proliferation
- Dense perivascular inflammatory cell infiltrates
- Increased vascularity due to angiogenesis
- Neutrophils and aggregates of organizing fibrin on the synovial surface
- Increased osteoclast activity in the underlying bone > bone erosion
- Pannus formed by
  - Proliferating synovial-lining cells
  - Inflammatory cells
  - Granulation tissue
  - Fibrous connective tissue
- May cause ankylosis



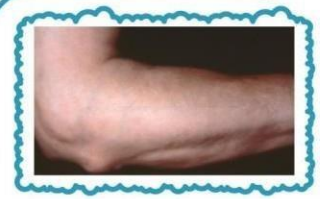
Prognosis
- The disease stabilize or regress (in minority of patients)
- It pursues a chronic, remitting-relapsing course (in most patients)
- Progressive joint destruction leading to disability after 10 to 15 years
- Cause reactive amyloidosis

Diagnosis
- X-ray
  - Loss of articular cartilage leading to narrowing of the joint space.
  - Joint effusions
  - Erosions

Clinical features
- Symmetric arthritis affecting small joints
- Most often, the proximal interphalangeal & metacarpophalangeal joints are affected
- Axial involvement
- Weakness, low grade fever
- Aching & stuffiness of the joint
- Enlarged joints, limited motion
- Characteristic deformities
  - Radical deviation at the wrist
  - Ulnar deviation at the fingers
  - Flexion & hyperextension deformities of the fingers (swan neck & boutonniere deformities).

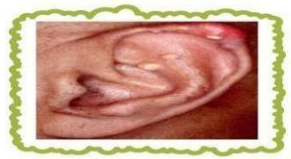


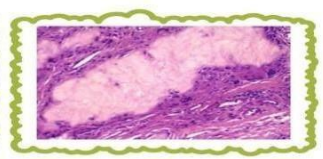
Subcutaneous nodules
- Develop in one fourth of patients
- Occurring along the extensor surface of the forearm
- Firm, nontender, oval or rounded masses(2cm in diameter)
- Characterized microscopically by fibrinoid necrosis surrounded by a palisade of macrophages, which is rimmed by granulation tissue & lymphocytes

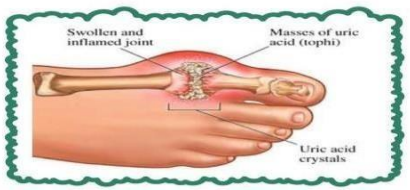


Goat

- *Definition*: Monosodium urate crystals precipitate from supersaturated body fluids and induce an acute inflammatory reaction
- *Etiology*: Caused by excessive amounts of uric acid
- *Marked by*
  - Recurrent episode of acute arthritis
  - Formation of large crystalline aggregates called **tophi**
- *Risk factors*
  - Obesity
  - Excess alcohol intake
  - Consumption of Purine-rich foods
  - Diabetes
  - The metabolic syndrome
  - Renal failure
- *Types*
  - 90% Primary
    - Enzyme defects - Unknown (85-90% of cases)
      - Overproduction of uric acid, normal or increased excretion
      - Underexcretion of uric acid with normal production
    - Known enzyme defect - e.g. partial HGPRT deficiency (rare): Overproduction of uric acid
  - 10% Secondary
    - Associated with increased nucleic acid turnover - e.g. leukemia's: Overproduction of uric acid with increased urinary excretion
    - Chronic renal disease: Reduced excretion of uric acid with normal production
    - Inborn errors of metabolism: Overproduction of uric acid with increased urinary excretion e.g. complete HGPRT deficiency (Lesch-Nyhan syndrome)
- *Morphology*
  - Acute arthritis
    - Characterized by a dense neutrophilic infiltrate permeating the synovium & synovial fluid
    - Long, slender, needle-shaped monosodium urate crystals
  - Chronic tophaceous arthritis
    - Repetitive precipitation of urate crystals during acute attacks
    - The synovium becomes hyperplastic, fibrotic & thickened by inflammatory cells
  - Tophi
    - Pathognomonic for goat
    - Appear in the articular cartilage of joints & soft tissues (ear lobes & nasal cartilage
    - Formed by
      - large aggregations of urate crystals
      - intense inflammatory reaction of lymphocytes
      - macrophages
      - foreign-body giant cells

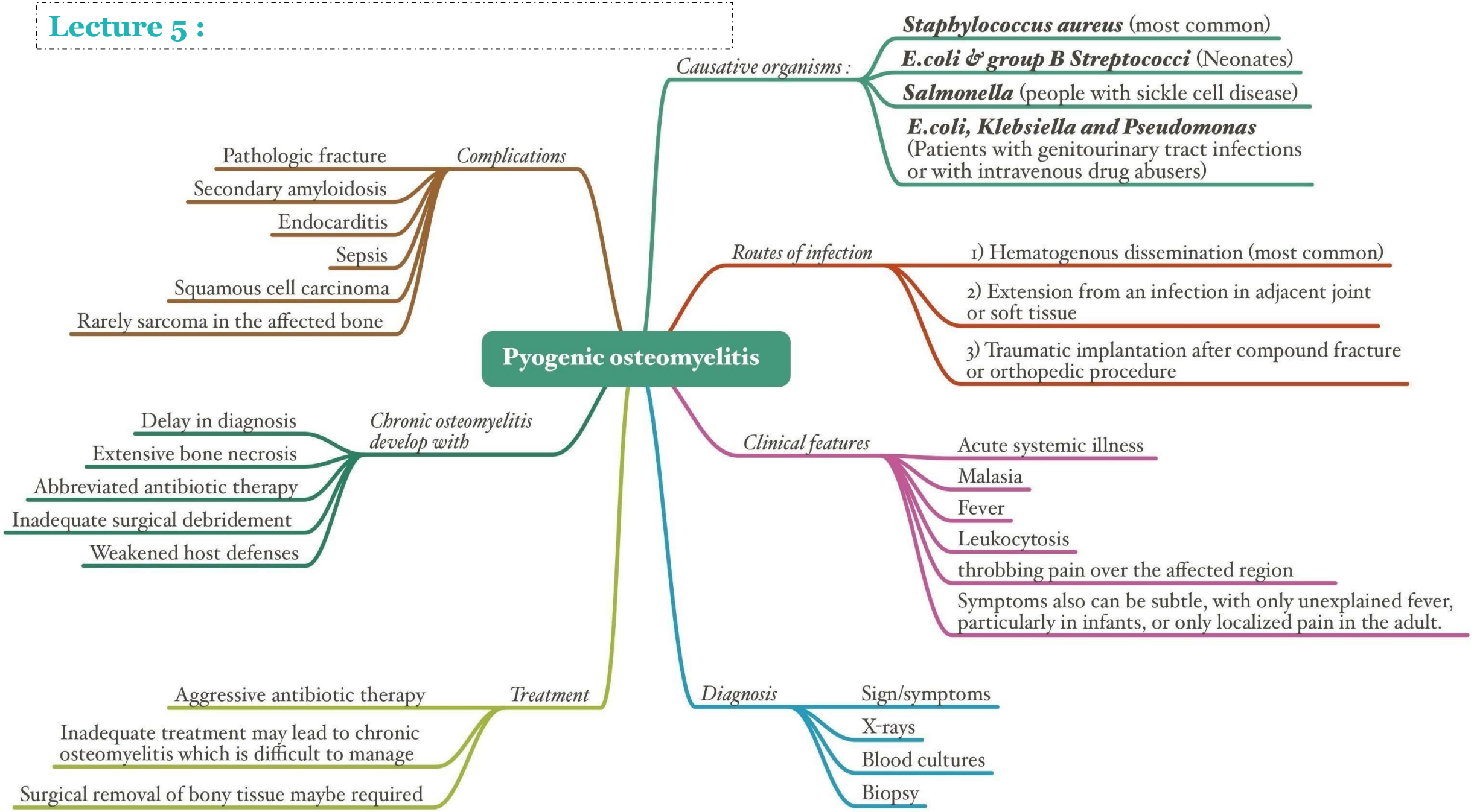






- *Clinical features*
  - Most common affected site: first metatarsophalangeal joint
  - Swollen, red & very painful
  - Renal manifestation of goat appears as renal colic, associated with passage of gravel & stones

Lecture 5 :


Pyogenic osteomyelitis
Causative organisms :
Staphylococcus aureus (most common)
E.coli & group B Streptococci (Neonates)
Salmonella (people with sickle cell disease)
E.coli, Klebsiella and Pseudomonas
(Patients with genitourinary tract infections or with intravenous drug abusers)
Routes of infection
1) Hematogenous dissemination (most common)
2) Extension from an infection in adjacent joint or soft tissue
3) Traumatic implantation after compound fracture or orthopedic procedure
Clinical features
Acute systemic illness
Malasia
Fever
Leukocytosis
throbbing pain over the affected region
Symptoms also can be subtle, with only unexplained fever, particularly in infants, or only localized pain in the adult.
Diagnosis
Sign/symptoms
X-rays
Blood cultures
Biopsy
Treatment
Aggressive antibiotic therapy
Inadequate treatment may lead to chronic osteomyelitis which is difficult to manage
Surgical removal of bony tissue maybe required
Chronic osteomyelitis develop with
Delay in diagnosis
Extensive bone necrosis
Abbreviated antibiotic therapy
Inadequate surgical debridement
Weakened host defenses
Complications
Pathologic fracture
Secondary amyloidosis
Endocarditis
Sepsis
Squamous cell carcinoma
Rarely sarcoma in the affected bone

Tuberculous osteomyelitis

Routes of entry
- Blood borne usually and originate from a focus of active visceral disease
- Direct extension or spread via draining lymphatics

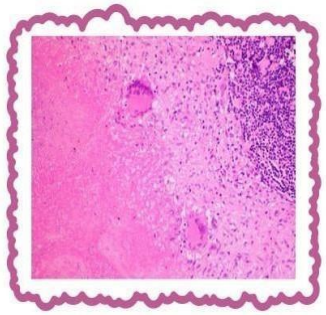
Common sites involved
- **Thoracic and lumber vertebrae** followed by the **knees and hips**
- Pott's disease is the involvement of **spine**
- In patients with AIDS frequently **multifocal**

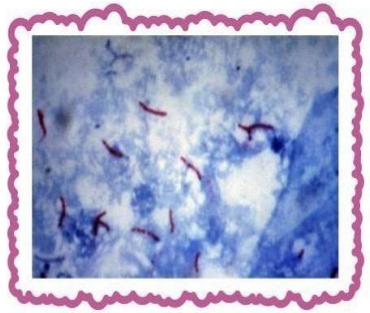
Complications
- Bone destruction
- Tuberculous Arthritis
- Sinus tract formation
- Amyloidosis

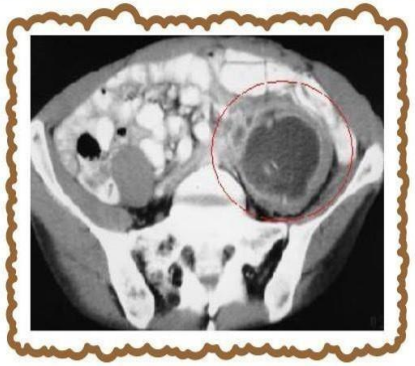
Clinical features
- Pain
- Fever
- Weight loss
- May form an inguinal mass "psoas abscess"

Histopathology
- Collections of epithelioid histiocytes
- Lymphocytes with caseation necrosis

Pott's disease
The infection breaks through the intervertebral discs and extends into the soft tissues forming abscesses or into the muscle forming **Psoas abscesses**

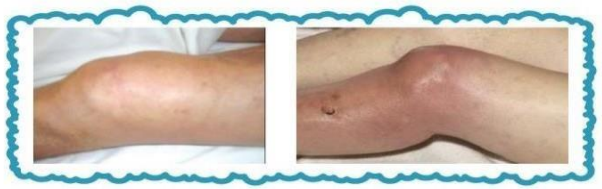






Infectious Arthritis

- *Routes of infection*
  - 1) Hematogenous
  - 2) Contiguous spread from osteomyelitis
  - 3) Contiguous spread from a soft tissue abscess
  - 4) Iatrogenic
  - 5) Traumatic
- *Common sites*
  - The infection involves only a single joint.
  - The knee-followed by hip, shoulder, elbow, wrist and sternoclavicular joints.
- *Causative organisms*
  - Bacterial infections almost always cause an **acute suppurative arthritis**
  - *Haemophilus influenzae* (children under 2 years)
  - *S. aureus* (older children & adults)
  - *Gonococcus* (late adolescence & young adulthood)
  - *Salmonella* (people with sickle cell disease)
- *Risk factors*
  - Immune deficiencies (congenital & acquired)
  - Debilitating illness
  - Joint trauma
  - Intravenous drug abuse
- *Clinical features*
  - Fever
  - Sudden onset of pain
  - redness, and swelling of the joint with restricted range of motion
  - Leukocytosis and elevated erythrocyte sedimentation rate



- *Treatment*
  - prompt antibiotic therapy
  - joint aspiration or drainage
- *Complications*
  - Septic arthritis can lead to ankylosis and even fatal septicemia.

MED437
KING SAUD UNIVERSITY

PATHOLOGY
TEAM 437

GOOD LUCK ! ☺

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