# MUSCULOSKELETAL PATHOLOGY-1 CONGENITAL DISEASES

Prof. Tariq Aladily

Department of Pathology

The University of Jordan

tnaladily@ju.edu.jo

# CONGENITAL DISEASES

- **Dysostosis** خلل العظم: localized abnormal bone formation
- Failure of migration and condensation of mesenchyme
- Examples: absence of bone or digit (aplasia)
- Supernumerary digits or ribs
- Abnormal fusion of bones (craniosynostosis, syndactyly)
- Results from mutations in homeobox genes, cytokines or cytokine-receptors genes.

# CONGENITAL DISEASES

- **Done Dysplasia:** abnormal pattern of growth
- Not a premalignant lesion
- Generalized abnormality, affecting the entire skeleton
- Disorganization of bone and/or cartilage
- Mutations in genes that control development or remodeling of the entire skeleton

# OSTEOGENESIS IMPERFECTA

- Most common inherited disorder of connective tissue
- Mutation in type-1 collagen gene, protein becomes defective and prematurely degraded
- Different types of mutations, variable in severity, may affect α1 or α2 subunits
- Bone matrix amount is too little, results in bone fragility, deformity

# SYMPTOMS

- Skeletal deformity
- Repeated fractures
- Also affects skin, joints, and eyes (blue sclera)
- Hearing loss (conduction defects in the middle and inner ear bones)
- Small misshapen teeth are a result of dentin deficiency
- Type 1: most common, normal life expectancy
- Type 2: severest, death  early in life or in utero (severe fractures)

# ACHONDROPLASIA

- Most common skeletal dysplasia
- Major cause of dwarfism
- Autosomal dominant transmission
- 90% of cases represent new acquired mutation, mostly paternal side

# PATHOGENESIS

- Point mutation in the fibroblast growth factor receptor 3 (FGFR3) that results in permanent activation
- Activated FGFR3 inhibits chondrocyte proliferation; as a result, the normal epiphyseal growth plate of the long bones is suppressed
- Patients have normal head and trunk, but short bowing limbs
- Normal life expectancy and mental function

# THANATOPHORIC DYSPLASIA

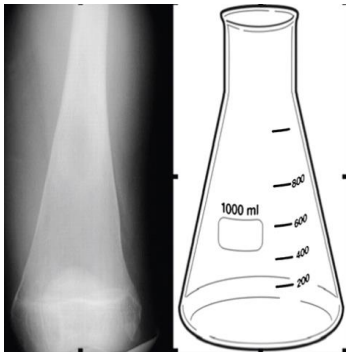
- A lethal form of dwarfism
- FGFR3 mutation, but more increase in signaling activity
- Short limbs, frontal bone bossing, microcephaly, small chest, belly-like abdomen
- Respiratory insufficiency
- Die at birth or shortly after

# OSTEOPETROSIS تصخر العظم

- Marble-like bone
- Rare genetic disorders characterized by reduced osteoclast-mediated bone resorption and therefore defective bone remodeling
- Bone shows diffuse symmetric sclerosis, yet can fracture easily

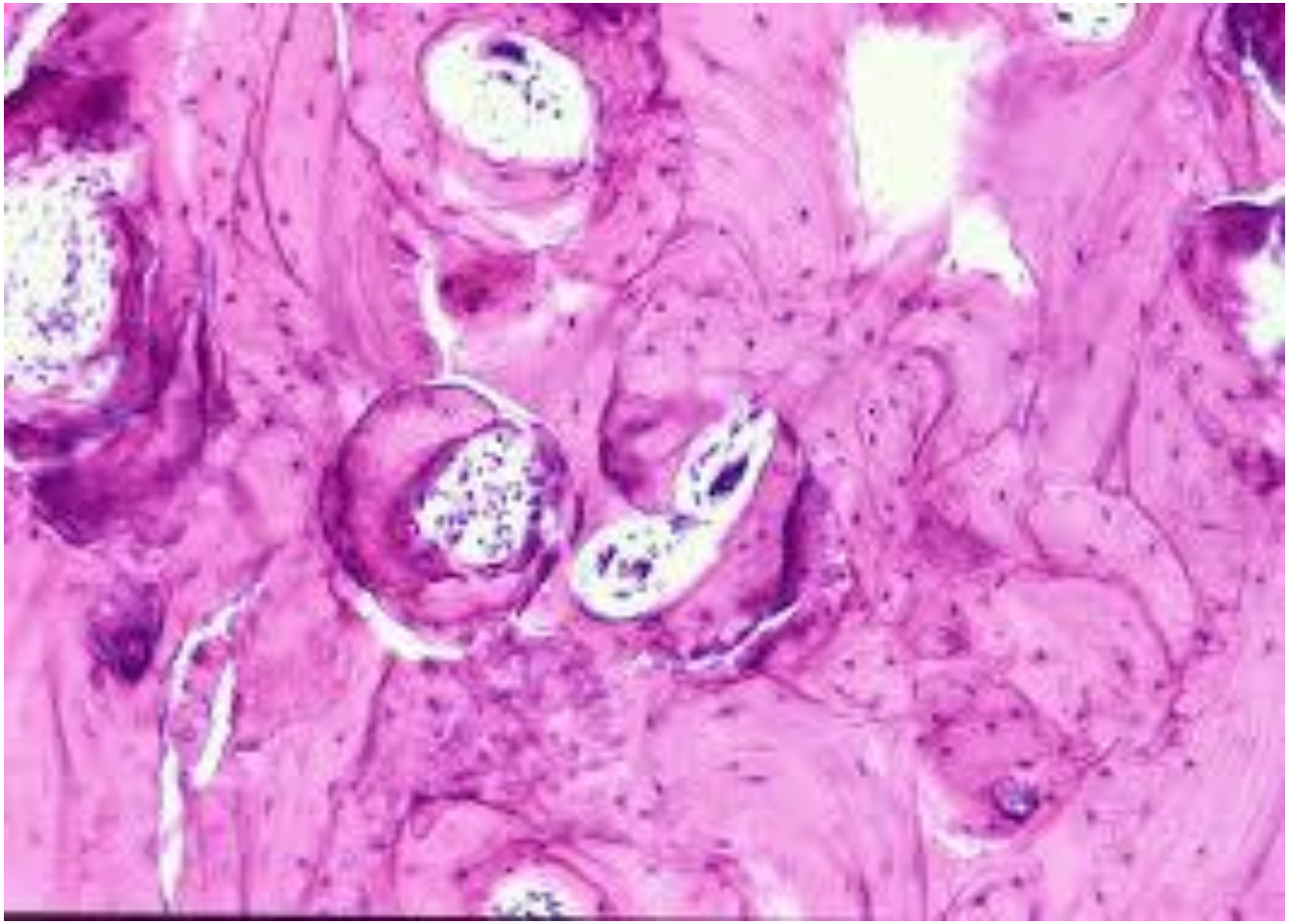
# INHERITANCE

- Multiple variants based on both the mode of inheritance and severity of symptoms
- All variants share a problem in the acidification process of osteoclasts that is responsible for bone resorption
- Autosomal dominant variant is the mildest (symptoms appear in adolescence or adulthood)
- Repetitive fractures
- Cranial nerve deficits
- Anemia
- Erlenmeyer-Flask deformity of long bones



# SEVERE INFANTILE OSTEOPETROSIS

- Autosomal recessive
- Severe symptoms, appear early in life
- Leukopenia
- Hepatosplenomegaly (extramedullary hematopoiesis)
- Fatal



- Osteopetrosis: markedly thickened bone trabeculae, marrow spaces are minimal