MSS

Musculoskeletal System

Doctor 2019 | Medicine | JU

NO.

Pathology

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CONGENITAL DISORDERS

There are two major category of congenital disorder:

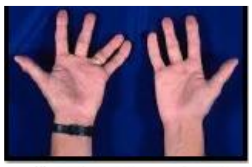
1. DYSOSTOSIS
2. DYSPLASIA

DYSOSTOSIS (dys: wrong , ostosis: bone)

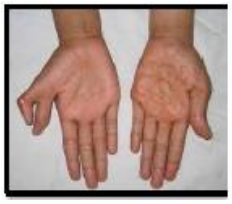
It is an abnormal condensation and migration of **mesenchyme** due Genetic abnormalities of certain group of genes called **homeobox genes**, which are affecting Inflammatory cytokines and its **receptors** .

Example of dysostosis:

- **Aplasia:** lack of synthesis of certain group of bone

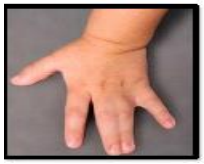


- **Supernumerary digit** : A child has an additional finger or toe



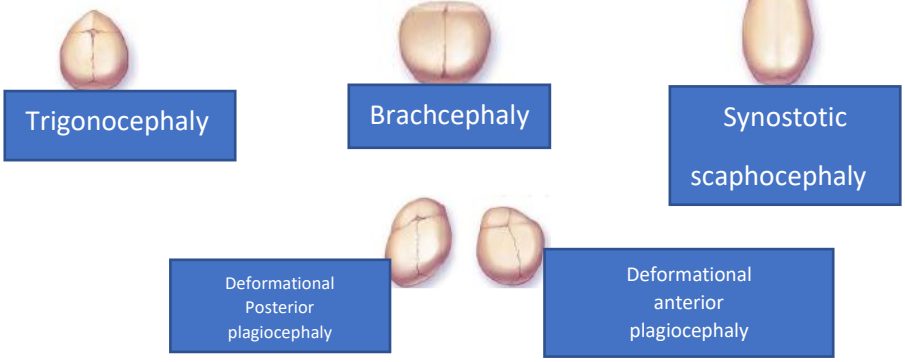
- **Syndactyly & craniosynostosis** :

⇒ **Syndactyly**: Fusion of the fingers



Syndactyly and Supernumerary digit

⇒ **craniosynostosis**: an abnormality In formation of the skull



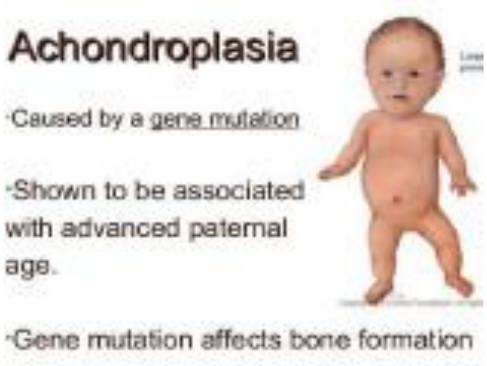
- You don't need to memories them but remember that they under the heading of dysostosis which is an abnormality in homeobox gene.

DYSPLASIA not premalignant (not cancer)

It is disorganized bone and cartilage, due to gene mutations that control development and remodeling.

Example of dysplasia:

- **Achondroplasia (dwarfism)**: most common



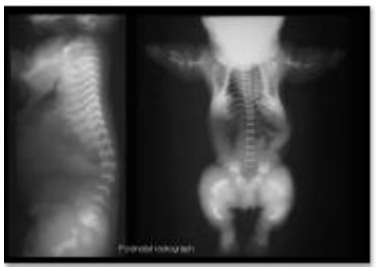
Mutations in Fibroblast Growth Factor Receptor #3 **(FGFR3)**

The most important concept that you have to understand that there is no impact on longevity, intelligence or reproductive status. بعيشوا زينا زيهم

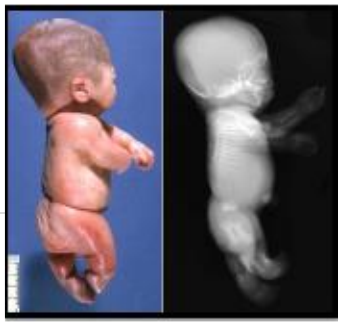
Peter Dinklage: 48-years-old, married with 2 children from USA, New Jersey
"Game of thrones

- **THANATOPHORIC DYSPLASIA** Most common lethal form of dwarfism

This is a severe form of dwarfism affecting another gene in the **FGFR3** (it is the same group of receptor but in **different** location than the Achondroplasia)



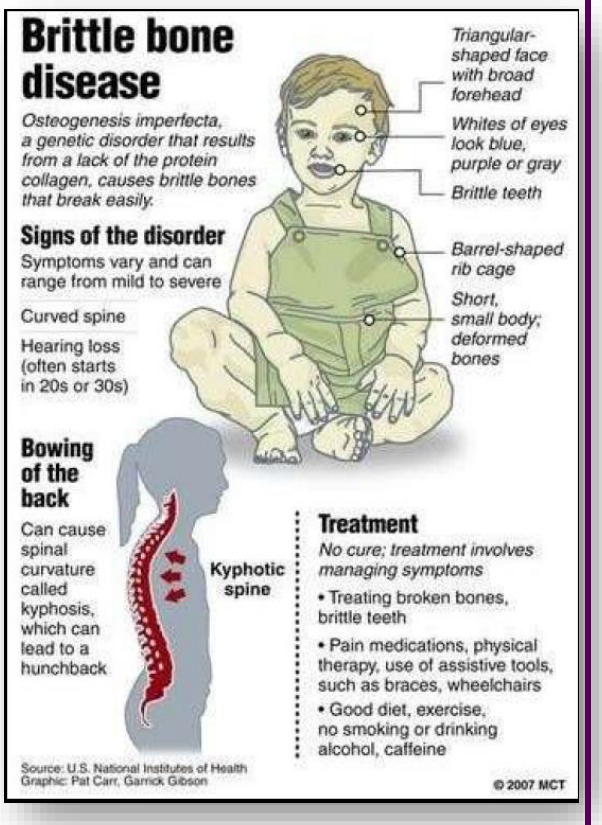
most of the baby die in the uterus or shortly after birth because inability of having normal respiration ➡ their chest wall is collapsing (small chest leading to resp. insufficiency)



Characteristics:

1- Big head
2- Small hand
3- Very sever restriction in the chest wall

- **OSTEOGENESIS IMPERFECTA** Most common inherited disorders of connective tissue



- it has another name "**brittle bone disease**".

- it is a group of disorders, autosomal dominant AD

-it's deficiency of type I collagen synthesis

-**Too little bone**; **fragility** in association with these, patient have Blue **sclera**; **hearing loss**; **teeth abnormalities**

- Type 2 (lethal) and type I (relatively normal life)

Signs of the disorder:

1-curved spine

2.trianguler shaped face with broad forehead

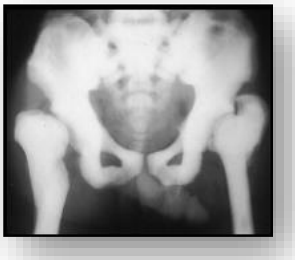
3.blue sclera

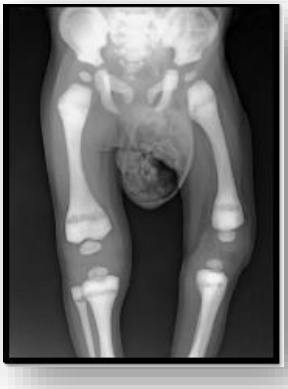
4.brittle teeth

5. barrel-shaped rib cage

6.small body ; deformed bone

- **OSTEOPETROSIS** Marble bone disease "stone bone"





• exactly the opposite of osteoporosis we will talk later about it.
•group of disorders; rare
• Impaired osteoclast function: reduced bone resorption leading to diffuse sclerosis
• Dx: X-ray
• Fractures and leukopenia (penia: deficient) in severe forms (immune deficiency they will be exposed to more opportunistic bacterial infection).

Summary

Congenital Disorders of Bone and Cartilage

Abnormalities in a single bone or a localized group of bones are called **dysostoses** and arise from defects in the migration and condensation of mesenchyme. They manifest as absent, supernumerary, or abnormally fused bones. Global disorganizations of bone and/or cartilage are called **dysplasias.** Developmental abnormalities can be categorized by the associated genetic defect.

- FGFR3 mutations are responsible for achondroplasia and thanatophoric dysplasia, both of which manifest as dwarfism.
- Mutations in the genes for type I collagen underlie most types of osteogenesis imperfecta (brittle bone disease), characterized by defective bone formation and skeletal fragility.
- Mutations in *CA2* and *TCIRG1* result in osteopetrosis (in which bones are hard but brittle) and renal tubular acidosis.

Metabolic disorder:

Osteopenia: decreased bone mass (1-2.5SD below the mean).

Osteoporosis: severe osteopenia; > than 2.5 SD below the mean with increase risk for fractures.

Osteo: bone

Penia: loss

Osteoporosis could be:

Primary osteoporosis(generalized)

- Much more common

- as a general disease of icting the whole community

associated with: senile(aging) postmenopausal

Osteoporosis is a multi-factorial disease; the factors could be:

1-Genetic factors: some people are susceptibleto osteoporosis depending on their genes.

2-Nutrition: low intake of dairy products contains calciumAlso low vitamin D levels and sun exposure.

3-Physical activity: it can prevent osteoporosis to a big extent.
4-Aging
5-Menopause

secondary osteoporosis:

-Much less common

-less serious

-easily treatable Associated with:

Hyperthyroidism (causesystemic osteoporosis)

Malnutrition (low intake ofcalcium from dairy products)

Steroids (for auto immune disease) …. they activation of osteoclast.

***Also, after **fractures** wherebone gets weaker, and in this case, osteoporosis is localized.

* NOW, how do aging and menopause contribute to osteoporosis?

Remember: IL-1 increases osteoclast differentiation, Thus more osteoclasts = osteoporosis

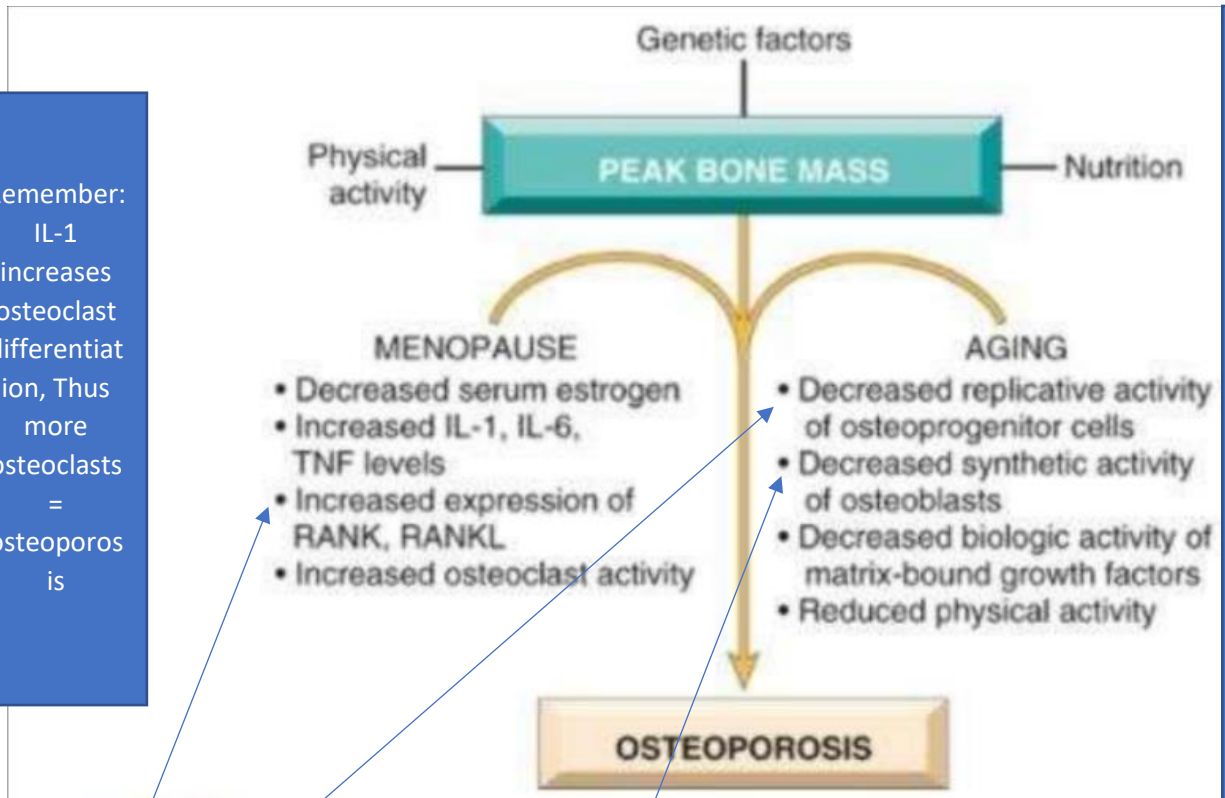


FIG. 21.5 Pathophysiology of postmenopausal and senile osteoporosis (see text).

Remember : estrogen decreases osteoclasts differentiation , thus its decrease leads to more osteoclasts = weakening of bone = osteoporosis

*They contribute in the formation of osteoclast precursor formation.

* Note : Osteoprogenitor cells are bone stem cells that form osteoblasts (bone forming cells)

*Decreased formation of osteoid and hydroxyapatite.

A normal vertebral body

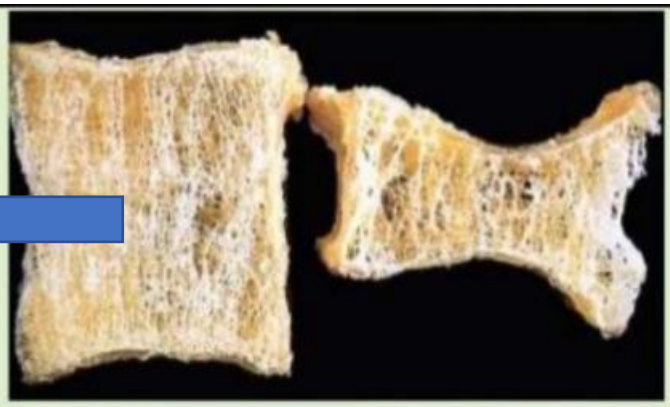


FIG. 21.6 Osteoporotic vertebral body *(right)* shortened by compression fractur..

*sever osteoporosis

*the space is 3 times less than normal .

*Fraction at all level vertebra.

*more matrix

*less spongy bone

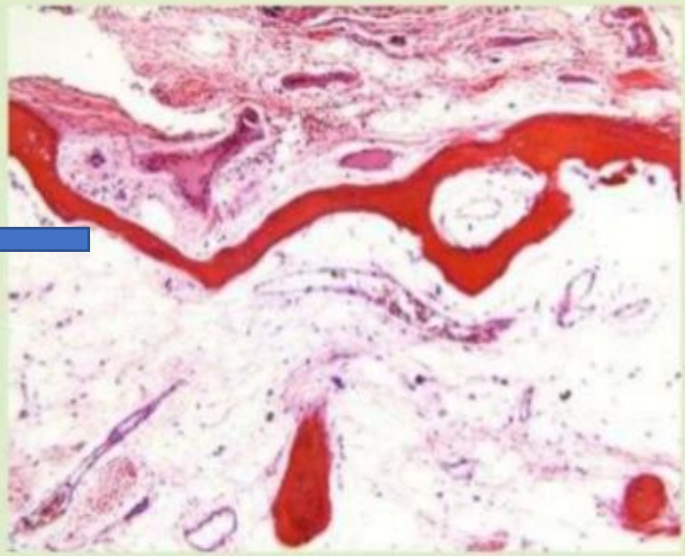


FIG. 21.7 In advanced osteoporosis, both the trabecular bone of the medulla *(b.*

* The red portion is the bone trabeculae, the quantity of them is much lower than normal + the thickness of trabeculae is very thin in osteoporosis.

OSTEOPOROSIS CLINICALLY:

There are many severe outcomes that can be developed from osteoporosis:

1-Vertebral fractures (as shown in the picture above)

2- variable fractures

3- Femur and Pelvic fractures

4- (it's a very serious situation and it is associated with a number of diseases) what are

they??

Femur and Pelvic fractures can result in:

- immobility

- PE (pulmonary embolism) due to DVT=Deep Venous Thrombosis, where a thrombosisin one vein of the body (formed from prolonged bed rest) would travel to reach the pulmonary vein and block it, thus causing death in some cases and its called “the silentkiller”

- pneumonia (40-50K death/yr in USA): due to the long stay in the hospital = hospitalpneumonia = caused by: ex: pseudomonas, klebsiella …

Diagnosis

- special imaging technique, bone mineral density (BMD scan), dualenergy X-ray absorptiometry (DXA or DEXA scan) or bone densitometry

examples:

-If the bone density readings of a patient were -1.5 below SD what would the diagnosis be?

The patient would most probably have

osteopenia

* if the bone density readings of a patient were – 2.7 SD what would the diagnosis be?

The patient would most probably have

Osteoporosis

* if the bone density was -2.3 ……. → Osteopenia

* if bone density was +2.5 ……. → There is no problem in the bone

The rule is:

Osteopenia: (1-2.5)SD in minus = below the mean (mean=normal)

PREVENTION AND TREATMENT:

- Exercise
- Calcium & vitamin D
- Bisphosphonates: reduce osteoclast activity and induce its apoptosis

Denosumab: anti-RANKL; blocking osteoclast activation

- (blocks RANK-L)Hormones (estrogen): =HRT (Hormonal Replacement Therapy)

risking DVT and stroke

-Thus, usually estrogen is combined with another hormone to reduce the sideeffects such as progesterone.
-this will not only help in osteoporosis treatment, but also it helps in decreasing menopausal symptoms.

(Prevention is more important than treatment)