



no.4



MSS

Musculoskeletal System

Pathology

Doctor 2018 | Medicine | JU

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In the last lecture, we Talked about OSTEOPOROSIS, which is a weakening In bones due to a decrease of bone density. Today's lecture will discuss a new bone disorders.

Prevention and treatment

*By **exercising** and a diet rich in calcium and **vitamin D**.

How does exercise affect bones?

physical activity causes new **bone** tissue to form, and this makes **bones** stronger.

Prevention is much more important than treatment.

* **Bisphosphonates**: as they reduce osteoclastic activity and induce its apoptosis.

Remember: **Osteoclasts** are the cells that degrade bone to initiate normal bone remodeling.

***Denosumab**: anti RANKL; blocks osteoclasts activation.

***Hormones (Estrogen)**. *WHY ESTROGEN?*

It inhibits bone resorption.

Treatment with *ESTROGEN* increases the risks of Deep Vein Thrombosis (DVT) and strokes.

Rickets and Osteomalacia

Caused by **vitamin D** deficiency or abnormal metabolism of **vitamin D**.

In children, we call this disorder **Rickets**, while in adults it is called **Osteomalacia**.

decreased mineralization of bone, unmineralized matrix. So, there is less content of calcium than normal bone tissue.

Decreased *mineralization* of bone increases risks of fractures.



Notice *HOW* curved are these bones.

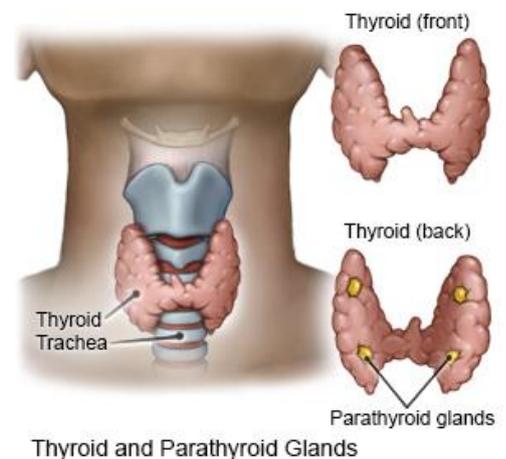
HYPERPARATHYROIDISM (HPT)

Parathyroid is a hormone that raises blood calcium (hypercalcemia) by breaking down the bone.

Thyroid and parathyroid hormones are secreted by different glands and have different functions.

- **HPT** is classified into 3 major categories.
- *Primary HPT is a cause of hyperplasia, adenoma or carcinoma of PTH gland.*
- In both **Secondary** and **tertiary HPT**, parathyroid glands are normal and the problem is the positive feedback due to hypocalcemia.
- Secondary HPT is due to **PHYSIOLOGICAL** stimulation of parathyroid gland due to hypocalcemia.
- As your plasma calcium level is low, your body tries to compensate by secreting parathyroid hormone.

If secondary HPT is untreated, it turns into tertiary HPT.



This table summarizes what we are required to know.

Hyperparathyroidism classification

Different causes and features of hyperparathyroidism - raised parathormone (PTH).

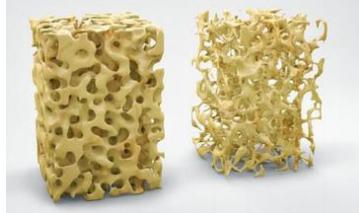
	primary	secondary	tertiary
pathology	Hyperfunction of parathyroid cells due to hyperplasia, adenoma or carcinoma.	Physiological stimulation of parathyroid in response to hypocalcaemia.	Following long term physiological stimulation leading to hyperplasia.
associations	May be associated with multiple endocrine neoplasia.	Usually due to chronic renal failure or other causes of Vitamin D deficiency.	Seen in chronic renal failure.
serum calcium	high	low / normal	high
serum phosphate	low / normal	high	high
management	Usually surgery if symptomatic. Cinacalcet can be considered in those not fit for surgery.	Treatment of underlying cause.	Usually cinacalcet or surgery in those that don't respond.

HPT clinically

BROWN TUMOR



OSTEOPOROSIS



* **Brown tumor**, a bone lesion that is a result of HPT. not a neoplasm but rather simply a mass.

* **osteoporosis**.

* **OSTEITIS FIBROSA CYSTICA (OFC)**, very rare condition, also called **osteitis fibrosa**, **osteodystrophia fibrosa**, and **von Recklinghausen's disease of bone** (not to be confused with **von Recklinghausen's disease**, **neurofibromatosis type I**).

Cause weakening of the bone.



Summary

Metabolic Disorders of Bone

- **Osteopenia** and **osteoporosis** represent histologically normal bone that is decreased in quantity. In osteoporosis the bone loss is sufficiently severe to significantly increase the risk of fracture. The disease is very common, with marked morbidity and mortality from fractures. Multiple factors including peak bone mass, age, activity, genetics, nutrition, and hormonal influences contribute to its pathogenesis.
- **Osteomalacia** is characterized by bone that is insufficiently mineralized. In the developing skeleton, the manifestations are characterized by a condition known as **rickets**.
- **Hyperparathyroidism** arises from either autonomous or compensatory hypersecretion of PTH and can lead to **osteoporosis**, **brown tumors**, and **osteitis fibrosa cystica**. However, in developed countries, where early diagnosis is the norm, these manifestations are rarely seen.

Paget disease (Osteitis Deformans)

- It is *BADLY FORMED* Bone structure without itis (inflammation).

Can be divided into 3 phases:

1. **Lytic**: More osteoclastic activity; bone is being resorbed.
2. **Mixed**: *Osteoblastic and Osteoclastic activity at the same time.*
3. **Sclerotic**: Very High Osteoblastic activity; Bone is being built at very high rate which may lead to Osteosclerosis (more bone mass)

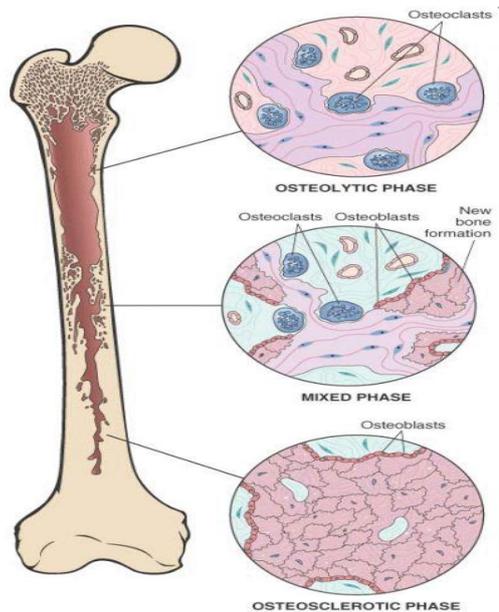
**Note: these phases could be sequential or non-sequential but the usual clinical scenario is:

Lytic → Mixed → sclerotic.

-We don't know the etiology (the cause) of Paget disease, some scientists blame viruses such as measles and RNA viruses, but if you are asked about the cause you will answer that the cause is unknown but there are some geographic variations (1% in USA), many environmental and acquired factors and many genetic factors

-50% of familial Paget regardless of the severity and 10% of sporadic have *SQSTM1* gene mutations.

* Paget disease Causes increase in **RANK** expression (stimulation), and decrease in **OPG** (**osteoprotegerin**) expression "inhibition" which will increase the osteoclastic activity.



This picture shows the 3 phases of Paget disease.

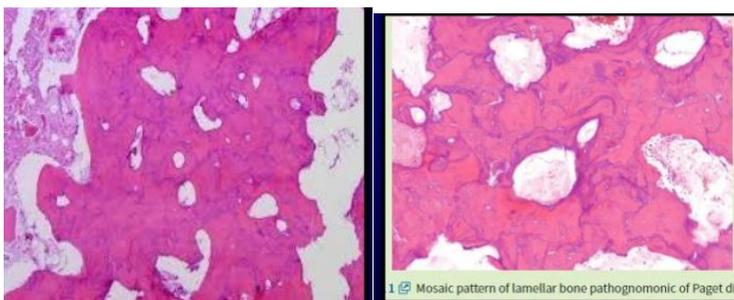
1. Osteolytic phase:

osteoclastic activity is very active and lytic lesions in the bone will be formed.

2. Mixed phase: osteoclastic Vs. osteoblastic activity.

3. osteosclerotic phase: more osteoblastic activity (increased bone density)

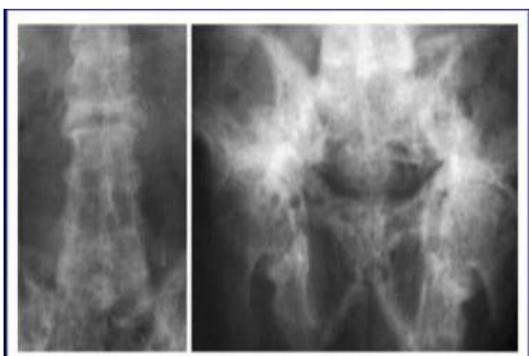
If your patient comes up with radiograph or histological sections such as those in pictures below you should be able to know that he is absolutely has paget diseas.



Very abnormal bone appearance (mosaic appearance).

Notice that it is thick bone trabeculae.

Note: mosaic bone appearance is different from woven bone as the doctor said 😊



As you can see that there are some translucent (radiolucent) areas: more black so it is in osteolytic phase.

and there are some dense areas: more white so it is in osteosclerotic phase.

There are also mixed areas 😊

Paget clinically : what happens with paget's patients:

- Paget is **polystotic** (more than one bone is involved (generalized)) in 85% of patients; 15% Monostotic (one bone is affected only).
- *Axial Skeleton is more affected than the rest (vertebral body, pelvic bone, prox. Femur).*
- *Most are mild and asymptomatic and Pain is caused by micro fractures or nerve compression.* This is very important point 😊
- Severe forms can affect the skull and cause **Leontiasis ossea (lion face)** or **platybasia**. (invagination of skull base), Other symptoms are secondary **osteoarthritis, fractures** and **osteosarcoma** (primary bone sarcoma) (1%)



Liontiasis ossea (lion face), platybasia

- DX: x-ray; **increase** in serum **Alkaline Phosphatase**, Normal **Ca** and **PO4**
- * you can differentiate between hyperparathyroidism's patients and Paget's patients by the amount of **alkaline phosphatase** (increased in Paget's patients)
- * Minimal traumas can cause fractures for Paget disease patients.

Good luck