

Part 5:

Regulation of calcium metabolism (Bone mineral homeostasis)

1. Primary hormonal regulators of Ca^{2+} metabolism and bone mineral homeostasis:

Parathormone (PTH)	Calcitonin (CT)	Vitamin D
It is a single chain polypeptide secreted by the parathyroid glands. Its secretion is not under pituitary control but controlled by the level of serum Ca^{2+}. Mechanism and effects: PTH acts on specific receptors in bone and kidney leading to $\uparrow$ serum Ca^{2+} and $\downarrow$ PO_4 through: Bone: $\uparrow$ bone resorption. Intestine: $\uparrow$ Ca^{2+} absorption (through activation of vit D). Kidney: $\uparrow$ Ca^{2+} reabsorption and PO_4 excretion. Therapeutic uses:	It is a single chain polypeptide secreted by the C-cells of the thyroid. Its secretion is not under pituitary control but controlled by the level of serum Ca^{2+} and vitamin D. Mechanism and effects: CT acts on specific receptors in bone and kidney leading to $\downarrow$ serum Ca^{2+} and PO_4 through: Bone: $\downarrow$ bone resorption. Intestine: $\downarrow$ Ca^{2+} absorption. Kidney: $\downarrow$ reabsorption of Ca^{2+} and PO_4. Therapeutic uses:	It is fat-soluble vitamin found in 2 forms: Vitamin D₂ (ergocalciferol): plants. Vitamin D₃ (cholecalciferol): animals, and can be synthesized in human skin by the action of UV rays. The two forms must be activated by 2 OH at site 25 (liver) and 1 (kidney). Mechanism and effects: Vit D acts on DNA receptors to synthesize proteins necessary for Ca^{2+} transport. Bone: the effect is complex: when bone Ca^{2+} is deficient (rickets), vit D $\uparrow$ Ca^{2+} deposition (calcification) but excess vit D in normal subjects leads to bone resorption and hypercalcemia. Intestine: $\uparrow$ Ca^{2+} absorption from the intestine. Kidney: $\uparrow$ Ca^{2+} and PO_4 reabsorption. Therapeutic uses:

VD3 $\leftarrow$ $\frac{1000}{1000000}$ mg/dL

S.C

S.C

oral

From $\frac{1}{2}$ dehydro cholesterol found in the keratinocyte

Calcibindin / PMP-6 / PMCAbl

$\leftarrow$ تخفيض $\leftarrow$ $\frac{1000}{1000000}$ mg/dL

if Plasma Ca^{2+} is normal, VD3 activate ob. if P. Ca^{2+} is low, VD3 release RANKL + IL-6 to activate O.C.

DCP PCP

| Hypercalcemia

Causes: In over 90% of cases hypercalcemia is due to either **hyperparathyroidism** or **malignancy** (especially myeloma). Hypercalcemia normally suppresses PTH and so PTH is therefore the best first test to identify the cause of hypercalcemia.

Management of acute hypercalcemia

- ! Saline diuresis: 500-1000 ml/hour plus furosemide to increase urine flow and enhance Ca^{2+} excretion.
- ! Hydrocortisone: 100 mg i.v. to enhance Ca^{2+} excretion.
- ! Intravenous bisphosphonates.
- ! Hemodialysis especially when renal failure is present.

| Hypocalcaemia

Causes: Hypoparathyroidism (N.B. tetany occurs when serum Ca^{2+} falls $< 7\text{mg/dl}$), chronic renal failure, vitamin D deficiency, etc.

Treatment

① Diet rich in calcium and low in phosphate

② Calcium gluconate: slowly (i.v.) (in acute conditions). Toxic effect

③ Vitamin D: to $\uparrow \text{Ca}^{2+}$ absorption from intestine

④ Thiazide diuretics.

⑤ Glucocorticoids.

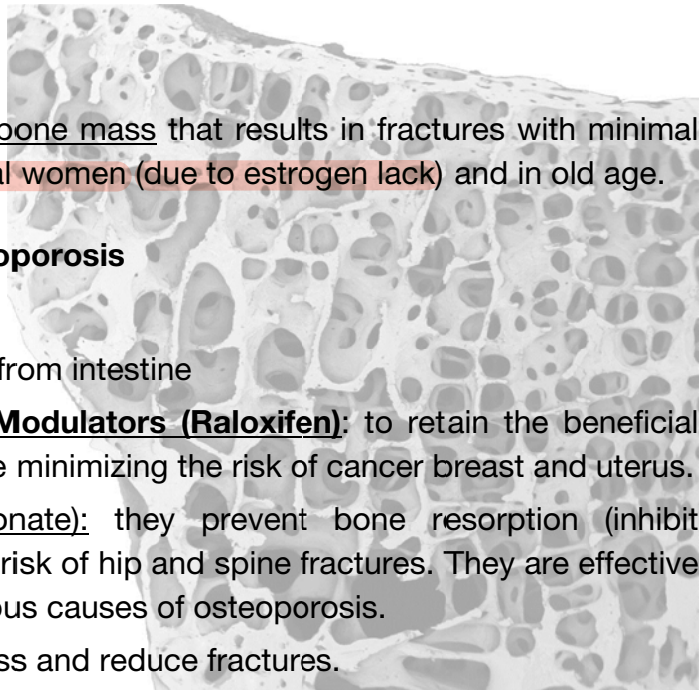
⑥ Acid.

| Osteoporosis

Definition: it is a condition of low bone mass that results in fractures with minimal trauma. It occurs in postmenopausal women (due to estrogen lack) and in old age.

Prevention and treatment of osteoporosis

- ! Diet rich in **calcium**.
- ! **Vitamin D**: to $\uparrow \text{Ca}^{2+}$ absorption from intestine
- ! **Selective Estrogen Receptor Modulators (Raloxifen)**: to retain the beneficial effects of estrogen on bone while minimizing the risk of cancer breast and uterus.
- ! **Bisphosphonates** (e.g. risedronate): they prevent bone resorption (inhibit osteoclastic activity) and reduce risk of hip and spine fractures. They are effective in both men and women for various causes of osteoporosis.
- ! **Calcitonin**: to increase bone mass and reduce fractures.
- ! **Teriparatide**: a recombinant form of PTH that has been recently approved for treatment of osteoporosis. It stimulates new bone formation and reduces risk of fractures.



يعني للمو بيا لج

1- HypoCalcemia

2- $\uparrow \text{K}^+$ Toxic effect.

3- Tetany.

B T W

ال Ca^{2+} يقل ال Toxic effect
Hyperkalemia
تبع effect
على القلب

السبب لو واحد مع Kidney
Alphacalcidol أو Calcitriol
بأعطيه

Orally منه أغراض

أبون
ال Ca^{2+}
مع حمض
Gluconic
Acid

- ! **Slow release fluoride preparation:** is a new treatment. It may reduce rates in postmenopausal osteoporosis.

Drug-induced osteoporosis

1. Corticosteroids.
2. Heparin.
3. Interferons.
4. Alum containing antacids.

**Part 6: Sex Hormones****Estrogen**

- ! **Natural estrogens:** estradiol, estrone and estriol
- ! **Semisynthetic estrogens:** Ethinyl estradiol and mestranol.
- ! **Synthetic estrogens:** diethyl stilbesterol.

Physiologic effects

- ! Normal development of genital tract and breast.
- ! Development of ♀ secondary sex characters.
- ! Metabolic effects:
 - ! Increase bone mass and prevent bone resorption.
 - ! Increase blood glucose and TGs.
 - ! Salt and water retention.
- ! Increase blood coagulation and platelet adhesiveness.

Therapeutic uses

- ! Contraceptive pills.
- ! Dysfunctional uterine bleeding.
- ! Replacement therapy in ovarian hypofunction.
- ! Postmenopausal symptoms e.g. atrophic vaginitis and osteoporosis.
- ! Cancer prostate.

Adverse effects and contraindications: see contraceptive pills.

Anti-estrogens:**1. Clomiphene citrate (Clomid)**

- ! Clomiphene blocks estrogen receptors in hypothalamus and pituitary → ↑ FSH and LH → stimulate ovulation.
- ! It is used to **stimulate ovulation** in infertile women with normal pituitary function.
- ! **Adverse effects:** Ovarian enlargement and hot flushes.