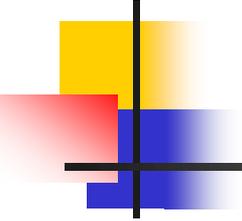


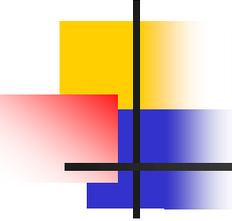
Pharmacology of Parathyroid Gland, Vitamin D & Calcium

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Faculty of Medicine, Mutah University



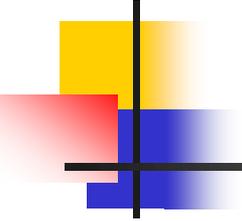
Content

- Calcium metabolism; Ca homeostasis
- Parathyroid glands
- Vitamin D
- Calcium and bone related-diseases



Calcium metabolism or calcium homeostasis

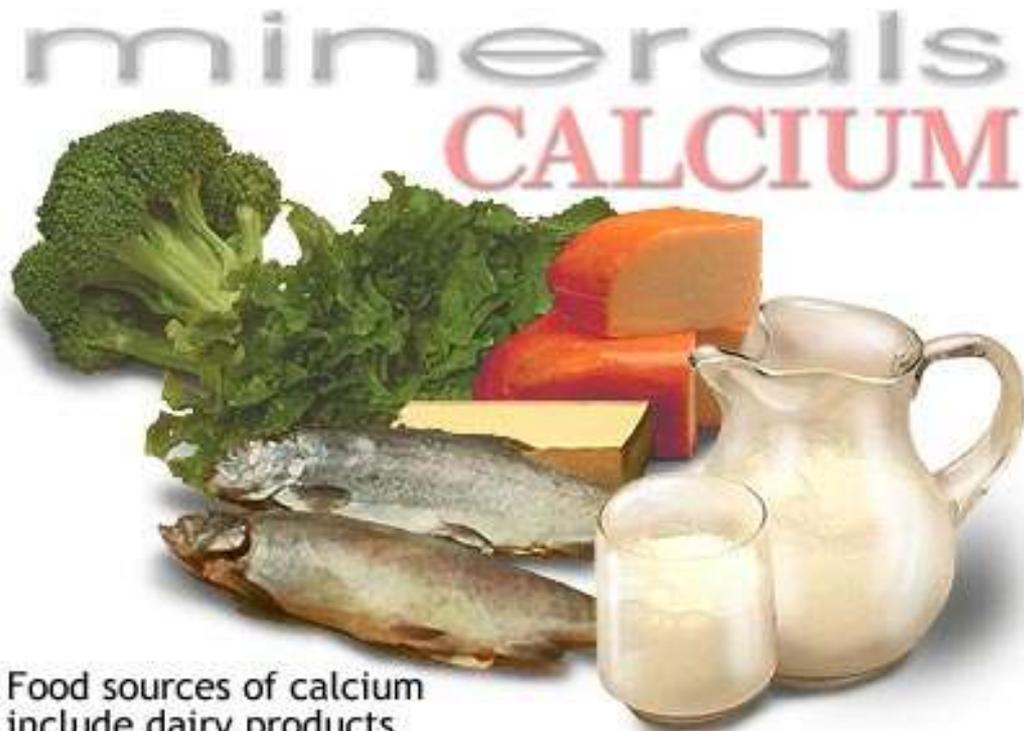
- Is the mechanism by which body maintains adequate levels of Ca
- Disturbance of this mechanism leads to:
 - **Hypercalcemia**
 - **Hypocalcemia**



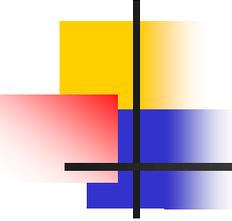
Importance of Ca in body

- One of **the most important minerals for general cellular function**
- **Ca controls membrane excitation**: there is influx of Ca through specific Ca channels during excitatory process in **nerve & muscle**
- It is necessary for **muscle contraction**
- Ca is a major **constituent of bone & teeth**

Calcium Sources

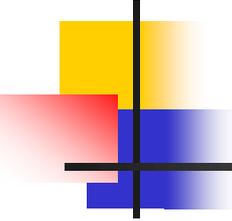


Food sources of calcium include dairy products, green leafy vegetables, and salmon, and sardines



Calcium Distribution in the Body

- Average adult body contains **1000g** of Ca
- Over **99%** of Ca is stored in **skeleton**
- The remaining **1%** in **extracellular fluid & cellular cytoplasm**
- The total **Ca in plasma** is about **9-10 mg/dL**



Regulators of Ca homeostasis

1. Principal regulators:

- **Parathyroid hormone (PTH), Vitamin D**

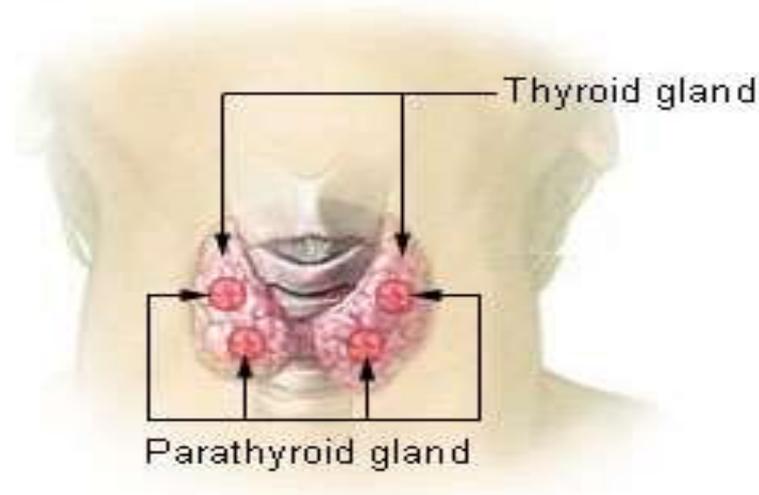
2. Second regulators: calcitonin, glucocorticoids & sex steroids (estrogens)

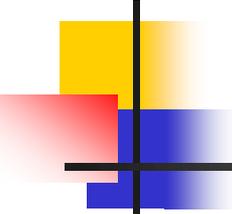
3. Other ions such as sodium, fluoride

Parathyroid hormone (PTH)

- Is a single chain peptide hormone, composed of 84 amino acids
- It is produced in **parathyroid glands**

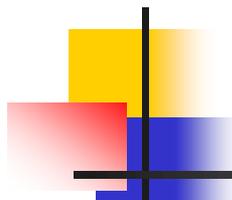
Thyroid and Parathyroid Glands





Parathyroid hormone (PTH)

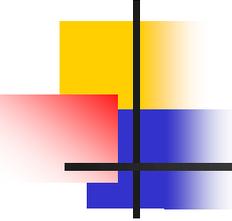
- **When plasma Ca levels are low, PTH secretion increases:**
 - releases of Ca from bones
 - increases Ca reabsorption from kidney
 - stimulates Ca absorption from small intestine
- **If plasma Ca is high, PTH secretion is inhibited & Ca is deposited in bones**



Parathyroid hormone (PTH)

1. Effects on bone:

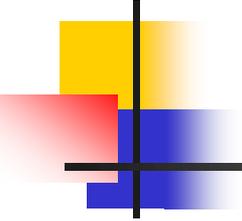
- PTH is involved in **remodeling of bone** (bone resorption & formation)
- **Bone resorption** is process by which **osteoclasts** (responsible for bone resorption), breakdown bone & releases minerals
- PTH **increases activity & number of osteoclasts**, which results in **increased Ca in plasma**



Parathyroid hormone (PTH)

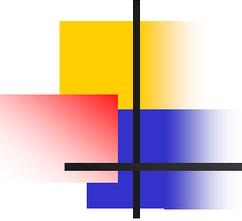
2. Effects on the kidney:

- PTH promotes active reabsorption of Ca & magnesium by ascending loop of Henle
- Increases phosphate excretion
- Stimulates synthesis of **1,25-dihydroxyvitamin D (1,25(OH)₂D)**



Vitamin D

- Is a prohormone that serves as a precursor to a number of biologically active metabolites
- It is produced in **skin**, from conversion of **7-dehydrocholesterol** to **previtamin D3** by action of **sunlight**, and then is converted to **vitamin D3 (cholecalciferol)**

- 
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- Many of **dairy products** in diet are fortified with **ergocalciferol**, **a synthetic vitamin D2** that has activity equal to **vitamin D3**

Vitamin D Sources

vitamin **D**

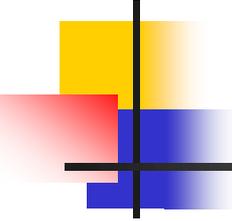


The body itself makes vitamin D when it is exposed to the sun

Cheese, butter, margarine, fortified milk, fish, and fortified cereals are food sources of vitamin D

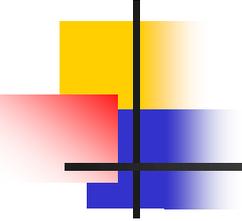


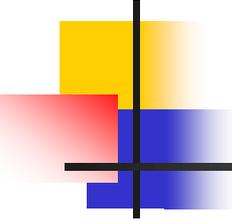
ADAM.



Vitamin D

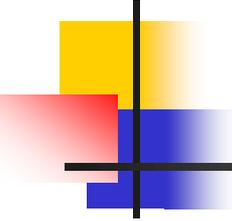
- **Vitamins D2 and D3 are made more active by two hydroxylation reactions:**
 - **1 α -hydroxylation in kidney**
 - **25-hydroxylation in liver**
 - to form **1 α -25-dihydroxycholecalciferol (calcitriol)** (the most active natural form of vitamin D)

- 
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- **Alfacalcidol (one-alpha)** requires only **hepatic hydroxylation** to become highly active **calcitriol**,
 - therefore, it is effective in **renal failure** since defective renal hydroxylation stage is bypassed



Vitamin D

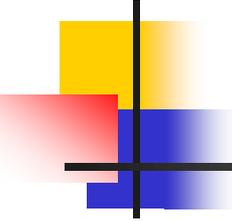
- **Biological actions of vitamin D:**
 - Promotes absorption of Ca & Phosphate from gut
 - Promotes renal tubular reabsorption of Ca and P



Vitamin D

■ **Indications:**

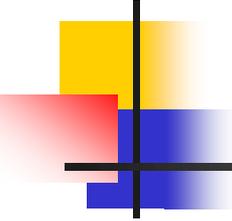
- Prevention & cure of **rickets & osteomalacia**
- **Psoriasis**
- **Calcitriol** is licensed for management of **postmenopausal osteoporosis**



Vitamin D

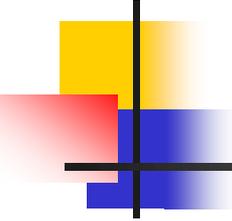
- **Doses and preparations:**

- **Simple vit D deficiency** can be prevented by taking orally **10 micrograms of ergocalciferol** daily
- **Alfacalcidol & calcitriol** should be prescribed if patients with **severe renal impairment** require vitamin D therapy



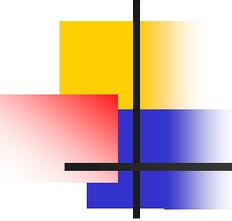
Calcitonin

- A hormone secreted by **parafollicular cells of thyroid gland**
- Effects of **PTH & calcitonin** are **antagonistic**
- Principal effects of calcitonin are to **lower serum Ca & P** by actions on **bone & kidney**
- It **inhibits** osteoclastic bone resorption
- In kidney, it **reduces** both Ca & P reabsorption



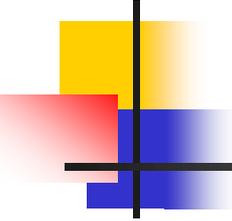
Calcitonin

- **It is a useful drug for treatment of:**
 - **Hypercalcemia** (rapid effect)
 - **Paget's disease of bone** (relief of pain & to relieve compression of nerves)
 - Metastatic bone cancer pain
 - Postmenopausal osteoporosis



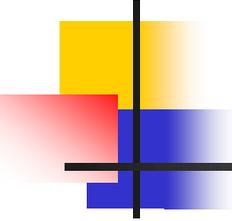
Glucocorticoids

- **Alter bone mineral homeostasis by:**
 - Antagonise vitamin D-intestinal Ca absorption
 - Stimulate renal Ca excretion
- **Prolonged administration** causes osteoporosis in adults, retarded skeletal development in children



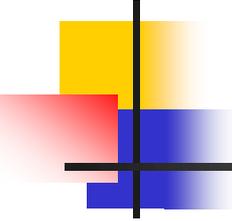
Estrogens

- Estrogens **reduce bone resorbing action of PTH**
- Estrogen administration leads **to increased 1,25(OH)₂ D level in blood**
- The principal therapeutic application for estrogen **treatment or prevention of postmenopausal osteoporosis**



Bisphosphonates

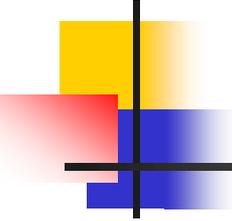
- **Action:** inhibit activation & function of osteoclasts
- **Alendronate, pamidronate, risedronate** are licensed for the treatment of osteoporosis
- Others are used in Paget's disease of bone & hypercalcemia due to cancer



Calcium and Bone-Related Diseases

1. Hypocalcemia

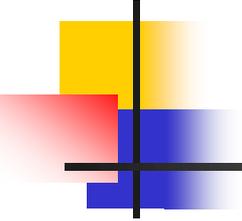
- **Features are neuromuscular:** tetany, paresthesis, laryngospasm, muscle cramps, & convulsions
- **Causes of hypocalcemia:**
 - Hypoparathyroidism, vitamin D deficiency, renal failure, malabsorption



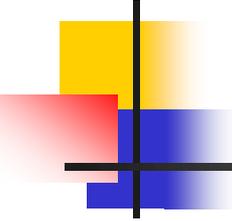
Treatment of hypocalcemia

1. Calcium (i.v, oral)

- **Calcium gluconate** is preferred for **i.v. use** because it is less irritating to veins (in acute hypocalcemia)
- **Calcium carbonate** is preferred for **oral use** because of its high percentage of Ca, low cost

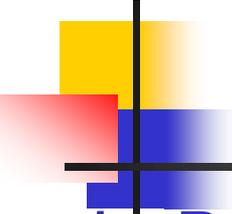


2. Vitamin D: when rapid action is required, $1,25 \text{ (OH)}_2 \text{ D}$ (calcitriol) is vitamin D metabolite of choice, it is capable of raising serum Ca within **24-48 hrs**



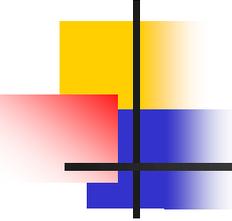
2. Hypercalcemia

- Hypercalcemia causes CNS depression, including coma, and is potentially lethal (**cardiac arrest**)
- **Causes of hypercalcemia:**
 - Hyperparathyroidism, cancer, hypervitaminosis D, sarcoidosis, immobilisation



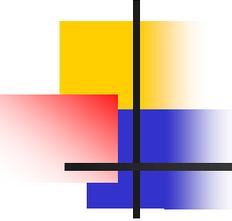
Treatment of hypercalcemia

1. Rehydration with **saline solution** (restores urine flow) & **diuresis** with a loop diuretic such as furosemide (enhance urine flow & increase renal Ca excretion)
2. **Bisphosphonates**
3. **Calcitonin**



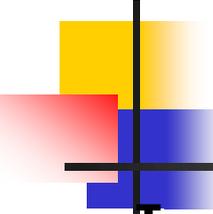
Treatment of hypercalcemia

4. **Phosphate**: i.v. should be used only after other methods have failed to control symptomatic hypercalcemia
5. **Dialysis** is quick and effective in severe cases or with renal failure



3. Nutritional rickets

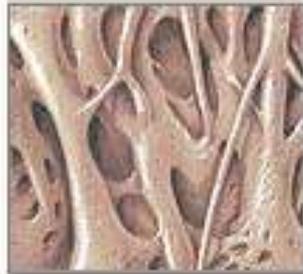
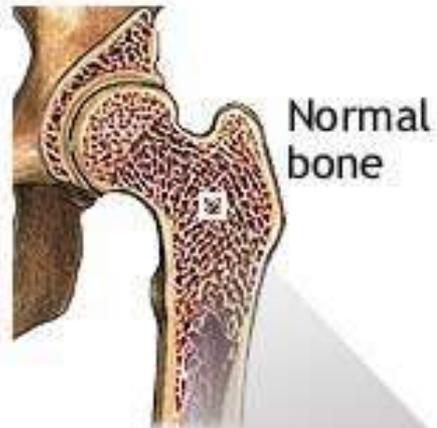
- Is a softening of bones in children, potentially leading to fractures & deformity
- It can occur in adults
- Causes: vitamin D deficiency, lack of adequate Ca in diet
- **Treatment:**
 - Daily intake of 400 units of vitamin D
 - Diet should contain Ca & P

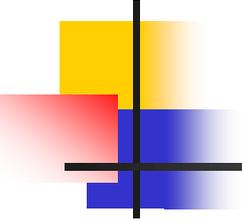


4. Osteoporosis

- **Is abnormal loss of bone predisposing to fractures**
- **bone mineral density is reduced**, bone microarchitecture is disrupted
- It is **common in women after menopause** (post-menopausal osteoporosis) but may develop in men & premenopausal women
- **1 in 3 women & 1 in 12 men** over age of 50 have osteoporosis

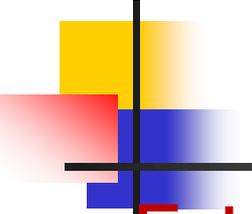
7. Osteoporosis





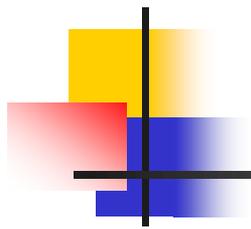
Causes of Osteoporosis

- Side effect of chronic administration of glucocorticoids
- Manifestation of endocrine disease such as hyperparathyroidism
- Feature of malabsorption syndrome
- Alcohol abuse
- Idiopathic (without obvious cause)



Treatment of Osteoporosis

- **Estrogen replacement therapy**
 - Postmenopausal osteoporosis is due to estrogen deficiency & is treated with estrogen
- **Bisphosphonates:** alendronate & more recently risedronate
- **Calcitonin:** reduces bone resorption acutely
- **Dietary Ca supplements & vitamin D**



Thank you