FAT SOLUBLE VITAMIN DEFICIENCIES

BY AFRAH ALI
ROLL NO. 9

INTRODUCTION

- Organic compounds with vital roles as cofactors in certain metabolic pathways
- Fat soluble vitamins: vitamins A, D, E and K
- Water soluble vitamins of the B complex group and vitamin C

22.28 Summary of clinically important vitamins and WHO recommended daily intakes[1]

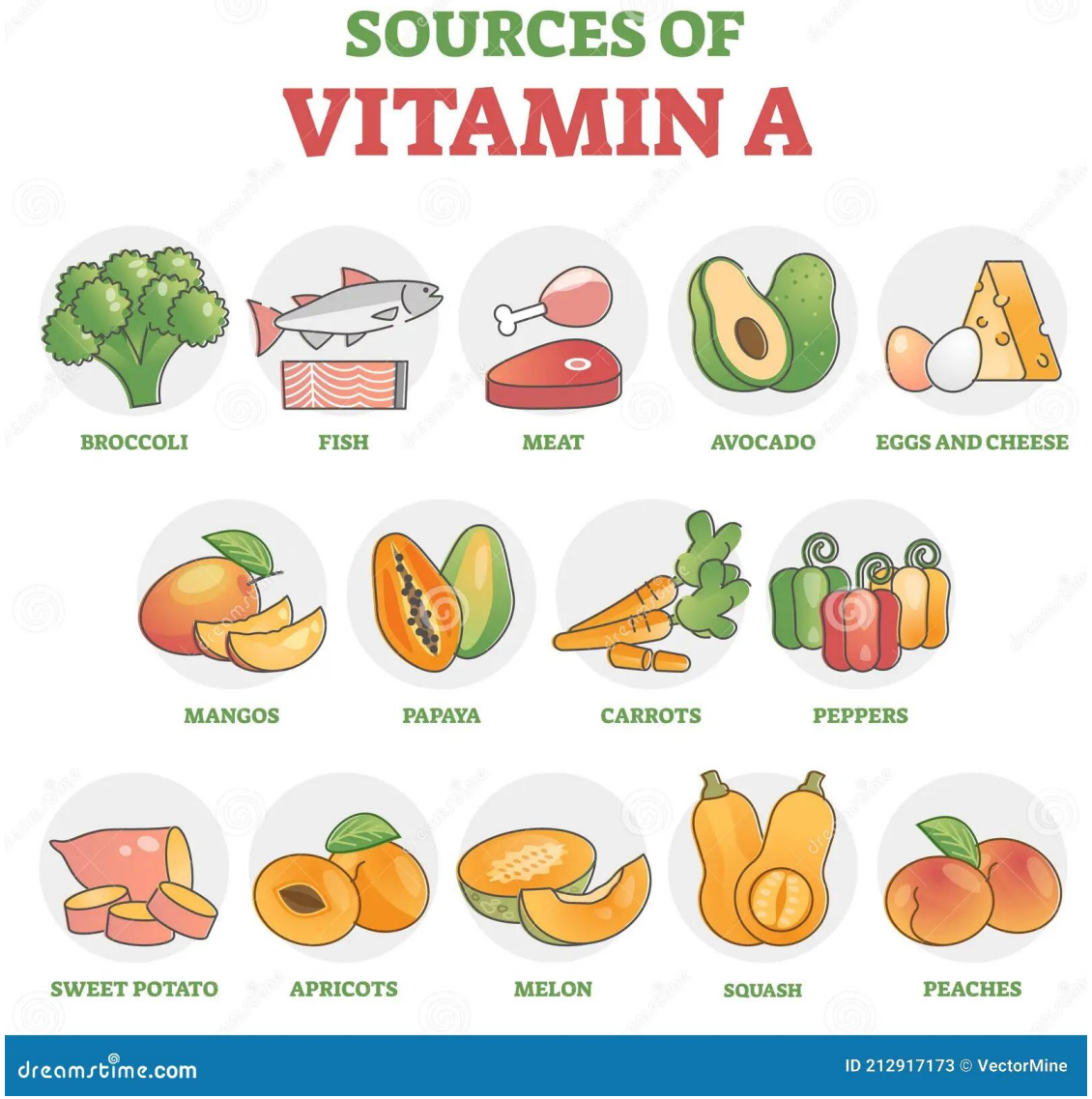
Vitamin	Sources[2]		Reference nutrient intake (RNI)[3]
	Rich	Important	
Fat-soluble			
A (retinol)	Liver	Milk and milk products, eggs, fish oils	700 µg men 600 µg women
D (cholecalciferol)	Fish oils	Ultraviolet exposure to skin Egg yolks, margarine, fortified cereals	10 µg if >65 years or no sunlight exposure
E (tocopherol)	Sunflower oil	Vegetables, nuts, seed oils	No RNI. Safe intake: 4 mg men 3 mg women
K (phylloquinone, menaquinone)	Soya oil, menaquinones produced by intestinal bacteria	Green vegetables	No RNI. Safe intake: 1 µg/kg

VITAMIN A (RETINOL)

Preformed vitamin A (retinyl esters) → Organ meats (especially liver, kidney)

Provitamin A carotenoids → fruits and vegetables, especially *yellow-orange vegetables* (pumpkin, carrot, sweet potato), and *leafy green vegetables* (spinach, broccoli)

One of the most abundant carotenoids is **β-carotene**



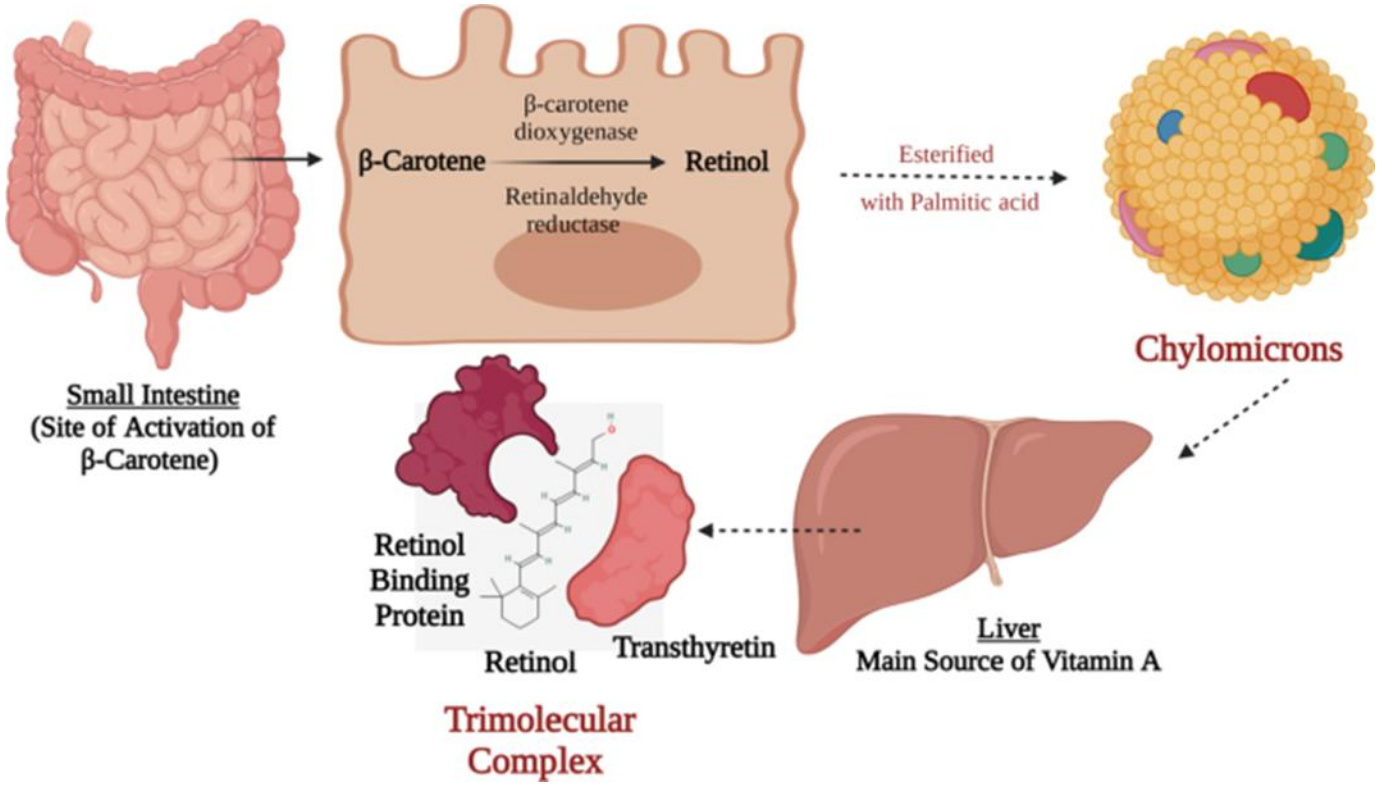
VITAMIN A IN THE BODY

- Three forms → the alcohol retinol, the aldehyde retinal, and retinoic acid.

The 2 essential metabolites of vitamin A in the body are :

- All-trans retinoic acid - for cell differentiation and regulation of gene transcription and is the ***most bioactive form of vitamin A***
- 11-cis retinal - the light-absorbing chromophore of the ***visual pigments rhodopsin and iodopsin***

VITAMIN A METABOLISM

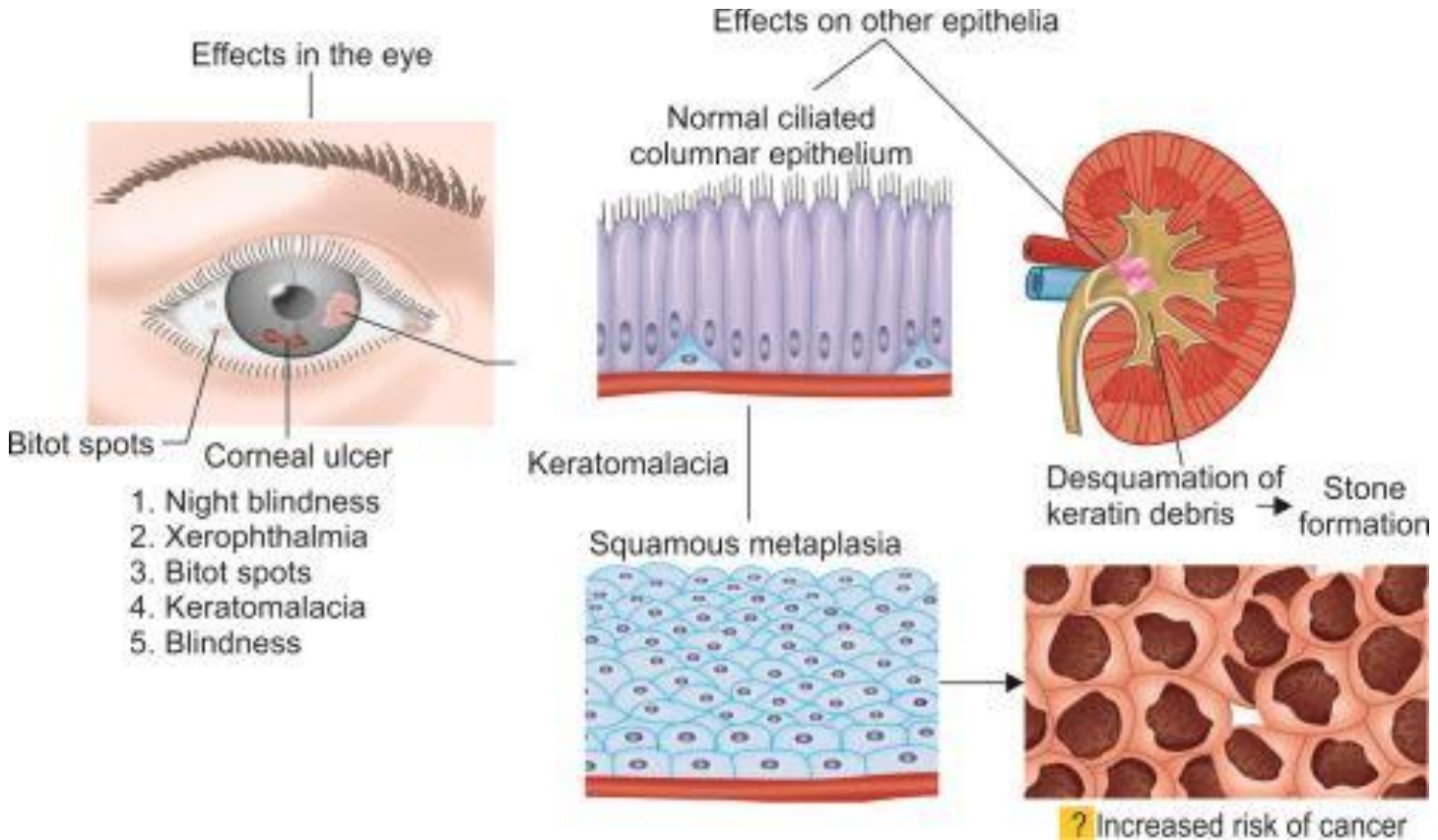


CAUSES OF VITAMIN A DEFICIENCY:

- Inadequate dietary intake
- Impaired intestinal absorption
- Reduced storage in liver
- Chronic alcholism

VITAMIN A DEFICIENCY

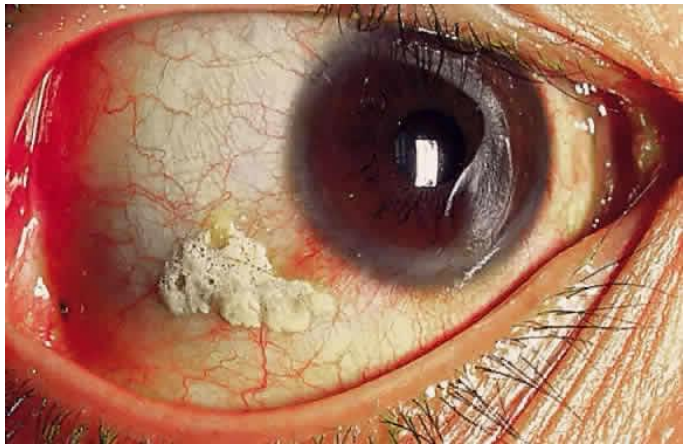
The most obvious symptoms of vitamin A deficiency are associated with **changes in epithelial cell morphology and functions**



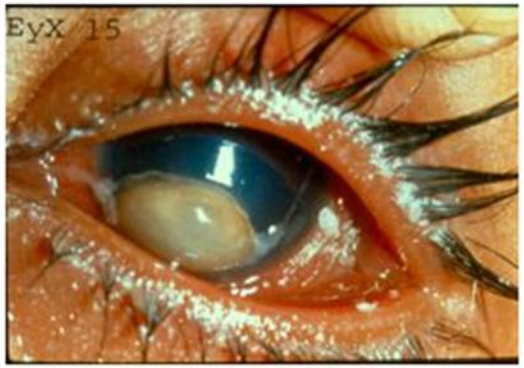
Xerophthalmia

XN	Night blindness
X1A	Conjunctival xerosis
X1B	Bitot's spot
X2	Corneal xerosis
X3A	Corneal ulceration/keratomalacia (< $^1/_3$ corneal surface)
X3B	Corneal ulceration/keratomalacia (≥ $^1/_3$ corneal surface)
XS	Corneal scar
XF	Xerophthalmic fundus

Treatment with vitamin A, up to the stage of keratomalacia, is effective in rapidly repleting the individual and saving vision.



Corneal Xerosis(X2)



Keratomalacia (X3)

DIAGNOSIS AND TREATMENT

- **Serum retinol:** <0.7 µmol/L (0.35-0.7 µmol/L – deficient, <0.35 µmol/L – very deficient)
- In children:

  <6 months: 50,000 IU

  6 months – 12 months: 1,00,000 IU

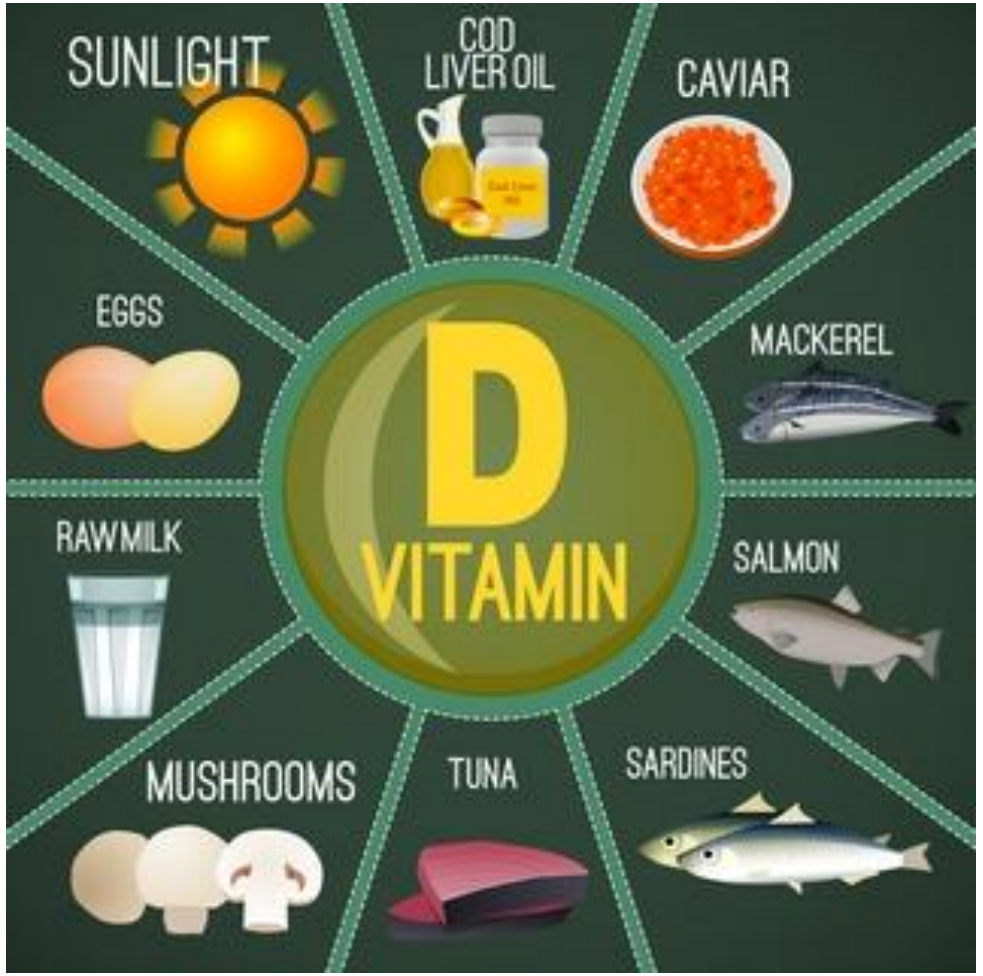
  >12 months: 2,00,000 IU

- Repeated moderate or high doses of retinol can cause liver damage, hyperostosis and teratogenicity
- Acute overdose leads to nausea and headache, increased intracranial pressure and skin desquamation. Excessive intake of carotene causes harmless orange pigmentation of the skin (hypercarotenosis).

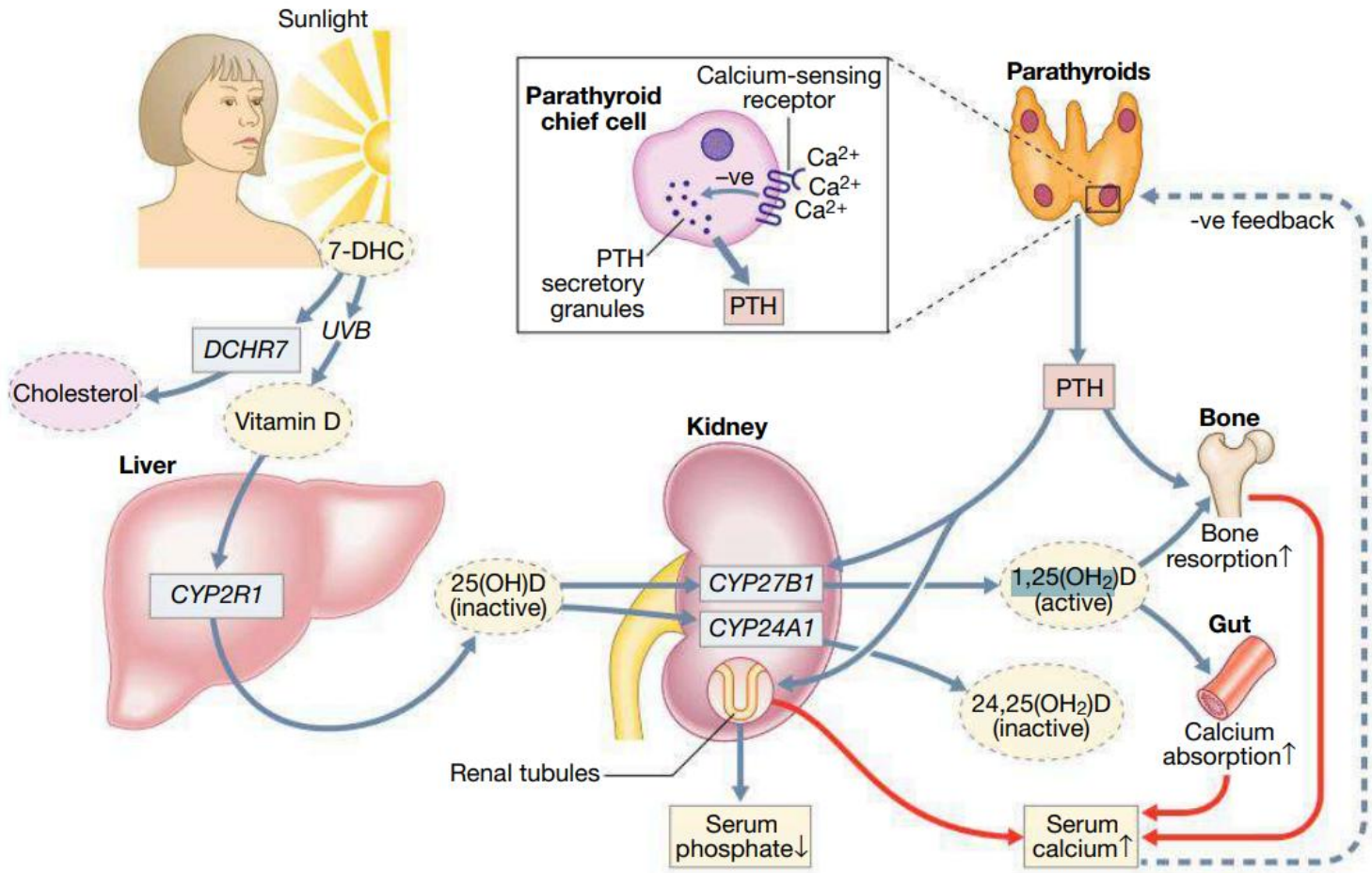
VITAMIN D

- Normal level is above **50 nmol/L**

- Vitamin D (also known as cholecalciferol) comes from two sources: *70% is made in the skin*, where 7-dehydrocholesterol is converted to cholecalciferol under the infuence of ultraviolet light, whereas the remaining *30% is derived from the diet*

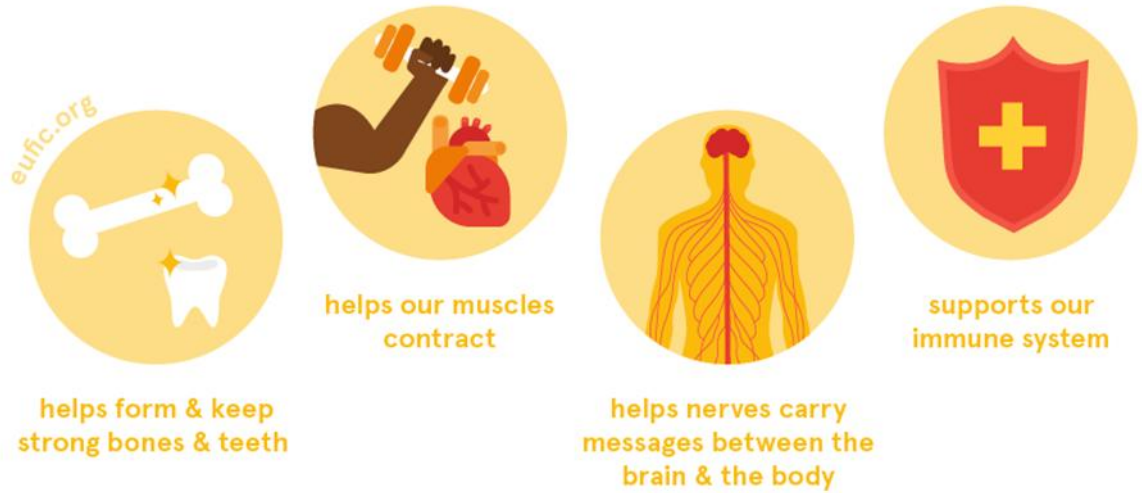


METABOLISM


Sunlight
7-DHC
DCHR7
UVB
Cholesterol
Vitamin D
Liver
CYP2R1
Parathyroid chief cell
Calcium-sensing receptor
Ca2+
Ca2+
Ca2+
–ve
PTH secretory granules
PTH
Parathyroids
-ve feedback
PTH
Kidney
25(OH)D (inactive)
CYP27B1
CYP24A1
1,25(OH2)D (active)
24,25(OH2)D (inactive)
Renal tubules
Serum phosphate↓
Serum calcium↑
Bone
Bone resorption↑
Gut
Calcium absorption↑

FUNCTIONS

- Necessary for GI absorption of calcium
- Increases absorption of phosphate
- Direct actions on bone, including mediating resorption



CLINICAL FEATURES AND INVESTIGATIONS

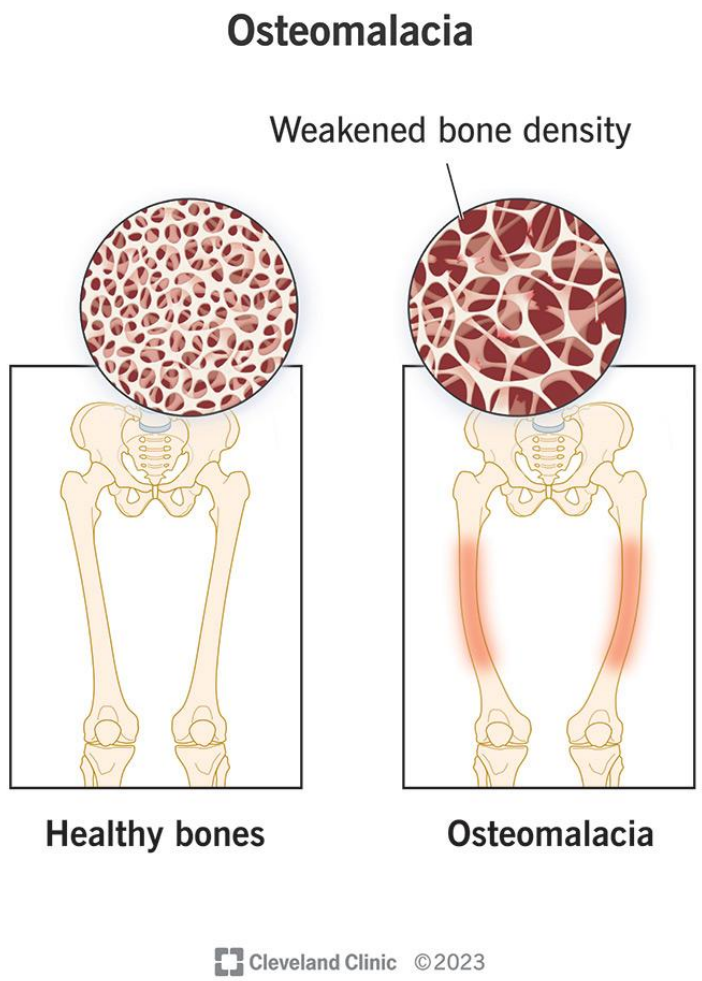
- Low circulating levels of vitamin D do not cause symptoms unless the vitamin D deficiency is severe, so the diagnosis of vitamin D deficiency is primarily made as the result of biochemical testing
- If vitamin D deficiency is prolonged and severe, then osteomalacia, rickets and hypocalcemia may occur
- Investigations for serum 25(OH)D, PTH, serum calcium, phosphate and ALP are to be made

MANAGEMENT

- Vitamin D supplements should be considered in patients who have low 25(OH)D levels and raised levels of PTH
- In most young adults, greater exposure to UV light and cholecalciferol in a dose of 800 IU daily should be suffcient
- Short courses of high-strength vitamin D can also be used, such as 20,000 IU once weekly for 4–6 weeks.
- Similarly, patients who are receiving intravenous bisphosphonates and denosumab for osteoporosis should have vitamin D deflciency corrected by supplementation to reduce the risk of hypocalcaemia

OSTEOMALACIA

- *Bone softening and weakness*
- They remain prevalent in older housebound individuals, who may have a poor diet and limited sunlight exposure, in people who wear facial coverings, and in people with malabsorption
- Result of chronic secondary hyperparathyroidism, invariably associated with Vitamin D deficiency



PATHOGENESIS

- The sustained elevation in PTH levels maintains normal levels of serum calcium by increasing bone resorption, which eventually causes progressive demineralisation of the skeleton.
- Phosphate released during the process of bone resorption is lost through increased renal excretion, resulting in hypophosphataemia
- The raised levels of PTH stimulate osteoblast activity and cause new bone formation, but the matrix is not mineralised properly because of defciency of calcium and phosphate.
- The undermineralised bone is soft, mechanically weak and subject to fractures, particularly stress fractures

CLINICAL FEATURES

Osteomalacia in adults can present with :

- Fractures and low bone mass density, mimicking osteoporosis
- Bone pain and general malaise
- Proximal muscle weakness is prominent and the patient may walk with a waddling gait and struggle to climb stairs or stand up from a chair
- Bone and muscle tenderness on pressure and focal bone pain can be due to fissure fractures of the ribs and pelvis.

INVESTIGATIONS AND MANAGEMENT

- Typically, serum ALP levels are raised, 25(OH)D levels are undetectable and PTH is markedly elevated
- X-rays often show osteopenia or vertebral crush fractures and, with more advanced disease, focal radio lucent areas (pseudofractures or Looser zones) may be seen in ribs, pelvis and long bones
- Treatment with between 10,000 and 25,000 IU daily for 2–4 weeks is associated with rapid clinical improvement, an elevation in serum 25(OH)D and a reduction in PTH.
- The dose of vitamin D can usually be reduced to a maintenance level of 800–1600 IU daily (10–20 µg), except in patients with malabsorption, who may require higher maintenance doses.

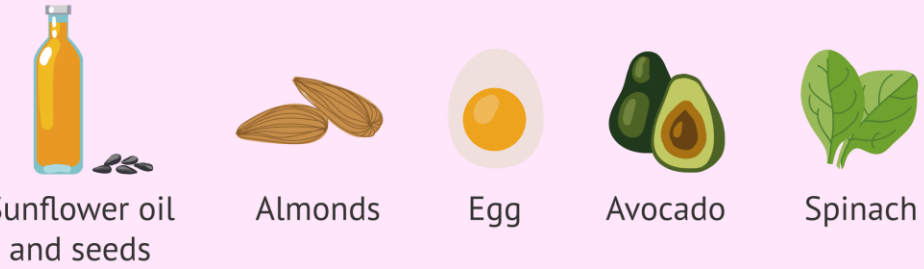
Fig. 26.63 Osteomalacia. A Photomicrograph of a toluidine blue-stained bone biopsy from a patient with osteomalacia showing thickened osteoid seams, stained light blue (arrows) covering most of the bone surface (left). Calcified bone is stained purple. B X-ray of a patient with osteomalacia showing a stress fracture of the tibia (arrow).

VITAMIN E

- The most important dietary form is ***α – tocopherol***
- Functions:

- Prevents oxidation of polyunsaturated fatty acids in cell membranes by free radicals.
- Helps maintain cell membrane structure.
- Affects DNA synthesis and cell signalling.
- Involved in the anti-inflammatory and immune systems

Vegetable oils, seeds, nuts, green leafy vegetables



DEFICIENCY

- Human deficiency is rare and has been described only in premature infants and in malabsorption, notably with abetalipoproteinaemia
- It can cause a mild haemolytic anaemia, ataxia and visual scotomas
- Vitamin E intakes of up to 3200 mg/day (1000 fold greater than recommended intakes) are considered safe
- Diets rich in vitamin E (e.g. vegetable oils, nuts and seeds) are consumed in countries with lower rates of coronary heart disease, but randomised controlled trials have not demonstrated cardioprotective effects of vitamin E or other antioxidants.

VITAMIN K

- Only fat soluble vitamin with a specific coenzyme function
- *Vitamin K1 (phylloquinone)* is present in plants. *Vitamin K2 (menaquinone)* is produced by the intestinal bacteria and also found in animals. Vitamin K3 (menadione) is a synthetic form
- Vitamin K is taken in the diet or synthesized by the intestinal bacteria. Its absorption takes place along with fat (chylomicrons) and is dependent on bile salts. Vitamin K is transported along with LDL and is stored mainly in liver and, to a lesser extent, in other tissues.

FUNCTION

- It brings about the *posttranslational modification* of certain blood clotting factors
- The clotting *factors II (prothrombin), VII, IX and X* are synthesized as inactive precursors (zymogens) in the liver
- Vitamin K acts as a coenzyme for the carboxylation of glutamic acid residues present in the proteins and this reaction is catalysed by a carboxylase
- It involves the *conversion of glutamate (Glu) to γ-carboxyglutamate (Gla)* and requires vitamin K, O2 and CO2

DEFICIENCY

- Vitamin K deficiency leads to delayed coagulation and bleeding
- In obstructive jaundice, dietary vitamin K is not absorbed and it is essential to administer the vitamin in parenteral form before surgery
- Vitamin K is given routinely to newborn babies to prevent haemorrhagic disease
- Symptoms of excess have been reported only in infants, with synthetic preparations linked to haemolysis and liver damage.

REFERENCES

- Davidson's Principles and Practice of Medicine, 25th Edition
- Textbook of Biochemsitry by U. Satyanarayana and U. Chakrapani

THANK YOU