University of Baghdad
College of Medicine
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Title: deficiency of Fat-soluble vitamins

Grade: third

Module: Nutritional, Water& Electrolyte Imbalance Module

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objective

- ✓ List the fat soluble vitamins & why called as that?
- ✓ What are the biochemical assessments of vitamin status?
- ✓ Clarify the clinical consequences of fat soluble vitamins.
- ✓ Clarify the causes of fat soluble vitamins deficiency.
- ✓ Define vitamin D deficiency & explain the clinical features & pathogenesis.
- ✓ What are the biochemical findings in vitamin D deficiency.
- ✓ Define osteomalacia / rickets & explain the pathogenesis, clinical , biochemical, & radiological features.
- ✓ Clarify the preventive measures & lines of management of fat soluble vitamins.

Fat-soluble vitamins

- Vitamins A, D, E, and K are called the fat-soluble vitamins, because they are soluble in organic solvents and are absorbed and transported in a manner similar to that of fats.

19.32 Biochemical assessment of vitamin status

Nutrient	Biochemical assessments of deficiency or excess
Vitamin A	Serum retinol may be low in deficiency Serum retinyl esters: when vitamin A toxicity is suspected
Vitamin D	Plasma/serum 25-hydroxyvitamin D (25(OH)D): reflects body stores (liver and adipose tissue) Plasma/serum $1,25(OH)_2D$: difficult to interpret
Vitamin E	Serum tocopherol:cholesterol ratio
Vitamin K	Coagulation assays (e.g. prothrombin time) Plasma vitamin K

Vitamin A (retinol)

- Pre-formed retinol is found only in foods of animal origin. Vitamin A can also be derived from carotenes, which are present in green and coloured vegetables and some fruits.

consequences of vitamin A deficiency

- the most important consequences is irreversible blindness in young children. Asia is most notably affected. Adults are not usually at risk because liver stores can supply vitamin A when foods containing vitamin A are unavailable.
- Early deficiency causes impaired adaptation to the dark (night blindness). Keratinization of the cornea (xerophthalmia) gives rise to characteristic Bitot's spots and progresses to keratomalacia, with corneal ulceration, scarring and irreversible blindness

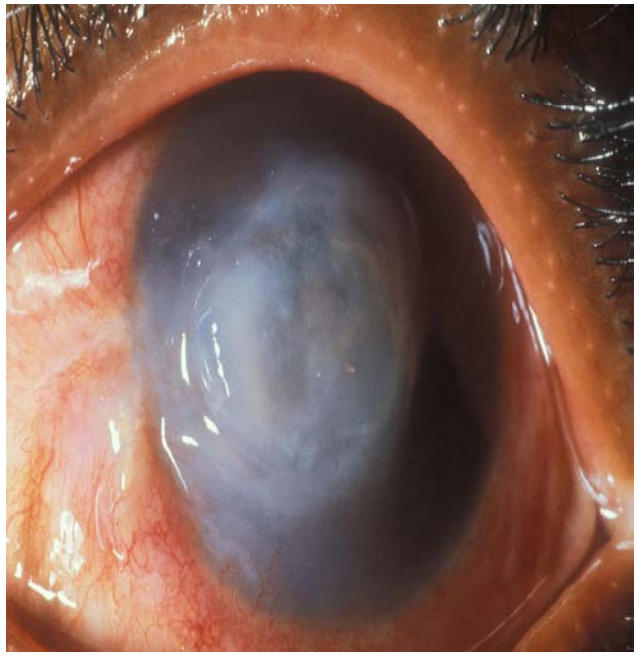
- Subclinical forms of vitamin A deficiency (VAD) may not cause any symptoms, but:

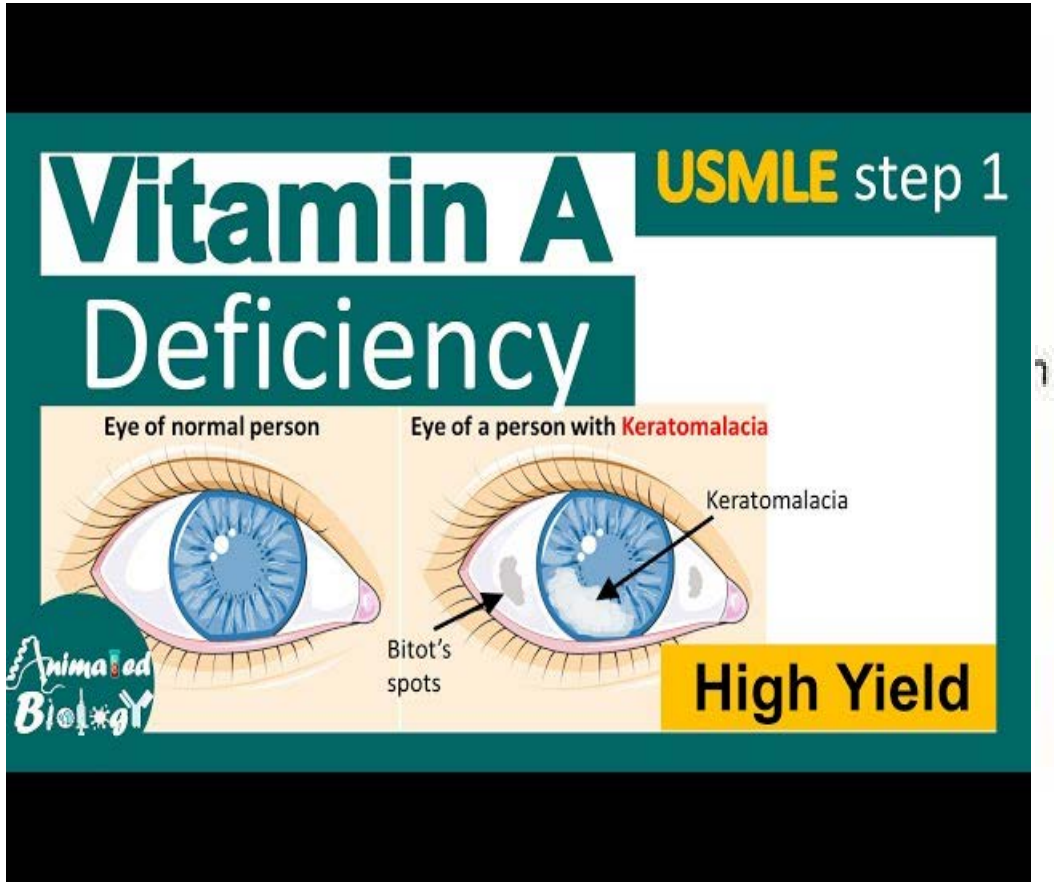
✓ the risk of respiratory and diarrheal infections is increased,

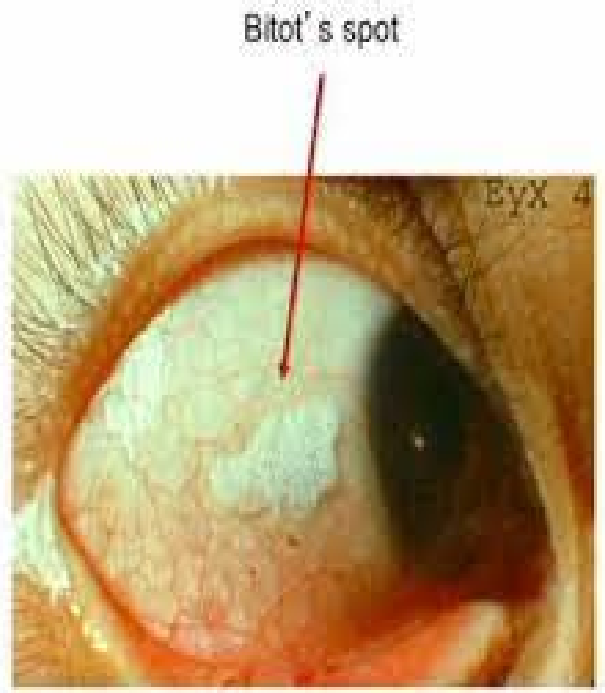
✓ the growth rate is reduced, and bone development is slowed

✓ dry skin, dry hair, broken fingernails, and

✓ decreased resistance to infections are among the first signs of VAD




Vitamin A
USMLE step 1
Deficiency
Eye of normal person
Eye of a person with Keratomalacia
Keratomalacia
Bitot's spots
Animated Biology
High Yield


Bitot's spot

prevention

- In countries where vitamin A deficiency is endemic, pregnant women should be advised to eat dark green, leafy vegetables and yellow fruits (to build up stores of retinol in the fetal liver),
- The WHO is giving a high priority for prevention in communities where xerophthalmia occurs, giving single prophylactic oral doses of 60 mg retinyl palmitate (providing 200 000 U retinol) to pre-school children. This also reduces mortality from gastroenteritis and respiratory infections.

Treatment

- Treatment for subclinical VAD includes the consumption of vitamin A–rich foods, such as liver, beef, chicken, eggs, fortified milk, carrots, mangoes, sweet potatoes, and leafy green vegetables.
- Therapeutic doses for severe disease include 60,000 mcg (200,000 IU)

Vitamin D deficiency

- Vitamin D deficiency is defined to exist when serum 25(OH)D concentrations are below 25 nmol/L (10 ng/mL).
- vitamin D levels in the range 25–50 nmol/L (10–20 ng/mL) is classified as vitamin D insufficiency.
- levels above 50 nmol/L (20 ng/mL) is classified as normal vitamin D status.
- In the elderly, a more appropriate normal threshold may be 75 nmol/L (30 ng/mL) or more.

Causes of deficiency

- The likelihood of developing vitamin D deficiency is strongly related to sunlight exposure.
- Dietary lack.
- Vitamin D deficiency is more common in the winter and spring, and less common in summer and autumn.

Pathogenesis

- When vitamin D levels fall – as the result of lower sunlight exposure or dietary lack – production of 1,25(OH)2D is reduced, causing a reduction in calcium absorption from the gut. This causes a transient fall in serum calcium, which is detected by calcium sensing receptors on the parathyroid chief cells; this increases PTH secretion, which restores calcium levels to normal. Vitamin D deficiency is, therefore, usually characterized by a low level of 25(OH)D and a raised level of PTH.

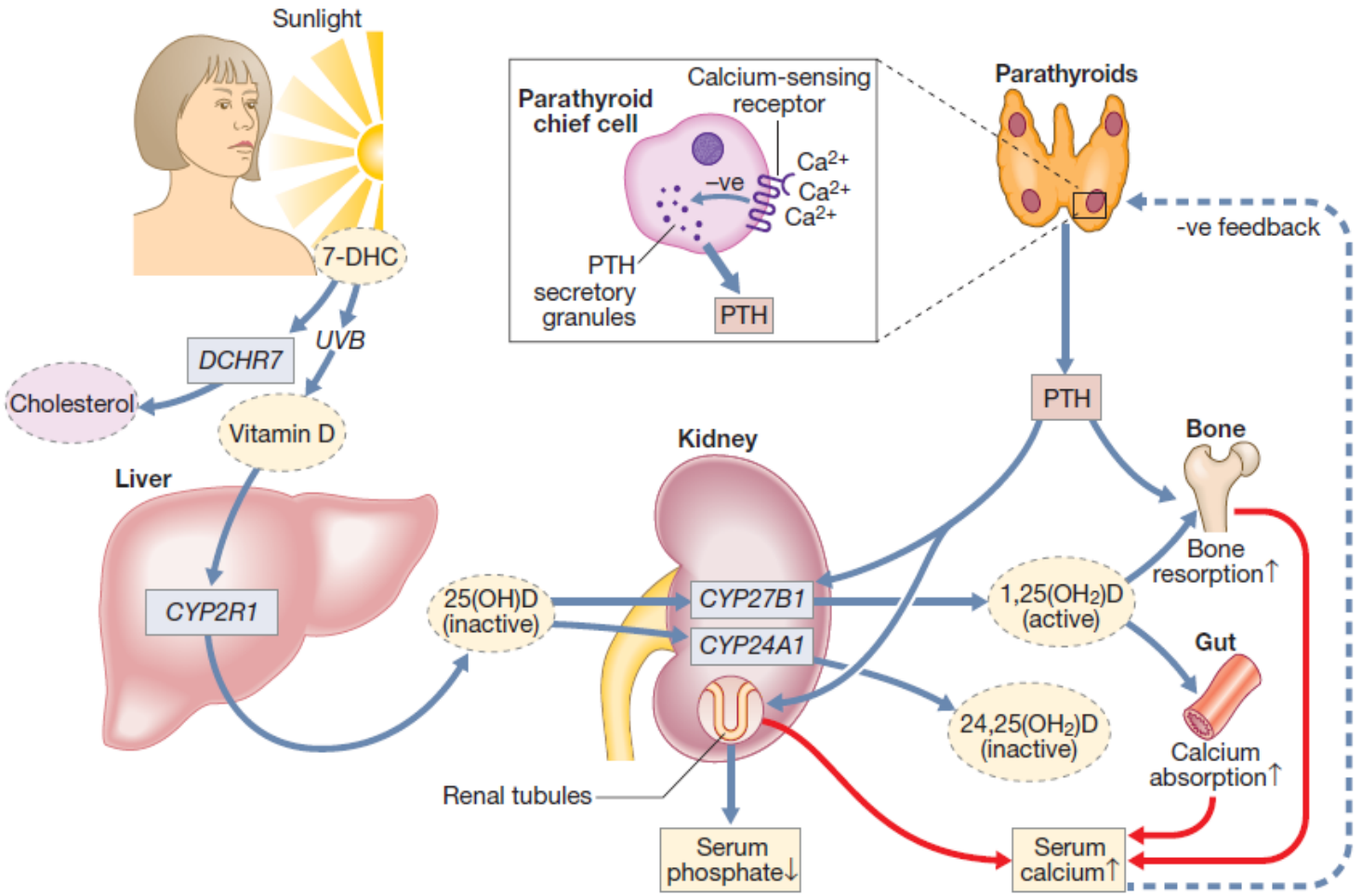


Fig. 24.61 Vitamin D metabolism. Vitamin D is produced in the skin from 7-dehydrocholesterol (7-DHC) by ultraviolet B (UVB) light. The 7-dehydrocholesterol reductase enzyme, which is encoded by the *DHCR7* gene, opposes the effect of UVB by converting 7-DHC to cholesterol. The vitamin D then undergoes hydroxylation steps in the liver and kidney to form the active metabolite $1,25(OH)_2D$, which regulates calcium homeostasis by stimulating calcium absorption from the diet and bone resorption. See text for details.

Clinical features

- Vitamin D deficiency does not cause symptoms and the diagnosis is made as the result of biochemical testing.
- If vitamin D deficiency is prolonged and severe, then osteomalacia and rickets may occur & their related clinical features become apparent.

Investigations

- measurement of serum 25(OH)D. Inpatients with low 25(OH)D, measurements of PTH, serum calcium, phosphate and ALP should also be considered.
- Low levels of 25(OH)D in the absence of other abnormalities is unlikely to be of any clinical significance and may be due to low levels of vitamin D-binding protein.
- If low 25(OH)D levels are combined with raised levels of PTH, this is of more significance since it indicates secondary hyperparathyroidism.
- Serum ALP, calcium and phosphate levels are normal in uncomplicated vitamin D deficiency.

Management

- The clinical benefit of treating biochemical vitamin D deficiency is uncertain.
- Vitamin D supplements should be considered in patients who have low 25(OH)D levels and raised levels of PTH.
- In most patients, cholecalciferol in a dose of 800 IU daily should be sufficient to correct the deficiency.
- In patients who are receiving intravenous bisphosphonates and denosumab for osteoporosis, vitamin D deficiency should be corrected by supplementation to reduce the risk of hypocalcaemia, in such a case give higher doses of vitamin D, such as 20 000–25 000 IU once a week for 4 weeks or to give lower doses over a more prolonged period.

Osteomalacia and rickets

- A disease characterized by the softening of the bones caused by impaired bone metabolism primarily due to inadequate levels of available phosphate, calcium, and vitamin D, or because of resorption of calcium. The impairment of bone metabolism causes inadequate bone mineralization.
- Severe and prolonged vitamin D deficiency can result in the occurrence of osteomalacia in adults and rickets in children, may be nutritional, more prevalent in elderly housebound individuals and people with malabsorption.

Pathogenesis

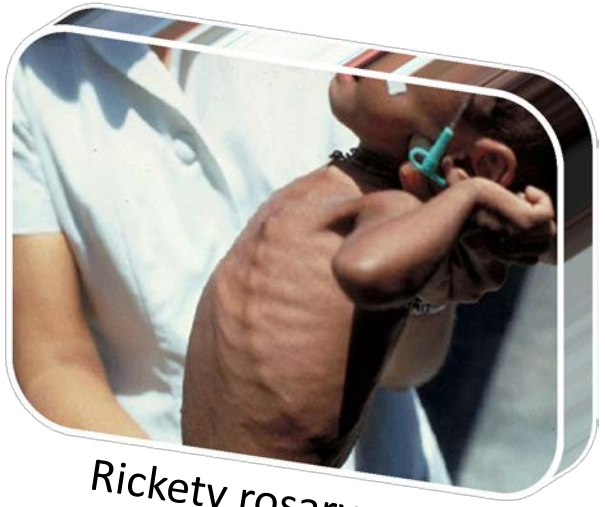
- The sustained elevation in PTH levels (secondary to vit. D deficiency) maintains normal levels of serum calcium by increasing bone resorption, which eventually causes progressive demineralization of the skeleton.
- Phosphate that is released during the process of bone resorption is lost through increased renal excretion, resulting in hypophosphatemia.

- The raised levels of PTH stimulate osteoblast activity and cause new bone formation but the matrix is not mineralized properly because of deficiency of calcium and phosphate.
- The under- mineralized bone is soft, mechanically weak and subject to fractures, particularly stress fractures. Normal levels of serum calcium tend to be maintained until a very advanced stage, when hypocalcaemia may occur.

Clinical features

- Vitamin D deficiency in children causes delayed development, muscle hypotonia, craniotabes (small unossified areas in membranous bones of the skull that yield to finger pressure with a cracking feeling), bossing of the frontal and parietal bones and delayed anterior fontanelle closure, enlargement of epiphyses at the lower end of the radius, and swelling of the rib costochondral junctions (‘rickety rosary’).

Widened epiphyseal plate



Rickety rosary

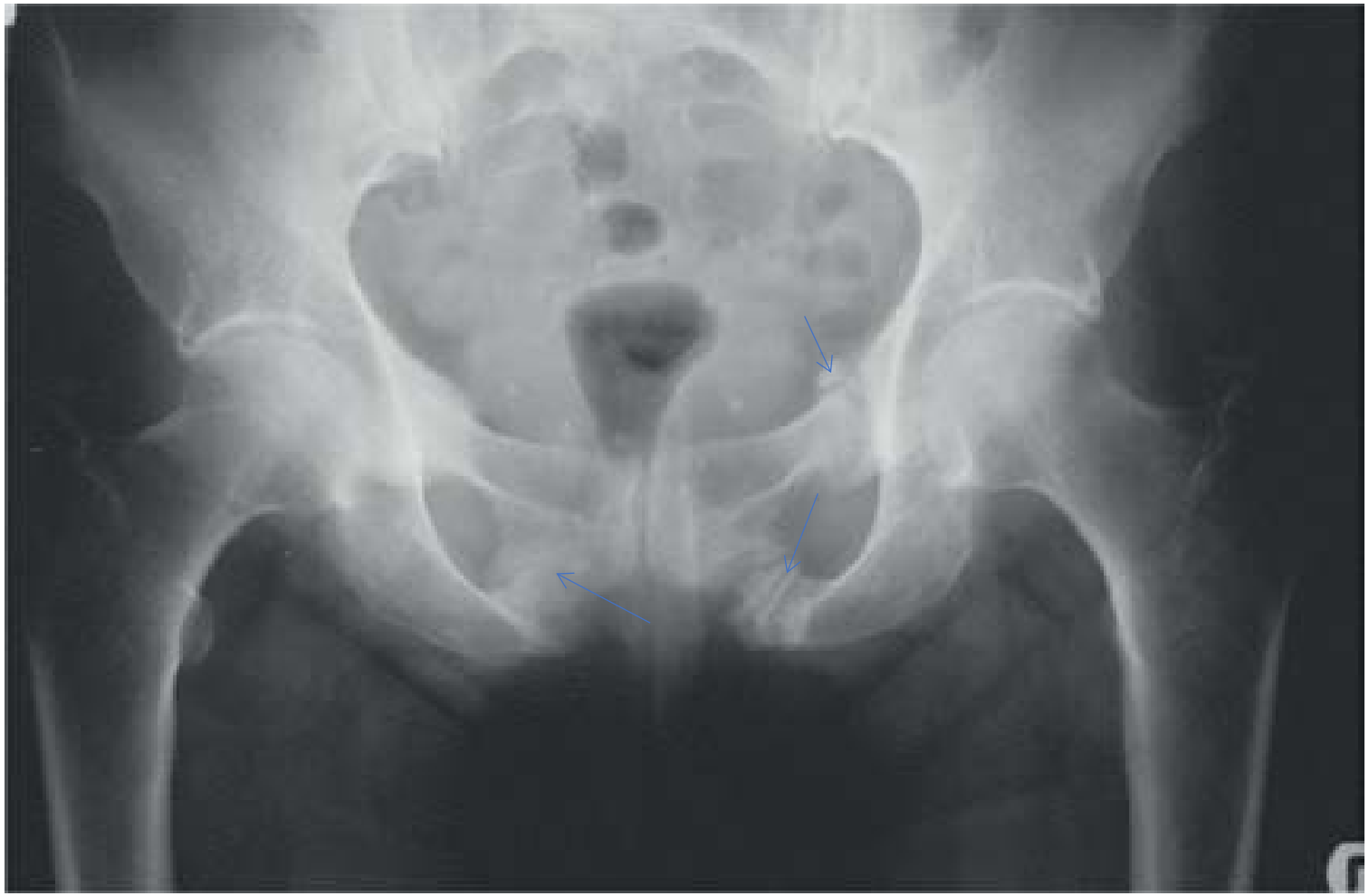
- Osteomalacia in adults can present with fractures and low BMD, mimicking osteoporosis. Other symptoms include bone pain and general malaise. Proximal muscle weakness is prominent and the patient may walk with a waddling gait and struggle to climb stairs or stand up from a chair. There may be bone and muscle tenderness on pressure, and focal bone pain can be due to fissure fractures of the ribs and pelvis.

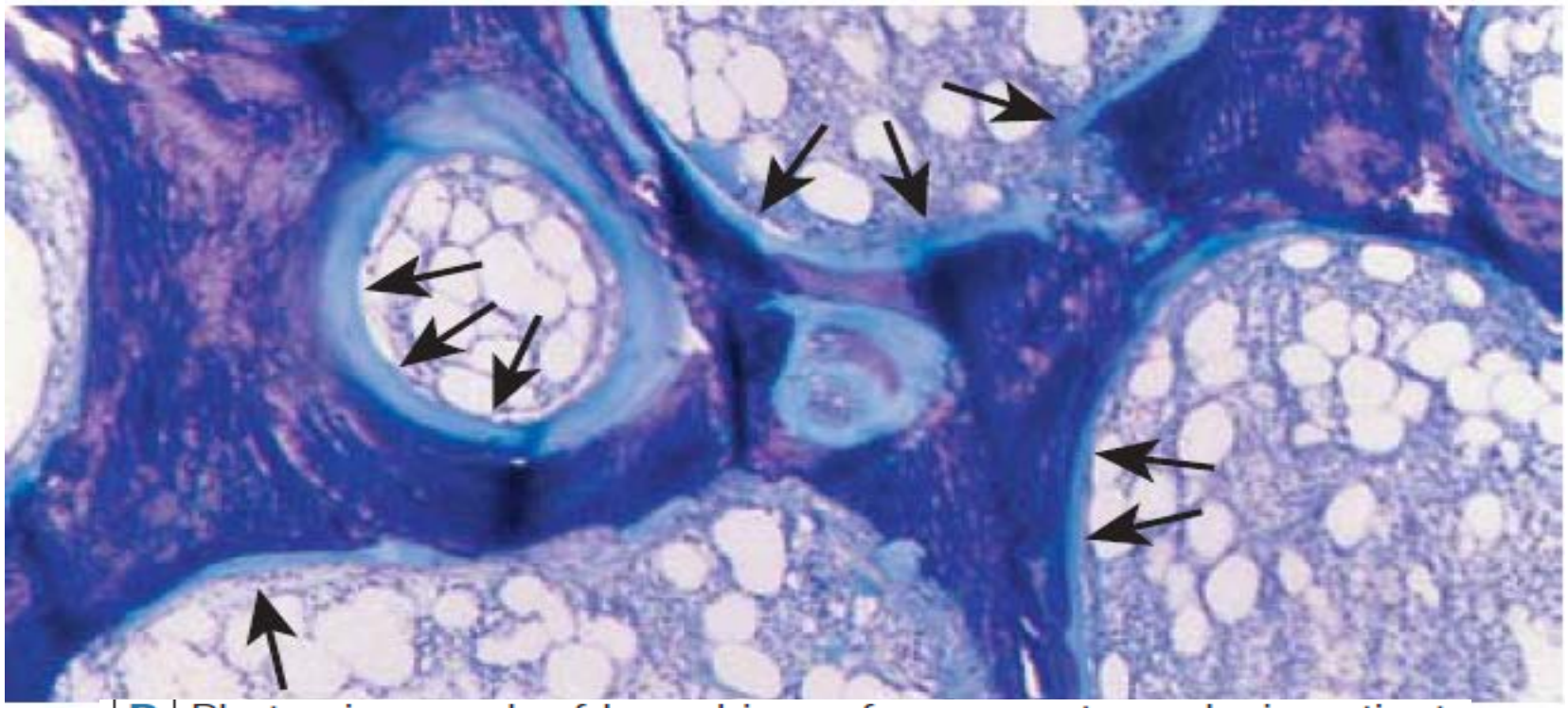
Investigations

- Biochemically
  - Typically, serum ALP levels are raised, 25(OH)D levels are undetectable and PTH is markedly elevated. Serum phosphate levels tend to be low but serum calcium is usually normal, unless the disease is advanced.
- Radiologically:
  - X-rays often show osteopenia or vertebral crush fractures and, with more advanced disease, focal radiolucent areas (pseudofractures or Looser's zones) may be seen in ribs, pelvis and long bones

- In children, there is thickening and widening of the epiphyseal plate.
- A radionuclide bone scan may show multiple hot spots in the ribs and pelvis at the site of fractures and the appearance may be mistaken for metastases.

❑ Where there is doubt, the diagnosis can be confirmed by bone biopsy, which shows the pathognomonic features of increased thickness and extent of osteoid seams.





B Photomicrograph of bone biopsy from an osteomalacic patient showing thick osteoid seams (stained light blue, arrows) that cover almost all of the bone surface. Calcified bone is stained dark blue.

Management

- Osteomalacia and rickets respond promptly to treatment with vitamin D. A wide variety of doses can be used. A dose of 10 000 - 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.
- Serum ALP levels sometimes rise initially as mineralization of bone increases but eventually fall to within the reference range as the bone disease heals.
- Subsequently, 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 doses.

Vitamin E

- Human deficiency is rare and has been described only in premature infants and in malabsorption. It can cause a mild hemolytic anaemia, ataxia and visual scotomas. Vitamin E intakes of up to 3200 mg/day (1000-fold greater than recommended intakes) are considered safe.

Vitamin K

- 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.
- Warfarin and related anticoagulants act by antagonizing vitamin K.
- Vitamin K is given routinely to newborn babies to prevent hemorrhagic disease.

Thanks for All