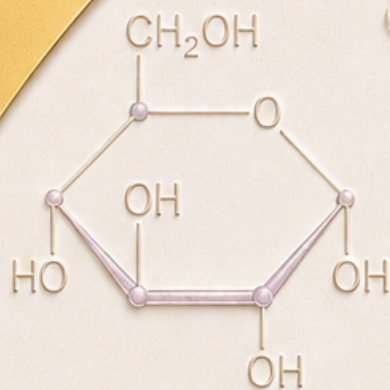




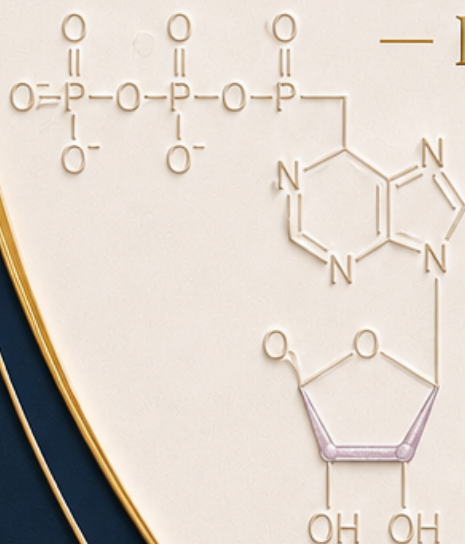
QUESTION BANK



• SEMESTER 3 •

MSK MODULE

— BIOCHEMISTRY —



Lecture 1 - Vitamins Essential for Bone Health

Part 1: MCQs (Choose the correct answer):

1. Which of the following statements concerning vitamins is correct?

- A. They are required in large amounts in the diet
- B. They are utilized as structural units of the cell and tissue
- C. They act as cofactors for enzymes in biochemical reactions
- D. They are a major source of energy for growing tissues
- E. They are all synthesized in adequate amounts inside the body

2. A 2-year-old boy is brought to the outpatient clinic for nutritional assessment. His mother states that his diet is rich in carrots and dark green leafy vegetables. The carotenes present in this diet act as an inactive precursor of which of the following vitamins?

- A. Vitamin A
- B. Vitamin D3
- C. Vitamin E
- D. Vitamin K
- E. Vitamin C

3. 7-dehydrocholesterol, the provitamin of vitamin D3 in man, is derived from which of the following?

- A. Ergosterol of plants and yeast
- B. Cholesterol by the intestinal mucosa
- C. Carotenes of dietary origin
- D. Retinol stored in the liver
- E. 25-hydroxycholecalciferol of the liver

4. A 45-year-old man with obstructive jaundice caused by a stone impacted in the common bile duct is found to have low serum levels of vitamins A, D, E and K. Which of the following best explains this finding?

- A. Increased urinary excretion of these vitamins
- B. Consumption of these vitamins as structural units of the cell
- C. Defective emulsification of fat with impaired absorption of these vitamins
- D. Failure of hydroxylation of these vitamins in the kidney
- E. Increased storage of these vitamins in the liver

5. Which of the following statements concerning water soluble vitamins is correct?

- A. They are stored in large amounts in the liver
- B. Their storage in the body is limited except for vitamin B12
- C. They are transported in the blood in lipoproteins
- D. Their deficiency manifestations appear later than those of fat soluble vitamins
- E. They commonly accumulate to toxic levels in the body

6. A 3-year-old boy whose diet is almost free of fresh fruits and vegetables presents with bleeding gums and delayed wound healing. Deficiency of which of the following water soluble vitamins, which is needed for connective tissue formation, is most likely?

- A. Thiamine
- B. Riboflavin
- C. Ascorbic acid
- D. Biotin
- E. Cobalamin

7. A newborn baby is given an intramuscular injection of a fat soluble vitamin that is needed for both blood clotting and bone health. Which of the following vitamins was most likely given?

- A. Vitamin A
- B. Vitamin C
- C. Vitamin D
- D. Vitamin E
- E. Vitamin K

8. A 30-year-old woman on a strict vegan diet takes a vitamin D supplement prepared from irradiated yeast. Which of the following is correct concerning the form of vitamin D that she is taking?

- A. It is ergocalciferol (D₂) and is of equal potency to cholecalciferol
- B. It is ergocalciferol (D₂) and is much less potent than cholecalciferol
- C. It is cholecalciferol (D₃) obtained from a plant source
- D. It is calcitriol and needs no further activation
- E. It is 25-hydroxycholecalciferol and is the active form of the vitamin

9. The mother of a 9-month-old infant with early signs of rickets states that the infant is fed mainly on unfortified cow's milk. Which of the following is correct as regards the dietary sources of vitamin D?

- A. Milk is a poor source of vitamin D
- B. Milk is the richest source of preformed vitamin D₃
- C. Egg yolk contains no vitamin D
- D. Fish liver oils are poor sources of vitamin D
- E. Liver is a poor source of vitamin D

10. Which of the following is the major storage form of vitamin D and the predominant form of the vitamin in the circulation?

- A. 7-dehydrocholesterol
- B. Cholecalciferol
- C. 25-hydroxycholecalciferol
- D. 1,25-dihydroxycholecalciferol
- E. Ergosterol

11. A 55-year-old man with advanced liver cirrhosis develops bone demineralization, and his physician decides to give him 25-hydroxycholecalciferol instead of cholecalciferol. Which of the following steps of vitamin D metabolism is defective in this patient?

- A. Conversion of 7-dehydrocholesterol into vitamin D₃ in the skin
- B. Hydroxylation at the 25-position in the liver
- C. Hydroxylation at the 1-position in the kidney
- D. Intestinal absorption of calcium and phosphate
- E. Conversion of ergosterol into vitamin D₂

12. The final rate limiting step in the conversion of vitamin D into its active form is catalysed by which of the following enzymes?

- A. 25-hydroxylase in the liver
- B. 1 α -hydroxylase in the kidney
- C. Alkaline phosphatase in bone
- D. 7-dehydrocholesterol reductase in the skin
- E. 24-hydroxylase in the intestine

13. A 50-year-old man is found to have a serum phosphate level below the normal range. Which of the following is the expected direct effect of this finding on vitamin D metabolism?

- A. Stimulation of the renal hydroxylase
- B. Inhibition of the renal hydroxylase
- C. Inhibition of parathormone release
- D. Inhibition of the hepatic 25-hydroxylase
- E. Increased urinary excretion of calcitriol

14. A 40-year-old woman is found to have a below-normal blood calcium level. Which of the following is the expected sequence of events that follows?

- A. Release of parathormone, which stimulates the renal hydroxylase and increases calcitriol formation
- B. Release of parathormone, which inhibits the renal hydroxylase
- C. Suppression of parathormone with increased calcitriol formation
- D. Release of parathormone, which stimulates the 25-hydroxylation step in the liver
- E. Increased calcitriol formation, which inhibits calcium uptake from the gut

15. Calcitriol acts as a lipid soluble hormone and induces the synthesis of calcium binding proteins in which of the following cells?

- A. Duodenal epithelial cells
- B. Parathyroid chief cells
- C. Hepatocytes
- D. Osteoclasts of the epiphysis
- E. Keratinocytes of the stratum basale

16. Which of the following best describes the effect of vitamin D on bone?

- A. It enhances bone mineralization at low levels and increases bone resorption at higher levels
- B. It enhances bone mineralization at all levels
- C. It increases bone resorption at low levels only
- D. It has no effect on bone in the presence of parathormone
- E. It decreases the intestinal absorption of calcium and phosphate

17. A 14-month-old infant who is exclusively breast fed and takes no supplements presents with bowing of the legs, broad tender wrists and muscle weakness. Which of the following best explains the bone changes in this child?

- A. Deficient mineralization of the newly formed bone matrix
- B. Decreased bone mass in the presence of normal mineralization
- C. Defective synthesis of type I collagen
- D. Failure of osteoclastic bone resorption
- E. Excessive deposition of calcium in the soft tissues

18. Which of the following statements correctly differentiates osteoporosis from osteomalacia?

- A. Osteoporosis is a decrease in bone mass with normal mineralization, while osteomalacia is deficient mineralization of bone
- B. Osteoporosis is deficient mineralization of bone, while osteomalacia is a decrease in bone mass with normal mineralization
- C. Both conditions are due to deficient mineralization of bone
- D. Osteoporosis occurs in children, while osteomalacia occurs before epiphyseal fusion
- E. Osteoporosis produces much more bone deformity than osteomalacia

19. A 2-year-old child has been given vitamin D drops in a dose that continuously exceeds ten times the recommended daily allowance for several months. He now complains of polyuria, polydipsia and nocturia. Which of the following is most likely to be found in this child?

- A. Hypocalcemia and hypophosphatemia
- B. Hypercalcemia and hypercalciuria
- C. Prolonged bleeding time
- D. Night blindness and dry gray plaques on the conjunctiva
- E. Megaloblastic anemia

20. A 9-year-old boy with rickets fails to respond to large oral doses of cholecalciferol and is found to have a genetic deficiency of the 1α -hydroxylase enzyme. Which of the following is the most appropriate treatment for this patient?

- A. Ergocalciferol
- B. 25-hydroxycholecalciferol
- C. 1,25-dihydroxycholecalciferol
- D. Retinol
- E. Ascorbic acid

Part 2: Essay / Short-Answer Questions:

1. Classify vitamins according to their solubility, mentioning the vitamins included in each group. (1 mark)

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2. Compare between water soluble and fat soluble vitamins as regards the following: (1.5 marks)

Point of comparison	Water Soluble Vitamins	Fat Soluble Vitamins
Storage		
Deficiency manifestation		
Removal		

3. List 2 provitamins (vitamin precursors), mentioning the vitamin formed from each. (1 mark)

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4. Describe the activation of vitamin D, mentioning the site and the enzyme of each hydroxylation step, and name both the storage form and the active form of the vitamin. (2 marks)

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5. Enumerate the factors that regulate the formation of 1,25-dihydroxycholecalciferol in the kidney. (1 mark)

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6. According to the mechanism of vitamin D and parathyroid hormone action, list the functions of vitamin D under the effect of PTH activity at: (1 mark)

A. Bone

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B. Intestine and kidney

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7. A 10-month-old girl is being evaluated for the bowed appearance of her legs. The parents report that the baby is still being breast fed and takes no supplements. Radiologic studies confirm the suspicion of vitamin D deficient rickets. (2 marks)

A. Explain the underlying defect in the bone in this condition.

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B. Mention two other clinical features expected in this child.

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C. Mention the line of treatment.

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8. A 62-year-old woman complains of bone pain and muscle weakness. She gives a history of chronic foul-smelling fatty diarrhea, and her investigations reveal a low serum level of 25-hydroxycholecalciferol. (1.5 marks)

A. What is your provisional diagnosis?

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B. Mention two differences between this condition and rickets.

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9. Mrs. Salma, 68 years, postmenopausal, sustained a fracture of the right wrist after a minor fall at home. She does not practise any exercise and takes no calcium or vitamin D supplements. (2 marks)

A. What is your provisional diagnosis, and mention two predisposing factors in this patient?

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B. Mention two lines of treatment of this condition, explaining the mechanism of action of one of them.

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10. A mother has been giving her child a vitamin D supplement in a dose far exceeding the recommended daily allowance for six months. (1.5 marks)

A. Mention two biochemical abnormalities expected in this child.

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B. Mention the early signs of the impaired renal function that may result.

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C. What is the direct effect of the excess vitamin D on bone?

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11. Give reason for each of the following: (1.5 marks)

A. Hypervitaminosis occurs with fat soluble but not with water soluble vitamins.

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B. Patients with severe liver disease may be given 25-hydroxycholecalciferol instead of cholecalciferol.

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C. Patients with end stage renal disease must be given 1,25-dihydroxycholecalciferol.

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Part 1: MCQ Answer Key

- 1 **C** – They act as cofactors for enzymes in biochemical reactions Slides 3 & 4 (Vitamins are required in small amounts, are not utilized as structural units and do not provide energy; they act as cofactors for enzymes)
- 2 **A** – Vitamin A Slide 5 (Pro-vitamins are inactive precursors converted to active vitamins inside the body: carotenes are provitamin A)
- 3 **B** – Cholesterol by the intestinal mucosa Slides 5 & 19 (7-dehydrocholesterol is derived from cholesterol by the intestinal mucosa and passes to the skin, where UV rays convert it into vitamin D3; it is provitamin D3)
- 4 **C** – Defective emulsification of fat with impaired absorption of these vitamins Slides 10 & 13 (Fat soluble vitamins are absorbed efficiently only when normal fat absorption is taking place; biliary system disorders and steatorrhea lead to avitaminosis)
- 5 **B** – Their storage in the body is limited except for vitamin B12 Slides 12 & 13 (Storage of water soluble vitamins is limited (except vitamin B12), excesses are excreted in urine and they must be provided regularly)
- 6 **C** – Ascorbic acid Slides 8 & 16 (Vitamin C is the water soluble vitamin needed for connective tissue and is therefore required for bone health)
- 7 **E** – Vitamin K Slides 8 & 15 (Vitamin K is a fat soluble vitamin whose functions include blood clotting and bone health)
- 8 **A** – It is ergocalciferol (D2) and is of equal potency to cholecalciferol Slides 17 & 18 (D2 (ergocalciferol) is obtained from plants, fungi and yeasts; vitamin D2 and vitamin D3 are of equal potency)
- 9 **A** – Milk is a poor source of vitamin D Slide 20 (Fish liver oils are rich in vitamin D3 and liver and egg yolk are good sources, whereas milk is a poor source of vitamin D)
- 10 **C** – 25-hydroxycholecalciferol Slides 17 & 22 (25-OH D3 formed in the liver is the major storage form of vitamin D and the predominant form of the vitamin in the circulation)
- 11 **B** – Hydroxylation at the 25-position in the liver Slides 22 & 35 (Patients with severe liver disease are given 25-DHCC or 1,25-DHCC because of the defective 25-hydroxylation step in the liver)
- 12 **B** – 1α -hydroxylase in the kidney Slides 23 & 30 (25-OH D3 is further hydroxylated at the one position by 25-hydroxycholecalciferol 1-hydroxylase in the kidney; this is the final rate limiting step in the formation of calcitriol)
- 13 **A** – Stimulation of the renal hydroxylase Slide 26 (Level of serum phosphate acts directly: a decreased phosphate level stimulates the renal hydroxylase)
- 14 **A** – Release of parathormone, which stimulates the renal hydroxylase and increases calcitriol formation Slides 26 & 30 (Level of serum calcium acts indirectly: hypocalcemia stimulates parathormone release, which induces the renal 1α -hydroxylase)
- 15 **A** – Duodenal epithelial cells Slide 31 (Calcitriol acts on duodenal epithelial cells; its intracellular receptor induces the synthesis of calcium binding proteins that stimulate calcium uptake from the gastrointestinal tract)
- 16 **A** – It enhances bone mineralization at low levels and increases bone resorption at higher levels Slide 27 (Functions of vitamin D: enhances intestinal absorption of Ca^{2+} and PO_4 , enhances bone mineralization at low levels and increases bone resorption at higher levels)
- 17 **A** – Deficient mineralization of the newly formed bone matrix Slides 37 & 43 (Deficiency of vitamin D in childhood produces rickets: bowing of the soft bones due to abnormal bone ossification, with muscle weakness; rickets and osteomalacia are deficient mineralization of bone)
- 18 **A** – Osteoporosis is a decrease in bone mass with normal mineralization, while osteomalacia is deficient mineralization of bone Slide 43 (Osteoporosis is a decrease in the mass of bone in the presence of normal mineralization, whereas osteomalacia is deficient mineralization of bone)
- 19 **B** – Hypercalcemia and hypercalciuria Slides 39 & 40 (Vitamin D is highly toxic at levels continuously exceeding $10\times$ the RDA, resulting in hypercalcemia and hypercalciuria; hypercalcemia impairs renal function and early signs include polyuria, polydipsia and nocturia)
- 20 **C** – 1,25-dihydroxycholecalciferol Slides 23 & 36 (Genetic deficiency of the 1α -hydroxylase (vitamin D resistant rickets) must be treated with 1,25-DHCC or an analogue that does not require metabolism in the kidney)

Part 2: Essay Answer Key (with slide references)

1. Classification of vitamins — Slides 8 & 9

- Basis of classification: the solubility of the vitamin.
- Fat soluble vitamins: A, D, E and K.
- Water soluble vitamins: vitamin B group (complex) and vitamin C.

2. Water soluble versus fat soluble vitamins — Slide 13

- Storage: cannot be stored (except B12) / can be stored in the liver.
- Deficiency manifestation: appears quickly after diet restriction / appears later.
- Removal: excreted in urine / cannot be excreted in urine (hypervitaminosis might appear).

3. Provitamins — Slide 5

- Carotenes = provitamin A.
- 7-dehydrocholesterol = provitamin D3.

4. Activation of vitamin D — Slides 17, 21, 22 & 23

- Vitamins D2 and D3 are not biologically active; they are activated by two hydroxylation reactions.
- I- Hydroxylation at the 25-position by a specific hydroxylase in the LIVER gives 25-OH D3 (25-hydroxycholecalciferol) = the major storage form and the predominant circulating form.
- II- Further hydroxylation at the one position by 25-hydroxycholecalciferol 1-hydroxylase in the KIDNEY gives 1,25-(OH)₂ D3 (calcitriol) = the active form.

5. Regulation of 1,25-dihydroxycholecalciferol formation in the kidney — Slide 26

- Level of serum phosphate (direct): low PO₄ stimulates the renal hydroxylase.
- Level of serum calcium (indirect): low Ca stimulates parathormone release, which stimulates the renal hydroxylase.
- Parathormone: stimulates the renal hydroxylase.
- Level of serum 1,25-di-OH D3: acts by a feedback mechanism.

6. Functions of vitamin D under the effect of PTH — Slides 27, 29, 31 & 32

- A. Bone: with PTH present it mobilizes calcium from bone (osteoclastic resorption at higher levels), while at low levels it enhances bone mineralization.
- B. Intestine (duodenum): induces calcium binding proteins, increasing the absorption of Ca²⁺ and PO₄; Kidney: facilitates calcium reabsorption. All these actions bring blood calcium back to the normal range.

7. Vitamin D deficient rickets — Slides 27 & 37

- A. Deficiency of vitamin D in childhood, with deficient intestinal absorption of calcium and phosphate, leads to abnormal bone ossification (deficient mineralization) so the soft bones bow.
- B. Deformities of the legs and other developing bones, muscle weakness, prominent forehead, broad tender wrists and swellings at the costochondral junctions (any two).
- C. Supplementation with calcium and vitamin D, together with sunlight exposure.

8. Osteomalacia — Slides 10, 38 & 43

- A. Osteomalacia (vitamin D deficiency after epiphyseal fusion, secondary to fat malabsorption / steatorrhea).
- B. It occurs in adults after epiphyseal fusion, while rickets occurs in children before fusion; it produces less deformity than rickets and presents mainly as bone pain and muscle weakness (bone demineralization) rather than bowing of the soft bones.

9. Osteoporosis — Slides 41, 42 & 43

- A. Osteoporosis: a gradual loss of bone mass with normal mineralization. Predisposing factors here: postmenopausal loss of estrogen stimulation, aging, lack of exercise and inadequate calcium / vitamin D intake.
- B. Exercise; calcium and vitamin D supplements; estrogen receptor drugs or hormone replacement therapy; bisphosphonates (alendronate, ibandronate), which combine with hydroxyapatite in bone so that bone becomes more resistant to osteoclast induced breakdown.

10. Vitamin D toxicity — Slides 39 & 40

- A. Hypercalcemia and hypercalciuria (with increased intestinal absorption of calcium and phosphate).
- B. Polyuria, polydipsia and nocturia; prolonged hypercalcemia causes calcium deposition in soft tissues, notably the kidney, with irreversible kidney damage.
- C. The direct effect of excessive vitamin D on bone is resorption, similar to that seen in vitamin D deficiency.

11. Give reason — Slides 11, 12, 35 & 36

- A. Fat soluble vitamins are adequately stored in the body and cannot be excreted through urine, so excess amounts accumulate and produce toxic effects; water soluble vitamins are excreted in urine and rarely accumulate to a toxic level.
- B. Because of the defective 25-hydroxylation step in the diseased liver, so the already hydroxylated 25-DHCC (or 1,25-DHCC) is given.
- C. End stage renal disease means insufficiency of 1,25-DHCC (renal osteodystrophy), so 1,25-DHCC or an analogue that does not require metabolism in the kidney must be given.