Frequently asked questions:

1) What is the role of membrane barriers and what are the different methods by which molecules are transported across the membrane?

Ans: Absorption is a complex process in which the nutrients pass through the intestinal mucosal cells into the bloodstream. Mammalian epithelia are enveloped by a plasma membrane composed of a phospholipid bilayer interspersed frequently with cholesterol molecules. Integral transmembrane proteins span the lipid bilayer in a weaving fashion and account for most membrane-associated receptors, transporters and certain enzymes. Tight junctions prevent the passage of water and molecular solutes between adjacent epithelial cells. The plasma membrane constitutes a selective barrier to the transcellular movement of molecules and ions between the extracellular and intracellular fluid compartments. Fat-soluble substances, water, and small uncharged polar solutes can simply diffuse through the membrane, but ions and water-soluble molecules having five or more carbon atoms cannot pass through. The transportation of high molecular weight compounds occur by active transport. Active transport requires the expenditure of metabolic energy. Primary active transport is driven directly by metabolic energy and is carried out exclusively by ion pumps, such as the calcium pumps, the sodium pump, and the proton pumps. Ion pumps are ATPases, which utilize the energy released by the hydrolysis of ATP. Secondary active transport is indirectly linked to metabolic energy through a coupling of the solute to the pump-driven movement of an inorganic ion (usually Na^+). Therefore, depending on the molecular weight and solubility, vitamins are transported or absorbed in different ways and membrane barriers play a significant role in controlling the transmembrane movement of molecules.

2) What is the role of protein transporters in the absorption of vitamins?

Ans: Most biologically important water-soluble substances such as glucose, amino acids, water-soluble vitamins, and certain inorganic ions are translocated across the plasma membrane by means of protein transporters, which exert their effect through a change in their three-dimensional shape. Specific transporters are responsible for the translocation of a specific molecule or a group of closely related molecules. Specificity is imparted by the tertiary and quaternary structures of the transporter molecule — only if a solute's spatial configuration fits into the protein, will the solute be transferred across the membrane. Transporters fall into two main classes: carriers and ion channels. Ion pumps are a type of carrier protein, which is also an enzyme. At physiological concentrations, the translocation of several water soluble vitamins (thiamin, riboflavin, pantothenic acid, biotin, and vitamin C) across cell membranes is mediated by carrier proteins. Therefore, specificity imparted by change in tertiary structure helps in transporting specific molecule or vitamin across the membrane.

3) Explain the structure of Vitamin A.

Ans: The parent vitamin A compound, retinol, has the empirical formula $C_{20}H_{30}O$. The molecule comprises a β-ionone (cyclohexenyl) ring attached at the C-6 position and side chain containing two isoprene units with four conjugated double bonds which give rise to cis and trans isomerism. Carotenoids can be considered chemically as derivatives of lycopene, a $C_{40}H_{56}$ polyene composed of eight isoprenoid units. Derivatives are formed by a variety of reactions that include cyclization, hydrogenation, dehydrogenation, and insertion of oxygen. Hydrocarbon carotenoids are known as carotenes, and the oxygenated derivatives are termed xanthophylls. In nature, carotenoids exist primarily in the all-trans configuration.

4) Explain the structure of Vitamin D.

Ans: All forms of Vitamin D belong to a family of lipids called secosteroids. Secosteroids are very similar in structure to steroids except that two of the B-ring carbon atoms of the typical four steroid rings are not joined. The structural difference between vitamin D_2 and vitamin D_3 is the side chain of D_2 contains a double bond between carbons 22 and 23, and a methyl group on carbon 24.

5) Explain the structure of Vitamin E.

Ans: Tocopherols are methyl-substituted derivatives of tocol, which comprises a chroman-6-ol ring attached at C-2 to a saturated isoprenoid side chain. Tocotrienols are analogous structures whose side chains contain three trans double bonds. In nature, there are four tocopherols and four corresponding tocotrienols; these are designated as alpha- (α), beta- (β), gamma- (γ) and delta- (δ) according to the number and position of the methyl substituents in the chromanol ring. They differ in methyl groups in positions 5, 7, and 8 of chromanol ring. α-tocopherol has three methyl groups in positions, 5, 7 and 8 of chromanol ring. The chromanol ring of β- and γ-tocopherols contains two methyl groups in 5, 8 and 7, 8 respectively. However δ-tocopherol has one methyl group in position 8 of chromanol ring.

6) Explain the structure of Vitamin K.

Ans: Vitamin K is a derivative of naphthoquinone and differ in side chain. Phylloquinone contain phytyl side chain whereas menaquinone contains polyisoprenoid side chain made up of 7 isoprene units. Several variants of vitamin K_2 containing more than 7 isoprenoid units in the side chain are also identified.

7) What is the role of micelles on intestinal absorption of fat soluble vitamins?

Ans: Absorption of the fat-soluble vitamins takes place mainly in the proximal jejunum and depends on the proper functioning of the digestion and absorption of dietary fat. The stomach is the major site for emulsification of fat. The coarse lipid emulsion, on entering the duodenum, is emulsified into smaller globules by the detergent action of bile. Pancreatic lipase hydrolyses triglycerides at the 1 and 3 positions, yielding 2-monoglycerides and free fatty acids. During their detergent action, bile salts exist as individual molecules. Above a critical concentration of bile salts, the bile constituents i.e., bile salts, phospholipids, and cholesterol form aggregates called micelles, in which the polar ends of the molecules are orientated toward the surface and the nonpolar portion forms the interior. The 2-monoglycerides and free fatty acids are sufficiently polar to combine with the micelles to form mixed micelles. These are stable water-soluble structures, which can dissolve fat-soluble vitamins and other hydrophobic compounds in their oily interior. Mixed micelles do not cross the brush-border membrane of enterocytes as intact structures, the products of lipolysis must dissociate from these structures before they can be absorbed. Therefore, micelles mainly help in solubilizing fat soluble vitamins thus, facilitating absorption.

8) Write the different forms and functions of Vitamin A.

Ans: *Forms of Vitamin A:* Vitamin A-active compounds include retinoids (designated as vitamin A) and their carotenoid precursors (provitamin A carotenoids). The retinoids comprise retinol, retinaldehyde, and retinoic acid, together with their naturally occurring and synthetic analogs. In plant foods it is present in provitamin form which is known as carotenes. There are three types of carotenes present in plants. They are α-carotenes, β-carotenes and γ-carotenes. β-carotenes are most potent source of retinol because one molecule of β-carotene yields two molecules of Vitamin A *in vivo.* Dietary vitamin A is obtained from animal-derived foods, while plant foods provide carotenoid precursors such as β-carotenes, β-Cryptoxanthin, z-carotene, zeinoxanthin, zeaxanthin, neoxanthin, and violaxanthin.

Functions of Vitamin A: Vision is a non-hormonal, biochemical process involving a different vitamin A metabolite. Vitamin A is an essential dietary factor for normal embryogenesis, cell growth and differentiation, reproduction, maintenance of the immune system, and vision. Retinol is required for differentiation and function as steroid hormone. Retinol and retinoic acid are involved in regulation of gene expression. Vitamin A is required for maintenance of nervous tissue particularly myelin sheath formation.

9) Write the different forms and functions of Vitamin D.

Ans: *Forms of Vitamin D:* Vitamin D is present as cholecalciferol (vitamin D_3) and ergocalciferol (vitamin D_2) which is structurally similar secosteroids derived from the UV irradiation of provitamin D sterols. Exposure of the skin to sunlight converts 7-dehydrocholesterol to vitamin D_3, which, on reaching the blood capillaries of the dermis, is conveyed to the liver on a specific plasma transport protein. Vitamin D_2 is produced in plants, fungi, and yeasts by the solar irradiation of ergosterol. On irradiation, the provitamins are initially converted to previtamin D, which undergoes thermal transformation to vitamin D.

Functions of Vitamin D: Vitamin D in its active form 1, 25-dihydroxy cholecalciferol or calcitriol acts as a steroid hormone. It is synthesized from ergocalciferol and cholecalciferol. Vitamin D binds to chromatin of target tissue and expresses the genes for calcium binding protein and Ca^{2+}-ATPase (Calcium ion-ATPase) in the intestinal cells which increases calcium absorption by actively transporting Ca^{2+} across the plasma membrane. It is essential for mineralization of bones by stimulating the transcription of mRNA for calcium binding protein and alkaline phosphatase thus increasing the absorption calcium and phosphate ions in bone mineralization. Vitamin D decreases the pH of the lower gastrointestinal tract. It helps in the excretion of phosphate and citric acid. Calcitriol is an immuno regulatory hormone. It stimulates cell mediated immunity. It plays a vital role in monocyte/macrophage activation.

10) Write the different forms and functions of Vitamin E.

Ans: *Forms of Vitamin E:* The term vitamin E refers to group of four compounds that exhibit vitamin E activity. They are α-tocopherol, β-tocopherol, γ-tocopherol and δ-tocopherol. *Functions of Vitamin E:* α-tocopherol present in cell membrane, membrane of subcellular organelle and in cytosol functions as antioxidant or free radical scavenger. It is present in high concentration in tissues which are exposed to high O_2 pressure like erythrocytes, lungs, retina etc. It prevents peroxidation of membrane lipids particularly polyunsaturated fatty acid (PUFA) of membrane phospholipids. Vitamin E is required for fertility in animals. Vitamin E increases synthesis of hemeproteins by increasing synthesis of ALA synthase and ALA dehydratase. Vitamin E prevents dietary vitamin A and carotenes from oxidative damage.

11) Write the different forms and functions of Vitamin K.

Ans: *Forms of Vitamin K:* Different forms of Vitamin K are Vitamin K_1 and K_2. Vitamin K_1 is also called as phylloquinone which is the major form of vitamin found in plants particularly in green leafy vegetables. Vitamin K_2 also known as menaquinone is the vitamin K present in animals and synthesized by intestinal flora. Menadione is a synthetic analog of vitamin K. It is also called as vitamin K_3. It lacks characteristic side chain present in vitamin K_1 and K_2. It is converted to vitamin K_2 by alkylation in the body.

Functions of Vitamin K: Vitamin K is essential for the activation of specific proteins such as prothrombin involved in blood clotting and in bone mineralization through its role as a cofactor for γ-glutamylcarboxylase. This enzyme catalyzes a unique post-translational conversion of selected glutamate residues in the proteins to γ -carboxyglutamate residues, allowing the proteins to bind calcium and thus become activated.

12) What factors affect the stability of vitamins A and D?

Ans: *Vitamin A:* Retinol is readily oxidized by atmospheric oxygen, resulting in an almost complete loss of biological activity. Retinyl esters are more stable towards oxidation when compared to retinol. Retinol is extremely sensitive towards acids, which can cause rearrangement of the double bonds and dehydration. They undergo photoisomerization however, they are stable in the dark. Irradiation also rearranges double bonds to form inactive retro structures. The carotenoids become unstable due to degradation by heat, light, oxygen, trace amounts of acids, and active surfaces such as silica. They are sensitive to enzymatic and non-enzymatic oxidation. Moderate heat treatments such as blanching and cooking denature carotenoid binding proteins, thereby releasing the carotenoids so that they can be more readily extracted. Blanching of fruits and vegetables before processing inactivates lipoxygenase and other enzymes (e.g., peroxidase) that are involved in carotenoid destruction.

Vitamin D: It is sensitive to oxygen and light. In the presence of mild acid, vitamin D undergoes isomerization.

13) What factors affect the stability of vitamins E and K?

Ans: *Vitamin E:* Tocopherols are alkaline sensitive and their vitamin activity is destroyed by oxidation. Cooking and food processing may destroy vitamin E to some extent. Tocopherols and tocotrienols are destroyed fairly rapidly by sunlight and artificial light containing wavelengths in the UV region. The vitamers are slowly oxidized by atmospheric oxygen to form mainly biologically inactive quinones; the oxidation is accelerated by light, heat, alkalinity, and certain trace metals. The tocotrienols, by virtue of their unsaturated side chains, are more susceptible to destruction than the tocopherols. Vitamin E is the most radiation-sensitive of the fat-soluble vitamins. Presence of lipoxygenase destructs the vitamin.

Vitamin K: Compounds of vitamin K are decomposed by UV radiation, alkali, strong acids, and reducing agents, but are reasonably stable to oxidizing conditions and heat. Phylloquinone is sensitive to both fluorescent light and sunlight. However they are stable to cooking, γ-irradiation and freezing.

14) Explain the factors that affect the bioavailability of fat soluble vitamins.

Ans: Active forms of vitamins are better absorbed than their provitamin forms. Individuals with poor nutritional status generally are deficit in fat soluble vitamins since; protein and fat are required for absorption and transportation of fat soluble vitamins. Dietary fibre decreases the bioavailability whereas dietary fat enhances the bioavailability of fat soluble vitamins. Health habits such as alcohol and smoking decreases the bioavailability of fat soluble vitamins.

15) Write a note on absorption of fat soluble vitamins.

Ans: After the formation of micelles, lipids along with fat-soluble vitamins can passively be absorbed across the brush-border membrane. In the enterocytes, a cytosolic fatty acid-binding protein (FABP) facilitates intracellular transport of fatty acids by directing them from the cell membrane to the smooth endoplasmic reticulum, where triglyceride synthesis takes place. The triglycerides are packaged into chylomicrons, together with free and esterified cholesterol, phospholipids, apolipoproteins, fat-soluble vitamins, and carotenoids. After further processing, the chylomicrons are discharged from the enterocyte by exocytosis across the basolateral membrane and enter the central lacteal of the villus. They pass into the larger lymphatic channels draining the intestine, into the thoracic duct, and ultimately into the systemic circulation. The liver has the capacity to rapidly remove chylomicron remnants from the circulation.