



Dietary supplements

Clinical Pharmacy

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Lecture 8

Dietary Supplements include:

- Vitamins such as vitamin A, B, C, E, K &D.
- Minerals such as calcium, selenium, zinc and iron.
- Botanicals or herbs such as ginger.
- Botanical compounds such as curcumin and caffeine.
- Amino acids such as tryptophan and glutamine.

- **Vitamins** are chemically unrelated families of organic compounds that are essential in small amounts for normal metabolism.



- Because vitamins (with the exception of vitamin D) cannot be synthesized by humans, they need to be ingested in the diet to prevent disorders of metabolism.
- The prevalence of vitamin deficiency among those consuming a typical Western diet is **higher** than generally presumed, particularly in older adults.

Vitamins function as:

- ✓ **Antioxidants** – antioxidants can inhibit the process of oxidation, which frequently produces free radicals that can start chain reactions that damage lipids and proteins, and affect cellular function. Antioxidants interrupt such processes by being oxidized themselves, and thus removing free radicals.

- ✓ **Gene transcription elements** – factors that affect the first step in gene expression, the process of “transcription” by which a complementary RNA copy of a DNA sequence is made.(like vitamins A and D)

- ✓ **H/e donors/acceptors** – factors that can undergo changes in oxidation state in metabolism by being oxidized (losing electrons to an acceptor) or reduced (accepting electrons to a donor acceptor) in metabolism.(vitamins E& C)
- ✓ **Hormones** – metabolites released by cells or glands in one part of the body that affect cell function in another part of the body.
(like vitamins A and D)
- ✓ **Coenzymes** – metabolites that link to enzymes and are required for enzyme activity.(vitamin B)

The two fundamental ways in which vitamin deficiencies can be caused are:

Primary deficiencies ... involve failures to ingest a vitamin in sufficient amounts to meet physiological needs.

- Poor food habits
- Poverty
- Lack of vitamin-rich foods
- Vitamin destruction (e.g., during storage, processing, and/or cooking)
- Anorexia (e.g., homebound elderly, dental problems)

Secondary deficiencies ... involve failures to absorb or otherwise utilize a vitamin post- absorptively.

- Poor digestion (– absence of stomach acid)
- Malabsorption (impaired intestinal absorption of nutrients; e.g., as a result of diarrhea, intestinal infection)
- Increased metabolic need (e.g., pregnancy, lactation, infection)
- Increased vitamin excretion (e.g., diuresis, excessive sweating).

VITAMIN DEFICIENCY

- Occur in several special populations, including older adults; vegans; the very poor, malabsorption, little sun exposure, history of gastric bypass surgery, and those undergoing haemodialysis or receiving parenteral nutrition.

VITAMIN D

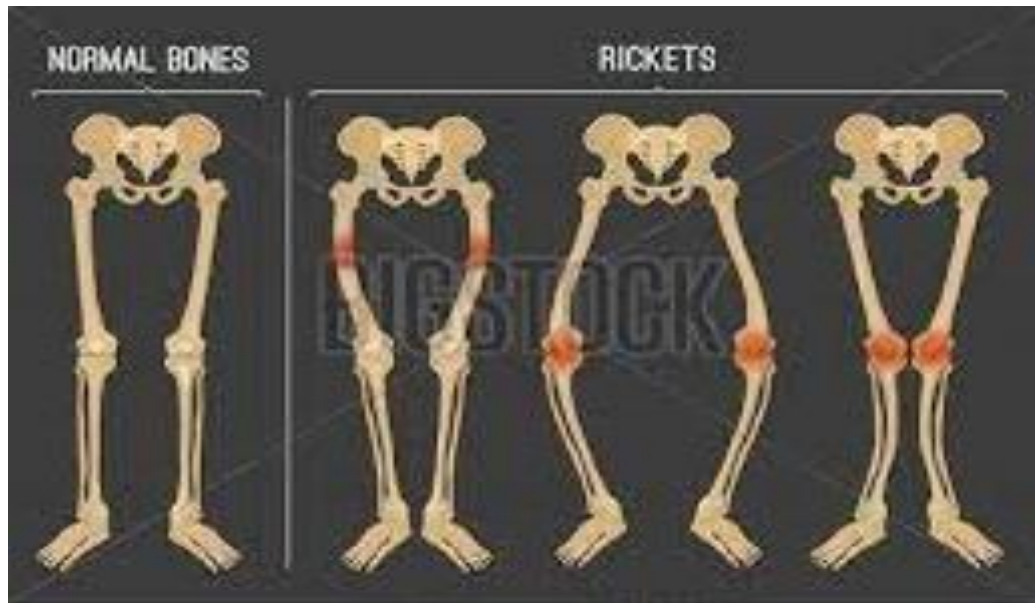


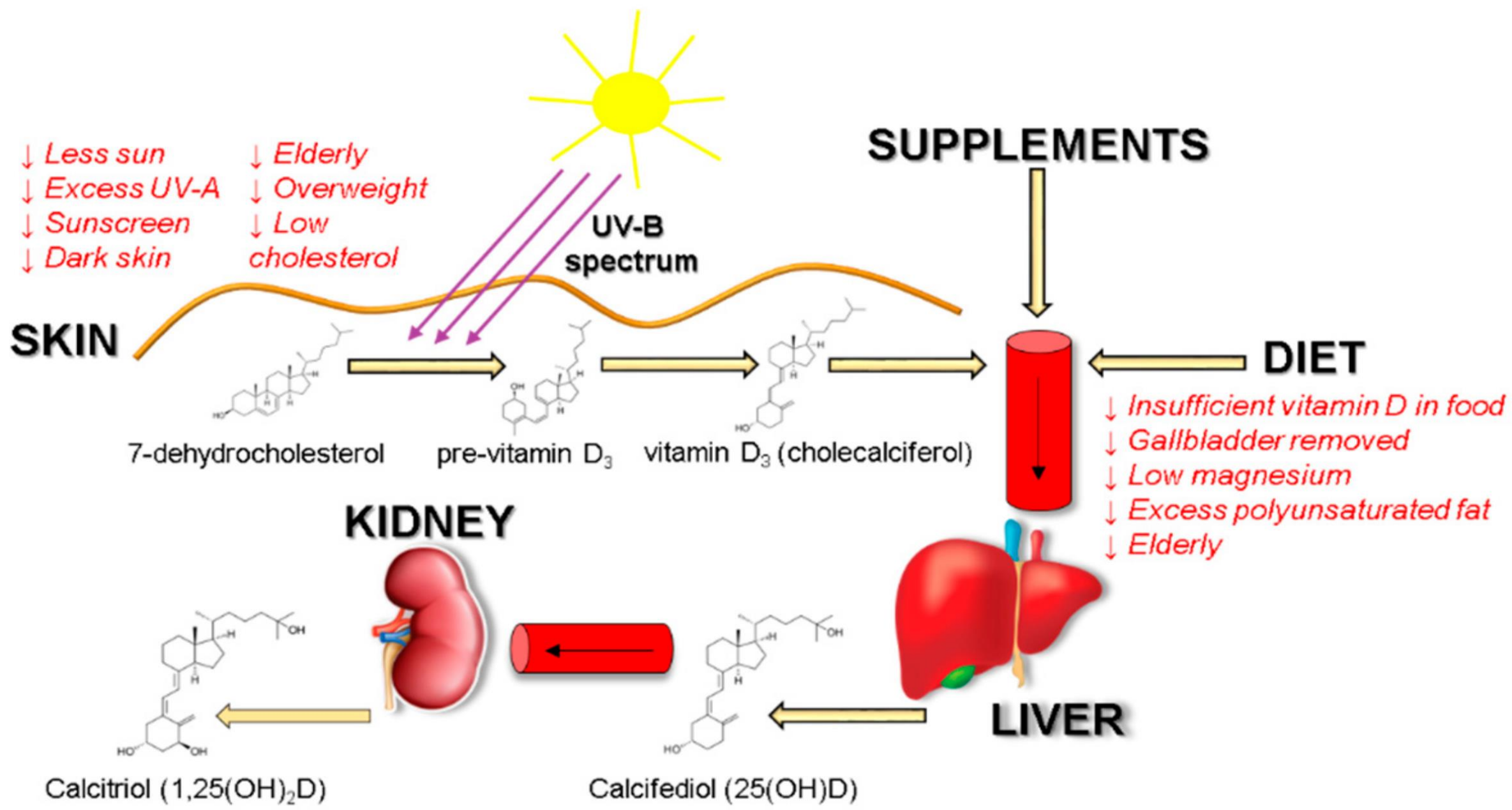
- Vitamin D, the “**sunshine vitamin**” is actually a hormone produced from sterols in the body by the photolytic action of ultraviolet light on the skin. Individuals who receive modest exposures to sunlight are able to produce sufficient amounts of vitamin to meet their physiological needs.



- Sources: Egg, liver, fish, cod liver oil.
- Vitamin D plays an important role, along with the essential minerals calcium (Ca), phosphorus (P), and magnesium (Mg), in the maintenance of healthy bones and teeth.

- Vitamin D deficiency increased risks of the metabolic bone diseases rickets and osteoporosis, falls, and fractures in older adults.
- Rickets, the deforming and debilitating disease involving delayed or failed endochondral ossification (mineralization at the growth plates) of the long bones, remains a problem in many countries.





Determinants of vitamin D3 biogenesis:

- **Exogenous factors** affecting sunlight exposure: season, time outdoors, sun screen use
- **Endogenous factors** affecting UVB responsiveness: skin thickness, pigmentation

DEFINING VITAMIN D SUFFICIENCY

- Vitamin D sufficiency is estimated by measuring Serum 25-hydroxyvitamin D (or calcidiol) concentrations.

25 (OH) Vitamin D Concentrations	Vitamin D Status
0-10 ng/ml	Deficient
10-30 ng/ml	Insufficient
30-150 ng/ml	Sufficient
>150 ng/ml	Potentially Toxic
The reference interval for 1, 25 (OH) ₂ vitamin D is 25-66 pg/ml.	

The calculation of dose is based on the formula as follows:

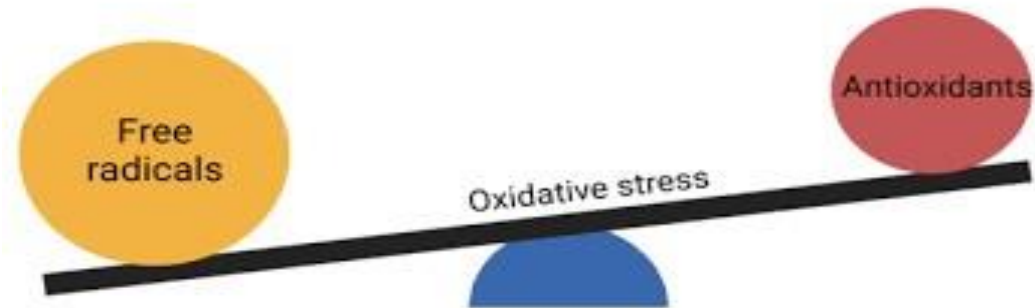
➤ **Vitamin D dose (IU)** = (target vitamin D level – current vitamin D level in ng/mL) X body weight in Kg/70 X 10,000

➤ **Vitamin D Dose (IU)** = [(8.52 - Desired change in serum 25-hydroxyvitamin D level) + (0.074 × Age) - (0.20 × BMI) + (1.74 × Albumin concentration) - (0.62 × Starting serum 25-hydroxyvitamin D concentration)]/(-0.002).

- ✓ Because dietary vitamin D intake is often low in older adults, suggest supplementation with **1000 units of vitamin D3** (cholecalciferol) {=0.025mg (25mcg)} daily, with downward adjustment in this dose.
- ✓ The supplement can be taken daily, or the adjusted dose can be taken as a once-weekly or monthly preparation, depending on the dosage strength used.(like 5000-600,000 should not be used daily.)
- ✓ It is important to ask patients about additional dietary supplements (some of which contain vitamin D) before prescribing supplemental vitamin D
- ✓ Vitamin D stores decline with age, especially in the winter.
- ✓ Thus, identification and treatment of vitamin D deficiency is important for musculoskeletal health and possibly even extra skeletal health, including the immune and cardiovascular systems.

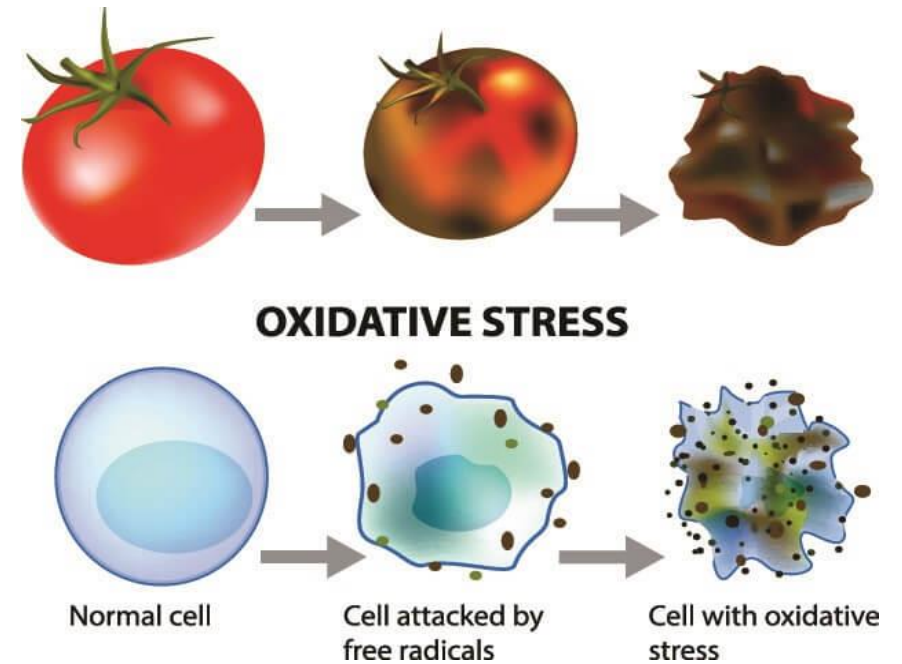
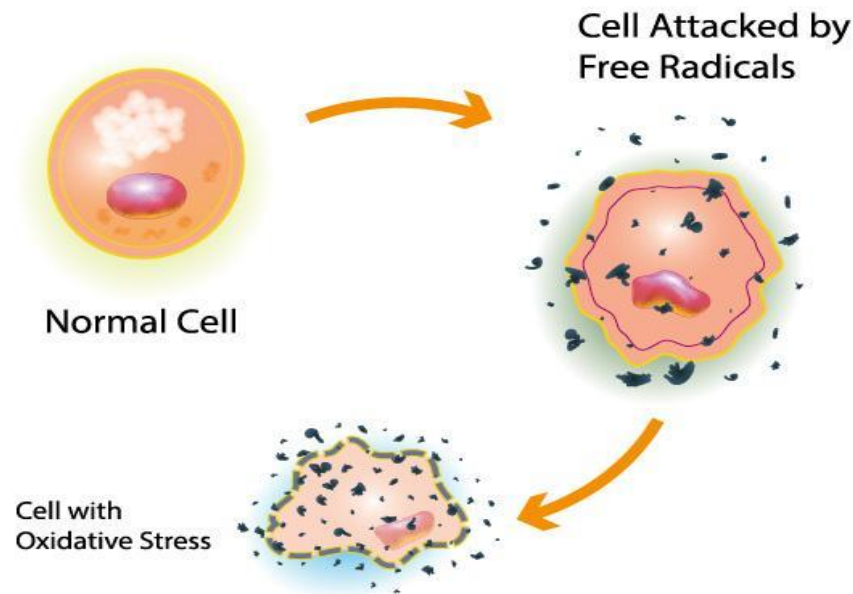
ANTIOXIDANT VITAMINS

- The antioxidant vitamins include vitamin A ,vitamins C and E. Many other compounds found in food, especially vegetables and fruits, also have antioxidant properties.



- Antioxidants can prevent cancer and cardiovascular disease by augmenting the body's ability to dispose of toxic free radicals, thereby retarding oxidative damage.

- Diets high in vegetables and fruits that are rich in antioxidants are associated with a reduced risk of cancer and cardiovascular disease. However, the association may be due to non-vitamin antioxidants, other compounds such as **flavonoids**.



Vitamin A

- Total vitamin A consists of preformed vitamin A (retinol) and the carotenoids such as beta-carotene.



Sources

- Provitamin A (carotenes) in pigmented vegetables and fruits e.g. Carrots, dark green leafy vegetables and apricots. Preformed vitamin A (Retinol) in animal origin e.g. liver and milk, egg yolk, and butter.
- **Vitamin A function** -- promotes vision, Integrity of epithelial cells, growth, bone remodelling, immune system

- In addition to antioxidant properties, retinol may also decrease cancer risk via other mechanisms such as inducing cellular differentiation.
- Carotenes (pro vitamin A) has antioxidants effect and give protection against cancers.
- Vitamin A deficiency causes :1- Epithelium changes: The skin will be characteristically dry, scaly and rough. 2- Eye changes Night blindness, xerophthalmia.
- For adult men, the recommended daily intake of vitamin A is 900 mcg(3,000 IU), while for adult women, it is 700 mcg(2,333 IU)
- ✓ 1 IU = **0.3 mcg** of retinol

- ✓ Neither retinol nor *b*-carotene is directly bioactive. Both compounds must be metabolized to generate the bioactivity of vitamin A.
- ✓ Supplements with preformed vitamin A in doses >10,000 international units taken in the first trimester of pregnancy have been shown to increase the risk of **congenital anomalies**
- ✓ Several synthetic retinoids that are prescribed for therapeutic use are known to be **teratogenic** and contraception is essential when they are used by women capable of becoming pregnant.
- **Note:** all lipid soluble vitamin require fat for proper absorption.

- **Vitamin C** (Ascorbic acid) is the most active reducing agent in living tissues. Vitamin C is commonly found in citric fruits and many types of vegetables.



- Its high concentrations are in the pituitary and adrenals, the eye and white blood cells. It is very easily destroyed by heat, alkalies such as sodium bicarbonates.
- **Function** as coenzyme , collagen formation(so improve healing of injury) & potent antioxidant(so inhibit aging process).
- **Deficiency of vitamin C** result in a disease termed **Scurvy**.

This disease is characterized by:

- 1- Looseness of teeth, inflammation of gums (gingivitis) and bleeding from gums.
- 2- Delayed healing of wounds and easy fracturability of bones.
- 3- Haemorrhage and increased liability for infections.
- 4- Iron deficiency anaemia (vit c keeps iron in ferrous state).



- Scurvy appears in person after 3-5 months of ascorbic acid deficiency due to slow metabolism of pre-existed vitamin C in body. Its deficiency results in defective formation of collagen due to failure of hydroxylation of proline to hydroxyproline, the characteristic amino acids of collagen.
- The normal adult body contains about 1.5 gm of vit C, so **250 mg TDS** orally will saturate the tissues quickly.



- Very large doses of vitamin C can lead to gastric irritation, diarrhea and oxalate stones as it is metabolized to oxalate.
- **Kidney stones** — Vitamin C increases urinary oxalate excretion and may increase the risk of kidney stones.

Vitamin E

- There are a number of biologically active vitamin E compounds in nature, including alpha-, beta-, gamma-, and delta- **tocopherol**.
- Vitamin E is a fat-soluble compound and protects cell membranes from **oxidation** and **destruction**.
- Vitamin E is found in a variety of foods including almonds, vegetable oils, and cereals. The form that is best known for its role in human health is alpha-tocopherol, which is abundant in soybean and corn oil and is common in the abundance of olive and sunflower oils.



- In addition, individuals taking anticoagulants should be particularly advised against high doses of vitamin E because of the synergistic action of vitamin E with these drugs.
- **Function of vitamin E** -antioxidant, protects lipids and cell membrane, Scavenger of Free Radicals & maintenance of membrane integrity in virtually all cells of the body.
 - Deficiency of vitamin E lead to neuropathy & increase bleeding risk
 - Daily requirement for adult is 15 mg (22.4 units).

Vitamin B1 (Thiamine)

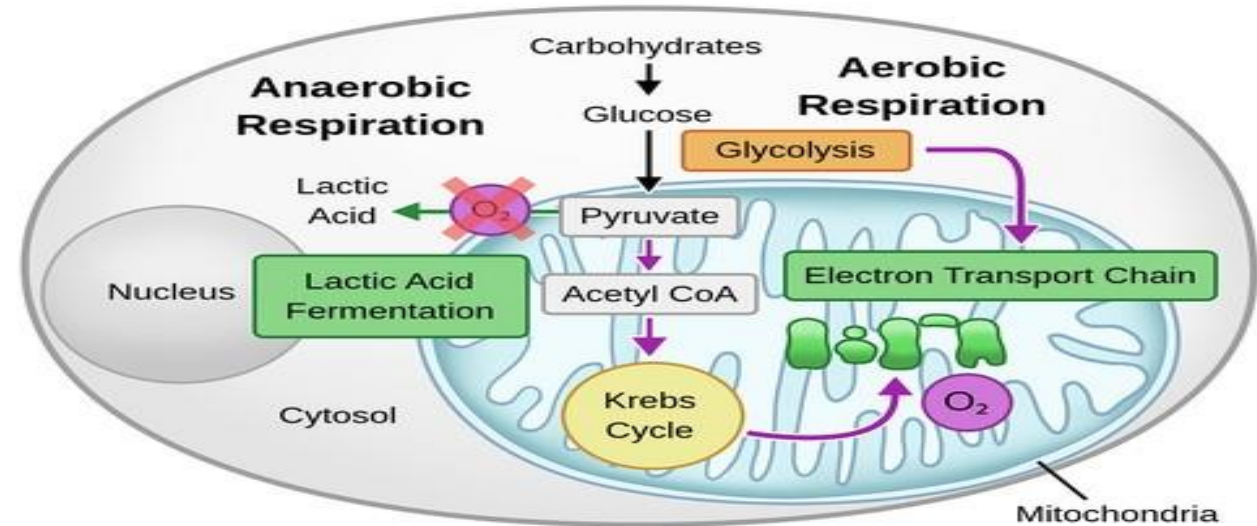
- **Dietary source.**-- Wheat, Nuts, Oatmeal, White bread, legumes and yeast.



Vitamin B1

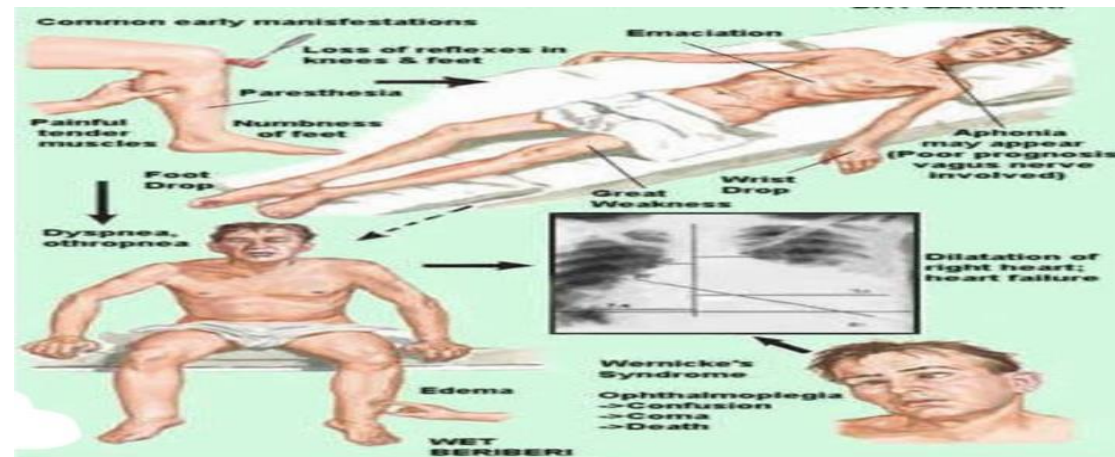
- **Deficiency results in a disease called beri-beri.**
- High CHO diets, intravenous glucose infusion predispose to and aggravate thiamine deficiency.

- The major manifestations of beri-beri are produced from accumulation of pyruvic and lactic acid (peripheral vasodilatation ~ hyperdynamic circulation) in blood as a result of failure to form thiamine pyrophosphate (TPP) which is a coenzyme for the decarboxylation of pyruvate to acetyl coenzyme A. So, the cells can't metabolise glucose aerobically, this is likely to affect the nervous system first, since it depends entirely on glucose.



Beri-beri is characterized by changes in peripheral nervous system, GIT and CVS including:

- 1- Peripheral polyneuritis with numbness, tender calf muscles and muscle wasting.
 - 2- Oedema
 - 3- Palpitation and high cardiac output, heart failure.
 - 4- Gastrointestinal disturbances e.g.: anorexia, nausea & vomiting.
- Treatment of *Beri-beri* -- **50 mg** thiamine 1M for 3 days then **10 mg** 3 *time/d* oral.



- **VITAMIN B2(Riboflavin)** is found in many commonly consumed foods, including milk, meat, eggs, Mushrooms, cereal, and green leafy vegetables. This may explain why overt riboflavin deficiency is rare.



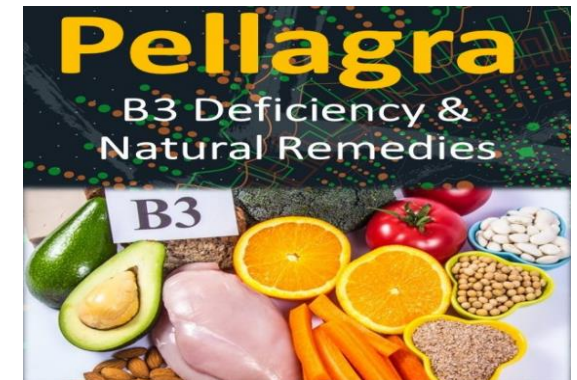
- ✓ Deficiency *results in non-specific manifestations that include:*
**Stomatitis and fissures at angles of mouth (angular stomatitis),
Seborrheic dermatitis of the face, Glossitis.**
- ✓ Dose of Riboflavin **5 mg** TDS orally.

Niacin (Nicotinic acid) or B3

It is called pellagra preventive factor (p.p. factor)

- Dietary Sources: liver, fish, meat, peanuts, yeast and coffee.
- Additional source is by synthesis from the amino acid tryptophan in body (60 mg tryptophan can give rise to 1 mg nicotinic acid).

- Requirements: 20 *mgl* day.
- Function –nutrient metabolism & cholesterol, FA synthesis
- Deficiency --*Results in a disease called pellagra which is characterized by:*
 - 1) Skin (erythema resembling severe sunburn)



2) Alimentary tract

- Diarrhea and other gastrointestinal disturbances

- ✓ **Dose of Nicotinamide** 100 mg/6 hrs orally.
- ✓ *Pellagra occurs in maize eating population due to:*
 - Maize is deficient in nicotinic acid.
 - Maize is deficient in tryptophan (from which nicotinic acid can be synthesized).
 - Maize contains nicotinic acid antagonists.



Pyridoxine -Vitamin B6

- Sources: liver, cereals, peanuts and bananas.
- Daily Requirements: 2 mg / day.



- **Functions:** The active form of the vitamin is pyridoxal 5 phosphate which is an important coenzyme involved in many metabolic reactions in amino acids metabolism including aminotransferases.
- **Deficiency** 1. neuropathy. 2. Hyperirritability and gastrointestinal distress. 3. Anemia, leucopenia, 4. depression in females under pills
- Dose -10 to 25 mg orally every six to eight hours
- Uses in Treatment of nausea and vomiting during pregnancy

Biotin (vitamin B7)

- Is an essential micronutrient vital to energy production, nervous system health, and other bodily functions.



- Biotin acts as an essential cofactor for five carboxylases which are involved in the catabolism of amino acids and fatty acids, synthesis of fatty acids, and gluconeogenesis
- Biotin is most famous for strengthening hair and nails and combatting alopecia due to effect of increasing protein synthesis, more specifically, keratin production.

- Biotin Deficiency cause hair thinning, hair loss and brittle nail, a red, scaly rash, usually around the eyes, nose, and mouth.
- A daily adequate intake 30 -100 mcg



- Biotin is a water-soluble vitamin, meaning excess biotin is usually excreted from your body.

FOLIC ACID (vitamin B9)

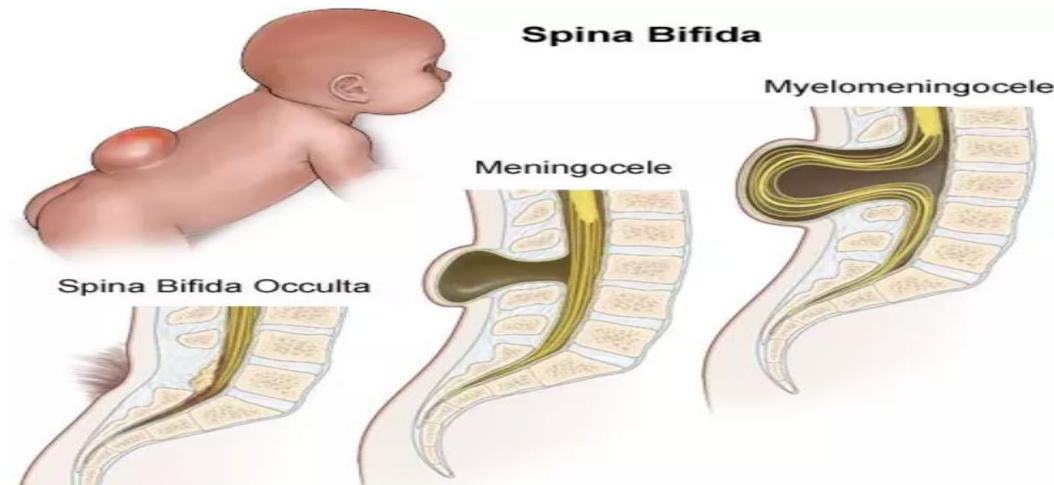
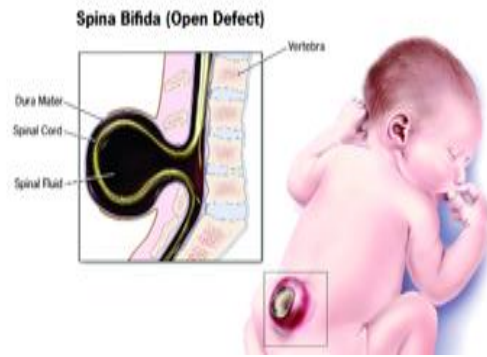
- *Folate* is the natural form of the vitamin found in food and is present in green, leafy vegetables, fruits, cereals, grains, nuts, and meats.



- **Folic acid** is the synthetic form of the vitamin that is included in supplements and food fortification, and has the same biologic effects as folate, but is more bioavailable and therefore more effective.
- Gross deficiency of folate leads to megaloblastic anaemia.

➤ **Neural tube defects** — Folic acid supplementation reduces the risk of neural tube defects, probably because folate is required for normal cell division.

- They recommend a folic acid supplement of **400 to 800** micrograms/day for all individuals planning or capable of pregnancy
- Excess folate intake (approximately twice the recommended dose) has been associated with peripheral neuropathy



VITAMIN B12 (COBALAMIN)

- Suboptimal vitamin B12 level is most commonly caused by poor absorption and inadequate intake of vitamin B12-containing food sources (e.g., liver, milk, fish, meat).



- Malabsorption of cobalamin is primarily the result of inability to release cobalamin from dietary proteins, especially in the presence of autoimmune antibodies against intrinsic factor or reduced gastric acid secretion.
- Vitamin B12 deficiency can also be seen among people following a vegan diet.

- Severe vitamin B12 deficiency causes neurologic disease (neuropathy) and megaloblastic anaemia.
- Measuring vitamin B12 levels may be indicated in individuals at increased risk for poor vitaminB12 intake, including vegans, and people with little dietary variation or poor-quality diets (such as some older adults and people living in poverty).
- Vitamin B12 deficiency may also be an important cause of hyperhomocysteinemia, particularly in older adults.
- ✓ High levels of homocysteine are associated with an increased risk of cardiovascular disease. Supplementation with folic acid, vitamin B6, and vitamin B12 can lower homocysteine levels.
- ✓ Daily requirement 2.4 mcg/day , Sever deficiency **1000mcg**



Vitamin K (The coagulation Vitamin)

Sources:

- Vit. K1 (phytomenadione) is present in green leafy vegetables e.g. spinach, cabbages, peas and cereals, tomatoes, egg yolk, and liver.
- Vit. K2 (menaquinone) synthesized by bacteria flora in the large intestine.

Vit K functions:

- Essential for prothrombin (factor II) & also essential for synthesis of other plasma clotting factors (VII, IX and X).
- It is required for synthesis of an amino acid (**carboxyglutamic**), which is part of the protein molecule of the mentioned four coagulation factors.

Vitamin K has important roles in these situations

- ✓ In newborn, primary deficiency can occur because placental transfer of vitamin K is inefficient, the neonatal bowel has not yet acquired bacteria and breast milk contains little amount of the vitamin. Vitamin K is given routinely to newborn babies to prevent haemorrhagic disease of the newborn.
- ✓ Oral anticoagulants act by antagonizing vitamin K.
- ✓ Deficiency of vitamin K lead to internal bleeding
- Dose for newborn **0.5mg – 1mg** IM at birth, then **2 – 4mg** PO vitamin K after first feeding then **2mg** at 2 – 4 weeks and again at 6 – 8 weeks
- Adult dose - **5 to 10 mg/d**



MULTIVITAMINS

- Most multivitamins contain 50 to 150 percent of the Recommended Dietary Allowance (RDA) for all vitamins, including folic acid and vitamins A, C, D, E, B2, B6, and B12.
- However, there are several variations of multivitamins, such as B vitamins alone, multivitamins with minerals, and multivitamins for specific groups (e.g., females, males, younger and older populations).
- The proposed rationale for taking a daily multivitamin for adults includes known or potential effectiveness for some of the component vitamins, relative safety in low doses, low cost.

SPECIAL DIETS

- A balanced diet with fruits and vegetables promotes health not only by providing known vitamins, but also because it contains fiber and thousands of other less well-defined micronutrients.
- However, people on restricted or special diets may have additional needs for vitamin supplementation.
- As an example, adequate vitamin B12 levels are strongly affected by dietary intake in addition to absorption. **In younger adults**, low consumption of animal-source food is the main cause of low vitamin B12 levels; **in older adults**, malabsorption of vitamin B12 from food is the most common cause.

Some special diets include:

- **Semi-vegetarian** – Meat occasionally is included in diet(not eat red meat but may eat fish and chicken).
- **Lacto- ovo vegetarian** – Eggs, milk, and milk products(no meat is consumed).
- **Lacto-vegetarian** – Milk and milk products, but no eggs or meat are consumed.
- **Macrobiotic** – Whole grains, especially brown rice, vegetables, fruits, and seaweeds are included. Animal foods limited to white meat or fish (once or twice a week).
- **Vegan** – All animal products, including eggs, milk, and milk products, are excluded from the diet.
- ✓ People who consume a vegan diet, Lacto ovo vegetarians and lactovegetarians should be supplemented with vitamin B12 (at the RDA of 2.4micrograms/day)

Toxicity At High Doses

- Water soluble vitamins (folate, vitamin C, B vitamins) can generally be tolerated at high doses, with toxicity occurring only at doses thousands of times the Recommended Dietary Allowance(RDA).
- A possible exception is the risk of kidney stones, which may be increased after doses of vitamin C that are 10 to 25 times the RDA.
- Fat soluble vitamins (vitamins A, D, E, K) are generally more toxic than water soluble vitamins and some may be risky even at doses short of toxicity. Vitamin D may cause hypercalcemia at doses as low as 4000 units/day (recommended upper limit) in some people.
- high-dose vitamin E (≥ 400 units/day) might increase all-cause mortality, patients without special indications should not take vitamin E supplements for disease prevention.