Sources and Diseases of Vitamin Deficiencies: A Review

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A. Introduction:

Vitamins are organic compounds that are required in small amounts in our diet but their deficiency causes specific diseases. Most of the vitamins cannot be synthesized in our body but plants can synthesize almost all of them, so they are considered as essential food factors. However, the bacteria of the gut can produce some of the vitamins required by us. All the vitamins are generally available in our diet. Different vitamins belong to various chemical classes and it is difficult to define them on the basis of structure. They are generally regarded as organic compounds required in the diet in small amounts to perform specific biological functions for normal maintenance of optimum growth and health of the organism. Vitamins are designated by alphabets A, B, C, D, etc. Some of them are further named as sub-groups e.g. B1, B2, B6, B12, etc. Vitamin A keeps our skin and eyes healthy. Vitamin C helps body to fight against many diseases. Vitamin C gets easily destroyed by heat during cooking. Vitamin D helps our body to use calcium for bones and teeth. Excess of vitamins is also harmful and vitamin pills should not be taken without the advice of doctor. The term “Vitamine” was coined from the word vital + amine since the earlier identified compounds had amino groups. Later work showed that most of them did not contain amino groups, so the letter ‘e’ was dropped and the term vitamin is used these days. Vitamins are classified into two groups depending upon their solubility in water or fat.

B. UNANI CONCEPT OF IMMUNITY

According to the concept of Unani Medical, nature has given the power to protect health. It provides thousands of systems and control mechanisms for each cell, tissue and the entire body. Some of these functions work within cells, some functions work between cells, and other functions work throughout the body to maintain health. The famous Unani scholar Ali Bin RabbanTabri wrote in his book Firdousal Hikmat: "Tabiat is considered the governing power of the body and Tabiat performs the governing function of the body with the help of many physical forces called QuwawateTabaiyya. Physical Faculty), Quwwate Haiwania (Vital Faculty) and Quwwate Nafsania (Nervous Faculty) ". Therefore, the main function of Tabiyat is to provide general management and defense or immunity against organisms.

Tabiat is defined as a collection of human structure, function and psychological characteristics. Hippocrates believed that everyone has a special ability called the body's defense mechanism, or expressed in the language of Unani Tabiat Muddabare Badan. This Tabiat is the best doctor and maintains the balance of four humours of the body. To maintain health, the quantity and body fluids must be adjusted according to the quality of the body's natural chemical components. Tabiat or the effectiveness of Quwwat-e-Muddabira Baden is due to diet, physical, psychological stress, hormones, etc. It will be affected by many exogenous and endogenous factors. Tabiyat-e-Insaniah controls all biochemical processes and physiological functions of the human body and also protects Aetidal Mizaj. strengthen tabiat (immunity) through immunomodulators, maintain a balanced temperament, maintain a humorous balance of quality and quantity, and the Asbabe Sitta Zarooriya (six of life essential elements) and adoption of maddiwa gair madditadabeer (i.e. regimenal therapy and counselling) Munzijwa Mushil (concoctive and purgative) therapy and Ilajbilghiza (Dieto-therapy)

Zakaria Razi said in “Kitabul Murshid” that "Tabiat relieves diseases and expels waste materials from human body and living beings." The existence of Tabiat can be understood through examples such as the healing of small wounds without any treatment and the improvement or cure of various pains and diseases after deep sleep or over time. All this comes from the administrative and managing power of Tabiat. Life-related functions such as regeneration, growth and development are found only in living bodies.

Regimental therapy (Ilaj-bil-tadbeer) is one of the most popular treatment methods and has been practiced by ancient Unani scholars since ancient times. Basically, the application of certain special technologies or physical methods improves the structure of the human body by eliminating waste and improving the body's defense mechanism. Fasd (blood draw / puncture), Ta'aleeq (hirudotherapy) and Hijaamat (cupping) are important parts of the treatment. Ibn-e- Sina, an eminent Unani scholar wrote in his famous book “Canon of Medicine”, that there are almost 36 regimens, amongs them “hammam” is one of the beneficiary regimes for increasing immunity. The "Hammam" (Turkish bath), also known as the healing bath, is one of the oldest Unani therapies used in the treatment of some diseases. The bathhouse is held in a

place reserved for the bath. The bathroom consists of several rooms, each opening into an adjacent room / another room, with special arrangements and conditions personalized according to the disease to be treated.

C. Deficiencies and Diseases of Vitamins.

These are essential organic nutrients, most of which are not made in the body, or only in insufficient amounts, and are mainly obtained through food. When their intake is inadequate, vitamin deficiency disorders are the consequence. Although vitamins are only present and required in minute quantities, compared to the macronutrients, they are as vital to health and need to be considered when determining nutrition security. Each of the 13 vitamins known today have specific functions in the body: vitamin A, provitamin A (Beta-carotene), vitamin B1, vitamin B2, vitamin B6, vitamin B12, biotin, vitamin C, vitamin D, vitamin E, folic acid, vitamin K, niacin and pantothenic acid. A person may be getting enough food to eat, but sometimes the food may not contain a particular nutrient. If this continues over a long period of time, the person may suffer from its deficiency. Deficiency of one or more nutrients can cause diseases or disorders in our body. Diseases that occur due to lack of nutrients over a long period are called deficiency diseases.

1. Vitamin A——— Night blindness
2. Vitamin B1———Beriberi
3. Vitamin B2——— Ariboflavinosis
4. Vitamin B3 ———Pellagra
5. Vitamin B5 ———Paresthesia
6. Vitamin B6 ———Anemia
7. Vitamin B7 —— Dermatitis, enteritis
8. Vitamin B9 & Vitamin B12 —— Megaloblastic anemia
9. Vitamin C —— Scurvy, Swelling of Gums
10. Vitamin D —— Rickets & Osteomalacia
11. Vitamin E —— Less Fertility
12. Vitamin K —— Non-Clotting of Blood**.**

Micronutrients, as opposed to macronutrients (protein, carbohydrates and fat), are comprised of vitamins and minerals which are required in small quantities to ensure normal metabolism, growth and physical well-

D. Basics in clinical nutrition, Physiological function and deficiency states of vitamins

I. Thiamine (vitamin B1)

Thiamine, usually in the form of thiamine pyrophosphate functions in the metabolism of carbohydrates and branched chain amino acids. It is absorbed mainly in the jejunum, and is transported in the blood in plasma and erythrocytes. Clinical signs of efficiency are widespread, initially with anorexia and weight loss, mental changes and muscle weakness. Severe deficiency has a number of clinical presentations:

1. Wet beri-beri, with cardiac failure and oedema
2. Dry beri-beri with neurological changes and muscle weakness.
3. Shoshin beri-beri is a fulminant cardiac failure with severe

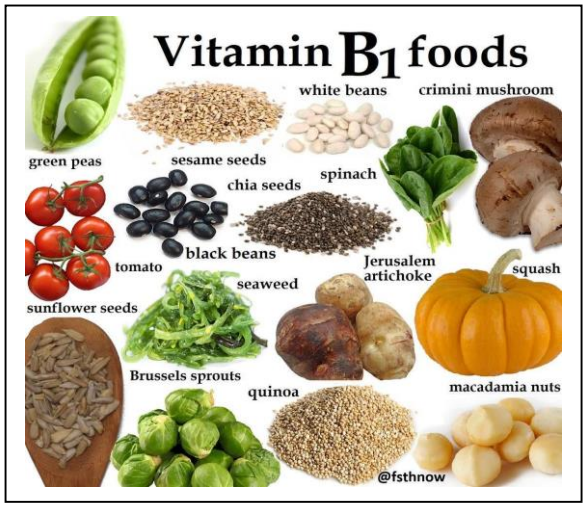

Fig. 1 Sources of Vitamin B1

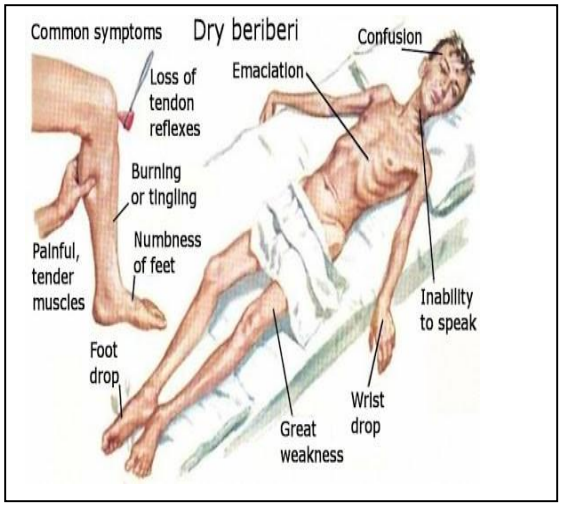

Fig. 2 Disease causes Vitamin B1

lactic acidosis, sometimes seen in intensive care units. Metabolic stress as a result of severe illness acutely increases the need for thiamine, as a result of increased oxidative metabolism and increased carbohydrate provision in the diet. Thiamine status is best assessed clinically, supported by measurements of erythrocyte thiamine, or the effect of added thiamine on erythrocyte transketolase activity in vitro.

II. Riboflavin (vitamin B2)

Riboflavin is an integral part of the co-enzymes flavine mononucleotide (FMN) and flavine adenine dinucleotide (FAD) e it is therefore a catalyst for redox reactions throughout metabolic pathways. Riboflavin is absorbed from the gut after hydrolysis of the bound co-enzymes. It circulates bound to albumin and immunoglobulins, and is converted to active co-enzyme within the cytoplasm of most tissues. Excess riboflavin is excreted in the urine. Signs of deficiency include cheilosis, angular stomatitis and glossitis and a seborrheic dermatitis. There is assumed to be a link with energy intake and therefore also with increased metabolism in stress. The best test for riboflavin status is erythrocyte riboflavin, or the activation in vitro of erythrocyte glutathione reductase.

Fig. 3 Sources of Vitamin B2

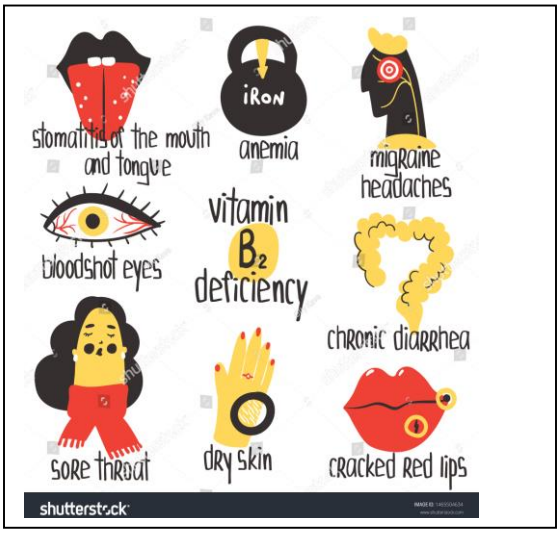

Fig. 4 Disease causes Vitamin B2

III. Niacin

Niacin (nicotinamide or nicotinic acid) has a central role in redox reactions, either as a hydride acceptor or donor, as part of the co-enzymes nicotinamide adenine dinucleotide (NAD), or its phosphate (NADP). These are of special importance in both carbohydrate and fat metabolism, and are synthesized in all tissues of the body. Excess niacin is excreted in the urine, mainly in the form of N-methyl nicotinamide. Severe niacin deficiency gives rise to pellagra, which has a typical symmetrical pigmented rash, a bright red tongue, gastrointestinal upsets, depression and memory loss. It would be unusual to measure niacin status, due to the complexity of tests, which include urinary excretion of metabolites, plasma concentration, or erythrocyte NAD. Metabolic stress is assumed to increase niacin requirement and recommendations for niacin intake are usually linked to those for energy intake.

Fig. 5 Diseases of Vitamin B3

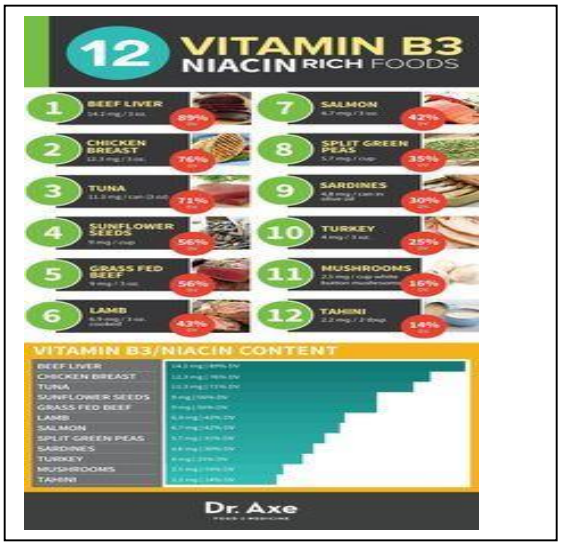

Fig. 6 Sources of Vitamin B3

VI. Vitamin B6

Vitamin B6 consists of pyridoxine and related compounds, the most metabolically active in man being pyridoxal phosphate (PLP). It is a co-enzyme for a large number of enzymes, primarily involved in amino acid metabolism. After absorption, pyridoxine metabolites are phosphorylated in the liver, and are transported in plasma bound to albumin. Excess pyridoxine is largely excreted in urine in the form of 4-pyridoxic acid. Deficiency of vitamin B6 leads to seborrheic dermatitis, and to a microcytic anaemia as a result of decreased haemoglobin synthesis. Serious illness leads to increased protein and amino acid turnover e this will lead to an increased requirement for

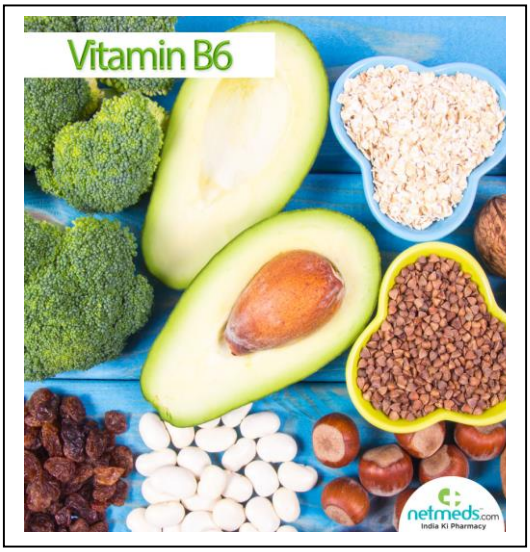

Fig. 7 Sources of Vitamin B6

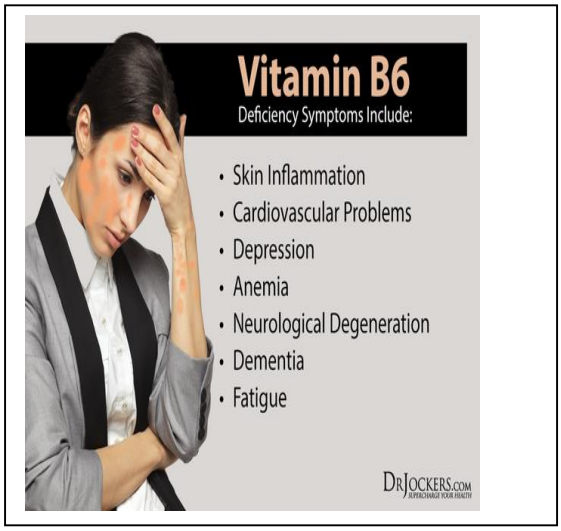

Fig. 8 Diseases of Vitamin B6

pyridoxine. The best markers of PLP status are plasma PLP that reflects the tissue stores of PLP, especially in the liver, but its concentration is subject to the effects of the acute phase response on plasma albumin. Alternatively, erythrocyte amino transferase has been widely used.

V. Folate

Folate is the term used to describe a group of vitamins related to folic acid. Folic acid itself rarely occurs in food, but is the form used in nutritional supplements. Food folate contains 1e6

additional glutamate residues. Folate co-enzymes take part in many reactions involving 1-carbon transfers, nucleic acid synthesis and amino acid inter-conversions. Food folates are hydrolysed to monoglutamate (folic acid) before absorption. Circulating folate is either free or bound to low affinity protein binders, especially albumin. For activity as a co-enzyme, folate monoglutamate must be converted intracellularly to polyglutamate forms. Folate deficiency leads to a rise in homocysteine concentration due to interference of the pathway, which regenerates methionine from homocysteine. Elevated homocysteine is currently recognized as being an independent risk

marker for coronary artery disease. There is much current interest in the potential beneficial

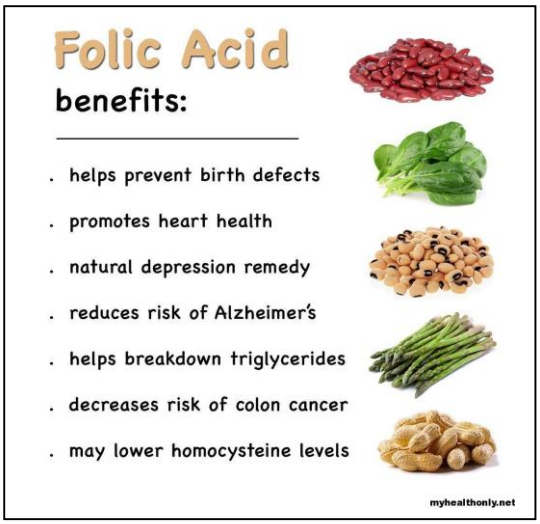

Fig. 10 Diseases of Vitamin B9

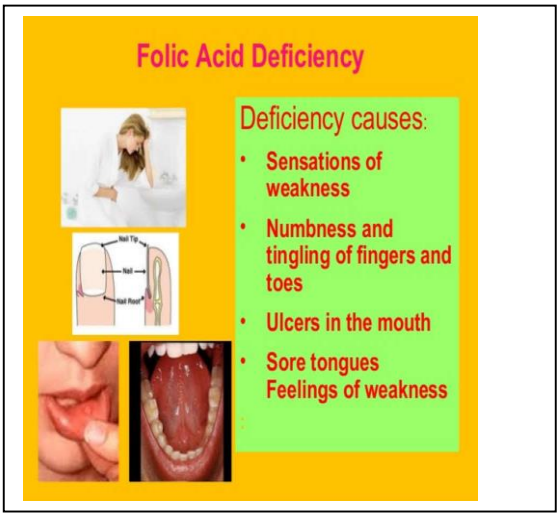

Fig. 9 Sources of Vitamin B9

effect of reducing homocysteine concentration by increasing folate intake. Clinical effects of folate deficiency include megaloblastic changes in bone marrow due to failure of DNA synthesis, leading to macrocytic anemia. The best markers of folate status are erythrocyte folate, which reflects whole body folate status, plasma homocysteine, with plasma folate being regarded as an indicator of recent folate intake.

VI. Vitamin B12

Cobalamin is a general term for cobalt containing vitamin B12 compounds. The main commercial form is cyanocobalamin. The active forms in the body are co-enzymes methylcobalamin or 5-deoxyadenosyl cobalamin, which are cofactors, especially for methyl transfer from methyltetrahydrofolate to homocysteine. Vitamin B12 absorption is a complex process.

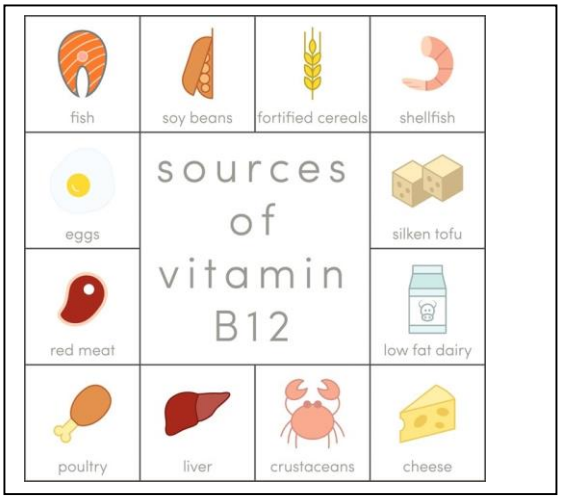

Fig. 11 Sources of Vitamin B12

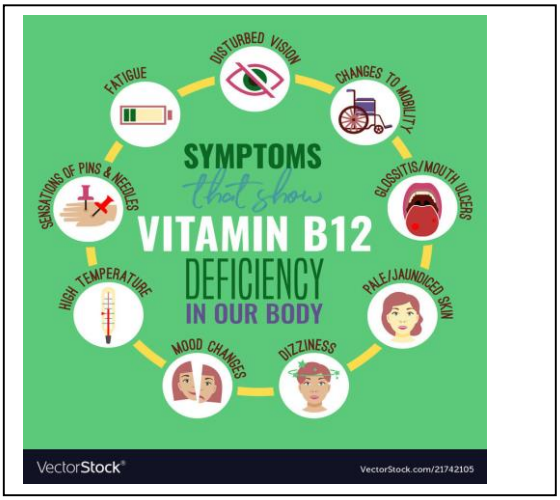

Fig. 12 Diseases of Vitamin B12

This involves dissociation of B12 from proteins in the stomach, complexing in the small intestine of B12 to Intrinsic factor, which has been secreted from the stomach, and absorption via specific receptors in the terminal ileum. Approximately 50% of dietary vitamin B12 is absorbed in the healthy adult and B12 ultimately is excreted in the urine or in the bile. B12 circulates in the plasma bound to transcobalamin. Deficiency of vitamin B12 gives rise to two clinical presentations. Pernicious anaemia is a macrocytic anaemia, similar to folate deficiency and results from failure of DNA synthesis. There may also be neutropenia and thrombocytopenia. Neurological changes on the other hand may include sensory disturbances especially in the lower limbs, gait abnormalities, memory loss and disorientation. About 25% of cases may only have neurological changes. The haematological changes are fully reversible although neurological changes may not. The best estimate of B12 status is serum B12 concentration. Metabolic markers of increased methylmalonic acid and homocysteine in serum may be helpful but lack specificity.

VII. Biotin

Biotin is a cofactor for carboxylase enzymes, mainly present in mitochondria. In cell turnover, biotin is released by the action of biotinidase, which is also involved in release of the protein-bound biotin in the diet.

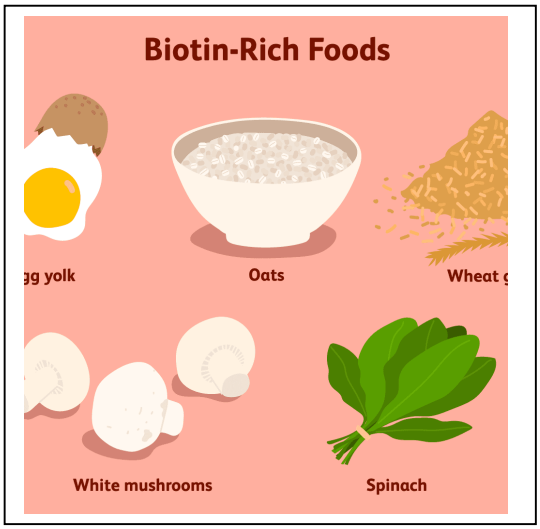

Fig. 13 Sources of Vitamin Biotin

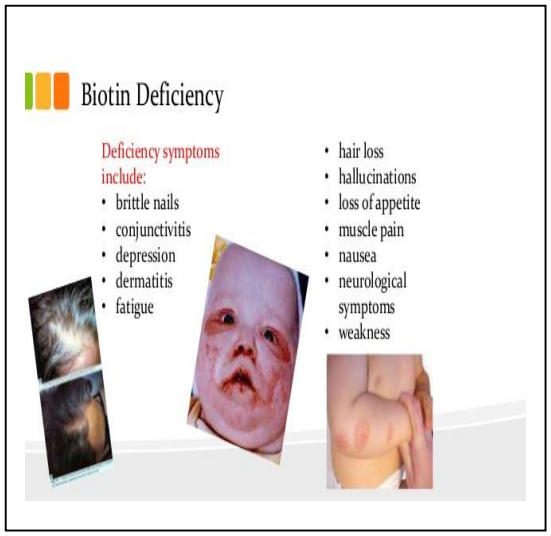

Fig. 14 Diseases of Vitamin Biotin

Most biotin is absorbed in the small intestine, but some may also be synthesized by gut microflora and absorbed in the colon. Deficiency of biotin has been observed in clinical nutrition and is characterized by dermatitis, conjunctivitis, alopecia and other abnormalities of the central nervous system. Plasma biotin is rarely measured and is a poor marker.

VIII. Vitamin C

Vitamin C comprises both ascorbic acid and dehydroascorbic acid (DHA). The most important biochemical function is to act as a reducing agent e as a cofactor for certain metallo enzymes, especially those involved in collagen hydroxylation, and as an aqueous phase antioxidant. It is also important for regeneration of other antioxidants, alpha-tocopherol and glutathione. Ascorbic acid

Fig. 15 Sources of Vitamin C

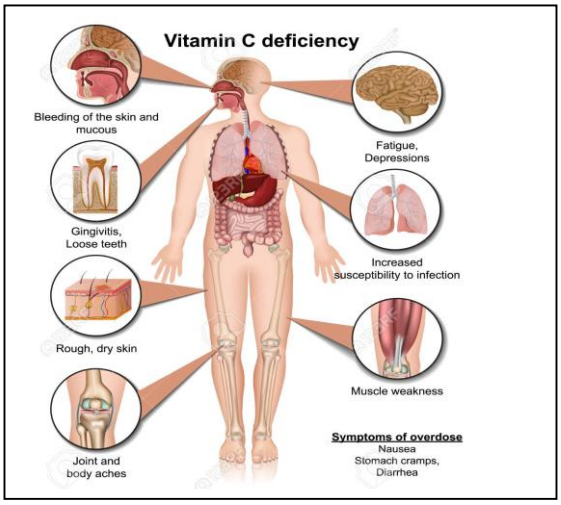

Fig. 16 Diseases of Vitamin C

is well absorbed in the small intestine. It exists in the plasma in the free reduced form, and is readily taken up into cells. Excess amounts of ascorbic acid are excreted in the urine. Deficiency of vitamin C leads to scurvy, which has multiple clinical features, including petechiae, bruising, inflamed and bleeding gums, and arthralgia and impaired wound healing. Less severe deficiency may present as gingival inflammation and fatigue. In infants there may be impaired bone growth and ossification. Assessment of vitamin C status consists of a range of functional measures as well as direct analysis. Functional measures include markers of oxidative damage of polyunsaturated fatty acids and DNA, and the extent to which these can be improved by vitamin C supplements. Greater specificity can be derived from direct measurement, either of plasma vitamin C for recent intake, or leukocyte vitamin C for whole body assessment. Cigarette smoking significantly lowers plasma vitamin C due to increased turnover and current recommendations are for higher intakes in such individuals.

XI. Vitamin A

Vitamin A is a fat-soluble vitamin comprising a family of complex 20-carbon molecules (retinol, retinal, retinoic acid). The term vitamin A includes pro-vitamin A carotenoids which are present in the diet and are converted to vitamin A in the intestinal mucosa after absorption. Vitamin A has a number of roles e for transduction of light into neural signals, to ensure normal structure of the

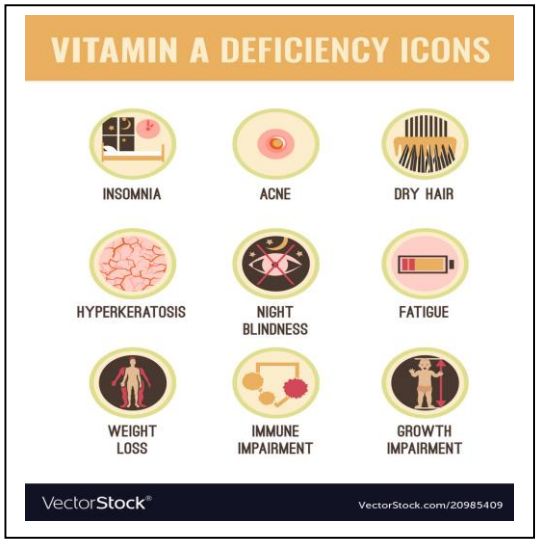

Fig. 17 Diseases of Vitamin A

Fig. 18 Sources of Vitamin A

cornea, and to maintain epithelial cell structure and function. Retinoic acid is a key regulator of gene expression for structural proteins, and has immune enhancing properties. Vitamin A is absorbed as retinol during the absorption of fats in chylomicrons, and partly as retinoic acid directly to the liver bound to albumin. Deficiency of vitamin A leads to exophthalmia, a condition that passes through stages of increasing severity: night blindness, conjunctival dryness, local damage (Bitot's spots), corneal ulceration and scarring, and finally blindness. The best marker for assessment of vitamin A status is dark adaptation.

X. Vitamin D

Vitamin D exists in two main forms:

1. Cholecalciferol (vitamin D3) is the main form in man, being synthesized in the skin under the action of ultraviolet light.
2. Ergocalciferol (vitamin D2) is the main form ingested in the diet, primarily from plants.

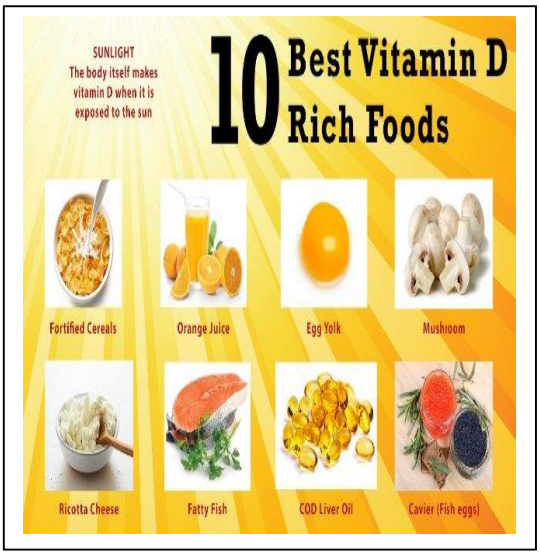

Fig. 19 Sources of Vitamin D

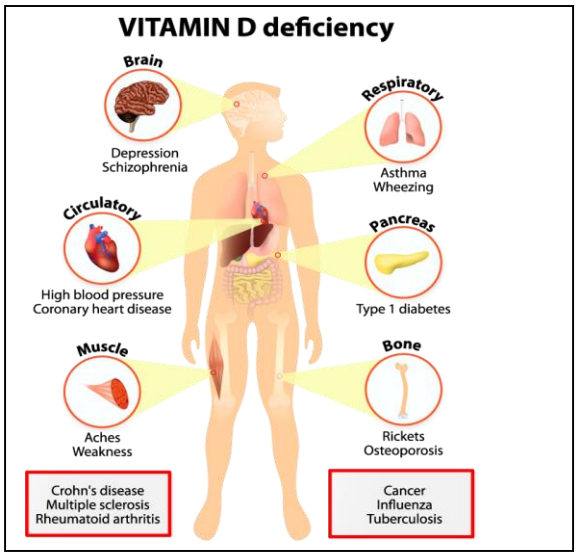

Fig. 20 Diseases of Vitamin D

Neither form is biologically active until it is converted in the liver to the 25-OH derivative, and this to the 1,25 (OH)2 derivative in the kidney. 1,25 (OH)2 vitamin D is the active form of the vitamin, and it controls plasma calcium concentration by modulating calcium absorption from the small intestine, phosphate excretion in the kidney and calcium release from bone. Vitamin D may also have other effects not related to calcium metabolism. Vitamin D deficiency is characterized by osteomalacia, where there is a defect in mineralization of bone matrix, pseudo-fractures may occur causing bone pain, and there may be psychological changes such as depression, and a proximal neuromyopathy. There is a risk of bony fracture following minimal trauma. The best assessment of vitamin D status is measurement of plasma 25eOH vitamin D, assuming renal function is normal. In addition, measurement of serum calcium, alkaline phosphatase and parathyroid hormone will give a good indication of the control of calcium metabolism. In severe disease or organ failure, vitamin D metabolism may be markedly affected. Either liver failure or kidney failure may prevent hydroxylation of vitamin D, so that the active form is not produced, leading to a fall in serum calcium.

XI. Vitamin E

Vitamin E comprises eight naturally occurring forms, but only the alpha forms are maintained in human plasma e tocopherols have a ring system with a long saturated side chain whereas tocotrienols have an unsaturated side chain. Vitamin E supplements are esters of alpha-tocopherol. Vitamin E functions as a non-specific chain breaking antioxidant. This prevents propagation of free radical reactions, especially in polyunsaturated fatty acids in membrane lipids and plasma lipoproteins. Vitamin E is relatively poorly absorbed and depends upon adequate micelle formation

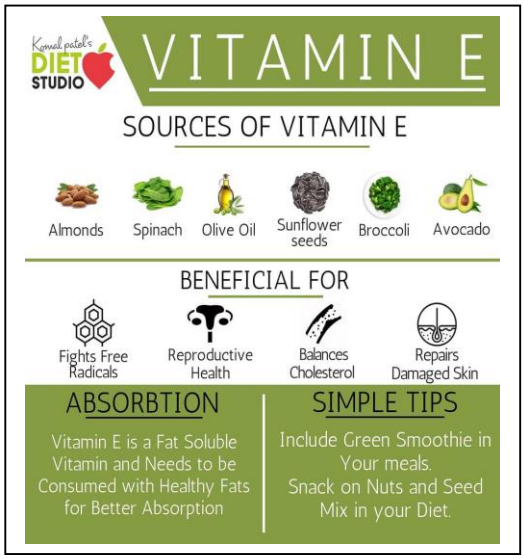

Fig. 22 Diseases of Vitamin E

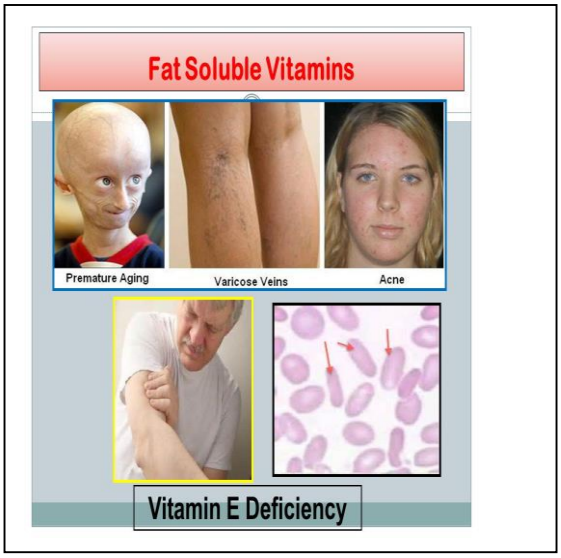

Fig. 21 Sources of Vitamin E

and uptake into enterocytes, and chylomicron production and absorption. Chylomicron remnants containing vitamin E are taken up by the liver, and vitamin E is then released into the circulation within very low density lipoproteins. Vitamin E rapidly transfers between lipoproteins and tissue lipids. Deficiency is rare in humans. The main signs are peripheral neuropathy, ataxia, skeletal myopathy and pigmented retinopathy. Assessment of vitamin E status includes biomarkers of resistance to haemolysis using hydrogen peroxide, or an increase in lipid peroxidation. Plasma vitamin E can be readily measured, but its relationship to intake is not clear, although plasma concentration may be suitable to confirm a very low intake. Vitamin E status is particularly affectedin situations where there is fat malabsorption e.g. short bowel or coeliac disease.

XII. Vitamin K

Vitamin K consists of two main families of compounds, each based on substituted naphthoquinones; phylloquinones, the plant form, contain a phytyl group, and menaquinones, produced by bacteria in the bowel contain polyisoprenyl side chains. Vitamin K is essential for gamma-carboxylation of glutamic acid residues in certain proteins e especially blood coagulation factors. Osteocalcin and matrix-Gla protein in bone also require vitamin K for gamma-carboxylation to achieve optimal function. Phylloquinone is absorbed from the diet as a component

Fig. 23 Sources of Vitamin K

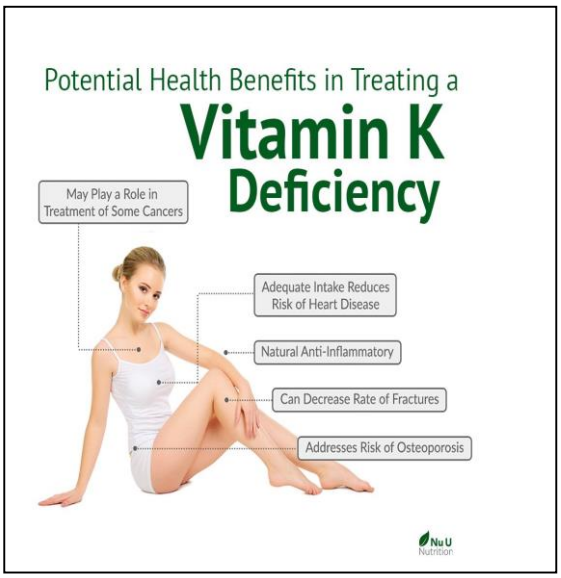

Fig. 24 Diseases of Vitamin K

of chylomicrons and circulates in VLDL and LDL. The relative contribution to the total intake of menaquinones produced by bacteria is not known, but some exogenous vitamin K is usually required. Deficiency of vitamin K leads to hypoprothrombinaemia, an increase in prothombin time, and increased bleeding. Vitamin K status is classically measured by prothrombin time, but this is not a sensitive indicator. It may be suitable for diagnosis of gross deficiency, but increasingly plasma phylloquinone concentration and an estimate of under carboxylated prothombin or osteocalcin are used for research purposes. Vitamin K status is of most concern in patients with severe liver disease, where high dose vitamin K intake may be necessary for production of blood coagulation factors, or where a low intake is coupled with the use of non-absorbed antibiotics, leading to reduced gut derived vitamin K.

E. Food-Based Approaches to Nutrition Management

Food-based strategies are the most obvious way to overcome multiple nutrient deficiencies. One such food-based strategy is dietary diversification, which aims to broaden the diet to include foods that are naturally rich in micronutrients. Another is food fortification, in which micronutrients are added to foods that form part of the existing diet. Whereas food fortification often targets a specific micronutrient, dietary diversification addresses multiple micronutrient deficiencies simultaneously.

Dietary diversification is the most sustainable way of addressing micronutrient undernutrition, although the benefits are not immediate and implementation should simultaneously include short-term strategies, such as micronutrient supplementation. Production of micronutrient-rich foods can occur through various approaches: small-scale community vegetable and fruit gardens; school-based gardens; production of fish, poultry, and small animals; and the commercial production of micronutrient-rich foods. Key resources needed to ensure the success of these projects include access to water, a regular supply of seeds, capital, or

credit to purchase inputs, training on how to grow and care for crops, an adequate labour force, fencing, access to markets, and availability of fertilizer and pesticides. A nutrition education component should be linked to these projects to ensure the increased consumption of micronutrient-rich foods.

Dark green, leafy vegetables are important sources of folate, vitamins A and C, and calcium, and the consumption of legumes can improve iron, folate, thiamine, and riboflavin status. While the consumption of fruit and vegetables should therefore be encouraged, meat and dairy products are often a better source of multiple micronutrients. For example, the inclusion of dark green, leafy vegetables, orange-fleshed vegetables, and red and orange fruits in the diet can increase the intake of provitamin A carotenoids, which are converted to retinol, the active form of the vitamin; however, liver, eggs, and milk are the richest source of preformed vitamin A. In addition, organ meats provide vitamins D, E, and folate. The consumption of meat and dairy products can also lead to improvements in the status of iron, calcium, zinc, thiamine, riboflavin, and vitamins B6, and B12; this is true for both infants and adults.

Other factors can either enhance or inhibit the absorption of micronutrients. For example, in countering iron-deficiency anaemia, it is important not only to encourage the intake of iron-rich foods, such as legumes, green leafy vegetables, and meat, but also to encourage the intake of vitamin C (in the form citrus fruits, for example), which promotes iron absorption. At the same time, because tea is high in tannins that can inhibit iron absorption, it is best not to drink it with foods that would otherwise be excellent sources of iron. Although legumes are a good source of protein as well as iron, they contain phytate, an antinutrient that inhibits the absorption of iron, zinc, and other minerals. Impoverished people tend to consume a diet high in both cereals and legumes, staple foods that are often associated with unsatisfactory growth, probably owing to their high fibre and phytate content. These substances bind to minerals and as a result reduce their intestinal absorption. Household food preparation methods that involve soaking cereals and legumes prior to cooking help promotes the enzymatic hydrolysis of phytate, while also deactivating certain antinutrients, thereby increasing the bioavailability of iron and zinc.

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