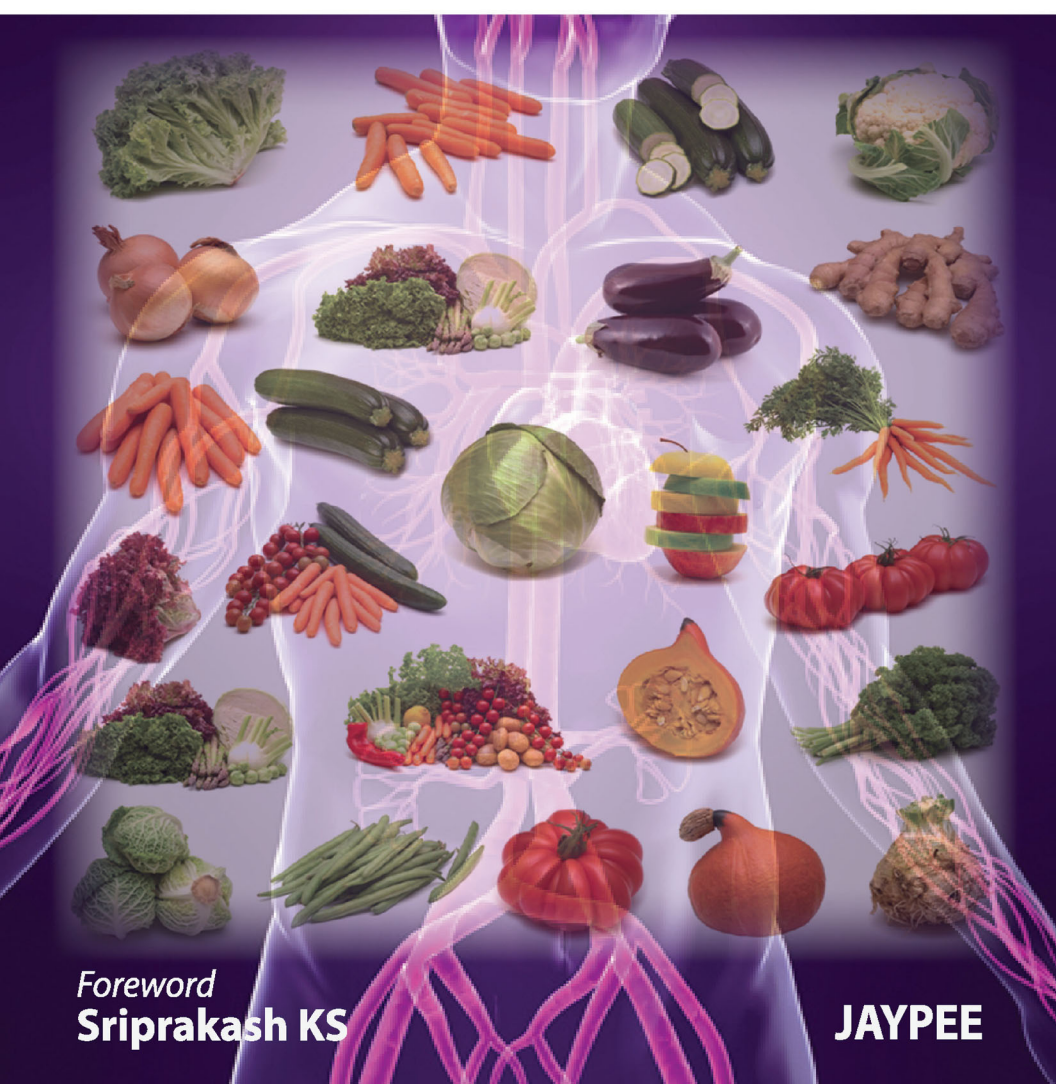
Vitamins in Health & Disease

ML Kulkarni



Foreword
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Chapter 4

Vitamin E

INTRODUCTION AND HISTORY

In 1922, HM Evans and Katherine S Bishop reported from California University that pregnant rats, which were fed on formulated diets containing most of the known nutritional factors, did not reach term gestation. With dietary supplementation of fresh lettuce, deaths of the fetuses were prevented, thus implying the probable existence of an unknown nutritional component. This component was later designated as vitamin E. This fat-soluble vitamin was first isolated from wheat germ oil in 1936 by Evans. In 1922, the substance was proved essential for normal reproduction. The generic name tocopherol was given, when it was recognized that more than one compound possessed vitamin E activity. Tocopherol is a Greek word meaning "to bring forth in child birth". Hence it is also known as "antisterility vitamin". Fernholz discovered the structure of this vitamin in 1937 and the synthesis was done by Karrer in 1938. It is an essential nutrition because body cannot make its own vitamin E. In 1968, Food and Nutrition Board of the National Research Council established that vitamin E is an essential vitamin.

BIOCHEMISTRY AND METABOLISM

Vitamin E, an essential fat-soluble vitamin, includes eight naturally occurring compounds in two classes designated as tocopherols and tocotrienols with different biological activity. All are derivatives of 6-chromanol and differ in the number and position of methyl groups on ring structure.

d-alpha-tocopherol has the highest biologic activity and is the most widely available form of vitamin E in food. The other isomers (beta, gamma and delta) are the most abundant in typical western diet. Gamma-tocopherol, the second most plentiful form of vitamin E has only 20 percent of bioactivity of alpha-tocopherol. The commercially available synthetic form of vitamin E comprise of approximately an equal mixture of eight stereo isomeric forms of alpha-tocopherol.

There are four-tocopherol homologues and four tocotrienols (Fig. 4.1). Collectively they are referred as tocochromanols. The homologues

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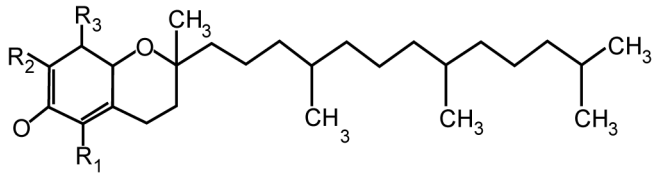


Fig. 4.1: Structure of alpha, beta, gamma and delta-tocopherol

are designated as α, β, γ and δ based on number and position of methyl groups on the chromanol ring (Table 4.1).

Table 4.1: Position of methyl groups in alpha, beta, gamma and delta tocopherol

Compound	R_1	R_2	R_3
α	CH_3	CH_3	CH_3
β	CH_3	H	CH_3
γ	H	CH_3	CH_3
δ	H	H	CH_3

Metabolism

The vitamin is absorbed from the gastrointestinal tract by a mechanism, similar to that of other fat-soluble vitamins and its absorption is dependent on digestion and absorption of fat. Before intestinal absorption, most esters of vitamin E are hydrolyzed by esterases secreted by pancreas or found in intestinal mucosa. It is absorbed into the intestinal mucosa by a non-saturable, non-carrier-mediated passive diffusion process. It is transported in association with newly synthesized chylomicrons and VLDL (Fig. 4.2). These pass by the mesenteric lymphatics and thoracic duct into systemic circulation. Newly absorbed vitamin E accumulates in almost all the tissues, largely in adipose tissue, liver and muscle. These tissue stores can protect against deficiency for a long time. Thus alpha-tocopherol is transferred to target tissues. The alpha and gamma-tocopherol remaining in chylomicron remnants are transported to the liver. Alpha-tocopherol is resecreted in hepatically-derived VLDL and HDL. Gamma-tocopherol is not resecreted, but appears to be metabolized or excreted by the liver. Hepatic tocopherol-binding protein (TBP) may play a role in why alpha-tocopherol is incorporated in lipoproteins and not gamma-tocopherol. Approximately, three fourth of vitamin is excreted in bile and the rest is excreted as glucoronides in urine.

Alpha-tocopherol Equivalent (α-TE)

For dietary purposes, vitamin E activity is expressed as α-tocopherol

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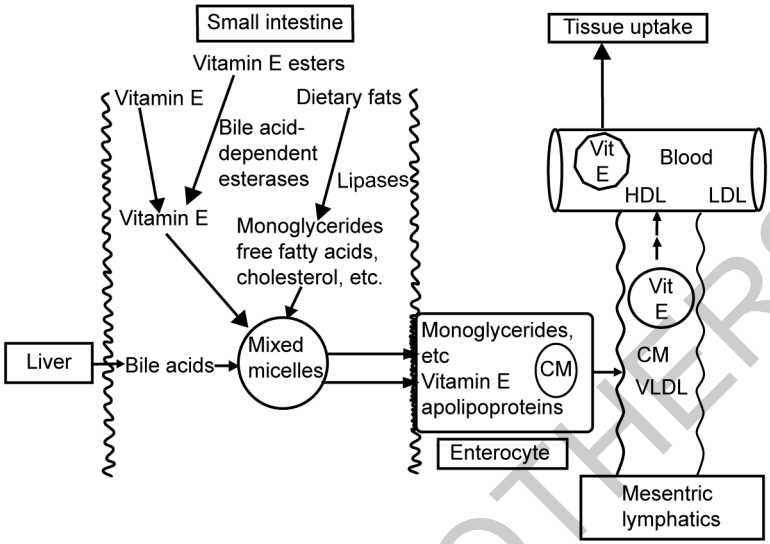


Fig 4.2: Intestinal absorption of vitamin E

equivalents (α-TEs). One α-TE is the activity of 1 mg RRR-α-tocopherol. In a diet containing natural forms of vitamin E, it is estimated by multiplying the number of milligrams of β-tocopherol by 0.5, γ- tocopherol by 0.1 and α-tocotrienol by 0.3. Synthetic forms of α-tocopherol should be multiplied by 0.74.

α-TE = alpha-tocopherol (mg × 1.0) + beta-tocopherol (mg × 0.5) + gamma-tocopherol (mg × 0.1) + alpha-tocotrienol (mg × 0.3).

SOURCES

The richest natural sources of vitamin E are vegetable oils, cereal grains, sunflower oils and seeds, wheat germs, nuts and whole grains. Wheat germ oil is the single richest source (Table 4.2).

Table 4.2: Vitamin E content of vegetable oils (mg tocopherol/100 g)

Oil	α-tocopherol	γ-tocopherol	δ-tocopherol	α-tocotrienol
Coconut	0.5	0	0.6	0.5
Corn	11.2	60.2	1.8	0
Palm	25.6	31.6	7	14.3
Olive	5.1	Trace	0	0
Peanut	13	21.4	2.1	0
Soybean	10.1	59.3	26.4	0

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Oil	α-tocopherol	γ-tocopherol	δ-tocopherol	α-tocotrienol
Wheat germ	133	26	27.1	2.6
Sunflower	48.7	5.1	0.8	0

Animal origin foods are generally low in vitamin E. Liver and eggs contain moderate quantity. Other sources include polyunsaturated fatty acids (PUFA), corn and spinach. Vitamin E is destroyed by oxygen, heat and light. Freezing also decreases vitamin E. During refining, processing and storage of foods, some of the vitamin E content is lost. Other sources include salad dressings, peanut butter, whole milk, tomato products and apples.

REQUIREMENT

Vitamin E is not a typical vitamin and differs from other vitamins in many ways. Most other vitamins have little benefit if taken in above recommended dietary allowances (RDA). Vitamin E however is an antioxidant, so the amount needed by an individual varies. Diseases like scurvy, beriberi and rickets have been linked to the deficiency of a particular vitamin. Deficiency due to lack of vitamin E is very rare. Vitamin E deficiency causes symptoms in persons with fat malabsorption, preterm infants and patients on total parenteral nutrition.

The RDA of alpha-tocopherol is 10 mg (15 IU) for men, 8 mg (12 IU) for women. In healthy children, RDA is 5 mg alpha-tocopherol/day. RDA of vitamin E is only a recommendation and individual needs vary. RDA does not take into consideration factors that may increase a person's need, e.g. diet, lifestyle, diseases, stress, exposure to pollutants, all which increase free radicals in the body. Those living in typical urban environment have higher requirement. RDA for low birth weight (LBW) infants is 0.5 mg/100 Kcal of alpha-tocopherol and oral administration of 5 to 25 IU of alpha-tocopherol acetate per day.

Vitamin E requirement increases as intake of poly unsaturated fatty acids (PUFA) increases. Increased cell membrane, PUFA enhances membrane susceptibility to free radical oxygen damage. Hence to prevent lipid peroxidation, vitamin E dose depends on dietary PUFA content. Iron catalyses cell lipid oxidation through generation of free radicals and it also interferes with vitamin E absorption from the gut. Therefore, dietary supplementation of iron increases vitamin E requirements.

DEFICIENCY

Preterm infants have increased vitamin E requirement. Vitamin E deficiency is almost entirely restricted to preterm infants as their body

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stores are low and associated fat malabsorption decreases vitamin E levels. Also preterm diets are generally rich in PUFA to improve fat absorption. Preterms receiving supplemental oxygen are at a risk of oxidative tissue injury. It has also been reported in preterms with low vitamin E : PUFA ratios. The manifestations are mild generalized edema, mild hemolytic anemia and thrombocytopenia. Recommended commercial infant formulas provide a vitamin E: PUFA ratio greater than 0.4, sufficient to prevent lipid peroxidation.

The protein-energy malnutrition (PEM) is associated with low vitamin E levels, but a claim that megaloblastic anemia responds to vitamin E has not been substantiated. When deficiency is observed in older children and adults, it is related to defective lipid absorption or transport. Secondary deficiency may occur in patients with steatorrhea in celiac disease, cystic fibrosis, short bowel syndrome, biliary atresia and abetalipoproteinemia and patients on total parenteral nutrition. It is seen that 50% to 75% children with chronic cholestasis are vitamin E deficient. During cholestatic liver disease, impaired secretion of bile acids by liver result in intraluminal bile acid concentration below critical micellar concentration, causing severe malabsorption of vitamin E. In both children and adults, degree of malabsorption of vitamin E is related directly to the severity of cholestasis and inversely to the duration of cholestasis. Sokol has summarized evidence of a unique inborn error, probably an autosomal recessive inheritance of vitamin E metabolism, termed as "isolated vitamin E deficiency". There is no fat malabsorption or gastrointestinal, liver or lipoprotein abnormality. Neurological symptoms appear in the first decade. Response to vitamin E is satisfactory.

The manifestations of vitamin E deficiency are as follows:

1. Hemolytic anemia
2. Fat malabsorption
   a. Cystic Fibrosis
   b. Short Bowel Syndrome
   c. Abetalipoproteinemia
3. AVED—Ataxia with vitamin E deficiency

Hemolytic Anemia

Due to limited transfer of vitamin E through placenta, it was found out that newborn infants had low serum vitamin E levels. At higher risk are those fed on formula feeds with low vitamin E and abundant PUFA and iron. Infants usually develop hemolytic anemia at 8 to 10 weeks of age

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which is correctable by administration of vitamin E. Clinical features comprises the triad of hemolytic anemia, edema and skin lesions. Other clinical features include an irritable and restless infant, noisy breathing, nasal discharge and edema involving face, lower limbs and genitalia. Skin lesions appear on face and extend to involve the scalp.

Pathogenesis

The main mechanism proposed is that due to low placental transfer of vitamin E, the life span of RBC's are shortened as a result of which there is a general increase in marrow activity.

How does Vitamin E help?

Vitamin E probably has the ability to protect cell membrane phospholipids from peroxidative degeneration. Studies have also proved that as the serum vitamin E levels increases, so does the survival of erythrocytes increase.

Complete eradication of hemolytic anemia is possible by adding vitamin E to infant milk formulas and by achieving an adequate vitamin E to PUFA ratio (> 0.4).

Fat Malabsorption

It has been observed that any condition that causes steatorrhea will lead to a secondary deficiency of vitamin E due to the association between intestinal dietary fat absorption and vitamin E.

Causes for fat malabsorption can be classified as genetic and non-genetic.

Genetic Cause

Abetalipoproteinemia: It is a rare inborn error of lipoprotein metabolism mainly due to defect in the production and transport of small amounts of apolipoprotein B (ApoB) containing lipoproteins (LDL, VLDL and chylomicrons) in the circulation. ApoB is the primary apolipoprotein of low-density lipoproteins (LDL or "bad cholesterol"), which is responsible for carrying cholesterol to tissues. Chylomicrons and VLDL contains principally two essential apolipoproteins (ApoB-48 and ApoB-100), which are encoded by the same gene which are synthesized in the intestine and liver respectively.

The genetic basis of abetalipoproteinemia is a mutation in the gene coding for microsomal triglyceride transfer protein. The microsomal triglyceride transfer protein plays a role in lipoprotein arrangement and assembly in Golgi apparatus.

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Non-genetic Causes

1. Chronic cholestatic hepatobiliary disorders
2. Cystic fibrosis
3. Short bowel syndrome

Chronic cholestatic hepatobiliary disorders: In chronic cholestasic disorders due to impaired bile flow, bile components are insufficient in the intestinal lumen; which leads to micelle production failure. Following micelle production failure there is malabsorption of dietary fat. Infants develop neuropathy as they have low stores of vitamin E. High doses of oral vitamin E (100–200 IU/kg/day)

Cystic fibrosis: It is a condition in which there is increased viscosity of pancreatic secretions. This leads to pancreatic duct obstruction and ultimately pancreatic enzyme secretion failure due to fibrosis of the exocrine pancreas. Steatorrhea develops which causes vitamin E deficiency characterized by posterior column neuroaxonal lesion.

Short bowel syndrome: It refers to the nutritional sequel of surgical small bowel resection. Surgeries are done mainly for Crohn's disease and mesenteric vascular thrombosis. Following surgical bowel resection there is decrease in bowel absorptive surface, leading to fecal bile acid loss.

Mechanism

Following a mutation in the gene coding protein, there is no lipoprotein secretion from liver and the intestine and there is absence of chylomicrons. This leads to a state of malabsorption and steatorrhea with impaired absorption of vitamin E. Important clinical features of abetalipoproteinemia are spiking erythrocytes, pigmented retinopathy, steatorrhea, progressive neurological disorder, ataxia and visual impairment.

Treatment of these patients with massive oral doses of vitamin E 100 IU/kg/day allows some absorption to take place resulting in in vitro erythrocyte hemolysis correction.

Ataxia with Vitamin E deficiency (AVED)

AVED syndrome was initially known as five deficiency (familial isolated vitamin E deficiency). It occurs due to mutation in the gene for alpha-tocopherol transfer protein on chromosome 8.

AVED is of two types

1. Complete absence of alpha-tocopherol transfer protein.
2. Defect in alpha-tocopherol binding region.

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Mechanism

The main mechanism proposed is that, following mutation there is impaired hepatic excretion of alpha-tocopherol leading on to removal of alpha-tocopherol from plasma to liver.

Neurologic symptoms appear between 4 to 18 years. Symptoms occur due to decreased delivery of vitamin E to nerve tissue. Patients can halt progression of damage by taking supplements of vitamin E but if they stop taking the drugs, damage continues.

FUNCTIONS

Antioxidant Action

The most widely accepted biological function of vitamin E is its antioxidant property and it prevents cell from free radical damage. Free radicals are unstable compounds formed in the body during metabolism and from exposure to environmental sources such as pollution and cigarette smoke.

Excess free radical in the body destroys healthy cells and leads to the development of diseases like cancer, heart disease and cataract and also leads to premature aging. Vitamin E is the most effective chain breaking lipid-soluble antioxidant in biological membranes where it contributes to membrane stability and protects cellular structures from damage by oxygen free radicals and reactive products of lipid peroxidation.

Cellular Response in Oxidative Stress

It has been found out that when cell growth is inhibited by lipid peroxidation, d-alpha tocopherol may restimulate cell growth and proliferation by removing inhibitors. In contrast, it may regulate cellular proliferation because of its ability to inhibit protein kinase C activity, which is a signaling factor that can regulate cellular proliferation. The modulation of signal transduction by d-alpha-tocopherol could contribute to anticancer and immunostimulatory effects of vitamin E. Oxidative stress leads to diminution of d-alpha-tocopherol from smooth muscle cells which results in growth and proliferation of these cells, which could contribute to the development of atherosclerosis.

Vitamin E and Retinopathy of Prematurity

The overgrowth of vessels in the posterior segment of the eye was shown to be precipitated by high levels of oxygen that was used to resuscitate preterm babies. Earlier work suggested that retrolental fibroplasias (RLF) were due to oxygen toxicity and an oxidant such as vitamin E was essential to provide protection. The evidence of vitamin E defi-

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ciency is conflicting. It is seen that although vitamin E deficiency does predispose to RLF, supplementation beyond sufficiency gives no added protection and may also be associated with toxic effects. Vitamin E serum levels should be maintained at 0.8 to 3.5 mg/dl and levels greater than these should be avoided. This can be accomplished by commercial preterm formulas which contain 20 to 35 mg vitamin E/100 Kcal or breastmilk which contains less vitamin E (2.3 mg/100 Kcal) but is a more bioavailable source.

Vitamin E and Hemolytic Anemia

Preterm infants with low serum levels of tocopherol, particularly those fed with formulas containing low vitamin E and abundant PUFA and iron, develop hemolytic anemia at 6 to 10 weeks of age, correctable by administration of vitamin E. Improvements in composition of infant formulas have virtually eliminated this.

Periventricular and Intraventricular Hemorrhage

Both these conditions are a major neonatal problem and often associated with respiratory distress syndrome. A recent trial (Sinha et al, 1987) has shown a significant reduction in intraventricular hemorrhage when vitamin E is administered. Probable risk is that vitamin E may scavenge free radicals generated during ischemic injury. Preferred route and optimum dose is uncertain. Preferred route is thought to be oral as tocopherol acetate needs to be de-esterified by hydrolytic enzymes in the gut to be made active. The efficacy of maternal vitamin E supplementation is under investigation.

Bronchopulmonary dysplasia occurs in 5% to 30% of survivors of respirators (therapy for RDS). It requires treatment with artificial ventilation. As in the case of retrolental fibroplasias, oxygen toxicity might play a part and vitamin E might be of benefit.

Vitamin E and Cancer

Several studies suggest that vitamin E may reduce the risk of cancer. Vitamin E inhibits mutagenesis and cell transformation through its antioxidant function by eliminating oxygen free radicals and decreasing DNA damage. Vitamin E may affect immune system—increasing natural killer cell activity. Studies of role of vitamin E have revealed inconsistent results and the exact role of antioxidants in prevention of cancer is yet to be determined.

Vitamin E and Immune System Function

Vitamin E is also essential for the normal functioning of the immune

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system. In preterm and deficient patients, it is seen that polymorphonuclear cells have impaired phagocytic ability, depressed oxidative, metabolic and bactericidal responses and decreased chemotactic movements towards stimuli. Deleterious effects of vitamin E deficiency on immune response are the effect on peroxide tone, causing defects in membrane stability of cells. It also decreases prostaglandin production in immune cells and increases cell-mediated immunity.

Vitamin E and Spinocerebellar Syndromes

Degenerative neurological disease associated with deficiency was first observed in abetalipoproteinemia. Similar changes have been found in children with cholestatic jaundice, cystic fibrosis and blind-loop syndromes. Prolonged deficiency of vitamin E in cholestatic children leads to a degenerative neuromyopathy involving spinocerebellar tracts, cranial nerves three and four, large caliber myelinated axons in peripheral nerves, posterior column of spinal cord, skeletal muscle and ocular retina with pigmentary retinopathy. The degenerative process begins within the first 2 years of life and is usually heralded by hyporeflexia at approximately 18 to 24 months of life. Within 2 to 4 years, truncal limb ataxias, gait disturbances, dysmetria and impairment in balance and coordination occur.

After several more years, peripheral neuropathy, muscular weakness, ophthalmoplegia and retinal dysfunction develop. By 10 years of age, the child has incapacitating neurologic symptoms that are irreversible. This irreversibility mandates aggressive evaluation and correction of deficiency early in chronic cholestasis in children. In adults with cholestasis, it may take 1 to 2 years of vitamin E malabsorption to deplete stores and additional 5 to 10 years to result in degeneration of mature nervous system.

Vitamin E in Cardiovascular Disease

It has been found that there is a significant decrease in coronary events and LDL oxidation with high intake of antioxidants. Vitamin E may participate in prevention of several events associated with pathogenesis of cardiovascular disease including LDL oxidation, adhesion of monocytes to endothelial cells, foam cell formation, fatty streak development, platelet adherence and aggregation, smooth muscle proliferation and reperfusion injury. Oxidized LDL is a chemo-attractant. Indiscriminate uptake of oxidatively modified LDL by scavenger receptors of macrophages results in cholesterol laden foam cells and fatty streak formation. These events and potential cytotoxicity of oxidized LDL further promote the evolution of fatty streaks to a more complex lesion. Oral supplementa-

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tion of vitamin E increases LDL resistance to oxidation, but no decrease in LDL resistance is seen in vitamin E deficient subjects. Vitamin E also modulates platelet adherence and aggregation and thus prevents progression of fatty streak and cell proliferation to an advanced lesion. In diabetics, concentration of vitamin E tends to decrease with increased platelet aggregation. Vitamin E supplementation could reduce platelet aggregation. Similar changes occur with aging. Supplementation of high doses of dietary vitamin E has no effect on aggregation, but as little as 200 IU/day is effective in reducing adhesion of platelets. Presupplementation with vitamin E also helps to reduce size of myocardial infarct and tissue damage. The best clinical evidence for protection by vitamin E against reperfusion injury comes from vitamin E pretreatment of patients undergoing elective coronary bypass.

Vitamine E and Selenium

Selenium is required as the selenium analog of cysteine, selenocysteine in the catalytic site of glutathione peroxidase. The membrane isoenzyme of glutathione peroxidase catalyses the reduction of the tocopheroxyl radical back to tocopherol. Glutathione peroxidase also reduces hydrogen peroxide and therefore lowers the amount of peroxide available for the generation of radicals. However, vitamin E has a role in removing the products of attack by these radicals on lipid components. It has also been found out that in vitamin E deficiency, selenium has a beneficial effect in reducing alkyl-peroxyl radical levels. In contrast, in selenium deficiency, vitamin E has a protective effect in reducing the radicals. When vitamin E is reduced and selenium is adequate, central nervous system is susceptible to lipid peroxidase as the central nervous system tissues are low in glutathione peroxidase activity. In contrast, when vitamin E levels are normal and selenium is reduced, lipid peroxidation in membranes will be inhibited but tissues containing high peroxide production will be at risk from damage due to sulfhydryl proteins.

Vitamin E and Myopathy

Vitamin E also plays a role in mitochondrial superoxide generation. Studies in experimental animals have shown that vitamin E deficiency produces a progressive myopathy, which mimics muscular dystrophy. Both myopathy and neuropathy have occurred in humans who lack intake of vitamin E. Vulnerable individuals are those with chronic malabsorption, premature infants and those on long-term dialysis. It has also been found that treatment with high doses of vitamin E may reverse this process. In contrast, there has also been reports of myopathy occurring due to hypervitaminosis E.

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Vitamin E and Cataract

It was concluded from studies that cataract occurred due to oxidative damage to alpha-crystallin in the lens of the eyes. Many controlled trials were conducted, out of which half of them showed positive results to vitamin E while the rest showed no effects. Since vitamin E is an antioxidant it was thought that it might have role in preventing cataract.

Vitamin E and Neurodegenerative Diseases

Some studies were conducted which showed that both Parkinson's disease and Alzheimer's disease occurred due to oxidative radical damage. Some studies also led to beliefs that Down's syndrome might also be related to radical damage because the gene for superoxide dismutase is on chromosome 21. Many controlled trials proved the fact that there was no beneficial effect of vitamin E in these conditions.

EVALUATION OF VITAMIN E STATUS

Serum-tocopherol level can now be easily measured by high performance liquid chromatography. Normal serum levels in older children and adults range from 5 to 20 microgram/ml and perhaps a little lower in infants. In children less than 0.5 mg/dl is considered as deficiency, but serum levels do not correlate with clinical signs with much certainity. In cholestasis, however serum vitamin E levels correlate directly with total serum lipids. Hyperlipidemia in a patient with normal vitamin E status results in elevated plasma vitamin E levels and vice versa. Thus a cholestatic patient who is vitamin E deficient and has severe hyperlipidemia, a normal serum vitamin E level may be obtained. Thus, ratio of serum vitamin E to total serum lipids is more accurate. Normal ratio in adults is 0.8 mg total tocopherol per gram of total lipid. In children under 12 years, less than 0.6 mg/ml may indicate adequacy.

There are several fundamental assays for vitamin E status. Red blood cells hemolyse when exposed to hydrogen peroxide if they are deficient in vitamin E. Normal is 5% to 10% hemolysis. In vitamin E deficiency, susceptibility of RBC's to hemolysis by hydrogen peroxide is increased to more than 30 percent. But selenium deficiency and other nutritional factors, e.g. PUFA also affect hydrogen peroxide hemolysis. Therefore the test is not specific for vitamin E deficiency. Another test has been proposed, wherein amount of malondialdehyde, a lipid peroxidation product released by RBC's exposed to hydrogen peroxide is measured. Serum lipid peroxide measurements have been made, but they are difficult to interpret during hyperlipidemia and may not normalize even when vitamin E status is corrected. Expired pentane gas, as a sensitive

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measure of total body lipid peroxidation of linoleic acid can be used for quantitative antioxidant deficiency, but selenium deficiency causes abnormal pentane gas excretion and the technology is tedious. Measurement of vitamin E content of adipose tissue is an accurate means of assessing vitamin E status, but it requires adipose tissue biopsy which is performed by a few laboratories only. Characteristic histological features of peripheral nerve and muscle are present in vitamin E deficiency.

VITAMIN E SUPPLEMENTATION

It is seen that normal healthy individuals receiving a normal diet showed significant decrease in cell damage when their diet was supplemented with vitamin E. This indicates that there may be damage from free radicals before disease symptoms are apparent. This can be avoided by vitamin E supplementation and when healthy individuals take vitamin E supplements, there is a reduction in the number of free radicals. Three to five times of the RDA may be required to prevent damage caused by free radicals in the body. High vitamin E supplementation is contraindicated when a coagulation defect is present due to vitamin K deficiency or in individuals with anticoagulant drugs.

Large oral parenteral doses of vitamin E may prevent permanent neurological abnormalities of children with biliary atresia or abetalipoproteinemia. 0.5 mg/kg/day is considered sufficient to meet requirements of vitamin E in childhood. In presence of overt deficiency, treatment should consist of 30 to 100 mg/day, unless malabsorption is the cause. Much larger doses (more than 100 mg/kg/day) have been used but they are associated with toxicity.

Synthetic vitamin E is called dl-alpha-tocopherol. It is a mixture of eight compounds, only one of which is molecularly equivalent to natural vitamin E. Natural vitamin E is 36 percent more potent than synthetic vitamin E. Vitamin E acetate is available in liquid-filled soft gelatin capsules of 200, 400, 600, 800, 1000 and 1200 IU. In US, 400 IU soft gelatin capsules are by far the most popular ones. Taking vitamin E in portions, several times a day will usually increase the body's use of the supplement.

TOXICITY

Vitamin E is least toxic of the fat-soluble vitamins. Very large doses (more than 1000 to 1500 IU/day) in adults who are deficient in vitamin K may be associated with increased coagulopathy. In neonates, large doses of more than 100 mg/kg/day has led to increased incidence of necrotizing enterocolitis and sepsis; presumably due to inhibition of

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bacterial and fungal killing by neutrophils through antioxidant suppression of neutrophil-derived free radicals. A new intravenous vitamin E product that has not been approved by the FDA has led to the death of preterm infants with pulmonary deterioration, thrombocytopenia, liver and renal failure.

ORAL VITAMIN E THERAPY IN CHILDREN

Oral vitamin E has been used for many years to treat number of diseases in children. Guidelines are lacking for dosage formulations and recommendation in children. There are no safety data on long-term effects. Research is still pending for recommendations regarding use of vitamin E in neonates and premature infants for prophylactic purposes. Clinical trials are in need for therapeutic use in premature infants and neonates.

CONCLUSION

Vitamin E has received a lot of attention because of its role in preventing a variety of cancers, heart disease, premature aging, cataracts and arthritis. It also helps to improve the immune system, relieve nocturnal cramps, relieve symptoms of premenstrual syndrome, control platelet adhesiveness in diabetics and patients on oral contraceptives and provide protection against air pollutants and other environmental toxins.

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Vitamins in Health & Disease

Vitamins are the essential organic compounds which are required in very small amounts and are involved in fundamental functions of the body such as growth, maintenance of health and metabolism. In recent years, there has been an explosion of knowledge regarding vitamins. Once considered as mere nutrient factors, vitamins are now recognized as playing a major role in the prevention and modification of lifestyle diseases, inborn errors of metabolism and even infectious diseases. The book covers these recent developments, at the same time has emphasized on nutritional role of these vitamins in health and disease. The book will not only help medical people but also paramedics, people involved in basic sciences like physiology, biochemistry, pharmacology and also common people at all levels.



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