The Vitamins
NHM 362

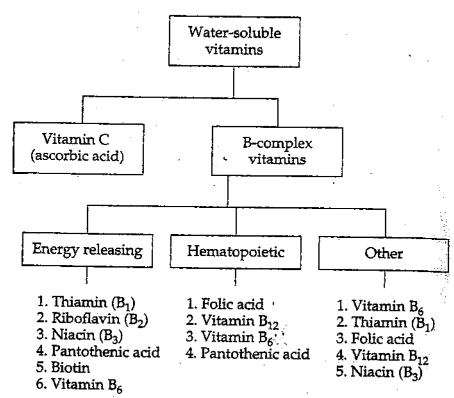
Vitamins

- Defined as essential organic micronutrients that are involved in fundamental functions of the body, such as growth, maintenance of health, and metabolism.
- Must be supplied wholly or partially by the diet.
- The broad classifications of the water and fat soluble vitamins are due to the fact that fat soluble vitamins are closely associated with the absorption and transport of lipids and are stored in body lipids.

2

- The water soluble vitamins are handled quite differently in the body with the exception of vitamin B_{12}, they cannot be retained by the body for long periods (excess is excreted).
- See table 9.1 for functions, coenzymes, deficiency symptoms and food sources of “water soluble vitamins”.

3



4

Water Soluble Vitamins

- Vitamin C and the members of the B complex are water soluble.

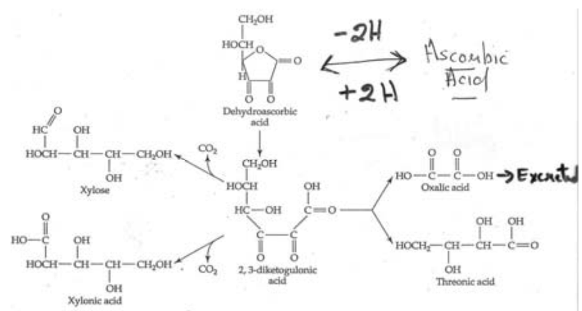
5

Vitamin C (Ascorbic Acid)

- **Humans are one of the few animals <u>unable</u> to synthesize vitamin C. Formula: $C_6H_8O_6$**
- **It is synthesized from glucose (fig. 9.2).**
- **Animals that cannot synthesize vitamin C lack <u>gulonolactone oxidase,</u> the last enzyme needed for the conversion of glucose to vitamin C.**
- **Vitamin C is synthesized by plants.**
- **Animal foods do not provide vitamin C. the only exception is liver, where vitamin C is stored in small amounts.**
- **Citrus fruits, dark green leafy vegetables, strawberries, cantaloupe, bell peppers are significant sources of vitamin C.**

6

Metabolism of Vitamin C



7

Absorption, Transport, and Storage

- **Absorption primarily occurs by an "<u>active transport</u>" system, but simple diffusion also occurs.**
- **Most absorption is in the distal part of the small intestine, with degree of absorption decreasing with increased intake (rate varies from 16% at high intake (1 -2 g) to 98% at low intakes (< 20 mg).**
- **In a range over usual intakes (20 - 120 mg/d), the average absorption is approximately 90%.**
- **Vitamin C is transported in the plasma as free anion, and equilibrates with the body pool (stores) of the vitamin.**

8

- The size of the pool varies with intake (1.4 - 5 g).
- The highest concentration of vitamin C is found in the adrenal gland (30 - 40 mg/100g wet tissue).
- Other tissues high in vitamin C are the pituitary gland and retina.
- An intermediate level of the vitamin is found in the liver, lungs, pancreas and leukocytes.
- Smaller amounts in kidneys, muscles and RBCs.
- The tissue concentration of vitamin C usually exceeds the plasma level by 3 to 10 times.
- Both plasma and tissue levels are related to vitamin C intake until intake exceeds 90 mg/day at which point the percentage absorption begins to decrease.

9

Functions of Vitamin C

1. Antioxidant and Pro-oxidant Activity.

- Acts as a reducing agent (antioxidant).

  Reverses the oxidation by donating electrons and H ions.

  Fe^{+++} + Ascorbate (AH^-) ------------> Fe^{++} + Dehydroascorbate radical($A^\cdot$)

- Free-radicals and reactive oxygen species($HO_2\cdot$, H_2O_2, $OH\cdot$ etc) formed during normal metabolism attack phospholipids and proteins in the cell membrane.

Ascorbate (AH^-) + OH $\cdot$ ⟶ Dehydroascorbate radical ($A^{\cdot-}$) + H_2O

- Peroxyl radicals induce oxidation of LDL (risk of CVD) and oxidation of RBC (hemolysis)

10

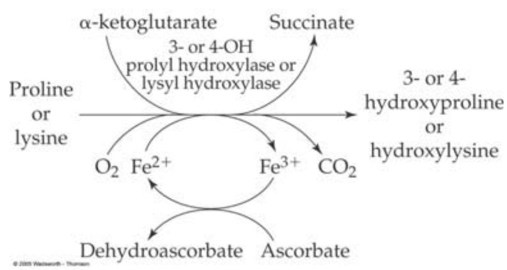
2. Collagen Synthesis

Vitamin C is needed in a number of hydroxylation" reactions.

- ***Vitamin C is particularly needed for hydroxylation" of various amino acids.***
- Two hydroxylation reactions needing vitamin C are necessary for **"Collagen"** formation (fig. 9.4).
- **The role of vitamin C in the hydroxylation of proline and lysine is of primary importance because it explains the protective role of vitamin C for scurvy.**

For collagen molecules to aggregate into a triple helix, selected "**proline**" residues on collagen α chains must be **hydroxylated.**

11



12

- **The importance of lysine hydroxylation is not clear, but hydroxy-lysyl residues permit cross linking of collagen.**

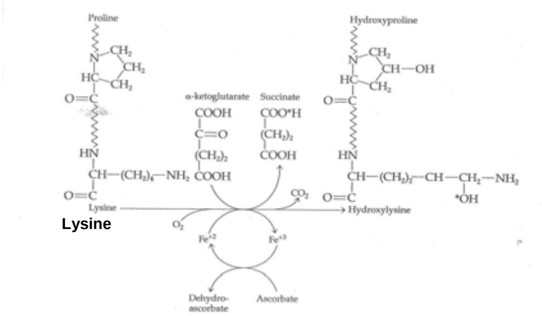


Figure 9.4 Ascorbate functions in the hydroxylation of peptide-bound proline and lysine in procollagen. The reaction is driven by α-ketoglutarate decarboxylation. One atom of oxygen* appears in the hydroxyl group of the product and the other in succinate.

3. Carnitine Synthesis

- **Vitamin C is involved in two reactions required for <u>carnitine synthesis</u>. Carnitine synthesis begins with <u>trimethyl lysine.</u>**

- **1. Iron containing enzyme trimethyl lysine dioxygenase (hydroxylase) catalyzes the conversion of tri-methyl lysine to 3-hydroxy tri-methyl lysine (fig. 9.5).**

- **2. Next to last step in carnitine synthesis, the iron containing enzyme 4- butryobetaine hydroxylase catalyzes the conversion of 4-butyrobetaine to carnitine.**

- **Carnitine is of significance in fat metabolism (fatty acid transport across mitochondria)**

15

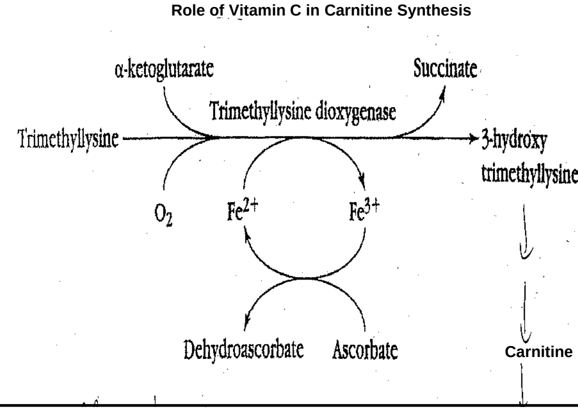
- **Hydroxylation of proline is catalyzed by "dioxygenases". These enzymes require Fe^{++} and a reductant (vitamin C is a reductant).**

- **Vitamin C indirectly functions to help keep enzyme active by keeping Fe in its reduced form (Fe^{++}).**

Fe^{+++} --------------------------------> Fe^{++}
Vitamin C

14

Role of Vitamin C in Carnitine Synthesis



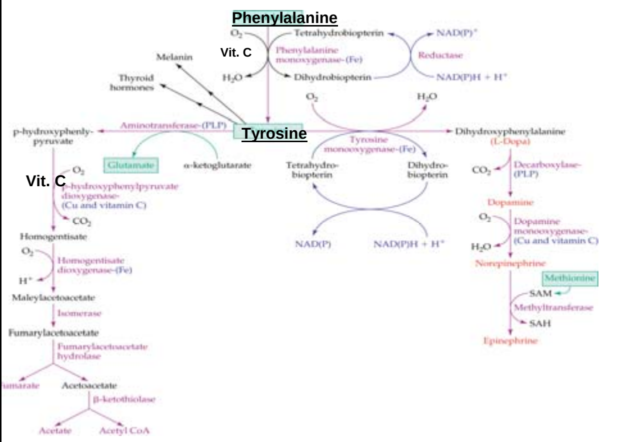
4. Tyrosine Synthesis

- **"Tyrosine"** is made from "**phenylalanine**" h**ydroxylation** via **phenylalanine mono-oxygenase** enzyme. Vitamin C is needed for this reaction. This reaction also needs folic acid.

- Another hydroxylation in which vitamin C participates is the **metabolism of tyrosine.**

  Vitamin C is needed for Cu^{++} dependent "p-hydroxyphenyl pyruvate hydroxylase" (fig. 9.6)

17



5. Neurotransmitter Synthesis

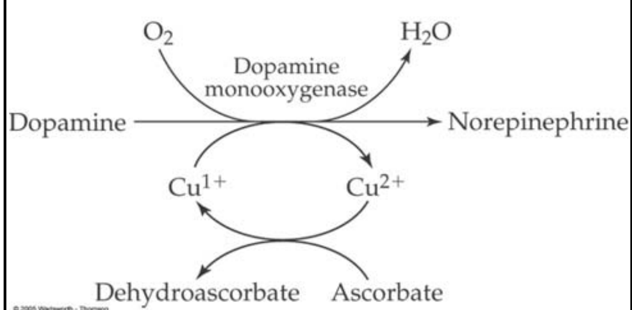
- **Vitamin C is also involved with the activity of two Cu^{2+} requiring enzymes *"dopamine mono-oxygenase"* and "*peptidyl glycine alpha amidating mono-oxygenase".***

- **Vitamin C probably acts to keep the Cu containing enzymes in its reduced state**.

(a) "**Dopamine mono-oxygenase**" converts **dopamine to norepinephrine** (fig. 9.6). Vitamin C is believed to donate a H in this conversion.

$$Cu^{++} \xrightarrow[\text{vitamin C}]{e^-} Cu^{+}$$

19



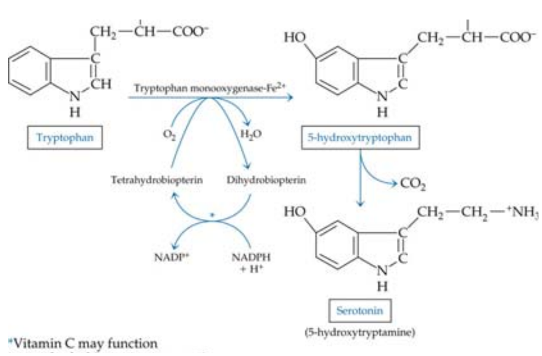
The role of Vitamin C in Norepinephrine Synthesis

20

(b) Serotonin Synthesis:

Vitamin C, folacin and O_2 are involved in hydroxylation of tryptophan for synthesis of neurotransmitter "serotonin" (5-OH Tryptamine) (fig. 9.7) in the brain

21



*Vitamin C may function

22

6. Cholesterol Degradation for Bile Synthesis

- **Hydroxylation of cholesterol's steroid nucleus by cholesterol 7 α-hydroxylase diminishes in vitamin C deficiency.**

23

Other Functions

- **Many other functions proposed.**

- **Pharmacological doses of vitamin C for treatment of common cold.**
  Megadoses of vitamin C are weakly prophylactic, if at all, and little or no use in the treatment of infections.

- **Cancer prevention ?**
  Increased intake of fruits and vegetables are associated with decreased risk of some cancers. Possible mechanism of vitamin C action against cancer development include a role in immunocompetence due to its ability to act as a free-radical scavenger or antioxidant.

24

- **Cardiovascular Disease and Vitamin C**

Many human studies report a relationship between low vitamin C status and increased plasma cholesterol levels. High plasma vitamin C also have been associated lower blood pressure and with higher HDL concentrations.

The mechanism by which vitamin C may protect against CVD in humans is not clear.

25

Recommended Dietary Allowances

- **In the U.S. RDA has varied from 75 mg/day in 1943 to 45 mg/day in 1974.**
- **The 1980 and 1989 RDA's for the vitamin C are based upon maintenance of a body pool of 1,500 mg.**
- **The current adult RDA is:**
  75 mg/day for female.
  90 mg/day for males

Deficiency Disease

- **Scurvy**

26

Interaction With Other Nutrients

- **Due to its powerful reductant effect, vitamin C prevents the oxidation of other easily oxidized vitamins such as A and E.**
- **Possibly strong interaction occurs with folate.**
- **Megaloblastic anemia in scurvy may be due to removal of tetrahydrofolate (THF) from the metabolic pool. Perhaps vitamin C assists in prevention of oxidation of THF and its coenzyme forms.**

27

- **The interaction between the mineral iron and vitamin C is related to the effects of vitamin C on absorption of non-heme iron but also on the distribution of iron in the body.**
- **Vitamin supplements can cause a change in Fe distribution in patients with Fe overload. Iron held in the reticuloendothelial cells of the spleen and liver may be mobilized and deposited in the parenchymal cell, causing a risk of liver damage.**

28

Pharmacological Effects of Vitamin C

- The vitamin C effect in the treatment of common cold has been refuted by many investigators.
- High doses (1-5 g/day) of vitamin C are only weakly prophylactic, if at all, and are of little use in the treatment of infection.
- 1 g of vitamin C/day is no more effective in protecting against common cold than 50 mg/day. there is no difference in the number of colds, severity or the duration.

29

- Pauling and Cameron have shown that the survival time in terminal cancer patients is prolonged by massive doses of vitamin C, others have demonstrated it to be unsuccessful.
- The fact that vitamin C when ingested with nitrates and or nitrites, can prevent formation of carcinogenic nitrosamines has resulted in a belief that vitamin C is protective against cancers of the stomach and esophagus.

30

Toxicity

- The frequency of recorded toxicity is quite low, though many potentially harmful effects have been reported due to excessive intakes of vitamin C.
- Though massive doses of vitamin C lead to excessive oxalate excretion in urine, thereby increasing the possibility of calcium oxalate kidney stones, the amount usually remains within a safe range.
- 4 g of vitamin C/day will increase the amount of uric acid excreted in urine. The resulting urine acidification with the excessive amount of urate being excreted could cause precipitation of urate crystals.

31

- Excessive doses of vitamin C can cause diarrhea, but not for a long time.
- Excretion of excessive vitamin C in urine and feces can interfere with a variety of clinical tests, false negative for fecal occult blood, test for glucose in the urine can be invalid.

32