### 3. Ascorbic Acid (Vitamin C)

The active form of vitamin C is ascorbic acid (Figure 28.8). The main function of ascorbate is as a reducing agent in several different reactions. Vitamin C has a well-documented role as a coenzyme in hydroxylation reactions, for example, hydroxylation of prolyl and lysyl residues of collagen. Vitamin C is, therefore, required for the maintenance of normal connective tissue, as well as for wound healing. Vitamin C also facilitates the absorption of dietary iron from the intestine by reducing $Fe^{3+}$ to $Fe^{2+}$. Also, Vitamin C is required as an activator in conversion of dopa to dopamine and dopamine to noradrenaline.

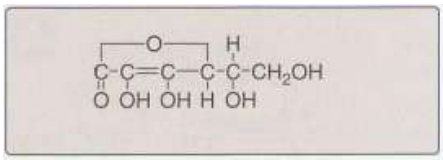


**Figure 28.8**
Structure of ascorbic acid.

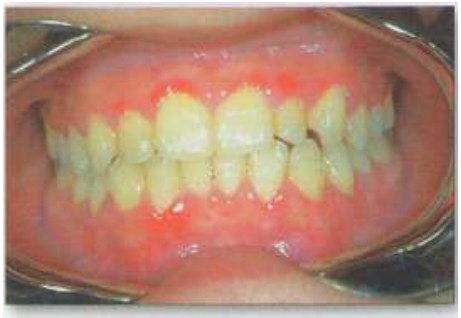
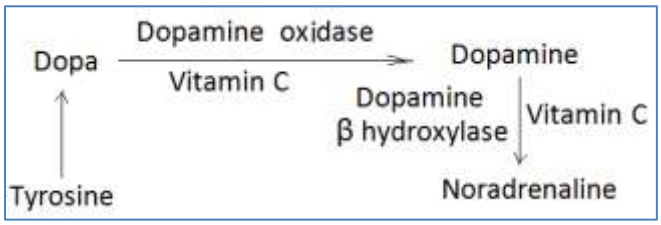


**Figure 28.9**
Hemorrhage and swollen gums of a patient with scurvy.




### A. Deficiency of Ascorbic Acid

A deficiency of ascorbic acid results in **scurvy**, a disease characterized by sore and spongy gums, loose teeth, fragile blood vessels, swollen joints, and anemia (Figure 28.9). Many of the deficiency symptoms can be explained by a deficiency in the hydroxylation of collagen, resulting in defective connective tissue.

### B. Prevention of chronic disease

Vitamin C is one of a group of nutrients that includes vitamin E and β-carotene, which are known as antioxidants. Consumption of diets rich in these compounds is associated with a decreased incidence of some chronic diseases, such as coronary heart disease and certain cancers. However, clinical trials involving supplementation with the isolated antioxidants have failed to determine any convincing beneficial effects.

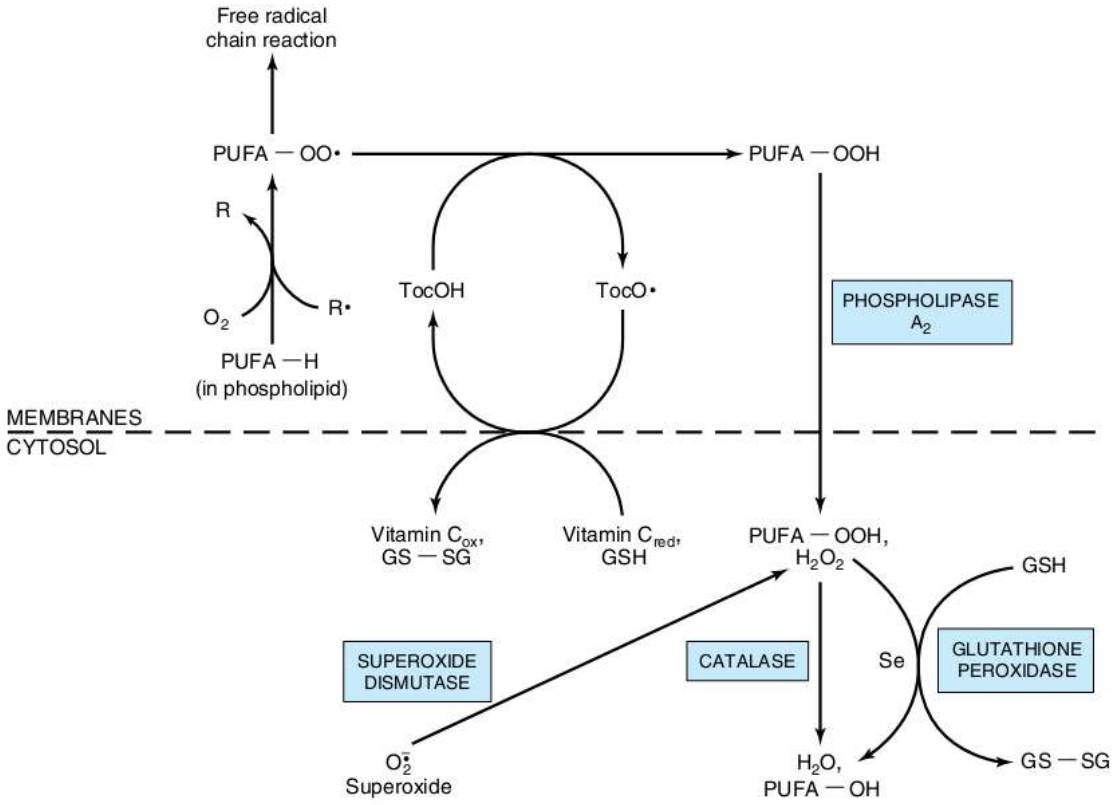
### Sources of Vitamin C

Citrus fruits ( orange, lemon), tomatoes, strawberries, green vegetables, guava fruit and green pepper.

### Recommended Dietary Allowance of Vitamin C

Children 40 µg/day.

Adults 60 µg /day.




**4. PYRIDOXINE (VITAMIN B6)**

Vitamin B6 is a collective term for pyridoxine, pyridoxal, and pyridoxamine, all derivatives of pyridine. They differ only in the nature of the functional group attached to the ring (Figure 28.10). Pyridoxine occurs primarily in plants, whereas pyridoxal and pyridoxamine are found in foods obtained from animals. All three compounds can serve as precursors of the biologically active coenzyme, pyridoxal phosphate. Pyridoxal phosphate functions as a coenzyme for a large number of enzymes, particularly those that catalyze reactions involving amino acids.

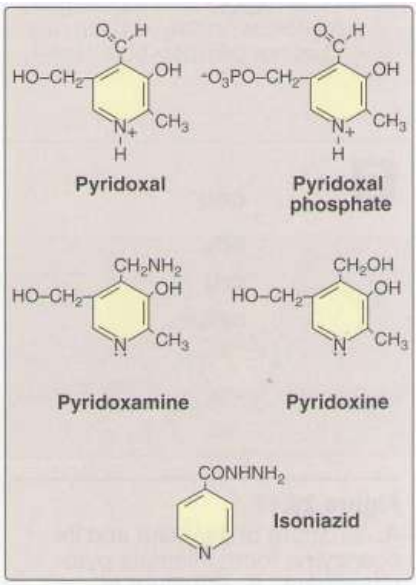



**Figure 28.10**
Structures of vitamin $B_6$ and the antituberculosis drug isoniazid.

| Reaction type | Example |
|---|---|
| Transamination | Oxaloacetate + glutamate ⇄ aspartate + |
| Deamination | Serine → pyruvate + $NH_3$ |
| Decarboxylation | Histidine → histamine + $CO_2$ |
| Condensation | Glycine + succinyl CoA → δ-aminolevulinic |

**A. Clinical indications for pyridoxine:**

Isoniazid (isonicotinic acid hydrazide), a drug frequently used to treat tuberculosis, can induce a vitamin B6 deficiency by forming an inactive derivative with pyridoxal phosphate. Dietary supplementation with vitamin B6 is, thus, an adjunct to isoniazid treatment. Otherwise, dietary deficiencies in pyridoxine are rare but have been observed in new-born infants fed formulas low in B6, in women taking oral contraceptives, and in alcoholics.

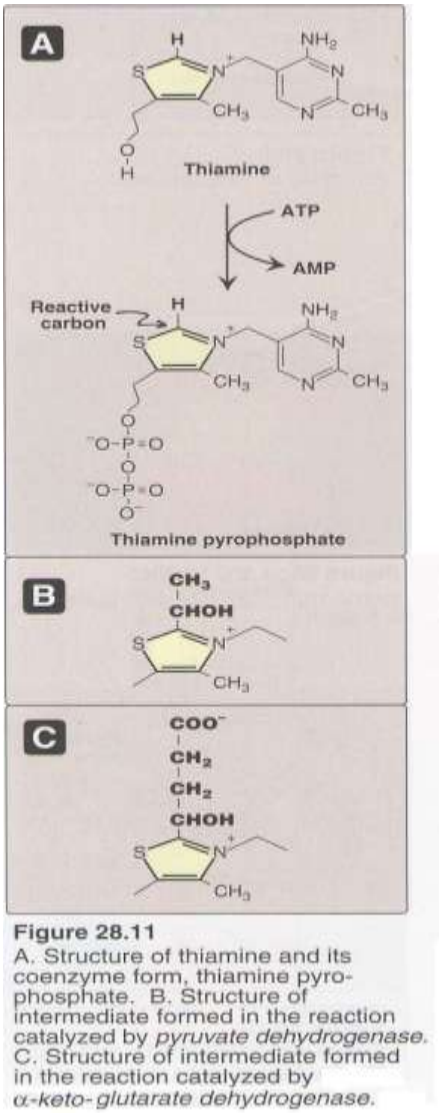



**Figure 28.11**
A. Structure of thiamine and its coenzyme form, thiamine pyrophosphate. B. Structure of intermediate formed in the reaction catalyzed by *pyruvate dehydrogenase*. C. Structure of intermediate formed in the reaction catalyzed by *α-keto-glutarate dehydrogenase*.

**B. Toxicity of pyridoxine**

Pyridoxine is the only water-soluble vitamin with significant toxicity. Neurologic symptoms (sensory neuropathy) occur at intakes above 200 mg/day, an amount more than 100 times the recommended dietary allowance (RDA).

Substantial improvement, but not complete recovery, occurs when the vitamin is discontinued.

**C. Sources of Pyridoxine (Vitamin B6)**

Whole grains, poultry fish, potatoes, meat , eggs and legumes.

**D. Recommended Dietary Allowance of Pyridoxine (Vitamin B6)**

Adults 2.2 mg/day.

Children 1.2 mg/day.

Infants 3.0 mg/day.

**5. THIAMINE (VITAMIN B1)**

Thiamine pyrophosphate is the biologically active form of the vitamin B1, formed by the transfer of a pyrophosphate group from adenosine triphosphate (ATP) to thiamine (Figure 28.11). Thiamine pyrophosphate serves as a coenzyme in the formation or degradation of α-ketols by transketolase (Figure 28.12A), and in the oxidative decarboxylation of α-keto acids (Figure 28.12B).

**A. Clinical indications for thiamine**

The oxidative decarboxylation of pyruvate and α-ketoglutarate, which plays a key role in energy metabolism of most cells, is particularly important in tissues of the nervous system. In thiamine deficiency, the activity of these two dehydrogenase-catalyzed reactions is decreased, resulting in a decreased production of ATP and, thus,

impaired cellular function. [Note: Thiamine deficiency is diagnosed by an increase in erythrocyte transketolase activity observed on addition of thiamine pyrophosphate.]

**1. Beriberi:** Beriberi literally means "I can't, I can't" in Singhalese (one of the three official languages used in Sri Lanka) .This is a severe thiamine-deficiency syndrome found in areas where polished rice is the major component of the diet. Signs of **infantile beriberi** include tachycardia, vomiting, convulsions, and, if not treated, death. The deficiency syndrome can have a rapid onset in nursing infants whose mothers are deficient in thiamine. Adult beriberi **(dry beriberi)** is characterized by dry skin, irritability, disordered thinking and progressive paralysis resulting from damaged peripheral nerves. **Wet beriberi** affects the heart and circulatory system. It is sometimes fatal, as it causes a combination of heart failure and weakening of the capillary walls, which causes the peripheral tissues to become edematous.

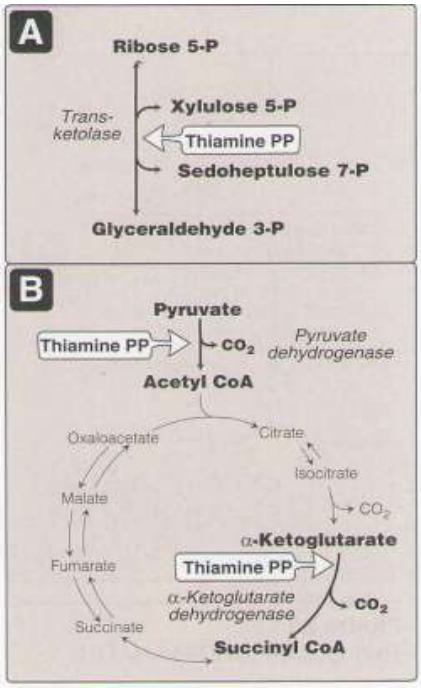



**Figure 28.12**
Reactions that use thiamine pyrophosphate (TPP) as coenzyme. A. *Transketolase.* B. *Pyruvate dehydrogenase* and α-*ketoglutarate dehydrogenase.* Note that TPP is also used by *branched-chain* α-*keto acid dehydrogenase.*

**2. Wernicke-Korsakoff Syndrome:** In the United States, thiamine deficiency, which is seen primarily in association with chronic alcoholism, is due to dietary insufficiency or impaired intestinal absorption of the vitamin B1. Some alcoholics develop Wernicke-Korsakoff syndrome- a thiamine deficiency state characterized by apathy, loss of memory, ataxia, and a rhythmic to-and-fro motion of the eyeballs (nystagmus). The neurologic consequences of Wernicke's syndrome are treatable with thiamine supplementation.

**B. Sources of Thiamine (Vitamin B1)**

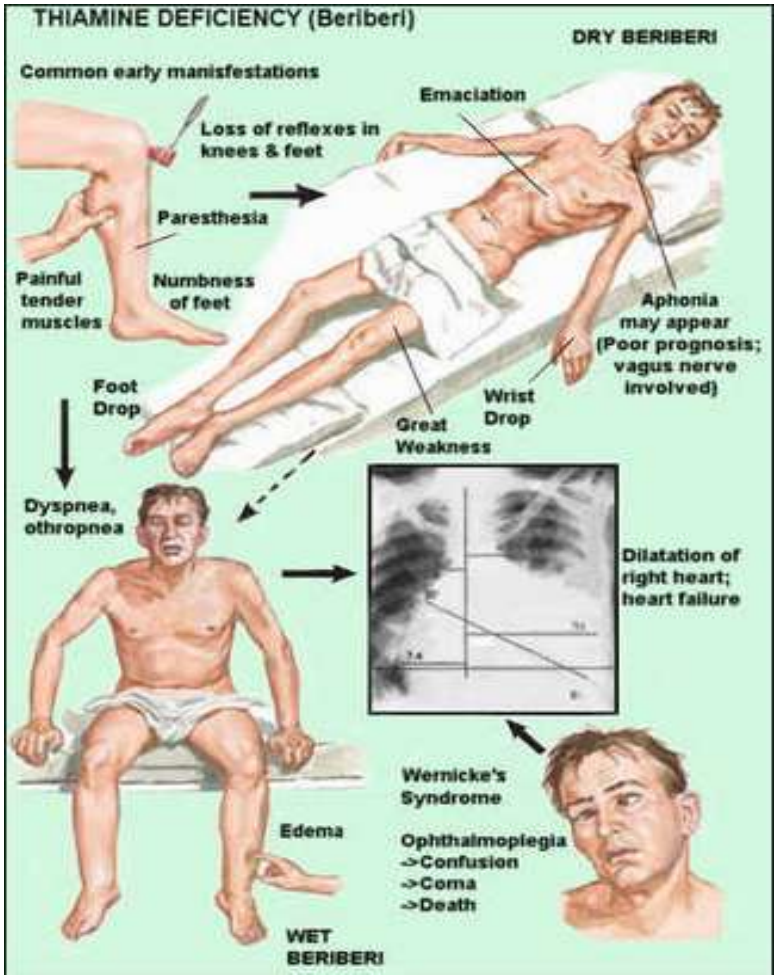
Whole grains (unpolished rice and wheat), legumes (beans and peas), meat ,bananas and soybeans.

**C. Recommended Dietary Allowance of Thiamine (Vitamin B1)**

Adults 1.5 mg/day.

Children 1.2 mg/day.

Pregnancy and lactation 2.0 mg/day.




**6. NIACIN or (NICOTINIC ACID) VITAMIN B3**

Niacin, or nicotinic acid, is a substituted pyridine derivative. The biologically active coenzyme forms are nicotinamide adenine dinucleotide ($NAD^+$) and its

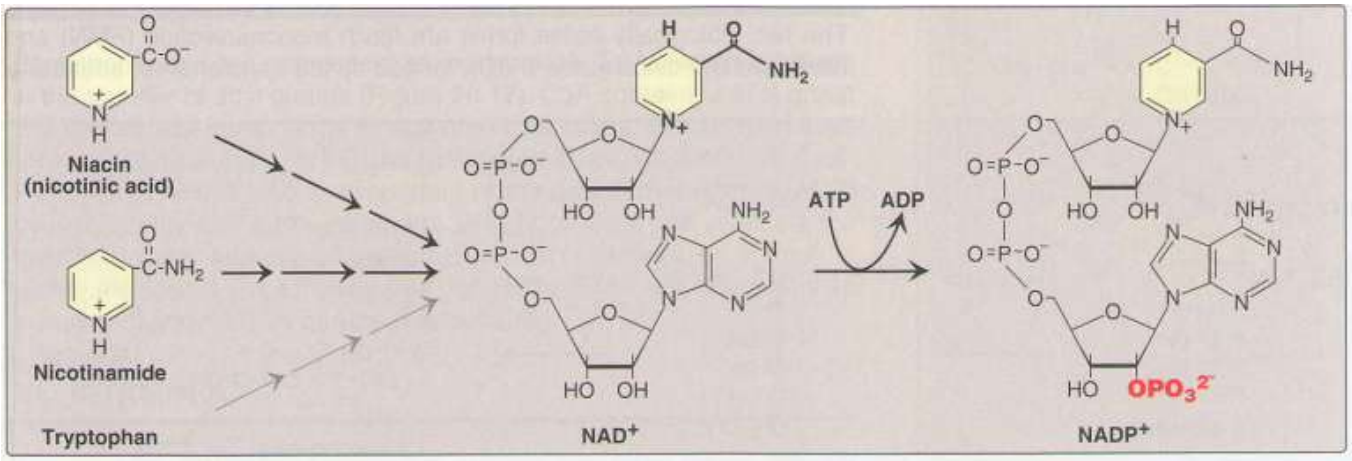



**Figure 28.13**
Structure and biosynthesis of $NAD^+$ and $NADP^+$. Note that a metabolite of tryptophan (quinolinate) can also be used in the synthesis of $NAD^+$.

phosphorylated derivative, nicotinamide adenine dinucleotide phosphate ($NADP^+$, Figure 28.13).

Nicotinamide, a derivative of nicotinic acid that contains an amide instead of a carboxyl group, also occurs in the diet. Nicotinamide is readily deaminated in the body and, therefore, is nutritionally equivalent to nicotinic acid. $NAD^+$ and $NADP^+$ serve as coenzymes in oxidation-reduction reactions in which the coenzyme undergoes reduction of the pyridine ring by accepting a hydride ion (hydrogen atom plus one electron, Figure 28.14). The reduced forms of $NAD^+$ and $NADP^+$ are NADH and NADPH, respectively.

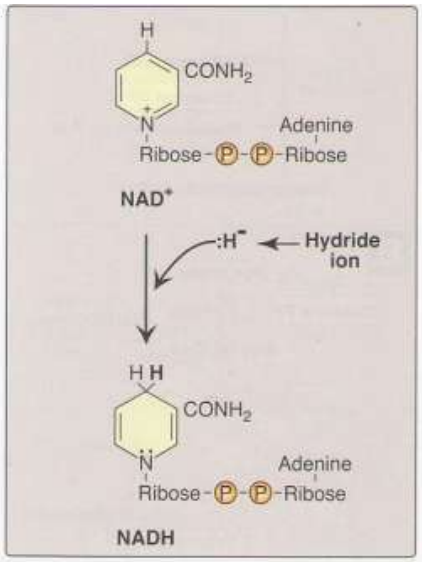


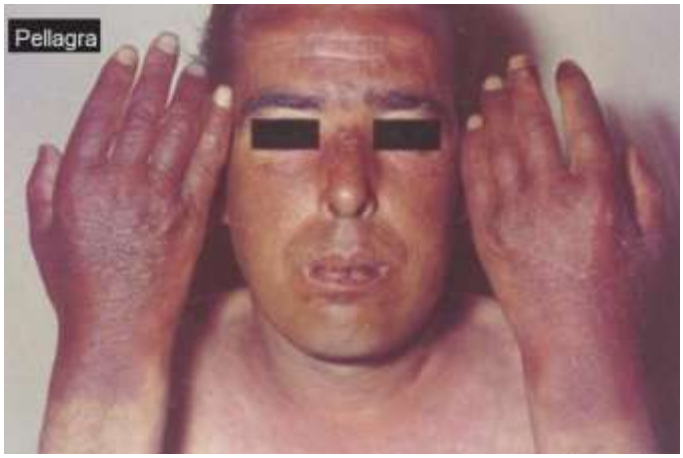

**Figure 28.14**
Reduction of $NAD^+$ to NADH.

**A. Distribution of Niacin (VITAMIN B3)**

Niacin is found in unrefined and enriched grains, milk, and lean meats, especially liver. [Note: Corn is low in both niacin and tryptophan. Corn-based diets can cause pellagra].

**B. Clinical Indications for Niacin (VITAMIN B3)**

**1. Deficiency of Niacin:** A deficiency of niacin causes **pellagra**, a disease involving the skin, gastrointestinal tract, and CNS. The symptoms of pellagra progress through the three Ds: dermatitis diarrhea, dementia- and, if untreated, death.




**2. Treatment of Hyperlipidemia:** Niacin (at doses of 1.5 g/day or 100 times the recommended dietary allowance or RDA) strongly inhibits lipolysis in adipose tissue-the primary producer of circulating free fatty acids. The liver normally uses these circulating fatty acids as a major precursor for triacylglycerol synthesis. Thus, niacin causes a decrease in liver triacylglycerol synthesis, which is required for very-low-density lipoprotein (VLDL) production. Low-density lipoprotein (LDL, the cholesterol rich lipoprotein) is derived from VLDL in the plasma. Thus, both plasma triacylglycerol (in VLDL) and cholesterol (in VLDL and LDL) are lowered. Therefore, niacin is particularly useful in the treatment of Type IIb hyperlipoproteinemia, in which both VLDL and LDL are elevated. [Note: Niacin raises HDL levels.]

**Recommended Dietary Allowance of Niacin (VITAMIN B3)**

Adults: 16-20 mg/ day

Children: 9-16 mg/ day

Infants: 5-8 mg/ day