

VITAMIN B₁ (THIAMIN)

Active form: Thiamin pyrophosphate (TPP)

Biochemical role: Decarboxylation

Example: Pyruvate → Acetyl-CoA + CO₂

Deficiency tests: alpha-keto acids- urine; Erythrocyte Transketolase Index

Adult repletion: 50 to 200 mg/d

Physiological Function: The two primary functions of thiamin are alpha-keto acid decarboxylation and transketolation.¹⁰ Decarboxylation reactions are an integral part of carbohydrate metabolism.³⁷ Thiamin is involved in the alpha-keto acid decarboxylation of pyruvate, alpha-ketoglutarate and the branched-chain alpha-keto acids (leucine, isoleucine and valine metabolites). Transketolation is involved in the pentose phosphate pathways and is an early marker of decreasing thiamin levels.^{7, 38} Thiamin is converted to its active form—thiamin pyrophosphate—the primary coenzymatic form (Figure 2.2).³⁸

Deficiency: Food processing, elevated pH and high temperatures result in significant losses of thiamin.¹⁰ The ease with which thiamin is depleted by processing rice creates an increased risk of deficiency among populations where rice is the staple food. A cross-sectional survey of an adult Mediterranean population found 6.4% deficient in thiamin according to the erythrocyte transketolase assay (described below).³⁹ Increased vigilance to ensure thiamin supplementation during pregnancy is suggested because sub-clinical thiamin hypovitaminemia is prominent during pregnancy despite vitamin supplementation.⁴⁰ During the third trimester among Spanish women, 25% of subjects were found to have intakes below recommended levels and 14% showed signs of severe thiamin deficiency.⁴¹ Because of the thiamin depleting effects of gestational diabetes, subclinical thiamin hypovitaminemia was also found in 19% of pregnant

mothers despite vitamin supplementation and prescribed glycemic control. These observations have led to the hypothesis that macrosomic neonates from mothers with gestational diabetes might display a fetal form of wet beriberi with symptoms of pudgy face, plump body, cardiomegaly and pitting edema.⁴⁰

Assessment of Status: Thiamin deficiency will occur when intake is insufficient to maintain tissue levels high enough to supply all enzymatic demands. The need for adequate functional thiamin to achieve optimal health for individuals is demonstrated in the growing list of known thiamin-responsive disorders of metabolism, which includes hyperkinetic cardiomyopathy, megaloblastic anemia and thiamin-responsive maple syrup urine disease.^{2, 42} Genetic polymorphisms of thiamin-dependent enzymes can alter thiamin binding affinity and enzyme function. This can result in abnormally rapid urinary losses of thiamin. Tissue and serum levels that are in the “normal range” may be insufficient in most individuals. In these people, providing higher-than-normal doses of thiamin can increase enzyme activity and correct functional deficiencies. Biochemical markers of functional sufficiency are therefore the most useful measure of adequacy. For example, three family members with dysautonomic symptoms, comparable to those seen in classical beriberi, required high doses of thiamin tetrahydrofurfuryl disulfide to restore biochemical function as measured by transketolase activity.⁴³

Transketolase — Erythrocytes heavily utilize the pentose phosphate pathway to produce reducing equivalents for maintaining reduced glutathione. This pathway involves two steps catalyzed by a transketolase enzyme that requires thiamin pyrophosphate (TPP). This enzyme may be used to perform a stimulation assay from a whole blood specimen. A “TPP stimulation” result greater than 14% demonstrates a significant risk

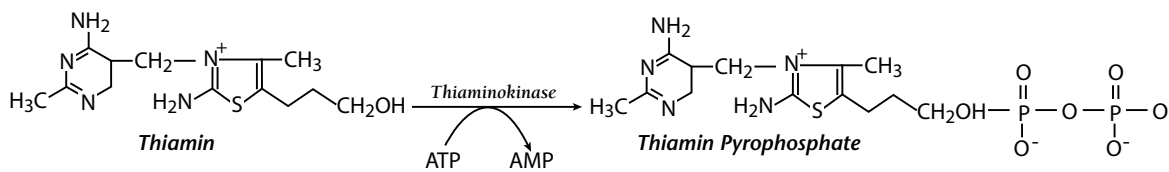


FIGURE 2.2 — Conversion of Thiamin to Thiamin Pyrophosphate

In the intestines, thiamin pyrophosphate is released from proteins and converted to thiamin. Thiamin is transported throughout the body and converted back to thiamin pyrophosphate.