

Thiamine (Vitamin B₁)

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Abstract

Thiamine (vitamin B₁) was the first B vitamin to have been identified. It serves as a cofactor for several enzymes involved in energy metabolism. The thiamine-dependent enzymes are important for the biosynthesis of neurotransmitters and for the production of reducing substances used in oxidant stress defenses, as well as for the synthesis of pentoses used as nucleic acid precursors. Thiamine plays a central role in cerebral metabolism. Its deficiency results in dry beriberi, a peripheral neuropathy, wet beriberi, a cardiomyopathy with edema and lactic acidosis, and Wernicke–Korsakoff syndrome, whose manifestations consist of nystagmus, ophthalmoplegia, and ataxia evolving into confusion, retrograde amnesia, cognitive impairment, and confabulation. Patients on a strict thiamine-deficient diet display a state of severe depletion within 18 days. The most common cause of thiamine deficiency in affluent countries is either alcoholism or malnutrition in nonalcoholic patients. Treatment by thiamine supplementation is beneficial for diagnostic and therapeutic purposes.

Keywords

thiamine, vitamin B₁, beriberi, Wernicke-Korsakoff syndrome, neuropathy, cardiomyopathy

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Vitamins are essential organic molecules that function as cofactors for enzymatic reactions. They generally cannot be synthesized by mammalian cells and, therefore, must be supplied in the diet. Vitamin B₁ is also known as thiamine, thiamin, and aneurine. Thiamine is the currently accepted name for vitamin B₁ in the United States. The chemical name for this water-soluble vitamin is 3-[(4-amino-2-methyl-5-pyrimidinyl)methyl]-5-(2-hydroxyethyl)-4-methylthiazolium. Thiamine consists of a pyrimidine ring and a thiazole ring, which are coupled by a methylene bridge (Figure 1).

Thiamine was the first B vitamin to have been identified, thus its designation B₁. The disease beriberi (which means “sheep”) was first described by Jacobus Bonitus, a Dutch physician, in Java, in 1630. He described patients “with their knees shaking and legs raised up, walk like sheep. It is a kind of paralysis, or rather tremor . . .”¹ The first insight into the real cause of beriberi came in the 1880s in the Japanese Navy, when a correlation between the sailors’ diet and beriberi was noted. After changing their diet, the incidence of beriberi dropped from 40% to 0% in 6 years.¹ Despite this compelling connection, most of the medical community continued to believe that beriberi was the result of a microbial infection or a toxin produced by a microorganism.^{2–6} In 1886, after months of searching for a toxic or microbial link to beriberi, a Dutch medical officer, Dr Christian Eijkman, noticed that some chickens walking freely outside his laboratory were inflicted with a beriberi-like ailment.⁷ He discovered that chickens fed with

white (polished or milled) rice developed polyneuritis, whereas red (partially polished) rice, unhusked rice (padi) and rice hulls prevented and even cured the disease. It was not until 1911 that a young chemist in London, Dr Casimir Funk, crystallized an amine substance from rice bran.⁸ He was convinced that this was the anti-beriberi factor and dubbed it “vitamine” for “vital amine.”⁹ In 1926, vitamin B₁ was finally isolated from rice bran by Jansen and Donath and named aneurine.¹⁰ Unfortunately, those investigators missed the sulfur atom, and their published incorrect formula for aneurine caused confusion for several years. In 1936, Williams and Cline¹¹ published the first correct formula and synthesis for the vitamin. The American Medical Association did not accept any of the names by which it had been known until then, and Williams came up with a new name, “thiamin.”¹² To reflect the vitamin’s amine nature, the American Chemical Society added an “e,” and “thiamine” is now the accepted term.¹³

The thiamine-deficiency condition, beriberi, was considered a disease of the peripheral nervous system, heart, and muscles

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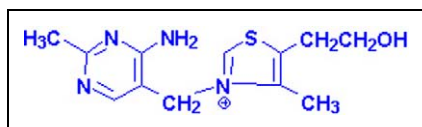


Figure 1. Thiamine is derived from a substituted pyrimidine and a thiazole, which are coupled by a methylene bridge

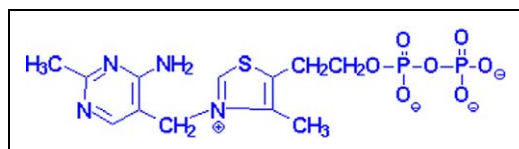


Figure 2. Thiamine pyrophosphate (TPP), the active form of thiamine. The hydroxyl group of thiamine is replaced by a diphosphate ester group

until the mid-1930s when it was realized that Wernicke's encephalopathy was actually the acute cerebral manifestation of severe thiamine deficiency.^{14,15} Beriberi remains a major problem in underdeveloped countries worldwide, and Wernicke-Korsakoff syndrome is a common consequence of alcoholism in the developed world.¹⁶

Biochemical Function of Thiamine

Thiamine occurs in the human body as free thiamine and as various phosphorylated forms: thiamine monophosphate, thiamine triphosphate, and thiamine pyrophosphate, which is also known as thiamine diphosphate. The hydroxyl group of thiamine in thiamine pyrophosphate is replaced by a diphosphate ester group (Figure 2). Thiamine pyrophosphate is the active form of thiamine and it serves as a cofactor for several enzymes involved in energy metabolism. These enzymes include the mitochondrial pyruvate dehydrogenase, the α -ketoglutarate dehydrogenase complexes, and the cytosolic transketolase, all of which participate in carbohydrate catabolism and all of which show reduced activity during thiamine deficiency (Figure 3). Pyruvate dehydrogenase complex is a key enzyme in the Krebs cycle that catalyzes the oxidative decarboxylation of pyruvate to form acetyl-coenzyme A (acetyl-CoA), which enters into the Krebs (citric acid or tricarboxylic acid) cycle. The rate-limiting Krebs cycle enzyme, α -ketoglutarate dehydrogenase, catalyzes the oxidative decarboxylation of α -ketoglutarate to succinyl-CoA. Transketolase functions in the pentose phosphate pathway, an alternate pathway for glucose oxidation. Deficiency of thiamine leads to a reduction in the activity of these enzymes, which is different for the different enzymes, and shows a strong cell-type dependency.¹⁷ These reductions have been demonstrated using cultured cells, experimental models of thiamine deficiency in rats, and autopsied human tissues.¹⁷⁻²¹

Decreases in pyruvate dehydrogenase and α -ketoglutarate dehydrogenase activity result in failure of adenosine triphosphate (ATP) synthesis and selective decreases in ATP levels

within brain regions leading to cell death.²² The reduced pyruvate entry into the Krebs cycle results in increased lactic acid concentrations within the brain and an associated acidosis^{23,24} localized to damaged regions.²⁵ The alterations in oxidative metabolism account for the mitochondrial damage observed both in rat cerebellar granule cells and mouse hippocampal neurons, as well as in cultured cells deprived of thiamine.²⁶⁻²⁸ Substantial cell death was attributed to necrosis due to compromised mitochondrial function and acidosis^{26,27} and to apoptosis.²⁹ Failure of the production of acetyl-CoA results in failure in the synthesis of acetylcholine, an essential neurotransmitter in the nervous system.^{30,31}

Loss of α -ketoglutarate dehydrogenase activity is thought to account for alterations in the intracellular and extracellular levels of several neurotransmitters, including γ -aminobutyric acid (GABA), glutamate, and aspartate, during thiamine deficiency.³²⁻³⁵ These and other findings have suggested that *N*-methyl-D-aspartate (NMDA) receptor-mediated excitotoxicity could play a role in thiamine deficiency-induced neuronal loss.³⁶

Transketolase participates in the pentose phosphate pathway, a pathway that produces reducing substances, such as reduced nicotinamide adenine dinucleotide phosphate (NADPH), for various cellular biosynthetic reactions, including for lipids, and for removal of oxygen radicals. Transketolase is critical for maintenance of the cellular redox state,³⁷ thus thiamine deficiency results in the production of oxidative stress.³⁸ The pentose phosphate pathway produces riboses for use in the synthesis of nucleotides, nucleic acids, coenzymes, and polysaccharides, thus a lack of thiamine results in defective ribonucleic acid (RNA) ribose synthesis.³⁹

Thiamine pyrophosphate is also a coenzyme for the enzyme branched-chain keto-acid dehydrogenase complex that catalyzes the oxidative decarboxylation of branched-chain α -keto acids derived from branched amino acids (eg, valine, isoleucine, leucine) and is responsible for maple syrup urine disease. Thus, thiamine deficiency has a major influence on the activities of this enzyme.⁴⁰

All known thiamine pyrophosphate-dependent enzymes also require a divalent cation, commonly magnesium (Mg^{2+}) that serves as a "coactivator" of the apoenzyme.⁴¹ Mg^{2+} is often depleted with chronic alcohol consumption,⁴² which explains the recognized refractoriness to thiamine treatment alone of hypomagnesemic alcoholics with Wernicke's encephalopathy.^{43,44}

The Effect of Thiamine Function on the Nervous System

Thiamine plays a central role in cerebral metabolism. The brain uses glucose as a primary fuel for energy generation. Glucose enters the brain by diffusion across the blood-brain barrier.⁴⁵ About 30% of the glucose absorbed by the brain undergoes a complete oxidation through the Krebs cycle.⁴⁶ The 3 thiamine-dependent enzymes that are essential for the cerebral metabolism of glucose use thiamine pyrophosphate as cofactor, accounting for 80% of the total thiamine present in nervous tissues.⁴⁷ It is found in both the central and peripheral nervous systems.

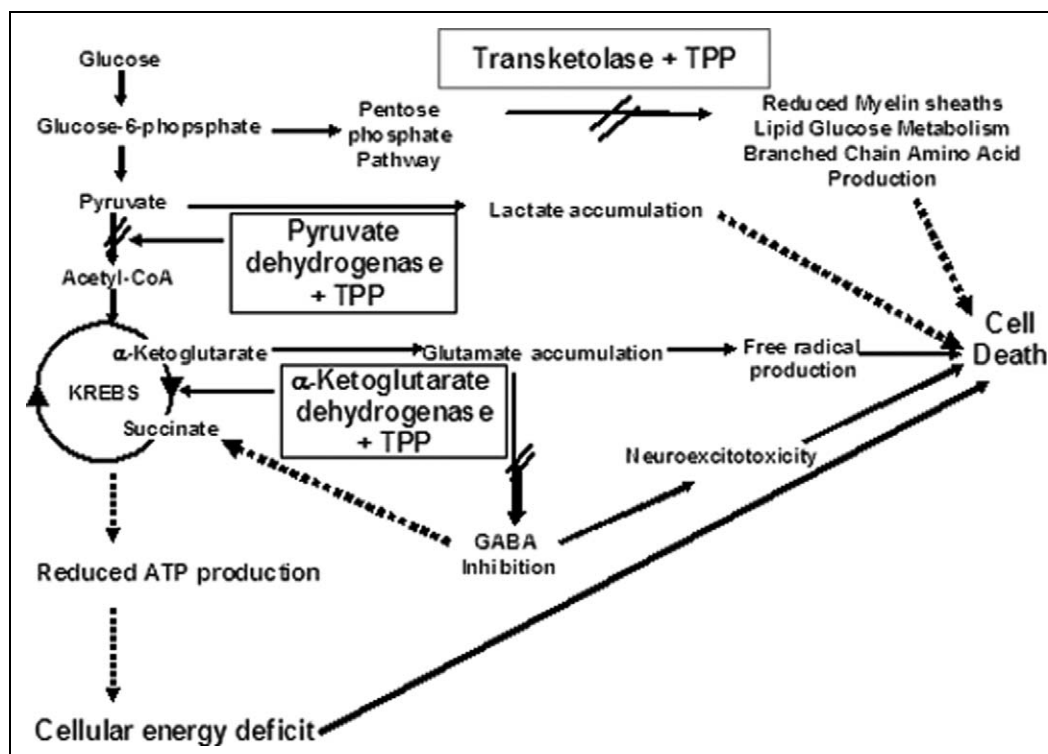


Figure 3. The 3 thiamine-dependent enzymes, transketolase, pyruvate dehydrogenase, and α -ketoglutarate dehydrogenase, and their role in the pathogenesis of cell death in thiamine deficiency

Over and above its coenzymatic function in metabolism, thiamine also has a structural role.^{48,49} It is involved in membrane structure and function, including axoplasmic, mitochondrial, and synaptosomal membranes, acts against agent-induced cytotoxicity, and fixes membrane sites.^{50,51} It intervenes in synaptic transmission and plays a role in cellular differentiation, synapse formation, axonal growth, and myelinogenesis.⁵²⁻⁵⁶ Thiamine-deficient rats displayed abnormal performance of a learning task⁵⁷ and functional disturbances in conduction velocities were demonstrated in their central and peripheral nervous systems.⁵⁸

Vitamins regulate brain development during fetal and early postnatal life, a fact that makes the brain particularly vulnerable to nutritional deficiencies.^{59,60} The results of studies in rat models indicate that maternal thiamine deficiency can indeed cause significant deficits in the spinal cord, brain enzymes, myelinogenesis, and lipogenesis,^{56,61-63} and there is evidence of thiamine involvement in specific brain regions.^{64,65} Deficits have also been reported in psychomotor and sensory abilities of murine pups.^{66,67} The storage of thiamine in the human body is minimal, and subjective symptoms appear in adults after 2 to 3 weeks of a thiamine-deficient diet.¹⁶

Bioavailability of Thiamine

Thiamine uptake by the small intestine is mediated by a transport system and is taken up by cells within liver, heart, and various other tissues from the blood, with the exception of

neuronal tissue, in which thiamine is transported from blood into cerebrospinal fluid via the blood-brain barrier. Once within the cell, further transport occurs through mitochondrial and nuclear membranes. The lack of a functional transporter results in thiamine-responsive megaloblastic anemia.^{68,69} Patients with thiamine-responsive megaloblastic anemia were found to have mutations in the *SLC19A2* gene that encodes a thiamine transporter protein.⁷⁰ Clinical improvements can be documented following administration of pharmacologic doses of thiamine for those patients. Once thiamine has been imported, it is rapidly converted to its active form (thiamine pyrophosphate) in the brain and liver by a specific enzyme, thiamine diphosphokinase.

Thiamine is found in various foods, including enriched bread and cereals (whole grain and enriched), peas, beans, nuts, brown rice, and meats (especially pork and beef), and is absent in polished rice and other highly purified cereal products. Some thiamine in foods is lost with cooking. Since this is a water-soluble vitamin, it is not stored in the body and the excess is excreted in the urine. Body storage of thiamine is minimal, and a state of severe depletion in patients on a strict thiamine-deficient diet becomes evident within 18 days.¹⁶

The dietary requirement for thiamine is proportional to the caloric intake of the diet and ranges from 1.0 to 1.5 mg/d for normal adults (Table 1).⁷¹ An increase in thiamine intake will be required if the carbohydrate content of the diet is excessive. A carbohydrate-rich diet coupled with low thiamine intake can precipitate thiamine deficiency.⁷²

Table 1. Recommended Daily Allowances (RDA) of Thiamine

	mg
Infants and children	
Birth to 6 months	0.3
6 months-1 year	0.4
1-3 years	0.7
4-6 years	0.9
7-10 years	1.0
Adolescents and adults	
Males	1.2-1.5
Females	1.0-1.1
Pregnant females	1.5
Breast-feeding females	1.6

Thiamine is water soluble and heat labile, and most of the vitamin is lost when rice is washed and when the cooking water is discarded. Several food products contain anti-thiamine factors (eg, thiaminases and thiamine antagonists) that inactivate thiamine. The thiaminase heat-labile enzyme is found in raw or fermented fish, shellfish, and some bacteria. These foods have anti-thiamine activity when consumed without heat treatment. Heat-stable thiamine antagonists occur in several plants, ferns, tea, and betel nut. They include polyphenols that are found in blueberries, red currants, red beets, brussel sprouts, red cabbage, betel nuts, coffee, and tea. They react with thiamine to yield the nonabsorbable thiamine disulfide. Tannins, a major component of fermented tea leaves, have anti-thiamine activity, which can be abolished by ascorbic acid, tartaric acid, and citric acid, all present in many vegetables and fruits.¹⁶ To decrease the influence of anti-thiamine factors and increase thiamine bioavailability, it is recommended to delay the consumption of tea or other tannin-containing products after a meal, to consume foods high in ascorbic acid, and to heat products containing thiaminase before consumption.¹⁶

Thiamine Deficiency States

Primary thiamine deficiency is caused by inadequate intake of thiamine, most commonly in underdeveloped countries. The great outbreaks of thiamine deficiency in Southeast Asia at the beginning of the 20th century followed the large-scale production of milled rice and its extensive distribution. The availability of milled rice as a cheap and popular food in the urban areas of those countries was also an important factor in the occurrence of thiamine deficiency. Thiamine deficiency was recorded in refugee populations of Thailand at the beginning of the 1980s and during the 1990s, in Guinea in 1990, in Djibouti in 1993, and in Nepal between 1993 and 1995.^{16,73-75}

Secondary thiamine deficiency is caused by increased requirement, as in hyperthyroidism, pregnancy, lactation, and fever. It is also associated with impaired absorption, as in prolonged diarrheas, and impaired utilization, as in severe liver disease.

The most common cause of thiamine deficiency in affluent countries is alcoholism: It has been found in up to 80% of alcoholics because of inadequate nutritional intake, reduced

absorption, and impaired utilization of thiamine.^{42,76,77} In nonalcoholics, malnutrition states are generally responsible for thiamine deficiency, such as those seen in end-stage malignancy, intractable vomiting after gastric bypass surgery, prolonged intravenous fluids without other sources of nutrition, hemodialysis, hyperemesis gravidarum, anorexia nervosa, and magnesium depletion.⁷⁸⁻⁸³ Elderly patients also appear to be vulnerable.⁸⁴

Thiamine deficiency is still common in developed countries. In the United Kingdom, the prevalence of thiamine deficiency in randomly selected patients on admission to an emergency department was found to be 21%, whereas their alcohol intake was similar to controls.⁸⁵ Fourteen percent of 75 elderly (64 years or older) emergency department admissions from a nursing home in Manhasset, New York were thiamine deficient.⁸⁴ Thiamine deficiencies can also occur in breast-fed infants when the mother has an inadequate intake of thiamine. As many as 12.5% of a population of critically ill Canadian children were found to have significant thiamine deficiency.⁸⁶

In 1997, thiamine deficiency was reported as a public health concern in the United States when the Centers for Disease Control and Prevention published a series of case reports of lactic acidosis traced to thiamine deficiency resulting from a nationwide shortage of multivitamins for total parenteral nutrition.⁸⁷⁻⁸⁹ In 2003, an "outbreak" of infantile thiamine deficiency was reported in Israel, induced by feeding with a thiamine-deficient soy-based infant formula.⁹⁰ Seasonal ataxia was recently reported in Nigerians as being because of their consumption of an African silkworm pupae, which possesses high activity of a heat-resistant thiaminase.⁹¹

Clinical Symptoms of Thiamine Deficiency

Early Symptoms

The earliest symptoms of thiamine deficiency are nonspecific and include fatigue, irritation, poor memory, sleep disturbances, precordial pain, anorexia, abdominal discomfort, and constipation. Five stages of the development of a vitamin deficiency were described by Brin in 1964.⁹² In the first or preliminary stage, inadequate thiamine availability because of faulty diet, malabsorption, or abnormal metabolism leads to a greatly reduced urinary thiamine loss. In the second, or biochemical stage, the activity of transketolase is significantly reduced. In the third, or physiologic stage, various general symptoms develop, such as reduced appetite, insomnia, increased irritability, and malaise. In the fourth, or clinical stage, a constellation of symptoms classically specific to thiamine-deficiency disease (beriberi) develops, including intermittent claudication, polyneuritis, bradycardia, peripheral edema, cardiac enlargement, and ophthalmoplegia. In the fifth, or anatomical stage, histopathological changes because of cellular structural damage are seen, such as cardiac hypertrophy, degeneration of the granular layer of the cerebellum, and swelling of the brain microglia. It is noteworthy that the first 3 stages do not involve specific signs of deficiency.

Clinical Syndromes

There are 2 major manifestations of thiamine deficiency: cardiovascular disease (“wet beriberi”) and nervous system disease (“dry beriberi” and Wernicke–Korsakoff syndrome). Symptoms of dry beriberi are bilateral and symmetric, predominantly involving the lower extremities, and beginning with paresthesias of the toes, burning of the feet (particularly severe at night), muscle cramps in the calves, and pain in the legs. Calf muscle tenderness, difficulty in rising from a squatting position, a decrease in the vibratory sensation in the toes, and plantar dysesthesia are early signs. A diagnosis of mild peripheral neuropathy can be made when ankle jerks are absent. Continued deficiency causes loss of knee jerk, loss of vibratory and position sensation in the toes, atrophy of the calf and thigh muscles, and finally foot drop and toe drop. That the arms can be affected after leg signs are well established.

Wet beriberi occurs in thiamine deficiency when myocardial disease is prominent. This causes a high cardiac output with peripheral vasodilation and warm extremities. Before heart failure occurs, tachycardia, a wide pulse pressure, sweating, warm skin, and lactic acidosis develop, leading to salt and water retention in the kidneys. The resulting fluid overload leads to edema of the dependent extremities. A more rapid form of wet beriberi has been termed acute fulminant cardiovascular beriberi or Shoshin beriberi, in which vasodilation continues, resulting in shock in a patient with heart failure.⁹³

Wernicke–Korsakoff syndrome or Wernicke encephalopathy is the thiamine-deficient disease seen most often in the Western hemisphere. It mainly affects alcoholics because of a number of reasons: (a) their diet is usually poor; (b) diets rich in carbohydrates (eg, alcohol or rice) increase the metabolic demands of thiamine; (c) alcohol inhibits intestinal ATPase, which is involved in the uptake of thiamine; and (d) magnesium, which is required for the binding of thiamine to the enzymes prior to their activation, is usually depleted in alcoholics.⁴² Wernicke’s encephalopathy, which describes the effects of thiamine deficiency in the acute phase, later progresses to Wernicke–Korsakoff syndrome in the chronic phase. Wernicke encephalopathy consists of nystagmus, total ophthalmoplegia, ptosis, aphonia, loss of vibratory sensation, decreased reflexes, loss of coordination, and ataxia.¹⁵ Hypothermia can also be present due to damage in the thermoregulatory centers. In late-stage beriberi, a patient can become confused and exhibit delusions, psychosis, confabulation, and impaired retentive memory and cognitive function. In severe cases, the patient can have seizures and coma, which, if untreated, can result in death. The unusual eye movements and ataxia of a patient with Wernicke encephalopathy can subside if thiamine replacement is provided, but it can be replaced by Korsakoff syndrome, which includes retrograde amnesia, impaired ability to learn, and confabulation.⁹⁴

Infantile beriberi usually occurs between the second and fourth month of life in infants who are breastfed by thiamine-deficient mothers. The onset of symptoms is often very rapid and the fatality rate is very high. Initially, an infant with

thiamine deficiency has a normal appearance with varying degrees of constipation, occasional vomiting, crying, and restlessness. Subsequently, the disease usually presents with cardiac manifestations or can display meningeal irritation accompanied by vomiting and convulsions (the pseudomeningitic form). Heart failure, aphonia, and absent deep tendon reflexes are characteristic of progressive disease.^{16,95}

Pathological Findings of Thiamine Deficiency

The most advanced neural changes occur in the peripheral nerves, particularly of the legs. The distal segments are characteristically affected earliest and most severely. Degeneration of the medullary sheath can occur in all tracts of the spinal cord, especially in the posterior columns and in the anterior and posterior nerve roots. Degenerative changes also occur in the anterior horn and posterior ganglion cells. The heart is dilated and enlarged, and muscle fibers are swollen, fragmented, and vacuolized, with interstitial spaces dilated by fluid. Vasodilation can result in some edema before high-output heart failure occurs.

The pathology of the brain in thiamine deficiency consists of bilaterally symmetrical midline hemorrhagic and/or necrotic lesions in selective brain regions, mainly the mammillary bodies, thalamus (medial dorsal, anterior medial, and pulvinar), periaqueductal region, and floor of the fourth ventricle, hypothalamus, and cerebellar vermis.^{96,97}

Neuroimaging in Thiamine Deficiency

The appearance of acute Wernicke encephalopathy on magnetic resonance imaging (MRI) is that of high signal intensities in the mammillary bodies, medial thalamus, periaqueductal gray matter, and cerebellar vermis on T2-weighted images (Figure 4). Fluid-attenuated inversion recovery-weighted MRI displays concurrent cytotoxic and vasogenic edema patterns. Diffusion-weighted MRI shows high signal intensities that correlate with low apparent diffusion coefficient mapping. Cerebral cortical involvement can be indicative of irreversible damage and poor prognosis.⁹⁸ In chronic Wernicke–Korsakoff syndrome, MRI can be normal or can show symmetric low-density abnormalities in periventricular areas, the diencephalon and the midbrain, with excessive mammillary body, cerebellar, and cerebral shrinkage. Although the MRI findings carry high specificity for Wernicke encephalopathy, its low sensitivity implies that normal MRI results should not be used to exclude the diagnosis of acute illness.

Diagnosis of Thiamine Deficiency

The diagnosis of thiamine deficiency is mainly clinical since routine laboratory tests are not available and awaiting the results of a diagnostic assay can lead to a delay in diagnosis. Thiamine is not measured in the blood since blood contains only about 0.8% of the total body thiamine, and the concentration is too low to allow precise extrapolation of the total



Figure 4. Magnetic resonance imaging (MRI) scan of a patient with thiamine deficiency showing a bilateral symmetrical hyperintense signal in the periaqueductal gray matter

thiamine status. Urinary excretion of thiamine is not a very reliable method for assessing tissue stores, and similar to the blood levels, it is a reflection of the immediately preceding intake. In contrast, transketolase activity, which is measured by the thiamine pyrophosphate effect assay, is the most reliable indicator of thiamine functional status. Erythrocyte transketolase activity is a sensitive indicator of tissue stores. Red blood cells, which lack mitochondria, have no alternative means of generating NADPH save the pentose phosphate pathway. Also, NADPH is required to reduce glutathione in order to maintain the normal structure of red blood cells and to maintain hemoglobin in the ferrous state. Transketolase is a thiamine pyrophosphate-requiring enzyme, which catalyzes reactions in the pentose phosphate pathway. As such, the level of transketolase activity in red blood cells is a reliable diagnostic indicator of thiamine status. The erythrocyte transketolase test requires a sample of hemolyzed blood to be incubated with excess ribose 5-phosphate in the presence of excess added thiamine pyrophosphate (matched with a control that has no added thiamine pyrophosphate). After the incubation period, the amounts of remaining substrate and the product formed are measured. Any enhancement in enzyme activity resulting from the added thiamine pyrophosphate indicates that the sample was originally deficient in thiamine to some extent. The extent of deficiency in thiamine is expressed in percentage stimulation over the control value (Table 2). An increase of more than 15% in enzyme activity is a definitive marker of deficiency.

Elevated blood pyruvate and lactate measurements are useful, but the many false positive test results make it difficult to establish a diagnosis. For example, sepsis, cardiogenic shock, and meningitis can imitate thiamine deficiency disease and are

Table 2. Classification of Thiamine Pyrophosphate Effect (TPPE)

	TPPE (%)
Normal	0-14
Marginally deficient	15-24
Severely deficient	25+

associated with lactic acidosis. However, the persistence of lactic acidosis and a rise following a glucose load strongly support the diagnosis and should alert the physician to the possibility of thiamine deficiency. Clinical response to thiamine administration is the most practical indication for diagnosis. If the patient responds to treatment, it is safe to assume that a measure of thiamine deficiency had been responsible for the condition. Thiamine is not toxic in high levels, which means that this approach carries little risk.

Treatment of Thiamine Deficiency

For mild polyneuropathy, 10 to 20 mg/d of thiamine is given in divided doses for 2 weeks followed by a nutritious diet. The dosage is 20 to 30 mg/d for moderate or advanced neuropathy and should be continued for several weeks after the symptoms disappear. The edema and congestion of Shoshin beriberi respond to 100 mg/d of thiamine intravenously, which should be continued for several days. Heart failure due to beriberi responds poorly to digitalis or diuretics. For Wernicke-Korsakoff syndrome, thiamine 50 to 100 mg intramuscularly or intravenously twice a day must usually be given for several days, followed by 10 to 20 mg daily until a therapeutic response is obtained. Anaphylactic reactions to intravenous thiamine unrelated to the dose are rare. Thiamine deficiency is often associated with other vitamin B-complex deficiencies, and multiple water-soluble vitamin therapy at 5 to 10 times the recommended daily allowances is usually advisable for several weeks. This regimen should be followed indefinitely by a nutritious diet supplying 1 to 2 times the recommended daily allowances. Magnesium, a cofactor for transketolase, should be given as magnesium sulfate (1 to 2 mL intramuscularly of a 50% solution) with thiamine to correct thiamine resistance and the frequently accompanying hypomagnesemia. Recovery from neurologic deficits is often incomplete in beriberi. Several inborn errors of metabolism respond to pharmacologic doses of thiamine (5 to 20 mg/d). These include thiamine-responsive megaloblastic anemia, lactic acidosis due to low activity of liver pyruvate dehydrogenase, and thiamine-responsive maple syrup urine disease due to low activity of branched-chain keto acid dehydrogenases.

In conclusion, clinicians should be vigilant and consider the possibility of thiamine deficiency in high-risk patients. If the diagnosis is questionable, it is recommended to treat the patient with thiamine anyhow, given that it is a safe and inexpensive therapeutic agent, which can prevent irreversible damage. Preventive strategies might be effective on the national level, and countries should consider this by supplementing staple foods with thiamine.

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