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What is This?
Thiamine in Nutrition Therapy

Krishnan Sriram, MBBS, FACS, FRCS(C)¹; William Manzanares, MD, PhD²; and Kimberly Joseph, MD, FACS, FCCM³

Abstract
Clinicians involved with nutrition therapy traditionally concentrated on macronutrients and have generally neglected the importance of micronutrients, both vitamins and trace elements. Micronutrients, which work in unison, are important for fundamental biological processes and enzymatic reactions, and deficiencies may lead to disastrous consequences. This review concentrates on vitamin B₁, or thiamine. Alcoholism is not the only risk factor for thiamine deficiency, and thiamine deficiency is often not suspected in seemingly well-nourished or even overnourished patients. Deficiency of thiamine has historically been described as beriberi but may often be seen in current-day practice, manifesting as neurologic abnormalities, mental changes, congestive heart failure, unexplained metabolic acidosis, and so on. This review explains the importance of thiamine in nutrition therapy and offers practical tips on prevention and management of deficiency states. (Nutr Clin Pract. 2012;27:41-50)

Keywords
thiamine; vitamin B₁; beriberi; metabolic acidosis; critical illness; micronutrients; enteral nutrition; parenteral nutrition; refeeding syndrome; congestive heart failure

Historical Facts
The term beriberi is often associated with thiamine deficiency, although the origin of the word is not clear. It has been suggested that it might come from Sinhalese meaning “I cannot” or from Arabic (“sailor’s asthma”). Carl Wernicke described the eponymous syndrome—Wernicke encephalopathy (WE)—in 1881. However, it took many more decades to establish a relationship between consumption of milled or polished rice and the development of beriberi due to thiamine deficiency in humans. It was only after the 1950s that enrichment of rice and other grains became common practice. After the advent of nutrition therapy in the mid- to late 1970s, thiamine deficiency was no longer a historic curiosity, especially in developed countries. It began to be recognized during or after nutrition therapy, both enteral and parenteral, even in patients who were seemingly well nourished or overnourished and not necessarily in the expected patient population—for example, alcoholics. This was especially true when a high carbohydrate intake is provided, as in parenteral nutrition with a high glucose content. We now also speak of gastrointestinal beriberi and bariatric beriberi, to be discussed later.

From ¹Division of Surgical Critical Care, Department of Surgery, Stroger Hospital of Cook County, Chicago, Illinois, ²Department of Critical Care, Hospital de Clinicas (University Hospital), Faculty of Medicine, Universidad de la Republica, Montevideo, Uruguay, ³Department of Trauma, Stroger Hospital of Cook County, Chicago, Illinois

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Corresponding Author: K. Sriram, Department of Surgery, Room 3350, Stroger Hospital, 1901 West Harrison St, Chicago, IL 60612; e-mail: ksriram@cookcountyhhs.org
Absorption of Thiamine

Thiamine is rapidly absorbed in the jejunum and ileum by an active, carrier-mediated, and rate-limited process, but at higher concentrations, the uptake is by passive diffusion. However, the clinical relevance of passive diffusion remains questionable.

The intestine is exposed to 2 sources of thiamine: a dietary source and a bacterial source in which the vitamin is generated by the normal intestinal microbiota. After hydrolysis of the phosphorylated forms of thiamine in the intestinal lumen, free thiamine enters the absorptive cells via a specialized sodium-independent, pH-dependent, and amiloride-sensitive carrier-mediated mechanism. Two thiamine intestinal transporters have been indentified: the human thiamine transporter–1 (hTHTR-1; the product of SLC19A2 transporters) and the hTHTR-2 (the product of SLC19A3). Both hTHTR-1 and hTHTR-2 are expressed in the small and large intestines. However, hTHTR-1 shows its maximal expression in the liver, followed in order by stomach, duodenum, jejunum, colon, and ileum.

The intestinal thiamine uptake process appears to be under the regulation of an intracellular calcium/calmodulin mediated pathway. Also, thiamine absorption is adaptively regulated by the extracellular thiamine level. In fact, thiamine deficiency was found to lead to an induction in intestinal carrier-mediated uptake. This effect was associated with a significant induction in the level of expression of THTR-2 (but not THTR-1).

Furthermore, chronic alcohol use leads to thiamine deficiency, and inhibition in intestinal thiamine absorption plays a role in causing this deficiency. This inhibition was associated with a marked decrease in the level of expression of THTR-1 (but not THTR-2). In addition, a similar mechanism of inhibition in thiamine uptake was demonstrated in kidneys. Thus, chronic alcoholism is characterized by inhibition in the intestinal absorption and in the reabsorption by the kidneys, which determine a negative impact on the thiamine balance in the body.

In summary, current knowledge indicates that active absorption of thiamine is the most important and significant. Thiamine transport seems to be at different capacities along the gastrointestinal tract: duodenum and jejunum > colon > stomach.

Biochemical Actions

Following absorption, thiamine is initially phosphorylated to thiamine diphosphate, also known as thiamine pyrophosphate (TPP), by a specific enzyme: thiamine pyrophosphokinase. TPP is the active form involved in several enzyme functions associated with metabolism of carbohydrates, lipids, and branched chain amino acids. TPP is a cofactor for multiple steps in the glycolysis and oxidative decarboxylation of carbohydrates. TPP is required as a coenzyme for the mitochondrial enzyme complexes α-ketoglutarate dehydrogenase and pyruvate dehydrogenase. Therefore, TPP is required for the conversion of pyruvate to acetyl CoA and entry to Krebs cycle, as well as the conversion of α-ketoglutarate to succinyl CoA (Figure 1). Both enzymes decrease its activity during thiamine deficiency states, but in general α-ketoglutarate dehydrogenase is more severely affected than the pyruvate dehydrogenase complex and is one of the earliest biochemical changes observed in thiamine deficiency. It is well known that TPP activates decarboxylation of pyruvate dehydrogenase complex. This complex is a group of enzymes and cofactors that form acetyl CoA, which then condenses with oxaloacetate to form citrate, the first component of the Krebs cycle. Thiamine’s important role in tricarboxylic acid cycle is explained in Figure 1.

Basically, thiamine is important for the conversion of lactate to pyruvate; in its absence, lactic acid accumulates. The acidosis is manifested both systemically and locally. An example of focal damage due to lactic acidosis is its effect on vulnerable brain structures (mammillary bodies and posteromedial thalamus) detectable by magnetic resonance imaging scanning. Apoptotic cell death due to N-methyl-D-aspartate toxicity is responsible for neurologic symptoms in thiamine deficiency.

Another important enzyme requiring TPP is erythrocyte transketolase, an enzyme of the pentose phosphate pathways. The functions of this pathway are to provide pentose phosphate for nucleotide synthesis and to supply reduced nicotinamide adenine dinucleotide phosphate for various synthetic pathways.

Risk Factors

Thiamine deficiency occurs due to poor oral intake, inadequate provision of thiamine in enteral or parenteral nutrition therapy, reduced gastrointestinal absorption due to disease or surgery, or increased metabolic requirements. Increased gastrointestinal or renal losses should also be considered. Often, multiple factors exist, predisposing the patient to thiamine deficiency, in addition to deficiencies of other micronutrients. Patients with a history of alcoholism, AIDS, and malignancies form a substantial group of patients in whom thiamine deficiency should be suspected. Although thiamine deficiency is often associated with alcohol abuse, it is being increasingly recognized that it can occur in patients without this history. Pregnancy and lactation, hyperthyroidism, renal failure especially on hemodialysis, systemic infections, advanced age, diabetes mellitus, and any critical illness are other major risk factors.

Obese patients, candidates for bariatric surgery, and postbariatric surgery patients are not exempt from developing thiamine deficiency even if routine multivitamin supplements are being taken. Because of its short half-life and poor stores, a continuous supply of thiamine is needed for optimal metabolism.
Some of these specific conditions are discussed in further detail in this review.

**Laboratory Diagnosis**

Serum thiamine level represents only a small portion of the total body thiamine and is not a reliable indicator of thiamine status. However, in clinical practice, serum and red blood cell thiamine levels are the only tests that can be ordered and obtained easily. A normal level does not exclude the diagnosis of thiamine deficiency. Erythrocyte transketolase activation assay, a functional test, is also mentioned in the literature. However, the current preferred test is measurement of thiamine diphosphate in erythrocyte (ie, red blood cell) hemolysates using high-performance liquid chromatography. It is more reproducible than the other tests and suitable for research and clinical purposes.

Considering the expense of these sophisticated tests and the delay in obtaining the results from a reference laboratory, the clinician should depend on clinical judgment and initiate treatment without waiting for a laboratory confirmation. Additionally, serum tests normalize rapidly after thiamine administration and must be obtained prior to treatment. We do not recommend routine testing. A high index of suspicion

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**Figure 1.** The glycolytic pathway and Krebs cycle pathways. TPP, thiamine pyrophosphate. Modified from Klooster A et al, Medical Hypothesis 2007; 69:873-878, and used with permission from Elsevier Ltd, Oxford, UK.
Clinical Features of Thiamine Deficiency

Central and Peripheral Nervous System

The neurologic manifestations of thiamine deficiency have recently been extensively reviewed by Kumar. Clinical manifestations are highly variable and involve the central and peripheral nervous systems (Table 1). Some symptoms may be permanent and not reversible even with thiamine administration. Although WE and Korsakoff psychosis have certain distinct clinical features, the term Wernicke-Korsakoff syndrome is often used in clinical practice. Korsakoff psychosis may sometimes be the initial presentation in some patients, or it may be a sequel to WE.

The classic triad of WE includes ocular abnormalities (nystagmus, partial or complete ophthalmoplegia, papillary abnormalities, fundoscopic changes, optic neuropathy), ataxic gait, and mental status changes. These may occur occurring acutely or subacutely. All components of the triad may not be seen. Gait and trunk ataxia are due to vestibular and cerebellar involvement. Various manifestations of peripheral neuropathy occur. Rarer neurologic manifestations include seizures, myoclonus and hypertonia, chorea, quadriparesis, and dysphagia. Tinnitus and hearing loss have also been reported.

Changes in mental status and sensorium are very often and constantly seen in WE and include apathy, inability to concentrate, spatial disorientation, confusion, and even frank delirium, psychosis, or coma. Thiamine deficiency must be suspected in any patient, especially one in the intensive care unit (ICU), with unexplained changes in sensorium or frank delirium.

About 80% of patients who initially survive WE end up with psychosis. Wernicke-Korsakoff syndrome is an amnestic confabulatory syndrome with severe amnesia and loss of recent and working memory, while remote or reference memory is preserved. The patient may appear to be alert and attentive with decent social behavior and the ability to learn new skills. Some degree of euphoria is seen. Kumar has described these features in detail in his excellent review.

Cardiovascular System

The association between CHF and thiamine deficiency is being recognized with increasing frequency even in present-day practice, although wet beriberi was described decades ago. Thiamine deficiency must be suspected and treated in all cases of unexplained CHF. Thiamine deficiency is highly prevalent among hospitalized patients with CHF and ranges from 13%–93%. Several potential factors have been associated with thiamine deficiency in CHF patients; among these, alcoholism, loop diuretic use, malnutrition, advanced age, and heart failure severity have been described. Among these patients, those with New York Heart Association functional class III/IV have a more severe deficiency than do class I/II patients, and furosemide treatment has been shown to exacerbate this deficiency, increasing urinary excretion. Diuretics are able to prevent reabsorption of thiamine and increase its urinary excretion. Zenuk et al found a 98% prevalence of thiamine deficiency with furosemide therapy at doses > 80 mg/d. However, thiamine deficiency may occur with smaller dosages of diuretics with long-term use. In 100 patients admitted to the hospital with diagnosis of CHF, Hanninen et al showed that thiamine deficiency was present in 33% of patients, compared with 12% of controls (P = .007). In this study, thiamine deficiency was associated with urine loss, nonuse of thiamine-containing supplements, preadmission spironolactone use, and preserved renal function. Nonetheless, according to multiple logistic regression analysis, increased urinary thiamine loss was the most important predictor of thiamine status among CHF patients. According to these data, thiamine supplementation should be considered a routine practice in the treatment of hospitalized CHF patients. In a study by Shimon et al, 30 patients with CHF who were receiving furosemide were given either thiamine in a daily dose of 200 mg or placebo. The authors observed a significantly improvement in left ventricular function, with an increase of 22% in ejection fraction. Furthermore, more research is warranted defining the safety and efficacy of thiamine supplementation in the CHF population. These studies should be capable of defining the effect of thiamine supplementation on illness severity in CHF patients.
Cardiac surgery provides another example of systemic inflammatory response syndrome. It was recently shown that coronary artery bypass graft surgery, a surrogate for critical illness and the stressed states, depletes plasma thiamine levels. In this small study, Donnino et al showed in 15 patients that plasma thiamine levels significantly decrease from preoperative period to 24 hours after surgery (mean difference, 10.14 mmol/L, \( P = .0004 \)). These results suggest that postoperative patients may require thiamine supplementation. However, more studies are warranted to define the need for routine thiamine supplementation after cardiac surgery.

**Metabolic Acidosis**

Thiamine deficiency must always be considered in cases of unexplained lactic acidosis. Thiamine deficiency is a rare cause of lactic acidosis, but it should be considered in alcoholism, patients receiving diuretics, total parenteral nutrition, or chemotherapy. Lactic acidosis and the inability to utilize the Krebs cycle are the major causes of dry beriberi and wet beriberi, both manifestations of thiamine deficiency. Additionally, an acute fulminant form of cardiac or wet beriberi known as *shoshin* is characterized by cardiogenic shock, leading to death in a short time. Also, lactic acidosis due to thiamine deficiency is often associated with nausea, emesis, and severe abdominal pain mimicking acute intestinal ischemia and may result in unnecessary surgery. This syndrome is referred to as gastrointestinal beriberi.

**Thiamine Deficiency in Specific Conditions**

**Thiamine in Pregnancy**

Thiamine requirement in pregnancy is increased. Hyperemesis gravidarum is especially a situation where thiamine deficiency can rapidly occur. Diagnosis can be difficult as presentation may be atypical. An elevation of transaminase levels suggesting liver function abnormality may also be seen. A high index of suspicion and prompt treatment even without confirmatory tests results in resolution of symptoms. Pregnancy after weight reduction following bariatric surgery is not uncommon and is reported to be associated with a reduced incidence of gestational diabetes. This is an additional reason why surgical options are offered to the obese patient planning to get pregnant. Thiamine deficiency should always be considered in the postbariatric surgery patient.

**Thiamine in Critical Illness**

More than 2 decades ago, Cruickshank et al showed, in a retrospective study on 158 patients admitted to the ICU, that thiamine deficiency was present in 20% of these patients. In addition, among patients with thiamine deficiency, mortality rate was significantly higher (72%) versus 50% of global mortality. In 1999, Jamieson et al concluded that thiamine deficiency at admission to the emergency room was present in 21% of patients. In a very interesting cohort study of 129 patients, Corcoran et al were unable to demonstrate any association between thiamine concentration and other vitamins based on the APACHE II (Acute Physiology and Chronic Health Evaluation II) score or the SOFA (Sequential Organ Failure Assessment) score after admission to the ICU. More recently, thiamine deficiency was recognized in critically ill patients with severe sepsis, and low thiamine levels have been associated with higher lactic acid levels in these patients even in the absence of hepatic dysfunction. In critically ill children, the incidence of low blood thiamine levels upon admission to ICU has been recently reported. In a Brazilian study, Lima et al found that 28.2% of patients upon admission to pediatric ICU had thiamine deficiency. In addition, low thiamine levels were not associated with malnutrition. However, the authors found a C-reactive protein concentration greater than 20 mg/dL as an independent risk factor for deficiency (\( P = .02 \)). These findings show that the magnitude of systemic inflammation is a risk factor for thiamine deficiency among critically ill children admitted to the ICU.

In burn patients, thiamine balance may be affected through reduced intestinal absorption, increased losses, tissue redistribution, and increased requirements. However, optimal nutrition requirements for burn patients are still unknown. Falder et al observed that thiamine supplementation is able to increase serum thiamine levels and concomitantly decrease pyruvate and lactate levels due to an increased utilization of pyruvate by pyruvate dehydrogenase activity. Likewise, thiamine supplementation showed a maximum benefit when its serum levels reach a concentration of 40 ng/mL.

Current guidelines suggest that thiamine supplementation at daily dose of 100–300 mg should be provided during the first 3 days in the ICU in patients with possible thiamine deficiency and especially when alcohol abuse is suspected (grade B).

**Thiamine in Refeeding Syndrome**

Refeeding syndrome is a potentially life-threatening complication of refeeding in severely starved individuals. This syndrome includes electrolyte abnormalities such as hypophosphatemia, hypokalemia and hypomagnesemia, heart failure, respiratory failure, neurologic and musculoskeletal abnormalities, hematological and hepatic dysfunction, vitamins deficiency, and death. Thiamine deficiency is often a component of refeeding syndrome. Upon the introduction of carbohydrates, there is a shift of metabolism from lipids to carbohydrates. In this context, acute thiamine deficiency may be precipitated due to increasing carbohydrate metabolism and consumption of thiamine during glycolysis, especially among patients suffering from chronic alcoholism who usually have chronic thiamine deficiency.
deficiency. Prior to initiating nutrition therapy cautiously, thiamine must be administered intravenously. It is likely that thiamine may be one of the contributing factors leading to sudden death in refeeding syndrome. Current guidelines for prevention of the refeeding syndrome suggest that adult patients at high risk should receive thiamine 300 mg intravenously at least 30 minutes before starting nutrition therapy and then 200–300 mg daily intravenously or orally until day 3. Nonetheless, other authors recommend continuing with a daily dose of 100 mg by enteral route. In the pediatric population, thiamine should also be replaced giving a daily dose of 10–25 mg during the first few days and, thereafter, 5–10 mg/d for 1 month.

**Thiamine in Acute Renal Failure and Renal Replacement Therapy**

Acute renal failure, or the preferred term, acute kidney injury, and its treatment by continuous renal replacement therapy (CRRT) are able to affect micronutrients status, including water-soluble vitamins. Furthermore, adult patients with chronic kidney disease requiring dialysis have shown poor intake and negative balance of thiamine. Nevertheless, Coveney et al compared serum levels of water-soluble vitamins in a group of extended- and conventional-hours hemodialysis adult patients. The authors showed that thiamine levels were lower in the extended group, although no cases of thiamine deficiency were reported. CRRT results in significant losses and negative balance of thiamine and other micronutrients, which contribute to thiamine deficiency. A prospective study from Switzerland evaluated 19 sessions in 11 critically ill patients and showed that the 24-hour balances were negative for thiamine (−4.12 mg, equivalent to 1.5 times the recommended intake). These data suggest that usual thiamine supplementation is not enough to substitute losses; hence, to optimize carbohydrate metabolism in critically ill patients who require CRRT, additional thiamine is needed. Current recommendations suggest a daily dose of 100 mg for patients treated by CRRT.

**Thiamine in Obese Patients and Bariatric Surgery**

Surgery for obesity is being performed with increasing frequency, not only for weight loss, but also as a treatment option for obese diabetic patients. Clinical and laboratory manifestations of diabetes are resolved or improved and maintained for more than 2 years. Many obese patients have deficiencies of micronutrients, including thiamine, even prior to surgery. Thiamine deficiency after bariatric surgery is actually substantially higher than previously recognized. This may occur as early as 4 weeks after surgery, and a new term has been coined: *bariatric beriberi*. Cerebral dysfunction due to thiamine deficiency after gastric restrictive and/or malabsorptive weight loss surgery occurs in 73.8% of cases.

Micronutrient deficiencies in general after bariatric surgery are more common after bypass procedures (eg, biliary-pancreatic diversion and Roux-en-Y gastrointestinal bypass) than restrictive procedures (eg, gastric banding and sleeve gastrectomy). This is true for thiamine deficiency too; thiamine levels decrease more rapidly after bypass procedures than restrictive procedures.

**Thiamine Deficiency in Parenteral Nutrition**

Inadvertent nonadministration of thiamine during parenteral nutrition is a serious and preventable situation. Several case reports are available to emphasize that this is not an uncommon occurrence, even with so many decades of experience in parenteral nutrition. The importance of a nutrition support team in the delivery of safe parenteral nutrition is emphasized. The multivitamin admixture used must contain adequate amounts of thiamine.

**Thiamine Deficiency in Trauma**

Little exists in the literature regarding the effects of thiamine deficiency with respect to major trauma specifically. In 1988, McConachie and Haskew looked at 5 previously healthy patients who sustained significant trauma with Injury Severity Score ≥ 12 requiring admission to the ICU. Each patient had daily measurements of erythrocyte transketolase activity performed as marker for thiamine status. In each patient, there was a statistically significant biochemical deficiency noted but no obvious clinical sequelae or attributable acidosis; wound healing was not specifically commented on. All patients made a full recovery from their illness. There is some suggestion that thiamine administration may play a role in recovery from trauma. A prospective, randomized, double-blinded, placebo-controlled trial conducted by Berger et al included 102 patients who were given supplemental selenium, zinc, vitamin C, and thiamine, with double doses of the supplements on days 1 and 2. Although there was no difference in early organ dysfunction as measured by the acute kidney injury score, there was a significant decrease in the inflammatory response noted in both trauma and cardiac surgery patients. Also, in contrast to the other studied groups, length of stay was noted to be shorter in the surviving trauma patients who received supplementation compared with controls. Supplemented trauma patients also appeared to have better perceived health status based on SF-36 health survey data collected at 3-month follow-up. This study did not separate out the effects of each supplement; thiamine, although not an antioxidant per se, was believed to be an important part of the supplement package due to its role as the coenzyme of all carbohydrate decarboxylation reactions. However, an earlier study done with supplementing only vitamin C, vitamin E, and selenium showed similar results with similar limitations. It remains unclear how important a role thiamine itself plays in recovery from major trauma; however, its
requirement for transketolase activity in the pentose phosphate pathway suggests that it likely has at least an indirect influence on oxidative stress.

Thiamine, along with riboflavin and pyridoxine, contribute to wound healing by functioning in antibody and leukocyte cell formation and collagen synthesis. Alvarez and Gilbreath demonstrated differences in lysyl oxidase activity and wound breaking strength between rats fed a normal versus thiamine-deficient diet in unwounded and wounded tissue. Thus, maintaining thiamine levels is important for patients with traumatic and other surgical wounds.

**Thiamine in Alcohol Withdrawal States**

Thiamine replacement has long been a mainstay of therapy for patients with suspected alcohol-related disease and for those who are at risk for or are undergoing alcohol withdrawal. Although a causal role of thiamine deficiency in delirium treamens has largely been excluded, a number of neuropsychiatric conditions common in alcoholic patients are directly attributable to thiamine deficiency, including Wernicke-Korsakoff syndrome and peripheral neuropathy. Torvik et al looked at postmortem findings in more than 500 alcoholic patients and found that 12.5% had WE and 3.9% died as a direct result of complications of the same.

As noted, daily administration of thiamine is standard in the care of patients with alcohol withdrawal syndrome; the purpose of this is not to address the autonomic hyperactivity often seen with the syndrome but rather to avoid the above-mentioned complications of thiamine deficiency. The standard replacement dose is 50–100 mg, but there can be significant variations in the amount required to treat active WE. This may be due to the existence of different forms of the apoenzyme of transketolase in different patients. As implied elsewhere in this review, the problem may become even more complex if critical illness, infection, and/or the need for renal replacement therapy is superimposed on the situation of a patient with alcohol-related comorbidity. In such cases, the standard replacement doses of thiamine may be inadequate to counter the deficits. Other metabolic concerns may manifest as well. In a study that looked at glucose regulation in infected rats, the authors found that thiamine-deficient animals exposed to endotoxin not only had decreased dietary intake but also had increased hyperlacticacidemia and a decrease in the expected rise of serum glucose expected with infection. Although they could not say why with certainty, they suspected that this might be due to the inability of pyruvate and lactate to enter gluconeogenesis. This impaired glucose response may have implications for chronically malnourished alcoholic patients who develop gram-negative sepsis.

A recent review by Zahr et al discusses in detail the clinical and alcohol-related damage to the brain.

**Dosage**

Table 2 summarizes our dosage recommendations based on several sources and clinical experience. There are wide variations in the dosages suggested; however, thiamine is safe to administer. The recommended daily allowance for thiamine is only 1.1–1.2 mg. This, however, is for oral or enteral administration. Parenteral multivitamin products usually contain 3.0–3.5 mg. Enteral formulas contain 2.2–2.9 mg per 1500 kcal/d of feed. The European Community directive for enteral nutrition suggests a thiamine minimum daily dose of 1.2 mg and a maximum dose of 10 mg. The exact requirement of thiamine in critical illness is not known, a fact that is true for most micronutrients. However, it is generally believed that thiamine requirements increase in critical illness.

In the prevention or treatment of WE, thiamine hydrochloride is formally indicated and supported by guidelines. Current guidelines suggest that thiamine is indicated for the treatment of suspected or manifest WE (level C). However, there is no evidence to recommend the best dosage, route of administration, and treatment time. Although it has been the practice to administer thiamine parenterally in dosages of 100 mg 3 times a day, more recent guidelines recommend that thiamine should be given intravenously 200 mg 3 times daily (level C). In all cases of WE, thiamine should be given before feeding, and standard diet should be started only after thiamine supplementation. After clinical improvement, the oral route is used with varying dosage recommendations, usually 50–100 mg per day.

The safety of thiamine is very good, regardless of route of administration (level B). In a retrospective analysis on adverse events due to thiamine supplementation, Wren et al have not identified serious side effects in more than 300,000

**Table 2. Thiamine Dosage Recommendations**

<table>
<thead>
<tr>
<th>Description</th>
<th>Dosage Recommendations</th>
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<tbody>
<tr>
<td>Recommended daily allowance</td>
<td>1.1–1.2 mg</td>
</tr>
<tr>
<td>Usual parenteral multivitamin additive</td>
<td>3.0–3.5 mg</td>
</tr>
<tr>
<td>Usual enteral formula content</td>
<td>2.2–2.9 mg per 1500 kcal/d of feed</td>
</tr>
<tr>
<td>Suggested range for enteral nutrition therapy</td>
<td>1.2–10 mg/d</td>
</tr>
<tr>
<td>At risk for deficiency</td>
<td>100 mg, 3 times a day, parenteral</td>
</tr>
<tr>
<td>High suspicion or proven deficiency</td>
<td>200 mg, 3 times a day, parenteral</td>
</tr>
<tr>
<td>Maintenance dose in proven deficiency</td>
<td>50–100 mg by mouth daily</td>
</tr>
<tr>
<td>Refeeding syndrome</td>
<td>300 mg intravenously before initiating nutrition therapy, 200–300 mg intravenously daily for at least 3 more days</td>
</tr>
<tr>
<td>Renal replacement therapy</td>
<td>100 mg daily</td>
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treatments. Anaphylactoid reactions may occur with doses > 400 mg given parenterally. Other symptoms and signs of overdosage include nausea, lethargy, ataxia, and diminution of gut tone.

**Conclusions**

We have highlighted the various clinical scenarios where thiamine deficiency should be suspected. Treatment should be initiated before laboratory confirmation, which is not always needed. Workup for other causes of the various manifestations of thiamine deficiency can be avoided in most cases. Early suspicion, recognition, and treatment are very important as some neurologic manifestations may become permanent. Wherever possible, such as in postbariatric surgery patients, preventive measures must be taken. Clinicians are encouraged to not only evaluate the macronutrient requirement of patients but also be aware of the crucial role that micronutrients play in enteral and parenteral nutritional therapy.

Based on clinical experience and practice, we recommend that thiamine be administered under the following circumstances:

- **Mucocutaneous changes suggestive of thiamine or other vitamin deficiencies**
- **History of excessive alcohol intake**
- **At risk of refeeding syndrome ( cachexia, malignancies, chronic malnutrition)**
- **Sensorium changes or delirium, especially in ICUs**
- **Unexplained CHF**
- **Unexplained metabolic acidosis**
- **Renal replacement therapy**

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**References**


