

Fact Sheet for Health Professionals

Introduction

Thiamin (or thiamine) is one of the water-soluble B vitamins. It is also known as vitamin B1. Thiamin is naturally present in some foods, added to some food products, and available as a dietary supplement. This vitamin plays a critical role in energy metabolism and, therefore, in the growth, development, and function of cells [1].

Ingested thiamin from food and dietary supplements is absorbed by the small intestine through active transport at nutritional doses and by passive diffusion at pharmacologic doses [1]. Most dietary thiamin is in phosphorylated forms, and intestinal phosphatases hydrolyze them to free thiamin before the vitamin is absorbed [1]. The remaining dietary thiamin is in free (absorbable) form [1,2]. Humans store thiamin primarily in the liver but in very small amounts [3]. The vitamin has a short half-life, so people require a continuous supply of it from the diet.

About 80% of the approximately 25–30 mg of thiamin in the adult human body is in the form of thiamin diphosphate (TDP; also known as thiamin pyrophosphate), the main metabolically active form of thiamin. Bacteria in the large intestine also synthesize free thiamin and TDP, but their contribution, if any, to thiamin nutrition is currently unknown [4]. TDP serves as an essential cofactor for five enzymes involved in glucose, amino acid, and lipid metabolism [1,3].

Levels of thiamin in the blood are not reliable indicators of thiamin status. Thiamin status is often measured indirectly by assaying the activity of the transketolase enzyme, which depends on TDP, in erythrocyte hemolysates in the presence and absence of added TDP [3]. The result, known as the TDP effect, reflects the extent of unsaturation of transketolase with TDP. The result is typically 0%–15% in healthy people, 15%–25% in those with marginal deficiency, and higher than 25% in people with deficiency. Another commonly used measure of thiamin status is urinary thiamin excretion, which provides data on dietary intakes but not tissue stores [5]. For adults, excretion of less than 100 mcg/day thiamin in urine suggests insufficient thiamin intake, and less than 40 mcg/day indicates an extremely low intake [6].

Recommended Intakes

Intake recommendations for thiamin and other nutrients are provided in the Dietary Reference Intakes (DRIs) developed by the Food and Nutrition Board (FNB) at the Institute of Medicine of the National Academies (formerly National Academy of Sciences) [7]. DRI is the general term for a set of reference values used for planning and assessing nutrient intakes of healthy people. These values, which vary by age and sex, include the following:

- Recommended Dietary Allowance (RDA): Average daily level of intake sufficient to meet the nutrient requirements of nearly all (97%-98%) healthy individuals; often used to plan nutritionally adequate diets for individuals
- Adequate Intake (AI): Intake at this level is assumed to ensure nutritional adequacy; established when evidence is insufficient to develop an RDA
- Estimated Average Requirement (EAR): Average daily level of intake estimated to meet the
 requirements of 50% of healthy individuals; usually used to assess the nutrient intakes of groups
 of people and to plan nutritionally adequate diets for them; can also be used to assess the
 nutrient intakes of individuals
- Tolerable Upper Intake Level (UL): Maximum daily intake unlikely to cause adverse health effects

Table 1 lists the current RDAs for thiamin [7]. For infants from birth to 12 months, the FNB established an AI for thiamin that is equivalent to the mean intake of thiamin in healthy, breastfed infants.

Table 1: Recommended Dietary Allowances (RDAs) for Thiamin [7]

Age	Male	Female	Pregnancy	Lactation
Birth to 6 months*	0.2 mg	0.2 mg		
7-12 months*	0.3 mg	0.3 mg		
1-3 years	0.5 mg	0.5 mg		
4-8 years	0.6 mg	0.6 mg		
9-13 years	0.9 mg	0.9 mg		
14-18 years	1.2 mg	1.0 mg	1.4 mg	1.4 mg
19-50 years	1.2 mg	1.1 mg	1.4 mg	1.4 mg
51+ years	1.2 mg	1.1 mg		

*AI

Sources of Thiamin

Food

Food sources of thiamin include whole grains, meat, and fish [2]. Breads, cereals, and infant formulas in the United States and many other countries are fortified with thiamin [2]. The most common sources of thiamin in the U.S. diet are cereals and bread [8]. Pork is another major source of the vitamin. Dairy products and most fruits contain little thiamin [3]. About half of the thiamin in the U.S. diet comes from foods that naturally contain thiamin; the remainder comes from foods to which thiamin has been added [9].

Heating foods containing thiamin can reduce their thiamin content. For example, bread has 20%–30% less thiamin than its raw ingredients, and pasteurization reduces thiamin content (which is very small to begin with) in milk by up to 20% [3]. Because thiamin dissolves in water, a significant amount of the vitamin is lost when cooking water is thrown out [3]. Processing also alters thiamin levels in foods; for

example, unless white rice is enriched with thiamin, it has one-tenth the amount of thiamin in unenriched brown rice [10].

Data on the bioavailability of thiamin from food are very limited [7]. Some studies do show, however, that thiamin absorption increases when intakes are low [1].

Several food sources of thiamin are listed in Table 2.

Table 2: Thiamin Content of Selected Foods [10]

Food	Milligrams (mg) per serving	Percent DV*
Breakfast cereals, fortified with 100% of the DV for thiamin, 1 serving	1.2	100
Egg noodles, enriched, cooked, 1 cup	0.5	42
Pork chop, bone in, broiled, 3 ounces	0.4	33
Trout, cooked, dry heat, 3 ounces	0.4	33
Black beans, boiled, ½ cup	0.4	33
English muffin, plain, enriched, 1	0.3	25
Mussels, blue, cooked, moist heat, 3 ounces	0.3	25
Tuna, bluefin, cooked, dry heat, 3 ounces	0.2	17
Macaroni, whole wheat, cooked, 1 cup	0.2	17
Acorn squash, cubed, baked, ½ cup	0.2	17
Rice, brown, long grain, not enriched, cooked, ½ cup	0.2	17
Rice, white, long grain, enriched, cooked, ½ cup	0.1	8
Bread, whole wheat, 1 slice	0.1	8
Orange juice, prepared from concentrate, 1 cup	0.1	8
Sunflower seeds, toasted, 1 ounce	0.1	8
Beef steak, bottom round, trimmed of fat, braised, 3 ounces	0.1	8
Yogurt, plain, low fat, 1 cup	0.1	8
Oatmeal, regular and quick, unenriched, cooked with water, ½ cup	0.1	8
Corn, yellow, boiled, 1 medium ear	0.1	8
Milk, 2%, 1 cup	0.1	8
Barley, pearled, cooked, 1 cup	0.1	8
Cheddar cheese, 1½ ounces	0	0
Chicken, meat and skin, roasted, 3 ounces	0	0
Apple, sliced, 1 cup	0	0

*DV = Daily Value. The U.S. Food and Drug Administration (FDA) developed DVs to help consumers compare the nutrient contents of foods and dietary supplements within the context of a total diet. The DV for thiamin is 1.2 mg for adults and children age 4 years and older [11]. FDA does not require food labels to list thiamin content unless thiamin has been added to the food. Foods providing 20% or more

of the DV are considered to be high sources of a nutrient, but foods providing lower percentages of the DV also contribute to a healthful diet.

The U.S. Department of Agriculture's (USDA's) <u>FoodData Central (https://fdc.nal.usda.gov/)</u> website [10] lists the nutrient content of many foods and provides a comprehensive list of foods containing thiamin arranged by <u>nutrient content</u> and by <u>food name</u>.

Dietary supplements

Thiamin is available in many dietary supplements. Multivitamin/mineral supplements with thiamin typically provide about 1.5 mg thiamin and sometimes more [12]. Supplements containing B-complex vitamins (including thiamin) or thiamin only are also available. The most commonly used forms of thiamin in supplements are thiamin mononitrate and thiamin hydrochloride, which are stable and water soluble [1,12].

Benfotiamine is a synthetic thiamin derivative that is used in some dietary supplements. Benfotiamine is not water soluble and is converted to thiamin in the body [13].

Thiamin Intakes and Status

Most people in the United States consume the recommended amounts of thiamin. An analysis of data from the 2003–2006 National Health and Nutrition Examination Survey showed that only 6% of the U.S. population has a usual intake below the EAR [9].

Among children and teens, the average daily thiamin intake from foods is 1.27 mg for ages 2–5 years, 1.54 mg for ages 6–11 years, and 1.68 mg for ages 12–19 years [14]. In adults age 20 and older, the average daily thiamin intake from foods is 1.95 mg in men and 1.39 mg in women. The average daily thiamin intake from foods and supplements in children and teens is 1.51 mg for ages 2–5 years, 1.76 mg for ages 6–11 years, and 1.95 mg for ages 12–19 years. In adults age 20 and older, the average daily thiamin intake from foods and supplements is 4.89 mg in men and 4.90 mg in women.

No current data on rates of thiamin deficiency in the U.S. population are available.

Thiamin Deficiency

In addition to insufficient intakes of thiamin from the diet, the causes of thiamin deficiency include lower absorption or higher excretion rates than normal due, for example, to certain conditions (such as alcohol dependence or HIV/AIDS) or use of some medications [3].

In its early stage, thiamin deficiency can cause weight loss and anorexia, confusion, short-term memory loss, and other mental signs and symptoms; muscle weakness; and cardiovascular symptoms (such as an enlarged heart) [7].

The most common effect of thiamin deficiency is beriberi, which is characterized mainly by peripheral neuropathy and wasting [1-3]. People with this condition have impaired sensory, motor, and reflex functions. In rare cases, beriberi causes congestive heart failure that leads to edema in the lower limbs

and, occasionally, death [1,3]. Although beriberi is rare in the United States and other developed countries, people in these countries do occasionally develop the condition [15-18]. Administration of supplemental thiamin, often parenterally, quickly cures beriberi [2,3].

A more common manifestation of thiamin deficiency in the United States is Wernicke-Korsakoff syndrome [2]. This disorder is about 8–10 times more common in people with chronic alcoholism than in the general population, but it can also develop in patients who have severe gastrointestinal disorders, rapidly progressing hematologic malignancies, drug use disorders, or AIDS [2]. In many patients, Wernicke-Korsakoff syndrome has two phases. The first, acute, and life-threatening stage, Wernicke's encephalopathy, is usually characterized by peripheral neuropathy [3,19]. Without treatment, up to 20% of people with Wernicke's encephalopathy die; those who survive develop Korsakoff's psychosis, although some people with Korsakoff's psychosis have not previously had Wernicke's encephalopathy [20,21]. Korsakoff's psychosis, an effect of chronic thiamin deficiency, is associated with severe short-term memory loss, disorientation, and confabulation (confusion between real and imagined memories) [1-3]. At this chronic state of the disorder, parenteral thiamin treatment does not lead to recovery in about one-quarter of patients [22].

The World Health Organization recommends daily oral doses of 10 mg thiamin for a week, followed by 3–5 mg/daily for at least 6 weeks, to treat mild thiamin deficiency [23]. The recommended treatment for severe deficiency consists of 25–30 mg intravenously in infants and 50–100 mg in adults, then 10 mg daily administered intramuscularly for approximately 1 week, followed by 3–5 mg/day oral thiamin for at least 6 weeks.

Groups at Risk of Thiamin Inadequacy

The following groups are among those most likely to have inadequate thiamin status.

People with alcohol dependence

In highly industrialized countries, chronic alcohol use disorders appear to be the most common cause of thiamin deficiency [1]. Up to 80% of people with chronic alcoholism develop thiamin deficiency because ethanol reduces gastrointestinal absorption of thiamin, thiamin stores in the liver, and thiamin phosphorylation [3,19]. Also, people with alcoholism tend to have inadequate intakes of essential nutrients, including thiamin.

Older adults

Up to 20%–30% of older adults have laboratory indicators that suggest some degree of thiamin deficiency [2,7]. Possible reasons include low dietary intakes, a combination of chronic diseases, concomitant use of multiple medications, and low absorption of thiamin as a natural result of aging [24,25]. Some small studies have found that the risk of deficiency is particularly high in elderly people who reside in an institution [26,27].

People with HIV/AIDS

People with HIV infection have an increased risk of thiamin deficiency and its sequelae, including beriberi and Wernicke-Korsakoff syndrome [1,28]. Autopsies of 380 people with AIDS found that almost 10% had Wernicke's encephalopathy [29], and some experts believe that thiamin deficiency is underdiagnosed in this population [30]. The association between thiamin deficiency and HIV/AIDS is probably due to malnutrition as a result of the catabolic state associated with AIDS.

People with diabetes

Some small studies have found that thiamin levels in plasma are up to 76% lower in people with type 1 diabetes than in healthy volunteers and 50%–75% lower in people with type 2 diabetes [31,32]. Other studies have shown a higher risk of thiamin deficiency in people with type 1 and/or type 2 diabetes based on tests of erythrocyte transketolase activity [33,34]. These lower thiamin levels might be due to increases in clearance of thiamin by the kidneys. The relevance of these effects to clinical prognosis or outcomes is not known.

People who have undergone bariatric surgery

Bariatric surgery for weight loss is associated with some risks, including severe thiamin deficiency due to malabsorption that can lead to beriberi or Wernicke's encephalopathy. A 2008 literature review identified 84 cases of Wernicke's encephalopathy after bariatric surgery (primarily gastric bypass surgery) between 1991 and 2008 [35]. About half of these patients experienced long-lasting neurologic impairments. Micronutrient supplements that include thiamin are almost always recommended for patients following bariatric surgery to avoid deficiencies [36].

Thiamin and Health

This section focuses on four diseases or disorders in which thiamin does or might play a role: Wernicke-Korsakoff syndrome, diabetes, heart failure, and Alzheimer's disease.

Wernicke-Korsakoff syndrome

Wernicke-Korsakoff syndrome is one of the most severe neuropsychiatric sequelae of alcohol abuse [37]. The authors of a 2013 Cochrane Review of thiamin to treat or prevent Wernicke-Korsakoff syndrome found only two studies that met their inclusion criteria, and one of these studies has not been published [37]. These randomized, double-blind, placebo-controlled trials compared 5 mg/day by mouth for 2 weeks or daily intramuscular doses of 5 to 200 mg/day thiamin over 2 consecutive days in a total of 177 people with a history of chronic alcohol use. The Cochrane Review authors concluded that the evidence from randomized clinical trials is insufficient to guide health care providers in selecting the appropriate dose, frequency, duration, or route of thiamin supplementation to treat or prevent Wernicke-Korsakoff syndrome in patients with alcohol abuse.

The authors of the European Federation of Neurological Societies guidelines for diagnosing, preventing, and treating Wernicke's encephalopathy note that even high doses of oral thiamin supplements might not be effective in raising blood thiamin levels or curing Wernicke's encephalopathy [38]. They recommend 200 mg thiamin, preferably intravenously, three times daily (total of 600 mg/day) until the signs and symptoms stop, along with a balanced diet. In its guidelines for managing

Wernicke's encephalopathy in emergency departments, the Royal College of Physicians in London supports the administration of oral thiamin hydrochloride (100 mg three times a day) in patients with adequate dietary intakes of thiamin and no signs or symptoms of Wernicke's encephalopathy [39]. However, the authors recommend parenteral thiamin supplementation for patients at high risk, such as those with ataxia, confusion, and a history of chronic alcohol misuse, because oral supplementation is unlikely to produce adequate blood levels.

Diabetes

The proportion of people with type 1 or type 2 diabetes who have poor thiamin status based on erythrocyte transketolase activity ranges from 17% to 79% in studies conducted to date [40]. In a study of 76 consecutive patients with type 1 or type 2 diabetes, for example, 8% had mild thiamin deficiency and 32% had moderate deficiency based on assays of the transketolase enzyme [33].

Some small studies have shown that oral supplementation with 150–300 mg/day thiamin can decrease glucose levels in patients with type 2 diabetes or impaired glucose tolerance [41,42]. However, the authors of these studies did not assess the potential clinical significance of these findings.

A few small randomized studies have assessed the effects of benfotiamine supplements on diabetic neuropathy. Three studies found that, compared to placebo, 120–900 mg/day benfotiamine with or without other B-vitamins decreased the severity of neuropathy symptoms and lowered urinary albumin excretion (a marker of early-stage diabetic nephropathy) [43-45]. However, another study found no effect of 900 mg/day benfotiamine on urinary excretion of albumin or kidney injury molecule-1, a marker of kidney injury [46].

Well-designed studies with larger sample sizes and longer durations are required to determine whether thiamin supplements can reduce glucose levels in patients with diabetes or decrease diabetic compications.

Heart failure

The rates of poor thiamin status in patients with heart failure have ranged in studies from 21% to 98% [47]. Explanations for this association include older age, comorbidities, insufficient dietary intake, treatment with diuretics, and frequent hospitalizations [48].

The authors of one study reported that 33% of 100 patients with chronic heart failure had thiamin deficiency compared to 12% of 50 healthy volunteers [49]. Rates of deficiency were even higher when the investigators excluded those who used thiamin supplements. The different rates of thiamin deficiency in patients with heart failure in these and other studies are probably due to differences in nutrition status, comorbidities, medications and dietary supplements used, and techniques used to measure thiamin status [48].

The authors of a systematic literature review and meta-analysis found two randomized, double-blind, placebo-controlled trials of thiamin supplementation in people with heart failure that met their eligibility

criteria [50]. In these trials, thiamin supplements significantly improved net change in left ventricular ejection fraction. The authors did not assess the clinical significance of this finding, however.

More research is needed to determine whether thiamin supplements might benefit people with heart failure, even if they have normal thiamin status.

Alzheimer's disease

According to animal model studies, thiamin deficiency might play a role in the development of Alzheimer's disease [51]. For example, thiamin deficiency produces oxidative stress in neurons, death of neurons, loss of memory, plaque formation, and changes in glucose metabolism—all markers of Alzheimer's disease. Autopsy studies have shown that transketolase and other thiamin-dependent enzymes have decreased activity in the brains of people with Alzheimer's disease [52,53].

Few studies have assessed the prevalence of thiamin deficiency in people with Alzheimer's disease. One of these studies found that 13% of 150 patients with cognitive impairment and acute-onset behavioral disturbances were considered thiamin deficient based on plasma levels [26].

The authors of a 2001 Cochrane Review assessed three double-blind, randomized trials (including two crossover trials) that compared the effects of 3 g/day oral thiamin to placebo on cognitive function in patients with Alzheimer's type dementia [54]. The three studies randomly assigned fewer than 20 patients each, and the two crossover studies did not include a washout period [55-57]. The review authors stated that it was not possible to draw any conclusions from these three studies because they were small and the publications describing them did not provide enough detail to combine these data in a meta-analysis.

Larger, well-designed studies are needed to determine whether thiamin supplements are beneficial for Alzheimer's disease.

Health Risks from Excessive Thiamin

The body excretes excess amounts of thiamin in the urine [2]. Because of the lack of reports of adverse effects from high thiamin intakes (50 mg/day or more) from food or supplements, the FNB did not establish ULs for thiamin [7]. They hypothesize that the apparent lack of toxicity may be explained by the rapid decline in absorption of thiamin at intakes above 5 mg. However, the FNB noted that in spite of the lack of reported adverse events, excessive intakes of thiamin could have adverse effects.

Interactions with Medications

Although thiamin is not known to interact with any medications, certain medications can have an adverse effect on thiamin levels. Some examples are provided below. Individuals taking these and other medications on a regular basis should discuss their thiamin status with their health care providers.

Furosemide

Furosemide (Lasix) is a loop diuretic used to treat edema and hypertension by increasing urinary output. Research has linked the use of furosemide to decreases in thiamin concentrations, possibly to deficient levels, as a result of urinary thiamin loss [49,58,59]. Whether thiamin supplements are effective for preventing thiamin deficiency in patients taking loop diuretics needs to be determined in clinical studies.

Chemotherapy with fluorouracil

Fluorouracil (also known as 5-fluorouracil; Adrucil) is a chemotherapy drug that is commonly used to treat colorectal and other solid cancers. The published literature includes several cases of beriberi or Wernicke's encephalopathy resulting from treatment with this drug, possibly because the drug might increase thiamin metabolism and block the formation of TDP, the active form of thiamin [60-63]. Thiamin supplements might reverse some of these effects.

Thiamin and Healthful Diets

The federal government's 2020–2025 *Dietary Guidelines for Americans* notes that "Because foods provide an array of nutrients and other components that have benefits for health, nutritional needs should be met primarily through foods. ... In some cases, fortified foods and dietary supplements are useful when it is not possible otherwise to meet needs for one or more nutrients (e.g., during specific life stages such as pregnancy)."

For more information about building a healthy dietary pattern, refer to the <u>Dietary Guidelines for</u>

<u>Americans (https://www.dietaryguidelines.gov)</u> and the USDA's <u>MyPlate. (https://www.choosemyplate.gov/)</u>

The Dietary Guidelines for Americans describes a healthy dietary pattern as one that

- Includes a variety of vegetables; fruits; grains (at least half whole grains); fat-free and low-fat milk, yogurt, and cheese; and oils.
 - Many whole grains are good sources of thiamin, and yogurt contains thiamin.
- Includes a variety of protein foods such as lean meats; poultry; eggs; seafood; beans, peas, and lentils; nuts and seeds; and soy products.
 - Pork, fish, and seafood are good or high sources of thiamin. Beef, beans, and seeds contain thiamin.
- Limits foods and beverages higher in added sugars, saturated fat, and sodium.
- Limits alcoholic beverages.
- Stays within your daily calorie needs.

References

- 1. Said HM. Thiamin. In: Coates PM, Betz JM, Blackman MR, et al., eds. Encyclopedia of Dietary Supplements. 2nd ed. London and New York: Informa Healthcare; 2010:748-53.
- 2. Bettendorff L. Thiamin. In: Erdman JW, Macdonald IA, Zeisel SH, eds. Present Knowledge in Nutrition. 10th ed. Washington, DC: Wiley-Blackwell; 2012:261-79.

- 3. Bemeur C, Butterworth RF. Thiamin. In: Ross AC, Caballero B, Cousins RJ, Tucker KL, Ziegler TR, eds. Modern Nutrition in Health and Disease. 11th ed. Baltimore, MD: Lippincott Williams & Wilkins; 2014:317-24.
- 4. Nabokina SM, Said HM. A high-affinity and specific carrier-mediated mechanism for uptake of thiamine pyrophosphate by human colonic epithelial cells. Am J Physiol Gastrointest Liver Physiol 2012;303:G389-95. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/22628036/)]
- 5. Allen L, de Benoist B, Dary O, Hurrell R, eds. <u>Guidelines on Food Fortification with Micronutrients</u> (http://www.who.int/nutrition/publications/micronutrients/9241594012/en/). Geneva: World Health Organization and Food and Agricultural Organization of the United Nations; 2006.
- 6. Gibson GE, Blass JP. Thiamine-dependent processes and treatment strategies in neurodegeneration. Antioxid Redox Signal 2007;9:1605-19. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/17685850/)]
- 7. Institute of Medicine. Food and Nutrition Board. Dietary Reference Intakes: Thiamin, Riboflavin, Niacin, Vitamin B6, Folate, Vitamin B12, Pantothenic Acid, Biotin, and Choline. Washington, DC: National Academy Press; 1998.
- 8. Sharma S, Sheehy T, Kolonel LN. Ethnic differences in grains consumption and their contribution to intake of B-vitamins: results of the Multiethnic Cohort Study. Nutr J 2013;12:65. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/23688109/)]
- 9. Fulgoni VL, 3rd, Keast DR, Bailey RL, Dwyer J. Foods, fortificants, and supplements: Where do Americans get their nutrients? J Nutr 2011;141:1847-54. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/21865568/)]
- 10. U.S. Department of Agriculture, Agricultural Research Service. <u>FoodData Central</u> (https://fdc.nal.usda.gov/), 2019.
- 11. U.S. Food and Drug Administration. <u>Food Labeling: Revision of the Nutrition and Supplement Facts Labels.</u> (https://www.federalregister.gov/documents/2016/05/27/2016-11867/food-labeling-revision-of-the-nutrition-and-supplement-facts-labels) 2016.
- 12. National Institutes of Health. <u>Dietary Supplement Label Database (https://dsld.od.nih.gov)</u>. 2014.
- 13. Aguilar F, Charrondiere UR, Dusemund B, Galtier P, Gilbert J, Gott DM, et al. Benfotiamine, thiamine monophosphate chloride and thiamine pyrophosphate chloride, as sources of vitamin B1 added for nutritional purposes to food supplements: Scientific Opinion of the Panel on Food Additives and Nutrient Sources added to Food (ANS). EFSA J 2008;864:1-31.
- 14. U.S. Department of Agriculture, Agricultural Research Service. <u>What We Eat in America, 2009-2010 (http://www.ars.usda.gov/Services/docs.htm?docid=18349)</u>. 2012.
- 15. Yang JD, Acharya K, Evans M, Marsh JD, Beland S. Beriberi disease: is it still present in the United States? Am J Med 2012;125:e5. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/22800868/)]
- 16. Howard AJ, Kulkarni O, Lekwuwa G, Emsley HC. Rapidly progressive polyneuropathy due to dry beriberi in a man: a case report. J Med Case Rep 2010;4:409. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/21176139/)]
- 17. Essa E, Velez MR, Smith S, Giri S, Raman SV, Gumina RJ. Cardiovascular magnetic resonance in wet beriberi. J Cardiovasc Magn Reson 2011;13:41. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/21838901/)]

- 18. Imai N, Kubota M, Saitou M, Yagi N, Serizawa M, Kobari M. Increase of serum vascular endothelial growth factors in wet beriberi: two case reports. Intern Med 2012;51:929-32. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/22504253/)]
- 19. Agabio R. Thiamine administration in alcohol-dependent patients. Alcohol Alcohol 2005;40:155-6. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/15550446/)]
- 20. Thomson AD, Marshall EJ. The natural history and pathophysiology of Wernicke's Encephalopathy and Korsakoff's Psychosis. Alcohol Alcohol 2006;41:151-8. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/16384871/)]
- 21. Thomson AD, Guerrini I, Marshall EJ. The evolution and treatment of Korsakoff's syndrome: out of sight, out of mind? Neuropsychol Rev 2012;22:81-92.

 [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/22569770/)]
- 22. Kopelman MD, Thomson AD, Guerrini I, Marshall EJ. The Korsakoff syndrome: clinical aspects, psychology and treatment. Alcohol Alcohol 2009;44:148-54. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/19151162/)]
- 23. World Health Organization. <u>Thiamine Deficiency and Its Prevention and Control in Major Emergencies (http://www.who.int/nutrition/publications/en/thiamine_in_emergencies_eng.pdf)</u>. Geneva; 1999.
- 24. Vognar L, Stoukides J. The role of low plasma thiamin levels in cognitively impaired elderly patients presenting with acute behavioral disturbances. J Am Geriatr Soc 2009;57:2166-8. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/20121971/)]
- 25. Wilkinson TJ, Hanger HC, George PM, Sainsbury R. Is thiamine deficiency in elderly people related to age or co-morbidity? Age and Ageing 2000;29:111-6. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/10791444/)]
- 26. O'Rourke NP, Bunker VW, Thomas AJ, Finglas PM, Bailey AL, Clayton BE. Thiamine Status of Healthy and Institutionalized Elderly Subjects: Analysis of Dietary Intake and Biochemical Indices. Age Ageing 1990;19:325-9. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/2251966/)]
- 27. Ito Y, Yamanaka K, Susaki H, Igata A. A cross-investigation between thiamin deficiency and the physical condition of elderly people who require nursing care. J Nutr Sci Vitaminol (Tokyo) 2012;58:210-6.
 - [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/22878392/)]
- 28. Lu'o'ng KV, Nguyen LT. The role of thiamine in cancer: possible genetic and cellular signaling mechanisms. Cancer Genomics Proteomics 2013;10:169-85.

 [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/23893925/)]
- 29. Boldorini R, Vago L, Lechi A, Tedeschi F, Trabattoni GR. Wernicke's encephalopathy: occurrence and pathological aspects in a series of 400 AIDS patients. Acta Biomed Ateneo Parmense 1992;63:43-9. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/1340667/)]
- 30. Larsen TR, Dragu D, Williams M. Wernicke's Encephalopathy: An Unusual Consequence of the Acquired Immune Deficiency Syndrome-Case Report and Literature Review. Case Rep Med 2013;2013:709474. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/23935638/)]
- 31. Thornalley PJ, Babaei-Jadidi R, Al Ali H, Rabbani N, Antonysunil A, Larkin J, et al. High prevalence of low plasma thiamine concentration in diabetes linked to a marker of vascular disease.

 Diabetologia 2007;50:2164-70. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/17676306/)]

- 32. Al-Attas OS, Al-Daghri NM, Alfadda AA, Abd-Alrahman SH, Sabico S. Blood thiamine and its phosphate esters as measured by high-performance liquid chromatography: levels and associations in diabetes mellitus patients with varying degrees of microalbuminuria. J Endocrinol Invest 2012;35:951-6. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/22107884/)]
- 33. Jermendy G. Evaluating thiamine deficiency in patients with diabetes. Diab Vasc Dis Res 2006;3:120-1. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/17058632/)]
- 34. Saito N, Kimura M, Kuchiba A, Itokawa Y. Blood thiamine levels in outpatients with diabetes mellitus. J Nutr Sci Vitaminol (Tokyo) 1987;33:421-30. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/3451944/)]
- 35. Aasheim ET. Wernicke encephalopathy after bariatric surgery: a systematic review. Ann Surg 2008;248:714-20. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/18948797/)]
- 36. Xanthakos SA. Nutritional deficiencies in obesity and after bariatric surgery. Pediatr Clin North Am 2009;56:1105-21. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/19931066/)]
- 37. Day E, Bentham PW, Callaghan R, Kuruvilla T, George S. Thiamine for prevention and treatment of Wernicke-Korsakoff Syndrome in people who abuse alcohol. Cochrane Database Syst Rev 2013;7:CD004033. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/23818100/)]
- 38. Galvin R, Brathen G, Ivashynka A, Hillbom M, Tanasescu R, Leone MA. EFNS guidelines for diagnosis, therapy and prevention of Wernicke encephalopathy. Eur J Neurol 2010;17:1408-18. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/20642790/)]
- 39. Thomson AD, Cook CC, Touquet R, Henry JA. The Royal College of Physicians report on alcohol: guidelines for managing Wernicke's encephalopathy in the accident and Emergency Department. Alcohol Alcohol 2002;37:513-21. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/12414541/)]
- 40. Page GL, Laight D, Cummings MH. Thiamine deficiency in diabetes mellitus and the impact of thiamine replacement on glucose metabolism and vascular disease. Int J Clin Pract 2011;65:684-90.
 - [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/21564442/)]
- 41. Gonzalez-Ortiz M, Martinez-Abundis E, Robles-Cervantes JA, Ramirez-Ramirez V, Ramos-Zavala MG. Effect of thiamine administration on metabolic profile, cytokines and inflammatory markers in drug-naive patients with type 2 diabetes. Eur J Nutr 2011;50:145-9. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/20652275/)]
- 42. Alaei Shahmiri F, Soares MJ, Zhao Y, Sherriff J. High-dose thiamine supplementation improves glucose tolerance in hyperglycemic individuals: a randomized, double-blind cross-over trial. Eur J Nutr 2013;52:1821-4. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/23715873/)]
- 43. Stracke H, Gaus W, Achenbach U, Federlin K, Bretzel RG. Benfotiamine in diabetic polyneuropathy (BENDIP): results of a randomised, double blind, placebo-controlled clinical study. Exp Clin Endocrinol Diabetes 2008;116:600-5. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/18473286/)]
- 44. Carpenter KJ. The discovery of thiamin. Ann Nutr Metab 2012;61:219-23. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/23183292/)]
- 45. Rabbani N, Alam SS, Riaz S, Larkin JR, Akhtar MW, Shafi T, et al. High-dose thiamine therapy for patients with type 2 diabetes and microalbuminuria: a randomised, double-blind placebo-

- controlled pilot study. Diabetologia 2009;52:208-12. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/19057893/)]
- 46. Alkhalaf A, Klooster A, van Oeveren W, Achenbach U, Kleefstra N, Slingerland RJ, et al. A double-blind, randomized, placebo-controlled clinical trial on benfotiamine treatment in patients with diabetic nephropathy. Diabetes Care 2010;33:1598-601. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/20413516/)]
- 47. Wooley JA. Characteristics of thiamin and its relevance to the management of heart failure. Nutr Clin Pract 2008;23:487-93.
 - [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/18849553/)]
- 48. DiNicolantonio JJ, Niazi AK, Lavie CJ, O'Keefe JH, Ventura HO. Thiamine supplementation for the treatment of heart failure: a review of the literature. Congest Heart Fail 2013;19:214-22. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/23910704/)]
- 49. Hanninen SA, Darling PB, Sole MJ, Barr A, Keith ME. The prevalence of thiamin deficiency in hospitalized patients with congestive heart failure. J Am Coll Cardiol 2006;47:354-61. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/16412860/)]
- 50. DiNicolantonio JJ, Lavie CJ, Niazi AK, O'Keefe JH, Hu T. Effects of thiamine on cardiac function in patients with systolic heart failure: systematic review and metaanalysis of randomized, double-blind, placebo-controlled trials. Ochsner J 2013;13:495-9. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/24357996/)]
- 51. Gibson GE, Hirsch JA, Cirio RT, Jordan BD, Fonzetti P, Elder J. Abnormal thiamine-dependent processes in Alzheimer's Disease. Lessons from diabetes. Mol Cell Neurosci 2013;55:17-25. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/22982063/)]
- 52. Gibson GE, Sheu KF, Blass JP, Baker A, Carlson KC, Harding B, et al. Reduced activities of thiamine-dependent enzymes in the brains and peripheral tissues of patients with Alzheimer's disease. Arch Neurol 1988;45:836-40. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/3395256/)]
- 53. Butterworth RF, Besnard AM. Thiamine-dependent enzyme changes in temporal cortex of patients with Alzheimer's disease. Metab Brain Dis 1990;5:179-84. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/2087217/)]
- 54. Rodriguez-Martin JL, Qizilbash N, Lopez-Arrieta JM. Thiamine for Alzheimer's disease. Cochrane Database Syst Rev 2001:CD001498. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/10796655/)]
- 55. Blass JP, Gleason P, Brush D, DiPonte P, Thaler H. Thiamine and Alzheimer's disease. A pilot study. Arch Neurol 1988;45:833-5. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/2969232/)]
- 56. Nolan KA, Black RS, Sheu KF, Langberg J, Blass JP. A trial of thiamine in Alzheimer's disease. Arch Neurol 1991;48:81-3. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/1986730/)]
- 57. Meador K, Loring D, Nichols M, Zamrini E, Rivner M, Posas H, et al. Preliminary findings of high-dose thiamine in dementia of Alzheimer's type. J Geriatr Psychiatry Neurol 1993;6:222-9. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/8251051/)]
- 58. Seligmann H, Halkin H, Rauchfleisch S, Kaufmann N, Motro M, Vered Z, et al. Thiamine deficiency in patients with congestive heart failure receiving long-term furosemide therapy: a pilot study. Am

- J Med 1991;91:151-5.
- [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/1867241/)]
- 59. Zenuk C, Healey J, Donnelly J, Vaillancourt R, Almalki Y, Smith S. Thiamine deficiency in congestive heart failure patients receiving long term furosemide therapy. Can J Clin Pharmacol 2003;10:184-8. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/14712323/)]
- 60. Cho IJ, Chang HJ, Lee KE, Won HS, Choi MY, Nam EM, et al. A case of Wernicke's encephalopathy following fluorouracil-based chemotherapy. J Korean Med Sci 2009;24:747-50. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/19654964/)]
- 61. Kondo K, Fujiwara M, Murase M, Kodera Y, Akiyama S, Ito K, et al. Severe acute metabolic acidosis and Wernicke's encephalopathy following chemotherapy with 5-fluorouracil and cisplatin: case report and review of the literature. Jpn J Clin Oncol 1996;26:234-6.

 [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/8765181/)]
- 62. Papila B, Yildiz O, Tural D, Delil S, Hasiloglu ZI, Ayan F, et al. Wernicke's Encephalopathy in Colon Cancer. Case Rep Oncol 2010;3:362-7.

 [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/21537379/)]
- 63. Rosen A, van Kuilenburg A, Assmann B, Kuhlen M, Borkhardt A. Severe encephalopathy, lactic acidosis, vegetative instability and neuropathy with 5-Fluorouracil treatment pyrimidine degradation defect or beriberi? Case Rep Oncol 2011;4:371-6. [PubMed abstract (https://pubmed.ncbi.nlm.nih.gov/21941485/)]
- 64. U.S. Department of Agriculture, US DHHS. <u>Dietary Guidelines for Americans, 2010</u>
 (http://www.cnpp.usda.gov/sites/default/files/dietary_guidelines_for_americans/PolicyDoc.pdf).
 Washington, DC: U.S. Government Printing Office; 2010.

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