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SURGERY FOR OBESITY AND RELATED DISEASES

ASMBS Guidelines

ASMBS literature review & clinical guidelines on prevention, diagnosis, and treatment of Wernicke's encephalopathy and Wernicke-Korsakoff syndrome

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Abstract The American Society for Metabolic and Bariatric Surgery (ASMBS) Wernicke's Task Force issues the following guidelines to enhance the quality of care in patients undergoing bariatric surgery and for other populations at risk of thiamine deficiency and Wernicke's encephalopathy (WE). This paper examines the current literature regarding the prevention, diagnosis, and treatment of WE. These guidelines intend to provide an objective summary of current peer-reviewed literature and provide clinical practice recommendations based on this literature and expert opinions. The goal is to enhance awareness and reduce the incidence of WE and the Wernicke-Korsakoff syndrome (WKS). This statement is not intended to establish a local, regional, or national standard of care and may be revised in the future as additional evidence becomes available. (Surg Obes Relat Dis 2025;21:707–718.)

Background

Thiamine is a water-soluble vitamin known as vitamin B1 since it was the first B vitamin discovered. Thiamine deficiency disorders (TDDs) may affect the cardiovascular system, manifesting as high-output congestive heart failure ("wet" beriberi), the peripheral nervous system leading to peripheral neuropathy ("dry" beriberi), the more new gastrointestinal beriberi that includes nausea, vomiting, abdominal pain, loss of appetite and lactic acidosis [1] or cerebral beriberi known as Wernicke's encephalopathy which carries a mortality rate approaching 17% and often leads to the permanent Werknicke-Korsakoff syndrome (WKS) [2].

Wernicke's encephalopathy (WE) is an acute neuropsychiatric syndrome caused by thiamine deficiency. Alarmingly, the diagnosis is often missed, delayed, or undertreated and

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is potentially fatal or permanently disabling if not adequately treated in a timely fashion, underscoring the critical need for more widespread clinical awareness. Since patients undergoing metabolic and bariatric surgery are at high risk of WE, bariatric surgeons and other providers caring for these patients must be vigilant to prevent and diagnose TDDs, including Wernicke's. High-risk patients include those with persistent vomiting or sudden and severe weight loss greater than the typical early postoperative weight loss of approximately eight percent of total body weight loss at 3 weeks after surgery.

Therefore, our society, the ASMBS, organized a Wernicke's Task Force comprised of experts to educate healthcare professionals across all medical specialties on the various aspects of thiamine deficiency and WE, an underdiagnosed medical emergency. Wernicke's is a low-frequency, high-severity preventable disease, and we aim to help educate the medical world on its prevention, diagnosis, and treatment.

This statement has been divided into the following eight sections:

1. Review of the literature regarding thiamine functions and physiology.
2. Recommended daily thiamine intake.
3. Review of the literature on the pathophysiology of thiamine deficiency, Wernicke's encephalopathy, and Wernicke-Korsakoff syndrome.
4. Review of the literature on the clinical presentation and diagnosis of Wernicke's encephalopathy and Wernicke-Korsakoff syndrome.
5. Review of the literature on populations at high risk of thiamine deficiency and Wernicke's encephalopathy.
6. Review of the literature on the prevalence and prevention of Wernicke's encephalopathy and Wernicke-Korsakoff syndrome.
7. Review of the literature on the treatment and prognosis of Wernicke's encephalopathy and Wernicke-Korsakoff syndrome.
8. Summary and recommendations.

Methods

A literature search was performed using Ovid MEDLINE® with the following search terms: "*Wernicke Encephalopathy" or "Wernickes" or "Korsakoff Syndrome" or "Thiamine Deficiency" or "Beriberi" and limited to those including human subjects, adults, and English language, and published in the past 10 years, from 2013-present. Article titles and abstracts were screened for inclusion. Case reports and series were included. Exclusion criteria included studies on children and studies on Wernicke's area, Wernicke's aphasia, or studies on other neurological conditions such as strokes or vascular malformations, or other causes of ataxia or cognitive impairment. Abstracts were evaluated independently by two physicians, and if either felt the article was relevant, it was included in the literature review. Secondary searching was performed using the bibliographies of relevant articles.

After applying the above search filters we identified 165 papers and 270 case reports for a total of 435 Wernicke's publications for review by the members of the ASMBS Wernicke's Task Force. Articles were narratively synthesized for this review. Since there are a paucity of experimental studies such as clinical trials evaluating the treatment of Wernicke's encephalopathy, a systematic review or meta-analysis (such as the PRISMA reporting guidelines) was not feasible. Similarly, assigning levels of evidence or recommendations was not advantageous.

This is a clinical guideline focused on the available evidence and the expert consensus of the ASMBS Wernicke's Task Force on the prevention, diagnosis and treatment of Wernicke's encephalopathy. Similar to the ASMBS guidelines on prevention and streatment of internal hernias, this paper has very high clinical relevance with a focus on prevention, which is usually feasible and effective.

Thiamine functions & physiology

Thiamine is an essential water-soluble vitamin (B1) that must be obtained through diet or supplementation. It plays a vital role in the production of ATP and, therefore, in cell growth and function and myelin sheath maintenance. Humans store only small amounts of thiamine in the liver (30-50 mg), with a short half-life of 9-18 days. Thus, regular dietary intake is necessitated to avoid thiamine depletion, which can occur in as short as 2 weeks. The human body excretes excess thiamine in the urine.

Thiamine from food is hydrolyzed into free thiamine in the lumen of the intestine, which passes through the wall of the proximal small intestine and enters erythrocytes, where it is converted to the biologically active form, thiamine diphosphate (TDP). Blood then carries TDP to the liver, heart, and muscles, and it passes through the blood-brain barrier to enter the cerebrospinal fluid (CSF), where it diffuses into the brain. TDP is a cofactor in metabolizing carbohydrates, branched-chain amino acids, and fatty acids. In addition, TDP plays a role in nerve structure, function, and brain metabolism. Magnesium is an essential cofactor for TDP metabolism, and magnesium deficiency can impair thiamine utilization and exacerbate the clinical effects of thiamine deficiency. Therefore, both thiamine and magnesium should be repleted contemporaneously. Due to the role of TDP in the Krebs cycle, one possibe sign of thiamine deficiency is lactic acidosis.

Recommended daily thiamine intake

According to the National Institutes of Health Office of Dietary Supplements, thiamine's recommended daily

allowance (RDA) is 1.2 mg/d for men, 1.1 mg/d for women, and 1.4 mg/d for those pregnant or breastfeeding. The recommended thiamine dosage for patients after metabolic and bariatric surgery (MBS) is above the RDA at a minimum of 12 mg per day and preferably 50 mg once or twice per day to maintain normal blood levels of thiamine [3,4]. These higher amounts of thiamine are found in specialized bariatric vitamins, whereas typical over-the-counter multivitamins contain about 1.5 mg of thiamine. Parenteral multivitamins contain 3 to 3.5 mg of thiamine, and the adult enteral formula contains 2.2 to 2.9 mg per 1500 kcal.

Pathophysiology of thiamine deficiency, Wernicke's encephalopathy & Wernicke-Korsakoff syndrome

Pathophysiology of thiamine deficiency

Thiamine must be obtained from the diet, is water soluble, and has small body stores. Therefore, people who are thiamine deficient, those with reduced intestinal absorption, or those with excessive thiamine metabolism or excessive losses can deplete their thiamine reserves in as little as 2 weeks, or even sooner in patients with pre-existing low thiamine levels, such as patients on a restrictive liquid diet in preparation for MBS [5].

Rich sources of thiamine include whole-grain cereals, legumes, beans, lentils, peas, nuts, lean pork, trout, and tuna. In the US, bread, cereals, and infant formulas have been fortified with thiamine since 1940. Some foods contain antithiamine factors (ATF) or thiaminases, which react with thiamine to form an oxidized, inactive product. Due to the presence of ATF, consuming large amounts of tea or coffee (even decaffeinated), chewing betel nuts, or raw fish can lower thiamine levels.

Drugs that reduce the intestinal transporter ThTR-2 can exacerbate thiamine deficiency, e.g., metformin, verapamil, quinapril, amitriptyline, sertraline, amoxapine, penicillamine, quinidine, trimethoprine and hydroxychloroquine [6]. Metronidazole acts as a thiamine analog and inhibits the absorption of thiamine, leading to a functional deficiency state, even with normal blood thiamine levels [7].

Inadequate consumption of thiamine is the predominant cause of thiamine deficiency in developed countries, such as high carbohydrate diets, anyone with chronic diarrhea or vomiting, including pregnant women with hyperemesis gravidarum, complications after bariatric surgery, and inflammatory bowel disease. Conditions resulting in an increased requirement for thiamine include fever, sepsis, pregnancy, breastfeeding, adolescent growth, and hyperthyroidism.

Excessive thiamine loss may cause deficiency, such as in patients on dialysis. It has long been thought that loop diuretics, such as furosemide, can increase the risk of thiamine deficiency by preventing the kidneys' reabsorption of thiamine and increasing its excretion in the urine. However, a recent study by Nazmi et al. found no association between furosemide use and thiamine concentration in 73 patients over 65 year old [8]. This remains an area of controversy.

Pathophysiology of Wernicke's encephalopathy

Thiamine is an essential factor for multiple enzymes involved in brain cell metabolism [9]. A deficiency in thiamine leads to decreased ATP production due to the depletion of intracellular TDP and, consequently, active thiamine (TPP). This deficiency impairs the activity of the tricarboxylic acid (TCA) cycle and the pentose phosphate pathway, resulting in cellular energy depletion, lowering the brain's resistance to oxidative stress, and triggering reactive gliosis throughout the brain.

Thiamine deficiency leads to lactic acidosis due to impaired enzymatic conversion of lactate to pyruvate, which may cause focal damage to specific brain structures such as mamillary bodies and the posteromedial thalamus. The accumulation of toxic intermediate metabolic products such as lactate, alanine, and glutamate, reduced cellular pH, and disruption of electrolytes results in cytotoxic edema [10]. The blood-brain barrier (BBB) plays a key role in preventing vasogenic edema. BBB dysfunction occurs when astrocytes are damaged by ATP depletion and oxidative stress in the setting of thiamine deficiency.

Pathophysiology of Wernicke-Korsakoff syndrome

While Wernicke's encephalopathy is an acute condition, Wernnicke-Korsakoff syndrome (WKS) refers to a chronic neurologic condition that usually occurs as a consequence of untreated or undertreated WE. It is a progression of the consequences of vasogenic edema that occurs with thiamine deficiency in the brain and spinal cord. It is thought to be primarily due to damage to the anterior nucleus of the thalamus, mammillary bodies, and corpus callosum. There is also evidence of decreased glucose metabolism in the cerebral cortex [11].

Clinical presentation & diagnosis of Wernicke's encephalopathy & Wernicke-Korsakoff syndrome

Presentation and diagnosis of Wernicke's encephalopathy

Wernicke's is diagnosed clinically via history and physical examination, and confirmatory testing with labs and imaging is insensitive. Previous clinical guidelines also recommend drawing a whole blood thiamine level before initiating treatment However, this should not delay treatment since the laboratory result currently takes about 4 days, and blood levels of thiamine do not reliably indicate the body's thiamine status [12]. Treatment should be started immediately, and follow up blood levels are not recommended as they will be normal once thiamine

is given and treatment duration is based on clinical response.

History

A triad of confusion, gait ataxia, and eye movement disorders classically characterizes Wernicke's encephalopathy. However, only 10-20% of patients present with the entire clinical triad, emphasizing the importance of a high clinical index of suspicion. Vomiting and extreme weight loss are strong predictors of nonalcoholic WKS [13].

The Caine criteria have been validated and are now widely used for diagnosis in Wernicke's encephalopathy and require only two of the following four signs for 85% sensitivity: (1) dietary deficiencies, (2) oculomotor abnormalities, (3) cerebellar dysfunction, and (4) either an altered mental state or mild memory impairment. Reproducibility and validity testing of these criteria were performed on 106 autopsies in patients with alcohol abuse and WE [14].

The most common presenting sign is an altered mental state, which is found in approximately 80% of patients with WE [15]. This presentation may be subtle, such as family members describing the patient as becoming withdrawn, depressed, or having memory issues.

Horizontal gaze-evoked nystagmus is the most common ocular finding in around 30% of patients. Other ocular abnormalities seen in patients with WE include papilledema, ophthalmoparesis, ophthalmoplegia, and rarely, ptosis.

Gait ataxia usually precedes other signs by a few days or weeks and is likely underreported at 23% as observing gait is often inappropriately omitted from the neurological exam. Polyneuropathy is seen in 11%, and rarely, lower extremity hyperalgesia or allodynia has been reported, such as pain with walking [16]. Other hallmark symptoms include nausea, food intolerance, cardiac dysfunction, and congestive heart failure (Fig. 1).

In about 80% of patients with WE, chronic axonal neuropathy symptoms can be found in the distal extremities, including decreased muscle strength and decreased deep tendon reflexes.

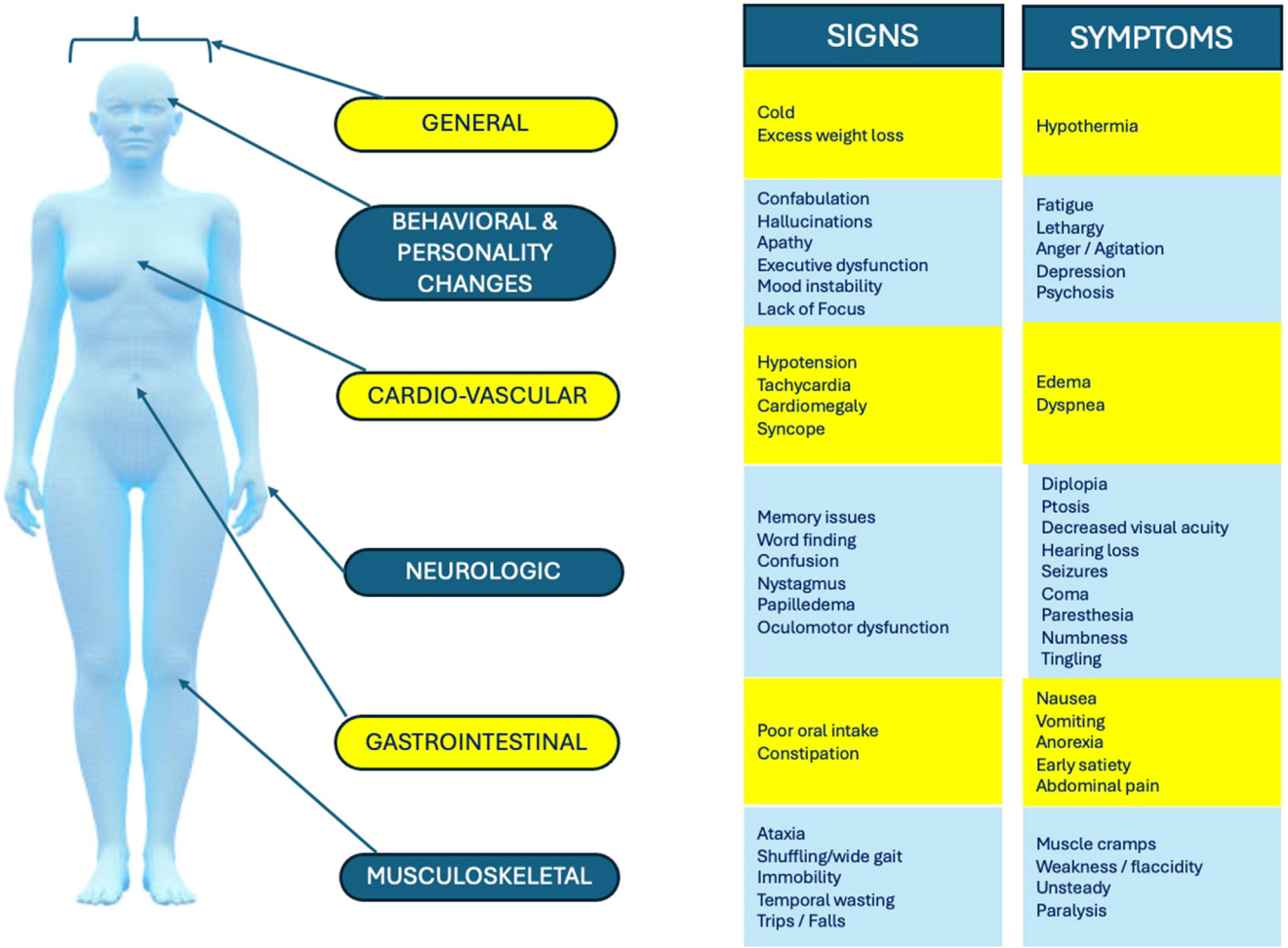

Fig. 1. Signs and symptoms of Wernicke's encephalopathy and Wernicke-Korsakoff syndrome.

Neurologic symptoms can be variable and severe, with headaches and sensorineural hearing loss, including sudden bilateral deafness, sudden blindness from optic neuropathy, seizures, and coma. Even such severe symptoms can resolve with appropriate and prompt treatment with high-dose intravenous thiamine [17].

Transient or prolonged hypotension has been reported as a rare autonomic dysfunction sign. Pulmonary hypertension has also been described due to thiamine deficiency and can resolve with thiamine [18]. Urinary incontinence and urinary retention have also been observed in WE.

Ataxia is a lack of voluntary coordination of muscle movements, including gait abnormalities, speech changes, and abnormalities in eye movements that indicate cerebellar dysfunction. A history of ataxia is elicited by asking questions about trouble walking, which may start with difficulty going up and down stairs, holding onto the railing, or experiencing frequent trips and falls. Patients may have blurry or double vision, slurred speech, and loss of dexterity, such as handwriting [19].

Physical examination

Physical examination for ataxia comprises several domains: eyes, speech, hands, legs, and gait [19].:

Eyes

Examine for nystagmus by holding a pen or other small object roughly one foot before the nose and moving it slowly from side to side, asking the patient to keep their head still.

Speech

Watch for scanning speech (words broken up into separate syllables with disrupted speech patterns), slowed speech, or variable volume.

Hands

1. Finger-nose-finger test: The patient points repeatedly with their index finger from their nose to the examiner's finger. Patients with ataxia will have intention tremors.
2. Finger chase: the patient's index finger follows the examiner's moving index finger as precisely as possible. Patients with ataxia will overshoot.
3. Fast alternating movements: the patient performs cycles of repetitive alternation of pronation and supination of their hand on their thigh. Patients with ataxia will have variable rhythm and speed.

Legs

In the heel-to-shin test, patients are asked to straighten one leg and use the heel of the other leg to slide down the shin from the knee smoothly and precisely. Patients with ataxia will have difficulty keeping the heel on the shin.

Gait

Observe the patient's walk, including turning corners. Patients with ataxia might veer toward one side and have a wide-based gait to compensate for impaired balance and a shortened stride.

Laboratory tests

Direct measurement of whole-blood TDP concentrations is the most sensitive and specific measurement of thiamine status. However, in Wernicke's encephalopathy, these concentrations may still be in the normal range, and there are no universally accepted reference values for cerebrospinal fluid (CSF) thiamine levels. Radiologic imaging is unnecessary to diagnose WE but can help confirm the diagnosis and rule out alternative diagnoses.

Radiologic imaging

Head CT scan is usually normal unless there is an intraventricular hemorrhage [20]. MRI is insensitive, detecting approximately 52%-65% of cases, and therefore should not be used to rule out WE [21,22]. Characteristic findings include hyperintense signals in the periaqueductal gray area and dorsal medial nucleus of the thalamus [10].

Cytotoxic and vasogenic edema are the most typical neuroimaging findings of WE, presenting as bilateral symmetric hyperintense on T2-weighted MR images involving the medial thalami, mamillary bodies, periaqueductal region, tectal plate, and floor of the fourth ventricle. Involvement of the cerebellum, brainstem nuclei, caudate, splenium, and cerebral cortex is significantly more common in nonalcoholics compared to alcoholics with Wernicke's. Preferential involvement of periventricular regions may be secondary to an inherently high rate of thiamine-dependent metabolism in these brain regions [23]. Signal abnormalities in WE usually resolve after successful thiamine replacement.

Presentation and diagnosis of Wernicke-Korsakoff syndrome

Approximately 56% to 84% of patients with Wernicke's encephalopathy progress to Korsakoff's syndrome (KS) due to lack of treatment or undertreated WE. Patients progressing to KS exhibit dementia, antegrade and retrograde amnesia, impaired short-term memory, learning disabilities, confabulation, apathy, anxiety, and irreversible neurologic deficits, collectively termed Wernicke-Korsakoff syndrome (WKS) [24].

The diagnosis of KS requires careful history taking and physical examination to identify neurological symptoms, such as peripheral neuropathy, cerebellar ataxia, or ophthalmological abnormalities. Moreover, collateral history is critical to establishing the patient's baseline functioning and timelines for decline. Neurocognitive testing of patients with WKS often yields difficulties with executive functioning and spatiotemporal deficits.

Given that WKS develops following WE, many WE symptoms can persist, including ataxia, peripheral neuropathy with paresthesias, balance issues, and tremors. Aggressive behavior is observed in 20% to 54% of patients with WKS. Approximately 18% of patients report depression, and 7% have psychotic symptoms [25].

WKS is a clinical diagnosis, but MRI may show atrophy of the mamillary bodies and midbrain tegmentum [23]. EEG is rarely performed but may show non-specific slowing. Nerve conduction studies may show sensory-motor axonal polyneuropathy, which improves after prompt treatment with thiamine [26].

Patient populations at high risk of thiamine deficiency & Wernicke's encephalopathy

A. Bariatric surgery & medical weight loss

With the rise of the obesity epidemic and the increasing number of bariatric procedures performed worldwide over the past 2 decades, we have seen an increase in cases of WE and also of missed cases of WE in malpractice claims. Interestingly, up to 29% of patients with obesity seeking metabolic and bariatric surgery have been reported to have thiamine deficiency before surgery, possibly due to high-carbohydrate diets (causing excessive thiamine metabolism) or calorie-restricted or liquid diets before surgery, which are often recommended to reduce intra-abdominal obesity [27]. The prevalence of thiamine deficiency after bariatric surgery is also alarmingly high at 25%

Thiamine deficiency leading to Wernicke's encephalopathy can manifest at any point after bariatric surgery, with most reported cases occurring within the first 3-4 months post-surgery. A common theme among these cases includes persistent nausea and vomiting, poor oral intake of nutrients, and a failure to thrive. Clinicians need to note that nausea and vomiting are both causes and effects of thiamine deficiency, and it becomes a vicious cycle analogous to dehydration and often occurs in the absence of any anatomic complications after bariatric surgery [28].

Oudman and colleagues reviewed literature from 1985 to 2017 and identified 118 Wernicke's encephalopathy (WE) reports [22]. The most common bariatric procedure cited was Roux-en-Y gastric bypass, which was the predominant procedure during this period. In this bariatric cohort with WE, 87% presented with vomiting, 85% had ataxia, 76% had altered mental status, and 74% had eye movement disorders. The whole triad was present in 54%, much higher than the 16% previously reported [22].

A more recent literature review of 129 cases of WE after bariatric surgery described that WE can occur after any bariatric operation but is more common in gastrointestinal procedures such as biliopancreatic diversion and gastric bypass than strictly gastric procedures such as gastric banding and sleeve gastrectomy [29].

The ASMBS 2017 nutrition guidelines recommend preoperative whole-blood thiamine testing for all WLS patients [3]. The ASMBS 2020 clinical practice guidelines recommend screening for thiamine deficiency in high-risk patients with malnutrition, rapid weight loss, or GI symptoms such as intractable nausea, vomiting, or constipation.

WE has also been reported after restrictive fad diets, endoscopic weight loss procedures such as intragastric balloon placement, and antiobesity medications (AOMs) [30]. At least one case report of WE due to rapid weight loss from semaglutide has been published, and the authors are aware of other unpublished cases [31].

B. Gastrointestinal disorders

WE can occur in almost any gastrointestinal condition, including surgery, cancer, inflammatory bowel disease, peptic ulcer disease, achalasia, hiatal hernia, intestinal obstruction, pancreatitis, and exocrine pancreatic insufficiency. Although classically associated with fat-soluble vitamin deficiencies, there are reports of water-soluble vitamin deficiencies due to cystic fibrosis [32].

Refeeding syndrome is an important complication in malnourished patients that may occur after extreme weight loss. It reflects the change from catabolic to anabolic metabolism after increased caloric intake from food or total parenteral nutrition (TPN). Major risk factors include unintentional weight loss of $>$15% over three to 6 months or little to no intake for more than 10 days. During refeeding, glycemia leads to glycogen, fat, and protein synthesis, a process requiring phosphate, magnesium, and cofactors such as thiamine, and the consequence is a fall in levels of all of these plus potassium [33].).

C. Alcohol abuse

Wernicke's is most commonly known to occur in patients with alcoholism, which accounts for 50% of cases. Thiamine deficiency is common in alcohol use disorder (AUD) because alcohol is high in calories but poor in nutrients [13].

AUD is universally recognized as a major risk factor for thiamine deficiency and WE. Up to 80% of patients with chronic alcoholism develop thiamine deficiency because alcohol reduces gastrointestinal absorption of thiamine

and the tendency for poor nutrition. Typical brain lesions of WE can be observed in 12.5% of autopsies of patients with AUD [34]. AUD is present in up to 25% of hospitalized patients on medical floors, and up to 59% of hospitalized patients with alcohol-related deaths have been found to have WE on autopsy [35].

D. Hyperemesis gravidarum

Nausea and vomiting affect up to 80% of pregnancies, and some are so severe that the diagnosis of hyperemesis gravidarum (HG) is established in .5-2.0% of pregnancies and may lead to WE. Criteria for diagnosing HG include vomiting that results in significant dehydration and weight loss (at least 5% of the patients' pre-pregnancy weight). A review of 82 cases of WE due to HG in pregnancy found that the mean gestational age was 16.5 ± 3 weeks with a mean vomiting duration of 6.6 ± 3.1 weeks. Complete remission has been reported in up to one-third of patients. Still, in a larger study of 177 cases of pregnant WE patients, a subtherapeutic dosage was noted in two-thirds, pregnancy loss occurred in 50%, and maternal death in 5%.

Failure to diagnose and treat can lead to maternal WKS and fetal demise [36,37].

E. Critically ill patients

Up to 30% of critically ill patients are thiamine deficient, and the frequency is as high as 70% in patients admitted to the Intensive Care Unit (ICU) with septic shock [38,39]. Infections are the presenting manifestation of thiamine deficiency in up to 50% of patients, and these patients are at risk of worse neuropsychological outcomes [40]. Trauma patients in the ICU have a high prevalence of alcoholism, and some recommend blood alcohol testing and thiamine prophylaxis in severely injured patients [41].

F. Cancer

A retrospective study of hospitalized oncology patients found thiamine deficiency occurred in 55%, 80% of whom demonstrated some mental status abnormality [42]. WE has also been reported in the caregivers and bereaved relatives of cancer patients who may develop a loss of appetite and nutritional deficiency due to the stress of caring for or losing a family member with cancer [43,44].

G. Psychiatric diseases

Patients who present with psychiatric histories may have symptoms disregarded or not evaluated fully due to symptom overlap. For example, in schizophrenia, delusions or hallucinations regarding their food or health status can lead to diminished intake. Access to care and food and reduced financial resources can significantly impact an individual's ability to obtain healthy food [45]. In contrast to patients with WE due to alcoholism, most WE schizophrenia cases present with the full triad of symptoms [46].

Depression is a major risk factor for WE, and if treated appropriately, WKS can be avoided. A systematic review of 21 patients with depression found none were treated with the recommended dose of 500 mg IV or IM three times a day. Of the 7 patients who received > 500 mg per day, only one developed Korskoff's syndrome, whereas 3 out of 5 patients who received less than 500 mg per day developed WKS [47].

Anorexia nervosa patients have the highest mortality of any psychiatric disorder and are at high risk of WE due to food restriction [48]. WE has also been described in patients with malnutrition due to crack-cocaine addiction [49].

H. Diabetes

Patients with type 2 diabetes have thiamine levels that are 50-75% lower than those without diabetes, possibly due to increased renal clearance since a greater deficiency of plasma thiamine has been documented with increasing albuminuria [50]. A double-blind, randomized clinical trial showed that oral supplementation with 150-300 mg of thiamine daily can decrease hyperglycemic individuals' blood glucose levels [51]. Furthermore, some studies have shown that high-dose thiamine has improved the vascular complications of diabetes, such as neuropathy, nephropathy, and retinopathy [52].

I. Heart failure

In addition to thiamine deficiency leading to heart failure (wet beriberi), heart failure is a risk factor for thiamine deficiency. One study showed that supplementation with 300 mg orally for 28 days improved left ventricular ejection fraction by 30% [53].

J. Dialysis

Patients on peritoneal dialysis or hemodialysis for either acute or chronic renal failure, are at high risk of thiamine deficiency and related disorders due to losses of thiamine during dialysis sessions [54].

Prevalence and prevention of Wernicke's encephalopathy & Wernicke-Korsakoff syndrome

The prevalence of Wernicke's encephalopathy in the general population ranges from .4 to 2.8% based on autopsy studies, which is higher than predicted by clinical studies (.04-.13%) [55]. Historically, only approximately 15% of cases were diagnosed before death [56]. A study by Lin

et al. of 262 psychiatric inpatients found that Caine-positive WKS prevalence was 12%, and only half used alcohol [57].

Prevention of thiamine deficiency, WE and WKS can be addressed within the classic public health paradigm of primary, secondary and tertiary prevention:

I. Primary Prevention: Prevent disease in susceptible people by ensuring thiamine intake from food, fortified foods, and vitamin supplements.
II. Secondary Prevention: Treat early when subclinical by giving medium-dose parenteral thiamine (IM or IV) to high-risk patients (such as a banana bag to ED patients with emesis).
III. Tertiary Prevention: Reduce the severity of the disease in patients diagnosed clinically with WE by treating them emergently with high-dose thiamine, 500 mg IV thrice daily for a minimum of 3 days.

Treatment and prognosis of Wernicke's encephalopathy & Wernicke-Korsakoff syndrome

Treatment and prognosis of Wernicke's encephalopathy

Although permanent neurologic damage and death can be prevented by timely thiamine replacement therapy, thiamine deficiency and Wernicke's encephalopathy often go undiagnosed and untreated. WE is a bona fide emergency as much as a myocardial infarction or stroke. If untreated, WE has a very high morbidity and mortality, with death in up to 20% of patients and WKS in 85% of survivors [58]. In a national population-based registry, the median survival in WKS was 10.7 years in comparison to 5.9 years in alcohol-related dementia.

Several published guidelines recommend high-dose IV (HDIV) thiamine for WE based largely on one randomized controlled trial, many case reports, plus expert opinions [59]. (Table 1).

Table 1
Summary of published guidelines on preventing, diagnosing, and treating Wernicke's encephalopathy

Society	Patients	Diagnosis	Initial Treatment	Further Treatment	Other Points and Recommendations
ASMBS Perioperative Nutrition and Micronutrient Guidelines	Post MBS patients with suspected TD.	Repletion dose & route vary by severity of symptoms.	Oral: 100-300 mg 2-3 times a day. IV: 200 mg tid or 500 mg od - bid for 3-5 d, then 250 mg per day for 3-5 d. IM: 250 mg od for 3-5 d or 100-250 mg monthly.	Continue initial treatment until symptoms resolve. Then, continue 100 mg orally daily indefinitely or until risk factors are resolved.	Treat before or in the absence of labs. Replacement of magnesium, potassium, and phosphorus for patients at risk for refeeding syndrome. Recommendations for TD, WE not reviewed.
ASPEN	Patients with or without AUD.	Clinical diagnosis. A high index of suspicion. Blood B1 levels do not evaluate body levels.	With AUD: 500-1500 mg IV, IM divided into 2-3 doses for 5 d Without AUD: 100-300 mg daily	Parenteral until symptoms resolve. 300 mg orally daily for 1-2 wk, then 100 mg daily for maintenance.	To reduce the risk of side effects, dilute B1 in 100 ml of NS and infuse over 30 min.
EFNS	Suspect in high-risk patients. Follow levels for 6 mo after MBS.	Caine criteria. MRI can support the diagnosis.	B1 200 mg IV tid for suspected WE before giving carbohydrates	Continue treatment until no further improvement in signs & symptoms	Draw whole blood B1 before treatment. IV B1 for high-risk pts in ED Encourage autopsy for death after WE.
RCP	ED patients with a history of AUD.	AUD plus any one of the classic triad: 1. Confusion 2. Ataxia 3. Eye signs	B1 250 mg IV tid for 3 d.	If no response, DC. If response, then continue for 5 d or until no further improvement.	Anaphylaxis is one in 5 million.
NIH	Acute TD with neurologic or cardiac symptoms.	Cardiac or neurologic symptoms.	Beri beri or WE: 200 mg IV or PO tid, or 50 mg IM for 2-3 d or resolution. WKS: 500 mg IV tid for 2 d, then 250 mg for 3 d.	Maintenance therapy of 10 mg per day orally.	Always give B1 in refeeding period in patients with AUD. WKS may persist for months or be permanent.

ASMBS = American Society for Metabolic and Bariatric Surgery(Mechanick et al, SOARD, 2020), (Parrott et al, SOARD, 2017); ASPEN = American society for enteral and parenteral nutrition (Polegato et al., Nutrition in Clinical Practice, 2019); EFNS = European Federation of Neurological Societies [60]; RCP = royal college of physicians [61]; NIH = National Institutes of Health (Wiley and Gupta, NLM, 2023); TD = thiamine deficiency; ED = emergency department; AUD = alcohol use disorder; MBS = metabolic and bariatric surgery; B1 = vitamin B1/thiamine.

A recent pair of randomized clinical trials from Australia aimed at comparing different doses of parenteral thiamine for the prevention and treatment of WE and WKS in patients with AUD. No differences were found between high and low-dose thiamine in over 500 patients, but as the authors acknowledge, several study limitations tempered the interpretation of their findings. Target enrollment was missed, exposing them to a potential type B error; 44% (173/393) of patients did not receive all of their study doses, and over 40% of patients were lost to follow-up [62].

Magnesium is an essential cofactor of transketolase, so serum levels should always be checked and supplemented in patients with WE since hypomagnesemia may cause thiamine-refractory WE [63]. Simultaneous administration of thiamine, magnesium, potassium, and phosphorus is required for patients at risk for refeeding syndrome, where these substrates are rapidly utilized and depleted [64].

While not reliably diagnostic, MRI may have a prognostic role in WE. A retrospective review of 34 cases of WE showed that patients who recovered early (within 4 weeks) showed a lower incidence of T2 weight image/FLAIR (fluid-attenuated inversion recovery) abnormality in typical brain locations compared with patients who recovered later (after 4 weeks). The early recovery group also had a lower incidence of cerebellar ataxia, suggesting a possible relationship between MRI features and clinical prognosis in WE [65]. After initiation of high-dose IV thiamine, WE symptoms usually start improving within 24 to 48 hours. In general, thiamine should be given before glucose administration because thiamine is rapidly depleted for glucose utilization. However, treatment of hypoglycemia should not be delayed for thiamine. Follow-up studies of patients with WE are sparse to nonexistent. Still, the authors have noted a high incidence of recurrent WE after hospital discharge, so 100 mg of oral thiamine after acute treatment of WE with HDIV B1 is likely inadequate in many patients, who should be followed closely after discharge. Further research is needed on the optimal thiamine dose to prevent and treat WE, but since thiamine has such a good safety profile, we have have recommended higher doses of oral thiamine after discharge, at 300 mg two or three times daily until the risk factors resolve.

Treatment and prognosis of Wernicke-Korsakoff syndrome

A summary of systematic reports of nonalcoholic WKS concluded that many physicians seemed to be either unaware of or underestimate the risk of nonalcoholic WKS and that doses of thiamine were often lower than published guidelines and frequently lead to chronic WKS and permanent disability [13].

A study of 32 psychiatric inpatients with Caine-positive WKS treated with high-dose thiamine demonstrated clinically and statistically significant neurocognitive improvement after 6 months, measured with pre and post-treatment Montreal Cognitive Assessment, delayed five-item recall, and gait and coordination score [57]. Auto-populated EMR order sets can significantly increase appropriate care practices such as high-dose parenteral thiamine in patients with AUD [66].

Given the functional, behavioral, psychiatric, and somatic problems that occur with WKS, an integrated approach to symptom management involving a multidisciplinary team is required. A large study showed that nursing home patients with WKS are often on psychotropic drugs to help manage behaviors [67]. There are case reports of positive effects of physical rehabilitation to improve strength, ambulation, and self-care activities in patients with WKS [68]. Several studies have shown that errorless learning can help patients with WKS relearn everyday skills, such as making a pot of coffee, known as ‘instrumental activities,’ which can improve autonomy and independent living [69].

WKS is widely believed to be irreversible, but there is a case report of a man with AUD making a complete recovery in higher mental functioning after aggressive treatment with high dose thiamine for 2 months (600 mg/d orally and 300 mg/d intramuscularly) [70]. In practice, we have found that IM is rarely tolerated at more than 100 mg IM daily due to pain at the injection sites.

Summary and recommendations

Wernicke’s encephalopathy is an acute syndrome requiring emergency treatment to prevent permanent neurologic damage or death. WE is clinically comparable to venous thromboembolism (VTE) in that they are both low-prevalence, high-risk conditions, but VTE prevention has become routine in medicine, in contrast to WE prophylaxis which is more likey to be overlooked.

WE is often preventable, simple, and inexpensive to treat, yet it is often missed or undertreated. Perioperative WE prophylaxis with thiamine should be considered routine in many patients, such as those purposely restricting food intake to lose weight via bariatric surgery or weight loss medications (Table 2). Auto-populated order sets focused on appropriate thiamine supplementation should be more widely utilized within electronic medical records (EMRs).

Due to the dire potential consequences of a missed WE diagnosis, a high index of suspicion is paramount. Any patient presenting to the ED with poor food intake, rapid weight loss, protracted vomiting, altered mental status, or hemodynamic instability should be treated empirically for presumptive diagnosis of thiamine deficiency with high-dose intravenous thiamine [71].

Based on our literature review and our combined expertise in preventing, diagnosing, and treating WE, this task force makes new recommendations for the prevention and treatment of thiamine deficiency and Wernicke’s

Table 2
ASMBS Wernicke's Task Force recommendations for preventing, diagnosing, and treating thiamine deficiency and Wernicke's encephalopathy

Society	Patients	Diagnosis	Initial Treatment	Further Treatment	Other Key Points
ASMBS Wernicke's Task Force	**Prevent Thiamine Deficiency** (Primary prevention) Patients at high risk of TD. Thiamine 100 mg PO daily, at least 2 weeks before weight loss treatment. Continue while on medications and for at least 3 months after surgery, followed by at least 12 mg PO daily indefinitely.	Symptoms of Thiamine Deficiency Abdominal pain, nausea, vomiting, or weakness with nutritional deficiency. Caine Criteria for Wernicke's Two of four: 1. Confusion 2. Ataxia 3. Eye signs 4. Nutritional deficiency.	**Treat Thiamine Deficiency** (Secondary Prevention) Thiamine 100 mg IV or IM daily for 1-3 doses, or until symptoms resolve, & adequate oral intake. **Treat Wernicke's** (Tertiary Prevention) Thiamine 500 mg IV tid for at least 5 d & continue until no further improvement.	Thiamine 300 mg orally 2-3 times daily until risk factors resolve. Continue 100 mg po daily indefinitely. Reassess the patient in person frequently for symptom relapse, which may require hospital admission and high-dose IV treatment.	Wernicke's is an emergency. Draw labs and treat simultaneously. Give before or with glucose if hypoglycemia. Replace Mg, K, and Ph. Daily physical exam, including observing gait & performing tests for ataxia.

Mg = Magnesium, K = Potassium, and Ph = Phosphorus.

encephalopathy. Here, we have presented a new paradigm for categorizing the stages of TDDs and WE into primary, secondary, and tertiary prevention, a common public health strategy. As such, we have clearly distinguished prevention of thiamine deficiency, treatment of thiamine deficiency, and treatment of Wernicke's encephalopathy (Table 2).

In keeping with ASMBS nutritional guidelines, we recommend higher doses and duration of thiamine for prophylaxis and treatment of TD and WE compared with non MBS patients.

Expanding on prior guidelines, we have recommended even higher doses of thiamine prior to MBS or starting medical weight loss, since thiamine deficiency is highly prevalent before and after MBS and cases of Wernicke's are on the rise. Further research is needed to determine the optimal thiamine dosage and route to prevent and treat thiamine deficiency, Wernicke's encephalopathy, and Wernicke-Korsakoff syndrome.

Disclosures

The authors have no commercial associations that might be a conflict of interest in relation to this article.

References

[1] Nisar S, Tanvir M, Ganie MA, Kareem O, Muzaffer U, Wani IA. Clinical profile of patients presenting with thiamine-responsive upper-gastrointestinal upset: a pointer toward gastric beriberi. Nutrition 2022;102:111730. https://doi.org/10.1016/j.nut.2022.111730.

[2] Smith TJ, Johnson CR, Koshy R, et al. Thiamine deficiency disorders: a clinical perspective. Ann N Y Acad Sci 2021;1498(1):9–28. https://doi.org/10.1111/nyas.14536.

[3] Parrott J, Frank L, Rabena R, Craggs-Dino L, Isom KA, Greiman L. American society for metabolic and bariatric surgery integrated health nutritional guidelines for the surgical weight loss patient 2016 update: micronutrients. Surg Obes Relat Dis 2017;13(5):727–41. https://doi.org/10.1016/j.soard.2016.12.018.

[4] Mechanick JI, Apovian C, Brethauer S, et al. Clinical practice guidelines for the perioperative nutrition, metabolic, and nonsurgical support of patients undergoing bariatric procedures – 2019 update: cosponsored by American association of clinical endocrinologists/American college of endocrinology, the obesity society, American society for metabolic & bariatric surgery, obesity medicine association, and American society of anesthesiologists. Surg Obes Relat Dis 2020;16(2):175–247. https://doi.org/10.1016/j.soard.2019.10.025.

[5] Kerns JC, Gutierrez JL. Thiamin. Adv Nutr 2017;8(2):395–7. https://doi.org/10.3945/an.116.013979.

[6] Vora B, Green EAE, Khuri N, Ballgren F, Sirota M, Giacomini KM. Drug-nutrient interactions: discovering prescription drug inhibitors of the thiamine transporter ThTR-2 (SLC19A3). Am J Clin Nutr 2020;111(1):110–21. https://doi.org/10.1093/ajcn/nqz255.

[7] Dhar A, Manoila I, Dugay MH, Sellal F. Mystery case: metronidazole-induced encephalopathy. Neurology 2016;87(9):e89–90. https://doi.org/10.1212/WNL.0000000000003030.

[8] Nazmi A, Weatherall M, Wilkins B, Robinson GM. Thiamin concentration in geriatric hospitalized patients using frusemide. J Nutr Gerontol Geriatr 2014;33(1):47–54. https://doi.org/10.1080/21551197.2013.875501.

[9] Isenberg-Grzeda E, Kutner HE, Nicolson SE. Wernicke-korsakoff-syndrome: under-recognized and under-treated. Psychosomatics 2012;53(6):507–16. https://doi.org/10.1016/j.psym.2012.04.008.

[10] Ota Y, Capizzano AA, Moritani T, Naganawa S, Kurokawa R, Srinivasan A. Comprehensive review of Wernicke encephalopathy: pathophysiology, clinical symptoms and imaging findings. Jpn J Radiol 2020;38(9):809–20. https://doi.org/10.1007/s11604-020-00989-3.

[11] Paller KA, Acharya A, Richardson BC, et al. Functional neuroimaging of cortical dysfunction in alcoholic Korsakoff's syndrome. J Cogn Neurosci 1997;9(2):277–93. https://doi.org/10.1162/jocn.1997.9.2.277.

[12] National Institutes of Health. Office of dietary supplements - thiamin. https://ods.od.nih.gov/factsheets/thiamin-consumer/. Accessed November 1, 2024.

[13] Oudman E, Wijnia JW, Oey MJ, van Dam M, Postma A. Wernicke-Korsakoff syndrome despite no alcohol abuse: a summary of systematic reports. J Neurol Sci 2021;426:117482. https://doi.org/10.1016/j.jns.2021.117482.

[14] Caine D, Halliday GM, Kril JJ, Harper CG. Operational criteria for the classification of chronic alcoholics: identification of Wernicke's encephalopathy. J Neurol Neurosurg Psychiatry 1997;62(1):51–60. https://doi.org/10.1136/jnnp.62.1.51.

[15] Scalzo SJ, Bowden SC, Ambrose ML, Whelan G, Cook MJ. Wernicke-Korsakoff syndrome not related to alcohol use: a systematic review. J Neurol Neurosurg Psychiatry 2015;86:1362–8. https://doi.org/10.1136/jnnp-2014-309598.

[16] Vogrig A, Zanoni T, Moretto G. Nystagmus and lower extremity hyperalgesia after colectomy. JAMA 2016;316(14):1488. https://doi.org/10.1001/jama.2016.13658.
[17] Xu J, Li F, Xue Y. Acute hearing and visual loss caused by thiamine deficiency. BMC Neurol 2023;23(1):285. https://doi.org/10.1186/s12883-023-03337-w.
[18] Asakura T, Kodera S, Kanda J, Ikeda M. Thiamine-responsive pulmonary hypertension. BMJ Case Rep 2013;2013:bcr2012007938. https://doi.org/10.1136/bcr-2012-007938.
[19] Kuo SH. Ataxia. Continuum (Minneap Minn) 2019;25(4):1036–54. https://doi.org/10.1212/CON.0000000000000753.
[20] Al-Bayati AR, Nichols J, Jovin TG, Jadhav AP. Thiamine deficiency presenting as intraventricular hemorrhage. Stroke 2016;47(6). https://doi.org/10.1161/STROKEAHA.116.013048.
[21] Antunez E, Estruch R, Cardenal C, Nicolas JM, Fernandez-Sola J, Urbano-Marquez A. Usefulness of CT and MR imaging in the diagnosis of acute Wernicke's encephalopathy. Am J Roentgenology 1998;171(4):1131–7. https://doi.org/10.2214/ajr.171.4.9763009.
[22] Oudman E, Wijnia JW, van Dam M, Biter LU, Postma A. Preventing Wernicke encephalopathy after bariatric surgery. Obes Surg 2018;28(7):2060–8. https://doi.org/10.1007/s11695-018-3262-4.
[23] Bathla G, Hegde AN. MRI and CT appearances in metabolic encephalopathies due to systemic diseases in adults. Clin Radiol 2013;68(6):545–54. https://doi.org/10.1016/j.crad.2012.05.021.
[24] Singh S, Kumar A. Wernicke encephalopathy after obesity surgery: a systematic review. Neurology 2007;68(11):807–11. https://doi.org/10.1212/01.wnl.0000256812.29648.86.
[25] Gerridzen IJ, Moerman-van den Brink WG, Depla MF, et al. Prevalence and severity of behavioural symptoms in patients with Korsakoff syndrome and other alcohol-related cognitive disorders: a systematic review. Int J Geriatr Psychiatry 2017;32(3):256–73. https://doi.org/10.1002/gps.4636.
[26] Liang H, Wu L, Liu LL, Han J, Zhu J, Jin T. A case report: non-alcoholic Wernicke encephalopathy associated with polyneuropathy. J Int Med Res 2017;45(6):1794–801. https://doi.org/10.1177/0300060517699039.
[27] Kerns JC, Arundel C, Chawla LS. Thiamin deficiency in people with obesity. Adv Nutr 2015;6(2):147–53. https://doi.org/10.3945/an.114.007526.
[28] Milone M, Di Minno MND, Lupoli R, et al. Wernicke encephalopathy in subjects undergoing restrictive weight loss surgery: a systematic review of literature data. Eur Eat Disord Rev 2014;22(4):223–9. https://doi.org/10.1002/erv.2292.
[29] Yu AT, Gross A, Park K, Harvey EJ. Wernicke encephalopathy after bariatric surgery: a literature review. Obes Surg 2023;33(11):3621–7. https://doi.org/10.1007/s11695-023-06840-8.
[30] Patel S, Gómez V. A case of ascending sensory neuropathy due to acute onset thiamine deficiency after intragastric balloon placement. Obes Surg 2019;29(10):3404–5. https://doi.org/10.1007/s11695-019-03967-5.
[31] Foster SK. From weight loss to neurological deficits: a case of Wernicke's encephalopathy stemming from prescription weight loss medication. https://www.emra.org/emresident/article/wernicke-july-2023. Accessed November 1, 2024.
[32] Vijayavel N, Koh SW, Goodman EL. Cystic fibrosis associated with Wernicke's encephalopathy in an older adult. BMJ Case Rep 2022;15(7):e249727. https://doi.org/10.1136/bcr-2022-249727.
[33] Chiappetta S, Stein J. Refeeding syndrome: an important complication following obesity surgery. Obes Facts 2016;9(1):12–6. https://doi.org/10.1159/000442534.
[34] Torvik A, Lindboe CF, Rogde S. Brain lesions in alcoholics. J Neurol Sci 1982;56(2-3):233–48. https://doi.org/10.1016/0022-510X(82)90145-9.
[35] Naidoo DP, Bramdev A, Cooper K. Autopsy prevalence of Wernicke's encephalopathy in alcohol-related disease. S Afr Med J 1996;86(9):1110–2.
[36] Fiorentini M, Nedu B, Dapoto F, Brunelli E, Pilu G, Youssef A. When time is brain: a systematic review about Wernicke encephalopathy as a dramatic consequence of thiamin deficiency in hyperemesis gravidarum. The J Maternal-Fetal Neonatal Med 2023;36(2):2223678. https://doi.org/10.1080/14767058.2023.2223678.
[37] Oudman E, Wijnia JW, Oey M, van Dam M, Painter RC, Postma A. Wernicke's encephalopathy in hyperemesis gravidarum: a systematic review. Eur J Obstet Gynecol Reprod Biol 2019;236:84–93. https://doi.org/10.1016/j.ejogrb.2019.03.006.
[38] Donnino MW, Andersen LW, Chase M, et al. Randomized, double-blind, placebo-controlled trial of thiamine as a metabolic resuscitator in septic shock: a pilot study. Crit Care Med 2016;44(2):360–7. https://doi.org/10.1097/CCM.0000000000001572.
[39] Costa NA, Gut AL, Pimentel JAC, et al. Erythrocyte selenium concentration predicts intensive care unit and hospital mortality in patients with septic shock: a prospective observational study. Crit Care 2014;18(3):R92. https://doi.org/10.1186/cc13860.
[40] Wijnia JW, Oudman E, van Gool WA, et al. Severe Infections are common in thiamine deficiency and may be related to cognitive outcomes: a cohort study of 68 patients with wernicke-korsakoff syndrome. Psychosomatics 2016;57(6):624–33. https://doi.org/10.1016/j.psym.2016.06.004.
[41] Blackmore C, Ouellet JF, Niven D, Kirkpatrick AW, Ball CG. Prevention of delirium in trauma patients: are we giving thiamine prophylaxis a fair chance? Can J Surg 2014;57(2):78–81. https://doi.org/10.1503/cjs.020112.
[42] Isenberg-Grzeda E, Shen MJ, Alici Y, Wills J, Nelson C, Breitbart W. High rate of thiamine deficiency among inpatients with cancer referred for psychiatric consultation: results of a single site prevalence study. Psychooncology 2017;26(9):1384–9. https://doi.org/10.1002/pon.4155.
[43] Ishida M, Uchida N, Yoshioka A, et al. Wernicke encephalopathy in a caregiver: a serious physical issue resulting from stress in a family member caring for an advanced cancer patient. Palliat Support Care 2022;20(4):600–2. https://doi.org/10.1017/S1478951521001784.
[44] Onishi H, Uchida N, Takahashi T, et al. Thiamine deficiency in the bereaved after cancer-related spousal loss. Palliat Support Care 2019;17(6):738–40. https://doi.org/10.1017/S147895151900018X.
[45] Crespo K, Barton J, Ireland S. C - 30A case of undiagnosed Wernicke's encephalopathy due to avoidant restrictive food intake disorder in a patient with persistent complex bereavement disorder. Arch Clin Neuropsychol 2018;33(6):703–94. https://doi.org/10.1093/arclin/acy061.183.
[46] Oudman E, Wijnia JW, Oey MJ, van Dam MJ, Postma A. Wernicke Encephalopathy in schizophrenia: a systematic review. Int J Psychiatry Clin Pract 2021;25(3):233–7. https://doi.org/10.1080/13651501.2020.1819333.
[47] Oudman E. Wernicke encephalopathy in patients with depression: a systematic review. Psychiatry Clin Neurosci 2020;74(10):569–72. https://doi.org/10.1111/pcn.13113.
[48] Brown K, Everwine M, Nieves J. A case of Wernicke encephalopathy secondary to anorexia nervosa complicated by refeeding syndrome and takotsubo cardiomyopathy. Am J Case Rep 2021;22:e929891. https://doi.org/10.12659/AJCR.929891.
[49] Sukop PH, Kessler FHP, Valerio AG, Escobar M, Castro M, Diemen LV. Wernicke's encephalopathy in crack–cocaine addiction. Med Hypotheses 2016;89:68–71. https://doi.org/10.1016/j.mehy.2016.01.023.
[50] Waheed P, Naveed AK, Ahmed T. Thiamine deficiency and its correlation with dyslipidaemia in diabetics with microalbuminuria. J Pak Med Assoc 2013;63(3):340–5.
[51] 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(7):1821–4. https://doi.org/10.1007/s00394-013-0534-6.

[52] Luong KV, Nguyen LT. The impact of thiamine treatment in the diabetes mellitus. J Clin Med Res 2012;4(3):153–60. https://doi.org/10.4021/jocmr890w.

[53] Jain A, Mehta R, Al-Ani M, Hill JA, Winchester DE. Determining the role of thiamine deficiency in systolic heart failure: a meta-analysis and systematic review. J Card Fail 2015;21(12):1000–7. https://doi.org/10.1016/j.cardfail.2015.10.005.

[54] Aomura D, Kurasawa Y, Harada M, Hashimoto K, Kamijo Y. Early detection of thiamine deficiency by non-thyroidal illness syndrome in a hemodialysis patient. CEN Case Rep 2022;12(1):110–5. https://doi.org/10.1007/s13730-022-00729-8.

[55] Sechi G, Serra A. Wernicke's encephalopathy: new clinical settings and recent advances in diagnosis and management. Lancet Neurol 2007;6(5):442–55. https://doi.org/10.1016/S1474-4422(07)70104-7.

[56] Donnino MW, Vega J, Miller J, Walsh M. Myths and misconceptions of Wernicke's encephalopathy: what every emergency physician should know. Ann Emerg Med 2007;50(6):715–21. https://doi.org/10.1016/j.annemergmed.2007.02.007.

[57] Lin S, Leppla IE, Yan H, et al. Prevalence and improvement of caine-positive wernicke-korsakoff syndrome in psychiatric inpatient admissions. Psychosomatics 2020;61(1):31–8. https://doi.org/10.1016/j.psym.2019.08.002.

[58] 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;2013(7):CD004033. https://doi.org/10.1002/14651858.CD004033.pub3.

[59] Ambrose ML, Bowden SC, Whelan G. Thiamin treatment and working memory function of alcohol-dependent people: preliminary findings. Alcohol Clin Exp Res 2001;25(1):112–6.

[60] Galvin R, Bråthen G, Ivashynka A, Hillbom M, Tanasescu R, Leone MA. EFNS guidelines for diagnosis, therapy and prevention of Wernicke encephalopathy. Eur J Neurol 2010;17(12):1408–18. https://doi.org/10.1111/j.1468-1331.2010.03153.x.

[61] Thomson AD. The royal college of physicians report on alcohol: guidelines for managing Wernicke's encephalopathy in the accident and emergency department. Alcohol Alcohol 2002;37(6):513–21. https://doi.org/10.1093/alcalc/37.6.513.

[62] Dingwall KM, Delima JF, Binks P, Batey R, Bowden SC. What is the optimum thiamine dose to treat or prevent Wernicke's encephalopathy or Wernicke–Korsakoff syndrome? Results of a randomized controlled trial. Alcohol Clin Exp Res 2022;46(6):1133–47. https://doi.org/10.1111/acer.14843.

[63] Coughlan JJ, Mross T, Wafer M, Liston R. Thiamine refractory Wernickes encephalopathy reversed with magnesium therapy. BMJ Case Rep 2016;2016:bcr2016218046. https://doi.org/10.1136/bcr-2016-218046.

[64] Frank LL. Thiamin in clinical practice. J Parenter Enteral Nutr 2015;39(5):503–20. https://doi.org/10.1177/0148607114565245.

[65] Kitaguchi T, Ota Y, Liao E, et al. The role of MRI in the prognosis of Wernicke's encephalopathy. J Neuroimaging 2023;33(6):917–25. https://doi.org/10.1111/jon.13143.

[66] Wai JM, Aloezos C, Mowrey WB, Baron SW, Cregin R, Forman HL. Using clinical decision support through the electronic medical record to increase prescribing of high-dose parenteral thiamine in hospitalized patients with alcohol use disorder. J Subst Abuse Treat 2019;99:117–23. https://doi.org/10.1016/j.jsat.2019.01.017.

[67] Gerridzen IJ, Goossensen MA. Patients with Korsakoff syndrome in nursing homes: characteristics, comorbidity, and use of psychotropic drugs. Int Psychogeriatr 2014;26(1):115–21. https://doi.org/10.1017/S1041610213001543.

[68] Genç A, Özdemir EC, Moustafa E, Küçükdeveci AA. Is physical rehabilitation effective for Wernicke–Korsakoff syndrome? A case report. Int J Rehabil Res 2018;41(4):373–6. https://doi.org/10.1097/MRR.0000000000000303.

[69] Oudman E, Nijboer TCW, Postma A, et al. Acquisition of an instrumental activity of daily living in patients with Korsakoff's syndrome: a comparison of trial and error and errorless learning. Neuropsychol Rehabil 2013;23(6):888–913. https://doi.org/10.1080/09602011.2013.835738.

[70] Paparrigopoulos T, Tzavellas E, Karaiskos D, Kouzoupis A, Liappas I. Complete recovery from undertreated Wernicke-Korsakoff syndrome following aggressive thiamine treatment. In Vivo 2010;24(2):231–3.

[71] Chisolm-Straker M, Cherkas D. Altered and unstable: wet beriberi, a clinical review. J Emerg Med 2013;45(3):341–4. https://doi.org/10.1016/j.jemermed.2013.04.022.