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Micronutrients and Gastric Bypass – What We Have Learned

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Bariatric surgery is a leading treatment for severe obesity, yet brings with it the risk for micronutrient deficiencies due to resection of primary absorption sites, reduced intake, and a number of other factors. Micronutrient deficiencies can have serious, sometimes irreversible consequences if left untreated. Clinician education about signs and symptoms of deficiencies, supplementation guidelines, and recommendations for repletion and monitoring is paramount in preventing micronutrient deficiencies and the resulting complications.

CASE STUDY

A 60-year-old male was admitted to our hospital for gastrostomy tube placement into his remnant stomach 14 months after Roux-en-Y gastric bypass (RYGB) due to persistent poor intake, weakness, and a nearly 200-pound weight loss. On average, he consumed less than 500 calories and 20 grams of protein per day and was non-adherent with his vitamin and mineral regimen. Since his surgery, he had become wheelchair-bound because of lower extremity weakness, ataxia, neuropathy, and regular falls. Prior to gastric bypass surgery, he walked independently except on uneven surfaces which required a cane. Given these symptoms and his altered anatomy, several micronutrient deficiencies were suspected including vitamin B12, copper, vitamin E, thiamine, vitamin B6, and niacin.

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INTRODUCTION

The prevalence of obesity in adults in the United States was 42.4% in 2017-2018, a notable increase from 30.5% in 1999-2000. Obesity is associated with a number of comorbid medical conditions including heart disease, type 2 diabetes, and stroke, and places a significant burden on the healthcare system.[1] Bariatric surgery is recognized as the most effective treatment for severe obesity.[2] The number of bariatric surgeries performed each year rises with the increasing prevalence of obesity. In 2019, it is estimated that 256,000 bariatric surgeries were performed in the U.S., 17.8% of which were RYGB.[3] It is well established that RYGB places

Table 1. Routine Supplementation Guidelines

Nutrient	Routine Supplementation Guideline
Multivitamin w/ minerals	• Twice daily[12]
Vitamin B12	• Oral: 350-1000 mcg daily OR • Intramuscular: 1000 mcg monthly[12] • *Currently, there are insufficient data to recommend nasal or sublingual B12 supplementation after RYGB[13,56]
Vitamin D	• 3000 IU vitamin D3 daily until serum 25(OH)-vitamin D is >30 ng/mL • Ongoing dosage should then be based on serum levels • Note: vitamin D3 is preferred over vitamin D2[12]
Calcium	• 1200-1500 mg calcium daily in divided doses[12]
Thiamine	• 12 mg daily (Grade C)[11]
Iron	• Menstruating females: 45-60 mg daily of elemental iron (includes iron from vitamin/mineral supplements) • Take in divided doses separate from calcium, acid-reducing medication, foods high in phytates or polyphenols[12]

patients at risk for micronutrient deficiencies, and many patients are noncompliant with recommended vitamin/mineral supplementation.[4-6] Clinicians must be aware of recommendations for screening, assessment, and treatment of micronutrient deficiencies in RYGB patients. A summary of specific recommendations can be found in tables 1-4. Acute inflammation may affect laboratory data for some micronutrients, details of which are included in the tables for each respective nutrient. Updated Clinical Practice Guidelines were published in 2019 and will hereafter be referred to as "CPGs."[12]

Vitamin B12 (Cyanocobalamin)

Vitamin B12 (B12) is necessary for neurological function, growth and development of red blood cells, and DNA synthesis.[7] A significant number of patients develop B12 deficiency after RYGB as a result of impaired absorption, decreased oral intake, lack of intrinsic factor, and reduced gastric acid.[8,9] Use of certain medications, including metformin, proton pump inhibitors, and H2 receptor antagonists, may increase the risk of B12 deficiency.[7]

B12 deficiency is associated with dementia, paralysis, and mood disturbance, and if left untreated can result in severe, irreversible neurological complications.[7,8,10] Other signs and symptoms of deficiency include megaloblastic and macrocytic anemias, fatigue, numbness and paresthesia in extremities, ataxia, magenta "beefy red" tongue, glossitis, pale skin, and slightly icteric skin and eyes.[11]

In the first year postoperatively, screening for B12 deficiency is recommended every three months according to the CPGs, followed by yearly screening thereafter or as indicated.[11,12] Recommended laboratory assessments are serum vitamin B12 and, in some cases, methylmalonic acid (MMA).[10,11,13] Serum B12 may be falsely elevated in the setting of alcoholism, liver disease, and cancer.[13] Deficiency may be present even when serum B12 is normal, since serum levels are maintained at the expense of tissue stores.[8,11] MMA should be considered in patients with normal or low-normal vitamin B12, macrocytosis, or clinical suspicion for B12 deficiency.[13] Elevated MMA can be indicative of B12 deficiency, however, MMA levels are also increased with renal disease, so should therefore be interpreted with caution.[8,11]

The CPGs recommend routine B12

Table 2. Water-Soluble Vitamins

Nutrient	Signs/Symptoms of Deficiency	Lab Assessment
B12	• Megaloblastic anemia, fatigue, numbness and paresthesia in extremities, ataxia, altered mental status, dementia, paralysis, mood disturbance • Magenta "beefy red" tongue, glossitis, pale skin, slightly icteric skin and eyes[7,8,10,11]	• Serum B12[7] • Methylmalonic acid (MMA)[7,8,11,13] • Note: serum levels of B12 are maintained at expense of tissue stores, and therefore deficiency may be present even when serum B12 appears normal[8] • Serum levels may be elevated in acute inflammation, liver disease, malignancies, or other disease states[57,58]
B6 (Pyridoxine)	• Seborrheic dermatitis, glossitis, lip and angular cheilitis, impaired immune function, peripheral neuropathy, seizures, hypochromic microcytic anemia • Pellagra-like symptoms are possible in severe cases[10,31,32]	• Plasma, erythrocyte, or urinary pyridoxal-5-phosphate[10] • Decreased plasma levels may be seen in acute inflammation[59]
B2 (Riboflavin)	• Angular and lip cheilitis, glossitis, nasolabial dermatitis, scrotal and vulvar eczema, anemia, peripheral neuropathy[31,32]	• Preferred: Erythrocyte glutathione reductase activity coefficient (EGRAC); cannot be used in patients with glucose-6-phosphate-dehydrogenase deficiency • Serum riboflavin (should be performed after an overnight 12-hour fast)[10]
B3 (Niacin)	• Pellagra • 4 D's: dermatitis, dementia, diarrhea, death • Weakness, fatigue, depression, hyperpigmentation of sun-exposed areas of skin ("glove," "boot," and "Casal's necklace")[10,31]	• Urinary N1-methylniconatinamide and N1-methyl-2-pyridone-5-carboxamide[10]
Vitamin C	• Scurvy • Perifollicular hemorrhages, ecchymosis, petechiae, xerosis, poor wound healing, corkscrew or swan-neck hairs, bleeding gums, fatigue, malaise, weakness[32,36]	• Treat if deficiency is suspected • Serum or leukocyte vitamin C[10] • Plasma levels may be decreased in acute inflammation, particularly in sepsis and after cardiac arrest[59,62,63]
B1 (Thiamine)	• Ataxia, confusion, nystagmus, ophthalmoplegia, peripheral neuropathy, weakness usually in lower extremity[21]	• Treat if deficiency is suspected; if levels are checked, use whole blood or erythrocyte[22,23]

	Various Guidelines for Repletion of Deficiency
	• 1000 mcg daily until normal serum B12 is achieved (recheck every 3-6 months) • Then return to maintenance supplementation[12]
	• 100 mg oral pyridoxine daily[32] • 25-600 mg daily depending on severity of symptoms[10] • Consider IV supplementation for patients with severe symptoms (i.e., seizures)[10] **Caution with long term high dose* supplementation:** Associated with sensory neuropathies and movement disorders[10] *High dose supplementation not clearly defined • "Toxic dose" is defined as 1000 mg/day and is associated with sensory neuropathy[33,34] • Tolerable Upper Intake Level is 100 mg/day for adults[60] • Use caution with higher doses or prolonged supplementation[33,61] • Higher doses below 1000 mg/day may have adverse effects, including indigestion, nausea, and photosensitivity[33]
	• No consensus[10] • 10-60 mg oral vitamin B2 daily[32] **Caution with high dose supplementation (>100 mg/day):** Chronic use may lead to damage of the ocular lens proteins and the retina[10]
	• 250-500 mg oral nicotinamide daily[31] • 500 mg oral nicotinic acid daily[32] • 100-300 mg subcutaneous niacinamide in 3 doses for patients with pellagra[10]
	• 1-2 g vitamin C daily for 2-3 days, followed by 500 mg daily for 1 week, followed by 100 mg daily for 1-3 months[31] • 1-2 g daily[64] • 300 mg daily for 3 months[10] • 2 g daily for 3 days followed by 500 mg daily for 1 week, followed by 100 mg daily for 3 months[10] Note: absorption decreases with doses >1g/day[10]
	• Dose is based on route and severity of symptoms: 100-500 mg 2-3x daily[11,12]

supplementation for all RYGB patients.[12] Patients with deficiency should receive additional supplementation.[12] The need for B12 supplementation beyond what is contained in a standard multivitamin is addressed in a systematic review of the literature by Mahawar et al., which showed that oral doses up to 15 mcg daily were insufficient to prevent deficiency. Doses of 600 mcg daily proved superior to 350 mcg daily, and 1000 mcg daily was sufficient to prevent deficiency in most patients.[9] Concerning the route of supplementation, there is evidence to suggest that vitamin B12 sufficiency can be maintained with oral supplementation in RYGB patients.[8] Regardless of route, it is important to monitor B12 status as vitamin/mineral non-adherence is common.

Vitamin D

Vitamin D is a steroid hormone and nutrient which is involved in bone metabolism as well as a number of other body processes.[14] Humans primarily obtain vitamin D through exposure to UVB light, in addition to dietary intake.[14,15] A review of the literature by Peterson et al. demonstrates that up to 90% of RYGB patients are vitamin D deficient (<20 ng/mL) in the pre-operative period.[14] Many studies indicate ongoing vitamin D deficiency after bariatric surgery, however, some have demonstrated improvement in vitamin D status in the post-operative period purported to result from release of sequestered vitamin D from adipose tissue as patients lose weight. However, this is often followed by high prevalence of deficiency or insufficiency.[14-16]

RYGB patients may have decreased absorption of vitamin D due to decreased surface area of the small intestine as well as altered mixing with pancreatic secretions and bile. Additionally, risk of vitamin D deficiency may be increased as a result of sequestration of vitamin D in adipose tissue and lack of sun exposure.[15]

Vitamin D deficiency can result in increased risk of osteopenia and osteoporosis, muscle weakness, falls, and generalized pain and discomfort.[15] Symptoms of deficiency may also include hypocalcemia, tetany, tingling, or cramping.[11]

Literature shows that dosages below 800 IU (20 mcg) of vitamin D3 daily are not sufficient to raise 25(OH)-vitamin D beyond 30 ng/mL in RYGB patients.[14,15] Higher doses have proven effective in some patients, but others may require even greater supplementation to maintain optimal serum levels.[15,17] The CPGs recommend routine supplementation and continued monitoring of vitamin D status.[12] Ongoing dosage should be based on serum levels. Vitamin D3 (cholecalciferol) is the preferred form of vitamin D for supplementation due to its higher potency, according to the CPGs.[12] Short term, high dose supplementation is not likely to be a comprehensive solution for vitamin D deficiency in RYGB patients; they will likely need supplemental vitamin D in the long term to maintain optimal serum levels.

Vitamin B1 (Thiamine)

Thiamine is a water-soluble vitamin essential for glucose metabolism, ATP production, and plays a role in maintaining the integrity of the nervous system. When oral intake is reduced, thiamine stores may be consumed quickly (9 to 18 days).[18] Thiamine deficiency is a clinical diagnosis and if undetected and untreated, may result in Wernicke-Korsakoff Syndrome.[19,20]

Recognizing risk factors and early signs and symptoms are the keys to detecting thiamine deficiency. RYGB patients with persistent vomiting are at risk for thiamine deficiency since vomiting precludes adequate intake. In addition, the primary sites of absorption which include the duodenum and first part of the jejunum are bypassed. These factors, combined with limited storage, may quickly lead to thiamine deficiency after surgery. Rapid weight loss and non-compliance with vitamins are also contributing factors.[18,21]

Wernicke's Encephalopathy (WE) is a neurological disorder caused by thiamine deficiency. Hallmark symptoms include the triad of mental status changes, ataxia, and eye movement disorders. In a recent study of WE after bariatric surgery, ataxia was the most common characteristic found in patients.[21] The full triad of symptoms may be seen in an estimated 20-50% of patients with WE.[21] In addition, patients may experience paresthesias, peripheral neuropathy, and weakness, usually in the lower extremities.

Thiamine diphosphate, or thiamine

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pyrophosphate (TPP), is the biologically active form of thiamine. Because TPP is found in erythrocytes and accounts for 90% of thiamine in whole blood, the use of whole blood or erythrocytes to measure thiamine stores is the most sensitive and specific method for testing.[22,23] However, given the long turnaround time for lab assays and the acute urgency to treat suspected thiamine deficiency, clinical suspicion and awareness of risk factors should be used to diagnose and treat patients. In addition, there is no thiamine level that correlates with the diagnosis of WE.

The American Society for Metabolic and Bariatric Surgery (ASMBS) treatment for thiamine deficiency depends on the route and severity of symptoms. There is a paucity of scientific data to support recommendations for treatment.[12]

Vitamin A

Vitamin A is involved in cell growth and development, immune function, vision, and functions as an antioxidant against free radicals.[24-26] The prevalence of deficiency in the first 4 years post-RYGB is up to 70%.[12] Deficiency commonly presents as night blindness and can result in complete blindness if left untreated.[10,12,24] In fact, vitamin A deficiency is the leading preventable cause of blindness.[24] Patients deficient in vitamin A may also exhibit Bitot's spots, hyperkeratinization of the skin, and poor wound healing.[11,24] Risk factors for vitamin A deficiency associated with RYGB are decreased intestinal surface area for absorption, decreased overall food intake, and low fat diet in the post-operative period.[26] Zinc deficiency, alcohol ingestion, and cholestyramine use can impair vitamin A absorption.[24]

The CPGs recommend routine supplementation of 5,000-10,000 IU vitamin A daily to prevent deficiency after RYGB, which can be attained with a multivitamin.[12,27] It is noteworthy that toxicity can occur with high-dose or chronic supplementation of vitamin A.[10]

Vitamin E

Vitamin E functions as an antioxidant and plays important roles in neurological health, specifically in the central nervous system.[28,29] Vitamin E deficiency is uncommon in bariatric surgery patients in the pre- and post-operative periods.[11,12,28] However, RYGB patients may be at increased risk for deficiency due to resection of primary absorption sites, altered mixing with pancreatic and biliary secretions, steatorrhea, or small intestinal bacterial overgrowth.[28] In a systematic review of the literature, Sherf-Dagan found deficiency rates of up to 65.7% in 1-5 years after bariatric surgery.[28]

Signs and symptoms of vitamin E deficiency include spinocerebellar ataxia, peripheral neuropathy, gait disturbances, decreased sensation, ophthalmologic disorders, nystagmus, impaired immune response, and hemolytic anemia.[11,28,29] The CPGs recommend supplementation for all bariatric surgery patients, which can be attained with a multivitamin.[12] Most supplements provide alpha-tocopherol, which is the most common form of vitamin E in human tissues and is the most biologically active form.[28,29] Additional supplementation may be needed to replete deficiency, however therapeutic dosing is not clearly defined.[11,12,28] Prompt supplementation of vitamin E can stop progression of, or even normalize, neuromuscular deficits resulting from deficiency.[29] High dose vitamin E supplementation (>1000 mg/day) may increase risk for competition with vitamin K and has been associated with hemorrhage.[10,30]

Vitamin B6 (Pyridoxine)

Vitamin B6 participates in protein and carbohydrate metabolism, gluconeogenesis, and neurotransmitter synthesis.[31,32] Factors that may increase the risk for deficiency are alcoholism and use of certain medications, including isonizid (antituberculosis), hydralazine, penicillamine, contraceptives, levo/carbidopa, and antiepileptic medications.[10,31,32]

Signs and symptoms of B6 deficiency include seborrheic dermatitis, glossitis, lip and angular cheilitis, impaired immune function, peripheral neuropathy, seizures, and hypochromic microcytic anemia.[10,31,32] Pellagra-like symptoms are possible in severe cases, since B6 is necessary for synthesis of nicotinic acid (see Niacin section).[31,32]

Treatment of deficiency varies within the literature depending on the severity of symptoms. IV supplementation should be considered for patients with severe symptoms, such as seizure.[10] Long-term high dose supplementation is associated

with sensory neuropathies and movement disorders, among other symptoms, and should be used with caution.[10] "Toxic dose" is defined as 1000 mg/day, however there are case reports of neuropathy with lower doses.[33,34] The Tolerable Upper Intake Level for vitamin B6 is 100 mg/day for adults.

Vitamin B2 (Riboflavin)

Vitamin B2 is involved in numerous reduction-oxidation reactions as well as the conversion of pyridoxine phosphate to vitamin B6.[31,32] The primary absorption site is the proximal small intestine, putting RYGB patients at risk for deficiency.[32] Alcoholism and diets low in meat and dairy can put patients at greater risk.[31] Symptoms of deficiency include angular and lip cheilitis, glossitis, nasolabial dermatitis, scrotal and vulvar eczema, anemia, and peripheral neuropathy.[31,32] The

Table 3. Fat-Soluble Vitamins

Nutrient	Signs and Symptoms of Deficiency	Lab Assessment	Various Guidelines for Repletion of Deficiency
Vitamin D	• Osteopenia, osteoporosis • Muscle weakness, falls, generalized pain and discomfort, hypocalcemia, tetany, tingling, cramping[11,15]	• 25(OH)-vitamin D[12] • Decreased plasma concentrations can be seen in acute inflammation or stress[59,63,65,66]	• 3000-6000 IU vitamin D3 daily OR • 50,000 IU vitamin D2 1-3x weekly[12]
Vitamin A	• Night blindness, xerophthalmia, Bitot's spots • Hyperkeratinization of skin, poor wound healing[10-12,24]	• Plasma retinol and carotenoid[10] • Decreased plasma concentrations of vitamin A (retinol) may be seen in infection, trauma, critical illness, inflammation, or acute stress[59,62,63,67,68] • Retinol binding protein (RBP) is a negative acute phase protein[67]	• Without corneal changes: 10,000-25,000 IU daily orally • With corneal changes: 50,000-100,000 IU IM for 3 days, followed by 50,000 IU IM daily for 2 weeks[12] **Caution with high dose supplementation:** Toxicity can occur with long-term use or with single dose >660,000 IU[12]
Vitamin E	• Spinocerebellar ataxia, peripheral neuropathy, gait disturbances, decreased sensation, ophthalmologic disorders, nystagmus, impaired immune response, hemolytic anemia[11,28,29]	• Serum alpha-tocopherol when serum lipids are normal • Adjust for serum lipids in patients with hyperlipidemia (serum alpha-tocopherol divided by total lipids)[10-12] • Decreased plasma concentrations may be seen in acute stress, however this decrease may not be observed when alpha-tocopherol levels are adjusted for changes in plasma lipids[59,62,63]	• Optimal dose not clearly defined[11,12,28] • 100-400 IU/d recommended[12] **Caution with high dose supplementation (>1000 mg/d):** May compete with vitamin K for absorption; risk for hemorrhage[10,30]

Table 4. Minerals

Nutrient	Signs and Symptoms of Deficiency	Lab Assessment	Various Guidelines for Repletion of Deficiency
Copper	• Peripheral neuropathy, myelopathy, ataxia, muscle weakness, anemia, neutropenia, optic neuropathy[42-45]	• Serum copper and/or ceruloplasmin (positive acute phase reactants) • MRI-showing increased T2 signal in the posterior dorsal column of the spinal cord[40,42]	• Dose is based on route and severity of symptoms: 3-8 mg/d oral; 2-4 mg/d IV[11,12,40,42] • 8 mg oral x 1 week, 6 mg for second week, 4 mg for third week, 2 mg thereafter; if symptoms persist, use 2 mg IV over 2 hours for 5 days[41]
Zinc	• Alopecia, taste changes, white spots on the nails, dermatitis, skin plaques and diarrhea[48]	• Plasma or serum levels (levels may not reflect cellular zinc due to tight homeostatic control)[10,49]	• 2-3 mg/kg/d elemental zinc; IV: 7-10 mg daily • Monitor copper levels[10,50-53] **Caution with high dose supplementation:** May cause nausea, vomiting, and gastric irritation[10,50-53]
Iron	• Microcytic anemia, fatigue, dyspnea, spoon-shaped nails[10]	• Microcytic, hypochromic anemia (not specific for iron deficiency) • Iron studies which may include serum iron*, TIBC, transferrin*, transferrin saturation and serum ferritin**	• 100-200 mg elemental iron up to 300 mg 2-3 times daily[10,12] • Adding a source of vitamin C may improve iron absorption • Consider taking single dose iron on alternate days vs daily or twice daily[55] • Parenteral iron if there is a lack of response to oral therapy; monitor patient for anaphylactic reaction

*May decrease during acute phase response
**May increase during acute phase response[10]

clinical presentation of B2 deficiency may mimic that of B3 or B6 deficiencies due to its role in their metabolism.[31] Supplementation recommendations vary, and there is limited data.[31,32] Caution should be used with long term supplementation at doses >100 mg/day due to potential effects on the ocular lens proteins and retina.[10]

Vitamin B3 (Niacin)

Vitamin B3 has essential roles in metabolism including ATP synthesis and glycolysis.[31] In a study by Ledoux et al. (2020), B3 deficiency was observed in 13.1% and 19.8% of patients within 1 year and ≥ 3 years, respectively, after RYGB.[35] The clinical manifestation of deficiency is pellagra, which is characterized by dermatitis, dementia, diarrhea, and potentially death.[10,31] Early symptoms of deficiency include weakness, fatigue, and depression. Physical exam findings may resemble sunburn on the face, neck, and dorsal extremities, hyperpigmented areas on the extremities known as the "glove" and "boot" of pellagra, or hyperpigmented areas on the neck known as Casal's necklace.[31] Additional risk factors for deficiency include alcoholism, use of isoniazid, azathioprine, or 6-mercaptopurine.[31]

Vitamin C (Ascorbic Acid)

Vitamin C functions as an antioxidant, supports osteoblast formation in bones and teeth, and is essential for the formation of collagen.[31,36,37] It is absorbed in the upper third of the intestine, and deficiency has been observed in the RYGB population in both the pre- and post-operative

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periods.[32,35,38] Patients may be at increased risk for deficiency in cases of alcoholism, ulcerative colitis, Crohn's disease, or dialysis. Smoking also increases risk for deficiency due to decreased intestinal absorption and increased catabolism.[31,32] Vitamin C deficiency in its most severe form is scurvy, which is characterized by perifollicular hemorrhages, ecchymosis, petechiae, xerosis, poor wound healing, corkscrew hairs, swan-neck hairs, bleeding gums, fatigue, malaise, and weakness.[32,36] If left untreated, vitamin C deficiency can be fatal, therefore supplementation should be started if there is clinical suspicion for deficiency rather than waiting for a lab result to return.[37] Upon initiation of therapeutic supplementation, symptoms are expected to resolve quickly, some within the first 24 hours and others taking weeks to months.[31,37] It should be noted that high dose vitamin C supplementation can be associated with diarrhea, other GI upset, or falsely elevated blood glucose readings on point-of-care glucose monitors.[10,31,39] Absorption of vitamin C decreases with doses over 1 g/day.[10]

Copper

Copper is an essential trace element that plays a role in neurotransmission, hematopoiesis, hemoglobin synthesis, and the formation of connective tissue. It is primarily absorbed in the stomach and proximal duodenum, placing a gastric bypass patient at risk for deficiency since these sites are reduced or bypassed after surgery.[40] Kumar reported on 34 cases of symptomatic copper deficiency occurring an average of 9 years after surgery with 97% of the cases *non-compliant* with taking multivitamins and minerals.[41]

Symptoms of copper deficiency include neurological deficits such as peripheral neuropathy, ataxia, and muscle weakness. Myelopathy and myeloneuropathy seen with copper deficiency closely resemble vitamin B12 deficiency. Symptoms may also include anemia and/or neutropenia. Optic neuropathy and blindness as a result of copper deficiency have also been reported.[42-45]

To diagnose a deficiency, serum copper levels are used. Another marker often used is ceruloplasmin, a protein that transports 80-95% of copper. It is, however, an acute phase protein that increases during inflammation which in turn leads to an elevated serum copper level. To diagnose deficiency, one author recommends using serum copper, ceruloplasmin < 20 mg/dL, and elevated C-reactive protein.[42] An MRI showing increased T2 signal in the posterior dorsal column of the spinal cord may enhance lab data when determining a diagnosis.[40]

Other than case studies, little scientific evidence is available on the route, amount, or timing of copper supplementation. Supplementation halts the progression of neurological deficits, but may not reverse them. It usually takes 4-12 weeks for hematologic consequences of copper deficiency to resolve.[40,42,46] Several strategies and guidelines for replacement of copper are available.[41,42,47] Copper levels should be checked periodically after levels return to normal and supplementation stops since cases of relapse have been reported.[12]

Zinc

Zinc is a mineral that plays a role in DNA and protein synthesis, immune function, wound healing, and more than 300 enzyme systems. It is primarily absorbed in the duodenum and proximal jejunum which may lead to a deficiency since these areas are bypassed after RYGB. Poor intake and non-compliance with vitamins and minerals may also contribute. Symptoms of deficiency include alopecia, taste changes, white spots on the nails, dermatitis, skin plaques and diarrhea.[48]

In a recent summary, only 6 cases of symptomatic zinc deficiency were found in the literature. On average, patients became symptomatic 6 years after surgery, 67% were female, and all had a skin rash. Information on vitamin compliance was available for 2 patients; one had stopped taking

her supplement, and the other was compliant.[48]

Since it is a component of various proteins and nucleic acids, zinc levels are difficult to measure. Plasma or serum levels are often used, but levels do not necessarily reflect cellular zinc due to tight homeostatic control. Also, clinical signs can be present in the absence of abnormal laboratory indices. Some suggest pairing clinical correlation with lab values and risk factors to aid in the diagnosis of a deficiency.[10,49]

ASMBS guidelines do not issue a recommendation due to insufficient evidence, however, they advise caution when repleting zinc as it can induce a copper deficiency over time. Excess amounts of enteral zinc may cause nausea, vomiting, and gastric irritation. Skin lesions usually improve within days to weeks of supplementation.[10,50-53]

A Word about Iron

Iron deficiency is the leading cause of anemia after RYGB. Factors contributing to this include decreased hydrochloric acid production in the gastric pouch, decreased meat consumption, and bypassing the duodenum and jejunum which are the primary sites of absorption.[54] Iron deficiency may occur despite routine supplementation and should be monitored within 3 months after surgery followed by every 3 to 6 months for the first year and then annually thereafter unless clinical signs and symptoms of deficiency are present.[12] Adherence to supplementation may be affected by side effects which can include constipation, nausea, vomiting and a metallic taste.[10] Many oral iron preparations are available, but none have been shown superior to ferrous sulfate. A recent article suggests absorption of oral iron improves when taken on alternate days in single doses versus daily or twice daily in healthy women with depleted iron stores.[55]

CASE STUDY CONCLUSION

A serum copper level was drawn and found to be low at 57 mcg/dL (normal 75-145 mcg/dL). The patient was anemic, but not neutropenic. He was treated with 2 mg/d oral copper gluconate. He also received 0.5 mg of copper in his multivitamin and 1.92 mg in his tube feeding for a total of 4.42 mg/d copper. Copper levels returned to normal 1.5 months after supplementation began. In addition, the patient did not experience any more falls after initiation of both copper supplementation and tube feeding. His ambulation improved to the point that he was able to walk using a cane, but remained wheelchair-dependent outside of the home. Copper levels continued to rise, and supplementation was discontinued after 7 months as the patient's ability to ambulate without falls remained stable. Levels were checked regularly every 3 months thereafter.

SUMMARY

It is well documented that patients who have undergone RYGB are at risk for micronutrient deficiencies. There is a paucity of data regarding the treatment of micronutrient deficiencies in the RYGB population, and most evidence to date comes from case studies rather than RCTs. Clinicians should be aware of signs and symptoms of micronutrient deficiencies as they collect a detailed patient history and perform a physical exam. Adherence to vitamin and mineral supplementation should be assessed. It should also be noted that micronutrient deficiencies rarely exist in isolation; if a patient presents with one deficiency, there are likely others. Lastly, vitamin and mineral supplementation is not benign and should be monitored and adjusted as clinically appropriate. ■

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Answers to this month's crossword puzzle: