Mineral Malnutrition Following Bariatric Surgery\textsuperscript{1,2}

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**ABSTRACT**

Moderate/severe obesity is on the rise in the United States. Weight management includes bariatric surgery, which is effective and can alleviate morbidity and mortality from obesity-associated diseases. However, many individuals are dealing with nutritional complications. Risk factors include: 1) preoperative malnutrition (e.g., vitamin D, iron); 2) decreased food intake (due to reduced hunger and increased satiety, food intolerances, frequent vomiting); 3) inadequate nutrient supplementation (due to poor compliance with multivitamin/multimineral regimen, insufficient amounts of vitamins and/or minerals in supplements); 4) nutrient malabsorption; and 5) inadequate nutritional support (due to lack of follow-up, insufficient monitoring, difficulty in recognizing symptoms of deficiency). For some nutrients (e.g., protein, vitamin B-12, vitamin D), malnutrition issues are reasonably addressed through patient education, routine monitoring, and effective treatment strategies. However, there is little attention paid to other nutrients (e.g., zinc, copper), which if left untreated may have devastating consequences (e.g., hair loss, poor immunity, anemia, defects in neuro-muscular function). This review focuses on malnutrition in essential minerals, including calcium (and vitamin D), iron, zinc, and copper, which commonly occur following popular bariatric procedures. There will be emphasis on the complexities, including confounding factors, related to screening, recognition of symptoms, and, when available, current recommendations for treatment. There is an exceptionally high risk of malnutrition in adolescents and pregnant women and their fetuses, who may be vulnerable to problems in growth and development. More research is required to inform evidence-based recommendations for improving nutritional status following bariatric surgery and optimizing weight loss, metabolic, and nutritional outcomes. *Adv. Nutr.* 4: 506–517, 2013.

**Introduction**

**Popularity and Benefits of Bariatric Surgery**

Weight loss through bariatric surgery is a popular treatment for moderate (BMI \(\geq 35 \text{ kg/m}^2\)) and severe (BMI \(\geq 40 \text{ kg/m}^2\)) obesity across most higher income countries and in 2011, \(>340,000\) procedures were performed worldwide (1). In the United States, a leading country for bariatric surgery, there were \(~160,000\) bariatric procedures performed in 2010 (2). Bariatric surgery was developed in the 1960s and 1970s (3,4), but its popularity began to increase in 1990 due to the dramatic rise in severe obesity (5,6), improved safety of the operations (7), and a consensus statement by the NIH, which offered endorsement and guidance (8). Since 1990, United States data from the Nationwide Inpatient Sample and the American Society for Metabolic and Bariatric Surgery estimate that a total of 1,426,268 persons have undergone bariatric surgery (1,9–12). The burden of severe obesity and comorbid cardio-metabolic disease, including type 2 diabetes (T2DM)\textsuperscript{4}, atherosclerosis and cancer, is lifted from most of these individuals (13–17). Moreover, decreased prevalence of morbidity, including athropathy, depression, poor quality of life (18–20), and mortality (21–24), following bariatric surgery is well documented.

**Drawbacks of Bariatric Surgery: Nutritional Complications**

Eligibility for bariatric surgery is described by a 1991 NIH consensus statement and includes individuals who have a BMI \(\geq 40 \text{ kg/m}^2\) or a BMI \(\geq 35 \text{ kg/m}^2\) and suffer from comorbid disease (8). In 2010, the US FDA expanded the criteria for eligibility by approving the use of a device used in the adjustable banding surgery (described below) for individuals who have a BMI \(\geq 30\) and have T2DM or other comorbidities (25). Despite the demonstrated benefits of bariatric surgery, it remains underutilized by eligible patients \((\sim 1%\) have undergone surgery (2)) due to lack of accessibility (26), high costs and questionable cost-effectiveness (27,28), and adverse outcomes that limit acceptability among patients, doctors, and third-party payers. The major adverse events relate to the complications of gastrointestinal surgery that typically occur within 30 d of the procedure and include wound infection, deep-vein thrombosis, small bowel

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3 Abbreviations used: AGB, adjustable gastric banding; BPD, bilipancreatic diversion; RYGB, roux-en-y gastric bypass; SG, sleeve gastrectomy; T2DM, type 2 diabetes.
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obstructions, abdominal leaks, and death. Severely obese individuals undergoing major elective surgery are at a high risk for complications due to preexisting medical conditions (29); however, due to advances in laparoscopy, which is less invasive and traumatic, the operative mortality and morbidity has reduced to 0.1–0.3 and 4.5%, respectively, in recent years (7,30). Despite improvement in perioperative safety, longer term complications are an important issue for patients undergoing bariatric surgery. These complications can be subdivided into those that are general or gastrointestinal surgery related (e.g., hernia, bowel obstruction, cholecystitis, slippage of gastric band/pouch dilation, ulcer, nausea, vomiting, diarrhea) (30), nutritional (hypoglycemia, loss of lean body mass, weight regain, vitamin and mineral deficiencies) (31,32), or other (e.g., psychosocial issues, neisidioblastosis hyperinsulinemia, bacterial overgrowth) (24,33,34). The frequency of long-term complications following bariatric surgery is difficult to ascertain, because this has been mostly determined through retrospectively obtained data with poor patient follow-up and the various complications are specific to the type of surgery performed (14,35). However, as evidenced by a growing body of case reports, retrospective studies, and a few prospective studies, poor nutritional outcomes are relatively common after surgery and prevalence of upwards of 82% has been reported (36–38). Some nutritional complications are well known to the surgeons and other key practitioners (dietitians, primary care doctors, and endocrinologists) who provide postoperative support as well as to the patients themselves; these include malnutrition in protein, vitamin B-12, vitamin D, calcium, and iron. Thus, most clinical practices provide adequate patient counseling for prevention and routinely monitor patients for deficiency. However, for many other nutrients, including B vitamins (thiamine, pyridoxal phosphate, folate), fat-soluble vitamins (A, K), essential fatty acids, and minerals (zinc, copper), awareness of risk of deficiency by patients and providers is low and prophylactic protocols and monitoring are insufficient, leading to debilitating consequences including long-term disability (39). Moreover, as acknowledged by consensus guidelines from experts within the American Society for Metabolic and Bariatric Surgery, The Obesity Society and the American Association of Clinical Endocrinologists, there is need for more and better quality evidence behind recommendations for the prevention and treatment for malnutrition after bariatric surgery (35,40).

The issues of nutritional deficiency following bariatric surgery were recently comprehensively reviewed (32,35). However, this present review will focus on the problem of essential mineral deficiencies following specific surgery procedures, especially highlighting the complexities involved in monitoring and risk factors, as well as protocols for prevention and treatment. The issues in recognizing nutritional complications using clinical signs and symptoms as well as sensitive biomarkers will be discussed. We discuss the confounding issues related to symptoms and biomarkers of deficiency, including the masking of deficiency by other nutrients and by inflammation. Information is provided regarding strategies for prophylactic supplementation and interactions between nutrients that affect absorption and bioavailability. Finally, we discuss concerns of mineral malnutrition following bariatric surgery in special populations, namely adolescents and pregnant women.

Information in this review included published original articles and review papers that were collected using PubMed searches containing the subject headings bariatric surgery (gastric bypass surgery, adjustable gastric banding (AGB), sleeve gastrectomy (SG), bioliopancreatic diversion) and nutritional deficiencies (malnutrition, micronutrients, nutritional status) published between 1990 and May 2013. The impact of bariatric surgery on magnesium, phosphorus, electrolytes (e.g., potassium, sodium, chloride), and trace elements (e.g., selenium, iodine) is important, but the data were not sufficiently robust to be discussed in the review.

**Current Status of Knowledge**

**Types of Bariatric Surgery Procedures**

Bariatric surgeries are defined as procedures that alter the gastrointestinal tract to reduce caloric intake or absorption and can be classified by the mechanism of action for promoting weight loss as restrictive or malabsorptive. Restrictive procedures reduce the volume or capacity of the stomach and thereby limit caloric intake by promoting early satiety. Malabsorptive procedures reduce the amount of calories absorbed by altering the flow of food to limit contact with pancreatic secretions and bile acids and/or bypass the absorptive regions of the duodenum and proximal jejunum. Surgical alteration of the gastrointestinal to restrict energy intake or promote malabsorption of macronutrients is achieved but with varying effectiveness and durability for sustained weight loss, as well as resulting nutritional side effects, depending on the extent of manipulation of the gastrointestinal system. The common bariatric surgery procedures are described herein along with features that may impair nutritional status.

The roux-en-y gastric bypass (RYGB) is the most popular surgical procedure in the United States at 47% of annual cases in 2011 (1). RYGB has a dual restrictive and malabsorptive mode of action as the stomach is reduced to a volume of 20–30 mL and stomach contents are rerouted to the distal jejunum via an anastomosis connection (Fig. 1) (41). The physiological mechanisms of RYGB for promoting weight loss are under intense investigation given the acute resolution of T2DM following surgery (42,43), and potential mechanisms include caloric restriction and alterations in secretion of incretins, satiety gastrointestinal hormones, and bile acids and in the microbiome of the gut (44). Although malabsorption of proteins and fats occurs after RYGB, restricted dietary intake plays a much larger role in the reduction of energy intake (45), and following RYGB, patients dramatically reduce caloric intake to ~1000 kcal/d (46,47). Studies have shown decreased appetite and increased post-meal satiety following RYGB, likely due to decreases in ghrelin, an orexigenic hormone, and increases in glucagon-like peptide 1 and polypeptide YY, which are satiety hormones (48–50). However,
malabsorption may indirectly contribute to the reduction in dietary intake observed after RYGB. In the remnant stomach pouch, the reduced availability of stomach secretions of pepsin, rennin, and hydrochloric acid leads to a decreased capacity for digestion (51). Also, the shunting of undigested food directly to the lower gut, particularly if high in simple carbohydrates or fat, can produce an osmotic imbalance that triggers severe gastrointestinal symptoms such as bloating, nausea, vomiting, flatulence, and diarrhea, known as dumping syndrome (52). The uncomfortable gastrointestinal side-effects of mal-digestion and -absorption may cause patients to develop food intolerances and avoid nutrient-dense foods such as meat, milk, and high-fiber foods (53,54). The processes of micronutrient absorption can be impaired following RYGB, because bioavailability requires digestive juices and acids in the stomach and small intestine and because absorption occurs primarily in the duodenum. Taken together, there are various reasons why RYGB can affect the status of macro- and micronutrients, including malabsorption, reduced dietary intake, and avoidance of nutrient-dense foods.

The AGB procedure has decreased in popularity in recent years (from 44% in 2008 to 27% in 2011) (1). AGB restricts intake of food as a band is placed around the proximal stomach, encompassing the upper portion of the fundus and creating a temporary holding pouch of 30 mL; when food is ingested, the pouch expands and creates intraluminal pressure and satiety signals are triggered (Fig. 1) (55). An important feature of this surgery is that the surgeon, or an appropriate surrogate, is able to periodically tighten the band around the stomach so that the feeling of fullness is maintained; without this adjustment, the surgery is ineffective for weight loss (35,56,57). Nutritional complications related to AGB occur if the flow of food is obstructed by the narrowness of the band, which causes reflux, nausea, and/or vomiting. For this reason, patients tolerate softer foods compared with foods with a coarser texture, leading to an avoidance of red meats and fibrous fruits and vegetables (54,58,59). A large study of patients who underwent AGB demonstrated that two-thirds experience an inability to eat certain foods and one-third reported regurgitation several times per week (58). Persistent vomiting following AGB has been shown to be a major cause of undernutrition following AGB (60).

The SG is an emerging restrictive procedure that is growing in popularity, reaching 19% in 2011 (1). The larger curvature of the stomach is dissected, leaving a narrow vertical tube that can hold a volume of 150 mL, thus similar to AGB, early satiety is achieved following a small meal (Fig. 1) (61). Increased satiety may also occur through mechanisms similar to those following RYGB, because the appetitive hormone ghrelin is decreased (62,63) and the satiety hormone PYY is increased following SG (61). Moreover, a decrease in gastric emptying and small bowel transit time has been demonstrated after SG, which would limit the digestion and bioavailability of some nutrients (64). Indeed, poor diet quality is an expected outcome following SG, because patients experience difficulties with eating certain foods, as has been observed following RYGB (54).

The biliopancreatic diversion (BPD) and the more recent version, the BPD with duodenal switch, are primarily malabsorptive surgeries that are highly effective for weight loss but associated with nutritional complications that are difficult to treat (65). The popularity of this surgery is low in the United States (0.8% in 2011) and other countries, but historical cases exist (1). In the operation, the stomach is resected as is done for the SG (Fig. 1). In fact, SG is derived from the BPD but without alteration of the intestine (66). Immediately following exit from the stomach, the food chyme is diverted and then rejoined with biliary and pancreatic juices in a common channel that begins at the ileum. Thus, the nutritional consequences of BPD are similar to those encountered following RYGB but are more severe (67–69) due to greater malabsorption, particularly of fat and fat-soluble vitamins (70).

Other Factors That Promote Poor Nutritional Status Following Bariatric Surgery

Candidates for bariatric surgery are often malnourished despite an overconsumption of calories, and obesity is a known risk factor for nutrient deficiency (71). Mechanisms besides poor dietary intake explain the association between obesity and poor nutritional status. The bioavailability of vitamin D is reduced in the obese state, because vitamin D is sequestered in adipose tissue (72,73). Inflammation associated
with obesity induces the production of hepcidin, an acute-phase protein made in the liver, which blocks iron absorption in the intestine (74). Also in obesity, hyperinsulinemia is associated with excessive urinary excretion of zinc, thus lowering plasma zinc concentrations (75). Assessment of nutritional status of severely obese patients before bariatric surgery has revealed varying rates of deficiencies, which is complicated by the lack of standardization of analytical tests and different referent ranges that were used. Typically vitamin D deficiency is high [ranging from 23 to 83%, using the cutoff of 50 nmol/L (76)] (77–83). Deficiencies in vitamin B-12, iron, and zinc are not uncommon, ranging from 2 to 18% for vitamin B-12, 1 to 18% for iron, and 12 to 32% for zinc (77,79–81,84–88). Thus, preexisting nutritional deficiency may put patients undergoing bariatric surgery at risk for further nutritional complications. Although patients lose weight after bariatric surgery, many patients experience inadequate weight loss or weight regain (89,90), so obesity-induced inflammation may still be an issue following surgery. Following bariatric surgery, expert recommendations are for a life-long regimen of daily micronutrient supplementation (35). However, compliance with this recommendation is mixed (59,69,91), because some patients: 1) do not recognize the need; 2) cannot bear the costs; or 3) are misled or confused by the large variety of commercial supplements, some of which are incomplete in specific vitamins or minerals (81,85). Moreover, many patients do not undergo routine monitoring for deficiencies and thus the effectiveness of prophylactic supplementation is not clear (35). Thus, although surgery-induced dietary restriction or malabsorption is the major factor leading to malnutrition in the bariatric surgery patient, several nonsurgical factors can further exacerbate the issue.

Malnutrition in Calcium and Vitamin D
Calcium is an essential macromineral, making up to 2% of the human body, and functions in cell signaling and the mineralization of bone and teeth (92). Vitamin D is important for calcium homeostasis by regulating the absorption of calcium in the small intestine (93,94). In addition to calcium metabolism, vitamin D has been implicated in the regulation of insulin action, immune function, and cell proliferation (95). Although blood concentration of calcium is often used as a marker of calcium status, this is not a good indicator because blood concentrations are tightly regulated (92). Bone represents a storage reservoir of calcium; thus, bone density, measured by dual X-ray absorptiometry, is better for assessment of calcium status and reference ranges for normal healthy individuals have been established using bone mineral density Z-scores (96). The impact of bariatric surgery on calcium and vitamin D is complicated, with surgery-induced changes in body weight, dietary intake, and gut absorption as influential factors. Compared with individuals of normal weight, obese individuals have higher bone density due to the positive effect of weight bearing on bone mineral accretion (97). Weight loss is known to reduce bone density, but this may not produce negative effects, because bone density may remain within the normal range (98–100). With regards to absorption of calcium and other divalent metals (iron, copper, zinc) in the gastrointestinal, acidic conditions are required for solubilization and transporters are most prevalent in the duodenum; therefore, decreased calcium absorption has been demonstrated after RYGB (100). Because it is fat soluble, vitamin D absorption may be decreased as well, although this has not yet been shown. However, a positive effect of surgery may be the decreased amount of body fat available for sequestration of vitamin D or a potential for release of vitamin D from fat stores during weight loss in the immediate period following surgery (101). Nevertheless, findings related to vitamin D status following bariatric surgery, measured by blood concentrations of 25-hydroxyvitamin D, have been conflicting, with decreases following BPD with duodenal switch (69) and RYGB (101) but an increase (102) or no change (72,82) reported in other studies. The inconsistency in findings may relate to the large variation in supplementation of calcium and vitamin D reported in studies of bariatric surgery patients, ranging from doses close to the recommended dietary allowance to high-dose vitamin D supplementation (103–105). Despite the equivocal findings for vitamin D, several studies have shown that bone mineral density decreases following restrictive (106) and malabsorptive (107–109) surgeries due to weight loss and secondary hyperparathyroidism. However, a 3-y study of women undergoing RYGB demonstrated that although bone loss occurred, bone mineral density remained in the normal range and the risk of osteoporosis was low (109). Some studies have demonstrated that calcium and vitamin D supplementation may attenuate the risk of bone loss following bariatric surgery (110,111) and expert recommendations are for daily supplementation of 1200–1500 mg calcium and at least 3000 international units of vitamin D (35) (Table 1). More research is needed to determine the optimum dosages for prophylactic supplementation to avoid adverse outcomes related to bone as well as nonsusosseous effects of calcium and vitamin D. It is also important to determine the longer term effects of bariatric surgery on calcium and vitamin D status, as well as bone mineral density, in growing adolescents.

Malnutrition in Iron
Iron is an essential micromineral in the human body (at 0.005% by weight) and functions in heme and nonheme proteins involved in oxygen and electron transport. Iron deficiency is highly prevalent in developing countries but is also common in industrialized countries, especially in women of childbearing age (up to 16%) (112). Obesity increases the risk of iron deficiency, which may be explained by obesity-associated, low-grade inflammation and the induction of hepcidin, which blocks iron absorption proteins (74). Iron deficiency is therefore prevalent before surgery and is exacerbated following malabsorptive and restrictive procedures. In a recent retrospective analysis, the medical insurance claims of a large population of RYGB patients (17,930 cases) who had undergone nutritional testing for
Iron deficiency were obtained up to 36 mo following surgery (113). Although the rate of preoperative testing and postoperative follow-up was low (21, 53, 39, and 31% at baseline, and at 12, 24, and 36 mo following RYGB, respectively), iron deficiency increased from 5 to 22%. A strength of this study was the large sample size; a limitation was that the measures used to define iron deficiency were not specified and may have included serum iron, which is not sensitive, or serum ferritin, which can be elevated during inflammation, a common feature of obesity. However, the findings of this study are consistent with others that show exacerbation of iron deficiency when followed from before surgery and up to 60 mo following RYGB, where rates of deficiency between 10 and 45% were reported (77,80,81,86,87,114,115). Although restrictive procedures, including the SG, are thought to induce less malabsorption compared with the RYGB, a similar worsening of iron status and increased prevalence of deficiency (18–24%) following SG surgery has been reported (80,81,113). However, not all studies have shown a deterioration of iron status following SG surgery (77). Iron deficiency can occur without symptoms; however, symptomatic iron deficiency including anemia and feeling fatigue, cold, and a desire to eat ice are commonly reported following bariatric surgery (61,114,116,117).

The complication of iron deficiency post bariatric surgery is difficult to diagnose and treat due to its multifactorial etiology and because its signs and symptoms, such as anemia, are shared with other nutrient deficiencies (114). Because of iron loss through menses, premenopausal women who have bariatric surgery are at increased risk for iron deficiency. Dietary intake of iron following surgery was reported to be lower than the recommended amount (81), possibly because patients avoid red meat, a good source of highly bioavailable heme iron (53). Using stable isotopes, it was demonstrated that absorption of heme and nonheme iron was shown to be reduced following RYGB and SG (118,119), probably due to decreased acidity of the stomach pouch and bypass of the absorptive regions in the intestine. Also important is that iron absorption and metabolism are affected by the availability or status of other nutrients, including zinc, vitamin C, and copper. Excess dietary intake of zinc can compete with iron for absorption (120,121), dietary vitamin C enhances the absorption of nonheme iron (122), and copper is needed for ceruloplasmin, which catalyzes the conversion of Fe^{2+} to Fe^{3+} so that it can be transported by transferrin into circulation (123,124). Regarding diagnosis, total iron-binding capacity or serum transferrin receptor are better measures of iron deficiency compared with serum iron or ferritin; the latter can be elevated in the inflammatory condition of obesity (125). As suggested by recent guidelines, for the correct interpretation of anemia following bariatric surgery, a comprehensive nutritional assessment of iron as well as vitamins B-6 and B-12, folate, copper, selenium, and zinc is warranted, because anemia can result from each of these nutrients (35) (Table 1). The interrelatedness of iron and other nutrients, especially copper, must be considered during treatment using iron oral supplementation, particularly if symptoms persist. Some studies have shown that supplementation with i.v. iron has been shown to be successful (80,111), but this needs to be done with caution to prevent iron overload and in a hospital setting (126).

Malnutrition in Copper

Copper is an essential micromineral that acts as a cofactor in many enzymes that function in electron transfer. These enzymes include cytochrome c oxidase (in the electron transport chain), superoxide dismutase (an antioxidant), amine oxidases (for synthesis of neurotransmitter norepinephrine), and lysyl oxidase (involved in collagen crosslinking) (127). Copper is also needed for iron mobilization in the body; thus, copper deficiency manifests as iron deficiency, resulting in low concentrations of RBCs and white blood cells. Patients undergoing malabsorptive bariatric surgery are at risk for impaired copper status due to hypoacidity in the remnant stomach pouch and bypass of the duodenum. Studies have shown that the concentration of blood copper decreases following RYGB (86,128) and BPD (129,130) surgery and case reports of severe cases of copper deficiency after these surgeries exist in the literature (131–133). Despite the lowering of blood copper concentrations that occurs after malabsorptive surgery, the frequency of copper deficiency after surgery is not clear because copper status is not commonly assessed. The prevalence of copper deficiency ranged from 10 to 15% in cross-sectional studies (128,134) and 4 to 18% (86,128,129) in longitudinal studies. Risk factors for copper deficiency include RYGB and BPD surgery (128,129) (although there is no data on SG), high zinc supplementation (135), and insufficient copper in micronutrient supplementation (81,85). The optimum dose of copper supplementation for prevention of copper deficiency is not known, but recent guidelines (35) suggest that multivitamin and -mineral supplementation for bariatric surgery patients contain copper at doses close to the RDA (0.9 mg), which is not always the case (81,85). Another concern is that anemia resulting from copper deficiency is often misdiagnosed as iron or vitamin B-12 deficiency until serious neurological symptoms, such as unsteady gait, extremity numbness, paresthesias, or paralysis, occur that may be irreversible (132). Current methods for assessing copper deficiency rely on blood copper and ceruloplasmin, which are confounded by obesity-induced inflammation (136) and thus may be falsely elevated during deficiency (Table 1). Also, care must be taken to use metal-free blood collection tubes that are commercially available and to avoid environmental contamination when processing (137). Studies in mice with marginal copper deficiency suggest that the cupro-protein, copper chaperone for superoxide dismutase in erythrocytes, may be a more sensitive biomarker than copper and ceruloplasmin, but confirmation is needed in humans (138).

Malnutrition in Zinc

Zinc is a trace mineral used as a co-factor in a diverse list of enzymes, including those involved in protein synthesis,

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<th>Mineral</th>
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<th>Suggested treatment</th>
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<tbody>
<tr>
<td><strong>Calcium</strong></td>
<td>Preexisting or current deficiency in vitamin D, RYGB, BPD-DS, SG, AGB, insufficient supplementation with calcium and/or vitamin D</td>
<td>Low bone density, osteoporosis, muscle contractions, pain, spasms, paresthesias</td>
<td>Bone densitometry using dual X-ray absorptiometry and referent Z-scores for age, parathyroid hormone, 25-hydroxyvitamin D for vitamin D status, plasma calcium is a poor indicator</td>
<td>Oral supplementation of 1200–1500 mg calcium and at least 3000 IU vitamin D, high-dose vitamin D supplementation (50,000 IU/wk)</td>
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<td><strong>Iron</strong></td>
<td>Preexisting deficiency, menstruation (especially if excessive), BPD-DS, RYGB, SG, gastrointestinal bleeding, insufficient supplementation with iron, avoidance of meat, copper deficiency</td>
<td>Fatigue, impaired work performance and productivity, anemia, inability to regulate body temperature, increased desire to eat ice and non-food items, white finger-nail beds</td>
<td>Serum/plasma transferrin receptor and total iron binding capacity, serum/plasma iron is a poor indicator, serum/plasma ferritin may be elevated in inflammation, also screen for deficiency in vitamins B-6, B-12, folate, protein, copper, selenium, and zinc, and C-reactive protein (to assess inflammatory status)</td>
<td>Oral ferrous sulfate, fumerate, or gluconate to provide 150–200 mg elemental iron daily, vitamin C, i.v. iron infusion, if severe</td>
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<tr>
<td><strong>Zinc</strong></td>
<td>Preexisting deficiency, BPD-DS, RYGB, SG, avoidance of meat, high use of antacids</td>
<td>Poor wound healing, dermatitis, blunting of taste sense, hair loss, impaired immunity</td>
<td>Serum/plasma zinc (care must be taken to avoid contamination), inflammation can decrease zinc concentrations (also measure C-reactive protein)</td>
<td>Oral zinc gluconate, sulfate, or acetate to provide 8–15 mg elemental zinc, 1 mg copper should be given for each 8–15 mg of zinc received</td>
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<tr>
<td><strong>Copper</strong></td>
<td>BPD-DS, RYGB, SG, high use of antacids, high use of zinc supplementation or zinc lozenges</td>
<td>Anemia, leukopenia, unsteady gait, numbness and tingling in hands and feet, painful paresthesias, poor wound healing, paralysis</td>
<td>Serum/plasma copper (care must be taken to avoid contamination, serum/plasma ceruloplasmin, both copper and ceruloplasmin are elevated in inflammation (also measure C-reactive protein)</td>
<td>Oral copper gluconate, oxide, or sulfate to provide 2–8 mg elemental copper, i.v. copper if severe</td>
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1 AGB, adjustable gastric banding; BPD-DS, biliopancreatic diversion with duodenal switch; RYGB, roux-en-y gastric bypass; SG, sleeve gastrectomy.
digestion, immunity, and regulation of gene transcription (139). Like other divalent cations (iron, copper, calcium), zinc absorption requires an acidic environment in the stomach and is absorbed in the proximal intestine. Not surprisingly, zinc absorption was demonstrated to have decreased to 42 and 65% of baseline at 6 and 18 mo after gastric bypass surgery, respectively, in a study using stable isotopes (140). In this study, various markers of zinc status were used, including plasma zinc, hair zinc, erythrocyte membrane alkaline phosphatase, erythrocyte metallothionein, and the exchangeable zinc pool, although the validity of each of these measures has been questioned (141). Nevertheless, using these measures, the prevalence of zinc deficiency increased from preoperative rates of 4–9% to 20–24% at 18 mo following surgery. When serum or plasma zinc was used as an indicator, comparable rates of zinc deficiency were reported by other studies at 24 mo following RYGB (20–35%) and SG (18–34%) surgeries and higher rates were found following BPD (74–91%) (80,81,115,129,142). Also zinc deficiency was found to persist as late as 60 mo following surgery in SG (12.5%), RYGB (21–33%), and BPD (45%) patients (81,115,129). Not all studies have found a decrease in blood concentrations of zinc in patients undergoing malabsorptive bariatric surgery; Rojas et al. (86) showed substantial increases in plasma zinc at 6 mo following RYGB. Assessment of zinc status using systemic zinc concentrations in bariatric surgery patients may be problematic, because serum zinc is decreased in states of obesity-induced inflammation (141,143). Also, zinc is fairly ubiquitous in the environment and care must be taken not to contaminate samples during assessment; use of metal-free blood collection tubes is advised (137,144).

Moreover, it is important to determine the importance of observations of decreased zinc status following bariatric surgery and the associations with concomitant symptoms of zinc deficiency. Signs and symptoms related to zinc deficiency, including hair loss, poor wound healing, and changes in taste acuity, have been reported in patients after bariatric surgery (145,146), but these symptoms may not be specific to malnutrition in zinc and may result from deficiencies in other micronutrients, protein, or fatty acids. Like iron, dietary intake of zinc following bariatric surgery can be lower than the recommended amounts due to avoidance of meat and low compliance with adequate supplementation (142,147). In the study by Rojas et al. (86), extra zinc supplementation has prevented undernutrition in zinc that is normally observed following RYGB. However, a caveat with zinc supplementation is that excess zinc can lead to the sequestration of copper in gut enterocytes due to zinc-induced upregulation of metallothionein, which binds copper and prevents uptake into the circulation (135). In recognition of this phenomenon, consensus guidelines recommend that patients undergoing zinc supplementation receive 1 mg of copper for each 8–15 mg of zinc provided (35) (Table 1). Additional studies are needed to better describe zinc deficiency following bariatric surgery, including methods for screening that are not confounded by inflammation, the recognition of signs and symptoms, and effective strategies for prevention and treatment.

Concerns in Special Populations

Individuals who are eligible for bariatric surgery include adolescents who are in a life stage of growth and development and there are special concerns regarding the risk of malnutrition in this population. The number of children and teenagers undergoing bariatric surgery is currently at 0.13% of the total number of cases but is expected to increase given trends in pediatric severe obesity and popularity of bariatric surgery (30,148,149). Although adolescents experience similar benefits from bariatric surgery related to metabolic health and quality of life (150,151), data on nutritional variables following surgery are scarce (151–153). Nutritional outcomes to date are available mostly from patients undergoing AGB or RYGB surgeries, because the SG is emerging (154,155). The risk of nutritional complications is high because of preexisting malnutrition in vitamin D (156) [and presumably also in iron (74)], the increased nutritional requirements of adolescents (147), and compliance issues that may relate to eating disorders and other psychosocial factors that have been reported in presurgical candidates (157). In teenagers who have RYGB surgery, poor compliance with the postoperative dietary and supplementation regimen has been reported (158). A recent study described the dietary intake and supplement use of adolescents undergoing RYGB and reported low compliance with recommendations for prophylactic calcium supplementation, so intakes of this nutrient were lower than recommended (153). In this same study, participants met or exceeded dietary requirements for intake of folate, iron, and thiamin and vitamins B-12, E, and D, but biochemical indices of these nutrients were not determined. In a separate study, bone mineral content decreased by 7.4% in adolescents 24 mo after RYGB, although Z-scores remained within the normal range. Given the importance of dietary calcium intake during adolescence for bone health (159,160), longer studies are needed to monitor and improve the adequacy of calcium and vitamin D in this population. Similarly, a comprehensive evaluation of other nutrients, especially iron and zinc, is critically needed in the pediatric population because of the detrimental impact of bariatric surgery on these nutrients in adults (32). Consensus guidelines for nutritional support have been developed by experts in pediatric obesity, surgery, and nutrition, incorporating available data from pediatric and adult literature, and the critical need for additional evidence-based research was acknowledged (155,161).

The issue of pregnancy following bariatric surgery is two-sided. On the positive side, bariatric surgery is beneficial for improving reproduction function and fertility (162,163) and also for decreasing obesity-related maternal complications during pregnancy, such as gestational diabetes and preeclampsia as well as macrosomia in the fetus (164,165). Children born to obese mothers are more susceptible to cardio-metabolic disease in adulthood due to fetal programming (166). Exciting developments in this area from studies of genes and other biomarkers obtained from offspring of women before and after gastric bypass surgery are that children born after surgery showed
less predisposition to insulin resistance and other metabolic pathways (167,168). On the negative side, numerous studies have found adverse fetal outcomes after bariatric surgery, such as shorter gestational age, higher risk of being small for gestational age, and lower birth weight compared with fetal outcomes from women with similar BMI, age, and parity who had not undergone bariatric surgery (164,169–172). Some studies have suggested that RYGB leads to worse outcomes (169) compared with restrictive surgeries, including AGB, but other studies did not find a difference (173–175). Adverse fetal outcomes may reflect poor nutritional status of pregnant women who have had bariatric surgery; one study found deficiencies in vitamin B-12, folic acid, iron, and calcium after RYGB (176) and another found higher rates of anemia in bariatric surgery patients compared with nonsurgical controls (164). Another study reported that 85% of women who had undergone bariatric surgery had lower than recommended intake for calcium (177). Thus, although bariatric surgery is promoted as a solution for morbidly obese women who wish to conceive (178), there is a high risk for developmental problems in the fetus related to deficiencies in iron, copper, and zinc and other nutrients with long-term consequences on physical and mental function (179).

In conclusion, the benefits of bariatric surgery are tempered by the high frequency of nutritional deficiencies that occur, some of which are under-recognized and left untreated and lead to devastating consequences to bone health and to the functioning of the immune, nervous, and muscular systems. Bariatric surgery exacerbates preexisting malnutrition in calcium and vitamin D as well as iron due to reduced bioavailability and malabsorption and poor dietary intake and compliance with micronutrient supplementation following surgery. Deficiencies in copper and zinc are difficult to diagnose, because laboratory assessment may be confounded by inflammation and signs and symptoms are shared with deficiencies in other nutrients. These issues are of great importance, especially in special populations such as adolescents as well as pregnant women and their fetuses who may be at risk for developmental problems that affect physical and mental function. Additional research is needed to establish recommendations for prevention and treatment to optimize nutritional outcomes following bariatric surgery.

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**Literature Cited**


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