

# MANAGEMENT OF PATIENTS RECEIVING BARIATRIC SURGERY

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## Learning Objectives

1. Discuss the worldwide prevalence and clinical effect of obesity.
2. Distinguish the differences between bariatric surgical procedures and clinical outcomes among different procedures.
3. Analyze the safety, efficacy, and associated complications of contemporary bariatric procedures in managing obesity.
4. Evaluate the perioperative management of patients undergoing bariatric surgery.
5. Assess the continued effect of bariatric surgery on the absorption and disposition of nutrients and drugs.
6. Construct a patient-specific nutritional and pharmacotherapeutic monitoring plan to minimize adverse events and maximize therapeutic outcomes for a given bariatric surgery recipient.

## Introduction

During the past decade, no other disease or medical condition has attracted more national and worldwide attention than obesity. The public perception and approach toward obesity have changed from regarding it as a minor health problem that mostly affects physical appearance to a global health issue that now drives government policy and the political process. Accordingly, interest in conducting obesity-related research has significantly increased. In addition to a heightened effort to develop safer and more effective weight-loss drugs, many clinical scientists and researchers have expanded their research to understand and compare the safety and effectiveness of different bariatric surgery procedures. Greater interest in obesity-related research has substantially increased knowledge in both the pathophysiology of obesity as well as complications associated with surgical and nonsurgical interventions.

Clinical outcome data on the effect of bariatric surgery on the mortality and morbidity associated with obesity have been very encouraging. The short-term positive effect of some procedures on certain chronic diseases,

such as gastroesophageal reflux, type 2 diabetes mellitus (DM), hypertension, and polycystic ovarian syndrome, is unequivocal and unmatched by pharmacotherapy or other conventional interventions. It appears likely that the indication for some procedures will be expanded beyond morbid obesity in the future. Nevertheless, the long-term (over 15 years) effects of bariatric surgery, such as the development of chronic diseases, cancer, and long-term survival, require further investigation. The focus of this chapter is clinical management issues in obese patients who have received bariatric surgery.

### Using Body Mass Index to Define and Classify Obesity

Body mass index (BMI) is a simple, convenient, and widely accepted measurement of total adiposity; it is commonly used as a threshold to initiate or exclude specific interventions. Currently recommended classifications of obesity based on BMI are summarized in Table 1-1.

**Table 1-1. Summary of Current Classification of Obesity based on BMI and Their Recommended Therapeutic Modalities**

BMI (kg/m <sup>2</sup> )	Weight Category	Recommended Weight-Loss Treatment Modality
< 18.5	Underweight	N/A
18.5–24.9	Normal weight	N/A
25.0–29.9	Overweight	Dietary changes, exercise, behavioral therapy, counseling; consider pharmacotherapy in the presence of comorbidities
30.0–34.9	Class I obesity	Similar to above, plus pharmacotherapy
35.0–39.9	Class II obesity	Similar to above; bariatric surgery to be considered in the presence of comorbidities
≥ 40.0	Class III obesity	Bariatric surgery

BMI = body mass index; N/A = not applicable.

## Abbreviations in This Chapter

BMI	Body mass index
DM	Diabetes mellitus
GI	Gastrointestinal
LAGB	Laparoscopic adjustable gastric banding
NSAID	Nonsteroidal anti-inflammatory drug
PPI	Proton pump inhibitor
RYGB	Roux-en-Y gastric bypass
VTE	Venous thromboembolism

Nevertheless, BMI is only a crude index and has several practical limitations. More importantly, BMI does not differentiate fat mass from muscle mass, nor does it describe the distribution of body fat. There is considerable evidence to suggest that abdominal obesity and waist circumference may have a higher prognostic value for some obesity-related complications, such as type 2 DM and metabolic syndrome, compared with BMI alone, although the exact cutoff point for these values requires further validation.

Although 18–25 kg/m<sup>2</sup> has been widely adopted as the normal range of BMI, including by the World Health Organization, it is also subject to debate. These values were initially determined based on historic U.S. mortality data. Subsequent research has suggested that a regional variation in mortality and morbidity risks of different populations exists despite having the same BMI. For example, data from the Asia-Pacific region have shown that the incidence of type 2 DM and hypertension becomes unacceptably high once the BMI is greater than 23 kg/m<sup>2</sup>. As a result, it is now generally accepted that the upper normal limit of BMI for Asians should be below 25 kg/m<sup>2</sup>. However, a clear BMI cutoff point for overweight and obesity in all Asians cannot be determined based on subanalysis of the regional data. Therefore, the expert panel established ethnic-specific cutoff points for waist circumference as triggers for interventions instead of redefining cutoff points for each population.

Although it has been suggested that future epidemiologic research should apply these ethnic-specific cutoff points to all ethnic groups regardless of their country of residence, the use of these values as triggers for clinical intervention requires further validation. Because North America is an ethnically diverse continent, future interventional research should compare the mortality and morbidity of different ethnic groups using different cutoff points. The value of these cutoff points and how they are defined are important because BMI is not only an integral component of the treatment algorithm for obesity, it is also used as one of the criteria by the government and insurance companies to determine and approve the patient's eligibility and reimbursement for bariatric surgery.

### Prevalence of Overweight and Obesity

According to the current disease definition and epidemiologic statistics, more than 60% of the U.S. population is considered overweight, and more than 33% is obese. Compared with the data available 2 decades

ago, these numbers have doubled. Not surprisingly, the trend observed in the United States is not specific, and the incidence of obesity is rapidly rising in many Western countries at a rate similar to that in the United States. The prevalence of adult obesity in Canada, for example, has more than doubled in the past 3 decades and is now about 24%. A similar trend has been observed in many European and developed countries and regions. The latest data from the World Health Organization indicate that about 1.6 billion adults (15 years of age and older) worldwide are overweight, with at least 400 million being obese. These numbers are expected to double by 2015. Therefore, managing obesity and its associated health complications is a growing global challenge.

Obesity also is a major economic burden to society and health care systems because it is an established risk factor for many chronic diseases and cancers. It is also an independent factor for lengthening hospital and intensive care unit stays, as well as increasing consumption and use of health care resources. From the pharmacotherapeutic standpoint, optimizing drug therapy is challenging in obese patients. Accurate determination of the optimal dosing regimens for obese patients, including patients receiving bariatric surgery, is often difficult. Suboptimal therapy leads to delayed recovery and increased use of health care facilities. However, increased frequency of monitoring, such as therapeutic drug monitoring and laboratory tests, also leads to higher health care costs.

Given that the material, manpower, and financial resources of our society are limited, the continued steep upward trend of obesity and obesity-related illnesses is a huge social and economic burden and must be reversed. Some studies have shown that bariatric surgery decreases overall health care costs by reducing the number and severity of comorbidities in obese patients, resulting in decreased prescription drug costs and hospitalization-associated expense. Modeled cost-effectiveness analysis has also suggested that the two leading bariatric procedures are cost-effective at less than \$25,000 per quality-adjusted life-year.

## Current Treatment for Obesity

### Indications, Treatment Goals, and Treatment Approaches

Measurement of BMI and waist circumference should be incorporated into routine health screening. The primary goal of screening is to prevent excessive weight gain (i.e., maintaining a BMI of less than 25 kg/m<sup>2</sup> with waist circumference below cutoff point for age, gender, and ethnicity) and delay or treat comorbid factors such as type 2 DM, hypertension, or hypercholesterolemia. Indicators suggesting the need for intervention in the obese patient include obesity-related clinical and laboratory abnormalities and the patient's dietary pattern. Inadequately controlled clinical depression, eating disorders, and mood disorders are all risk factors for significant weight gain. Patient readiness to change behaviors and barriers to weight loss should be carefully examined. This evaluation is especially important for candidates for bariatric surgery because lifelong lifestyle

**Table 1-2. Off-label Use of FDA-Approved Drugs for Weight Loss**

Drug	Dosage Studied
Bupropion	300–400 mg daily
Fluoxetine	60 mg daily
Metformin	850 mg twice daily
Sertraline	150–200 mg daily
Topiramate	96–192 mg daily
Zonisamide	100 mg daily initially; titrate up to 600 mg daily

changes are necessary to maintain weight loss and minimize the risks of surgery-related complications. The treatment plan and goals must be individualized.

The overall goals of therapy for obesity should include weight loss, weight maintenance, and control of other weight-related illnesses. The current recommended treatment approach for overweight individuals is primarily lifestyle modification, which includes physical activity, nutritional interventions, and cognitive behavior therapy. The addition of pharmacotherapy is recommended for patients with a BMI of 27 kg/m<sup>2</sup> or greater with comorbidities or a BMI greater than 30 kg/m<sup>2</sup>. Bariatric surgery is indicated for patients with class II obesity and at least one obesity-associated comorbidity or for patients with class III obesity. Because recent studies in obese patients have shown a markedly higher remission rate of type 2 DM in bariatric surgery recipients, the clinical indications for these procedures will likely be expanded in the future.

It is vital for bariatric surgery candidates to fully understand that the surgery is merely a tool to facilitate weight loss and weight maintenance. Both clinicians and patients must fully acknowledge the importance of continued lifestyle modifications and work together over time to optimize the benefits and minimize the long-term risks of bariatric surgery.

### Lifestyle Modifications and Pharmacotherapy

In general, lifestyle modifications alone lead to a 5% to 10% weight loss; their efficacy in weight-loss maintenance varies, but the long-term benefit is usually poor, mostly because of inability to maintain lifestyle changes. This magnitude and duration of weight loss are inadequate for overweight patients with significant comorbidities or for obese patients with a high BMI. The addition of pharmacotherapy may increase total weight loss to up to 10% and maintain weight loss for 1–4 years. Among patients with significant but not life-threatening comorbidities, pharmacotherapy offers more substantial short-term weight loss and additional benefits in glycemic and blood pressure control for a few years.

Only three drugs (phentermine, orlistat, and sibutramine) are currently labeled for use by the U.S. Food and Drug Administration (FDA) for weight loss, with orlistat being the only one also approved for over-the-counter sale. Rimonabant, a cannabinoid-1 receptor antagonist available by prescription in several European countries, has demonstrated good efficacy in inducing weight loss and in improving the metabolic profile of overweight and obese individuals in several international trials. However, the FDA

found the high incidence of neurologic adverse effects—especially the reported cases of suicide, severe depression, and other psychiatric symptoms—to be unacceptable and in 2007 voted against its approval in the United States. Efficacy for weight loss has also been demonstrated by several other marketed drugs (Table 1-2); however, none of these drugs is labeled for use in treating obesity.

### Surgical Therapy

Bariatric surgery is the most effective treatment for class II and class III obesity; it is also the most effective intervention to achieve long-term weight-loss maintenance. In addition, a significant improvement or even remission of many obesity-associated complications (e.g., hypercholesterolemia, hypertension, type 2 DM, gastroesophageal reflux disease, polycystic ovarian syndrome, degenerative joint diseases, nonalcoholic fatty liver disease, obstructive sleep apnea) is observed in many who receive a contemporary bariatric procedure. More impressively, some studies have shown that bariatric surgery leads to a relative reduction of 5-year mortality rate by 89% compared with age- and sex-matched obese patients who have not undergone weight-reduction surgery. With improved surgical techniques, and with better effort to prevent treatment-related complications, the mortality rate associated with bariatric surgery has decreased substantially during the past decade. With careful patient selection, the current reported surgery-associated mortality rate is just below 0.2%. Although outcomes are affected by the type of concurrent medical conditions the patient has, as well as the experience of the treatment center and the performing surgeon, bariatric surgery is a safe and potentially life-saving intervention in treating obesity.

In 2006, it was estimated that at least 177,600 people in the United States received bariatric surgery; the number is believed to be more than 200,000 for 2007. This means that less than 1% of the U.S. population meeting the criteria for bariatric surgery has actually received surgery. It is believed that many more have received bariatric procedures overseas. With the continued increase in the number of obese children and adolescents, the number of bariatric surgery candidates is likely to increase even further during the next decade. When taken with the low procedure-related mortality rate and the expected survival benefit for the surgery, it is likely that most clinicians, regardless of area of practice, will take part in managing patients who are either candidates for bariatric surgery or who are recipients of the surgery.

## Evolution of Bariatric Surgery

### General Principles and Historic Aspect

All current bariatric surgical procedures that result in significant weight loss and weight maintenance involve either (1) malabsorption or decreased absorptive capacity of the gastrointestinal (GI) tract or (2) restriction or limiting of food intake. Some procedures involve both elements with one as the primary mechanism (Table 1-3). Roux-en-Y gastric bypass (RYGB), for instance, is a primary restrictive procedure with a mild malabsorption component.

**Table 1-3. Classifications of Bariatric Procedures**

Type	Mechanism	Procedure
Malabsorptive	Weight loss is accomplished by significant nutrient malabsorption	Jejunioleal bypass Biliopancreatic diversion (malabsorption is the primary mechanism as the flow of food from the remaining stomach into the small intestine is not regulated due to the absence of the pyloric sphincter)
Restrictive	Weight loss is accomplished by decreased food intake due to the reduced food reservoir in the gastrointestinal tract, especially the stomach	Vertical-banded gastroplasty Adjustable gastric banding (including laparoscopic adjustable gastric banding)
Combined restrictive and malabsorptive		Roux-en-Y gastric bypass (restriction is the primary mechanism because it is the rate-limiting step for food intake; malabsorption component is only mild with proximal Roux-en-Y) Biliopancreatic diversion with duodenal switch (pylorus is preserved and thus increases the significance of the restrictive component) Sleeve gastrectomy

Knowledge gained from an understanding of the physiologic changes associated with bariatric surgery further suggests that, in addition to caloric intake reduction, an alteration of the neuroendocrine system, especially the regulation of gut peptides, is an important reason for achieving and maintaining weight loss and improving metabolic disorders. The emerging “hindgut hypothesis” suggests that the anatomic rearrangement of the gut from bariatric surgery leads to a relatively early arrival of food in the distal ileum and the hindgut, which includes the terminal ileum and colon. The distal part of the intestine then sends early signals to trigger the “ileal brake” or “neuroendocrine brake,” which contributes to early satiety and establishes a new homeostasis of gut hormones. These changes in neuroendocrine signaling and regulation affect insulin secretion, release, and sensitivity, as well as nutrient use. This hypothesis is at least partially supported by research using the model of ileal transposition. Future surgical procedures may also emerge based on this theory.

Historically, jejunioleal bypass was the prototype of malabsorptive surgery. First performed in the 1950s at the University of Minnesota, this procedure involves connecting the intact stomach to the terminal ileum, thus bypassing most of the small intestine to cause profound food malabsorption. Although the magnitude of weight loss was substantial, severe complications including malnutrition, wasting, dumping, and dehydration were common and sometimes life threatening. Today, this procedure has essentially been abandoned.

The currently performed bariatric procedures include vertical-banded gastroplasty, biliopancreatic diversion with duodenal switch, and RYGB. Laparoscopic adjustable gastric banding (LAGB), which involves surgical insertion of an implanted device consisting of a hollow silicone band, tubing, and an access port, is the latest procedure; performed extensively in many countries, it received FDA approval for marketing in 2001. Sleeve gastrectomy is a variant of gastroplasty that involves subtotal gastric resection for creation of a long, lesser curve–based gastric conduit. Its

possible role as an accepted alternative procedure in the treatment of morbidly obese patients is being investigated. At present, RYGB remains the leading bariatric procedure performed in the United States, whereas LAGB is more common worldwide. These two procedures are discussed in detail in the following paragraphs.

### Contemporary Procedures

#### Roux-en-Y Gastric Bypass

The RYGB is a combined restrictive and malabsorptive procedure, with restriction likely the leading mechanism in inducing weight loss. The procedure involves gastric volume reduction by creating a small gastric pouch, typically between 15 mL and 30 mL, and staple partition or staple transection of the stomach. A narrow anastomosis is formed between the pouch along the lesser curvature and the jejunum, usually divided 30–40 cm distal to the ligament of Treitz. This bypass limb, also known as the alimentary limb or the Roux-limb, allows the passage of food and other swallowed matter. The biliary limb, which includes the remnant stomach, the intact duodenum, and the portion of the proximal jejunum where food is excluded, is reattached to the jejunum distally through a jejunojejunal anastomosis to allow the entrance of pancreatic enzymes, bile salts, and other enterohepatic hormones (Figure 1-1).

It is widely speculated that weight loss is achieved and maintained by early satiety because of the small capacity of the stomach pouch. In addition, because the food passage bypasses most of the upper GI tract (i.e., gastric antrum, duodenum, and part of the proximal jejunum) where digestive enzymes, bile salts, and some gut hormones (e.g., gastrin, ghrelin) are actively secreted, incomplete digestion and exclusion of some functional absorptive units for nutrients may lead to mild to moderate nutrient malabsorption, further promoting weight loss.

In today’s practice, a standard proximal Roux-en-Y is the most commonly performed version of this procedure, with the length of the Roux-limb typically between 75 cm and 90 cm. This length allows more than two-thirds of the

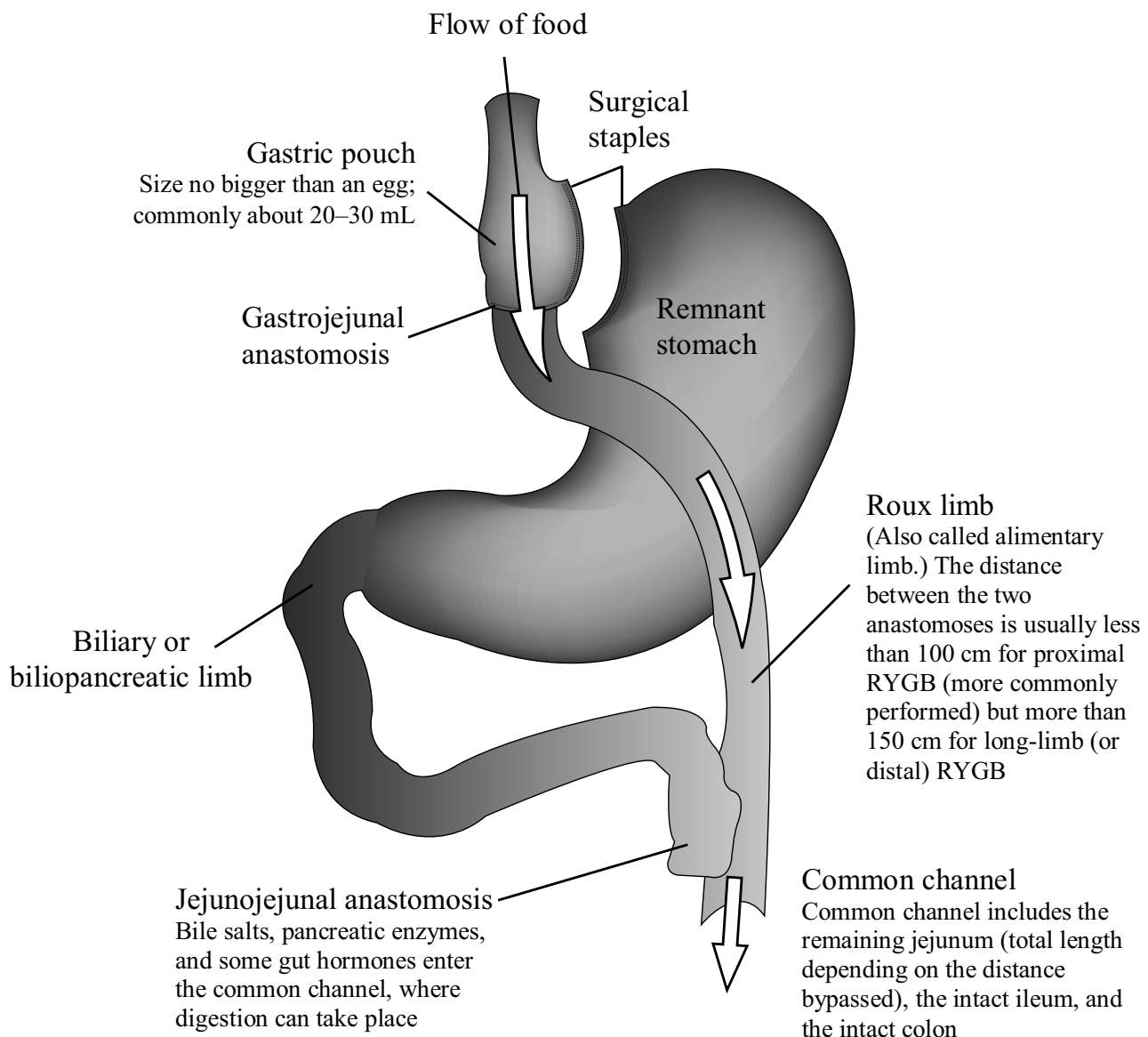


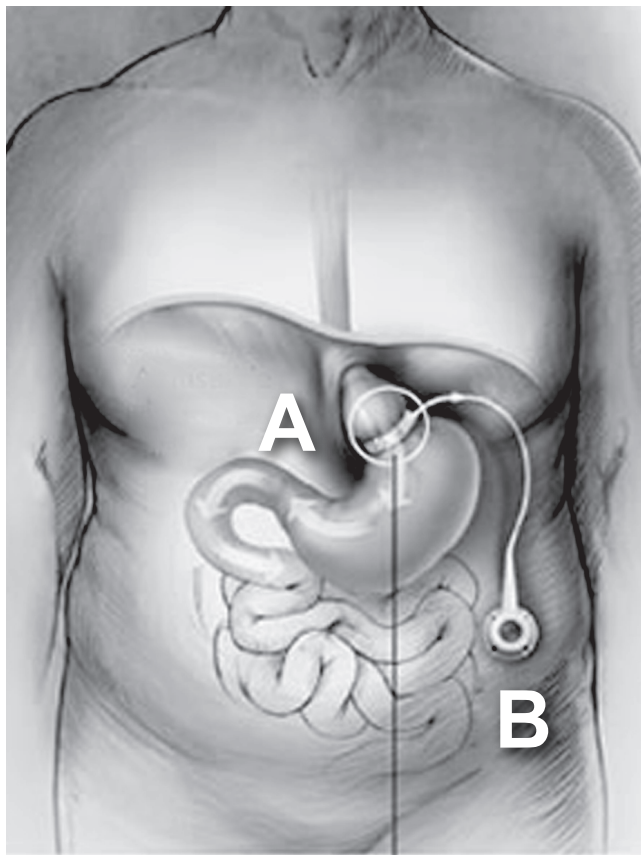
Figure 1-1. Roux-en-Y gastric bypass surgery.  
RYGB = Roux-en-Y gastric bypass.

functional small intestine to be in contact with food for digestion and nutrient absorption. A longer Roux-limb (i.e., longer than 150 cm; sometimes referred to as distal RYGB) tends to increase the magnitude of malabsorption and is usually reserved for superobese patients in whom more profound weight loss is desired. Nonetheless, increasing the length of the Roux-limb also tends to increase the risk of developing dumping syndrome and other malabsorptive disorders.

Dumping syndrome is associated with malabsorption and sometimes severe discomfort. Other common GI-related symptoms include early satiety, nausea, cramps, and explosive diarrhea. Some patients may also experience vasomotor symptoms, which include profuse sweating, flushing, palpitation, dizziness, and an intense desire to lie

down. Mild dumping could be a desirable adverse effect of bariatric surgery because patients can learn what foods to avoid. Nevertheless, persistent and uncontrolled dumping can lead to severe electrolyte disturbances, dehydration, and malnutrition.

Although a “take-down” procedure can be performed if medically necessary, RYGB is generally an irreversible surgery. Recipients must commit to lifelong dietary and lifestyle adjustments to achieve long-term weight maintenance and, more importantly, prevent chronic and sometimes life-threatening complications. Overall, the procedure is generally safe and effective for weight loss and for reducing obesity-related complications, including death. The rate of weight loss is rapid. Maximal weight loss is commonly achieved within the first 2 years, with about



Band Unfilled

Band Filled

Figure 1-2. Laparoscopic adjustable gastric banding (LAGB). The band (A) is inserted laparoscopically. The gastric pouch is about 20 mL to 30 mL. The remaining part of the GI tract remains intact and functional. The access port (B) is implanted under the skin, similar to an intravenous access device. Saline solution is used to inflate the donut-shaped balloon and decrease the size of the stoma, thus restricting food intake. Removal of saline deflates the balloon and opens the stoma to allow more food intake. Complications specific to LAGB placement include slippage of the band, worsening of reflux, gastroesophageal erosion, and port-related complications.

*Adapted with permission from St. Alexius NewStart, St. Louis, MO.*

40% excess weight loss. More than 60% of patients usually maintain a comparable amount of weight loss at 5 years. Long-term data from the Swedish Obese Subjects Study Group showed that the average weight loss from RYGB after 15 years is 27%, which is significantly higher than banding (around 14%) and conventional therapy (2%). A survival

benefit was also observed in RYGB recipients compared with those receiving conventional therapy. Despite these positive results, data on long-term complications after RYGB are limited. The average hospital length of stay for an uncomplicated RYGB procedure is about 3 days.

### Laparoscopic Adjustable Gastric Banding

In principle, LAGB involves inserting a silicone band lined with an inflatable donut-shaped balloon around the neck of the stomach. The balloon is filled with an isotonic liquid and connected to a port implanted under the skin of the abdomen. The degree of restriction provided by the band is controlled by increasing or decreasing the amount of liquid inside the balloon (Figure 1-2). A plain LAGB is a purely restrictive procedure that does not involve bypassing or “reconnecting” any part of the GI tract. Patient adherence to frequent follow-up visits for band adjustments is essential to achieve target weight loss and minimize complications such as dysphagia, erosive esophageal injuries, and port-related complications.

For obese women who wish to bear children, LAGB is usually preferred to other bariatric procedures because it allows adaptation to the altered nutritional and caloric needs of different stages of pregnancy. If necessary, LAGB essentially allows normal nutrient intake and absorption if the stoma is maximally dilated. Several published reports suggest that pregnancy after LAGB is safe, and LAGB may even have a positive effect on obstetric outcomes compared with obese women with excessive weight gain. Nevertheless, no trial has directly compared pregnancy outcomes between restrictive and malabsorptive procedures.

It is rare and generally not recommended to remove the band in LAGB recipients even if adequate weight loss is achieved; the exception is the patient who has developed severe complications necessitating its removal. The patient with a history of poor adherence for follow-up is not a good candidate for LAGB. In addition, patients with severe obesity (e.g., those having BMI greater than 50 kg/m<sup>2</sup>), the presence of severe abdominal adiposity, or chronic dysfunction of the GI tract (e.g., chronic uncontrolled gastroesophageal reflux) are poor candidates for LAGB. The mortality risk associated with LAGB placement is 0.1%, slightly less than with RYGB.

The rate of excessive weight loss is slower than with RYGB or malabsorptive procedures, but the maximal amount of weight loss is thought to be comparable. The rate of weight loss typically plateaus at about 50% between the fourth and fifth year after the procedure. In a recent Australian study, obese patients with type 2 DM receiving LAGB had a 5.5 times higher rate of remission of type 2 DM compared with those receiving conventional therapy. Nevertheless, improvement in overall obesity-related comorbidities is generally less favorable with LAGB than with RYGB, and further research is necessary to determine the long-term clinical and survival benefits of LAGB.

Because the procedure is relatively simple, most centers treat LAGB as an outpatient procedure, and patients are discharged home on the same day. The most common short-term complications associated with the procedure include band failure, band slippage, gastric erosion, infection, and difficulty swallowing.

# Perioperative Management

## Cardiac Management

Because many patients have underlying cardiovascular risk factors, a thorough cardiovascular evaluation is crucial for the success of bariatric surgery. In patients at risk of cardiac complications, perioperative  $\beta$ -blockade may reduce the risk of myocardial infarction and ischemia associated with the surgery. Based on the patient's risk stratification according to the guidelines established by the American College of Cardiology/American Heart Association,  $\beta$ -blockers should be initiated at least 1 week before surgery and continued throughout the perioperative period. Abrupt withdrawal of  $\beta$ -blockers can precipitate angina or even ischemic events. Therefore, each patient's list of chronic medications should be screened before the surgery. Unless otherwise contraindicated, the dosage and regimen for the  $\beta$ -blocker during the perioperative period should be comparable with the patient's chronic regimen. Sustained-release dosage forms should be converted to the equivalent immediate-release dosage forms to allow adequate absorption. Accumulating evidence suggests that the goal of dose titration is to maintain tight heart rate control at less than 65 beats/minute without evidence of bradycardia.

## Glycemic Management

In patients undergoing surgery, poor glycemic control is associated with a higher incidence of infection, delayed wound healing, and increased hospital length of stay. A well-maintained euglycemic state during the perioperative period is therefore essential to improve the outcomes of bariatric surgery. The ideal perioperative glycemic range for these patients is unknown. A target upper limit for serum glucose of 150 mg/dL should offer reasonable outcome benefits for most bariatric surgery recipients, but it may not be practical or attainable in large institutions where one-on-one nursing care is rare.

Patients who received insulin as part of their chronic regimen preoperatively should be instructed to withhold or decrease the basal insulin by 50% the night before the scheduled surgery to prevent profound hypoglycemia. Continuous insulin infusion should be used postoperatively to attain glycemic goal. Once an oral diet is initiated, the regimen can be gradually transitioned back to subcutaneous insulin. It is common to see a patient's insulin requirement decrease to an amount lower than the presurgery dose even as early as hospital discharge. Much of this is mostly the result of a significant reduction of glucose and caloric intake during the immediate postoperative period. Any changes made to the presurgery insulin regimen should be communicated to the patient to prevent drug errors, adverse event, or confusion at home.

For patients taking chronic oral hypoglycemic drugs, the doses should be withheld throughout the perioperative period starting with the dose just before surgery. Short-acting insulin is used to achieve and maintain euglycemia. Once the patient tolerates a reasonable amount of caloric intake, oral hypoglycemic agents may be slowly reinstated. However, because of the risk of hypoglycemia, the long-acting sulfonylurea class of agents should not be restarted unless oral intake becomes stable with no signs of vomiting

or dumping. The same considerations should be considered before reinitiating metformin because dehydration may cause acute renal failure, which can precipitate lactic acidosis. Many patients receiving only oral hypoglycemic agents before the surgery will experience remission of type 2 DM within 1 year after the surgery; these patients will no longer require the continued use of oral hypoglycemic agents. For patients who do not experience disease remission, the requirement for oral hypoglycemic drugs will be substantially reduced.

## Surgical Wound Infection

Another potentially preventable postoperative complication is postoperative wound infection. The effort to decrease the number of surgical site infections in this patient population includes not only proper antibiotic selection but also optimal dosing. A recent study showed that, in patients with a BMI of 30 kg/m<sup>2</sup> or higher, the rate of surgical site infections was significantly higher than in those with a BMI less than 30 kg/m<sup>2</sup> when standard doses of cefotetan and ertapenem were administered before abdominal surgery. Similarly, when cefazolin 2 g was given preoperatively as the prophylactic antimicrobial regimen, a negative relationship between serum antimicrobial concentrations and BMI was observed. Therefore, in the obese patient, doses must be carefully calculated to provide adequate antimicrobial concentrations without causing toxicity. Tight glycemic control also has a complementary effect in reducing the rate of surgical site infections.

For purposes of this chapter, it is not possible to provide a specific dosing regimen for every antimicrobial agent used in the setting of bariatric surgery because the pharmacokinetics of many drugs have not been reported in obese patients, especially those with BMI greater than 40 kg/m<sup>2</sup>. Each regimen must be individualized: rather than using a "standard" adult dose, individualize and optimize a loading dose before surgery. The dose should be determined based on the pharmacokinetic profile specific for the patient's weight and organ function, if data are available in the literature. If data are not available, review the pharmacokinetic profile of the drug (e.g., volume of distribution, tissue distribution) to assess whether the dose can be empirically adjusted.

Obesity is associated with an increase in creatinine clearance and glomerular filtration rates. Thus, it may be necessary to administer a supplemental dose of the antimicrobial agent in a patient with very high BMI, especially if the time of surgery is prolonged (e.g., multiple procedures or intraoperative complications). Therapeutic drug monitoring is imperative, when possible.

## Thromboembolic Complications

Venous thromboembolism (VTE) is one of the leading early causes of death after bariatric surgery. Documented incidence of VTE after bariatric surgery varies from 0.3% to 5.8% within the first 30 days after surgery, depending on the procedure the patient has received as well as the presence of coexisting risk factors. Postoperative VTE incidence is higher after RYGB than LAGB (less than 1%). A national guideline on postoperative VTE prophylaxis after initial hospital discharge has not been established. The reasons for the higher risk of VTE in patients undergoing bariatric surgery are 2-fold. Obesity, in general, increases



the risk of VTE. There is also an increase in venous stasis caused by the pneumoperitoneum, as well as an increase in fibrinogen, factor VIII, and von Willebrand factor related to hypercoagulability caused by the surgery itself. Patients with a previous history of thromboembolic events, BMI over 60 kg/m<sup>2</sup>, hospital length of stay over 5 days, or who have received conversion surgery (i.e., laparoscopic procedure converted to open abdominal procedure intraoperatively) are at especially high risk to develop VTE after surgery. Therefore, VTE prophylaxis and early ambulation are essential components of the overall management plan during the early postoperative period for bariatric surgery recipients.

Appropriate dosing strategies for VTE prophylaxis in severely obese patients remain controversial. The experience of using unfractionated heparin as monotherapy in patients with BMI greater than 50 kg/m<sup>2</sup> is very limited. Based on available research conducted in patients receiving RYGB, enoxaparin 40 mg subcutaneously twice daily appears to be the most efficacious without causing excessive bleeding. Because the risk of VTE and pulmonary embolism appears to be highest within 1 month after surgery, some institutions have begun using an extended postoperative VTE prophylaxis regimen for up to 4 weeks. The ultimate judgment regarding the appropriateness of any specific procedure or pharmacotherapeutic regimen must be individualized in light of all the circumstances presented. An extended VTE prophylaxis regimen, however, does not appear to be necessary for patients undergoing LAGB unless they experience complications requiring hospitalization.

### **Nutritional Management**

Nutritional management is essential and perhaps the most important aspect for the success of bariatric surgery. A comprehensive nutritional management plan must be in place before surgery, and specific nutritional education should begin at the presurgery clinic visits. Although there is no controlled clinical trial to determine the benefit of presurgery caloric restriction, a period of 2–4 weeks of a low-calorie diet immediately before surgery may promote abdominal fat loss, reverse nonalcoholic hepatic steatosis, and optimize the likelihood of performing the surgery through a laparoscopic technique, which has fewer risks and complications compared with an open abdominal procedure. In addition, presurgical caloric restriction serves as a transitional period for patients to adapt to the smaller meals they will be able to tolerate after surgery. In patients with type 2 DM, reduction in total food and caloric intake also allows the gradual tapering of insulin and oral hypoglycemic agents.

Postoperatively, patients may progress from a clear liquid diet to full liquids and eventually to pureed foods within days to a few weeks, as tolerated. With such a restrictive diet, emphasis must be made on maintaining adequate hydration. Encouraging and monitoring hydration status is especially important after intravenous access is removed. In LAGB recipients, serious dehydration and electrolyte disorders may occur if the stoma of the band is too small because this will lead to severe obstruction and aphagia. Therefore, swallowing evaluation should be performed before discharge from the surgery center. In RYGB recipients, the cause of dehydration is usually a lack

of desire to drink or an inability to tolerate the usual volume of fluid intake because of the small gastric pouch. Patient education, especially on adjusting the approach toward fluid consumption (i.e., smaller sips on a more frequent basis), is essential to minimize severe dehydration and other fluid- and electrolyte-related disorders.

### **Drug Management**

Postoperatively, all patients should be transitioned to liquid or crushable formulations of drugs until the anastomoses are healed and the risk of stressing or tearing of the anastomotic sites is minimal. It can take up to 2 months before the patient is able to swallow whole pills again. To increase drug adherence and minimize adverse events, the pharmacist should carefully evaluate the patient's chronic drugs, consider adjusting dosage form, and work closely with the patient and prescribers to ensure a smooth transition. Barriers such as palatability and convenience may play a role in patient adherence and should be considered when designing a regimen. Special attention should be paid to enteric-coated tablets and extended-release formulations. These formulations should be changed to the equivalent dosing regimen using the immediate-release capsules, crushable tablets, or oral liquids. It is generally not recommended to use sustained-release dosage forms in RYGB recipients because of the potential for erratic absorption. In theory, the oral bioavailability of drugs for LAGB recipients should not be affected by the procedure as long as the dosage form can pass through the stoma. Suppositories should be avoided in case the patient develops diarrhea or dumping syndrome. Once the patient's new drug regimen has been instituted, the patient should be informed of all formulation and dosing changes; this can minimize potential drug errors and confusion surrounding postoperative drugs versus preoperative drugs.

Postoperative use of drugs associated with increased risk of GI bleed (e.g., nonsteroidal anti-inflammatory drugs [NSAIDs], corticosteroids, antiplatelet agents) and the need for short-term ulcer prophylactic therapy remain controversial. The reported incidence of post-RYGB marginal ulceration, a type of gastric ulcer developed in the jejunal mucosa near the site of a gastrojejunal anastomosis, is between 2% and 7%, although a 16% incidence was reported in one study. The incidence of epithelial bleeding in the remnant stomach is unclear, although it is considered very rare. Smoking, use of NSAIDs or clopidogrel, and history of *Helicobacter pylori* infection have been identified as risk factors predisposing to marginal ulceration. A retrospective study of 1001 RYGB recipients showed that recent NSAID use was associated with an 11-fold higher risk for developing marginal ulcers as diagnosed by endoscopy. Based on these findings, the short-term use of NSAIDs should be discouraged, and their chronic use should be avoided in RYGB recipients. The benefits versus risks of using corticosteroids and other antiplatelet agents should be carefully assessed.

Proton pump inhibitors (PPIs) have a demonstrated protective effect against marginal ulceration and are also effective in treating patients who have developed marginal ulcers. Therefore, if the use of corticosteroids, antiplatelet agents, or NSAIDs is medically indicated in RYGB recipients, it is advisable that a PPI be prescribed for ulcer prophylaxis.



Histamine<sub>2</sub>-receptor antagonists may also be used, although their efficacy in ulcer prevention is not as established as PPIs. The protective effect of sucralfate is highly doubtful in these patients because the short transit distance from the gastric pouch to the jejunum and the luminal pH of the small gastric pouch are unlikely to fully activate the drug. In addition, sucralfate use in this setting may further alter or impair the absorption many drugs and nutrients. Therefore, its use is not recommended. The benefit of empirical postoperative PPI use in patients without a known risk factor for marginal ulceration has not been determined.

Bisphosphonate use in bariatric surgery recipients is also a controversial topic. Given the risk associated with gastroesophageal injuries, bisphosphonate use after RYGB may be an independent risk factor for developing marginal ulceration. However, with the increased risk of osteoporosis in bariatric surgery recipients, bisphosphonate therapy may be beneficial in maintaining the patient's bone mass. Unfortunately, the clinical effect of bisphosphonate therapy in preventing or retarding osteoporosis in bariatric surgery recipients has not been assessed. Thus, the empirical use of oral bisphosphonates cannot be recommended for all bariatric surgery recipients, and the decision to use a bisphosphonate should be evaluated on a case-by-case basis. Because pill esophagitis (i.e., a form of injury to the esophageal lining caused by prolonged contact with a caustic oral agent) is one of the proposed mechanisms of bisphosphonate-associated GI injuries based on endoscopic findings, it is important to ensure these pills can pass through the esophageal junction unobstructed in bariatric surgery recipients, especially those with LAGB. In patients considered at high risk of developing esophageal or marginal ulceration, intravenous bisphosphonate therapy (e.g., zoledronic acid 5 mg yearly, ibandronate 3 mg every 3 months) would be a safer choice.

## Effects on Nutrient and Drug Absorption

### Nutrient Absorption

Bariatric surgery is associated with an increased risk of developing macro- and micronutrient deficiencies. In today's practice standard, with adequate clinical follow-up and route laboratory monitoring, profound macronutrient deficiencies are rare unless the patient does not adhere to dietary guidance, experiences a relapse of psychiatric illnesses (especially eating disorders), or suffers from severe surgical complications such as anastomotic leaks. Micronutrient deficiencies, however, are far more common. Insufficient knowledge of micronutrient homeostasis by the health care provider; inadequate understanding by practitioners, especially primary care providers other than the surgical team, of the differences and risks among various surgical procedures; insidiousness of the symptoms associated with micronutrient deficiencies; and the misconception by both patients and care providers that trace elements and vitamins are merely dietary supplements with little therapeutic value are all important factors that lead to insufficient prevention and to a delay in the diagnosis of micronutrient deficiencies.

There are three basic principles that should guide clinicians when managing recipients of bariatric surgery. The first principle is that, because vitamin and other micronutrient deficiencies are common in obese patients, bariatric surgery candidates are predisposed to clinically significant micronutrient deficiencies. Second, the GI tract anatomy after surgery is important because it influences the pattern and extent of nutrient absorption. Finally, procedures that involve a more profound malabsorptive component possess a higher risk of chronic malabsorption and malnutrition. Therefore, patients who received a jejunoileal bypass, biliopancreatic diversion, or any combination of procedures involving extensive small bowel resection or bypass are more prone to develop nutrient deficiencies than RYGB recipients.

Similarly, the risk of having nutrient malabsorption is also higher in patients receiving distal RYGB (e.g., Roux-limb longer than 150 cm) compared with proximal RYGB or LAGB. More importantly, the anatomic changes to the gut associated with the surgery also affect how nutrients should be replaced and supplemented. A procedure with an extensive malabsorptive component could decrease the overall absorptive capacity for nutrients because of the loss of surface area for absorption and possibly saturation of the remaining transport mechanisms. Specific minerals or vitamins may need to be given several times each day to allow optimal absorption. It is therefore critical to obtain a complete surgical history of the patient through face-to-face discussion and careful review of all records, if possible, before making clinical assessment and implementing the management plan.

The presence or history of depression, psychiatric illness, and particularly eating disorders in patients must also be recognized. Severe postoperative nutrient malabsorption suggests that drug malabsorption may also occur; this can lead to a relapse of previously controlled psychiatric illnesses and eating disorders. Chronic malabsorption associated with changes to the texture and quality of the food, drugs, and supplements should also be investigated. For instance, replacing solid food with too many sugar-containing oral liquids, including those containing nonabsorbable sugars, can lead to chronic diarrhea and dumping. Many liquid drugs and rehydration solutions also contain a significant amount of sorbitol, which can cause diarrhea and malabsorption. Exclusion of the gastric parietal cells, such as in the case of sleeve gastrectomy or RYGB, also affects absorption of nutrients, especially those with a pH-sensitive absorption pattern such as cobalamin.

### Cobalamin, Folate, and Iron

Chronic anemia in bariatric surgery recipients is usually associated with a deficiency of cobalamin, folate, iron, or a combination of these micronutrients. The incidence of hypcobalaminemia is reportedly between 26% and 70% in recipients of RYGB. Symptomatic clinical deficiency usually does not occur until much later after surgery. The incidence has not been quantified with LAGB, although it is expected to be much lower. Decreased food intake partially contributes to the clinical deficiency; however, the primary mechanism is functional malabsorption of the nutrients, especially iron and cobalamin, from the GI tract. In cobalamin malabsorption after RYGB, two mechanisms

are commonly involved. The failure to separate protein- and foodstuff-bound cobalamin because of the absence of gastric acid reduces the quantity of absorbable dietary cobalamin. The overall decrease in the release of intrinsic factor further impairs the magnitude of cobalamin absorption from the terminal ileum because the efficiency of cobalamin transcellular uptake in the terminal ileum is much lower for free cobalamin than when it is complexed with intrinsic factor.

With an estimated incidence of less than 30%, folate deficiency is less common than hypcobalaminemia. The cause is primarily from reduction of dietary folate intake. Conversely, iron deficiency is far more common after bariatric surgery. Some studies have suggested that symptomatic iron deficiency occurs in more than 40% of recipients of RYBG within 4 years. Patients who received a longer Roux-limb, primary malabsorptive procedures, and significant gastric resection are particularly at risk of developing iron malabsorption and clinical deficiency. The etiology of iron deficiency is multifactorial. Reduced dietary intake; decreased conversion of ferric ion to the ferrous state because of achlorhydria; and, in patients with RYGB and other malabsorptive procedures, the exclusion of duodenum and proximal jejunum (where the highest efficiency of iron absorption takes place) all contribute to iron deficiency.

Preoperative screening followed by postoperative monitoring is the most effective approach in preventing vitamin and mineral deficiencies. All bariatric surgery candidates should be screened for chronic anemia; if found, the cause of anemia should be identified. If micronutrient deficiency associated anemia is confirmed, treatment with appropriate supplementation should be initiated before surgery. Postoperatively, these minerals should be monitored at least yearly in the first 5 years during the active weight-loss period. In patients at high risk of these deficiencies, more frequent monitoring should be performed. It must be recognized that monitoring of mean corpuscular volume alone is insufficient to assess the body stores of these micronutrients because this laboratory test result may be affected by the concurrent presence of several nutrient deficiencies.

Prevention of hypcobalaminemia includes daily supplementation of at least 350 mcg of cyanocobalamin as oral tablets or orally disintegrating tablets. Alternatively, intramuscular injection of 1000 mcg of hydroxocobalamin monthly, 3000 mcg intramuscularly every 6 months, or weekly inhalation of the nasal formulation (500 mcg) may be used, depending on each patient's preference, financial resources, and clinical response. Because its absorption occurs throughout the small intestine, folate deficiency can usually be prevented by daily supplementation of 1–2 mg of oral folate or a prenatal vitamin tablet.

Most iron deficiency can be prevented or improved by a multivitamin supplement that contains at least 65 mg of elemental iron. For severe or persistent iron deficiency, additional iron supplementation (300 mg of ferrous sulfate three times daily) should be given. To maximize oral absorption, patients should be instructed to take the iron supplement with juices, applesauce, or another acidic liquid or snack but separate from calcium and magnesium supplements. There is a theoretical benefit of using iron in other salt forms (e.g., fumarate, gluconate, polysaccharide) because the oral bioavailability of elemental iron in these

compounds is less affected by pH; however, the clinical relevance has not been examined. In addition, bariatric surgery affects the physiology of the GI tract, which also affects micronutrient absorption and homeostasis independent of gastric acid release. Therefore, the highest priority is to customize an iron supplementation regimen to prevent chronic iron deficiency according to affordability, adherence, and GI tolerance.

### Calcium and Vitamin D

Bariatric surgery is an important risk factor for accelerating bone loss leading to osteoporosis. Some studies have detected a mean increase in parathyroid hormone concentration of 90% from baseline in all patients within the first year after bariatric surgery. Bone mineral mobilization was evident by a significant rise in the serum bone-specific alkaline phosphatase and C-telopeptide. Worsening of hyperparathyroidism was noted postoperatively in many patients despite calcium and vitamin supplementation. The accelerated bone loss is likely caused by calcium and vitamin D malabsorption. Although calcium absorption takes place throughout the entire GI tract, the proximal region of the small intestine provides the most active and regulated area for calcium absorption.

Calcium absorption is mediated by two processes: vitamin D–regulated transcellular active transport, which takes place in the duodenum and upper jejunum; and concentration gradient–driven paracellular diffusion processes, which occur throughout the intestine. Dietary calcium availability and absorption is reduced after bariatric surgery because of decreased food consumption, which is likely the primary cause of increased bone resorption. Nevertheless, procedures with a malabsorptive component (e.g., RYGB) also redirect the flow of food away from the duodenum and proximal jejunum where transcellular calcium transport is most active and efficient. Accordingly, a functional impairment of calcium absorption is present, which further augments total body calcium deficiency.

Serum calcium concentration is not a reliable indicator of total body calcium status because a normocalcemic state is often maintained at the expense of bone loss. Given the reduction in food intake, calcium supplementation is necessary in all bariatric surgery recipients regardless of the procedure. Daily supplementation with at least 1200 mg of elemental calcium in divided doses should be given. Clinicians should remind patients to take their calcium supplement with food but not with their iron supplement, because calcium may impair iron absorption. Although, in theory, calcium citrate is preferred over calcium carbonate because its oral absorption is less affected by pH, the clinical benefit has not been proved, and absorption kinetics studies comparing relative calcium oral bioavailability among different formations and salt forms report conflicting results. Because calcium carbonate generally costs less than calcium citrate, is available as chewable tablets, and offers more elemental calcium than calcium citrate on a per gram basis, it is a more practical form of calcium supplementation.

Given the volume of literature consistently showing a high incidence of hypovitaminosis D in obese patients, the accelerated bone loss after bariatric surgery, and the increased recognition of the importance of vitamin D in general health, a baseline serum 25-hydroxyvitamin D concentration should be measured and hypovitaminosis D

**Table 1-4. Reported Nutrient Deficiencies and Their Common Signs and Symptoms in Bariatric Surgery Recipients**

Nutrient Deficiency	Associated Signs and Symptoms
Protein energy malnutrition	Marasmus; anasarca; ascites; wasting
Essential fatty acid deficiency	Scaly and cracking skin; hair loss; brittle nails; dry mucous membranes; immunosuppression
Calcium	Usually asymptomatic unless severe deficiency has occurred, in which case altered mental status, tetanus, and generalized weakness can occur
L-Carnitine	Lipid intolerance; hyperammonemia without other hepatic dysfunction; encephalopathy
Cobalamin	General weakness; anemia, especially megaloblastic anemia, unless iron deficiency is also present
Copper	Fatigue; unexplained bleeding under the skin; anemia; cardiomegaly
Folate	General weakness; anemia, especially megaloblastic anemia, unless iron deficiency is also present; GI discomfort
Iron	Tiredness; shortness of breath; general malaise; anemia, especially microcytic anemia
Thiamin	Numbness sensation in fingers and/or toes; neuropathy; irritation; beriberi; Wernicke encephalopathy in severe cases
Vitamin A	Night blindness
Vitamin D	Usually asymptomatic; possibly bone and joint pain; depression; laboratory test may reveal hyperparathyroidism
Zinc	Nonspecific symptoms; skin disorders; hair loss; dysgeusia; anemia unexplained by iron, folate, or cobalamin deficiency

GI = gastrointestinal.

corrected before bariatric surgery. If the 25-hydroxyvitamin D serum concentration is marginal (i.e., between 20 ng/mL and 25 ng/mL), the parathyroid hormone concentration should also be checked. In patients with hypovitaminosis D or secondary hyperparathyroidism, oral vitamin D 50,000 IU weekly for 8 weeks should be initiated before the surgery. In patients with severe deficiency (i.e., serum 25-hydroxyvitamin D concentrations less than 8 mcg/mL), 50,000 IU can be given twice weekly. A repeat serum vitamin D concentration should be checked in 8–12 weeks to evaluate adequacy of replacement.

The goal is to maintain serum 25-hydroxyvitamin D concentration at 30 mcg/mL or higher and prevent secondary hyperparathyroidism. Postoperatively, recipients of standard RYGB and LAGB should receive no less than 400 IU of vitamin D supplementation daily, although most patients will require doses closer to 1000 IU, especially for patients living in cities in the northern and southern regions of the planet during the winter months. Higher maintenance dosages should be given to patients with confirmed hypovitaminosis D before the surgery. In patients receiving long-limb RYGB or other primary malabsorptive procedures, at least 2000 IU of vitamin D should be taken daily. The dosage should be adjusted based on repeat serum 25-hydroxyvitamin D concentrations, which should be monitored no less than yearly.

#### Other Nutrients

Thiamin deficiency has been increasingly recognized and reported in bariatric surgery recipients. It is usually manifested as progressive joint and muscle pain; peripheral neuropathy; beriberi; acute psychosis; and, in some serious cases, as Wernicke encephalopathy. Thiamin deficiency is a chronic disorder that develops over weeks or even months insufficient nutrient intake. Among patients who receive at least the daily recommended amount of thiamin (1.5 mg daily or more) in a multivitamin supplement, clinical deficiency is rare. Therefore, all bariatric surgery recipients

should receive a daily thiamin-containing multiple vitamin supplement.

Thiamin deficiency is usually diagnosed by reviewing dietary history and evaluating clinical symptoms. Although plasma thiamin concentration may be measured, the more sensitive and preferred laboratory test for thiamin deficiency is either erythrocyte transketolase activity or total erythrocyte thiamin concentration. The turnaround time for these tests is usually delayed, making them less useful for clinical monitoring. Given the relatively safe profile of thiamin, supplementation in patients with suspected clinical deficiency should be empirically initiated as soon as blood samples have been drawn. An initial regimen of 100 mg of thiamin twice daily either intramuscularly or intravenously can be instituted. Note that intestinal thiamin absorption is saturable at doses around 25 mg; therefore, larger doses must be given parenterally for maximal effect on serum thiamin concentrations. The dosages may be reduced to 50–100 mg daily after 2 weeks or when clinical improvement is observed.

More recently, there have been isolated reports of clinical deficiencies of vitamin A, vitamin C, carnitine, essential fatty acids, and zinc. These disorders are more likely to occur in patients who have an extensive history of malnutrition or dumping associated with a primarily malabsorptive surgery. The signs and symptoms of these deficiencies are summarized in Table 1-4. Treatment and monitoring plans are similar to other documented cases of severe malnutrition.

#### Effect on Drug Absorption

Despite a half-century of clinical experience with millions of surgeries performed, the effects of bariatric surgery on drug absorption remain poorly understood. Clinical data, such as those from descriptive pharmacokinetic studies or patient case reports, are scarce. Among the 20-some reports published in this area, the quality of the data varies significantly. Most importantly, most of these reports suffer

from a common limitation because either the anatomy of the patients studied was not described or the data from patients receiving significantly different procedures were combined, making meaningful clinical interpretation and extrapolation of the results impossible.

Exclusion of drugs from the stomach per se, as in RYGB (and, arguably, sleeve gastrectomy), should have a negligible effect on overall oral bioavailability because most drugs are reasonably well absorbed in the rest of the small intestine. One known exception is ethanol: both the rate and extent of oral absorption of ethanol are increased in RYGB recipients. These surgical procedures, however, lead to achlorhydria, which may negatively affect the dissolution of solid dosage forms of several drugs and hypothetically reduce the total amount absorbed. Nevertheless, based on very limited historic data, the influence of achlorhydria on the oral bioavailability of drugs, including acidic drugs, appears minimal. Absorption of liquid dosage forms is not expected to be affected. Whether the increase in luminal pH in the gastric pouch and the Roux-limb associated with RYGB changes the absorption kinetics and duration of effect of newer drugs with a pH-dependent delivery system (e.g., duloxetine) is unknown. Close and continued monitoring of a patient's clinical response to any orally administered drug after surgery is highly recommended.

In principle, the region of the intestine with the highest absorptive efficiency and capacity for drugs is the proximal small intestine. Therefore, malabsorptive procedures that involve significant exclusion of the proximal small intestine would have the most negative effect on oral drug absorption. This fact is supported by a few published reports of patients who have received a jejunioileal bypass. The effect caused by restrictive procedures and mild malabsorptive procedures should be minimal. For RYGB, given the lack of published data, a negative effect on drug absorption may become more clinically significant with a longer Roux-limb and shorter common channel (i.e., shorter distance between jejunojunal anastomosis and the terminal ileum). Again, careful preoperative evaluation, confirmation of the postoperative GI tract anatomy, and close follow-up are essential. When therapeutic drug monitoring is an option, it should be performed.

### **Effect on Drug Metabolism and Transport**

The overall effect of bariatric surgery on intestinal drug metabolism and transport is unknown. Although the exclusion of intestinal lumen may decrease the total absorptive surface area for drugs, increased drug concentrations delivered to the remaining functional segment of the small intestine may cause saturation of the intestinal enzymes and transporter systems. This saturation may possibly compensate for the loss of absorptive surface caused by the bypass. Similarly, the overall effect of bariatric surgery on hepatic clearance is unknown. In obese patients with nonalcoholic steatohepatitis, hepatic CYP2E1 activity was shown to decline after vertical-banded gastroplasty, a form of restrictive bariatric procedure. This change in enzymatic activity is likely the result of significant weight loss and the resolution of non-alcoholic fatty liver diseases such as steatohepatitis and is not necessarily specific to the bariatric procedure.

## **Role of the Pharmacist**

Obesity is a chronic disease that affects millions of people. Bariatric surgery has proved to be a safe and effective method for managing obesity. Nevertheless, these procedures are potentially associated with many surgical, medical, and nutritional complications. A multidisciplinary approach is necessary to maximize the benefits and minimize the risks of bariatric surgery. Pharmacists are the health care professionals most qualified to facilitate the transition from drugs taken before surgery and during the immediate perioperative period to the postoperative period. Issues such as dosage form selection, dose conversion, and the need for therapeutic drug monitoring during the transitional period are essential for bariatric surgery success and for optimal maintenance of therapy for other concurrent medical conditions.

Postoperatively, most patients will experience an improvement of other chronic diseases such as type 2 DM, dyslipidemia, and hypertension. With good understanding of the basic principles and complications of the surgical procedures, as well as the training in pharmacotherapy for chronic medical disorders such as hypertension, pharmacists are able to bridge the gap between the surgical and medical teams and serve as the facilitator of patient care. Pharmacists have the training and experience to take a major part in the continuing management of these patients. In addition, pharmacists should work closely with clinical dietitians in selecting the dosage and dose forms of mineral and vitamin supplementation to optimize long-term treatment outcomes. With the continued increase in the volume of bariatric surgery performed, there is no boundary to the potential opportunity for pharmacists to become involved in direct patient care.

Bariatric surgery is an area of unlimited opportunities for research and generation of new knowledge. For example, data describing the effects on drug pharmacokinetics are virtually nonexistent. Clinicians are encouraged to report and publish any relevant clinical observations they encounter, whether they are in the format of a conference abstract, research letter, case report, or descriptive trial. Any experience and information shared would be helpful in guiding and refining patient management and could lead to improved clinical outcomes.

From the clinical application standpoint, especially regarding making dose adjustments and the specific monitoring plan for individual drugs, the authors cannot offer standardized dose adjustment algorithms for the following patient-specific: the effect on drug absorption is specific to the procedure performed; the patient's nutritional status and magnitude of weight loss can affect drug disposition and response; the absorption profile of a drug may change with time because of intestinal adaptation; and the improvement or worsening of other comorbid conditions after bariatric surgery, or the presence of surgery-related complications, may alter drug response.

Clinicians must use all the knowledge they possess (including, but not limited to, physiology, pharmacology, pharmacokinetics, pathophysiology, and anatomy), monitor each patient's clinical response, and exercise sound clinical judgment to individualize therapy. When therapeutic

drug monitoring is available or applicable, it should be performed to guide clinical decision-making. If therapeutic drug monitoring is not possible for a specific drug, closely monitoring the patient's clinical response, symptoms, and any other relevant laboratory results will assist in the clinical decision-making process.

## Conclusion

Obesity is a chronic disease state that affects many aspects of health. Preparation for bariatric surgery and the lengthy weight-loss period, especially in patients with several comorbidities, is a complex and challenging process. Successful management of this process will require the integration of many areas of the health care system that include nutritional management, surgical care, medical management of chronic diseases, and social support.

With the projected increase in the number of bariatric surgeries to be performed, the need for clinicians skilled in the care of these patients during the postoperative period will continue to rise. Practitioners who will be in high demand are those who are proficient in disease state management and chronic health maintenance, knowledgeable in pharmacotherapy, and able to assess patients and function independently. Pharmacists appear to be the perfect fit for this role.

Bariatric surgery is a dynamic specialty. In addition to being directly involved in typical patient care activities, practitioners specialized in this area have the obligation to disseminate knowledge to continue to improve the quality of health care delivery and affect public health policy. With many opportunities available, pharmacists must be actively involved and become an integral part of any successful bariatric surgery program.

## Annotated Bibliography

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This article is an updated systematic review and meta-analysis of the important studies comparing the effectiveness of different weight-loss modalities, which included diet alone, diet and exercise, exercise alone, meal replacements, very-low-energy diets, pharmacotherapy, and counseling alone. All major interventional trials with at least a 1-year follow-up were analyzed. The results show that reduced-energy intake and/or pharmacotherapy lead to only modest weight loss of 5% to 9% of total body weight. Peak weight loss occurs at about 6 months after initiation of therapy. Long-term weight-loss maintenance is 3–6 kg in 2 years. Counseling alone and exercise alone generally have lower efficacy for weight loss at any time point. This study confirms the speculation and the results of many smaller trials because most of the current weight-loss methods do not lead to a clinically significant reduction and maintenance in body weight for morbidly obese patients. The results provide further support for adopting and expanding the role of bariatric surgery in the long-term management of obesity.

2. Bult MJ, van Dalen T, Muller AF. Surgical treatment of obesity. *Eur J Endocrinol* 2008;158:135–45.

This article is highly recommended for clinicians who would like to better understand each of the bariatric surgical procedures currently performed. The biggest strength of this article is that it also provides a systematic comparison and review of the effect of obesity on other clinical outcomes, such as improvement in glycemia and lipid profile by each procedure. The results are current and well organized according to different disease states.

3. Sjöström L, Narbro K, Sjöström CD, Karason K, Larsson B, Wedel H, et al. Effects of bariatric surgery on mortality in Swedish obese subjects. *N Engl J Med* 2007;357:741–52.

This study, one of the most important and influential in the field of bariatric surgery and obesity, shows the long-term benefit and safety of bariatric surgery, particularly for RYGB and adjustable gastric banding. This is a follow-up report for the Swedish Obese Subjects study published in 2004. That study included 10-year follow-up data. This current article provides the results of a 15-year follow-up. The results essentially are similar to the 2004 results and further support that restrictive surgery, including RYGB, is safe and effective in inducing and maintaining long-term weight loss. More importantly, this current article provides comprehensive results on long-term morbidity and mortality. The findings are very encouraging. Of note, the adjustable gastric band used in the Swedish study is a different product from the band currently used in the United States, although the principle is similar. This is a must-read article for anyone interested in research related to obesity and metabolic disorders.

4. Dixon JB, O'Brien PE, Playfair J, Chapman L, Schachter LM, Skinner S, et al. Adjustable gastric banding and conventional therapy for type 2 diabetes: a randomized controlled trial. *JAMA* 2008;299:316–23.

This landmark trial, published in early 2008, uses data from a well-respected Australian research group. The researchers compared the effect on type 2 DM of conventional care by lifestyle change with the addition of LAGB. The 2-year follow-up results show that the addition of LAGB to conventional therapy leads to a 5.5 times higher remission rate for type 2 DM (73% vs. 13%). The LAGB procedure also leads to 10 times more weight loss than conventional therapy without serious complications. Although the study sample was relatively small (n=60; 92% completion rate) and the results need to be confirmed in larger-scale trials in a more diverse population, the potential implication of the findings is very significant. Most of all, because this study exclusively focuses only on patients with class I and class II obesity (i.e., BMI between 30 kg/m<sup>2</sup> and 40 kg/m<sup>2</sup>), the results suggest that even the relatively “less-obese” patients with type 2 DM could benefit substantially from LAGB. It is possible that the indications for LAGB will be expanded partially based on these results.

5. Compher CW, Badellino KO, Boullata JI. Vitamin D and the bariatric surgical patient: a review. *Obes Surg* 2008;18:220–4.

This article is an up-to-date and focused systematic review of the current issues surrounding the need for vitamin D assessment and supplementation in patients undergoing and those who have received bariatric surgical procedures. The results suggest that most bariatric surgery candidates have baseline hypovitaminosis D, and many will have secondary hyperparathyroidism. Recipients of bariatric surgery procedures with malabsorptive components are at higher

risk of developing further hypovitaminosis D and bone loss, and calcium and vitamin D supplementation at currently recommended dosages is often inadequate to restore the deficiency and suppress secondary hyperparathyroidism. The authors raise important questions on the current postoperative management approach toward bariatric surgery patients, especially for RYGB and other malabsorptive surgery recipients. Based on the findings, vitamin D screening and monitoring should be a part of all patient management plans both pre- and postoperatively. The question on how to better manage vitamin deficiency requires further investigation.

- Schweitzer DH, Posthuma EF. Prevention of vitamin and mineral deficiencies after bariatric surgery: evidence and algorithms. *Obes Surg* 2008;18:1485–8.

This article provides several excellent algorithms and decision-making tables on micronutrient monitoring after bariatric surgery. That the schedule for follow-up monitoring and the supplementation regimens are mostly based on opinion rather than evidence can be viewed as a weakness of this article. Nevertheless, information provided offers a logical starting point for patient care and is particularly helpful for clinicians and centers beginning a bariatric surgery program. Further validation of the suggested approaches is definitely necessary.

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This review is a more comprehensive discussion on general nutritional deficiencies in patients after RYGB. The focus is broader than the article discussed in reference 6, with a more comprehensive summary of clinical data and results. The authors have also addressed issues on nutritional management of pregnant women who previously have received an RYGB procedure, an area in which research and data are desperately needed. Overall, it is a good article to help clinicians establish a more structured monitoring program for postoperative nutrient deficiencies.

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This study is one of the most important articles to address the effect of RYGB on bone health and is one of the very few articles to include clinical values specific to measuring bone mobilization. The investigators studied a total of 230 patients who underwent preoperative baseline bone mineral density scans. At 1 year after surgery, the data showed that total forearm, total hip, and total lumbar spine bone densities decreased by 0.55%, 9.27%, and 4.53%, respectively, although radius bone density increased overall by 1.85%. By the second postoperative year, total forearm bone density suffered from an additional 3.62% reduction, whereas no further changes in the radius were detected. Parathyroid hormone concentration increased persistently in the 2-year follow-up, although no significant changes to serum 25-hydroxyvitamin D concentrations were detected, possibly because of supplementation. This study confirms the negative effect of weight loss on bone health and emphasizes the importance of a comprehensive and patient-specific longitudinal follow-up plan for patients receiving RYGB.

- Riedt CS, Brodin RE, Sherrell RM, Field MP, Shapses SA. True fractional calcium absorption is decreased after Roux-en-Y gastric bypass surgery. *Obesity* 2006;14:1940–8.

One of the most important questions from a nutritional and endocrine standpoint is whether calcium and vitamin D deficiencies are the result of reduced dietary intake alone or impaired intestinal absorptive capacity. The latter suggests that the conventional supplementation methods may be inadequate in restoring the deficiency because the body cannot absorb the nutrients adequately. This elegantly designed and conducted study addressed this issue with a focus on calcium fractional absorption. Using a tracer method, a relative 33% reduction in fractional calcium absorption with significantly increased bone turnover rate was observed in 25 extremely obese women. More importantly, the change in fractional calcium absorption correlated with the concentrations of estradiol and calcitriol, suggesting the involvement of the hormone-regulated transcellular calcium absorption process. The study results appear to suggest that oral calcium supplementation results in better absorption when given in smaller dosages at more frequent intervals.

- Aasheim ET, Hofsø D, Hjelmsaeth J, Birkeland KI, Bøhmer T. Vitamin status in morbidly obese patients: a cross-sectional study. *Am J Clin Nutr* 2008;87:362–9.

The magnitude and frequency of deficiencies appear to correlate with the magnitude of obesity. This article is important because it shows that many obese patients have underlying vitamin deficiencies. In addition to 25-hydroxyvitamin D deficiency, morbidly obese women and men had significantly lower concentrations of vitamin B<sub>6</sub>, vitamin C, and lipid-standardized vitamin E compared with healthy control subjects; the status of vitamins A, B<sub>1</sub>, B<sub>2</sub>, and B<sub>12</sub> and folic acid was adequate in most of the patients. Of interest, the depressed concentrations of vitamins A, B<sub>6</sub>, and C appear to be correlated with the mild inflammatory state associated with obesity. This study further confirms the importance of presurgical screening for vitamin deficiencies in bariatric surgery candidates.

- Merhi ZO. Challenging oral contraception after weight loss by bariatric surgery. *Gynecol Obstet Invest* 2007;64:100–2.

The most effective contraceptive method for childbearing women after bariatric surgery has not been investigated. Based on a few studies published in the 1980s, it is known that malabsorptive procedures are associated with impaired absorption of oral contraceptive drugs, leading to an increased risk of unintended pregnancy. The goal of this article was to explore whether contemporary bariatric procedures negatively impair the efficacy of oral contraceptive drugs. As expected, the author could only identify very limited data based mostly on anecdotal experience or case reports. It appears that lower oral contraception dosages and surgical gastrointestinal disturbances place patients at higher risks of unintended pregnancy. Higher dosages (e.g., 50 mcg of ethinyl estradiol) may theoretically provide more hormones to be absorbed to maintain efficacy. However, clinical and pharmacokinetic evidence of oral estrogen and progestin absorption in RYGB recipients does not exist. The concern about increased thromboembolic events associated with the higher hormone dosage preparations further complicates the decision-making process. Etonogestrel implant and depo-medroxyprogesterone implant are both alternatives; however, there are no published data showing whether the pharmacokinetics of etonogestrel implant is altered by severe obesity. Until more data become available, except for

abstinence, using a barrier method or contraceptive vaginal ring together with or without a hormone implant device may be the most reliable contraceptive approach for patients after bariatric surgery.

12. Karmon A, Sheiner E. Pregnancy after bariatric surgery: a comprehensive review. *Arch Gynecol Obstet* 2008;277:381–8.

Whether bariatric procedures are associated with negative perinatal outcomes has been a topic of debate. This timely article addresses the currently published data that compare the risks and benefits of pregnancy after bariatric surgery with the risks in nonobese and obese women who have not undergone a bariatric surgical procedure. Pregnancy after malabsorptive procedures appears safe, although nutrient deficiencies, especially hypovitaminosis and hypoalbuminemia, are common. There may also be an increased risk of developing an internal hernia and small bowel ischemia. Purely restrictive procedures (e.g., LAGB) appear to be safe and may actually have a positive effect on obstetric outcomes. More frequent band adjustment may be necessary to alleviate nausea or vomiting or to allow more dietary intake. The effect of bariatric surgery on fertility is not as clear. Studies show both increased and decreased fertility in patients who have undergone bariatric surgery. Among the studies showing a higher fertility rate, it is unclear whether the correction of anovulation or the alteration of pharmacokinetics and pharmacodynamics of oral contraceptive drug plays a more important role. Regarding the incidence of pregnancy-related and fetal complications, the data again are unclear with only very few relevant concerns having been definitively addressed. The patient's underlying medical or surgical history, type of bariatric procedure performed, and frequency of additional perinatal care and monitoring may all affect clinical outcomes. Overall, many questions remain unanswered.

13. Voelker M, Foster TG. Nursing challenges in the administration of oral antidepressant medications in gastric bypass patients. *J Perianesth Nurs* 2007;22:108–21.

A significant number of bariatric surgery candidates and recipients take psychotropic drugs to control depression, eating disorders, social anxiety disorder, or other psychiatric illnesses. The dosage of these agents must continue to be optimized after the surgery to ensure continued optimal therapy. It is often a challenging task, however, because very few of these agents are available in an oral liquid dose form. In addition, food intake may affect the oral bioavailability of some of these agents. The article's table 1 and the brief discussion on the pharmacokinetics of different antidepressants provide the most helpful information.

14. Rogers CC, Alloway RR, Alexander JW, Cardi M, Trofe J, Vinks AA. Pharmacokinetics of mycophenolic acid, tacrolimus and sirolimus after gastric bypass surgery in end-stage renal disease and transplant patients: a pilot study. *Clin Transplant* 2008;22:281–91.

Obesity has a negative effect on graft function and survival. In addition, obesity increases the cardiovascular risks associated with transplantation as well as posttransplant management. Currently, there are at least a few studies suggesting that bariatric surgery appears safe and effective in improving candidacy in morbidly obese patients awaiting transplantation. However, how bariatric surgery affects the dosing strategy for immunosuppressive agents is unknown. This pilot study was aimed to profile the pharmacokinetics of tacrolimus, sirolimus, and mycophenolic acid in renal

transplant candidates and recipients who have previously received RYGB. However, this was not a controlled study. Rather, it was an observational study in six cohorts who were RYGB recipients—four renal transplant candidates and two renal transplant recipients. Overall, a large intersubject variation in the pharmacokinetics of the three study drugs was observed. Compared with historic data, it appears that RYGB is associated with altered transit time and reduced oral bioavailability based on maximal achieved concentrations (using whole blood for tacrolimus and sirolimus and plasma for mycophenolic acid) and area-under-the curve for all three drugs.

Despite the importance and relevance of this study, there are a few notable issues. Although the authors referenced the surgical technique used in the RYGB procedure at their institution, they did not report the length of the Roux-limb for each study subject. Of interest, based on the linked reference for the surgical technique, the length of the Roux-en-Y limbs was made to approximate, in centimeters, each patient's weight in pounds, with one-half the length being in the biliopancreatic limb and one-half in the Roux-limb. Therefore, for a patient with a pre-RYGB weight of 136 kg (300 lb), the biliopancreatic limb and the Roux-limb would each be 150 cm, whereas the biliopancreatic limb and Roux-limb would each be 180 cm for a patient whose pre-procedure weight was 163 kg (360 lb). Accordingly, the large interindividual variation in pharmacokinetics may be explained by the variable lengths of the Roux-limb. It is also likely that some of these patients received procedures with a more profound malabsorptive component, depending on their preoperative weight. It is possible that the differences in postoperative anatomy significantly contributed to the wide range of pharmacokinetic results.

Although the results of the study cannot lead to a generalizable dose adjustment strategy for immunosuppressive drugs, the overall message is quite clear: perform therapeutic drug monitoring whenever possible to individualize dosing.

15. Mechanick JI, Kushner RF, Sugerma HJ, Gonzalez-Campoy JM, Collazo-Clavell ML, Guven S, et al, and American Association of Clinical Endocrinologists; Obesity Society; and the American Society for Metabolic & Bariatric Surgery. Executive summary of the recommendations of the American Association of Clinical Endocrinologists, the Obesity Society, and the American Society for Metabolic & Bariatric Surgery medical guidelines for clinical practice for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient. *Endocr Pract* 2008;14:318–36. Also available at [www.aace.com](http://www.aace.com). Accessed November 8, 2008.

These guidelines are a working document based on both published literature as well as expert opinions. The recommendations are endorsed by the American Association of Clinical Endocrinologists, the Obesity Society, the American Society for Metabolic & Bariatric Surgery, and the American Society for Parenteral and Enteral Nutrition. Clinicians will find this document helpful if they are working in an institution where a bariatric surgery program is being established or standardized patient management guidelines for bariatric surgery recipients are being developed. Although there are a total of 166 recommendations in this article, many of the recommendations are rated Grade D (i.e., based on expert opinion because of a lack of conclusive clinical evidence). There are many opportunities for further research and validation of current practice in this field. Some of the recommendations are very conservative and should only be used as starting points because the recommendations are based on older studies. For instance, the daily recommended



vitamin D intake according to the document is 400–800 IU/day. This regimen is likely to be insufficient for most patients as reflected by the more recent data from epidemiologic and clinical research. It is definitely helpful, however, to use the information from this document to establish minimal practice standards.

# SELF-ASSESSMENT QUESTIONS

- Which one of the following patients has the highest risk of developing symptomatic cobalamin malabsorption?
  - A patient who recently received laparoscopic adjustable gastric banding (LAGB) surgery.
  - An obese patient with hyperlipidemia and hypertension taking orlistat 120 mg three times/day for weight loss for the past 3 months.
  - A patient who received a Roux-en-Y gastric bypass (RYGB; Roux-limb, 85 cm) 3 months ago with a 15-mL gastric pouch.
  - A patient who received a biliopancreatic diversion 3 months ago.

## Questions 2–6 pertain to the following case.

J.B. is a 34-year-old woman admitted to the hospital for an RYGB procedure. She has no history of peripheral vascular disease, venous thromboembolism (VTE), or coagulation disorders. Her body mass index (BMI) is 52.1 kg/m<sup>2</sup>, and she has normal renal function. J.B.'s concurrent medical conditions include seasonal allergy, epilepsy, hypertension, type 2 diabetes mellitus (DM), and obstructive sleep apnea.

- Based on current clinical evidence and experience described in this chapter, which one of the following postoperative VTE prophylaxis regimens is the best choice for J.B.?
  - Enoxaparin 40 mg subcutaneously once daily.
  - Enoxaparin 40 mg subcutaneously twice daily.
  - Enoxaparin 1 mg/kg subcutaneously once daily.
  - Unfractionated heparin 500 units subcutaneously three times/day.
- J.B.'s epilepsy has been well controlled with valproic acid capsules 500 mg every morning and 750 mg at bedtime and phenytoin capsules 200 mg at bedtime. She has been seizure free for 9 years. On postoperative day 1, which one of the following orders written for her valproic acid is the best for J.B.'s antiepileptic drug therapy?
  - Give valproic acid oral capsules 500 mg every morning and 750 mg at bedtime; crush the contents of each capsule and administer with small sips of liquid.
  - Give valproic acid oral liquid 500 mg in the morning and 750 mg at bedtime; administer with a small amount of water.
  - Give valproate sodium intravenously 500 mg in the morning and 750 mg at bedtime.
  - Discontinue valproic acid; increase phenytoin to 100 mg three times/day.
- Based on J.B.'s medication profile, she is at significantly higher risk of developing which one of the following nutrient deficiencies than other patients undergoing the same procedure?
  - Folic acid and vitamin D.
  - Iron and thiamin.
  - L-Carnitine.
  - Vitamin D and vitamin B<sub>12</sub>.
- On postoperative day 4, J.B. is clinically stable and ready to be discharged from the hospital. During the discharge counseling session, you discover that before surgery, she was taking an over-the-counter product containing ibuprofen and pseudoephedrine for chronic sinus pain and allergies. Which one of the following would be the best information to give J.B. regarding her use of over-the-counter preparations containing ibuprofen or other anti-inflammatory drugs?
  - She can continue to take these preparations as directed on the packages.
  - She should avoid these preparations because they will increase her risk for dumping syndrome.
  - She should avoid these preparations because they will increase the risk of ulceration around the gastrojejunostomy site.
  - She should avoid these preparations because they will increase her risk of developing ulceration in the remnant stomach.
- Which one of the following is the best plan for J.B.'s anticonvulsant therapy on discharge?
  - Restart the previous home drug regimen using the same formulations, dosages, and intervals. No further action is necessary unless J.B. develops seizures.
  - Restart the previous home drug regimen using the same dosages and frequencies but change the formulations to phenytoin chewable tablets and divalproex tablets. Check serum phenytoin and valproic acid concentrations weekly until she is able to tolerate a normal diet.
  - Restart the previous home drug regimen at the same dosages and frequencies but using oral liquid formulations. Check serum phenytoin and valproic acid concentrations in 1 week.
  - Restart the previous home drug regimen but increase the dosages by 50% and change to oral liquid formulations at the same dosing frequency. Check serum valproic acid and phenytoin concentrations in 1 month.
- Which one of the following bariatric surgery procedures would have the least effect on the oral bioavailability of itraconazole capsules?
  - LAGB.
  - Biliopancreatic diversion.
  - Standard (proximal) RYGB.
  - Long-limb (distal) RYGB.

8. Which one of the following is the most likely explanation for the development of microcytic anemia in an RYGB recipient?
- Inadequate thiamin absorption because of the small gastric pouch.
  - Insufficient vitamin B<sub>12</sub> absorption because of insufficient intrinsic factor.
  - Insufficient iron absorption because of the absence of intrinsic factor.
  - Lack of gastric acid and absorption sites to optimize iron absorption.
9. A 37-year-old woman with class II obesity who received an LAGB 3 months ago returns to the weight-loss clinic for a routine follow-up. She has lost 10 kg since the surgery and is doing well. She is able to tolerate semisolid food and tuna salad. Her most recent serum vitamin B<sub>12</sub> concentration was 253 pg/mL (normal, 210–700 pg/aL), which is lower than her preoperative concentration checked 3 months before her LAGB. The nurse practitioner would like to initiate vitamin B<sub>12</sub> supplementation. The patient is belonephobic; therefore, she would prefer not giving herself frequent intramuscular injections. Which one of the following recommendations is best for this patient?
- Do nothing; wait until her next follow-up visit in 2 months; then recheck her vitamin B<sub>12</sub> concentration.
  - Do nothing; vitamin B<sub>12</sub> supplementation is not warranted until she develops clinical symptoms of anemia.
  - Initiate intramuscular cyanocobalamin injections 1000 mcg monthly.
  - Initiate an oral vitamin B<sub>12</sub> supplement 500 mcg/day.

**Questions 10–12 pertain to the following case.**

G.G. is a 23-year-old woman who returns to the surgery clinic for her follow-up visit 1 year after receiving a long-limb RYGB (Roux-limb, 180 cm). Her current BMI is 27.4 kg/m<sup>2</sup> and weight is 71.4 kg, which is 63% of her preoperative weight. G.G. is currently taking two chewable multiple vitamin tablets daily, atenolol 50 mg daily, and four calcium carbonate tablets (500 mg each) daily. She claims that she becomes tired very easily and short of breath after climbing half a flight of stairs. She also has had a recurrent morning headache during the past few weeks even though she does not have a history of migraine or tension headaches. She reports that she has regular bowel movements with no diarrhea. Her blood pressure was 102/60 mm Hg and 100/60 mm Hg at supine and upright positions, respectively. Her heart rate is stable at 64 beats/minute. Serum chemistries, including blood urea nitrogen and serum creatinine, are within normal limits except for hemoglobin, 10.2 g/dL; mean corpuscular volume, 82 fL; and mean corpuscular hemoglobin concentration, 30 g/dL.

10. Based on the information provided, which one of the following differential diagnoses is the most likely cause of G.G.'s recent symptoms and complaints?
- She has developed dumping syndrome, a common complication associated with long-limb RYGB.
  - Her hypertension is improving, and the dosages of her antihypertensive drugs may be excessive.
  - She has chronic anemia associated with micronutrient deficiency.
  - She has chronic dehydration caused by increased gastrointestinal (GI) fluid losses secondary to the long-limb RYGB.
11. Which one of the following statements is the correct assessment of G.G.'s hematologic laboratory results?
- Microcytic anemia suggesting iron deficiency.
  - Megaloblastic anemia suggesting folate deficiency.
  - Megaloblastic anemia suggesting hypcobalaminemia.
  - Chronic anemia caused by erythropoietin deficiency.
12. Which one of the following actions is best for G.G.?
- Initiate iron supplementation and recheck laboratory results in 3 months.
  - Check folate and cobalamin profile; then empirically initiate folate and cobalamin supplementation while awaiting results.
  - Check iron, folate, and cobalamin profiles; then empirically initiate iron supplementation while awaiting results.
  - Transfuse 2 U of packed red blood cells; then initiate darbepoetin and iron supplementation.
13. A patient who received an RYGB 3 years ago is currently doing well and has lost 48% of his preoperative body weight. His current BMI is 28.2 kg/m<sup>2</sup>. He will be traveling to the Amazon in 1 month and, according to recommendations from the Centers for Disease Control and Prevention, he will need to take drugs for malaria prophylaxis. Based on the absorption kinetics of each of the following drugs, which regimen would be the best choice for his malaria prophylaxis?
- Atovaquone 250 mg/proguanil 100 mg one tablet daily.
  - Chloroquine 500 mg once weekly.
  - Doxycycline 100 mg twice daily.
  - Mefloquine 250 mg once weekly.
14. S.J. received an RYGB procedure 3 days ago and has had an uneventful recovery. Her diet has been advanced to 30 mL of clear liquid by mouth every 2 hours. She seems to be tolerating the fluid intake well with no sign of dehydration, nausea, or vomiting. Her diet will be advanced, and she will be maintained on a full liquid diet, which includes skim milk, water, and artificially sweetened liquids, as tolerated. Her most recent vital signs include blood pressure, 117/85 mm Hg, and heart rate, 78 beats/minute, which are similar to her preoperative vital signs. S.J. has a history of bipolar disorder, hypertension, and type 2 DM. Preoperatively, S.J.'s drug regimen included lithium, atenolol, fosiopril, insulin, glipizide, and metformin. She is to be discharged from the hospital with a follow-up clinic appointment scheduled in 5 days. Which one of S.J.'s home drugs should not be continued on discharge?

- A. Fosinopril.
- B. Glipizide.
- C. Lithium.
- D. Metformin.

**Questions 15 and 16 pertain to the following case.**

K.T., a 34-year-old woman with class III obesity and bipolar mania, underwent an LAGB procedure 4 weeks ago and was discharged home on postoperative day 3. She developed a relapse of her bipolar disorder earlier this week. She has been taking ziprasidone 60 mg every morning and 80 mg every evening and 750 mg of divalproex as delayed-release tablets once daily. Her regimen has not been changed for more than 3 years, and her symptoms were well controlled for the past 2 years until the current relapse episode. Her psychiatrist asks if the pharmacokinetics of divalproex and ziprasidone are affected by LAGB and what follow-up action should be considered for K.T.

15. Which one of the following assessments and recommendations for divalproex is best for K.T.?
  - A. LAGB causes achlorhydria, which led to the early release of valproic acid from the current formulation, resulting in a shorter duration of action. K.T. should be changed to twice-daily dosing.
  - B. LAGB causes malabsorption, which led to an inadequate absorption of valproic acid. K.T. should be changed from divalproex delayed-release tablets to extended-release tablets.
  - C. K.T.'s reduction in food intake has significantly decreased the oral bioavailability of valproic acid. K.T. should be instructed to take divalproex with a liquid protein shake to increase absorption.
  - D. It is unlikely that K.T.'s relapse is associated with the divalproex regimen, because LAGB does not alter the pharmacokinetics of divalproex and valproic acid. Check her serum valproic acid concentration.
16. Which one of the following best describes how K.T.'s ziprasidone therapy would be affected by her surgery?
  - A. LAGB causes achlorhydria, which reduces the oral bioavailability of ziprasidone.
  - B. LAGB causes mild malabsorption, which leads to inadequate ziprasidone absorption.
  - C. The reduction in food intake after LAGB significantly decreases the oral bioavailability of ziprasidone.
  - D. The pharmacokinetics of ziprasidone are not altered by LAGB.
17. Which one of V.K.'s concurrent chronic illnesses may significantly worsen after RYGB?
  - A. Hypertension.
  - B. Osteoporosis.
  - C. Gastroesophageal reflux disease.
  - D. Hyperlipidemia.
18. According to V.K.'s medical history, which one of her concurrent medical conditions makes her a poor candidate for LAGB?
  - A. Type 2 DM.
  - B. Gastroesophageal reflux.
  - C. Severe abdominal obesity.
  - D. Compulsive overeating disorder.
19. Which one of the following contraceptive regimens would have the lowest risk of failure in a 31-year-old woman (BMI, 28.3 kg/m<sup>2</sup>) who had a biliopancreatic diversion 3 years ago?
  - A. An implant such as depot medroxyprogesterone plus a contraceptive vaginal ring.
  - B. Norgestrel 0.075 mg orally daily.
  - C. Norelgestromin/ethinyl estradiol transdermal patch.
  - D. Ethinyl estradiol 35 mcg/norgestimate 250 mcg orally daily.
20. A 42-year-old man (BMI, 42 kg/m<sup>2</sup>) is being evaluated for RYGB. He has osteoarthritis, hypertension, and hypercholesterolemia. He is allergic to eggs and is lactose intolerant. His serum 25-hydroxyvitamin D concentration is 10 ng/mL. Which one of the following is the best action plan to minimize the risk of osteoporosis in this man?
  - A. Calcium citrate 400 mg plus vitamin D 600 IU three times/day with meals; recheck vitamin D concentration in 6 months.
  - B. Calcium citrate 400 mg twice daily plus vitamin D 1200 IU daily; recheck vitamin D concentration in 2 weeks.
  - C. Vitamin D<sub>2</sub> 50,000 IU orally twice weekly for 8 weeks with calcium carbonate 500 mg three times/day with meals; recheck serum concentration in 8 weeks.
  - D. Vitamin D<sub>2</sub> 50,000 IU orally daily for 2 weeks; recheck serum concentration in 4 weeks; add calcium citrate 400 mg daily once vitamin D concentration is normalized.

**Questions 17 and 18 pertain to the following case.**

V.K. is a 42-year-old woman (height, 163 cm; BMI, 43 kg/m<sup>2</sup>; waist circumference, 103 cm) with significant comorbid illnesses, including type 2 DM, depression, compulsive overeating disorder, gastroesophageal reflux disease, hypertension, hyperlipidemia, sleep apnea, osteoporosis, and polycystic ovarian syndrome. She is being evaluated for RYGB.