Nutritional Concerns Related to Roux-en-Y Gastric Bypass
What Every Clinician Needs to Know

Melanie Horbal Shuster, MSN, RN, APRN-BC; Jorge A. Vázquez, MD

Weight loss surgery, particularly the Roux-en-Y gastric bypass (REYGB), has become a popular treatment strategy for obesity. Often the only measure of success is the amount of weight lost following surgery. Unfortunately the nutritional adequacy of the postoperative diet has frequently been overlooked, and in the months to years that follow, nutritional deficiencies have become apparent, including protein-calorie malnutrition and various vitamin and mineral deficiencies contributing to medical illnesses and limiting optimal health. Therefore, patients require close monitoring following REYGB, with special regard to the rapidity of weight loss and vigilant screening for signs and symptoms of subclinical and clinical nutritional deficiencies. Several specific nutrients require close surveillance postoperatively to prevent life-threatening complications related to deficient states. This article addresses nutritional concerns associated with REYGB with fastidious focus on recognition and treatment of the nutritional deficiencies and promotion of nutritional health following REYGB. Recommendations regarding nutritional intake following REYGB are based on available scientific data, albeit limited. In cases where data do not exist, expert or consensus opinion is provided and recommendations for future research are given. Ultimately, clinical application of this information will contribute to the prevention of nutrition-related illness associated with REYGB.

Key words: ghrelin, morbid obesity, nutritional deficiencies, polyneuropathy, Roux-en-Y gastric bypass, Wernicke’s encephalopathy

The ultimate goal of obesity treatment is to reduce the complications associated with obesity, improve quality of life, and prolong life. To achieve these goals, normalization of body composition is desirable by reducing excess body fat while preserving lean body mass. This goal can be accomplished by producing a negative energy balance; however, obesity experts have debated for years—and have not yet reached a consensus—as to the optimal method to achieve fat loss while sparing muscle mass. Nonetheless, it has become apparent that weight loss surgery (WLS) is the most effective treatment option available to patients who are severely obese. Weight loss surgery produces weight loss within a year after surgery, which is 3 to 4 times superior than what can be achieved with nonsurgical weight management programs. More important, patients who lose weight with WLS are more likely to maintain most of the weight lost and sustain their reduced weight for periods of up to 16 years. Comparatively, nearly 100% of the weight lost with nonsurgical weight loss programs is regained within 2 years. Therefore, greater and more sustained improvements in comorbidities are realized, and improvement in quality of life is noted with WLS when compared with nonsurgical weight management programs.

Because of the greater weight loss, WLS has become very popular and is the treatment
of choice for patients who are very obese (body mass index [BMI] \(>40\) kg/m\(^2\)) who cannot lose weight with nonsurgical methods. It is estimated that over 103,000 WLS procedures were performed in 2003, and this figure is expected to increase in the years to come.\(^5\) In addition to the effectiveness in reducing weight, the explosion in WLS is in part due to celebrity endorsement, advertising, improvements of surgical techniques, especially laparoscopic options, and greater availability of surgical centers. All of these factors together have made these procedures more appealing to patients. Unfortunately, the demand for WLS has outgrown the knowledge and research regarding the efficacy and safety of WLS.\(^6\) Although surgery-associated risks (ie, wound infection, anastomotic leak, deep vein thrombosis, pulmonary emboli, and death, etc) are well recognized and publicized by many in the field, less is known about the short- and long-term nutritional consequences of WLS.

The purpose of the gastrointestinal (GI) tract is to process the food that will nourish the body. Major concerns regarding the short- and long-term effects of WLS on nutritional and metabolic outcomes exist because of the significant alterations of the GI tract and the permanency associated with these procedures. Reports from centers with large series of patients who have undergone WLS suggest that WLS is safe and there are no major nutritional or metabolic problems in patients either in the short or long term.\(^7\)–\(^10\) However, the long-term effects of WLS on nutritional outcomes are not well known at this time, because longitudinal data that fully assesses nutritional outcomes are not available. In addition, there have been case reports of patients with significant nutrition and/or metabolic morbidity, raising the possibility that there is much subclinical nutritional morbidity that is both undetected and underreported and subsequently undertreated. These nutritional issues are of importance to anyone undergoing these procedures, but especially in adolescents, women of child-bearing age, and patients older than 55 as these subpopulations have additional nutritional needs.

The aim of this article is to critically analyze the published literature addressing nutritional issues and WLS. The focus of this review is on the nutritional concerns after Roux-en-Y gastric bypass (REYGB), because it is the most common WLS procedure performed in the United States.\(^11\) Review of background GI anatomy, physiology, and nutritional principles essential to understanding the implications of WLS will be undertaken. Since the open and laparoscopic REYGB yields the same alterations in GI anatomy and physiology the nutritional concerns of both types of surgeries will be considered together. Data related to other types of WLS will only be reviewed when pertinent. However, it is important to note that the REYGB is not a “standard” procedure, in that it is not performed in an identical fashion by every surgeon. Many differences in the surgical technique such as the size of the gastric pouch, size of the gastrojejunostomy, presence or absence of a silastic ring distal to the gastrojejunostomy, length of intestinal limbs, and the creation and size of the jejuno-jejunostomy to name a few, are likely to influence outcomes, particularly nutritional status.

**WEIGHT LOSS**

One of the main goals of any weight management program is weight loss, in particular fat loss. Surgical programs are more successful at producing greater amounts of weight loss in a relatively shorter period of time as compared to nonsurgical programs. Therefore, weight loss over time is the most commonly reported nutrition-related outcome in WLS studies. Unfortunately, interpreting the reported data of weight loss surgery is difficult, because not all the data are equal or comparable. Weight loss data are basically reported in 2 different ways: as an absolute amount (eg, pounds lost at 1 year) or as a relative weight (eg, percent weight lost from initial weight at 1 year or as a percentage of excess weight.
lost at 1 year). The excess weight is the difference between the actual and the “ideal” weight. Ideal weight is determined from the Metropolitan Life Insurance table using the midpoint of the medium frame build as the standard reference. The interpretation of weight loss data is further clouded by the homogenization of individual patient’s weight loss patterns. Finally, surgeons often combine weight loss data regardless of the type of procedure performed. Therefore, it is difficult to determine which surgical procedure was responsible for which weight loss outcome.

To date the best longitudinal weight loss data reported are those of Pories and associates, who used a standardized REYGB procedure: the Greenville gastric bypass (Fig 1). All the surgeries were done via open laparotomy using the same surgical technique, creating a 20- to 30-mL gastric pouch, a 0.8- to 1.0-cm gastrojejunostomy, and a 40- to 60-cm alimentary (Y) limb. Weight loss started immediately after surgery and continued at a relatively fast pace for 12 to 18 months. The average 300-lb patient, 65 to 68 in tall, experienced an average absolute weight loss of 125 lb at 1 year. This translates to a relative weight loss of 40% of the initial weight or a 75% to 80% loss of excess weight at 1 year. After the second year, patients began to gain weight and by the 5th year had gained an average of 25 lb, which was equal to a 20% regain of the initial weight loss. The weight loss remained relatively stable from the 5th to the 14th year of observation. The long-term (>5 years) absolute weight loss for morbidly obese patients with the Greenville gastric bypass was 100 lb, or a 53% decrease from the initial weight or a 66% decrease from the initial excess weight (IEW). Christou et al also reported 16 years of data on patients undergoing WLS at the McGill University Hospital in Montreal. These investigators combined data from open and laparoscopic REYGB, vertical banded gastroplasty, and vertical banded gastroplasty converted to REYGB. Follow-up from year 1 to year 11 was superior (>70% of cases), but after 12 years’ follow-up decreased to only 10% to 20% of cases. Patients on average lost 70.4% of IEW in the first 2 years and then gained a modest amount of weight, so from postoperative years 10 to 16 the weight loss was 55% to 60% of IEW.

Other investigators have reported patients’ weight loss data for more than 2.5 years following REYGB. However, in most of these reports the surgical procedure has not been standardized over time. Combined results of both open and laparoscopic procedures have been reported by some surgeons, and others have reported, in aggregate, the weight loss results of patients who have a standard 75-cm Y limb and a long 150-cm Y limb. Therefore, interpretation and generalization are difficult. In addition, the surgical technique has been evolving over the years in the majority of these studies. Reporting weight loss data from both

![Figure 1. Weight loss after REYGB. Redrawn from data reported by Pories et al.](image-url)
open and laparoscopic procedures together is not expected to affect the short- and long-term weight loss results. However, extending the alimentary limb from 75 to 150 cm or longer may result in greater weight loss. Nonetheless, the shape of the curve of weight loss results over time for the short (1 year) and medium term (2–5 years) for these studies is remarkably similar to that of the results with the Greenville gastric bypass. Patients on average lose approximately 62% to 70% of IEW at 1 to 2 years and maintain 50% of IEW lost for 2 to 5 years.

Unfortunately, reporting REYGB weight loss data as a mean or average of the group may mask important individual differences often seen between patients. More innovative and descriptive ways of presenting weight loss data after WLS has been presented by Sanyal et al,22 Ray et al,23 who have shown weight loss data by reporting the frequency of weight loss within various weight-loss categories. Higa et al has shown individual data in a graph categorized by BMI at the time of surgery and at follow-up.24 When data are viewed in this way, it is clear that the results of WLS are extremely variable and many patients have undesirable outcomes. Using a less than 50% excess weight loss at 1 year as a criterion for failure, it can be seen that 20% of patients can be considered as failures of WLS.2,22,24

The data of Higa et al also show that the result of REYGB depends on the initial BMI.2,24 The higher the BMI at the time of surgery the higher the initial absolute weight loss at 1 year, but a higher BMI preoperatively tends to result in a lower IEW lost at 1 year.2,25–27 Ballantyne28 and Kral29 have listed both positive and negative factors that influence weight loss after WLS. Preoperative presence of diabetes,30 depression,31 and other psychological and behavioral factors25 have recently been reported to affect the 1-year weight loss results after REYGB. In addition, weight loss after REYGB is influenced by gender, age, and ethnicity. Sugerman32 and Capella and Capella33 have shown that African American patients lose less weight than Caucasian patients after WLS. Younger patients experience greater weight loss than older patients.34 Weight loss after REYGB is also expected to be affected by the degree of compliance with dietary and physical activity recommendations, but these have not been adequately investigated. Furthermore, the results of REYGB may also be affected by surgical factors such as the experience of the surgeon, the size and position of the gastric pouch, the length of the alimentary limb, the length of the bypassed segment, and the presence or absence of a Silastic ring to prevent dilatation of the gastrojejunostomy.35

Another observation that can be made after analyzing the data of Sanyal et al22 and Higa et al24 is that only a few patients achieve a normal weight (ie, lose 90% to 100% of IEW) and 3% to 5% of patients lose greater than 100% of IEW. The latter group can be considered as malnourished after REYGB. Patients who reached normal weight and/or became malnourished postoperatively tended to be in the less than 40 kg/m² BMI weight range category preoperatively.24 Although these patients achieved large weight loss, they should also be considered as failures of WLS because of the excess morbidity and poor quality of life associated with malnutrition.

Most of the data regarding weight loss after WLS are measured at 1 to 2 years. This is when patients show the greatest weight loss. Very little is known about weight loss patterns during the first 3 months and up to 1 year after surgery. The weight data may indeed have been collected but not reported, because the most commonly reported protocol for postoperative office visits is 2 to 3 weeks, then 3, 6, and 12 months, and yearly thereafter. Weight loss data if obtained at these visits are relevant, because weight loss at the third month following WLS is a marker of hydration and reflects nutritional status and adequacy. In addition, this weight measurement may be a potential predictor of early morbidity, indicating the need for hospitalization, and may be prognostic of long-term weight loss.

Many REYGB patients, often with surgeons’ consent, want to lose the excess weight as soon as possible and purposely avoid eating or
drinking, while other patients, because of persistent nausea, vomiting, or anastomotic stricture cannot eat enough to produce a steady, slower, safe weight loss. Both of these situations can lead to rapid and greater-than-expected weight loss. However, the appropriate rate of weight loss during the first 3 postoperative months following WLS is unknown. Perhaps research data obtained from controlled starvation and very-low-calorie diets (VLCDs) may be of benefit in an attempt to calculate a rational weight-loss expectation during the first 3 months immediately following surgery. Drenik et al studied 11 men who underwent therapeutic starvation, only receiving water and vitamins under supervised conditions, in a metabolic ward from 12 to 117 days. The patients ranged in age from 32 to 71 years and weighed from 236 to 550 lb, with an average weight of 308 lb. All subjects experienced a very fast initial weight loss of 2 to 4 lb over the first 24 hours and continued to lose about 2 to 3 lb per day for the next 10 days. The following second 10 days had a progressive slowing in the rate of weight loss until it reached approximately 0.7 lb per day at the end of the second month, and the rate of weight loss tended to remain fairly constant. Thus, patients lost approximately 12%, 20%, and 27% of their initial weight at the end of 30, 60, and 90 days of total therapeutic starvation, respectively. Subjects who were on a weight-reducing diet before commencing starvation lost less weight.

Although weight loss is rapid with starvation, it is not without untoward effects and is not without risk. Starvation is associated with orthostatic hypotension, losses of lean body mass, and death if prolonged for more than 70 days in otherwise healthy adults. Therefore, near starvation postoperatively should be avoided. Ideally, it would be best if weight could be reduced without the losses of lean mass, hypotension, and death. Vazquez et al data suggest that the losses of lean body mass can be minimized by consuming at least 500 kcal/d, of which 200 to 280 kcal are from 50 to 70 g of protein and surfeit amounts of vitamins, minerals, electrolytes, and water. Interestingly, this is the nutritional composition of most VLCDs. Very-low-calorie diets produce on average a weight loss of 1.5 to 2.5 kg/wk in women and 2.0 to 2.5 kg/wk in men with average weight losses of 20 kg over 12 weeks. At 1, 2, and 3 months a VLCD is expected to produce weight losses that are 7%, 12%, and 15% of the initial weight, respectively, while preserving lean body mass and avoiding dehydration.

Utilizing these data, speculation regarding a reasonable time line for weight loss postoperatively is possible. An appropriate weight loss for the first 3 months after REYGB should be less than what is expected with total starvation and closer to what is expected with VLCDs. Therefore, weight loss ranging from 7% to 10%, 12% to 15%, and 17% to 20% of initial weight at 1, 2, and 3 months, respectively, would be within the expected limits. Women and subjects with BMI less than 50 kg/m² are expected to fall in the lower end of the expected limit, while males and subjects with BMI greater than 50 kg/m² are expected to fall in the upper end. Subjects with significant preoperative edema are likely to lose large amounts of weight in the first 2 to 3 postoperative weeks, which may exceed these expectations. However, weight loss in this group will be primarily water and should be easy to identify as the edema will dissipate.

**BODY COMPOSITION**

When an individual restricts energy intake and weight loss occurs, the mass lost is a combination of water, fat, and muscle. The composition of the weight loss after REYGB was recently assessed by Das et al. Thirty patients, with an average preoperative weight of 139 ± 35 kg had their body composition measured before and after the REYGB. The average amount of weight lost at 14 ± 2 months after the surgery was 53.4 ± 22.2 kg or 39% of initial weight. On average, 79% of the weight loss was fat and 21% was fat-free mass, and were not proportionally significant.
as related to the amount of weight loss. These results are in accordance with previous study by Raymond et al in patients after gastric partitioning. However, Raymond also measured body composition at earlier times after surgery and found higher lean body mass losses at 3 months. Thus, proportionally more lean body mass is lost in the first 3 months after surgery, but by 6 months and certainly by a year, the composition of the body mass lost is similar to the composition of body mass lost with dietary restriction. More important, the body composition of female patients after REYGB was similar to the composition of a reference woman, indicating an appropriate physiological weight loss. Nonetheless, it should also be pointed out that some patients do have abnormal body composition after WLS. For example, McLean et al examined the body composition of a group of patients with REYGB admitted to the hospital for complications after surgery. Some of these patients clearly showed evidence of excessive lean body mass loss and malnutrition. Preservation of lean mass and prevention of visceral protein wasting is of paramount importance when active weight loss is occurring.

**MECHANISM OF WEIGHT LOSS**

The mechanisms responsible for weight loss after REYGB surgery have not been fully elucidated. Weight loss generally occurs when greater amounts of energy are expended in comparison to energy ingested. Decreases in energy ingested may result from a decrease in food intake or maldigestion and malabsorption. Increased energy expenditure can be due to increased physical activity or increased metabolism secondary to infection, fever, trauma, or wasting illness such as cancer. Inadequate digestion and absorption can occur with illness such as chronic pancreatitis where inadequate enzyme secretion inhibits foods from being completely prepared for absorption. Therefore inadequate absorption of energy ingested will result in weight loss. Regardless of the mechanism, weight loss ensues.

Possible reasons for weight loss after REYGB may be higher energy expenditure, malabsorption, or lower energy intake as compared to preoperative intake. Das et al reported that total energy expenditure and resting energy expenditure (REE) decreased by 25% on average after REYGB and the decrease in energy expenditure is solely accounted for by the changes in fat-free mass, because an overall decrease in body mass results in a decrease in energy expenditure. Das et al and Klem and associates have also reported that physical activity is not significantly increased after REYGB, therefore this would not be an explanation for the weight loss.

Roux-en-Y gastric bypass is considered to be both a restrictive, limiting amount of food ingested at one time, and a malabsorptive, decreasing absorptive capacity of the intestine, WLS. However, the contribution of malabsorption to weight loss with REYGB has not been well defined, even though there are many anatomic and physiologic alterations induced by REYGB that could produce malabsorption. Roux-en-Y gastric bypass decreases the stomach size from more than approximately 500 mL to between 15 and 30 mL, thereby restricting the volume of food ingested. In addition, REYGB significantly alters many important physical properties and functions of the stomach, such as liquefaction of food by grinding. Grinding is very important in releasing vitamins and minerals from the food and serves as a preparatory step for further action of pancreatic enzymes. Gastric emptying is controlled by osmotic pressure and by the chemoreceptors located in the antrum of the stomach and the proximal small intestine, the pylorus. By bypassing this segment of the gut, patients lose the capacity to grind and sieve food.

Normally, the stomach will grind the food until it is less than 10 mm in size, thereby increasing the surface area for the pancreatic enzymes to act. By eliminating the body of the stomach, the patient loses storage capacity
and important gastric secretory products, in particular hydrochloric (HCl) acid, pepsinogen, intrinsic factor, gastrin, and mucus. HCl coagulates protein and along with pepsinogen starts the digestive process for proteins, which is further aided by salivary amylases and lipases. HCl is also important in the reduction of iron, which allows for more efficient absorption. By forming the Roux-en-Y anastomosis the coordination between gastric emptying and pancreatic enzymes release is lost, which could lead to maldigestion. Obviously, if nutrients are maldigested, they cannot be transported across the gut membrane, resulting in malabsorption. In a healthy individual, the pancreas produces enzymes in excess of what is normally needed for digestion. Pancreatic secretions are mediated by the vagus nerve, which may or may not be severed during REYGB. Neural release of secretions occurs in 2 phases, cephalic and gastric. The cephalic phase is initiated with the thought or suggestion of food and the gastric phase occurs with the presence of food. Finally, pancreatic secretions are influenced by the intestinal phase, where secretion is stimulated by the hormones secretin and cholecystokinin and inhibited by the hormone pancreatic polypeptide. The secretion and metabolism of all these hormones could be altered after REYGB.\textsuperscript{47}

Previous studies of patients with gastrectomy for peptic ulcer disease have found only mild malabsorption after the procedure.\textsuperscript{48} Considering the alteration in anatomy, this population can be used as a model for comparison, because the stomach and proximal small bowel are removed for ulcer disease. This is somewhat similar to REYGB, although not removed; the stomach and proximal small bowel are not directly participating in the digestive process. Malabsorption is measured by quantifying the amount of fat and protein lost in stool. Stool fat losses (steatorrhea) after gastric surgery are usually 5 to 10 g/d (normal <5 g/d when ingesting 100 g of fat per day) and nitrogen losses (azotorrhea) are usually 2 g/d (normal 1 to 2 g/d). Patients may also have carbohydrate malabsorption after gasterectomy, which may contribute to flatulence, while others may develop lactose intolerance. The large intestine can salvage the majority of undigested carbohydrates and is unlikely to contribute to weight loss after gastric surgery.

Patients with REYGB whose alimentary limb is 50 to 75 cm and biliopancreatic limb is 20 to 40 cm, rarely develop maldigestion and/or malabsorption of proteins, carbohydrates, and fats, which may contribute to weight loss, although it can be associated with micronutrient (vitamins, minerals) deficiencies. However, lengthening the limbs is associated with greater weight loss, as described above. The mechanism for the greater weight loss is presumably greater macronutrient malabsorption. Unfortunately, this has not been thoroughly investigated and an extensive review of the literature did not find any study that reported the degree of steatorrhea or azotorrhea after REYGB. However, with regards to the limb’s length, malabsorption of macronutrients is expected to be less than what is seen with pancreatic insufficiency and also less than what is seen with biliopancreatic diversion. Scopinaro reported an apparent absorption of 57%, 32%, and 56% for total energy, fat, and nitrogen, respectively, after biliopancreatic bypass.\textsuperscript{49}

Therefore, decreases in food and energy intake are the most important contributors to weight loss as observed in most studies after REYGB. Decreased oral intake often accompanied by anorexia after REYGB are commonly attributed to the small gastric remnant (15–30 mL) and small gastrojejunal anastomotic outlet (<1 cm) that reduces gastric emptying of both liquids and solids. Horowitz et al studied gastric emptying of liquids and solids and gastric remnant size after gastric bypass surgery and found no correlation between the rate of weight loss and the solid- or liquid-phase gastric emptying and the size of the pouch.\textsuperscript{50} Similarly, Miskowiak et al\textsuperscript{51} and Nasland and Beckman\textsuperscript{52} found no correlation with weight loss and the gastric emptying of liquid or solids after gastroplasty.
Taste acuity is another mechanism that has been offered as an explanation of weight loss in REYGB patients following surgery. Burge et al. found that many patients reported foods tasting sweeter after REYGB and others reported aversion to meat. There was a significant reduction in the threshold recognition for sucrose 6 months after surgery, which persisted at 12 months. There were no significant changes in the threshold recognition for urea (the end product of protein metabolism) over time, but there was a significant difference noted between the patients who reported aversion to meat and the ones that did not. However, opposite results were reported by Scruggs et al., who found significant decreases in the taste thresholds for HCl and urea post-REYGB but no changes for the thresholds for sucrose or sodium chloride. Interestingly, a change in taste acuity was also implicated as a mechanism of weight loss in patients with jejunoileal bypass.

Recently, changes in circulating levels of ghrelin have been implicated as at least one mechanism that may explain anorexia and weight loss after REYGB. Ghrelin is a peptide secreted primarily by the stomach fundus glands and to a lesser extent by the small intestine. Ghrelin activates neurons in the hypothalamus that in turn activate neuropeptide Y and agouti-related protein. Both of these mediators are known to stimulate food intake and promote weight gain. Circulating ghrelin levels are elevated in the fasting state and decrease abruptly after a meal. In addition, ghrelin has a diurnal pattern and levels normally fluctuate during the day and night with periods of peaks and troughs as it relates to feeding and fasting. Previous studies have shown that ghrelin levels are low in obese individuals as compared to lean individuals, and the levels increase after diet-induced weight loss. Therefore, it has been hypothesized that increased ghrelin levels may be one of the mechanisms responsible for amplified hunger after dieting. Cummings and Shannon reported that unlike diet-induced weight loss, REYGB-induced weight loss was associated with low baseline serum ghrelin levels and with a loss of the diurnal pattern that characterizes the 24-h ghrelin profile. These investigators hypothesized that the suppressed ghrelin levels may be one of the hormonal mechanisms by which REYGB produces weight loss, and a different factor that explains a greater weight loss with REYGB as compared with other restrictive surgeries such as Lap-band gastroplasty and vertical banded gastroplasty. Major limitations of the Cummings et al. findings were that only 5 patients with REYGB were studied and that they were not studied prospectively. Since the publication of this study, other groups have reported ghrelin data before and after REYGB and with other WLS. Geloneze et al. reported that ghrelin levels at 1 year post-REYGB were lower than preoperative values in both diabetic and non-diabetic patients. Frühbeck et al. found lower levels of ghrelin in REYGB patients than in matched obese patients who underwent adjustable gastric banding (AGB) or biliopancreatic diversion instead of REYGB. In this study, patients lost approximately the same amount of weight and the same amount of body fat. It was speculated that ghrelin levels after WLS would vary between the procedures, being lower in those surgical procedures that isolate the fundus area of the stomach the most, ie REYGB. This observation was validated by finding lower ghrelin levels 24 hours after REYGB than after AGB, and after Nissen fundoplication. Hanusch-Enserer reported no changes in ghrelin levels between before and 6 months after AGB, but an increase at 12 months has been reported by others when patients lost weight with no-surgical methods. Unfortunately, more recent studies have not shown such consistent findings. Lonetti et al. found ghrelin levels to be lower in individuals after both AGB and REYGB when compared with obese individuals who did not have WLS. However, ghrelin levels were lowest in AGB individuals, and although ghrelin was lowered with both surgeries, it was higher in the REYGB individuals, the antithesis of the expected. In addition, neither AGB nor REYGB patients showed the typical 24-hour ghrelin
profile seen in nonsurgical patients. Faraj et al. found that ghrelin levels after REYGB depend on the dynamics of weight loss. Patients who were actively losing weight at the time of measurement had higher ghrelin levels, but those who were no longer losing weight had no change in ghrelin levels compared with preoperative levels. In summary, ghrelin levels differ depending on the procedure and the surgeon performing the WLS. The results of ghrelin levels after WLS range from postoperative suppression, to inappropriately low levels despite large weight losses, to changes in the 24-hour profile, to increases or appropriate levels as seen in other weight-loss methods. These results suggest that ghrelin may have a role in energy homeostasis and body weight regulation but does not fully explain the anorexia experienced by many patients after REYGB. As a matter of fact, no studies today have correlated ghrelin levels after REYGB with any parameter of hunger or satiety. Many patients (but certainly not all), report less hunger immediately after REYGB and progressive increase in hunger and restoration of appetite with time. Perhaps other unknown factors released by the gut and adipose-related tissue are involved in the regulation of hunger contributing to decreased weight loss after REYGB. Unlike ghrelin, which is considered to be an appetite-stimulating hormone, other gut peptides are considered as appetite suppressants to decrease hunger.

**POSTOPERATIVE ORAL INTAKE**

The optimal oral intake for patients after REYGB is unknown. An extensive review of the scientific literature found only a few studies that systematically evaluated important elements of dietary intake, such as (1) composition of nutrients ingested (ie, the amount of macronutrients: carbohydrates, fat, and protein), which determines the energy ingested, (2) consistency of foods ingested (ie, liquids, pureed, semisolid, or soft), (3) frequency of intake, and (4) quantity of intake. The dietary guidelines given to patients following gastric bypass regarding oral intake are not based on research but on standard postoperative oral intake practices, and the experience previously obtained with other gastric surgeries. However, it should be pointed out that gastrectomies are usually performed in different types of patients (ie, gastric ulcers or cancer) and under much different circumstances than REYGB. The rationale for these dietary recommendations are for prevention of undesirable symptoms (ie dumping syndrome, nausea, vomiting) in contradistinction to the ultimate goal of REYGB, which is to produce safe and steady weight loss and facilitate healthy long-term changes in eating habits.

The purpose of eating is to live. Ingesting oral foods to nourish the body provides hydration, energy, protein, fat, vitamins, and minerals to allow optimal health. Ingesting foods in inadequate or excessive amounts contributes to less than optimal bodily function. However, the human body is quite resilient and can perform very well in spite of less than perfect oral intake, ignorance of adequate nutrition is not recommended. Although reducing oral intake to a necessity seems drastic, eating to live is essential, but most individuals associate eating with pleasure, happiness, social support, and comfort. However, in a social environment, food is often consumed in excess of need. Therefore, one must be cognizant of the need for food versus the want for food. The need of food clearly supports life while the want of food is dispensable, but can make life more worth living. The foods we eat that contain the essential nutrients for life are collectively referred to as a diet. The ideal diet provides all the nutrients necessary for survival in appropriate quantities to maintain an acceptable body weight for height, a BMI of 19 to 25 kg/m².

Presently, patients who have undergone REYGB are not prescribed a specific diet, but rather are given a set of guidelines or rules to regulate oral intake. The purpose of the guidelines is to prevent complications and undesirable side effects associated with anatomic restructuring and physiological alterations as a result of surgery. It is also interesting to note
that these guidelines change over time. More important, these guidelines give little significance to the nutritional composition and adequacy of oral intake postoperatively.

Most, if not all, REYGB patients are NPO 24 hours following surgery or until an oral gastrografin study demonstrates an intact gastrojejunostomy. Patients then begin a clear-liquid diet. The rationale for a clear liquid diet is to evaluate the patient’s ability to tolerate oral fluids. If slow gastric emptying occurs, which may be due to the effect of anesthesia, swelling, or stricture at the gastrojejunal anastomosis, vomiting may result. A clear-liquid diet may reduce the risk of vomiting; however, a study evaluating clear liquids as compared to full liquids or semisolids as the initial postoperative intake has not been completed. The clear liquid diet starts 24 hours after surgery and may continue for as long as 14 days postoperatively depending on the preference of the surgical team. Some patients, especially those after laparoscopic REYGB, are discharged to home within 24 to 48 hours after the surgery with instructions to continue a clear-liquid diet with further directions to advance to a full-liquid diet, followed by a semisolid or pureed diet, and finally progress to a solid diet. The decision regarding the progression of the oral diet or the timetable to advance from clear liquids to full liquids, and then to semisolids and solids, depends on the patient’s symptoms and tolerance to the various food consistencies ingested as well as the individual’s surgical program protocol. There is no standardized timetable regarding the progression of the diet; however, most patients are advanced to a full-liquid diet at their routine 2- to 3-week postoperative office visit, and by 3 months most patients are eating solid foods. The nutritional value of a clear-liquid diet for postoperative REYGB patients averages an energy intake of 400 calories with 5 g of protein per day while the full-liquid diet provides 1500 calories with 55 g of protein per day. There is great potential for inadequate nutrient intake after REYGB depending on the components of these diets as well as the duration.

Most large reports of REYGB procedures do not detail specifically the postoperative diet to be ingested or a diet-advancement protocol. Furthermore, the nutritional adequacy of the postoperative diet is not featured, and patients are not given targets for energy and protein intakes; therefore, it is expected that the resulting nutrient intake will be quite variable. However, a few studies do provide some information regarding the postoperative recommendations for energy and protein targets. Sugerman\textsuperscript{7} and associates recommended patients eat a blended diet for 6 weeks, with a minimum of 44 g of protein per day. In addition, patients were instructed to take multivitamins (MV) with minerals for the rest of their life.\textsuperscript{72} Flickinger\textsuperscript{26} started patients on a nutritional supplement (Ensure\textsuperscript{®}) a day after surgery and all patients continued supplementation for 7 to 10 days. When the consistency of the diet was advanced, the supplement was discontinued while stressing the importance of completely chewing food. Brolin et al recommended a modified liquid diet of no more than 1000 kcal/d for 4 weeks; then the diet was advanced to a “soft” diet.\textsuperscript{75}

Typically at the time of discharge from the hospital, patients are given a set of rules that are intended to control the composition of the meals as well as the length of time spent eating. For instance, patients are instructed to eat slowly, to chew well, to eat 3 to 5 small meals per day and to not drink liquids with meals. Many programs also give specific recommendations regarding the type of liquids to drink during the different stages of the diet advancement. For example, only decarbonated (flat) diet soda and sugar-free gelatin are allowed during the early stages of the postoperative diet, and the use of straws to drink the liquids is prohibited.\textsuperscript{74} Patients are also instructed to consume protein-containing foods at every meal every day (“Protein foods are to be eaten first”). All of these recommendations are designed to reduce the risk for nausea, vomiting, bloating, and dumping syndrome, but scientific evidence regarding the validity of these
recommendations are not available. Finally, patients are instructed to take nutritional supplements to reduce the risk for developing nutritional deficiencies.

Nutritional supplements are products taken in addition to food that contain 1 or several nutrients. They can be ingested as tablets, capsules, liquids, powders, or as complex drinks that contain macro- and micronutrients, eg Boost®, Ensure®, Resource®. Supplements are required when foods that naturally contain the nutrients are not consumed in a quantity that is adequate to restore or maintain health. These can include macronutrients such as protein as well as micronutrients such as vitamins and minerals. However, recommendations regarding nutritional supplementation vary widely depending on the surgeon. In 1999, Brolin and Leung surveyed the practice patterns of surgeons performing REYGB regarding nutritional supplementation. These authors found that 98% of surgeons recommended MV supplements to their patients. In contrast, iron, protein, vitamin B12, and calcium supplements were recommended by 64%, 56%, 50%, and 33% of the surgeons, respectively.

All required nutrients for life and health can be found in a diet that is well balanced, energy-appropriate for height, and includes a variety of foods. However, diets that are energy-restricted to less than 1200 kcal/d may not be adequate in 1 or more of the essential nutrients. Therefore, oral intake after REYGB may not be adequate and supplementation may be necessary. Unfortunately, only a few studies have investigated eating behaviors, and the composition of oral intake at various times after REYGB. Halmi et al used a structured interview to assess eating behaviors of 80 patients before and at 6 months and 1 and 2 years after gastric bypass. She summarized the results of the qualitative data as follows:

Before the operation, patients stated they could eat after their usual meal an additional full meal to one third of a meal. Postoperatively, they stated they could eat no additional food after a meal. Before the bypass operation, patients ate all the food on their plate at a meal; and after the operation, they rarely to never finished all the food on their plate. They always ate food they did not really desire before the operation, and never did this following the operation. Before surgery, the reason they stopped eating was because no food was available; and after the surgery, they stopped eating because they had no desire for any more food. The amount of willpower required to stop eating before the operation was considerable and, after, no willpower was required. They will stop abruptly. They were not uncomfortable after a meal either before or after the surgery. The patients were more conscious of what they were eating, and they felt hungry much less often after the bypass surgery compared to before. Other characteristic changes in eating followed surgery were that the patients ate much less often between meals, ate much slower, drank liquids much more often, and found it much easier to stop eating.

After the bypass there was significant reduction in the number and the types of meals consumed. Postoperatively, the patients ate less fats and carbohydrates and more protein rich foods such as low-fat meals. Foods in the category of high caloric dense fats or carbohydrates were no longer enjoyable and foods in the category of high fat meats, low-fat meats, fruits and vegetables were regarded as delicious.

Several other investigators have reported that patients tend to eat less meat after surgery than before surgery but no details were given about this phenomenon. For instance, it is not clear if this applied to all “meats” or if it is affected by the preparation of the food. Coughlin et al used diet histories to estimate preoperative intake and dietary recall and a checklist to estimate the energy intake and macronutrient composition of the diet after bypass surgery at 1, 3, 6, and 12 months in 25 morbidly obese women. The results are shown in Table 1. Patients in the study underwent a usual and customary REYGB procedure, which is defined as a divided and pouches stomach with a capacity of 30 mL with a Roux-en-Y limb of jejenum no greater than 1 cm in diameter attached 1.5 cm distally to the esophagogastric junction. The distal stomach, duodenum, and proximal jejenum
As expected, a dramatic reduction in food intake was noted when comparing the status before and after REYGB. The energy intake for the first and third month postoperation was less than 500 kcal/d with less than 20 g of protein per day. However, energy intake increased by the sixth month to approximately 1000 kcal/d with 38 g of protein. At 1 year the energy intake remained at approximately 1000 kcal/d, but the protein intake increased to 60 g of protein per day. The caloric intake essentially remained unchanged at 1 year, but the protein intake increased by approximately 30%. Coughlin et al also studied the time intervals throughout the day when meals were consumed by participants. Preoperation, approximately 45% of the daily energy intake was consumed at the evening meal (4–8 PM) as compared to 1 month postoperation, when energy intake of the evening meal decreased to 35% of the daily energy intake, and at 3 months energy intake at the evening meal was the lowest at 27%. However, by the 6th and the 12th month, the energy consumed at the evening meal had returned to 42% and 45% of the daily energy intake, respectively, with the latter equaling the preoperative level.

Brolin et al used a 1-day dietary recall to analyze oral intake after REYGB of 108 patients. Foods reported as ingested were evaluated for energy and composition preoperatively and postoperatively at 6, 12, 18, 24, and 36 months. At discharge, patients were instructed to follow a 1000-kcal modified liquid diet for 4 weeks and gradually advanced to a soft-solid diet, without specific dietary recommendations regarding nutrients. The data are shown in Table 2. Brolin et al reported energy intake at 6 months and 1 year to be approximately 900 and 1100 kcal/day, respectively, which is similar to the findings reported by Coughlin et al. The energy intake increased to about 1300 kcal after 18 months and remained at this level through the 36 months. Patients also reduced the consumption of sweets and soda (SWS), milk and ice cream (MIC), nonliquid sweets (NLS), and high-calorie liquids (HCL) after the surgery. However, it is interesting to note that the overall distribution of nutrients remained somewhat similar when comparing preoperative and postoperative oral intake at 36 months (see Table 2). The most significant change was in the amount of food ingested. Post-REYGB, patients ate on average 70% to 75% less than what they ate preoperation.

Lindroos et al used a dietary questionnaire to assess the oral intake of patients participating in the Swedish Obesity Study (SOS). Patients completed a questionnaire that assessed oral intake over 3 months prior to each of their 6-, 12-, and 24-month follow-up visits. Patients in the SOS who received a gastric bypass had mean daily energy intake at baseline of 2755 kcal, at 6 months 1410 kcal, at 12 months 1800 kcal, and at 24 months 1885 kcal. When comparing baseline to 2-year post-bypass intake, patients were consuming less energy from protein (16.7 ± 2.7 vs 15.4 ± 2.2%, \( P < .05 \)) and less prepared meals (28.9 ± 8.1 vs 23.3 ± 8.4%, \( P < .001 \)) but

---

**Table 1.** Quantity and composition of oral intake before and after REYGB*†

<table>
<thead>
<tr>
<th>Time variable</th>
<th>Preoperative</th>
<th>1 month</th>
<th>3 months</th>
<th>6 months</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy, kcal/d</td>
<td>3979 ± 492</td>
<td>352 ± 50</td>
<td>471 ± 60</td>
<td>932 ± 105</td>
<td>1091 ± 116</td>
</tr>
<tr>
<td>Protein, g/d</td>
<td>164 ± 123</td>
<td>15 ± 2</td>
<td>19 ± 2</td>
<td>38 ± 4</td>
<td>60 ± 12</td>
</tr>
<tr>
<td>CHO, g/d</td>
<td>432 ± 51</td>
<td>41 ± 7</td>
<td>56 ± 11</td>
<td>98 ± 13</td>
<td>112 ± 15</td>
</tr>
<tr>
<td>Fat, g/d</td>
<td>177 ± 25</td>
<td>14 ± 3</td>
<td>19 ± 4</td>
<td>43 ± 7</td>
<td>44 ± 5</td>
</tr>
</tbody>
</table>

*Data are expressed as average ± SEM. Data extracted from Coughlin.
†REYGB indicates Roux-en-Y gastric bypass; CHO, carbohydrate.
Table 2. Distribution of caloric intake before and after REYGB\(\ast,\dagger\)

<table>
<thead>
<tr>
<th>Time variable</th>
<th>Preoperative</th>
<th>6 months</th>
<th>12 months</th>
<th>18 months</th>
<th>24 months</th>
<th>36 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy, kcal/d</td>
<td>3120 ± 1168</td>
<td>890 ± 407</td>
<td>1116 ± 426</td>
<td>1256 ± 504</td>
<td>1319 ± 912</td>
<td>1386 ± 578</td>
</tr>
<tr>
<td>Protein, %</td>
<td>18 ± 6</td>
<td>20 ± 7</td>
<td>19 ± 6</td>
<td>19 ± 5</td>
<td>2 ± 7</td>
<td>18 ± 6</td>
</tr>
<tr>
<td>CHO, %</td>
<td>46 ± 9</td>
<td>48 ± 11</td>
<td>47 ± 12</td>
<td>46 ± 12</td>
<td>45 ± 13</td>
<td>50 ± 9(\dagger)</td>
</tr>
<tr>
<td>Fat, %</td>
<td>36 ± 8</td>
<td>31 ± 11(\dagger)</td>
<td>34 ± 11</td>
<td>35 ± 12</td>
<td>34 ± 11</td>
<td>33 ± 8(\dagger)</td>
</tr>
<tr>
<td>SWS, %</td>
<td>26 ± 17</td>
<td>15 ± 16(\dagger)</td>
<td>12 ± 13(\dagger)</td>
<td>15 ± 17(\dagger)</td>
<td>15 ± 17(\dagger)</td>
<td>23 ± 21</td>
</tr>
<tr>
<td>MIC, %</td>
<td>9 ± 9</td>
<td>4 ± 8(\dagger)</td>
<td>3 ± 6(\dagger)</td>
<td>2 ± 4(\dagger)</td>
<td>2 ± 5(\dagger)</td>
<td>1 ± 2(\dagger)</td>
</tr>
<tr>
<td>NLS, %</td>
<td>23 ± 27</td>
<td>9 ± 22(\dagger)</td>
<td>13 ± 23(\dagger)</td>
<td>13 ± 23(\dagger)</td>
<td>15 ± 25(\dagger)</td>
<td>17 ± 27(\dagger)</td>
</tr>
<tr>
<td>HCL, %</td>
<td>26 ± 33</td>
<td>24 ± 31(\dagger)</td>
<td>16 ± 29(\dagger)</td>
<td>19 ± 32(\dagger)</td>
<td>18 ± 27(\dagger)</td>
<td>26 ± 35</td>
</tr>
</tbody>
</table>

\(\ast\)Data are expressed as mean ± SD. Data extracted from Brolin et al.72

\(\dagger\)REYGB indicates Roux-en-Y gastric bypass; CHO, carbohydrate; SWS, sweet/soda intake; MIC, milk and ice cream products; NLS, nonliquid sweets; and HCL, high-calorie liquids.

\(\dagger\)Significant difference between preoperative and postoperative intake.

more carbohydrate (43.0 ± 4.6 vs 45.2 ± 6.5%, \(P < .01\)), especially monosaccharides and disaccharides (17.8 ± 5.2 vs 19.6 ± 5.7%, \(P < .01\)), more sweet foods (16.8 ± 10.4 vs 21.4 ± 8.7%, \(P < .01\)), and alcohol (1.7 ± 2.2 vs 2.9 ± 1.2%, \(P < .001\)). From these data it is clear that weight loss following REYGB is directly related to the amount of energy ingested.

**DUMPING SYNDROME**

Dumping syndrome refers to a group of symptoms that results when the stomach rapidly and without regulation empties its contents into the small intestine. These symptoms may occur early, within 15 to 30 minutes of eating, or can be delayed for as long as 2 hours after eating. The early dumping syndrome results in both vasomotor (tachycardia, palpitations, sweating, flushing, dizziness and syncope) and gastrointestinal (nausea, vomiting, crampy abdominal pain, diarrhea and belching) symptoms, which can be bothersome and disabling for many patients. Dumping syndrome was initially described in patients undergoing gastrectomy, pyloroplasty and vagotomy for ulcer disease or cancer but most recently has also been shown in patients undergoing REYGB for weight management.

The pathophysiological mechanism(s) responsible for the signs and symptoms associated with dumping syndrome include a rapid fluid shift from intravascular space to the gut lumen and release of vasoactive substances such as vasoactive intestinal polypeptides, neurotensin, and motilin.88 The signs and symptoms associated with late dumping syndrome are probably related to fluctuations in the blood glucose level. Rapid delivery of sugars into the small intestine cause the pancreas to release insulin into the bloodstream: a normal response. Unfortunately, not all the sugars in the small intestine are digested and absorbed; therefore, a decrease in blood glucose level results as insulin release is excessive in relation to the sugars absorbed. Several studies have investigated hormone response to a meal after gastric bypass. Kellum14 and associates measured gut-hormone release in a group of patients after gastric bypass surgery. Measurements were made before surgery and at 6 to 9 months after gastric bypass. Patients were fed a defined protein-fat meal on the first day and a 100 g glucose oral preparation on the second. All patients postoperatively developed symptoms compatible with the dumping syndrome after the glucose meal but not after the mixed meal. These symptoms were associated with a dramatic increase in enteroglucagon release. There was no difference in the release pattern for cholecystokinin, vasoactive intestinal peptide (VIP), or 5-hydroxytryptamine after the operation. The
surgery also produced a significantly lower fasting and integrated postprandial blood glucose level as well as a lower insulin response when compared with preoperative levels.

The symptoms associated with the dumping syndrome are greatest and most exaggerated after ingestion of high carbohydrate (greater than 100 g = 400 kcal), high-osmolality meals (concentrated fat and sugar content) and may worsen if large volumes of liquids are also consumed with the meal. The exact prevalence of dumping syndrome after REYGB surgery is unknown. Most large series of patients failed to mention the prevalence of this problem in their report. The highest prevalence of dumping syndrome in a large series reported is 70.9% by Pories and associates. However, very little information was provided regarding the occurrence and frequency of dumping syndrome and it is not clear if this number represents the number of episodes reported or the number of patients with persistent symptoms. Other authors have reported a significantly lower incidence of dumping syndrome after REYGB. Monteforte and Tulkelson completed a meta-analysis of 62 studies of bariatric surgery and found a combined incidence of 14.64% of dumping syndrome for combined restrictive and malabsorptive surgical procedures. Crowley reported 10% of patients experienced weakness and sweating after eating, suggesting dumping syndrome. Benotti et al reported 33% of patients with dumping syndrome. Sugerman et al reported that 50% of patients with REYGB experienced symptoms of dumping syndrome such as lightheadedness, nausea, flushing, sweats, or diarrhea after eating sweets, with another 25% stating they were either afraid to try sweets or had lost their taste for sweets, while three patients reported never developing dumping type symptoms. It is not clear from this report how severe the symptoms were and how long the symptoms lasted. Pories and others also reported a 3.5% incidence of hypoglycemia, which could be related to dumping syndrome.

Some authors believe that dumping syndrome is beneficial after REYGB surgery. It is postulated that the mechanism responsible for dumping can contribute to a lower energy intake producing a greater weight loss with REYGB as compared to other restrictive surgeries such as VBG. However, Mallory et al failed to showed greater weight loss in patients with dumping after REYGB as compared to patients with no symptoms of dumping syndrome. Furthermore, with time patients tended to increase the consumption of sweets and the symptoms of dumping syndrome became less frequent.

Both early and late dumping syndrome improve with minor dietary modifications such as avoidance of high-sugar and calorically dense foods as well as excessive fluid intake with meals. More important, it improves with time, but some patients may continue with symptoms for a long time. There are no long-term longitudinal data available addressing the issues of frequency and severity of symptoms or the importance of dumping syndrome in the overall management of patients post-REYGB. Patients who continue with symptoms after dietary education and modification of the diet may respond to the addition of fibers such as pectin, or ascarbose, to delay carbohydrate absorption. In addition, octreotide is useful in patients who have undergone partial or total gastrectomy who experience refractory symptoms.

MICRONUTRIENT DEFICIENCIES

Vitamins

Vitamins are chemical compounds required by the body to perform normal metabolic processes optimally. Most vitamins are coenzymes or cofactors in metabolic pathways involved in carbohydrate, fat, and protein metabolism. Other vitamins function in oxidation/reduction reactions, as antioxidants or as hormones (ie, vitamin D). Vitamins cannot be synthesized by the human body and need to be consumed in food as part of the diet on a regular basis. Humans require 13 vitamins to maintain health. Failure to consume adequate amounts of any and all vitamins results
in alterations of metabolism and yields typical clinical signs and symptoms of specific vitamin deficiencies.94

There is great concern regarding the potential for patients to develop vitamin deficiencies after REYGB, because of the anatomical alterations and the changes in food intake following WLS. Unfortunately, the incidence of vitamin deficiencies after REYGB other than folate and vitamin B12 is unknown. The majority of surgical weight loss programs do not routinely measure vitamin levels before or after surgery or routinely monitor the adequacy of oral vitamin intake. Furthermore, the signs and symptoms of many vitamin deficiencies are subtle and may be difficult to identify.

Several studies have assessed the average intake and blood levels of several vitamins before and after WLS.75,80–82,95 Miskowiak and associates assessed the oral intake of 32 women before and after gastroplasty, for treatment of morbid obesity, at 3 and 12 months by using a 7-day dietary check list.95 Preoperative intake of most vitamins was above the lower level of the recommended dietary allowances (RDAs) except for vitamins D and B6 and folate. Three months after surgery, the intake of all vitamins, except for vitamin K, were below the minimum RDA. At 12 months the intake of all vitamins except for vitamin K, niacin, and B12 remained below the minimum RDA, and for many, vitamin intake was less than 50% of the RDA.95,96

Boylan et al77 measured total vitamin intake (vitamins contained in oral food plus supplements) and plasma levels of vitamins E, B6, B12, and folate in 22 patients before and after REYGB.77 Patients were instructed to take a specific brand of MV or 2 chewable MVs per day, but 4 (18%) patients reported only rare consumption of the supplements. The pre-REYGB total vitamin intake of vitamin B6 and folate was 15% and 20%. Fifteen to 20% of the patients were below 67% of the RDA for these vitamins, whereas the intake of vitamins E and B12 were above the RDA in all patients. The intake of vitamin E (35.1 ± 13.6 vs 9.6 IU), vitamin B6 (2.3 ± 0.9 vs 0.8 ± 0.4 mg), vitamin B12 (6.5 ± 3.9 vs 1.7 ± 1.3 µg), and folate (348 ± 118 vs 149 ± 89 µg) were significantly higher before than after 12 months of the surgery, respectively. Oral intake of vitamins below requirements or below the RDA has been reported by others for folate,80 vitamins B6 and B12,79 vitamin C,79 vitamin D,79 and vitamin A78,79 after gastric bypass surgery.

Low postoperative vitamin intake may result in low serum vitamin concentration. Boylan et al found higher mean serum vitamin levels of vitamins E, B6, B12, and folate after REYGB as compared to those before surgery. However, not all patients had normal vitamin status postsurgery. Serial measurements of vitamin E showed marginal serum levels in 6 of 17 patients (35%) at 6 months and 2 of 16 patients at 12 months, respectively, despite MV supplementation. Eight of 17 patients had low folate levels at 6 months and 7 of 17 had low levels at 12 months, despite consuming vitamin supplements that contained adequate amounts of vitamins according to the RDA.77 Brown et al reported low serum carotene and vitamin A levels.78 MacLean measured several vitamins in a group of patients admitted for malnutrition or very rapid weight loss. He found that 50%, 65%, and 24% of the patients had low levels of serum thiamine, folate, and vitamin B12, respectively.44

Serum vitamin B12 is measured routinely by most surgeons and low levels have been commonly reported in many large series.91,97–100 The incidence of low serum vitamin B12 at 1 year after REYGB is 30% to 35% but estimates as high as 70% have been reported depending on the time of follow-up and whether the patient had received MV and/or vitamin B12 supplementation. Low levels of vitamin B12 can be seen as early as 6 months after surgery but most commonly occurs 12 months or longer after WLS.99

There are two sources of vitamin B12: food and pharmaceuticals. Unlike most other nutrients, the absorption of dietary vitamin B12 is an involved process that requires an intact stomach, coordinated pancreatic enzyme release, and an adequate amount of ileum, particularly the terminal portion.
The first step of vitamin B<sub>12</sub> absorption is the release of bound vitamin B<sub>12</sub> from the food via gastric acid and intestinal enzymes. The free vitamin B<sub>12</sub> attaches to salivary R-binder proteins in the stomach. The R-vitamin B<sub>12</sub> complex exits the stomach and enters into the small intestine where pancreatic enzyme releases R-proteins, allowing binding of vitamin B<sub>12</sub> to intrinsic factor (IF), which is a protein synthesized and secreted only by gastric parietal cells. This vitamin B<sub>12</sub>-IF complex moves through the intestine, where it attaches to receptors of the complex in the ileum. The complex is then taken up by the ileal enterocyte and diffuses, or is transported, across the enterocyte via transcobalamin II into the portal venous system, at which point it attaches to the vitamin B<sub>12</sub>-binding proteins. The mechanism of absorption for the pharmaceutical form of vitamin B<sub>12</sub> is diffusion. Approximately 1% of any free vitamin B<sub>12</sub> can be absorbed along the entire length of the intestine.<sup>100</sup>

Roux-en-Y gastric bypass alters the normal physiological mechanisms of absorption of vitamin B<sub>12</sub> in several ways: (1) by decreasing consumption of meat, milk, and other high vitamin B<sub>12</sub> containing foods<sup>85–87</sup>; (2) by decreasing gastric acid and pepsin release, thereby inhibiting the release of food-bound vitamin B<sub>12</sub><sup>101,102</sup>; (3) by causing incomplete release of vitamin B<sub>12</sub> from R-binders by the pancreatic enzymes<sup>102,103</sup>; and (4) by decreasing availability of IF because of bypassing the stomach.<sup>104</sup> Because of anatomic and physiologic restructuring, the majority of REYGB patients cannot maintain normal vitamin B<sub>12</sub> levels with an oral diet alone, and will require supplementation regardless of the mechanism responsible for inadequate absorption.

The body can store vitamin B<sub>12</sub>, with the average amount being between one and five mg, of which 50% to 90% is found in the liver. Daily vitamin B<sub>12</sub> requirements are approximately one micrograms/d; therefore deficiency may take years to develop. Absorption of pharmaceutical (crystalline) vitamin B<sub>12</sub> is normal after REYGB.<sup>105</sup> The amount of vitamin B<sub>12</sub> in adult MV preparations provides 6 µg and may not be enough to prevent low serum vitamin B<sub>12</sub> levels after REYGB.<sup>106,107</sup> Normal serum vitamin B<sub>12</sub> levels can be maintained by providing at least 350 to 500 µg of crystalline vitamin B<sub>12</sub><sup>106,108</sup> or 100 µg monthly via intramuscular injection.<sup>101</sup>

Vitamin B<sub>12</sub> deficiency after REYGB is usually detected by low serum levels, and is most frequently subclinical. However, early signs of deficiency could be detected if clinicians measured serum levels of methylmalonic acid and homocysteine<sup>109</sup> which are associated with an increased risk of cardiovascular disease. Vitamin B<sub>12</sub> deficiency after REYGB may cause megaloblastic anemia<sup>110</sup> or neuropsychiatric disorders without anemia.<sup>111</sup> The neuropsychiatric signs and symptoms associated with vitamin B<sub>12</sub> deficiency include paresthesia, especially numbness and tingling in the hands and feet, diminution of vibration and/or position sense (occurring first in ankles and feet, but not always), unsteadiness, mental slowness, poor memory, confusion, agitation, depression and central scotomata. Also, the neurological changes observed with vitamin B<sub>12</sub> deficiency tend to be symmetrical and not unilateral as in stroke, although extreme delusions and hallucinations and even overt psychosis may occur.<sup>101</sup>

Folate, another water-soluble vitamin, also has been known to be affected by WLS. The incidence of patients with low serum folate levels after REYGB has been reported to be anywhere between 6% and 35%<sup>97,98,107</sup> Folate is widely found in foods, including both animal and vegetable sources. Folate from food is absorbed primarily in the jejunum although it can be absorbed along the entire length of the small bowel. Folate is moved from the gut lumen through the enterocyte via an active transport mechanism.<sup>100</sup> Active transport is a more complex mechanism of absorption that requires energy and a carrier system unlike simple passive diffusion, which requires no energy and moves via a concentration gradient. But before folate can be absorbed chemical alterations must occur to liberate it from the food containing it.

Folate present in food is found primarily as a complex, with 1 or more glutamic
acid molecules. Before folate can be absorbed into the body, the excess glutamate must be released from the side chain of the folate molecule by enzymes. These enzymes are present in the intestinal lumen and intestinal mucosa, and are inhibited at high intraluminal pH (alkali or basic environment) and by certain drugs such as salicylazosulfapyridine, diphenylhydantoin, and alcohol. Therefore, folate deficiency can occur because of insufficient intake or interference in absorption secondary to chemicals or altered gastrointestinal function. The latter would be of greatest concern with WLS.

Folate deficiency can also cause megaloblastic anemia. Neurological damage is less common with folate as compared to that with vitamin B₁₂ deficiency, because folate deficiency does not affect the myelin of nerves. However, patients with folate deficiency frequently present with irritability, forgetfulness, hostility, and paranoid behaviors. As with vitamin B₁₂, most patients after REYGB with deficiency are asymptomatic or suffer from subclinical disease. Therefore, these deficient states are not recognized. The signs and symptoms of folate deficiency quickly improve after 24 hours of treatment. Ingestion of regular MV preparations, containing 400 µg of folate, usually prevents folate deficiency after REYGB. A below-normal serum folate level found in patients after REYGB is usually a sign of noncompliance with prescribed recommendations of oral vitamin supplementation. Patients who are found to have low folate levels with regular MV ingestion will quickly respond to additional oral folate at a dose of 1 mg/d.

Thiamine: Wernicke’s encephalopathy

Deficiencies of vitamin B₁₂ and folate are the most common after REYGB, but thiamine deficiency is the most dangerous and has greater clinical importance. Thiamine (vitamin B₁) is a water-soluble vitamin found in a large variety of animal and vegetable products, but is abundant only in a few foods. It is absorbed in the small intestine by two mechanisms: an active transport mechanism that is greatest in the jejunum and by passive diffusion. The total amount of thiamine present in a normal healthy adult is approximately 30 mg, 50% of which is found in the skeletal muscle, with the remainder found in the heart, liver, kidney, and brain. The biological half-life of thiamine in the body is 9 to 18 days. Thiamine is not stored in large amounts in any tissues of the body; therefore, a continuous supply of thiamine is necessary on a regular basis. Thiamine is essential for the metabolism of carbohydrates and branched-chain amino acids. Decreased food intake or malabsorption after REYGB results in thiamine deficiency. However, thiamine deficiency after REYGB can be subclinical, that is to say it can go undetected or can be quite blatant, if recognized by the knowledgeable practitioner as dry beriberi, Wernicke’s encephalopathy (WE), or as wet beriberi.

Patients with undiagnosed or subclinical thiamine deficiency often show irritability, frequent headaches and unusual fatigue. Patients with wet beriberi present with edema and congestive heart failure and those with dry beriberi present with peripheral neuropathy characterized by symmetrical impairment of sensory, motor, and reflex functions that primarily affects the distal segment of the extremities more severely than the proximal limb. Very often the patients have difficulty rising from a squatting position. Wernicke’s encephalopathy is a disease characterized by the triad of nystagmus, ophthalmoplegia, and ataxia of gait. Korsakoff psychosis refers to a mental disorder in which retentive memory is impaired out of proportion to other cognitive functions. Patients with features of both are referred to as Wernicke-Korsakoff syndrome. At autopsy, patients with WE have petechial hemorrhages and necrosis of the mammary bodies in the paraventricular regions.

Wernicke’s encephalopathy is diagnosed either clinically or at autopsy. Clinical diagnosis is established when patients present with 1 or more of the features of WE followed by clinical improvement with thiamine.
supplementation. Very few patients with WE present with the typical triad of nystagmus, ophthalmoplegia, and ataxia. Therefore, it is important to recognize the early stages of the disease when only 1 or 2 of these signs may be present. Low serum thiamine (B1) or erythrocyte transketolase levels, as well as deficiencies of other vitamin, folate, and B12 will support the diagnosis of WE, but often these laboratory measurements are not available to the clinician in a timely fashion. Peripheral neuropathy is present in a great number of patients with WE, and magnetic resonance imaging (MRI) can show typical lesions of WE in 50% of cases.116,117 However, it should be pointed out that many cases with typical WE presentation and response to thiamine have been reported when the MRI is normal.118,119

Patients with WE also may have a normal EEG, cerebrospinal fluid examination, and head CT.

Harper found that 80% of patients with WE at autopsy were undiagnosed prior to death.120 The main reason for this discrepancy is the lack of awareness of clinicians in recognizing situations conducive to the development of WE. Although most clinicians are aware of the high risk for WE in alcoholics they are not aware that WE is also common in other conditions associated with recurrent vomiting and malnutrition such as hyperemesis gravidarum,121–124 strict dieting,125–129 during childhood,130,131 after gastric surgery,132,133 and after WLS,134–145 including REYGB.144,145 Most of these conditions occurred in patients with persistent vomiting and excessive weight loss and/or who have received prolonged administration of intravenous (IV) fluids containing dextrose in water solutions without thiamine or MV supplementation. Because thiamine is needed for carbohydrate metabolism, administration of dextrose in water solutions without thiamine or MV supplementation may unmask a previously unrecognized or subclinical thiamine deficiency. Because there is no clear-cut definition of WE, and because routine surveillance is not done by most WLS programs, many cases of WE go unrecognized and/or unreported. Unfortunately, it is difficult with the currently available research data to estimate the frequency of WE after REYGB, but recent reports suggest that it may be higher than once thought.144,146

Once WE is diagnosed, or even suspected, treatment must be initiated immediately, because any delay may result in permanent neurological damage and/or death.114 Treatment consists of IV administration of 100 mg of thiamine daily for 5 to 10 days or until the patient is able to take thiamine by mouth. Oral thiamine supplementation must continue at a daily dose of 50 mg for an extended period of time, perhaps continuing for several months. It is also important to give patients intravenous MV because of the high possibilities that the patient has other subclinical deficiency of vitamins such as niacin or pyridoxine that may also be contributing to the clinical syndrome. Response to IV thiamine is variable but in some cases can nearly completely resolve all of the signs and symptoms observed. Victor et al147 in his experience with alcoholics found that after thiamine administration the recovery from the ophthalmoplegia began earlier, often within hours after administration, and recovery tended to be complete, except for a residual fine horizontal nystagmus in 60% of the patients. Recovery from ataxia was relatively delayed, and in 62% recovery was incomplete or entirely absent. Recovery from acute mental signs tended to begin within 2 weeks of therapy, but in many cases the global confusional state gave way to Korsakoff psychosis, with chronic impairment of retentive memory. Reported mortality in the Victor et al series was approximately 10%. Most of these patients were alcoholics and died in the acute phase of their illness, and other factors such as hepatic encephalopathy, gastrointestinal bleeding, pancreatitis, malnutrition, etc may have contributed to their death. Many other patients were left with permanent neurological damage that required institutionalization. Death has also been reported in the REYGB population after WE developed.148 These patients are also admitted to the hospital more
frequently, but the long-term disability is not known.

Most commonly WE will develop between the second and the eighth postoperative months in REYGB. Patients usually give a history of unremitting nausea and vomiting and inability to drink or eat. They are usually dehydrated and are admitted to the hospital for treatment. Many of them will have gastric outlet obstruction and/or a gastrojejunostomy stricture. However, not all patients with anastomotic stricture and/or frequent vomiting develop WE. The reasons for this are not totally understood. Potential explanations are differences in thiamine storage and genetic variations in thiamine-dependent enzymes. 148

According to the reviewed literature, wet beriberi has not been reported after REYGB but has been reported after gastrectomy and after poor diets. 149 This is likely due to underrecognition of this disorder. Many cases of polyneuropathies after REYGB have been reported and most of them are likely due to dry beriberi or thiamine deficiency, 137,144,150–155 but others have features that are atypical for thiamine deficiency. 146,156 Post-REYGB polyneuropathy is similar to cases of nutritional neuropathies described in an epidemic in Cuba from 1992 to 1994. 156 In this instance, otherwise-healthy patients developed polyneuropathy after consuming diets high in carbohydrate and low in meats, pork, egg, milk, and vegetable oils. In Cuba, the epidemic was halted when the diet was supplemented with a vitamin supplement containing the B-vitamins, folate, and vitamin A. 157,158 Although many patients had evidence of thiamine deficiency, some patients had normal thiamine levels, yet others with low thiamine levels did not develop the syndrome. This suggests that nutrients other than thiamine may have been responsible for the signs and symptoms of the epidemic. Some patients developed typical symptoms of vitamin B12 and niacin deficiencies, and it is believed that deficiencies of riboflavin and pyridoxine may account for some of the symptoms as well. Thus it is possible that post-REYGB polyneuropathy, as the Cuba epidemic, is due to multivitamin deficiency and not only thiamine deficiency. This is plausible since the intake of many foods and therefore most vitamins are reduced after surgery (see above). Except for Boylan et al, who measured levels of pyridoxine, no other researchers have studied the role of niacin, riboflavin, pyridoxine, biotin, etc in the pathogenesis of post-REYGB polyneuropathy has not been assessed. Another factor that has been implicated in post-REYGB polyneuropathy is carnitine deficiency. 159 Carnitine is a nutrient necessary for intracellular mitochondrial function. Therefore, it is important to consider that most patients with thiamine deficiencies and/or polyneuropathies post-REYGB suffer from multiple deficiencies of other nutrients, all of which needs to be treated.

MINERAL DEFICIENCIES

Iron: Anemia

Iron deficiency is the most common nutritional deficiency found after REYGB. This is not surprising, since iron deficiency is the most common nutritional deficiency in the world. Furthermore, REYGB anatomically alters many of the normal physiological mechanisms of iron absorption. The RDA for iron for men and non-menstruating women is 10 and 15 mg/d, respectively, and for menstruating and pregnant women is 15 and 45 mg/d, respectively. The average dietary intake of iron in the United States is between 10 and 30 mg/d or between 5 and 7 mg/1000 kcal/d. Thus, people who restrict their energy intake to 1000 to 1500 kcal/d may only consume 6 to 9 mg of iron from food ingested per day, clearly not an adequate amount by any standard. 160

Iron is primarily obtained from the foods we eat or from oral iron supplementation when oral intake of iron is inadequate. Dietary iron can be ingested in animal products as part of hemoglobin and myoglobin (heme iron) or in plant products such as cereals, fruits, and vegetable products (inorganic iron). Foods can also be fortified with iron,
which means that additional inorganic iron can be added to grains, cereals, or breads in the preparation or processing of foods. Fortification increases the quantity of iron above the levels that would naturally be found in these products. In addition, food can be contaminated with additional iron in the preparation process from iron-containing utensils and cookware (cast iron skillets). Iron adsorbed into the food in this way when consumed will be supplying additional iron to the individual. Once iron is ingested it is absorbed during the digestive process by different mechanisms depending on the form of iron. Heme iron is absorbed directly by intestinal mucosal cells after removal of the globin by proteolytic duodenal enzymes, or the protein portion of the hemoglobin molecule can be removed within the mucosal epithelium. Non-heme iron is absorbed by a more complex and elaborate process. First, reduction of iron from $\text{Fe}^{3+}$ to $\text{Fe}^{2+}$ by the acidic gastric juice must occur. Acidic substances that form low-molecular-weight iron chelates such as ascorbic acid, sugars, and amino acids promote inorganic iron absorption and will facilitate absorption. Absorption of iron may occur at any level of the intestine, but it is more efficient in the duodenum. Weight loss surgery, in particular REYGB, causes iron deficiency because it reduces the oral intake of foods that contain both heme iron and nonheme iron. Iron deficiency results from the inability of patients to eat meats, milk, and other high-iron-content foods. In addition, REYGB reduces non-heme iron absorption because the conversion of $\text{Fe}^{3+}$ to $\text{Fe}^{2+}$ is blunted owing to the reduction in gastric acidity, and because the duodenum, the site with the greatest potential for iron absorption, is bypassed. Iron deficiency can also be caused by gastrointestinal bleeding. Most experts agree that surgery-related bleeding is minimal, but gastrointestinal bleeding may occur with anastomotic ulcers, esophagitis, polyps, or other forms of GI bleeding as occurs in people without WLS. Bleeding from the bypassed stomach and proximal small bowel will be difficult to detect as this area is not accessible with standard endoscopic techniques. In addition, menstruation contributes to further blood loss.

The prevalence of iron deficiency after REYGB has been estimated to be between 30% and 50%, and is higher in menstruating women. Iron deficiency can be easily diagnosed with readily available laboratory analysis. Typically, iron deficiency is diagnosed when patients have low serum iron saturation, low serum iron level, elevated total iron-binding capacity (TIBC), low serum ferritin, and microcytosis. Frank anemia may or may not be apparent. Patients with iron deficiency complain of generalized fatigue, weakness and a feeling of being overtly tired even if anemia is not present. When anemia is present the symptoms are more exaggerated. Treatment of iron deficiency requires iron supplementation. Whenever possible, patients should be encouraged to eat meat to increase heme-iron availability and absorption. Avinoah et al have shown that patients who are able to tolerate meat have a lower risk for iron deficiency. Most patients, however, will require iron supplementation to prevent and/or to treat iron deficiency.

Available evidence indicates that MV with minerals, as recommended by many surgeons, is not enough to prevent iron deficiency, and would be even less effective for treatment of any iron deficiency that may already exist. Brolin et al investigated the role of iron sulfate in the prevention of iron deficiency and anemia after REYGB. Fifty-six menstruating women were randomized to receive 325 mg of ferrous sulfate twice a day or a placebo for 24 months. Hemoglobin and hematocrit decreased equally in both groups compared with preoperative values. Serum iron, TIBC, and iron saturation was similar in both groups at all times, but ferritin decreased by 24 months in the placebo group while it remained in the normal range in the ferrous sulfate group, suggesting inadequate iron absorption and storage. Thus, prophylactic iron supplements prevented iron deficiency but did not protect the women from developing anemia. Importantly, 8 women (14%)
developed anemia in the absence of iron deficiency. The majority of women (57%) who develop anemia responded to oral iron supplements. Iron is a difficult mineral to absorb even when anatomy and physiology are normal, and the addition of chewable vitamin C may increase iron absorption; it is unknown if this occurs after WLS. Finally, some patients are unable to tolerate oral iron supplements because of intestinal adverse effects and require intravenous iron administration to correct the deficiency.

**Calcium: Metabolic bone disease**

Metabolic bone disease and an increased risk of bone fractures are known complications after partial gastrectomy for ulcer disease or cancer. Bone biopsies in these patients often show features of both osteoporosis and osteomalacia. Osteoporosis is common with aging in patients with or without gastrectomy and is not a unique feature, but osteomalacia is less common in the general population and is a more characteristic feature of postgastrectomy metabolic bone disease. Studies on patients with partial gastrectomy have consistently shown features of osteomalacia, including bone pain, elevated serum alkaline phosphatase levels, decreased serum calcium levels, decreased serum 25-hydroxy vitamin levels, elevated levels of 1,25-hydroxy vitamin D, elevated serum concentrations of parathyroid hormone, widened osteoid seams on bone biopsies, and pseudofractures on bone films. Therefore, another major concern for patients who undergo REYGB is the possibility of metabolic bone disease in the future.

Ott et al assessed for features of metabolic bone disease in 26 women 10 years after REYGB as compared to 7 women who achieved weight loss with dietary restriction. The post-REYGB women had significantly higher serum alkaline phosphatase and serum osteocalcin levels, but lower serum calcium and 25-hydroxy vitamin D concentrations than women in the control group. The bone mineral density (BMD) was significantly higher in the REYGB group at the lumbar spine (L1-L4), but it was reduced at the femoral neck. Crowley et al also has shown elevated serum alkaline phosphatase levels and low serum calcium levels in patients 7 years post-REYGB. Thus preliminary evidence already exists suggesting patients with REYGB may be at a high risk for osteomalacia, and 1 such case has already been reported by Goldner et al. In addition, Shaker et al reported 2 cases with non-traumatic bone fracture and hyperparathyroidism after gastric bypass. Because the number of REYGB in the last 5 years has dramatically increased, it is likely that an increase in the incidence of osteomalacia and fractures will become apparent in the next decade.

There is also great concern regarding the risk of osteoporosis post-REYGB. Obesity is associated with a high bone mineral density (BMD) and a lower risk of osteoporosis. Weight loss has been reported to reduce BMD and potentially increase the risk for osteoporosis and fracture. A typical 10% weight loss is associated with 1% to 2% loss of BMD, and with higher weight loss, as seen in patients with REYGB, the risk for reduced BMD and fracture is higher. Research by Compston et al and Jensen et al has shown a decrease in BMD in patients consuming an energy-restricted diet of 400 to 452 kcal/d, which is similar to the diet consumed by REYGB patients in the early postoperative period. Goode et al performed bone density screening in 44 women (23 premenopausal and 21 postmenopausal) 3 to 5 years after REYGB and compared the findings to age-and weight-matched controls. Twenty-nine (66%) of the women were found to have low BMD at 1 or more skeletal sites. The premenopausal women had no significant difference in lumbar spine BMD or bone mineral composition (BMC) compared with the controls. The postmenopausal women had higher BMD and BMC at the lumbar spine but significantly lower BMD and BMC at the femoral neck than postmenopausal control women. Thirteen of the 44 initial subjects were then re-scanned 6 months later after receiving 600 mg elemental calcium per day in addition
to an MV with mineral supplement that contained 5 µg/d vitamin D and 160 mg/d of calcium. There were no differences in lumbar spine BMD or BMC in REYGB women between the baseline value and that at the 6-month follow-up. REYGB subjects had higher levels of serum PTH and higher levels of pyridinium crosslinks and deoxypyridinolines (markers of bone turnover) at baseline and after 6 months of calcium supplementation as compared to controls, questioning adequate absorption. This study also shows early evidence of osteoporosis and metabolic bone disease in patients after REYGB. However, these data should be considered preliminary evidence, since BMD were not measured before the surgery and the follow-up BMD scan was completed too soon after therapy. The effect of a therapy to alter bone metabolism is usually reflected by BMD changes 12 to 24 months after the initiation of therapy. Reductions in BMD and increases in deoxypyridinoline and osteocalcin have also been reported by von Mach et al.\textsuperscript{171}

The importance of preoperative metabolic assessment is underscored by the results of several studies that document that some morbidly obese patients have evidence of metabolic bone disease and altered vitamin D metabolism before surgery. Hamoui et al found that 25% of patients pre-WLS had elevated PTH, and 21% and 23.1% had low 25-hydroxy vitamin D and 1,25-hydroxy vitamin D levels respectively.\textsuperscript{172} Buffington et al found that 62% of patients had low 25-hydroxy vitamin D level before REYGB.\textsuperscript{173} The 25-hydroxy vitamin D levels were significantly and inversely correlated with BMI. Other investigators have also documented low 25-hydroxy vitamin D levels and an altered vitamin D metabolism axis.\textsuperscript{174,175}

Therefore, long-term surveillance for metabolic bone disease should be part of the postoperative medical management of REYGB patients. More important, postmenopausal patients are at higher risk of fractures, because they have the potential for metabolic bone disease in addition to osteoporosis. Therefore, patients who have undergone REYGB should be advised to take calcium and vitamin D supplements and engage in weight-bearing physical exercise as a component of routine medical care.

OTHER NUTRITIONAL DEFICIENCIES

Disorders in mineral and trace element metabolism other than iron and calcium have rarely been reported after REYGB. Crowley et al reported hypokalemia in 2.4% of his patients,\textsuperscript{91} and Schauer et al reported hypokalemia in 5% and hypomagnesemia in 0.7%.\textsuperscript{7} However, much higher prevalence of electrolyte imbalances were reported by Halverson, who reported 56% prevalence of hypokalemia and 34% of hypomagnesemia in patients at least 1 year after gastric bypass.\textsuperscript{98} Burge et al reported no change in zinc levels in patients after REYGB.\textsuperscript{53} Carnitine levels have rarely been measured.\textsuperscript{159}

MACRONUTRIENT CONCERNS

Protein-calorie malnutrition

Macronutrients are less affected with REYGB than micronutrients. Carbohydrate malabsorption has not been studied, but it could contribute to gas formation and bloating after REYGB. Some patients developed lactose malabsorption after REYGB.\textsuperscript{176} Fat absorption, except for patients with long- or very-long-limb gastric bypass, is also likely to be relatively well preserved, as discussed above.

The macronutrient of major concern after REYGB is protein. Protein-calorie malnutrition (PCM) can develop after REYGB. The prevalence or the incidence of PCM after a standard REYGB is unknown, but the general impression is that it is rare and occurs less frequently as compared to malabsorptive WLS. The main factor that hinders the estimation of the prevalence of PCM after REYGB is the lack of a working definition of PCM. The authors of a large series of WLS fail to report nonsurgical-related complications. In
addition, there is a lack of uniformity of laboratory and clinical data obtained on these patients at follow-up visits. For example, Brolin and Leung reported that 76% of bariatric surgeons ordered liver function tests and only 8% ordered measurement of protein or albumin levels routinely. Furthermore, measurement of the concentrations of plasma proteins that are considered to be better indicators of PCM such as prealbumin and or retinal binding protein are almost never done. Amaral reported that total protein and albumin levels significantly declined at 3 and 6 months, with return to baseline level at 12 months. Both total protein and albumin average levels remain within the normal range.

Close examination of the available data, however, clearly shows that some patients develop signs of PCM after REYGB, such as (a) losing more than 25% of excess weight at 3 months or more than 100% of excess weight at 18 months, (b) re-operation for persistent nausea, vomiting, or excessive weight loss, (c) development of edema, hypoalbuminemia, anemia, and hair loss, (d) extreme fatigue that results in inability to walk or to perform simple tasks, and (e) use of enteral or parenteral nutrition.

Pories and others reported a 4% overall incidence of dehydration/malnutrition in their series of 397 patients treated with the Greenville gastric bypass and a 5.9% incidence of pedal edema. MacLean and colleagues used body composition analysis using the multiple isotopes dilution technique to assess the incidence of PCM after WLS and reported malnutrition in 47 patients, 25% of which were 16 to 34 months after gastric bypass. Patients with REYGB lost more weight and developed malnutrition earlier (average 16.2 ± 0.9 months) than most types of surgery. It is interesting to note that most if not all of these patients developed stenosis or obstruction of the gastrojejunal anastomosis, which is presumed to contribute to the development of PCM. When comparing patients who did with those who did not develop malnutrition, it is necessary to assess weight loss.

Surprisingly, total body weight loss (25.9 vs 25.7%) and body fat loss (24.4 vs 36.2%) was similar, but higher body cell mass losses (29.4 vs 18.8%) and higher Na⁺/K⁺ (1.45 vs 1.10) over similar time periods were noted in the malnourished group. In these patients, malnutrition was also associated with lassitude, difficulty obtaining employment, and hair loss. Many of these malnourished patients also had laboratory and clinical evidence of vitamin deficiencies. Finally, many patients in this series presented with recurring vomiting owing to gastric outlet obstruction and required reoperation.

Recently Faintauch et al reported the prevalence of malnutrition after REYGB in a series of 236 consecutive patients over a 68-month period. Criteria for a diagnosis of malnutrition were the presence of 3 or more of the following objective findings: hypoalbuminemia, anemia, inability to walk, or difficulty performing simple tasks. Not one patient had a preoperative history of nutritional problems or organ failure, and all were discharged from the hospital in good condition. Eleven of the 238 patients (4.7%) developed PCM postoperatively. Sixty-three (63%) percent of the patients had external events that precipitated the development of malnutrition, the most common was anastomotic stenosis requiring endoscopic dilatation or eventual surgical revision, and the other 34% had persistent vomiting without demonstrable anatomic lesion. Other events, such as poor intake, that precipitated malnutrition were often present. These patients had demonstrated anemia (mean hemoglobin 9.7 ± 23.0 g/dL), hypoalbuminemia (2.4 ± 8.2 g/dL), and hypcholesterolemia (135 ± 41 mg/dL). Edema was present in 45.5% of the patients, and extreme weakness with patients termed as bedridden was present in 36.4% of the malnourished patient group. Fifty-four percent (54%) of the patients required additional rehospitalization for an average of 0.7 ± 1.4 months, and 36% required reoperation. Patients who were malnourished were treated with a combination of oral, enteral, or parenteral nutrition and required an average
of 3.1 ± 3.4 months of nutrition rehabilitation. Two patients died because of recalcitrant malnutrition, 1 late after surgical correction of gastric outlet stenosis, and another with anorexia nervosa as documented by psychiatry.

Another interesting series of patients with PCM has also been reported by Segal et al.\textsuperscript{182} They reported 5 cases of patients who lost large amounts of weight after gastric bypass as a result of anorexia. The average preoperative BMI of these patients was 50.2 ± 4.4 kg/m\textsuperscript{2} (range 46–52) and the lower postoperative BMI was 25.6 ± 4.3 kg/m\textsuperscript{2} (range 20–30). Despite a postoperative BMI in the normal range all had several signs of malnutrition, including low serum total protein, albumin, and vitamin concentrations. All showed a marked change in their relationship with food when comparing preoperative and postoperative intake that was associated with a fear of regaining weight. These patients chose foods that were palatable, easy to swallow, and of high calorie density, which was followed by (induced) vomiting, thereby reducing all nutrients ingested. These patients were noncompliant with nutritional directions and drug therapy, and missed or shortened their follow-up appointments.

Another sign of PCM commonly seen after REYGB is alopecia. Pories and associates reported a 4.5% incidence of hair loss after the Greenville gastric bypass.\textsuperscript{11} Halverson reported hair loss in 90% of the patients and Benotti et al reported alopecia in 19\%\textsuperscript{92} Amaral\textsuperscript{178} indicated that 75% of the patients in his series experienced hair loss. Hair loss is also common with strict weight reduction diets.\textsuperscript{185–186} Hair loss usually starts after the second postoperative month and can continue for few months. In the experience of Halverson, regrowth of hair usually occurs by the time the weight loss plateaus between 12 and 18 months.\textsuperscript{98} Hair loss may be the result of medications, anesthesia, or nutritional deficiencies, particularly of iron, protein, and vitamins.\textsuperscript{187} Neve et al\textsuperscript{188} reported that patients who developed hair loss after vertical banded gastroplasty responded to zinc sulfate 200 mg 3 times a day.\textsuperscript{188} However, zinc levels were not measured and no placebo control was included in the study; therefore, the improvements could be due to other factors including improvement in diet over time.

Although studies are lacking, it is likely that the absorption of protein after REYGB is preserved in most patients except in those with long or very long limb lengths. The main reason for developing PCM in association with REYGB is decreased protein intake. Most patients developing PCM have persistent nausea and vomiting and have limited oral intake, especially during the first 3 months postoperation. However, all REYGB patients are at risk for PCM, because the protein intake is inadequate even 12 months after surgery.\textsuperscript{87} Previous well-controlled studies of morbidly obese patients have indicated that 70 g of protein per day is necessary to maintain nitrogen balance in patients during severe calorie restriction.\textsuperscript{39} Untreated, severe PCM may lead to immunosuppression, leading to a greater risk for infection.\textsuperscript{189}

**PREGNANCY AND LACTATION**

Pregnancy is a normal physiological state associated with weight gain. Maternal weight gain is the most important variable that determines fetal outcome. In an average pregnancy 33% of the weight gain is accounted for by the weight of the fetus, placenta, and amniotic fluid, and 66% is accounted for by expansion of the maternal tissues, including increases in uterine and mammary tissues, blood volume, extracellular fluid, and fat stores.\textsuperscript{190} Recommendation for weight gain during pregnancy in women who are obese is 15 to 25 lb. Pregnancy increases the requirement for iron and to a lesser degree protein, zinc, and certain vitamins in addition to a small to moderate increase in energy intake. Women consuming a well-balanced diet do not need dietary supplements except for iron. Folate deficiency during pregnancy increases the risk of fetal neural-tube defects,\textsuperscript{191} and
supplementation in the months prior to conception is advisable.

REYGB is commonly performed in women of reproductive age. At the present time the long-term consequences of REYGB on pregnancy and on maternal and/or fetal outcomes are not known. Several case reports have documented that post-REYGB and after other types of WLS patients are fertile and capable of sustaining a normal pregnancy and delivering healthy babies. Nonetheless, women who have had a WLS are at higher risk for complications during pregnancy as compared with women of the same age and weight who have not undergone WLS, because of the difficulty in escalating oral intake to meet the demands of pregnancy. It is difficult for many post-REYGB patients, especially in the first 2 years, to eat a balanced diet that provides at least 1500 kcal and more than 70 g of protein per day, which is the recommended oral intake for pregnant women. Weight loss should not continue during pregnancy or lactation because of the potential deleterious effect on the offspring.

A natural experiment pertinent to understanding the possible effects of REYGB on pregnancy and fetal outcomes is the experience with semistarvation imposed in Rotterdam in 1944–1945. Owing to the famine, the energy and protein intake of pregnant women was 50% of their usual intake, especially during the second and third trimester. Malnutrition during these stages interfered with intrauterine growth and development of the fetus. The result was a 10% reduction in the mean birth weight of newborn infants. Malnutrition of the mother during the first trimester has been associated with the development of adult obesity of the offspring and the development of other chronic diseases. Therefore, malnutrition during pregnancy should be avoided at all costs.

Because of the lack of prospective observations and the limited experience in this area it is difficult to provide rational dietary recommendations for pregnancy after REYGB. The best advice is to avoid pregnancy for the first 2 years following REYGB when the food intake is erratic and often inadequate to sustain a normal pregnancy and lactation. Unfortunately, birth control methods may fail and those patients who become pregnant less than 2 years postoperation should receive additional medical and dietary surveillance. Pregnant patients after REYGB need to receive much higher doses of oral iron during pregnancy as compared to nonpregnant REYGB and normal pregnant women. It is important to ensure an adequate intake of folate owing to the high risk of neural tube defects. Wittgrove suggests that patients continue to take the MV with minerals prescribed post-REYGB and prior to conception in addition to a prenatal MV preparation. Deitel suggests greater amounts of vitamins, adequate amounts of vitamin B12, and vitamin A. However, intake of preformed vitamin A in excess of 10,000 IU per day is associated with higher risks for birth defects. However, vitamin deficiency during pregnancy is associated with immunosuppression and higher morbidity and mortality. Therefore, it is prudent to recommend that vitamin A levels be monitored in all women who become pregnant after REYGB, and vitamin A supplementation be initiated only after a careful analysis of all factors, and when the benefits clearly outweigh the risks of supplementation. Monitoring of vitamin levels needs to be performed in this select population as quickly as pregnancy is suspected or confirmed, since patients with REYGB may have developed vitamin deficiencies following WLS (but prior to conception). In addition to levels of vitamins, those of select minerals and trace elements have been known to be decreased; therefore, pregnant REYGB patients will also need more calcium and zinc supplementation. Most reports have failed to show an increased risk of maternal or fetal adverse outcomes with pregnancy after REYGB. However, these reports were not prospective and many lacked adequate controls. Two cases of neural tube defects and 1 case of severe microcytic anemia with severe iron and vitamin B12 deficiency after gastric bypass have been reported.
ADOLESCENTS

Adolescence is also a period of rapid growth. The average American girl experiences her most rapid linear growth between the ages of 10 and 13 and the average boy experiences his most rapid growth between the ages of 12 and 15. During this time both girls and boys gain a significant amount of weight. The recommended intake of energy and proteins for adolescents during this period is 2200 to 3000 kcal/d and 50 to 60 g/d, respectively. In addition, adolescents have a higher need for calcium to support skeletal growth, for iron to support the expansion of red cell and skeletal bone mass, and for zinc to generate new skeletal and muscle tissue.

Several case reports have shown that adolescents lose as much weight as adults after REYGB and other WLS. However, these reports did not study the patients prospectively and did not assess nutritional or growth issues. Therefore, it is not possible to assess the long-term risk of REYGB on growth, bone metabolism, and nutrition. It would be expected that adolescents would have higher long-term risks of developing nutritional complications after REYGB as compared to adults, including protein-calorie malnutrition, metabolic bone disease, iron deficiency anemia, and complications with pregnancy. In addition, many adolescents may not be compliant with MV and nutritional supplementation. Therefore, it seems prudent to delay WLS in children and adolescents until skeletal and sexual maturity (approximately 13 years for girls and 15 years for boys) have been reached. However, many obese adolescents experience early onset of puberty and are likely to reach maturity sooner than normal-weight age-matched individuals. When there is uncertainty, a bone-age study should be entertained to objectively measure skeletal maturity. Since data are lacking, to say otherwise, the current wisdom would be to choose restrictive over malabsorptive surgical procedures for the morbidly obese adolescent, but prior to any WLS the patient and the family requires evaluation by a multidisciplinary team.

SUMMARY

On average, REYGB patients lose 60% to 70% of their excess weight after surgery, but the results are variable and depend on age, sex, and ethnicity. Postoperative REYGB subjects eat 400 to 600 kcal including 30 to 40 g of protein per day for the first 3 months. After 12 months, energy and protein intake averages 800 to 1200 kcal with 50 to 80 g of protein per day. However, patients continue to eat the majority of their calories at the evening meal (45%), and the percentage of calories from fat remains the same as in the preoperative period, suggesting that overall eating behaviors are not improved by the surgery and just the quantity is decreased. After REYGB there is a marked reduction in vitamin and mineral intake, which are often below the RDA level. The majority of patients after REYGB can maintain a relatively normal nutritional status, but deficiencies of iron, vitamin B₁₂, and folate are common. Some patients develop subclinical micronutrient deficiency. Multivitamin with mineral supplements reduce but do not totally prevent development of iron, folate, or vitamin deficiencies. Some, but not all, patients develop dumping syndrome, and others have major nutritional complications. Three of the most clinically significant are protein-calorie malnutrition, Wernicke’s encephalopathy, and peripheral neuropathy. In the long term, patients are also at risk of metabolic bone disease. Pregnant women and adolescents are at higher risk for nutritional complications after REYGB because of the higher physiological nutrition needs. Therefore, long-term nutritional follow-up care is essential to promote a healthy optimal life following WLS.

RECOMMENDATIONS FOR DIET, SUPPLEMENTATION, AND MONITORING

The available data regarding diet and nutrition after REYGB are fragmented and do
not allow firm conclusion about the optimal diet, nutritional supplementation, or the appropriate nutritional surveillance needed for this population to produce controlled weight loss and minimize complications. Any recommendation therefore should be considered preliminary.

Weight loss greater than 10% of initial weight lost in the first month following surgery would be in excess of the expected weight loss, and closer monitoring is indicated, perhaps weekly weight checks for the next 1 to 4 weeks. Likewise, weight loss in excess of 15% of initial weight at 2 months would signal danger, and weight loss in excess of 20% at 3 months would warrant more careful observation. Weekly weight checks may be necessary during this time interval to initiate treatment quickly if weight loss is too rapid.

All patients should be informed about all the known short- and long-term nutritional risks before undergoing REYGB. In addition, patients should receive instructions on specific calorie and protein targets to avoid nutritional complications. On the basis of previous research data that were well controlled, it is suggested that 800 to 1000 kcal with 70 to 80 g of protein per day are reasonable targets since they have shown to minimize nutritional risks. All patients need to be monitored, with a critical eye for short- and long-term nutritional complications. More research is needed to determine the optimal composition of a post-REYGB diet that produces controlled weight loss while minimizing short- and long-term nutritional complications. In addition, clinical research to determine what nutritional parameters and nutritional markers are necessary to monitor, prevent, and predict complications is indicated. Furthermore, research regarding the most effective, efficient, and financially prudent method to monitor and treat nutritional status is recommended.

REFERENCES

46. Klem ML, Wing RR, Chang CC, et al. A case-control study of successful maintenance of a substantial


76. Coughlin K, Bell RM, Bivins BA, Wrobel S, Griffen WO Jr. Preoperative and postoperative assessment of nutrient intakes in patients who have...


