

Potential Impacts of Nutritional Deficiency of Postbariatric Patients on Body Contouring Surgery

Siamak Agha-Mohammadi,
M.B., B.Chir., Ph.D.
Dennis J. Hurwitz, M.D.
Pittsburgh, Pa.

Background: Bariatric surgery is currently the most effective method of sustainable weight loss for the morbidly obese patient. In the months to years that follow, many patients develop nutritional deficiencies of proteins, vitamins, and minerals as they present for plastic surgery and body contouring operations.

Methods: The aim of this review is to highlight the nutritional deficiencies of postbariatric patients as related to their planned body contouring surgery. This review was prepared by an extensive search of the PubMed and Ovid databases for terms such as “bariatric surgery,” “nutritional deficiency,” “wound healing,” and “immune response.”

Results: The current review indicates that many of the deficient macronutrients and micronutrients of postbariatric patients are implicated in wound healing and optimal immune response.

Conclusions: Although the optimal nutrient intake to promote wound healing is unknown, it is clear that proteins, vitamin A, vitamin C, vitamin B complex, arginine, glutamine, iron, zinc, and selenium can have significant beneficial effects on wound healing and optimization of the immune system. Furthermore, vitamin B complex can reduce homocysteine levels, which is inversely associated with the risk of venous thrombosis and endothelial cell dysfunction. The authors’ preliminary experience with a nutritional blend that contains all of the aforementioned ingredients has significantly reduced their complication rates. (*Plast. Reconstr. Surg.* 122: 1901, 2008.)

Obesity has reached epidemic proportions,¹ with 66.3 ± 1.1 percent of American adults classified as either overweight or obese, 32.2 ± 1.2 percent classified as obese, and 4.8 ± 0.6 percent classified as morbidly obese.² Bariatric surgery is the most effective strategy for obesity management because of its ability to provide sustained weight loss. Weight loss surgery produces weight loss within 12 to 18 months by means of restrictive intake, malabsorption, or both.³ More importantly, patients who lose weight with bariatric surgery are more likely to maintain most of the lost weight and benefit from amelioration of obesity-related comorbidities.⁴ The more common procedures include laparoscopic adjustable banding and Roux-en-Y gastric bypass. Other procedures include vertical banded gastroplasty and biliopancre-

atic diversion and biliopancreatic diversion with duodenal switch.⁵

The popularity of gastric bypass surgery has led to a large population of postbariatric patients seeking plastic and body contouring surgery.⁶ Although a number of surgical procedures have been developed and modified to treat the severe deformities of massive weight loss patients, optimal surgical results can only be obtained in the absence of obesity-related comorbidities, and in physiologically and nutritionally repleted patients. Given that weight loss surgery procedures significantly alter the nutritional status of the patient, many postbariatric patients develop chronic nutritional deficiencies that require continued management.⁷ Reports of significant nutrition

From the Hurwitz Center for Plastic Surgery.

Received for publication February 8, 2008; accepted June 9, 2008.

Copyright ©2008 by the American Society of Plastic Surgeons

DOI: 10.1097/PRS.0b013e31818d20d6

Disclosure: *None of the authors has a financial interest in any of the products, devices, or drugs mentioned in this article.*

and/or metabolic morbidity raise the possibility of much subclinical nutritional morbidity that is both undetected and unreported, and subsequently untreated. The aim of this article is to highlight the potential impact of nutritional deficiencies of weight loss surgery patients on their subsequent plastic surgery procedures.

PATIENTS AND METHODS

This review was prepared by an extensive search of the literature using the PubMed and Ovid databases for broad search terms including “bariatric surgery” and “nutrition deficiency.” A list of the nutritional deficiencies of postbariatric patients was then compiled. Individual searches were performed to identify the role of each nutrient in wound healing, immune response, and physiologic status relating to trauma and surgery.

Weight Loss Patterns after Bariatric Surgery

Before planning body contouring surgery, it is important to appreciate the pattern of weight loss after weight loss surgery. Longitudinal data by Pories et al.⁸ indicate that weight loss starts immediately and continues at a relatively fast pace for 12 to 18 months using a standardized Roux-en-Y gastric bypass procedure. The average 300-lb patient experienced an average absolute weight loss of 125 lb or 75 to 80 percent loss of excess weight at

1 year. Many patients began to gain weight after the second year and on average gained approximately 25 lb by the fifth postoperative year, possibly because of dilatation of the gastric pouch and gastrojejunal anastomosis.^{9,10} Afterward, weight loss remains relatively stable from the fifth year to the 14th year.⁸ Similar data have been reported by other investigators (Table 1).^{11–19}

Body Composition after Bariatric Surgery

Similar to the composition of body mass lost with dietary restriction, the composition of the weight lost after Roux-en-Y gastric bypass is approximately 79 percent fat and 21 percent fat-free mass at 1 year.²⁰ This indicates an appropriate physiologic weight loss. However, a small proportion of the Roux-en-Y gastric bypass patients are frequently admitted to the hospital for complications related to excessive lean body mass loss and malnutrition.²¹ Compared with the nonmalnourished patient, total body weight loss in the malnourished group was 25.9 percent versus 25.7 percent, and body fat loss was 24.4 percent versus 36.2 percent; however, a higher body cell mass loss of 29.4 percent versus 18.8 percent was noted.²¹ Recognition of the malnourished patient and prevention of protein wasting is of paramount importance in preparation of postbariatric patients for subsequent plastic surgery procedures. Typically,

Table 1. Longitudinal Data on Weight Loss Patterns

| Study Design | Sample Size | Weight Change | Excess Weight Loss | Reference |
|--------------------------|-----------------------|----------------|--------------------|-----------|
| Case series | 123 GB | | 1 yr, 36% | 11 |
| Case series | 713 GB | | 9 yr, 21% | 12 |
| Observational two-cohort | 841 RYGBP and 194 VBG | | 2 yr, 53% | 4 |
| | | | 6 yr, 57% | |
| | | | 2 yr, 78% | |
| | | | 10 yr, 65% | |
| | | | 16 yr, 60% | |
| Prospective controlled | 34 RYGBP | 1 yr, -38% | | 13 |
| | | 10 yr, -25% | | |
| | 156 GB | 1 yr, -21% | | |
| | | 10 yr, -13% | | |
| Retrospective controlled | 154 RYGBP | | 1 yr, 62% | 14 |
| | | | 14 yr 50% | |
| Case series | 608 RYGBP | | 2 yr, 70% | 8 |
| | | | 10 yr, 55% | |
| | | | 14 yr, 49% | |
| Case series | 1025 RYGBP | 1 yr, -35% | 1 yr, 66% | 15 |
| | | 5–7 yr, -31% | 5–7 yr, 59% | |
| | | 10–12 yr, -28% | 10–12 yr, 52% | |
| Case series | 39 RYGBP | 2 yr, -38% | 2 yr, 72% | 16 |
| | | 4 yr, -35% | 4 yr, 63% | |
| Case series | 157 RYGBP | 1 yr, -36% | | 17 |
| | | 3 yr, -30% | | |
| Case series | 100 RYGBP | | 1 yr, 78% | 18 |
| | | | 7 yr, 67% | |
| Case series | 500 RYGBP | | 1 yr, 77% | 19 |
| | | | 5 yr, 80% | |

RYGBP, Roux-en-Y gastric bypass; GB, gastric bypass; VBG, vertical banded gastroplasty.

these patients show excessive weight loss of more than 100 percent of excess weight at 18 months.^{22,23}

Postbariatric Oral Guidelines

At the present time, postbariatric patients are not prescribed a specific diet, but are given a set of instructions to prevent complications of anatomical restructuring and physiologic alterations of the weight loss surgery.²⁴ Patients are instructed to eat slowly, to chew well, to eat three to five small meals per day, and to not drink liquids with meals. Patients are also advised to consume protein-containing foods at every meal and to take nutritional supplements to reduce the risk of developing nutritional deficiencies. According to the studies of Coughlin et al.,²⁵ the energy intake for the first and third postoperative month is less than 500 kcal/day with less than 20 g/day of protein. These increase by the sixth month to approximately 1000 kcal/day, with 38 g of protein. At 1 year, the energy intake remains at approximately 1000 kcal/day, but the protein intake increase to 60 g/day. Similarly, Dias et al.²⁶ have shown that the daily energy intake at 3, 6, 9, and 12 months was 529.4 ± 47.4 , 710.9 ± 47.6 , 833.2 ± 72.0 , and 866.2 ± 95.1 kcal/day (mean \pm SEM). Protein intake was increased in the same proportion at 6 and 9 months but reduced at 12 months. Thus, patients do not meet standard recommendations regarding calories and proteins, even at the end of the first year.²⁶

With regard to supplemental nutrition, Brolin and Leung²⁷ noted that 98 percent of surgeons recommended multivitamin supplements to their patients. In contrast, iron, protein, vitamin B₁₂, and calcium supplements were recommended by 64, 56, 50, and 33 percent of the surgeons, respectively. Even when appropriate recommendations are made, intake of most vitamins and minerals are below 50 percent of the recommended daily average²⁸ and compliance is often poor in these patients.²⁹ Thus, it is not surprising that many macronutrient and micronutrient deficiencies have been noted with the various weight loss surgery procedures, as reviewed recently by Agha-Mohammadi and Hurwitz.⁷

Protein-Calorie Malnutrition

Up to 25 percent of weight loss surgery patients are at risk of developing protein-calorie malnutrition for many months after surgery,⁷ because their protein intake remains significantly lower than the daily recommended guidelines (1.5 g/kg ideal body weight) for a low-energy restrictive

diet.³⁰ Protein-calorie malnutrition is defined by a history of inadequate protein and energy intake, unintentional weight loss, or low body weight for height. Roux-en-Y gastric bypass patients commonly consume inadequate protein and less than 1000 kcal/day during the first year.³¹ The reduced protein intake may contribute to an excess loss of lean tissue and malnutrition.^{22,23}

In the postbariatric body contouring patient, protein deficiency impairs wound healing because protein is needed for fibroblast proliferation, angiogenesis, and collagen production (Table 2).^{32,33} Haydock and Hill³⁴ have reported significantly lower healing rates in 21 subjects with mild protein-calorie malnutrition (defined as 90 to 95 percent usual body weight) and nine subjects with moderate to severe protein-calorie malnutrition (<90 percent of usual weight), compared with 36 well-nourished subjects (defined as those with >95 percent of usual weight).³⁴ In addition, any consequent edema adversely affects perfusion of the healing tissues.³⁵ Another factor to consider is the association of severe protein-calorie malnutrition with immunosuppression (Table 2),³⁶⁻⁴¹ which in turn correlates clinically with increased wound complication rates and increased wound failure after clean surgical procedures.³⁹⁻⁴¹

In the context of weight loss surgery, previous studies have indicated that a minimum of 60 to 70 g/day of protein is needed to avert protein-calorie malnutrition.^{42,43} A higher protein intake is desirable during the time of stress and extensive wound healing of a postbariatric procedure. Although not directly related, several studies have shown that higher protein intakes, ranging between 1.25⁴⁴ and 2.1 ± 0.9 g of protein per kilogram,⁴⁵ can enhance the healing process of pressure ulcers.

Vitamin B₆, Vitamin B₁₂, and Folate Deficiencies

Vitamin B complex and folate deficiencies are fairly prevalent after bariatric operations.⁴⁶⁻⁴⁹ Folate deficiency has an incidence of 9 to 35 percent after bypass operations.⁵⁰ The incidence of vitamin B₆ deficiency is approximately 17.6 percent⁵¹ and that of vitamin B₁₂ deficiency ranges from 3.6 to 37 percent at 1 year after Roux-en-Y gastric bypass.⁷

In most Roux-en-Y gastric bypass patients, folate and vitamin B₁₂ deficiencies are asymptomatic or subclinical. However, those with severe deficiency can present with megaloblastosis. Megaloblastosis is a generalized disorder that also affects nonhematopoietic cells, such as gastrointestinal mucosal cells, which have megaloblastic features.

Table 2. Impact of Macronutrients and Micronutrients on Wound Healing and Immune Response Activity

| Primary Nutrient Deficiency | Associated Nutrient Deficiency | Wound Healing | Effect of Deficiency on Immune System | Effect of Deficiency on Immune Response | Comments | References |
|---|--|---|--|--|--|----------------------|
| Protein | Zinc, magnesium, selenium, copper, iron, vitamin A | Required for fibroblast proliferation, angiogenesis, and collagen production | Altered T-cell subsets, increased T-cell function, decreased phagocytic activity, decreased complements, increased IgA; IgG is normal or increased | Decreased skin test reactivity; decreased cytokine response; risk of bacterial, viral, parasitic, opportunistic infections | PCM leads to increased susceptibility to infections and greater morbidity from infections | 32, 33, 36-41 |
| Vitamin C (regulator of redox and metabolic checkpoints) | | Required for the hydroxylation of proline and lysine in collagen synthesis | Decreased plasma glutathione | Decreased phagocytic activity, increased risk of infections | Enhances phagocytosis and complement activity; regulates the phagocytic process by decreasing free radical production and thus potentially reduces the severity of the endotoxin response | 67-71 |
| Vitamin A | Zinc | Increases the inflammatory response in wounds, macrophage influx and activation, fibroplasia, collagen synthesis, and epithelialization | Lymphopenia, decreased mucosal barrier function | Decreased neutrophils, macrophages, and NK cell function; impairs both TH1- and TH2-mediated immune responses | Supplementation improves levels of serum IgA, CD40, ligand-activated IgG and also leads to reduced inflammatory cytokines | 76-84 |
| Vitamin E (strong antioxidant) | Selenium | Supports monocyte/macrophage-mediated responses; influences T-cell function by down-modulating PGE ₂ in elderly | Increased IgE levels, decreased antioxidant defense | Increased PGE ₂ production, increased viral virulence | Supports monocyte/macrophage-mediated responses; influences T-cell function by down-modulating PGE ₂ in elderly | 87-89 |
| Iron (critical for immune function) | Zinc | Required for the hydroxylation of specific prolyl and lysyl residues in collagen | Decreased T-cell response, decreased phagocytic activity | Decreased IL-2 production and cytokine response | Decreases risk of parasitic and opportunistic <i>Candida</i> species infections | 44, 93, 94 |
| Zinc (essential for activity of thymic hormones and many enzymes) | Rarely iron, copper | Required for nucleic acid metabolism, protein synthesis, synthesis of structural proteins such as collagen, function of several hundred zinc metalloenzymes and zinc finger proteins, DNA synthesis, and for normal insulin-like growth factor production | Reduced TH1 cytokines (IL-1) and thymic hormone activity, lymphopenia thymic atrophy | Decreased skin test reactivity, decreased cytokine response | Prolonged zinc deficiency leads to reprogramming of the immune system through activation of the HPA axis and chronic production of glucocorticoids; accelerate apoptosis among early T and B cells | 68, 99, 101, 103-106 |

Table 2. Continued

| Primary Nutrient Deficiency | Associated Nutrient Deficiency | Wound Healing | Effect of Deficiency on Immune System | Effect of Deficiency on Immune Response | Comments | References |
|-----------------------------|--------------------------------|---|---|---|--|----------------|
| Selenium | | | Decreased antioxidant host defense system affecting leukocyte and NK cell function | Increased viral virulence | | 97, 98 |
| Copper Arginine | Increased zinc | Indispensable amino acid in collagen synthesis and wound healing; at pharmacologic levels (17–24.8 g of free arginine per day), significantly increases the amount of total protein deposition at the wound site; increases plasma insulin-like growth factor, the peripheral mediator of growth hormone activity | Decreased IL-2 response Stimulation of the T-cell responses; T lymphocytes are essential for normal wound healing; stimulation of macrophage-induced bacterial killing mediated by NO | Lymphopenia and neutropenia | Catabolized by immune cells to NO or ornithine; NO is a powerful vasodilator, an autocrine stimulator of fibroblast-contraction and collagen-synthesis; ornithine can be used for collagen synthesis or converted to polyamines important for cellular proliferation and differentiation | 111 146–158 |
| Glutamine | | Plays significant roles in wound healing as a major respiratory fuel source in gluconeogenesis; serves as a nitrogen donor for the synthesis of amino acids, as a precursor for the synthesis of nucleotides in cells, including fibroblasts and macrophages | | | Glutamine levels fall rapidly after an injury, and supplementation appears to improve protein synthesis and decrease length of hospital stay | 159–167 |

IL-, interleukin; Ig, immunoglobulin; HPA, hypothalamic-pituitary-adrenal; NK, natural killer; NO, nitric oxide; PCM, protein-caloric malnutrition; PG, prostaglandin.

A common basis for megaloblastosis is impaired DNA and protein synthesis. Folate and vitamin B₁₂ are required for the formation of S-adenosylmethionine, which is critical for stabilization of DNA and many proteins, and for synthesis of other molecules, including creatine, methylcobalamin, phosphatidylcholine, melatonin, norepinephrine, coenzyme Q10, carnitine, polyamines, serotonin, and niacinamide.^{52,53} Thus, deficiencies of these vitamins can potentially contribute to poor cellular proliferation and repair in the postbariatric body contouring patient. Also, the associated megaloblastic anemia will adversely affect circulation in the healing tissues.^{54,55} Furthermore, anemia-related fatigue and weakness can exacerbate immobilization of the postbariatric body contouring patient, which can increase the risk of deep venous thrombosis. Given the fact that postbariatric body contouring patients can lose a significant amount of blood during multiple procedures, it is of paramount importance that the patient's ability to sustain erythropoiesis is not compromised by inadequate vitamin B₁₂/folate reserves.

Vitamin B₆ is an essential cofactor in DNA synthesis and various transamination, decarboxylation, and synthesis pathways involving carbohydrate, sphingolipid, sulfur-containing amino acids, heme, and neurotransmitter metabolism. Vitamin B₁₂, folate, and vitamin B₆ deficiencies can contribute to hyperhomocysteinemia, which has a direct effect on vascular endothelium dysfunction, an atherogenic process.⁵⁶ Subjects with hyperhomocysteinemia (>15 μM) have a two- to three-fold increase in risk of developing cardiovascular disease or thromboembolic disease.⁵⁷⁻⁵⁹ The latter is thought to be attributable to stimulation of procoagulant factors and/or impairment of anticoagulant mechanisms or fibrinolysis by homocysteine.⁶⁰

Thus, it is not surprising that homocysteine levels are noted to increase after weight loss surgery.^{61,62} Borson-Chazot et al.⁶³ reported raised plasma homocysteine concentrations in two-thirds of their vertical ring gastropasty patients at 1 year, with clear-cut hyperhomocysteinemia (>15 μM) in 32 percent. Furthermore, after weight loss surgery, there is a shift in the micronutrient-to-homocysteine dose-response curve, with higher concentrations of both folate and vitamin B₁₂ required to maintain normal homocysteine levels.⁶⁴ Thus, deficiency of vitamin B₆, vitamin B₁₂, and folate in postbariatric patients can potentially contribute to a hypercoagulable state in those with hyperhomocysteinemia. Recommendations for postsurgical

patients range from 500 to 600 μg/day of vitamin B₁₂ and 400 μg of folate.⁵¹

Thiamine

In postbariatric patients, thiamine deficiency is likely to be subclinical. Thiamine plays an essential role in the metabolism of carbohydrates and branched-chain amino acids⁶⁵ and thus may have an important role in the healing process.

Vitamin C Deficiency

The incidence of vitamin C deficiency in Roux-en-Y gastric bypass patients is 34.6 and 35.4 percent at the 1- and 2-year follow-up, respectively.⁵¹ A recent report has confirmed vitamin C deficiency in those Roux-en-Y gastric bypass patients who are not on multivitamin supplementation.²⁸

Although vitamin C deficiency is asymptomatic in postbariatric patients, humans lack long-term storage for vitamin C, and levels decrease with stress and severe injury.⁶⁶ This observation is obviously of concern in postbariatric body contouring patients because vitamin C plays an important role in wound healing by increasing collagen synthesis and angiogenesis.^{67,68} Vitamin C deficiency is also associated with capillary leakage caused by decreased collagen production and susceptibility to wound infections (Table 2).⁶⁷⁻⁷¹

Although the recommended daily average for vitamin C is 60 mg/day, in major burn victims, the requirement may be as much as 2 g/day to restore tissue levels to normal.⁷² Levenson and Demetriou⁷³ recommend supplements of 1 to 2 g/day for wounded patients until convalescence is completed.

Vitamin A Deficiency

Several studies have demonstrated deficiency of vitamin A in up to 69 percent of postbariatric patients 4 years after surgery, with a clear increase in deficiency over time.⁷⁴ Although prophylactic supplementation can prevent deficiency, it is important to realize that up to 10 percent of those patients who had distal Roux-en-Y gastric bypass do not respond to such supplementation.²⁷

Even though the clinical consequences of vitamin A deficiency following bariatric surgery are few, the continued deficiency will adversely impact the healing process of the postbariatric body contouring patient. In addition, the stress of surgery and injuries can lead to increased vitamin A requirements.^{65,74,75} Vitamin A is an essential factor in the healing patient, as it functions as an immu-

nostimulant, enhancing inflammation-driven wound healing (Table 2).^{76–84}

Although the recommended daily average for vitamin A is approximately 2000 to 3000 IU,⁸⁵ this amount may not be optimal to enhance wound healing in postbariatric body contouring patients. Some investigators have recommended 25,000 to 50,000 IU/day orally and 10,000 IU intravenously for severely to moderately injured patients or for malnourished patients before and after elective surgery.^{73,86}

Vitamin E

Vitamin E deficiency is clinically uncommon in most postbariatric patients who receive vitamin supplementation.⁷⁴ Vitamin E plays an important role in supporting monocyte/macrophage-mediated responses (Table 2),^{87–89} but excess supplementation can inhibit collagen synthesis and decrease tensile strength of wounds because vitamin E has antiinflammatory properties similar to steroids.^{90,91}

Iron Deficiency

There is a significant risk of iron deficiency, ranging from 30 to 50 percent, with all types of bariatric surgery, even in those who are advised to take a multivitamin daily.⁷ Patients with iron deficiency may present with microcytic anemia, which can affect circulation in the healing tissues. Also, anemia-related fatigue and weakness can exacerbate immobilization of the postoperative postbariatric body contouring patient, which can increase the risk of deep venous thrombosis. Given the fact that postbariatric body contouring patients can lose a significant amount of blood during surgical procedures, it is important that the patient's hemoglobin and hematocrit are optimized in the preoperative setting. In terms of wound contracture, severe iron deficiency can impair collagen production⁹² and increase the risk of opportunistic infections (Table 2).^{93,94} Thus, any iron deficiency should be clearly treated, and most patients would benefit from preoperative oral iron supplementation. Treatment is usually accomplished with single daily doses of 100 to 200 mg of elemental iron. Occasionally, patients who are refractory to oral iron supplementation require parenteral iron infusions.⁹⁵

Zinc Deficiency

A significant deficiency of this trace element is demonstrated in 36 percent of postbariatric patients despite vitamin supplementation,⁹⁶ which often

manifests itself as hair thinning and loss.⁹⁵ Zinc is required for multiple aspects of cellular growth and replication. Zinc-deficient subjects are at risk of decreased fibroblast proliferation and collagen synthesis, leading to decreased wound strength and delayed epithelization,⁶⁸ and supplementation has a positive effect on wound healing.⁹⁷

Zinc also plays an important role in supporting the immune system. Both cellular and humoral immune functions are impaired in zinc deficiency, resulting in an increased susceptibility to wound infection and the possibility of delayed healing.⁹⁸ Furthermore, zinc may have antioxidant and antiatherogenic properties^{99,100} and plays a vital role in leukocyte function and cell-mediated immunity.¹⁰¹ Patients receiving trace metals—zinc (20 mg/day) plus selenium (100 µg/day)—or trace metals and antioxidants had fewer infections over a 2-year period.^{102,103} Given the importance of this trace element in both wound healing and the immune system (Table 2),^{68,99,101,103–106} supplementation of this element is appealing in all body contouring patients.

Selenium Deficiency

Selenium deficiency exists in 3 percent of postbariatric patients despite supplementation.⁹⁵ Although no clinical consequences of selenium deficiency are noted, this trace element is important for thyroid function, muscle metabolism,⁴⁶ and immune function (Table 2).^{102,103,107,108}

Copper

Clinical copper deficiency presenting as myelopathy is rare after weight loss surgery,^{109,110} but subclinical deficiency rates are not known. There are no specific recommendations on the use of copper in postbariatric patients. Thus, patients should be encouraged to take the recommended daily average for copper. Like zinc, iron, and selenium, copper is important for optimal immune system function (Table 2).¹¹¹

DISCUSSION

Timing for Body Contouring Surgery

On average, Roux-en-Y gastric bypass patients lose 60 to 70 percent of their excess weight during the first year after surgery. Many patients regain some of the lost weight during the ensuing years. Thus, from the standpoint of plastic surgery, the best time for body contouring surgery is probably between 18 and 24 months after bariatric surgery. This is the time during which patients have lost most of their excess weight and have significant tissue excess and laxity. However, this is also the

period during which most patients have minimal nutritional reserves following months of continued malabsorption of proteins, vitamins, and minerals. With up to 50 percent of reported vitamin and mineral deficiencies occurring within the first year after weight loss surgery,¹¹² it is prudent to pay serious attention to the patient's nutritional status before any body contouring procedures. Body contouring should be contemplated only when the patient's weight has reached a plateau for several months. We consider this period critical for repleting the nutritional reserves of the patient. Furthermore, it is essential for the plastic surgeon to realize that only a few patients will ultimately achieve a normal weight (i.e., lose 90 to 100 percent of excess weight) and that, more importantly, 3 to 5 percent of patients will lose greater than 100 percent of their excess weight.^{113,114} The latter group of patients is considered malnourished and often has had a complicated postoperative course. Many of the patients who reach normal weight and/or become malnourished postoperatively tend to be in the less than 40 kg/m² body mass index weight range category preoperatively.¹¹⁵ Again, it is imperative to recognize this group of patients preoperatively, because any body contouring operation on a malnourished patient can potentially lead to more severe complications.

Nutritional Deficiency and Healing in the Body Contouring Patient

Several studies have demonstrated significant preexisting nutritional deficiency in medical and surgical patients.^{116,117} Furthermore, the incidence of either infectious or noninfectious complications, mortality, time to return to normal activities, and length of hospital stay are significantly higher in the malnourished surgical patients than in well-nourished ones.¹¹⁸⁻¹²¹ In a recent review, we highlighted the suboptimal nutritional status of morbidly obese patients and, more importantly, the nutrient deficiencies of postbariatric patients.⁷ As plastic surgeons, we are increasingly faced with the needs of postbariatric patients who have excessive tissue laxity. Any surgical procedure will require energy in the form of carbohydrates, protein, and/or fat for the healing process.¹²² In rats, reducing caloric intake by 50 percent results in decreased collagen synthesis, matrix protein deposition, and granulation tissue formation.^{123,124} The energy intake of the postoperative Roux-en-Y gastric bypass subjects is severely reduced by over 50 percent, averaging 800 to 1200 kcal during the first 12 months^{25,26} and increasing to approxi-

mately 1885 ± 770 kcal by 24 months.¹²⁵ In addition to the low-calorie intake of postbariatric patients, surgery itself elicits a series of reactions, including release of stress hormones and inflammatory mediators, increased metabolic rates and catecholamine levels, loss of total body water, and cellular protein turnover, resulting in an overall state of catabolism. For optimal rehabilitation and wound healing, the body needs to be in an anabolic state. Recent studies have shown that measures to reduce the stress of surgery can minimize catabolism and support anabolism throughout surgical treatment and allow patients to recover substantially better and faster, even after major surgical procedures.¹²⁶

Furthermore, the protracted protein-calorie malnutrition and the associated deficiencies of vitamins A, C, and B₁₂; folate; iron; zinc; and selenium are expected to adversely affect the healing process of postbariatric body contouring patients. In humans, modest protein-calorie malnutrition can impair fibroplasia.¹²⁷ Even a brief period of decreased nutritional intake preoperatively has a significant effect on postoperative collagen synthesis. Patients who are malnourished before an injury exhibit delayed wound healing and have increased rates of wound infection that can be reduced significantly by nutritional repletion before the planned operation.¹²⁸⁻¹³¹

In addition to its fundamental role in wound healing, protein-calorie malnutrition is also the major cause of secondary immune deficiency worldwide. Protein-calorie malnutrition leads to activation of the hypothalamic-pituitary-adrenal, an increase in serum glucocorticoid levels,¹³² atrophy of lymphoid organs, T-lymphocyte deficiency, and increased susceptibility to bacterial and viral pathogens and opportunistic infections.^{132,133} The effects of protein-calorie malnutrition on the immune system are broad, involving all limbs of the immune system, including mucous membrane defense barrier, altered immune regulation and cellular trafficking, altered microbial flora, and impaired cellular immune response.¹³³ In postbariatric patients, micronutrient deficiencies of vitamins A, B₆, B₁₂, C, and E; folate; niacin; zinc; iron; copper; and selenium further affect the adaptive antibody and cellular immune response and the innate immune response.¹³⁴⁻¹³⁸ This is of major concern when considering the additional effects of surgical trauma on the immune system, including both the specific and the nonspecific immune response. Although minor surgery is suggested to stimulate individual components of the immune system, it is generally agreed that major surgery causes immunosuppression.¹³⁹⁻¹⁴¹

Although many plastic surgical procedures progress uneventfully in postbariatric body contouring patients, a review of 75 of our postbariatric body contouring patients between 2001 and 2005 confirmed major complications in 66 percent of the patients, related to wound problems.¹⁴² It may be expected that optimal nutritional status may improve the healing process, wound tension, and scar quality and reduce potential complications. The primary goal, therefore, should be to provide every patient with optimal nutrition so that this prioritization of wound healing can occur within an ideal host environment.

CONCLUSIONS

It is well known that nutrition profoundly influences the process of wound healing, such that depletion exerts an inhibitory effect and nutritional supplementation has a positive effect. Multiple published studies in gastrointestinal surgery, cardiovascular surgery, and head and neck surgery have confirmed a significant reduction in postoperative infectious complications, length of hospital stay, and morbidity and mortality rates in subjects receiving nutritional supplementation. The greatest improvement in postoperative outcomes was observed in patients receiving specialized nu-

tritional support preoperatively.^{118–121,128–131} Even 12 hours of preoperative fasting has been associated with prolonged recovery after uncomplicated surgery.^{143,144} These observations have led to development of a specific guideline for enhanced recovery after surgery by the European Society of Clinical Nutrition and Metabolism.¹⁴⁵ The essence of the guideline is avoidance of long periods of preoperative fasting, reestablishment of oral feeding as early as possible after surgery, and integration of nutritional support into the overall operative management. In our practice, following a review of our postbariatric body contouring patients, major complications were noted in 66 percent of our patients.¹⁴² We then approached a number of nutritional manufacturers to formulate a suitable nutritional supplement for this patient subpopulation. Since January of 2006, we have attempted to optimize undernutrition of our body contouring patients with additional supplements formulated for postbariatric surgery patients, using ProMend (Bariatric Advantage, Irvine, Calif.) or ProCare Surgical Formula (NutrEssential, Inc., Wilmington, Calif.) (Table 3). The former is a supplement of protein, arginine, and glutamine that is taken in addition to the Bariatric Advantage multivitamin tablets. The latter is a comprehensive

Table 3. Ingredients of ProCare and ProMend Nutritional Supplements

| | ProCare | | ProMend† | |
|--------------------------------------|--------------------|---------------|--------------------|---------------|
| | Amount per Serving | % Daily Value | Amount per Serving | % Daily Value |
| Protein | 20 g | 40 | 10 g | 20 |
| L-Arginine | 4 g | * | 4 g | * |
| Glutamine | 1 g | * | 1 g | * |
| Free amino acids | 5 g | * | — | — |
| Dietary nucleotides | 0.5 g | * | — | — |
| Vitamin A | 5000 IU | 100 | — | — |
| Vitamin C (ascorbic acid) | 500 mg | 834 | 100 mg | 167 |
| Thiamin (vitamin B ₁) | 10 mg | 667 | — | — |
| Riboflavin (vitamin B ₂) | 5 mg | 294.1 | — | — |
| Niacin (vitamin B ₃) | 25 mg | 125 | — | — |
| Biotin | 100 µg | 33 | — | — |
| Pantothenic acid (B ₅) | 1.67 mg | 17 | — | — |
| Vitamin K ₁ | 16.7 µg | 21 | — | — |
| Folic acid | 200 µg | 100 | — | — |
| Vitamin D ₃ | 400 IU | 100 | — | — |
| Vitamin B ₆ | 2 mg | 100 | — | — |
| Vitamin B ₁₂ | 300 µg | 5000 | — | — |
| Zinc (oxide) | 20 mg | 133 | 10 mg | 67 |
| Copper (gluconate) | 0.7 mg | 35 | — | — |
| Calcium (carbonate) | 100 mg | 10 | — | — |
| Iron (ferrous fumarate) | 18 mg | 100 | — | — |
| Choline (bitartrate) | 66.7 mg | * | — | — |
| Selenium (AAC) | 66 µg | 94 | — | — |
| Chromium (picolinate) | 25 µg | 21 | — | — |
| Omega-3 fatty acids | 100 mg | * | — | — |
| Grape seed extract | 10 mg | * | — | — |
| Lycopene 5% | 0.3 mg | * | — | — |

*Daily value not established.

†ProMend Supplement is recommended in addition to Bariatric Advantage multivitamin tablets.

formula of protein, free amino acids, arginine, glutamine, and dietary nucleotides, and vitamins A, C, B₆, and B₁₂; folate; thiamine; iron; zinc; and selenium. Arginine and glutamine have been deemed essential in many studies to the healing of wounds and optimization of the immune system (Table 2).^{146–167} Vitamin B₁₂, folate, and vitamin B₆ are also supplemented to reduce homocysteine levels in postbariatric patients and thus the potential hypercoagulable state. We now use three scoops of ProCare supplement per day in all nonbariatric and bariatric body contouring patients starting at 3 weeks before the operation and continued until complete healing is achieved. We prefer ProCare because it provides all of the required nutritional ingredients in one powder form, rather than multivitamin tablets that may not be completely absorbed in postbariatric patients. This regimen provides approximately 90 g of protein and amino acids, in addition to vitamins at levels indicated for wound healing. A prospective ongoing study of 37 of our postbariatric body contouring patients who are supplemented with ProCare Surgical Formula indicated wound complication rates of 18.9 percent. This is in contrast to our 66 percent wound complication rate in those patients who did not receive supplementation before 2006.¹⁴² Both patient groups had an average of approximately eight procedures per patient at each surgical stage. Furthermore, we have also noted significantly fewer minor complications, accelerated wound healing, and higher energy levels as reported by the patients.

Siamak Agha-Mohammadi, M.B., B.Chir., Ph.D.
Plastic Surgery Body Contouring Center
400 Newport Center Drive, Suite 500
Newport Beach, Calif. 92660
dragha@plasticsurgerycal.com

REFERENCES

- Allison, D. B., Fontaine, K. R., and Manson, J. R. Annual deaths attributable to obesity in the United States. *J.A.M.A.* 282: 1530, 1999.
- Hedley, A. A., Ogden, C. L., Johnson, C., Carroll, M. D., Curtin, L. R., and Flegal, K. M. Prevalence of overweight and obesity among US children, adolescents, and adults, 1999–2002. *J.A.M.A.* 291: 2847, 2004.
- Buchwald, H., Avidor, Y., Braunwald, E., et al. Bariatric surgery: A systematic review and meta-analysis. *J.A.M.A.* 292: 1724, 2004.
- Christou, N. V., Sampalis, J. S., Liberman, M., et al. Surgery decreases long-term mortality, morbidity, and health care use in morbidly obese patients. *Ann. Surg.* 240: 416, 2004.
- Kushner, R. Managing the obese patient after bariatric surgery: A case report of severe malnutrition and review of the literature. *J. Parenter. Enteral Nutr.* 24: 126, 2000.
- American Society of Plastic Surgeons press release. Massive weight loss patients create mass appeal for body contouring procedures, 2007.
- Agha-Mohammadi, S., and Hurwitz, D. J. Nutritional deficiency of post-bariatric body contouring patients: What every plastic surgeon should know. *Plast. Reconstr. Surg.* 122: 604, 2008.
- Pories, W. J., Swanson, M. S., MacDonald, K. G., et al. Who would have thought it? An operation proves to be the most effective therapy for adult-onset diabetes mellitus. *Ann. Surg.* 222: 339, 1995.
- Schwartz, R. W., Strodel, W. E., Simpson, W. S., and Griffen, W. O., Jr. Gastric bypass revision: Lessons learned from 920 cases. *Surgery* 104: 806, 1988.
- Muller, M. K., Wildi, S., Scholz, T., Clavien, P. A., and Weber, M. Laparoscopic pouch resizing and redo of gastrojejunal anastomosis for pouch dilatation following gastric bypass. *Obes. Surg.* 15: 1089, 2005.
- Martikainen, T., Pirinen, E., Alhava, E., et al. Long-term results, late complications and quality of life in a series of adjustable gastric banding. *Obes. Surg.* 14: 648, 2004.
- O'Brien, P., Brown, W., and Dixon, J. Revisional surgery for morbid obesity: Conversion to the Lap-Band system. *Obes. Surg.* 10: 557, 2000.
- Sjöström, C. D., Peltonen, M., Wedel, H., and Sjöström, L. Differentiated long-term effects of intentional weight loss on diabetes and hypertension. *Hypertension* 36: 20, 2000.
- MacDonald, K. G., Jr., Long, S. D., Swanson, M. S., et al. The gastric bypass operation reduces the progression and mortality of non-insulin-dependent diabetes mellitus. *J. Gastrointest. Surg.* 1: 213, 1997.
- Sugerman, H. J., Kellum, J. M., and DeMaria, E. J. Conversion of proximal to distal gastric bypass for failed gastric bypass for superobesity. *J. Gastrointest. Surg.* 1: 517, 1997.
- Balsiger, B. M., Kennedy, F. P., Abu-Lebdeh, H. S., et al. Prospective evaluation of Roux-en-Y gastric bypass as primary operation for medically complicated obesity. *Mayo Clin. Proc.* 75: 673, 2000.
- Waters, G. S., Pories, W. J., Swanson, M. S., Meelheim, H. D., Flickinger, E. G., and May, H. J. Long-term studies of mental health after the Greenville gastric bypass operation for morbid obesity. *Am. J. Surg.* 161: 154, 1991.
- van de Weijert, E. J., Ruseler, C. H., and Elte, J. W. Long-term follow-up after gastric surgery for morbid obesity: Pre-operative weight loss improves the long-term control of morbid obesity after vertical banded gastroplasty. *Obes. Surg.* 9: 426, 1999.
- Wittgrove, A. C., and Clark, G. W. Laparoscopic gastric bypass, Roux-en-Y-500 patients: Technique and results, with 3–60 month follow-up. *Obes. Surg.* 10: 233, 2000.
- Das, S. K., Roberts, S. B., Kehayias, J. J., et al. Body composition assessment in extreme obesity and after massive weight loss induced by gastric bypass surgery. *Am. J. Physiol.* 284: E1080, 2003.
- MacLean, L. D., Rhode, B. M., and Shizgal, H. M. Nutrition following gastric operations for morbid obesity. *Ann. Surg.* 198: 347, 1983.
- Halverson, J. D. Metabolic risk of obesity surgery and long-term follow-up. *Am. J. Clin. Nutr.* 55: 602S, 1992.
- Raymond, J. L., Schipke, C. A., Becker, J. M., Lloyd, R. D., and Moody, F. G. Changes in body composition and dietary intake after gastric partitioning for morbid obesity. *Surgery* 90: 15, 1986.
- Marcason, W. What are the dietary guidelines following bariatric surgery? *J. Am. Diet. Assoc.* 104: 487, 2004.

25. Coughlin, K., Bell, R. M., Bivins, B. A., Wrobel, S., and Griffen, W. O., Jr. Preoperative and postoperative assessment of nutrient intakes in patients who have undergone gastric bypass surgery. *Arch. Surg.* 118: 813, 1983.
26. Dias, M. C., Ribeiro, A. G., Scabim, V. M., Faintuch, J., Zilberstein, B., and Gama-Rodrigues, J. J. Dietary intake of female bariatric patients after anti-obesity gastroplasty. *Clinics* 61: 93, 2006.
27. Brolin, R. E., and Leung, M. Survey of vitamin and mineral supplementation after gastric bypass and biliopancreatic diversion for morbid obesity. *Obes. Surg.* 9: 150, 1999.
28. Trostler, N., Mann, A., Zilberbush, N., Charuzi I. I. Avinovich, V. Nutrient Intake following Vertical Banded Gastroplasty or Gastric Bypass. *Obes. Surg.* 5: 403, 1995.
29. Bloomberg, R. D., Fleishman, A., Nalle, J. E., Herron, D. M., and Kini, S. Nutritional deficiencies following bariatric surgery: What have we learned? *Obes. Surg.* 15: 145, 2005.
30. Moize, V., Geliebter, A., Gluck, M. E., et al. Obese patients have inadequate protein intake related to protein intolerance up to 1 year following Roux-en-Y gastric bypass. *Obes. Surg.* 13: 23, 2003.
31. Kenler, H. A., Brolin, R. E., and Cody, R. P. Changes in eating behavior after horizontal gastroplasty and Roux-en-Y gastric bypass. *Am. J. Clin. Nutr.* 52: 87, 1990.
32. Spanheimer, R. G., and Peterkofsky, B. A specific decrease in collagen synthesis in acutely fasted, vitamin C-supplemented, guinea pigs. *J. Biol. Chem.* 260: 3955, 1985.
33. Irvin, T. T. Effects of malnutrition and hyperalimentionation on wound healing. *Surg. Gynecol. Obstet.* 146: 33, 1978.
34. Haydock, D. A., and Hill, G. L. Impaired wound healing in surgical patients with varying degrees of malnutrition. *J.P.E.N. J. Parenter. Enteral Nutr.* 10: 550, 1986.
35. Lawrence, W. T. Clinical management of nonhealing wounds. In I. K. Cohen, R. F. Diegelmann, and W. J. Lindblad (Eds.), *Wound Healing Biochemical and Clinical Aspects*. Philadelphia: Saunders, 1992.
36. Neumann, C. G., Gewa, C., and Bwibo, N. O. Child nutrition in developing countries. *Pediatr. Ann.* 33: 658, 2004.
37. Russell, B. J., White, A. V., Newbury, J., Hattch, C., Thurley, J., and Chang, A. B. Evaluation of hospitalisation for indigenous children with malnutrition living in Central Australia. *Aust. J. Rural Health* 12: 187, 2004.
38. Schneider, S. B., Erikson, N., Gebel, H. M., Wedner, H. J., Denes, A. E., and Halverson, J. D. Cutaneous anergy and marrow suppression as complications of gastroplasty for morbid obesity. *Surgery* 94: 109, 1983.
39. Kay, S. P., Moreland, J. R., and Schmitter, E. Nutritional status and wound healing in lower extremity amputations. *Clin. Orthop. Relat. Res.* 217: 253, 1987.
40. Dickhaut, S. C., DeLee, J. C., and Page, C. P. Nutritional status: Importance in predicting wound-healing after amputation. *J. Bone Joint Surg. (Am.)* 66: 71, 1984.
41. Casey, J., Flinn, W. R., Yao, J. S., Fahey, V., Pawlowski, J., and Bergan, J. J. Correlation of immune and nutritional status with wound complications in patients undergoing vascular operations. *Surgery* 93: 822, 1983.
42. DeMaria, E. J., Sugerman, H. J., Kellum, J. M., Meador, J. G., and Wolfe, L. G. Results of 281 consecutive total laparoscopic Roux-en-Y gastric bypasses to treat morbid obesity. *Ann. Surg.* 235: 640, 2002.
43. Vazquez, J. A., Kazi, U., and Madani, N. Protein metabolism during weight reduction with very-low-energy diets: Evaluation of the independent effects of protein and carbohydrate on protein sparing. *Am. J. Clin. Nutr.* 62: 93, 1995.
44. Bergstrom, N., Bennett, M. A., Carlson, C. E., et al. Pressure ulcer treatment: Clinical practice guideline. *Quick Reference Guide for Clinicians, No. 15*. Rockville, Md.: U.S. Department of Health and Human Services, Public Health Service, Agency for Health Care Policy and Research, 1994. AHCPR publication no. 95-0653.
45. Breslow, R. A., Hallfrisch, J., Guy, D. G., Crawley, B., and Goldberg, A. B. The importance of dietary protein in healing pressure ulcers. *J. Am. Geriatr. Soc.* 41: 357, 1993.
46. Amaral, J. F., Thompson, W. R., Caldwell, M. D., Martin, H. F., and Randall, H. T. Prospective hematologic evaluation of gastric exclusion surgery for morbid obesity. *Ann. Surg.* 201: 186, 1985.
47. Halverson, J. D. Micronutrient deficiencies after gastric bypass for morbid obesity. *Am. Surg.* 52: 594, 1986.
48. Brolin, R. E., Gorman, J. H., Gorman, R. C., et al. Are vitamin B12 and folate deficiency clinically important after Roux-en-Y gastric bypass? *J. Gastrointest. Surg.* 2: 436, 1998.
49. Herbert, V., and Das, K. C. Folic acid and vitamin B12. In M. E. Shill, J. A. Olson, and M. Shike (Eds.), *Modern Nutrition in Health and Disease*, 8th Ed. Philadelphia: Lea & Febiger, 1994. P. 402.
50. Marcuard, S. P., Sinar, D. R., Swanson, M. S., Silverman, J. F., and Levine, J. S. Absence of luminal intrinsic factor after gastric bypass surgery for morbid obesity. *Dig. Dis. Sci.* 34: 1238, 1989.
51. Clements, R. H., Katasani, V. G., Palepu, R., et al. Incidence of vitamin deficiency after laparoscopic Roux-en-Y gastric bypass in a university hospital setting. *Am. Surg.* 72: 1196, 2006.
52. Russell, R. M. Vitamin and trace mineral deficiency and excess. In D. L. Kasper, E. Braunwald, A. S. Fauci, et al. (Eds.), *Harrison's Principles of Internal Medicine*, 16th ed. New York: McGraw-Hill, 2005. P. 403.
53. Loenen, W. A. S-adenosylmethionine: Jack of all trades and master of everything? *Biochem. Soc. Trans.* 34: 330, 2006.
54. Crowley, L. V., and Olson, R. W. Megaloblastic anemia after gastric bypass for obesity. *Am. J. Gastroenterol.* 78: 406, 1983.
55. Boylan, L. M., Sugerman, H. J., and Driskell, J. A. Vitamin E, vitamin B6, vitamin B12, and folate status of gastric bypass surgery patients. *J. Am. Diet. Assoc.* 88: 579, 1988.
56. Dayal, S., and Leutz, S. R. ADMA and hyperhomocysteinemia. *Vasc. Med.* 10 (Suppl. 1): S27, 2005.
57. Gallistl, S., Sudi, K., Mangge, H., Erwa, W., and Borkenstein, M. Insulin is an independent correlate of plasma homocysteine levels in obese children and adolescents. *Diabetes Care* 23: 1348, 2000.
58. den Heijer, M., Blom, H. J., Gerrits, W. B., et al. Is hyperhomocysteinemia a risk factor for recurrent venous thrombosis? *Lancet* 345: 882, 1995.
59. Boushey, C. J., Beresford, S. A., Omenn, G. S., and Motulsky, A. G. A quantitative assessment of plasma homocysteine as a risk factor for vascular disease: Probable benefits of increasing folic acid intakes. *J.A.M.A.* 274: 1049, 1995.
60. Klerk, M., Verhoef, P., Verbruggen, B., et al. Effect of homocysteine reduction by B-vitamin supplementation on markers of clotting activation. *Thromb. Haemost.* 88: 230, 2002.
61. Dixon, J. B. Elevated homocysteine with weight loss. *Obes. Surg.* 11: 537, 2001.
62. Dixon, J. B., Dixon, M. E., and O'Brien, P. E. Elevated homocysteine levels with weight loss after Lap-Band surgery: Higher folate and vitamin B12 levels required to maintain homocysteine level. *Int. J. Obes.* 25: 219, 2001.
63. Borson-Chazot, F., Harthe, C., Teboul, F., et al. Occurrence of hyperhomocysteinemia 1 year after gastroplasty for severe obesity. *J. Clin. Endocrinol. Metab.* 84: 541, 1999.
64. Jacobson, P., Lindroos, A. K., Sjostrom, C., et al. Long-term changes in homocysteine following weight loss in the SOS study. *Int. J. Obes.* 224(Suppl. 1): S175, 2000.

65. Tanphaichtr, V. Thiamin. In M. E. Shill, J. A. Olson, M. Shike (Eds.), *Modern Nutrition in Health and Disease*. Philadelphia: Lea & Febiger, 1994. P. 359.
66. Goetzl, E. J., Wasserman, S. I., Gigli, I., et al. Enhancement of random migration and chemotactic response of human leukocytes by ascorbic acid. *J. Clin. Invest.* 53: 813, 1974.
67. Nicosia, R. F., Belser, P., Bonanno, E., and Diven, J. Regulation of angiogenesis in vitro by collagen metabolism. *In Vitro Cell. Dev. Biol.* 27A: 961, 1991.
68. Barbul, A., and Purtill, W. A. Nutrition in wound healing. *Clin. Dermatol.* 12: 133, 1994.
69. Hartel, C., Strunk, T., Bucsky, P., and Schultz, C. Effects of vitamin C on intracytoplasmic cytokine production in human whole blood monocytes and lymphocytes. *Cytokine* 27: 101, 2004.
70. Mizutani, A., Maki, H., Torii, Y., Hitomi, K., and Tsukagoshi, N. Ascorbate dependent enhancement of nitric oxide formation in activated macrophages. *Nitric Oxide* 2: 235, 1998.
71. Levenson, S. M., Green, R. W., Taylor, F. H. L., et al. Ascorbic acid, riboflavin, thiamin, and nicotinic acid in relation to severe injury, hemorrhage, and infection in the human. *Ann. Surg.* 124: 840, 1946.
72. Lund, C., Levenson, S., Green, R., et al. Ascorbic acid, thiamine, riboflavin and nicotinic acid in relation to acute burns in man. *Arch. Surg.* 55: 583, 1947.
73. Levenson, S. M., and Demetriou, A. A. Metabolic factors. In I. K. Cohen, R. F. Diegelmann, and W. J. Lindblad (Eds.), *Wound Healing Biochemical and Clinical Aspects*. Philadelphia: Saunders, 1992.
74. Slater, G. H., Ren, C. J., Siegel, N., et al. Serum fat-soluble vitamin deficiency and abnormal calcium metabolism after malabsorptive bariatric surgery. *J. Gastrointest. Surg.* 8: 48, 2004.
75. Moody, B. J. Changes in the serum concentrations of thyroxine-binding prealbumin and retinol-binding protein following burn injury. *Clin. Chim. Acta* 118: 87, 1982.
76. Connor, M. J. Retinoid stimulation of epidermal differentiation in vivo. *Life Sci.* 38: 1807, 1986.
77. Demetriou, A. A., Levenson, S. M., Rettura, G., Seifter, E. Vitamin A and retinoic acid: Induced fibroblast differentiation in vitro. *Surgery* 98: 931, 1985.
78. Patel, G. K. The role of nutrition in the management of lower extremity wounds. *Int. J. Low. Extrem. Wounds* 4: 12, 2005.
79. Cohen, B. E., Gill, G., Cullen, P. R., and Morris, P. J. Reversal of postoperative immunosuppression in man by vitamin A. *Surg. Gynecol. Obstet.* 149: 658, 1979.
80. Barbul, A., Thysen, B., Rettura, G., Levenson, S. M., and Seifter, E.,. White cell involvement in the inflammatory, wound healing, and immune actions of vitamin A. *J.P.E.N. J. Parenter. Enteral Nutr.* 2: 129, 1978.
81. Stephensen, C. B. Vitamin A, infection, and immune function. *Annu. Rev. Nutr.* 21: 167, 2001.
82. Quadro, L., Gamble, M. V., Vogel, S., et al. Retinol and retinol-binding protein: Gut integrity and circulating immunoglobulins. *J. Infect. Dis.* 182 (Suppl. 1): S97, 2000.
83. Kozakova, H., Hanson, L. A., Stepankova, R., Kahu, H., Dahlgren, U. L., and Weidemann, U. Vitamin A deficiency leads to severe functional disturbance of the intestinal epithelium enzymes associated with diarrhoea and increased bacterial translocation in gnotobiotic rats. *Microbes Infect.* 5: 405, 2003.
84. Stephensen, C. B., Jiang, X., and Freytag, T. Vitamin A deficiency increases the in vivo development of IL-10-positive Th2 cells and decreases development of Th1 cells in mice. *J. Nutr.* 134: 2660, 2004.
85. Aukrust, P., Muller, F., Ueland, T., Svoldal, A. M., Berge, R. K., and Froland, S. S. Decreased vitamin A levels in common variable immunodeficiency: Vitamin A supplementation in vivo enhances immunoglobulin production and downregulates inflammatory responses. *Eur. J. Clin. Invest.* 30: 252, 2000.
86. Levenson, S. M., Gruber, C. A., Rettura, G., Gruber, D. K., Demetriou, A. A., and Seifter, E. Supplemental vitamin A prevents the acute radiation-induced defect in wound healing. *Ann. Surg.* 200: 494, 1984.
87. Park, O. J., Kim, H. Y., Kim, W. K., Kim, Y. J., and Kim, S. H. Effect of vitamin E supplementation on antioxidant defense systems and humoral immune responses in young, middle-aged and elderly Korean women. *J. Nutr. Sci. Vitaminol.* 49: 94, 2003.
88. van Tits, L. J., Demacker, P. N., de Graaf, J., Hak-Lemmers, H. L., and Stalenhoef, A. F. Alpha-tocopherol supplementation decreases production of superoxide and cytokines by leukocytes ex vivo in both normolipidemic and hypertriglyceridemic individuals. *Am. J. Clin. Nutr.* 71: 458, 2000.
89. Wu, D., and Meydani, S. N. Mechanism of age-associated up-regulation in macrophage PGE2 synthesis. *Brain Behav. Immun.* 18: 487, 2004.
90. Havlik, R. J. Plastic Surgery Educational Foundation DATA Committee. Vitamin E and wound healing. *Plast. Reconstr. Surg.* 100: 1901, 1997.
91. Ehrlich, H. P., Tarver, H., and Hunt, T. K. Inhibitory effects of vitamin E on collagen synthesis and wound repair. *Ann. Surg.* 175: 235, 1972.
92. O'Dell, B. L. Roles for iron and copper in connective tissue biosynthesis. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* 294: 91, 1981.
93. Ekiz, C., Agaoglu, L., Karakas, Z., Gurel, N., and Yalcin, I. The effect of iron deficiency anemia on the function of the immune system. *Hematol. J.* 5: 579, 2005.
94. Thibault, H., Galan, P., Selz, F., et al. The immune response in iron-deficient young children: effect of iron supplementation. *Eur. J. Pediatr.* 152: 120, 1993.
95. Neve, H. J., Bhatti, W. A., Soulsby, C., Kincey, J., and Taylor, T. V. Reversal of hair loss following vertical gastroplasty when treated with zinc sulphate. *Obes. Surg.* 6: 63, 1996.
96. Madan, A. K., Orth, W. S., Tichansky, D. S., and Ternovits, C. A. Vitamin and trace mineral levels after laparoscopic gastric bypass. *Obes. Surg.* 16: 603, 2006.
97. Hallbook, T., and Lanner, E. Serum-zinc and healing of venous leg ulcers. *Lancet* 2: 780, 1972.
98. Prasad, A. Acquired zinc deficiency and immune dysfunction in sickle cell anemia. In S. Cunningham-Rundles (Ed.), *Nutrient Modulation of the Immune Response*. New York: Marcel Dekker, 1993. P. 393.
99. Powell, S. The antioxidant properties of zinc. *J. Nutr.* 130: 1447S, 2000.
100. Hennig, B., Toborek, M., McClain, C. J., and Diana, J. N. Nutritional implications in vascular endothelial cell metabolism. *J. Am. Coll. Nutr.* 15: 345, 1996.
101. Oleske, J. M., Westphal, M. L., Shore, S., Gorden, D., Bogen, J. D., and Nahmias, A. Zinc therapy of depressed cellular immunity in acrodermatitis enteropathica: its correction. *Am. J. Dis. Child.* 133: 915, 1979.
102. Girodon, F., Lombard, M., Galan, P., et al. Effect of micronutrient supplementation on infection in institutionalized elderly subjects: A controlled trial. *Ann. Nutr. Metab.* 1: 98, 1997.
103. Girodon, F., Galan, P., Monget, A. L., et al. Impact of trace elements and vitamin supplementation on immunity and infections in institutionalized elderly patients: A randomized controlled trial. MIN.VIT. AOX. Geriatric network. *Arch. Intern. Med.* 159: 748, 1999.

104. Mocchegiani, E., Ciavattini, A., Santarelli, L., et al. Role of zinc and alpha2 macroglobulin on thymic endocrine activity and on peripheral immune efficiency (natural killer activity and interleukin 2) in cervical carcinoma. *Br. J. Cancer* 79: 244, 1999.
105. Fraker, P. J. Roles for cell death in zinc deficiency. *J. Nutr.* 135: 359, 2005.
106. Fraker, P. J., King, L. E., Laakko, T., and Vollmer, T. L. The dynamic link between the integrity of the immune system and zinc status. *J. Nutr.* 130 (Suppl.): 1399S, 2000.
107. Ferencik, M., and Ebringer, L. Modulatory effects of selenium and zinc on the immune system. *Folia Microbiol.* 48: 417, 2003.
108. Singhal, N., and Austin, J. A clinical review of micronutrients in HIV infection. *J. Int. Assoc. Physicians AIDS Care (Chic. Ill.)* 1: 63, 2002.
109. Juhasz-Pocsine, K., Rudnicki, S. A., Archer, R. L., and Harik, S. I. Neurologic complications of gastric bypass surgery for morbid obesity. *Neurology* 68: 1843, 2007.
110. Kumar, N., Ahlskog, J. E., and Gross, J. B., Jr. Acquired hypocupremia after gastric surgery. *Clin. Gastroenterol. Hepatol.* 2: 1074, 2004.
111. Percival, S. S. Copper and immunity. *Am. J. Clin. Nutr.* 67 (Suppl.): 1064S, 1998.
112. Brolin, R. E., Gorman, R. C., Milgrim, L. M., and Kenler, H. A. Multivitamin prophylaxis in prevention of post-gastric bypass vitamin and mineral deficiencies. *Int. J. Obes.* 15: 661, 1991.
113. Higa, K. D., Boone, K. B., Ho, T., and Davies, O. G. Laparoscopic Roux-en-Y gastric bypass for morbid obesity: Technique and preliminary results of our first 400 patients. *Arch. Surg.* 135: 1029, 2000.
114. Sanyal, A. J., Sugeran, H. J., Kellum, J. M., Engle, K. M., and Wolfe, L. Stomal complications of gastric bypass: Incidence and outcome of therapy. *Am. J. Gastroenterol.* 87: 1165, 1992.
115. De Prisco, C., and Levine, S. N. Metabolic bone disease after gastric bypass surgery for obesity. *Am. J. Med. Sci.* 329: 57, 2005.
116. Ray, E., Nickels, M., Sayeed, S., and Sax, H. C. Predicting success after gastric bypass: The role of psychosocial and behavioral factors. *Surgery* 134: 555, 2003.
117. Brolin, R. E., Kenler, H. A., Gorman, R. C., and Cody, R. P. The dilemma of outcome assessment after operations for morbid obesity. *Surgery* 105: 337, 1989.
118. Pikul, J., Sharpe, M. D., Lowndes, R., and Ghent, C. N. Degree of preoperative malnutrition is predictive of post-operative morbidity and mortality in liver transplant recipients. *Transplantation* 57: 469, 1994.
119. Dempsey, D. T., Mullen, J. L., and Buzby, G. P. The link between nutritional status and clinical outcome: Can nutritional intervention modify it? *Am. J. Clin. Nutr.* 47(Suppl. 2): 352, 1998.
120. Heslin, M. J., Latkany, L., Leung, D., et al. A prospective, randomized trial of early enteral feeding after resection of upper gastrointestinal malignancy. *Ann. Surg.* 226: 567, 1997.
121. Snyderman, C. H., Kachman, K., Molseed, L., et al. Reduced postoperative infections with an immune-enhancing nutritional supplement. *Laryngoscope* 109: 915, 1999.
122. Kinney, J. Energy requirements of the surgical patient. In W. Ballinger, J. Collins, W. Drucker, S. Dudrick, and R. Zeppa (Eds.), *Manual of Surgical Nutrition*. Philadelphia: Saunders, 1975. P. 223.
123. Schäffer, M. R., Tantry, U., Ahrendt, G. M., Wasserkrug, H. L., and Barbul, A. Acute protein-calorie malnutrition impairs wound healing: A possible role of decreased wound nitric oxide synthesis. *J. Am. Coll. Surg.* 184: 37, 1997.
124. Kiyama, T., Efron, D. T., Tantry, U., and Barbul, A. Trauma and wound healing: Role of the route of nutritional support. *Int. J. Surg. Invest.* 2: 483, 2001.
125. Lindroos, A., Lissner, L., and Sjöström, L. Weight change in relation to intake of sugar and sweets before and after weight reducing gastric surgery. *Int. J. Obes.* 20: 634, 1996.
126. Fearon, K. C., Ljungqvist, O., Von Meyenfeldt, M., et al. Enhanced recovery after surgery: A consensus review of clinical care for patients undergoing colonic resection. *Clin. Nutr.* 24: 466, 2005.
127. Goodson, W. H., III, Lopez-Sarmiento, A., Jensen, J. A., West, J., Granja-Mena, L., and Chavez-Estrella, J. The influence of a brief preoperative illness on postoperative healing. *Ann. Surg.* 205: 250, 1987.
128. Braga, M., Gianotti, L., Vignali, A., and Carlo, V. D. Preoperative oral arginine and n-3 fatty acid supplementation improves the immunometabolic host response and outcome after colorectal resection for cancer. *Surgery* 132: 805, 2002.
129. Tepaske, R., Velthuis, H., Oudemans-van Straaten, H. M., et al. Effect of preoperative oral immune-enhancing nutritional supplement on patients at high risk of infection after cardiac surgery: A randomised placebo-controlled trial. *Lancet* 358: 696, 2001.
130. Gianotti, L., Braga, M., Nespoli, L., Radaelli, G., Beneduce, A., and Di Carlo, V. A randomized controlled trial of preoperative oral supplementation with a specialized diet in patients with gastrointestinal cancer. *Gastroenterology* 122: 1783, 2002.
131. Braga, M., Gianotti, L., Nespoli, L., Radaelli, G., and Di Carlo, V. Nutritional approach in malnourished surgical patients: A prospective randomized study. *Arch. Surg.* 137: 174, 2002.
132. Savino, W. The thymus gland is a target in malnutrition. *Eur. J. Clin. Nutr.* 56(Suppl. 3): S46, 2002.
133. Najera, O., Gonzalez, C., Toledo, G., Lopez, L., and Ortiz, R. Flow cytometry study of lymphocyte subsets in malnourished and well-nourished children with bacterial infections. *Clin. Diagn. Lab. Immunol.* 11: 577, 2004.
134. Rivera, M. T., De Souza, A. P., Araujo-Jorge, T. C., De Castro, S. L., and Vanderpas, J. Trace elements, innate immune response and parasites. *Clin. Chem. Lab. Med.* 41: 1020, 2003.
135. Fraker, P. J., and Lill-Elghanian, D. A. The many roles of apoptosis in immunity as modified by aging and nutritional status. *J. Nutr. Health Aging* 8: 56, 2004.
136. Kirkpatrick, B. D., Daniels, M. M., Jean, S. S., et al. Cryptosporidiosis stimulates an inflammatory intestinal response in malnourished Haitian children. *J. Infect. Dis.* 186: 94, 2002.
137. Guerrant, R. L., Lima, A. A., and Davidson, F. Micronutrients and infection: interactions and implications with enteric and other infections and future priorities. *J. Infect. Dis.* 182(Suppl. 1): S134, 2000.
138. Bhaskaram, P. Micronutrient malnutrition, infection, and immunity: An overview. *Nutr. Rev.* 60(Suppl.): S40, 2002.
139. Faist, E., Schinkel, C., and Zimmer, S. Update on the mechanisms of immune suppression of injury and immune modulation. *World J. Surg.* 20: 454, 1996.
140. Romeo, C., Cruccetti, A., Turiaco, A., et al. Monocyte and neutrophil activity after minor surgical stress. *J. Pediatr. Surg.* 37: 741, 2002.
141. Hensler, T., Hecker, H., Heeg, K., et al. Distinct mechanisms of immunosuppression as a consequence of major surgery. *Infect. Immun.* 65: 2283, 1997.
142. Hurwitz, D., Agha-Mohammadi, S., Ota, K., and Unadkat, J. A clinical review of total body lift surgery. *Aesthetic Surg. J.* 28: 294, 2008.

143. Ljungqvist, O., Nygren, J., and Thorell, A. Modulation of postoperative insulin resistance by pre-operative carbohydrate loading. *Proc. Nutr. Soc.* 61: 329, 2002.
144. Ljungqvist, O., Nygren, J., Thorell, A., et al. Preoperative nutrition elective surgery in the fed or the overnight fasted state. *Clin. Nutr.* 20(Suppl. 1): 167, 2001.
145. Weimann, A., Braga, M., Harsanyi, L., et al. ESPEN Guidelines on Enteral Nutrition: Surgery including organ transplantation. *Clin. Nutr.* 25: 224, 2006.
146. Rose, W. Amino acid requirements of man. *Fed. Proc.* 8: 546, 1949.
147. Seifter, E., Rettura, G., Barbul, A., and Levenson, S. M. Arginine: An essential amino acid for injured rats. *Surgery* 84: 224, 1978.
148. Barbul, A., Wasserkrug, H. L., Seifter, E., Rettura, G., Levenson, S. M., and Efron, G. Immunostimulatory effects of arginine in normal and injured rats. *J. Surg. Res.* 29: 228, 1980.
149. Barbul, A., Lazarou, S. A., Efron, D. T., Wasserkrug, H. L., and Efron, G. Arginine enhances wound healing and lymphocyte immune responses in humans. *Surgery* 108: 331, 1990.
150. Kirk, S. J., Hurson, M., Regan, M. C., Hold, D. R., Wasserkrug, H. L., and Barbul, A. Arginine stimulates wound healing and immune function in elderly human beings. *Surgery* 114: 155, 1993.
151. Schaffer, M. R., Efron, P. A., Thornton, F. J., Klingel, K., Gross, S. S., and Barbul, A. Nitric oxide, an autocrine regulator of wound fibroblast synthetic function. *J. Immunol.* 158: 2375, 1997.
152. Schaffer, M. R., Tantry, U., Thornton, F. J., and Barbul, A. Inhibition of nitric oxide synthesis in wounds: Pharmacology and effect on accumulation of collagen in wounds in mice. *Eur. J. Surg.* 165: 262, 1999.
153. Efron, D. T., Thornton, F. J., Steulten, C., et al. Expression and function of inducible nitric oxide synthase during rat colon anastomotic healing. *J. Gastrointest. Surg.* 3: 592, 1999.
154. Albina, J. E., Abate, J. A., and Mastrofrancesco, B. Role of ornithine as a proline precursor in healing wounds. *J. Surg. Res.* 55: 97, 1993.
155. Langkamp-Henken, B., Johnson, L. R., Viar, M. J., Geller, A. M., and Kotb, M. Differential effect on polyamine metabolism in mitogen-and superantigen-activated human T-cells. *Biochim. Biophys. Acta* 1425: 337, 1998.
156. Barbul, A., Fishel, R. S., Shimazu, S., et al. Intravenous hyperalimentation with high arginine levels improves wound healing and immune function. *J. Surg. Res.* 38: 328, 1985.
157. Agaiby, A. D., and Dyson, M. Immuno-inflammatory cell dynamics during cutaneous wound healing. *J. Anat.* 195: 531, 1999.
158. Langkamp-Henken, B., Herrlinger-Garcia, K., Stechmiller, J. K., et al. Arginine supplementation is well tolerated but does not enhance mitogen-induced lymphocyte proliferation in elderly nursing home residents with pressure ulcers. *J.P.E.N. J. Parenter. Enteral Nutr.* 24: 208, 2000.
159. Krebs, H. Glutamine metabolism in the animal body. In J. Mora and R. Palacios (Eds.), *Glutamine: Metabolism, Enzymology, and Regulation*. New York: Academic, 1980.
160. Abcouwer, S., Bode, B., and Souba, W. Glutamine as a metabolic intermediate. In J. Fischer (Ed.), *Nutrition and Metabolism in the Surgical Patient*. Boston: Little, Brown, 1996. P. 353.
161. Zetterberg, A., and Engstrom, W. Glutamine and the regulation of DNA replication and cell multiplication in fibroblasts. *J. Cell. Physiol.* 108: 365, 1981.
162. Zielke, H. R., Ozand, P. T., Tildon, J. T., Sevdalian, D. A., and Cornblath, M. Growth of human diploid fibroblasts in the absence of glucose utilization. *Proc. Natl. Acad. Sci. U.S.A.* 73: 4110, 1976.
163. Demling, R. H., and DeSanti, L. Involuntary weight loss and the nonhealing wound: The role of anabolic agents. *Adv. Wound Care.* 12(1 Suppl.): 1, 1999.
164. Askanazi, J., Carpentier, Y. A., Michelsen, C. B., et al. Muscle and plasma amino acids following injury: Influence of intercurrent infection. *Ann. Surg.* 192: 78, 1980.
165. Roth, E., Funovics, J., Muhlbacher, F., et al. Metabolic disorders in severe abdominal sepsis: Glutamine deficiency in skeletal muscle. *Clin. Nutr.* 1: 25, 1982.
166. Peng, X., Yan, H., You, Z., Wang, P., and Wang, S. Clinical and protein metabolic efficacy of glutamine granules-supplemented enteral nutrition in severely burned patients. *Burns* 31: 342, 2005.
167. Zhou, Y. P., Jiang, Z. M., Sun, Y. H., Wang, X. R., Ma, E. L., and Wilmore, D. The effect of supplemental enteral glutamine on plasma levels, gut function, and outcome in severe burns: A randomized, double-blind, controlled clinical trial. *J.P.E.N. J. Parenter. Enteral Nutr.* 27: 241, 2003.