Surgical Preparation

Surgery has been referred to as “benign violence” (Waldron EE 1985)—an appropriate term for the calculated and deliberate wounding of a human body, even when the goal is the noble one of curing disease.

Indeed, from a biological standpoint, surgery causes many of the same kinds of tissue damage that occur during a traumatic injury. While this injury may be necessary and beneficial, the body does not discriminate between a surgeon’s scalpel and any other kind of trauma. In fact, studies have shown that patients are under great physical stress both during and after their surgeries. Sadly, few conventional physicians recommend proven ways to speed recovery and produce better patient outcomes.

In general, surgery can be divided into three main phases: the preoperative period; the period during the surgery; and the postoperative, or recovery, period. At each of these stages, patients can take an active role in their own well-being by following documented steps to support their body’s antioxidant stores, reduce inflammation, and modulate the immune responses that accompany surgery. By paying careful attention to nutritional status, patients can speed their recovery and experience more successful results (Asher ME 2004; Schmiesing CA et al 2005).

THE PREOPERATIVE PERIOD

Each of the three phases of a surgical procedure poses different threats to the patient’s well-being, although there may be considerable overlap. The most variable phase is the preoperative, or preparatory, phase. In the case of emergency surgery, this period may be limited to a very few hours (and in the case of trauma even to a few minutes). In most cases, however, both the patient and the surgical team have longer to prepare, and it is during this period that many nutritional interventions can be made. One overlooked statistic is that up to 50 percent of patients admitted to hospitals are malnourished (Patel GK 2005). This startling statistic underscores the critical importance to the surgical patient of proper nutritional intervention.

Two significant threats to the patient’s well-being during the preoperative period are the continued progression of the disease that has made the operation necessary (for instance, a growing cancer) and the patient’s degree of apprehension and anxiety. Certain preoperative procedures, such as prolonged fasting, may also exert negative effects.

Disease progression. Virtually all disease processes that require surgery, including traumatic injury, impose substantial oxidative threats to tissue (DeWeese TL et al 2001). For instance, initial oxidative (free radical) damage can be caused by impaired blood supply as a tumor presses on major vessels or diverts blood from healthy tissues. Toxins may be released from infected or malignant tissue or by release of intracellular contents, including protein-damaging enzymes, from dying cells (Michalik L et al 2006).

Blood released from normal circulation into various body compartments, such as the abdomen, can itself produce oxidative damage (Potts MB et al 2006). An early response to oxidative damage is inflammation, which is aimed at destroying unhealthy tissue or invading infectious agents. As inflammation grows, however, additional oxidant damage is produced by white blood cells that are attracted to the area by signaling chemicals called cytokines and chemokines (Ceriello PA 2006). Many of these cells, particularly white blood cells called neutrophils, release toxic reactive oxygen species, which cause further tissue damage (De la Fuente M et al 2005).

Similarly, in the case of infections, the body’s powerful immune response calls inflammatory cells to the infected tissue, where they release agents that oxidize lipids in cell membranes, causing the membranes to leak and the cells to die (Stark G 2005). Inflammation also changes blood vessel walls, making them “leaky” and allowing blood components to seep into tissues, causing swelling and loss of plasma proteins (Thurston G et al 2000). These oxidative and inflammatory reactions impair local tissue function and also sap the body of the proteins, minerals, and other substances necessary for maintaining normal blood pressure and overall tissue health (Fall PJ et al 2005).

A healthy diet and appropriate nutritional supplements can help prepare a patient for surgery by maximizing reserves of proteins, essential fatty acids, vitamins, and minerals. Supplements can also help bolster the immune system, minimize oxidative damage, and keep inflammation under control. Specific nutrients and supplements for these purposes are discussed below.

Psychological stress. It is widely recognized that psychological and emotional stress reduces the body’s immune function and renders people more vulnerable to disease; scientists today understand that much of this effect is mediated by brain structures that influence the production of stress-induced hormones such as corticosteroids (Leonard BE 2005; Straub RH et al 2005). Every person who will be undergoing a surgical procedure, no matter how minor, has some degree of anxiety about the procedure, its outcomes, and potential complications. The outcomes of surgical procedures are almost always improved by a reasonably long preoperative planning period, which gives the surgical team and the patient the maximum opportunity for physical and technical preparation. Excessively long preoperative periods, however, may be associated with increased amounts of worry, anxiety, and stress; these factors can have a negative impact on surgical outcomes (Pucak ML et al 2005).

Unfortunately, the often-repeated phrase “just relax” is not only entirely ineffective—there is even evidence that patients who are “ordered” to relax actually experience increased stress levels. Instead, one of the most effective interventions to reduce patient stress levels is communication; patients with a high degree of so-called health literacy are known to have shorter hospital stays, fewer complications, and better overall outcomes (Wolf MS et al 2005; Schillinger D et al 2002). Health literacy is easy to attain; the Partnership for Clear Health Communication promotes a program called “Ask Me 3,” which recommends that patients get three simple questions answered by a physician regarding any disease or treatment:

1. What is my main problem?
2. What do I need to do?
3. Why is it important for me to do this?

Getting these questions answered is a major step in improving health literacy and reducing stress levels—and believe it or not, many physicians appreciate being asked to present information to patients in this format. More information for patients on the Ask Me 3 program is available at www.askme3.org.

Other nonmedical strategies for reducing preoperative anxiety and stress have been shown to be helpful in varying degrees. Hypnosis has been found to be effective in reducing both preoperative anxiety and postoperative complications (Lambert SA 1996; Rapkin DA et al 1991). A related technique called guided imagery, in which a skilled therapist works with the patient to envision low-stress and positive concepts, has also been documented to anxiety, safely lowering pulse and blood pressure, and even shortening hospital stays (Halpin LS et al 2002; Norred CL 2000). In other studies, patients using guided imagery required 50 percent less pain medication than did controls (Tusek D et al 1997a,b).

Preoperative fasting. Practically since the inception of general anesthesia for surgery, doctors have worried about the effects of a full stomach on an unconscious patient. The chief risk is aspiration of stomach contents into the lungs, which can cause severe inflammation, infection, and death. Modern anesthesia practices, however, such as careful control of the patient’s airway, close monitoring, and the selective use of appropriate anesthetic drugs, has dramatically reduced this risk (Brady M et al 2003). Periods of fasting, such as the traditional “nothing by mouth after midnight” on the night before surgery, can produce dehydration, low blood sugar, and a variety of other complications. Increasingly, anesthesiologists are recognizing both the biological and the psychological value of permitting patients a reasonable oral intake, at least of liquids, until about four hours before the procedure is to begin. Patients are encouraged to discuss this practice with their physicians well in advance of surgery.

THE OPERATION ITSELF

The surgical procedure itself is the phase over which patients have the least control. From the moment the patient enters the operating room, virtually all vital functions are taken over by members of the surgical team. The “ABCs,” or airway, breathing, and circulation, are typically managed by the anesthesiologist. While many anesthetic agents are aimed at attaining unconsciousness and managing pain, many other medications are given to support pulse and blood pressure, prevent infection and blood loss, and even counter the side effects of other medications. It is not unusual for a patient to experience the effects of more than 10 medications during a major surgical procedure. Blood transfusions can also have untoward effects, especially with regard to calcium status (Spiess BD 2004).

While each of these medications has its purpose, it also has inevitable unwanted effects, with many medications being potent oxidants and others stimulating immune or inflammatory responses, particularly in the lungs, which are directly exposed to inhaled anesthetic gasses (Patel AB et al 2002; Yang T et al 2001). Most medications have effects on the liver’s ability to detoxify other drugs and toxins. Anesthesiologists typically plan the array of medications carefully to minimize these effects, and it has recently been shown that certain of the most commonly used anesthetic gasses actually provide some protection against oxidative damage (Sivaci R et al 2006; Johnson ME et al 1996).

The oxygen that is provided during the procedure is itself a mixed blessing. Critical for maintaining normal cellular processes and proper wound healing, supplemental oxygen also produces increased levels of reactive oxygen species that can damage tissues. Surgical procedures themselves are known to reduce circulating levels of vitamins A and E and other naturally occurring antioxidants (Luyten CR et al 2005; Schindler R et al 2003). Good pre- and postoperative nutrition, with special attention to maintaining adequate antioxidant status, can help minimize these effects, and studies of administration of antioxidants during surgery are showing some promise (Canbaz S et al 2003; Xia Z et al 2003).

The majority of the physiological stress produced by an operation is the result of direct tissue damage from cutting, clamping, suturing, and otherwise manipulating organs and other structures. Reduced blood flow produces ischemia (lack of oxygen), resulting in cell death and release of intracellular components that produce an acidic environment. Enzymes released from injured cells can further damage adjacent tissue.

When blood flow is restored to an ischemic area, reperfusion injury occurs, with the suddenly elevated oxygen levels causing transient oxidative damage and the restored flow of blood sweeping tissue toxins into the general circulation (Michalik L et al 2006). Oxidant molecules produce the same sort of damage to cell membranes (lipid peroxidation) as that caused by the disease process itself (Stark G 2005). Similarly, oxidant damage results in stimulation of inflammatory processes and release of cytokines, with further oxidant injury caused by inflammatory cells attacking injured tissue (Michalik L et al 2006; Potts MB et al 2006; De la Fuente M et al 2005). While this inflammatory response represents the first stages of the healing process, it can often become exaggerated and contribute to both local and systemic stressors that impede, rather than improve, recovery (Angele MK et al 2005).

Finally, although not a major factor during the operation, bacterial and fungal organisms may gain access to normally sterile body areas, especially during so-called dirty cases, in which the bowel or other naturally contaminated organs must be opened. Drainage of abscesses and other infected tissue can also allow infectious organisms entry into otherwise sterile tissue, setting the stage for a postoperative infection, with its attendant oxidative and inflammatory consequences (Angele MK et al 2005).

Oxidant and inflammatory stresses are not limited to the region undergoing the surgical procedure. It is now widely recognized that surgery itself can be a systemic inflammatory stress that can cause injury in areas far removed from the site of the operation (Frass OM et al 2001; Kawahito K et al 2000). For example, surgery can impact the function of blood vessels during the procedure, causing blood pressure instability (Williams MA et al 1999).

Some of the most profound effects of surgical procedures may impact the gastrointestinal tract. There is now good evidence that surgery (and anesthesia) may produce “leaky gut” effects, permitting entry of toxins and microorganisms into the circulation and affecting long-term outcomes (Mangiante G et al 2005). Many surgeons and anesthesiologists are now interested in the use of antioxidant and immune-modulating nutrients during surgery to ameliorate these effects (Angele MK et al 2005; Calder PC 2004).

THE POSTOPERATIVE (RECOVERY) PERIOD

During the postoperative phase, the patient and the surgical team have many opportunities to collaborate in maximizing nutrient contributions to the healing and recovery process. As in the preoperative period, considerable benefit has been demonstrated from nonmedical interventions such as hypnosis and guided imagery. The latter in particular has been shown to reduce pain, anxiety, and length of stay in patients undergoing diverse surgical procedures (Antall GF et al 2004; Halpin LS et al 2002; Lambert SA 1996).

The greatest biological threats to the postoperative patient arise from the intricate relationships between regrowth of healing tissue, inflammation, and infection. A certain amount of inflammation is necessary for proper wound healing—cytokines and other inflammatory mediators are required for the production of vascular endothelial growth factor, which is vital for assuring a strong blood supply to new tissue, for example (Khanna S et al 2001, 2002). Inflammatory cells and their chemical products are also required to fight the ever present threat of infection. But excessive inflammation can also impair the healing process.

Supplemental oxygen is a very frequent part of the postoperative treatment regimen; surgeons are naturally anxious to provide adequate oxygen for the increased metabolic demands of rapidly healing tissue (Alleva R et al 2005; Gottrup F 2004). Wound healing is known to be accelerated by moderately elevated tissue oxygen levels, and in fact hyperbaric oxygen therapy (oxygen treatment at higher-than-normal pressures) is now used for treatment of slow-healing wounds and many burns (Gajendrareddy PK et al 2005), where it has been shown to increase vascular endothelial growth factor levels (Patel V et al 2005).

As with intraoperative oxygen therapy, however, this benefit is not without its costs in terms of increased tissue levels of reactive oxygen species. A judicious mix of increased oxygen supply with antioxidant supplementation seems to provide maximum wound healing benefits with minimum systemic exposure to free oxygen radicals (Alleva R et al 2005; Patel V et al 2005; Muth CM et al 2004; Sen CK et al 2002).

In addition to the wounds and tissue damage inflicted by the surgery itself, postoperative patients are at risk for a number of complications caused by their decreased mobility. Early complications include partial lung collapse that results from shallow, painful breathing (Westerdahl E et al 2005), bladder infections from indwelling catheters (Green RJ et al 1995), local inflammation of the healing wound (Larsen JW et al 2003), and inflammation caused by blood clots developing in nonmoving lower extremities (Vucic N et al 2003). These complications are so common, in fact, that surgical interns are taught the mnemonic “wind, water, wound, walk” when considering likely sources of a fever in the first few postoperative days (Pile JC 2006). All of these complications are the result of inflammatory processes that have been amplified by the surgery. Nutritional modulation of the inflammatory response may help blunt these complications (Calder PC 2004).

Perhaps the most severe postoperative complication is the development of pressure ulcers, or bedsores. These ulcers develop at pressure points in patients who are unable or unwilling (because of pain) to shift their positions in the bed; early signs of their development can be present within two hours of pressure being applied (Bansal C et al 2005). Constant pressure reduces local blood flow, producing ischemia (reduced oxygen levels) and lack of nutrients. This situation rapidly produces increased tissue levels of metabolic waste products such as lactic acid and eventually results in cell death, with release of toxins and enzymes into adjacent tissue. Once again, inflammation is triggered in previously healthy tissue, attracting inflammatory cells that cause still further tissue damage. Necrosis (cell death) can occur very rapidly in these ulcers, resulting in the development of potentially large masses of dead and dying tissue, which are a breeding ground for bacteria.

For these reasons, bedsores can be life threatening. Their prevention is one of the chief priorities of the surgical team in the postoperative period. Poor nutritional status is a major risk factor for their development (Domini LM et al 2005), and many nutritional interventions are known to be helpful (Desneves KJ et al 2005; Breslow RA et al 1993).

Proper wound healing also requires both energy and an adequate supply of the chemical building materials of new tissue. Requirements for calories, protein, and vitamins in the postoperative period are higher than at practically any other period in the lifetime of an adult (Ellis LM et al 1991). Formerly, surgeons sharply limited the amount and pace of postoperative feedings, believing that the gut needed a lengthy recovery period from anesthesia and surgery. Today most surgeons recognize the critical nature of early restoration of feedings, preferably by the gastrointestinal route (Grimble RF 2005; Fearon KC et al 2003). This practice has been shown not only to maximize nutritional intake but also to reduce the “leaky gut” effects produced by the systemic inflammation that occurs in response to surgery (Mangiante G et al 2005).

Finally, surgery also suppresses immune response (Angele MK et al 2005). For this reason, the risk of infection, already elevated by the operation itself, rises still higher in the postoperative period as all branches of the immune system slowly emerge from their depressed state. Many nutrients contribute to the recovery of the immune system postoperatively, and indeed the new field of immunonutrition has developed around a growing understanding of the effects of certain nutrients on immune and inflammatory responses (Alvarez W et al 2003).

IMMUNONUTRITION

Most surgeons now recognize that good attention to nutrition, including its effects on antioxidant and inflammatory status, can have major positive impact on the outcome of a surgical procedure (Calder PC 2004). No longer a minor part of the postoperative orders, a comprehensive nutritional program begun in the weeks prior to surgery and continued at the earliest possible postoperative moment is known to increase survival, reduce complications, minimize length of hospital stays, keep costs down, and significantly enhance patients’ quality of life (Ellis LM et al 1991).

The field of immunonutrition aims to provide the proper mix of nutrients to boost healthy immune function while suppressing the exaggerated inflammatory response (Chen da W et al 2005; Grimble RF 2005). A variety of nutrient formulas and routes of delivery have been tested. The most promising results come from nutrient formulas that are provided by mouth or by feeding tube (the enteral route) rather than by intravenous feedings. Such feedings reduce atrophy of the intestinal lining and prevent the increase in gut permeability that is a consequence of the inflammatory response (Mangiante G et al 2005).

Patients given enteral (orally administered) supplements have been shown to have fewer infections (Fukushima R et al 2004), shorter stays in intensive care, and fewer overall hospital days (Grimble RF 2005). They have improved wound healing compared with patients receiving standard nutrition (Farreras N et al 2005). Of particular importance from the patient’s standpoint, starting immunonutrition supplements up to five days before surgery may provide even greater benefits (Sax HC 2005), including beneficial immune system effects (Matsuda A et al 2006), fewer postoperative infections (Moskovitz DN et al 2004), and reduced costs (Braga M et al 2005).

Omega-3 fatty acids. While many different mixtures of nutrients have been used in immunonutrition, several main components appear to provide maximum benefit. The goal of reducing the exaggerated inflammatory response to surgery is met through the provision of omega-3 fatty acids, largely derived from fish oils (Grimble RF 2005). These fatty acids can shift the production of cytokines away from those that stimulate inflammation (Heller A et al 2000). They also make cell and mitochondrial membranes more resistant to oxidant stress (Ates E et al 2004), which reduces tissue damage and prevents amplification of the inflammatory response. Most effective immunonutrient supplements contain substantial quantities of omega-3 fatty acids.

Amino acids. The amino acids arginine, glutamine, and taurine are conditionally essential amino acids, which means that under certain stressful conditions (including trauma and surgery), the body cannot synthesize them in normal amounts and must therefore rely on external supplemental sources (Kendler BS 2006; Sole MJ et al 2002).

- *Arginine*. This amino acid provides a substrate for nitric oxide production, which enhances blood flow by relaxing blood vessels (Grimble RF 2005). It also stimulates and activates immune system cells (Fukushima R et al 2004). Trauma and surgery increase levels of the enzyme arginase, which reduces arginine levels (Bansal V et al 2005). Arginine supplementation, alone or in combination, has been observed to enhance wound healing (Moskovitz DN et al 2004) and prevent pressure ulcers (Singer P 2002).

- *Glutamine*. Glutamine is a major component of proteins produced during clotting (Weisel JW 2005). Supplementation with glutamine also speeds wound healing (Peng X et al 2004).
- *Taurine*. Taurine is required for mitochondrial energy production and efficient utilization of other nutrients (Jeejeebhoy F et al 2002). It has been documented to improve outcomes after cardiac surgery by protecting heart muscle against ischemic damage (Keith M et al 2005).

Ribonucleic acids. Ribonucleic acids (RNA) are crucial to protein synthesis in wound healing, as well as the expression of gene products of immune system cells. While the precise mechanism is unknown, immunonutritional supplements containing RNA appear to improve immune responses and more rapidly overcome the immune depression induced by surgery (Kemen M et al 1995). Like other nutrient combinations, these supplements are effective when given both preoperatively (Matsuda A et al 2006) and in the early postoperative period (Farreras N et al 2005).

More than 170 studies have been published on various immunonutrient combinations that have shown positive results (Grimble RF 2005). Patients given a preoperative formula containing omega-3 fatty acids and arginine had significantly improved systemic immune responses, gut oxygen levels, and gut perfusion compared with control patients (Braga M et al 2002). In a different study, patients supplemented with arginine, glutamine, and omega-3 fatty acids had higher postoperative total protein and immunoglobulin levels, higher levels of infection-fighting white blood cells, and lower levels of pro-inflammatory cytokines and tumor necrosis factor than did unsupplemented controls, demonstrating that these supplements enhanced host defenses while modulating the exaggerated inflammatory response (Chen da W et al 2005).

Wound healing is also improved by immunonutritional mixtures. A 2005 study demonstrated that patients given a postoperative formula containing arginine, omega-3 fatty acids, and RNA increased synthesis of protein in surgical wounds and experienced fewer wound healing complications than did unsupplemented control patients (Farreras N et al 2005). The enhancement of host defenses by immunonutritional supplements (Ates E et al 2004) results in many fewer postoperative complications, such as pneumonia (Klek S et al 2005) and pressure ulcers (Singer P 2002).

OTHER NUTRIENTS THAT ENHANCE SURGICAL OUTCOMES

In addition to the specific immunonutrients discussed above, supplementation with many other biologically active materials can help prepare a person for upcoming surgery. Assuring that the body is replete with antioxidants is one easy and powerful way to avoid the antioxidant depletion that occurs during the surgical procedure (Pechan I et al 2004). Maximizing the anti-inflammatory status and boosting immune function to achieve the proper balance of host defense against infection while minimizing the exaggerated inflammatory response to surgery is another. And, of course, ensuring adequate protein intake prior to surgery is an important way of providing the soon-to-be-healing body with the building blocks of new tissue. All of these effects can be achieved with a reasonable program of supplementation in the weeks prior to surgery.

Amino acids are the building blocks of proteins, which are themselves the chief components of structural tissue. The enzymes that catalyze all biological processes are also proteins. Surgery dramatically increases the daily requirement of protein, particularly if there is substantial blood loss; and supplements containing amino acids or whole proteins have been shown both in animal models and human clinical trials to enhance the outcomes of surgical procedures (Collins CE et al 2005; MacKay D et al 2003; Scholl D et al 2001). Supplements may improve wound healing (Collins CE et al 2005), reduce the rate and severity of pressure ulcers (Frias SL et al 2004; Bourdel-Marchasson I et al 2000; Breslow RA et al 1993), and improve fat mass (a good thing following surgery; de Luis DA et al 2005).

Almost all of the known vitamins are essential in each of the phases of surgery, either as vital cofactors in protein or nucleic acid synthesis for rapidly healing tissue or as potent antioxidants that can minimize tissue damage and the heightened inflammatory response caused by surgery. Blood levels of many of the vitamins are markedly reduced during surgery, and there is good evidence for both pre- and postoperative supplementation.

Vitamin C. This vitamin is an antioxidant that is also an absolute requirement for protein synthesis, making it indispensable in wound and fracture healing; fractures in animal models heal faster when the animals receive vitamin C supplementation (Sarisozen B et al 2002; Yilmaz C et al 2001). In humans, vitamin C contributes to the strength of healing wounds and reduces the degree and severity of postoperative pressure ulcers (Desneves KJ et al 2005; Frias SL et al 2004; MacKay D et al 2003).

Vitamin E. Vitamin E is a potent antioxidant and fat-soluble vitamin that is found in large amounts in skin, where it may improve wound healing and scar appearance (Chen MA et al 2005; MacKay D et al 2003). By scavenging reactive oxygen species, vitamin E can reduce tissue damage caused by free radicals, thereby reducing surgically induced inflammation. Like vitamin A, vitamin E levels are depleted during surgical procedures, especially those that require the use of a heart-lung machine (Schindler R et al 2003). In animal models, supplements containing vitamin E promote fracture healing (Turk C et al 2004; Sarisozen B et al 2002) and mitigate the deleterious effects of hyperbaric (high pressure) oxygen (Patel V et al 2005). In humans, vitamin E also assists in the healing of bone necrosis following radiation treatment (Delanian S et al 2005). Vitamin E has even been administered directly into coronary blood vessels during open-heart surgery, where it was shown to reduce reperfusion oxidative injury to cardiac muscle cells (Canbaz S et al 2003).

Because vitamin E can inhibit platelet aggregation, patients should discuss vitamin E supplementation with their surgeons well in advance of the surgery to determine whether the benefit exceeds the risk in their specific cases. Another way to enhance vitamin E function without direct vitamin E supplementation is to consider alpha-lipoic acid, which has been shown to support vitamin E's antioxidant function in patients undergoing hyperbaric oxygen treatment (Alleva R et al 2005).

Vitamin A. This vitamin is essential for surgical patients; it stimulates the production of transforming growth factor beta-1, which accelerates skin and intestinal wound healing (Yuen DE et al 2004). Supplements containing vitamin A have been especially useful in the prevention of pressure ulcers (Singer P 2002) and in treatment of burn patients (Grau CT et al 2005). Vitamin A has also been shown to mitigate the effects of inflammation caused by radiation treatments that often accompany cancer surgery (Ehrenpreis ED et al 2005).

Lipoic acid. Lipoic acid is an effective antioxidant that may have a role in preoperative care. In a rat model of skin injury, pretreatment with lipoic acid sped the healing of skin wounds by protecting skin cells from oxidant damage (Lateef H et al 2005). In humans, lipoic acid helped combat the free radical damage caused by high tissue concentrations of oxygen (Alleva R et al 2005).

In addition to vitamins, a number of other micronutrients and conditionally essential nutrients, many with antioxidant or anti-inflammatory effects, have been found to improve surgical outcomes and prevent complications.

Omega-3 fatty acids. These have already been mentioned as key components of immunonutrient formulas. Fish oil supplements have independently been documented to reduce the exaggerated inflammatory response caused by surgery, producing decreased cytokine levels (Aiko S et al 2005; Babcock TA et al 2005; Bansal V et al 2005). Supplementation with fish oil rich in omega-3 fatty acids reduced infection rates and showed promise for shortening hospital length of stay (Heller A et al 2000). The same group of investigators also demonstrated improvements in liver and pancreatic function postoperatively in cancer patients supplemented with fish oil (Heller AR et al 2004). Cancer patients given five days of omega-3 supplementation before their surgery had dramatically reduced blood levels of inflammatory mediators in the postoperative days (Nakamura K et al 2005). Perhaps the most dramatic demonstration of fish oil's efficacy is a 2004 study of preoperative supplementation, which demonstrated a decrease in deaths following surgery in the group that received preoperative fish oil supplements (Tsekos E et al 2004). This study also showed a lower requirement for mechanical ventilation postoperatively and a shorter length of hospital stay in the group supplemented preoperatively.

Coenzyme Q10. Coenzyme Q10 (CoQ10) is an antioxidant molecule intimately involved in intracellular energy management. Like other antioxidants, its levels plummet sharply during surgery, presumably because of rapid consumption by oxidant species (Pechan I et al 2004). Diminished levels of CoQ10 and other conditionally essential antioxidants may also worsen cardiac output, especially in people with preexisting heart disease (Sole MJ et al 2002). Poor cardiac output results in poor perfusion of other organs and can delay healing and set the stage for other complications. Preoperative treatment with CoQ10 can restore cardiac muscle function and protect against hypoxic (low oxygen) damage (Keith M et al 2005; Rosenfeldt F et al 2005). One study of a supplement containing CoQ10, taurine, and carnitine demonstrated improved cardiac blood volumes in cardiac surgery patients (Jeejeebhoy F et al 2002).

Zinc. This mineral functions as an important coenzyme in the production of collagen, the chief protein in healing wound tissue; it has also recently been determined to have an important antioxidant function in skin (Rostan EF et al 2002). The earliest sign of zinc deficiency in humans is often the development of skin breakdown, and topical zinc treatments have been used for centuries with good effect (Schwartz JR et al 2005). Animals made zinc deficient have slower rates of collagen accumulation in wounds and diminished wound strength, while zinc supplementation prior to creation of the wound (preoperatively) increased the strength of the healing wound (Kaplan B et al 2004; Iriyama K et al 1982). Quantitative studies of the effects of zinc supplementation in mice demonstrate that adequate zinc has an antioxidant function and hastens wound healing, while deficiency or very high doses delay healing (Lim Y et al 2004; Cario E et al 2000). Zinc may help in the healing, not only of skin wounds, but also of bone: one study demonstrated that zinc supplementation hastened the healing of leg fractures in rats (Igarashi A et al 1999).

In studies of patients who already had pressure ulcers, supplementation with a combination of zinc, arginine, and vitamin C produced significant improvement in treated patients compared with controls given placebo (Desneves KJ et al 2005; Frias SL et al 2004). A similar supplement was shown to delay the onset of pressure ulcers in a group of patients recovering from hip surgery (Houwing RH et al 2003). This combination is now widely recognized for patients undergoing surgery of any kind (Singer P 2002).

Melatonin. This is a pineal gland hormone that also has antioxidant functions (Macchi MM et al 2004). It appears to fundamentally affect a variety of brain functions related to relaxation, sleep, and anxiety, and its natural secretion is perturbed both by surgery (Guo X et al 2002) and by anesthesia (Karkela J et al 2002). These disturbances may contribute to the well-known phenomena of postoperative delirium (Shigeta H et al 2001) and “ICU psychosis,” in which patients become agitated, confused, and combative while in intensive care. Melatonin supplementation has been suggested in this setting (Miyazaki T et al 2003), though no clinical trials have been conducted.

Melatonin has recently been demonstrated to be as effective at reducing anxiety before a procedure as the commonly used benzodiazepine drug midazolam (Acil M et al 2004). As a premedication, melatonin has the added advantage of not producing postoperative impairments in mental function, as do the benzodiazepines (Samarkandi A et al 2005). There is emerging clinical evidence that melatonin may positively modify surgically induced general inflammation. In a study of newborns, melatonin given postoperatively significantly reduced inflammatory cytokine levels (Gitto E et al 2004).

Curcumin. Curcumin is a major component of turmeric. It is an antioxidant and a potent inhibitor of nuclear factor kappa beta, which plays a central role in “translating” inflammatory stimuli into activation of the inflammatory response. There has been tremendous recent interest in the role of nuclear factor kappa beta inhibition as a means of reining in overactive inflammatory reactions in sepsis, cancer, and autoimmune diseases (Maheshwari RK et al 2006).

A study of topical curcumin delivered in a collagen-based film demonstrated enhanced wound healing and tissue proliferation in wounds covered with the film, as well as more-efficient free radical scavenging than in wounds covered with a non-curcumin-containing film (Gopinath D et al 2004). In an animal model of radiation-induced impaired wound healing, pretreatment with curcumin enhanced wound closure compared with controls (Jagetia GC et al 2004). This study has profound implications for human cancer surgeries that are often complicated by the effects of radiation treatment.

Curcumin has also demonstrated powerful antioxidant effects on skin cells in culture, protecting cells against damage caused by hydrogen peroxide (Phan TT et al 2001). These mechanisms together may explain the more rapid healing of experimentally-produced surgical wounds in animals treated with curcumin (Sidhu GS et al 1998, 1999). There are as yet no human trials of curcumin in the context of surgery, but it has been observed to be safe and well tolerated in human trials for other uses as an anti-inflammatory and chemoprotective agent (Holt PR et al 2005; Cheng AL et al 2001).

LIFE EXTENSION FOUNDATION RECOMMENDATIONS

In an ideal situation, patients undergoing surgery will have adequate time before the operation to prepare themselves emotionally and physically. This preparation will likely include dietary supplementation, as well as mental and emotional preparation. The healthier patients are when they go into surgery, the healthier they are likely to be during the postoperative phase.

Life Extension also recommends that patients with poor glucose control discuss intensive insulin therapy with the surgeon before surgery. Studies indicate that surgery-induced insulin resistance, leading to elevated glucose levels during surgery, raises the risk of complications and death. Intensive insulin therapy, a procedure in which glucose levels are closely monitored during surgery, can help reduce complications and lower the risk of death (van den Berghe et al 2001). The recommended glucose range is between 80 mg/dL and 120 mg/dL. However, this practice is not standard in hospitals and requires intensive administration from nurses and other members of the surgical team. Nevertheless, because of the benefits, patients may want to discuss intensive insulin therapy with their surgical team to see if it is warranted.

Patients may also want to discuss aspirin therapy before surgery. Aspirin is a well-known antiplatelet that is used for prevention of heart attack and to mitigate the damage of ongoing heart attacks. Some studies have suggested that aspirin therapy may benefit certain patients before surgery, especially heart patients and those undergoing carotid endarterectomy (Mangano DT 2002). However, because aspirin affects the blood's ability to clot, no surgery patients should begin aspirin therapy unless under the direct supervision of their surgical team.

Other nutrients might also be helpful before and after surgery:

- **EPA/DHA**—1400 milligrams (mg) EPA and 1000 mg DHA daily
- **Arginine**—3000 to 12,000 mg daily (in three divided doses)
- **Glutamine**—1000 to 3000 mg daily
- **Vitamin C**—2000 to 3000 mg daily
- **Vitamin E**—400 international units (IU) daily (with at least 200 mg gamma tocopherol)
- **Vitamin A**—25,000 IU daily
- **Lipoic acid**—150 to 300 mg daily
- **CoQ10**—300 mg daily
- **Zinc**—30 mg daily
- **Melatonin**—300 mcg to 10 mg, usually taken before bedtime; begin with the smallest possible dose
- **Curcumin**—800 to 1600 mg daily
- **Protein (derived from whey)**—up to 60 grams (g) daily

Importantly, the surgeon should be aware of any dietary supplements that are consumed. Some supplements, such as vitamin E and Ginkgo biloba, increase the risk of bleeding during surgery. Many physicians will recommend that patients discontinue these supplements up to 14 days before surgery.

PRODUCT AVAILABILITY

All the nutrients and supplements discussed in this section are available through the Life Extension Foundation Buyers Club, Inc. For ordering information, call anytime toll-free 1-800-544-4440, or visit us online at www.LifeExtension.com.

The blood tests discussed in this section are available through Life Extension National Diagnostics, Inc. For ordering information, call anytime toll-free 1-800-208-3444, or visit us online at www.LifeExtension.com.

SURGICAL PREPARATION SAFETY CAVEATS

An aggressive program of dietary supplementation should not be launched without the supervision of a qualified physician. Several of the nutrients suggested in this protocol may have adverse effects. These include:

Coenzyme Q10

- See your doctor and monitor your blood glucose level frequently if you take CoQ10 and have diabetes. Several clinical reports suggest that taking CoQ10 may improve glycemic control and the function of beta cells in people who have type 2 diabetes.
- Statin drugs (such as lovastatin, simvastatin, and pravastatin) are known to decrease CoQ10 levels.

Curcumin

- Do not take curcumin if you have a bile duct obstruction or a history of gallstones. Taking curcumin can stimulate bile production.
- Consult your doctor before taking curcumin if you have gastroesophageal reflux disease (GERD) or a history of peptic ulcer disease.
- Consult your doctor before taking curcumin if you take warfarin or antiplatelet drugs. Curcumin can have antithrombotic activity.
- Always take curcumin with food. Curcumin may cause gastric irritation, ulceration, gastritis, and peptic ulcer disease if taken on an empty stomach.
- Curcumin can cause gastrointestinal symptoms such as nausea and diarrhea.

EPA/DHA

- Consult your doctor before taking EPA/DHA if you take warfarin (Coumadin). Taking EPA/DHA with warfarin may increase the risk of bleeding.
- Discontinue using EPA/DHA 2 weeks before any surgical procedure.

L-Arginine

- Do not take L-arginine if you have the rare genetic disorder argininemia.
- Consult your doctor before taking L-arginine if you have cancer. L-arginine can stimulate growth hormone.
- Consult your doctor before taking L-arginine if you have kidney failure or liver failure.
- Consult your doctor before taking L-arginine if you have herpes simplex. L-arginine may increase the possibility of recurrence.

L-Glutamine

- Consult your doctor before taking L-glutamine if you have kidney failure or liver failure.
- L-glutamine can cause gastrointestinal symptoms such as nausea and diarrhea.

Lipoic Acid

- Consult your doctor before taking lipoic acid if you have diabetes and glucose intolerance. Monitor your blood glucose level frequently. Lipoic acid may lower blood glucose levels.

Melatonin

- Do not take melatonin if you are depressed.
- Do not take high doses of melatonin if you are trying to conceive. High doses of melatonin have been shown to inhibit ovulation.
- Melatonin can cause morning grogginess, a feeling of having a hangover or a “heavy head,” or gastrointestinal symptoms such as nausea and diarrhea.

Vitamin A

- Do not take vitamin A if you have hypervitaminosis A.
- Do not take vitamin A if you take retinoids or retinoid analogues (such as acitretin, all-trans-retinoic acid, bexarotene, etretinate, and isotretinoin). Vitamin A can add to the toxicity of these drugs.
- Do not take large amounts of vitamin A. Taking large amounts of vitamin A may cause acute or chronic toxicity. Early signs and symptoms of chronic toxicity include dry, rough skin; cracked lips; sparse, coarse hair; and loss of hair from the eyebrows. Later signs and symptoms of toxicity include irritability, headache, pseudotumor cerebri (benign intracranial hypertension), elevated serum liver enzymes, reversible noncirrhotic portal high blood pressure, fibrosis and cirrhosis of the liver, and death from liver failure.

Vitamin C

- Do not take vitamin C if you have a history of kidney stones or of kidney insufficiency (defined as having a serum creatine level greater than 2 milligrams per deciliter and/or a creatinine clearance less than 30 milliliters per minute.
- Consult your doctor before taking large amounts of vitamin C if you have hemochromatosis, thalassemia, sideroblastic

anemia, sickle cell anemia, or erythrocyte glucose-6-phosphate dehydrogenase (G6PD) deficiency. You can experience iron overload if you have one of these conditions and use large amounts of vitamin C.

Vitamin E

- Consult your doctor before taking vitamin E if you take warfarin (Coumadin).
- Consult your doctor before taking high doses of vitamin E if you have a vitamin K deficiency or a history of liver failure.
- Consult your doctor before taking vitamin E if you have a history of any bleeding disorder such as peptic ulcers, hemorrhagic stroke, or hemophilia.
- Discontinue using vitamin E 1 month before any surgical procedure.

Zinc

- High doses of zinc (above 30 milligrams daily) can cause adverse reactions.
- Zinc can cause a metallic taste, headache, drowsiness, and gastrointestinal symptoms such as nausea and diarrhea.
- High doses of zinc can lead to copper deficiency and hypochromic microcytic anemia secondary to zinc-induced copper deficiency.
- High doses of zinc may suppress the immune system.

For more information see the Safety Appendix