

Clinical Nutrition & Supplements For Wound Healing, Surgery Recovery and Scar Reduction

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Introduction to Clinical Nutrition for Wound Healing, Surgery Recovery, and Scar Reduction

Introduction

The population of the US is aging. This has led to a significant increase in certain healthcare sectors. One of the largest sectors of growth has been in wound care. Specialized wound care centers and wound care treatments have increased throughout all patient populations. This has also led to a great deal of research into wound healing, chronic wounds, and at risk patient populations.

Wound healing is a complex and multifaceted process. Adequate nutrition is an integral part to the wound healing process. There has been an abundance of literature in surgery that proper nutrition prior to surgery is critical to optimal patient outcomes. Currently, the American College of Surgeons recommends preoperative nutritional supplementation for patients that are undergoing major abdominal surgery and Medicare increases payments to medical facilities if they provide the nutritional supplements.

Wound healing follows 4 major steps:


Hemostasis- Blood clot formation. (30 min)

Inflammatory Phase- Immune cells migrate to the wound to clear the wound of debris and bacterial infection. (4-6 days)

Proliferation Phase- Rebuilding of the tissue begins with the recruitment of varied cell types. (4-24 days)

Remodeling Phase- Wound closure occurs and regeneration of the original tissue occurs. Cells involved the previous phases are destroyed through cell signals. (21 days- 2 years)

Each stage of wound healing must complete its job before the next stage can begin. Furthermore, if a single stage lasts longer than the next stage, it will not occur. The body will divert energy and protein from other tissues to the wound bed causing dysregulation and further slowing the healing process. Thus, disruptions in the process at any stage can lead to significant complications and a non-healing wound.^{2,3,4,5}



The role of nutrition in surgical recovery has become very significant in recent years. The first step in this has been the inclusion of nutritional “prehabilitation” for patients undergoing major abdominal surgery. The improvement in this space has led many other surgical specialties to focus on preoperative nutritional optimization. Many new products have been developed and brought to market that attempt to address this need. The second breakthrough was based on the bacterial flora at the time of bowel surgery. Data now shows that the bacterial microenvironment plays a direct role in surgical complications. While this has been well known with *C. diff* colitis, new data suggests the bacteria at the bowel anastomosis is the cause of anastomotic leaks and superficial wound infections. These studies linked a lack of appropriate amino acids and nutrients within the enterocyte leads to bacterial transformation to pathogen. Currently, numerous surgical societies recommend nutritional supplementation with specific proteins, amino acids, and vitamins both before and immediately after surgery for improved outcomes and faster healing.


Understanding the Role of Nutrition in Wound Care

An understanding of the role of nutrients in wound care enables healthcare professionals to offer advice to patients whose wounds are not progressing as expected. Nutrition should be part of a holistic wound assessment, with any malnourished patient being referred to a dietician. It is a misconception that only underweight individuals can be malnourished. Malnutrition occurs quickly in obese patients as the metabolic needs of fat cells are different and their ability to mobilize nutrients is diminished. Furthermore, they can often have underlying essential vitamin, mineral, and amino acid deficiencies in the setting of obesity. Elderly patients are at extremely high risk of malnutrition in spite of appearing well. Protein requirements rise as people age, but their ability to process complex proteins within their GI tract diminishes. Furthermore, multiple medications can negatively affect their ability to absorb, process, and use protein in their diet. The use of a robust assessment tool will assist healthcare professionals in deciding which patients require nutritional referral.

The link between malnutrition and wound complications has been well established.⁶ Malnutrition can be defined as an imbalance between nutritional requirements and intake, causing the body to experience measurable adverse effects. Chronic illnesses are often present in patients with non-healing wounds and can lead to protein-energy malnutrition, which has been outlined as a significant problem in hospitals.⁹

Wound Care

Nutritional assessment of any patient with a non-healing wound is considered standard within the wound care community. Furthermore, Enhanced Recovery After Surgery (ERAS™) strongly recommends pre-operative nutritional evaluation and intervention prior to surgical intervention.



Nutritional factors can affect many health conditions such as diabetes and heart failure, and optimal nutrition can aid in the maintenance of overall health. Guidance suggests that a nutritious diet aimed at promoting wound healing should ideally encompass hydration, nutrients such as proteins and amino acids, vitamin A, vitamin B complex, vitamin C, vitamin E, iron, zinc, copper, fats and carbohydrates.^{7,8}

Normal Wound Healing

Hemostasis- During the injury, blood vessels are damaged exposing platelets to the basement membrane. Platelets adhere to the basement membrane and to each other causing a platelet plug. The platelets degranulate releasing a large number of local stimuli. These stimuli cause vasoconstriction, start chemotaxis, and active the clotting cascade.

Inflammatory Phase- Immune cells migrate to the wound. Wound debris is cleared using phagocytosis, bacteria and other pathogens are destroyed both by immunologic means as well as oxygen free radicals. New blood vessels begin to form but have not reached the wound.


Proliferative Phase- The new blood vessels reach the peri-wound increasing nutrient delivery. Fibroblasts begin secretion and crosslinking of collagen. Vessels migrate through the crosslinked collagen allowing for skin islands to form and wound contracture.

Remodeling Phase- Collagen crosslinking rapidly accelerates. Laminin, elastin, and other structural proteins provide an enhanced 3D scaffold allowing stem migration, tissue maturation, and multifunctional return.

Understanding the Importance of Protein in Wound Care

Normal metabolism can be critical when considering both surgical patients as well as patients with a diabetic wound. One of the critical elements necessary for healing is energy, which is received via carbohydrates, fats, and proteins. Although energy is most efficiently processed from carbohydrates and fats, protein is by far the most important of the required dietary components for a healing wound because it helps to repair damaged tissue.¹⁹

Proteins are the “building blocks” or the tools used to create new tissue. With normal hormone activity, the body uses nearly all protein byproducts for synthesis and not for energy. Carbohydrates and fats enter the energy system and can be stored later for energy use. Protein makes up the critical cell structure in muscle, organs, red blood cells, immune cell function, and connective tissue. Most significantly, the skin is composed mainly of the protein collagen.²¹




A healthy adult requires 0.8 grams of protein per kilogram of body weight per day with the recommended intake falling between 1.2 to 2.0 grams per kilogram. Stressed patients (i.e. patients with wounds) require almost double the protein intake at 1.5 grams of protein per kilogram of body weight. The increased need originates from both the demand for protein synthesis and the increased loss of amino acids abnormally channeled for fuel and energy. Good sources of protein include lean meats, eggs, lentils, beans, peanut butter, and fish.

It is important to increase protein in one's diet while trying to heal a wound and prevent the loss of lean body mass. This can be deleterious to one's general health as well as to the wound healing process. A loss of more than 15 percent of lean body mass will impair wound healing, while a 30 percent loss of lean body mass can lead to the development of spontaneous wounds such as pressure ulcers and possibly wound dehiscence.²⁰ It is easy to appreciate the importance of proteins in regards to wound healing.

What Are The Roles Of Carbohydrates And Fats In Wound Healing?

In addition to protein, there are other dietary essentials to aid in wound healing. Carbohydrates tend to get a bad reputation in the diet world, but are essential in the diet of someone trying to heal a wound. Remember that proteins can be used for energy, but are better served in the anabolic process. Carbohydrates may fill that role for energy use. Wounds require energy for collagen synthesis, along with other things.²² Glucose is the major fuel used to generate cellular energy in the form of adenosine triphosphate (ATP), which drives the wound healing process. The use of glucose to generate adenosine triphosphate can be inefficient, but it is the caloric contribution of glucose that is essential for preventing the depletion of proteins.

Hyperglycemia in the setting of wound healing is extremely deleterious. It inhibits new blood vessel formation in the wound, reduced immune cell function for debris phagocytosis and bacterial clearance. Therefore, it is imperative that diabetic patients have tight glucose control and adequate protein intake. Patients with diabetes can therefore suffer from a decreased and prolonged inflammatory phase that results in delayed deposition of matrix components as well as delayed epithelialization and decreased collagen formation. This in turn will result in decreased wound remodeling and delayed closure. Hyperglycemia can also interfere with the transport of ascorbic acid into certain cells, specifically leukocytes and fibroblasts.²⁴ Structurally, ascorbic acid and glucose are similar, so there may be a competitive inhibition of ascorbic acid, which may help explain the decreased early inflammatory response that increases the delay in healing. Also, wound infection rates may be higher in those with diabetes because of immunocompromise and for this reason practitioners need to discuss sound nutritional goals early in the treatment plan to try to bring these factors under control quickly. Again, achieving normal glucose control is perhaps the most important goal for successful wound healing in a patient with diabetes.²⁵



Fats are another essential macronutrient necessary for exceptional wound healing. Demling has suggested that the demand for fatty acids likely increases when there is a wound.¹⁰ Linoleic and arachidonic acids are two fatty acids that have been recognized as essential for prostaglandin synthesis.²⁶ Phospholipids are also necessary for wound healing in that they are the key components of basement membranes while prostaglandins are important for cellular metabolism and inflammation. Researchers have studied omega-3 fatty acids for possible benefits in wound healing, but they do not appear to be as structurally strong as other fatty acids.¹¹ However, omega-3 fatty acids do show benefits in propelling stronger immunity in the host, thereby decreasing infection rates and improving healing.²⁷

Along with cell membrane formation, one needs extra fats to power a wound to heal. Lipid components are responsible for tissue growth and wound remodeling, including collagen and extracellular matrix production. Animal fats including cheeses, butter, and meat sources are excellent sources of fats, as well as other sources such as fatty fish, avocado, and nuts.

How Does Malnutrition Affect The Individual?

The effects of malnutrition can have a profound impact on health and wellbeing. Physical and mental health can both deteriorate rapidly when an individual is not able to provide their body with the nutrients and energy that is needed.²⁸


Weak bones and muscles can reduce mobility, making it more challenging to walk, navigate stairs, and bathe. A reduction in strength often means losing independence, as the individual's ability to lift grocery bags, carry laundry, move from sitting to standing, and do everyday activities is compromised.

Without adequate muscular strength, posture can become weakened causing strain and pain in the neck, back, and shoulders. The risk of falls increases with a reduction in strength and mobility as well.

When malnutrition is present, the immune system may also be impacted. Healing after an injury or surgery is typically much slower and individuals are more susceptible to illness and infection.²⁹

The fatigue and irritability that are present whenever energy needs are not met can set the stage for the co-occurrence of depression and anxiety. Preventing malnutrition should be a goal for providers with at risk patients. It is essential that good oral hygiene is practiced as well. This ensures that the individual can chew and swallow safely and with ease. Studies have shown that gum disease is often linked to heart disease.

Hydration is another factor that is essential to maintain optimal nutrition. Hydration improves sleep quality, cognition, and mood. Hydration is crucial for many reasons such as regulating



body temperature, keeping joints lubricated, preventing infections, delivering nutrients to cells, and keeping organs functioning properly. These suggestions can help achieve a healthier life and diet.³⁰

How Nutritional Deficiencies Can Affect the Progression of Wound Healing

The role of nutrition in wound healing has been an area of both interest and controversy for many years. Although deficiencies in certain nutrients have long been known to impair healing, supplementation of specific immunomodulating nutrients has not consistently yielded improvements in wound healing. Still, the prospect of optimizing nutrition to assist the immune system in wound repair bears great significance in both medical and surgical fields, as the costs of wound care and repair cannot be ignored. Adapting your diet can help support a faster recovery too.³¹ Better nutritional practices can facilitate the wound healing process, while malnutrition will delay, inhibit, and complicate it.

Many nutrients work in isolation or combination with others to assist wound healing. A healthy diet with good nutrition is very important to help any wounds heal. A lack of certain nutrients can slow down the healing process. With each successive phase in the normal sequence of wound healing, the immune system orchestrates a wide variety of processes.³²


The Demand for Adequate Nutrition in Wound Healing

Adequate nutrition during recovery from an injury can help to control inflammation, provide the necessary nutrients to rebuild and restore injured tissue, decrease the risk of muscle atrophy, and preserve muscle strength.

For athletes, it is important to maintain sufficient energy intake because their metabolic rate increases 15 to 20 percent after an injury or surgery as the body prepares to repair the injured tissues. Under-eating can slow your recovery and contribute to the loss of muscle as the body doesn't have sufficient energy from food intake to repair the tissues.

Nutrition experts recommend athletes eat a balanced, whole-food, antioxidant-rich diet of lean protein, fruits and vegetables, healthy fats, and unprocessed foods to promote overall optimal health. During the recovery stages after an injury, it is recommended to increase the intake of particular foods to supply the necessary nutrients, vitamins, and minerals for tissue repair and to preserve muscle mass.

Healing places extra demands on one's resources as the body replaces cells and tissues that are lost or damaged through illness, injury, or surgery. The added stresses imposed during the healing process can deplete your levels of certain key nutrients. Vitamins may help these depleted levels, aiding in the recovery process.



According to the World Health Organization, malnutrition refers to all forms of deficiency, excess, or imbalance in a person's intake of energy and/or nutrients.³⁰ Unfortunately, malnutrition is often difficult to diagnose, especially in hospital settings and for chronically ill patients where other symptoms may mask nutritional challenges. That means it's up to the healthcare team to look for symptoms such as poor appetite, lack of mobility, unusual fatigue, dry skin, and a distended abdomen.

Certain nutrients are essential to the immune system. Without them, the body's ability to heal and recover is reduced. The body requires macronutrients and micronutrients to support body functions and systems. Macronutrients refers to the energy-yielding nutrients such as carbohydrates, proteins, and fats; whereas micronutrients refers to non-energy yielding nutrients such as vitamins and minerals. Micronutrients generally support the functions of macronutrients and are vitally important to the wound healing process. Fluids and water serves as the solvent for vitamins, minerals, glucose, and other nutrients. Therefore, hydration plays an important role in wound healing as well.

Fundamental Nutrients to Support Wound Healing


Our growing knowledge of the physiological role of various nutritional elements has led to the recognition that certain nutrients, which have commonly been classified as nonessential, become essential in certain clinical situations. Most of the studies that have found benefits from nutrition have focused mainly on critical care populations, trauma victims, gastrointestinal cancer patients, or other groups at high risk for malnutrition.³⁴

Vitamin A

Vitamin A is an essential micronutrient that comes in multiple forms, including retinol, retinals, and retinoic acids. Dietary vitamin A is absorbed as retinol from preformed retinoids or as provitamin A carotenoids that are converted into retinol in the enterocyte.³⁶ These are then delivered to the liver for storage via chylomicrons and later released into the circulation and to its biologically active tissues bound to retinol-binding protein.

Vitamin A is a crucial component of many important and diverse biological functions, including reproduction, embryological development, cellular differentiation, growth, immunity, and vision. Vitamin A functions mostly through nuclear retinoic acid receptors, retinoid X receptors, and peroxisome proliferator-activated receptors.³⁷ Retinoids regulate the growth and differentiation of many cell types within the skin, and their deficiency leads to abnormal epithelial keratinization.

In wounded tissue, vitamin A stimulates epidermal turnover, increases the rate of re-epithelialization, and restores epithelial structure. Retinoids have the unique ability to reverse the inhibitory effects of anti-inflammatory steroids on wound healing.³⁸ In addition to its role in



the inflammatory phase of wound healing, retinoic acid has been demonstrated to enhance the production of extracellular matrix components such as collagen type I and fibronectin, to increase proliferation of keratinocytes and fibroblasts, and to decrease levels of degrading matrix metalloproteinases.³⁹

Vitamin A has multiple positive effects on wound healing even in non-deficient states. It increases collagen cross-linking and wound-breaking strength. Vitamin A increases the inflammatory response in wounds through enhanced lysosomal membrane ability, increased macrophage influx, and activation and stimulation of collagen synthesis. Vitamin A increases the number of monocytes and macrophages at the wound site early in the inflammatory phase, facilitating epithelial cell differentiation.⁴⁰ It also importantly reverses corticosteroid-induced inhibition of cutaneous wound healing. Ultimately, vitamin A supplementation facilitates wound healing and surgical recovery.

Vitamin C

Vitamin C, also known as ascorbic acid, is required for the synthesis of collagen.⁴¹ It is also a highly effective antioxidant protecting cells from damage due to free radicals. Studies have shown that this vitamin can help speed up the healing process of wounds. Vitamin C plays an essential role in recovery as it can help keep the skin, bones, and soft tissues in optimal condition. It also has antioxidant properties, which can reduce the negative effects that free radicals and other pollutants have on the body. Studies show that consuming more vitamin C can increase your blood antioxidant levels by up to 30%. This helps the body's natural defenses fight inflammation. Finally, vitamin C also shows anti-inflammatory properties, making it an ideal booster for patients recovering from a bad trauma.

Vitamin C is a cofactor in the hydroxylation of proline and lysine residues in procollagen, which is vital for the strength and stability of collagen fibers.⁴² Vitamin C helps the body produce collagen and is present in skin, muscle, and other tissues. People with a low intake of vitamin C may experience slower wound healing, as their bodies will be less capable of producing collagen. It has numerous cutaneous and wound manifestations due to its critical role in collagen formation and post-translational modification.

In addition, studies have shown that mice supplemented with vitamin C had improved full-thickness wound contraction time after radiation therapy along with increased collagen deposition and fibroblast numbers. In a prospective randomized controlled trial, surgical patients with pressure sores given large doses of ascorbic acid had a significant acceleration in the healing of the pressure sores. Overall, vitamin C supplementation has consistently shown to benefit the wound healing process.⁴²



Vitamin D3

Humans absorb vitamin D from exposure to sunlight, their dietary intake, and dietary supplements. The “D” indicates D2 or D3. Vitamin D2 is manufactured through the ultraviolet irradiation of ergosterol from yeast and vitamin D3 for the ultraviolet irradiation of 7-dehydrocholesterol (a zoosterol that functions in the serum as a cholesterol precursor) from lanolin.⁴³

While other vitamins and nutrients are generally introduced to the body through the foods we eat, vitamin D works slightly differently. The main source of this element is exposure to sunlight. Ultraviolet-B radiation waves stimulate the production of vitamin D from a chemical in the skin’s epidermis, 7-dehydrocholesterol. This promotes proper wound healing. As such, it acts more like a hormone than a vitamin.⁴⁷

Vitamin D is only found in a handful of ingredients, but it is necessary for reducing downtime from a fracture. This vitamin helps store minerals in the bones and increases the amount of calcium the blood can absorb.


Many elements come into play concerning skin synthesis of vitamin D.⁴⁸ The latitude, the air quality of where one lives and sunscreen habits may help determine how much of this nutrient is produced in the epidermis. For this reason, deficiency is not uncommon. However, there are other ways to increase the levels of this nutrient without spending an excessive number of hours in the sun, which can be dangerous to one's health.

Foods that are high in vitamin D include:

- Cod liver oil
- Swordfish, salmon, tuna, and other fatty fish
- Many fortified drinks, such as milk and orange juice.
- Beef liver
- Egg yolk
- Swiss cheese

Vitamin E

Vitamin E is a generic term for a group of tocol and tocotrienol derivatives.⁴⁹ Since it was discovered as the major lipid-soluble antioxidant in the skin, vitamin E has been tried for the treatment of almost every type of skin lesion imaginable. Anecdotal reports claim that vitamin E speeds up wound healing and improves the cosmetic outcome of burns and other wounds. Many patients use vitamin E regularly to improve the outcome of scars and physicians often recommend topical vitamin E after skin surgery or resurfacing. Vitamin E is one of the essential vitamins that the body needs to maintain proper function. It plays a key role in cellular structure




and the formation of DNA, RNA, and red blood cells.⁵⁰ As an antioxidant, it neutralizes free radicals that can cause wrinkles, age spots, and fine lines. It also protects against ultraviolet rays, pollution, drugs, radiation, and smoke that can oxidize cells and change their cellular structure to cause signs of aging and disease. Essentially, vitamin E makes the skin look younger and more vibrant.

Vitamin E is a fat-soluble vitamin that is stored in the liver, adipose, and muscles. Because it is fat-soluble, it requires fat to be transported to other areas of the body.⁵¹ Without the ability to freely move throughout the body, excess vitamin E in the body can be potentially toxic. Therefore, maintaining proper levels of vitamin E in the body is crucial. Vitamin E has several functions in the body including skincare and repair. Vitamin E can be absorbed through the food that we eat, as a vitamin supplement, or applied topically in lotions, creams, and gels. The best way to receive the daily allowance of vitamins is through the consumption of food. Even though the amount of vitamin E that the body requires is minuscule compared to other vitamins, it is very difficult to receive enough vitamin E through our diets. Some foods that are high in vitamin E include spinach, almonds, avocados, sunflower seeds, olive oil, olives, papaya, and blueberries. By ingesting foods rich in vitamin E, the body can protect the skin from the inside out. Vitamin E within the body eliminates free radicals, protects the liver from toxic chemicals, promotes good circulation, and boosts the immune system.

Vitamin E is easily absorbed by the skin.⁵² When applied directly to the skin, vitamin E promotes wound healing, prevents scar tissue, treats sunburns, and prevents UV ray damage. Although it can be used to prevent scars, it can also be used to soften the appearance of scars. Vitamin E also aids in the treatment of skin diseases and conditions. Psoriasis is an autoimmune disease that causes skin redness and irritation. Vitamin E can be applied topically to reduce the redness and inflammation and decrease the irritation while softening the skin.⁵³ Vitamin E also reduces the risk of skin cancer by protecting the skin against sun damage. It acts as a skin barrier and strengthens the outside layer of skin to protect against environmental exposure. Vitamin E should be applied to the skin 20-30 minutes before going into the sunlight. Additionally, sunscreen can be applied on top of vitamin E to increase the effectiveness of sunblock. It also reduces water loss through the skin and promotes oil balance within the skin layers.⁵⁴ Vitamin E has potential benefits in the wound healing process, in skin care, and in preventing scar formation.

Vitamin B12

Vitamin B12 aids in growth and cell development, particularly in the production of erythrocytes (red blood cells). Like other B vitamins, it is important in metabolism and also helps the formation of red blood cells and maintenance of the central nervous system.⁵⁵ Vitamin B12 enables the body to process carbohydrates and fats, it aids the nervous system in functioning properly, and improves memory and concentration. It also helps the body process



deoxyribonucleic acid (DNA).⁵⁶ Vitamin B12 can be obtained from fish, dairy products, pork, beef, lamb, and eggs.

Similar to other water-soluble vitamins, vitamin B12 plays an important role in cell division and growth.⁵⁷ It also increases our energy levels by metabolizing fats and carbohydrates. Vitamin B12 enters the body by binding to the protein found in food. During digestion, hydrochloric acid releases vitamin B12 from the protein.⁵⁸ After being released, vitamin B12 combines with a substance called intrinsic factor (IF). This complex is now capable of being absorbed through the gastrointestinal tract.⁵⁹

In a study, it was found that vitamin B12 increased the tensile strength of wounds during the early phases of healing in rats that were fed balanced diets containing 19% or 25% protein. This effect was evident at least by the third day in the wounds studied, and it was most noticeable by the sixth day. In this same study, there was no significant difference in healing rates at the eighth day between wounds that were studied in the saline control and rats treated with vitamins from the third to the eighth day.⁵


Biotin

Biotin is a water-soluble vitamin, generally classified as B-complex vitamin.⁶⁰ It is also known as vitamin B7, coenzyme R, W Factor, and vitamin H. Like other B vitamins, it helps cells in the body to produce energy. It helps metabolize fats, proteins (amino acids), and carbohydrates in the body. It is important in cell growth, the production of fatty acids, maintaining steady blood sugar levels, and strengthening hair and nails. It plays a role in the citric acid cycle, a process in which biochemical energy is created during aerobic respiration.

Studies have shown that vitamin B supplementation including biotin helps improve wound healing. A small placebo-controlled clinical trial involving 30 study participants with periodontitis who underwent access flap surgery were randomly assigned to either a test group given a vitamin-B complex supplement or a placebo. The supplement included 50 µg of biotin. Healing was assessed in all patients at baseline and at one-week, two-week, one-month, three month, and six month intervals. The results reported a positive correlation, indicating that the test-group patients had significantly better clinical attachment levels for both shallow and deep wound sites from the surgery. This suggests that vitamin B, including biotin, used after surgery may offer superior wound-healing capabilities.⁶¹

Iron

It has long been known that iron is essential for healthy skin, mucous membranes, hair, and nails. Iron serves as a cofactor in collagen synthesis and plays pivotal roles in oxygen transport, formation of hemoglobin, break-down of free radicals, oxidation-reduction processes, hydroxylation of collagen precursors, and mitochondrial respiration. Iron deficiencies have been



shown to compromise wound healing via hypoxia and decrease bactericidal effects of leukocytes. For these reasons, iron supplementation is especially recommended for patients with wounds.⁶²

Over recent years there has been some advancement in knowledge about iron in the skin and iron deficiency in cutaneous wound healing. Iron deficiency without inflammation is likely to affect one of the later stages of wound healing such as remodeling. Treating iron deficiency can be a potential therapeutic target in delayed cutaneous wound healing.

Selenium

Selenium boosts the immune system and inhibits cancer cell production, protects the cells from free radical damage, and repairs the DNA of damaged cells.⁶⁴


Selenium is an essential micronutrient and only small amounts of it are necessary for tissue oxygenation and protection against lipid peroxidation. It is involved in one of the main antioxidant defense systems of the body in the form of glutathione peroxidase, which is the main plasma selenoprotein. It consists of four identical subunits, each of which contains one covalently bound selenium atom.

Selenium has strong antioxidant properties. There are suggestions that it may expedite wound healing in burn patients. A prospective, randomized controlled trial investigated the effect of large intravenous doses of trace elements (copper, selenium, and zinc) on patients with major burns and found that cutaneous concentrations of those trace elements were increased, antioxidant status (as measured by normalization of plasma glutathione peroxidase level) was improved, and wound healing was augmented as measured by decreased graft requirements.⁶⁷ The antioxidant properties of selenium have been shown to benefit wound healing.

The beneficial effect of selenium has been demonstrated in the healing process in patients with leg ulcers. It has also been shown that selenium accelerates the healing of experimental skin wounds.⁶⁵ Enhanced wound healing occurs in the presence of the novel selenium compound. This enhancement was more marked in diabetics compared to wild-type mice in a recent study. The decrease in monocyte chemotactic activity, IL-6 expression, and improvements in tissue elasticity and tensile strength, suggest that this selenium compound may aid wound healing.⁶⁶

Bromelain

Bromelain is an anti-inflammatory pineapple enzyme that helps reduce post-operative bruising and swelling, lessen postoperative pain, and accelerate healing.⁶⁸ Diverse biological processes like anti-inflammatory, anti-oedematous, analgesic, anti-thrombotic, and exfoliation are involved in bromelain's therapeutic actions. Even though more research is needed to establish



bromelain's utility as an anti-inflammatory agent in surgical care, literature supports a promising role of bromelain. In Europe, it is approved for oral and topical use, mainly for surgical wounds, inflammation due to trauma and surgery, and debridement of deep burns. Bromelain can be used as an effective health supplement to promote and accelerate wound healing and can be used for pain relief.¹³

L-Arginine

L-Arginine has numerous effects on immune function and wound healing. Metabolically, arginine is a precursor to proline, which is recruited specifically for collagen synthesis. It is also a precursor for ornithine, which is critical for polyamine synthesis and for nitric oxide.⁷⁴ Numerous studies in rodents and humans show that supplemental arginine, administered either orally or parenterally, accelerates wound healing mainly by increasing collagen deposition in wounds. Not only is collagen accumulation increased by arginine supplementation, but peripheral blood lymphocytes show increased mitogenesis and activity as well.⁷⁵ Although arginine improves epithelial reconstitution after intestinal injury, it does not affect the re-epithelialization of skin graft donor sites in patients, whether given orally or parenterally. However, in a randomized study evaluating the effect of different doses of arginine supplementation on stage II-IV pressure ulcers, there was almost a twofold improvement in healing time in the group receiving arginine.⁷⁶ Arginine availability can affect the immune response in injured states and other disease processes, establishing its role as a nutrient. In clinical practice, arginine is included in most parenteral feeding formulas. As a single agent, it is the best-studied component of nutrition, and the weight of evidence suggests that arginine is beneficial to wound healing.⁷⁷

L-Glutamine

Glutamine, also known as L-glutamine, is the most abundant amino acid in the plasma and is a primary metabolic fuel for rapidly proliferating cells.⁷⁸ Glutamine supplementation decreases infectious complications, which is one of the clinical hallmarks of its use of nutrition. Glutamine protects against inflammatory injury by inducing the expression of heat shock proteins, which provide cellular protection in states of inflammation, injury, and stress. Furthermore, glutamine can modulate and preserve gut function, which is compromised in severe stress.

Glutamine, besides being an important metabolic fuel, can also be considered an important nutritional mediator of the inflammatory response.⁷⁹ When evaluating glutamine supplementation in wound healing specifically, numerous randomized trials have provided conflicting results. For example, oral supplementation of glutamine has been studied in treating oral mucositis for pediatric patients who received stem cell transplants. One study comparing glutamine supplementation with glycine supplementation, the control variable, found an overall decreased severity of mucositis and a shorter course of both analgesia and parenteral nutrition

needed.⁸⁰ Another study using a higher dose of enteral supplementation of glutamine did not show any benefit in terms of incidence or severity of mucositis in a population of pediatric oncology patients receiving chemotherapy.


Glutamine is one of twenty amino acids the human body uses for a variety of purposes.⁸¹ Unlike most amino acids and other nutrients, glutamine's importance in our diet fluctuates. Likewise, our nutritional goals should reflect this fluctuating need. This is why glutamine has become a popular dietary supplement, so it can be added to a healthy diet when our bodies require more of it.

L-glutamine doesn't fit precisely into the essential or nonessential categories of amino acids. Nonessential amino acids are the amino acids our bodies can synthesize; essential amino acids are the ones we cannot synthesize and must be consumed in our diet. Instead, glutamine is considered conditionally essential because stress and injury can result in our body needing more than it can synthesize.⁸² Without consuming more glutamine, the normally available levels of glutamine will begin to run out, making the human body less effective at healing itself.⁸³

Glutamine supplementation aids in the healing process. As glutamine is used up during recovery, our bodies scavenge it from other areas of the body. Muscles are a key resource for glutamine, which is why muscle loss often follows major surgery. By adding glutamine to a patient's diet, it can limit muscle loss. Glutamine supplementation also decreases recovery time. By consuming glutamine, patients have been shown to recover faster and experience fewer negative surgery outcomes. Finally, glutamine can provide a much-needed boost to the immune system during recovery. One of the major risks of surgery is that it opens up the body to infection. By increasing the intake of glutamine, patients have been shown to improve their immune system, thus decreasing the chances of infection.⁸⁴

Copper

The earliest recorded application of copper in wounds can be traced to Egyptian papyrus written between 2600 and 2200 BC. Copper is essential for the health of the heart and for making hemoglobin and collagen.⁸⁵ Copper has also potent biocidal properties and has been used as a biocide for centuries by many different civilizations. Both gram-positive and gram-negative bacteria, including antibiotic-resistant bacteria as well as hard-to-kill bacterial spores, fungi, and viruses, are killed when exposed to high copper concentrations. In some cases, they are killed within minutes of exposure to copper or copper compounds.⁸⁶ Consequently, copper biocides have become indispensable. Thousands of tons are used annually, all over the world in agriculture, wood preservation, and antifouling paints.⁸⁷ More recently, copper compounds have been introduced into textiles and solid surfaces for odor and microbial control, including for the



reduction of microbial bioburden in medical institutions. Copper is essential to wound healing, as it promotes angiogenesis and skin formation and stabilization.⁸⁸

Copper is also a catalytic cofactor, which plays an important role in physiological processes, including angiogenesis. This is required for reparative neovascularization and wound healing in response to injury. Copper directly stimulates cell proliferation and migration in cultured endothelial cells.

Zinc


Zinc is a micronutrient that is essential to overall health. It is a cofactor in several intracellular enzymatic reactions to wound healing.⁸⁹ It is also an antioxidant and confers resistance against epithelial apoptosis. It even has significant antibacterial properties. Zinc plays a major role in many biological functions such as growth, respiration, endocrine system function, healthy inflammation response, wound healing, reproduction, and supporting a healthy immune system.⁹¹ There are some suggestions that zinc takes part in the prevention of cancer of the esophagus, bronchi, and prostate. Zinc is abundantly found in beef, bread, wheat germ, soybeans, white beans, and lentils.⁹²

Zinc plays a major role in regulating every phase of the wound healing process, ranging from membrane repair, oxidative stress, coagulation, inflammation and immune defense, tissue re-epithelialization, angiogenesis, to fibrosis and scar formation. Due to the loss of zinc during injury, zinc therapy has been used in wound care to enhance healing in zinc-deficient patients. Topical zinc has been widely used in wound healing for its antioxidant effect, enhancement of healing abilities, and to increase collagen degradation in necrotic wounds. A standard regimen for severe burn care includes regular daily dietary zinc supplementation equivalent to or exceeding 22 mg, which has been shown to help these patients significantly.

Zinc deficiency can negatively affect wound healing and it is an issue clinicians need to consider in the overall care of patients with wounds. Because zinc plays a vital role throughout all wound healing phases, when zinc levels are low in the cellular environment, all four phases of healing are affected. In order to provide the highest quality patient care, the clinician should address any possibility of zinc deficiency and recommend dietary supplementation.

Chlorella

Chlorella vulgaris has a variety of properties that are beneficial to injured organs and tissues. The moniker "great normalizer" refers to the ability of *chlorella vulgaris* to restore various bodily functions to normal levels.⁹³ *Chlorella vulgaris* is thought to act as an anti-inflammatory agent because of its ability to reduce the secretion of cytokines associated with inflammatory activity, such as some types of interleukin (IL) as well as matrix metalloproteinase (MMP), a matrix that damages the tissue.⁹⁴ Some of the activities induced by the administration of *Chlorella vulgaris*



can also be related to the growth and development of fibroblasts.⁹⁵ Fibroblasts play an important role in the process of tissue repair, which is responsible for the preparation of producing protein products that will be used in tissue reconstruction. Therefore, the number of fibroblast cells is one of the parameters used to assess the wound healing process.

Some components of *Chlorella vulgaris* that affect wound healing, especially for wound moisture, are flavonoids and tannins. Flavonoids can stop bleeding in the wound and act as an anti-inflammatory agent that will affect the production of inflammatory cells in the wound healing phase. The presence of flavonoids in ointment can affect changes in the condition of wet wounds to become moist faster. The content of tannin as an astringent can affect the permeability reduction of the mucosa, making the bond between the mucosa strong so that it prevents irritation. Thus, indirectly, tannin affects the changes in each level of humidity. Apart from having an effect on mucosal permeability, tannins can also affect the permeability of the wall or membrane of bacteria so that bacteria shrink and die. This antibacterial property can prevent wound infections.


Saponins contained in *Chlorella vulgaris* can affect the production of collagen in the early stages of tissue repair and stimulate the regeneration of epithelial cells in the skin thereby accelerating the process of wound healing in animals. Phenol compounds play a role in preventing cell damage due to free radicals, thus preventing inflammation. *Chlorella vulgaris* also contains terpenoids, which are useful in reducing inflammatory activity. Several types of sterols extracted from *Chlorella vulgaris* can inhibit certain inflammation of the skin and can prevent prolonged allergies and regenerate skin cells. *Chlorella vulgaris* can support tissue repair and wound healing with its antioxidant and anti-inflammatory properties.

Calendula

Calendula is an herb that can also enhance the wound healing process. It is believed that the herb increases the flow of blood to the wound site, thereby providing the oxygen and nutrients essential to tissue regeneration.⁹⁶ Additionally, with its high amount of flavonoids, this herb can help reduce inflammation, speeding up the stages of healing. These flavonoids also protect against wound infection by fighting off bacteria, viruses, and other harmful foreign invaders. Other uses for calendula include acting as a soothing ointment, wash, or tincture, as it can help provide cooling relief on irritated wounds and reduce inflammation and swelling.⁹⁷

Grape Seed Extract

Grape-seed extract is known to help skin wounds heal faster and prevent scarring.⁹⁸ The extract has been shown to aid wound healing in two ways. Firstly, it helps the body make more of a compound used to regenerate damaged blood vessels. It also increases the number of free



radicals in the wound site. Free radicals help clear potentially pathogenic bacteria from a wound, leading to more optimal wound healing.

Organic Turmeric Powder

For hundreds of years, people around the world have linked turmeric to healing properties and cosmetic benefits.⁹⁹ The bright, yellow-orange spice is related to ginger. It's available as a ground spice or in supplements and other beauty and dermatology products.


Turmeric possesses health benefits primarily because of curcumin, a bioactive component. Curcumin has anti-inflammatory and antioxidant properties. Modern scientific research is just beginning to study the positive impact of turmeric, but many believe it has several beneficial uses for the skin. The curcumin found in turmeric can help wounds heal by decreasing inflammation and oxidation. It also lowers the response of your body to cutaneous wounds.¹⁰⁰ This results in your wounds healing more quickly and effectively. Studies have found that turmeric can positively affect tissue and collagen as well. The journal *Life Sciences* recommends applying curcumin as an optimized formula to best work on skin wounds.¹⁰¹ Overall, turmeric has potential wound healing properties that can support tissue repair.

Hyaluronic Acid

Hyaluronic acid can also aid in wound healing. In the proliferation phase to form granulation tissue, hyaluronic acid allows for the diffusion of nutrients and the elimination of waste products.¹⁰² Hyaluronic acid facilitates the migration and proliferation of fibroblasts and keratinocytes and represents a reservoir of growth factors. This is due to the ability of hyaluronic acid to absorb water, maintain wound moisture, and limit cellular adhesion to extracellular matrix molecules.¹⁰³ The extracellular matrix and fibroblasts maintain a bidirectional interaction. Since fibroblasts participate in the synthesis and remodeling of the extracellular matrix, this modulates the activity of these cells. In addition, it has been demonstrated that degradation products of hyaluronic acid are proangiogenic.¹⁰⁴ Subsequent remodeling of granulation tissue involves lowering hyaluronic levels and increasing the proportion of other proteoglycans and collagen to improve tissue resistance and elasticity. The properties of hyaluronic acid can promote adequate wound healing.

Arnica montana

Arnica montana is a plant that is native to the mountainous regions of Europe and southern Russia.¹⁰⁵ The flowers and leaves of this plant have many traditional medicinal uses. *Arnica montana*'s rootlets contain derivatives of thymol, which has anti-inflammatory effects. It promotes effective vasodilatation of subcutaneous blood capillaries and assists normal healing processes by facilitating the transport of blood and fluid accumulations through dilatation of



subcutaneous blood vessels. In a study, it was proven to be more effective than diclofenac for wound healing after foot surgery.¹⁰⁶ Arnica has been recommended by many homeopathic practitioners for treating injuries on account of its alleged ability to control bruising, reduce swelling, and promote recovery for many years. It is popular with patients undergoing surgery, potentially reducing postoperative complications. However, there is still more research to be conducted to prove its efficacy.

Probiotics (Lactobacillus and Saccharomyces)

Skin homeostasis is regulated by microorganisms called skin microbiota. This microbiota acts on keratinocytes and on their cytokine release, ensuring the skin health is in good condition. The alteration of skin homeostasis occurs in the presence of wound infection and during certain inflammatory diseases such as acne or psoriasis. It has been shown that specific lactobacilli strains have a beneficial role in the wound healing process, in defense against the inflammatory processes that affect skin, and in resistance to infections by interfering with pathogens.¹¹


In a recent study, researchers used *Lactobacillus reuteri* extracts to determine whether bacterial extracts could regulate the functions of gingiva mesenchymal stem cells (GMSCs) and promote wound healing. The concluding results indicated an acceleration in the process of wound healing.^{107, 108} The results of a clinical study on pediatric burn patients in the *Journal of Burn Care & Research* concluded that those treated with probiotics healed at a faster rate than those treated with a placebo. The study included 20 children, half of whom received a probiotic and half of whom were treated with a placebo. The treatment was administered daily, starting 10 days after their initial burn and lasting until their wounds were closed. These patients showed significant wound healing recovery.³

Conclusion

Nutrition plays an essential role in wound healing, scar reduction, and surgery recovery. Wound healing, scar formation, and surgery recovery implicate a well-orchestrated complex of events such as coagulation, inflammation, and remodeling. In each of these events, macronutrients and micronutrients are involved in the intricate processes. Lacking macronutrients such as protein can demote wound healing and is needed to help build and maintain new tissues.

Micronutrients such as vitamin A, B, C, and D, zinc, and iron are essential for the inflammatory process and the synthesis of collagen. Improving a patient's nutritional status can help the body to supply the necessary building blocks and cellular response for healing to take place. Given the evidence, optimal nutrition can enhance wound healing, scar reduction, and lead to a faster surgery recovery. The importance of eating well in order to heal well has been firmly established.

Nutritional requirements, especially when the body is in need of more during recovery, can not always be met through diet alone. WoundVite™ is an all-in-one effective oral supplement formula



for wound care, scar reduction, post-surgical healing, and tissue repair. Each capsule is formulated with 21 different pharmaceutical-grade vitamins, minerals, and herbs that have all been extensively researched through clinical studies. These high quality ingredients work together to help with wound healing, scar reduction, and post surgery recovery. Not only can this formulation aid in optimal wound recovery, but it can also correct any nutritional deficiencies. WoundVite™ can be the missing step in providing optimal wound care management.

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