Nutritional Aspects of Healing a Diabetic Foot Wound

This is an essential but often overlooked aspect of wound healing.

By Kenneth B. Rehm, DPM

In a patient who has diabetes, healing a foot ulcer, just like healing a problem in any other part of the body, requires incorporating basic principles and a systematic approach that must include medical nutrition therapy. In general, the clinical goals of medical nutrition therapy in a diabetic patient are to:

1. Achieve and maintain glycemic control by balancing food intake with insulin (exogenous or endogenous) or oral glucose-lowering medications and activity levels.

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Objectives

After reading this continuing education article, the podiatric physician should be able to do the following:

1) Be familiar with the clinical goals of medical nutritional therapy.

2) Identify the eight principles of healing a diabetic foot wound.

3) Be able to describe the basic principles of nutritional management of patients with diabetic foot wounds.

4) Describe a comprehensive nutritional assessment.

5) Be able to relate the phases of wound healing with basic nutritional needs.

6) To discuss the role of calories and weight loss in diabetic foot wound healing.

7) Understand the roles of proteins, fats, carbohydrates, vitamins, minerals and trace elements in diabetic foot wound healing.

8) To delineate the appropriate blood tests needed to assess nutritional status in a patient with a diabetic foot wound.

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Following this article, an answer sheet and full set of instructions are provided (p. 210).—Editor
Medical nutrition therapy is part of the systematic approach to healing a diabetic foot wound which incorporates the following basic principles:

1. There must be adequate circulation to the wound site.
2. A wound must be kept clean and free from contamination.
3. Necrotic tissue must be eliminated or reduced to a minimum.
4. A wound must be free from infection.
5. Dermatologic disease must be controlled or eliminated.
6. Shearing, friction and direct pressure on a wound must be kept at a minimum.
7. The external wound healing environment must be controlled and kept free from excess dryness and moisture.
8. The wound host must be nutritionally, metabolically and medically stable.

It is the nutritional aspects that are to be discussed in this paper.

The ability of a patient with a diabetic foot ulcer to heal is affected by the baseline nutritional status and pre-existing nutritional deficiencies. A resultant suboptimal outcome and poor healing prognosis is related to increased susceptibility to the development of foot ulcers, increased time needed for wound healing, increased likelihood for reoccurrence, decreased tensile strength of a closed wound, increased susceptibility to infection and post-surgical complications in general. Providers of care for diabetic foot wounds should closely scrutinize the nutritional status of these patients, and consider poor nutritional status a major causal element, especially in cases where the wound is not healing and all of the other factors for appropriate wound healing are in place. Basic principles of nutritional management of patients with diabetic foot wounds are the following: correction of inappropriate appetite, swallowing, as well as chewing and dentition abnormalities, control of serum glucose, hyperlipidemia, hypertension, metabolic status, appropriate supplementation of vitamins and trace minerals, and ascertaining and maintaining proper dietary requirements. Before these basic principles of nutritional management are implemented, proper nutritional assessment and its components must be accomplished.

A comprehensive nutritional assessment evaluates macro- and micronutrient intake, co-morbidities that could affect the actual ingestion of nutrients and/or the assimilation of nutrients, medications that affect wound healing and/or serum glucose levels, and the overall medical, nutritional and metabolic status of the patient. An optimal assessment should include relevant clinical and biochemical data, including the following blood tests: complete blood count with a differential, glycosylated hemoglobin levels, hematocrit, hemoglobin, lipid levels, blood urea nitrogen levels, serum creatinine, albumin, prealbumin, sodium and potassium levels, total protein and transferrin levels. Urine tests include quantitative values for protein, urine glucose and urine acetone. Blood

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pressure readings are important.

Determining the dietary prescription, restrictions, and level of compliance is essential information to be able to create proper nutritional status. It should be noted that poor nutritional status can be due to a poor appetite, a metabolic problem, or inability to digest or swallow appropriately. A close evaluation of food intake vs. caloric requirements should be performed, paying close attention to proteins, fats, carbohydrates, key vitamins, folic acid, and key minerals, trace elements and micronutrients. Because of all of these factors, it is imperative that a registered dietitian be involved in the assessment process.

Healing Phases

With the nutritional assessment made, the correction or prevention of malnutrition is critical in optimizing wound healing. Nutritional status is the reserve from which the patient will draw upon to close the skin defect. With the other principles of wound healing in place, if the patient is well nourished, and not challenged again, the wound is likely to close. If the patient is malnourished at the start of the healing process, the wound cannot be expected to close in a timely manner. The nutritional substrate is essential for tissue formation because nutrients are important to the appropriate completion of the four phases of wound healing.

These four phases are separate and overlapping. They are:

1. The hemostatic phase. This is the phase where platelet aggregation begins the process of blood coagulation in the wound.
2. The inflammatory phase. This phase is characterized by macrophage proliferation and their ingestion of bacteria and debris.
3. The connective tissue phase. This is when fibrous tissue and collagen forms to create a lattice work that supports new blood vessels. The wound now begins to contract and close.
4. The epithelial phase. Epithelial cells now begin to cover the surface of the wound until maturation occurs.

In order for these four phases of wound healing to progress, certain basic nutritional requirements must be met:
1. Proteins are required for tissue repair
2. Glucose is required for energy
3. Lipids (fats) are required for cellular integrity with pre-existing compromised nutritional status.

Marasmus is a type of undernutrition associated with chronic caloric deprivation. Depletion of somatic proteins and subcutaneous fat causes a decrease in body weight. Significant marasmus is indicated by a weight that is less than 85% of a person’s ideal weight. Weight loss that is less than 10% of a person’s usual weight is considered mild, moderate if it ranges from 10% to 20%, and severe if the weight loss is 20% or greater. Mild to moderate weight loss may, in fact, improve serum glucose levels even if desired weight is not reached. The problem is that without being able to bear weight, as is the case in many wound patients, it is difficult to achieve weight loss. In fact, it is often necessary to avoid purposeful weight reduction until the foot wound is closed.

Protein Requirements

In detailing the basic nutritional requirements, the first consideration is the protein and calorie requirements. The provision of sufficient calories is a priority so that protein will be spared for its critical roles in the stimulation of fibrin formation, cell multiplication, connective tissue formation, collagen formation and deposition, increasing of enzyme activity, diminishing catabolism, enhancing immunity and improving overall wound healing. Protein deficiency suppresses the immune response, inhibits angiogenesis, decreases fibroblast formation and remodeling of collagen and impairs overall wound healing.

A review of the components we’ve identified in the four phases of wound healing reveals that skin formation, white blood cell activity, immune function and collagen formation are all protein-based. The presence of all essential amino acids is required for protein synthesis. All aspects of wound healing are delayed under conditions of protein deficiency. Therefore, adequate protein intake is absolutely essential for wound healing.

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stress. It is usually associated with a catabolic stress situation without nutritional support. It is important to differentiate the type of protein-calorie malnutrition because each has a different effect on wound healing. Clinical studies have shown that any protein-calorie malnutrition leads to compromised wound healing and a greater risk for developing pressure-related ulcerations.

Various diseases can lead to all forms of protein-calorie malnutrition. Common diseases linked with this form of malnutrition include:

- cancer
- chronic illness
- protein loss in the gastrointestinal tract
- anorexia and other eating disorders
- multiple traumas
- liver disease
- obesity
- pancreatitis
- burns over 30% or more of your body

Overt signs of malnutrition may exist and include severe wasting, extreme weight loss, weakened resistance to infection, being unable to think clearly, or hair becoming brittle or falling out. In addition, the skin may be dry or yellowish, muscles may feel weak, and fainting spells may occur. In younger women, menstrual periods may stop.

Protein-calorie malnutrition poses a severe danger to the patient because it can occur very rapidly and without overt signs of malnutrition. Therefore it is important to appropriately monitor the nutritional status by examining serum levels of pre-albumin, albumin, total protein, and transferrin levels and by performing a CBC with a differential, hematocrit

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**Protein-Calorie Malnutrition**

There are basically three types of protein-calorie malnutrition: (1) **Marasmus** involves decreased calories and protein. It is usually associated with prolonged starvation, anorexia, chronic illness and the elderly. It takes months to years to develop. (2) **Kwashiorkor** involves decreased protein intake alone and is usually a result of fad diets, liquid diets, or long-term dextrose-containing IV fluid supplementation with nothing by mouth. It takes weeks to months to develop. (3) **Combined** is a result of decreased calories, protein intake and increased stress.

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**PROTEIN-CALORIE MALNUTRITION**

<table>
<thead>
<tr>
<th>Nutritional setting</th>
<th>Marasmus</th>
<th>Kwashiorkor</th>
<th>Combined</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased calories</td>
<td>Decreased protein intake</td>
<td>Decreased protein intake</td>
<td>Decreased calories, decreased protein intake and increased stress</td>
</tr>
<tr>
<td>and protein intake</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical setting</th>
<th>Prolonged starvation, anorexia, chronic illness, elderly</th>
<th>Fad diets, liquid diets, long-term dextrose-containing IV fluid supplementation with nothing by mouth</th>
<th>Catabolic stress without nutritional support</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time course to</td>
<td>Months to years</td>
<td>Weeks to months</td>
<td>Days to weeks</td>
</tr>
<tr>
<td>develop</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>Starved appearance</th>
<th>May look well-nourished or obese. Edema, ascites may be present. Normal anthropometrics.</th>
<th>Moderately to severely starved appearance Decreased anthropometrics</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Laboratory findings</th>
<th>Normal visceral proteins</th>
<th>Decreased visceral proteins, Decreased lymphocyte count, Anergic</th>
<th>Decreased immune function values Decreased visceral proteins</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Clinical course</th>
<th>Reasonably preserved and responsive to short-term stress</th>
<th>Diminished wound healing, Diminished immunocompetence, Increased infections, Increased overall complications</th>
<th>Diminished wound healing, Increased overall complications and slower recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality rate</td>
<td>Low unless complications of underlying disease process</td>
<td>High</td>
<td>High</td>
</tr>
</tbody>
</table>
and a hemoglobin.

The pre-albumin test measures a protein that reflects nutritional status. Pre-albumin is most often used to help diagnose protein-calorie malnutrition. In this condition, which can affect more than 30% of physiologically stressed or wounded patients, the body breaks down muscle, protein, and body fat. This type of malnutrition can lead to complications and even death if not treated.

The test also is used to monitor changes in patients who are receiving parenteral nutrition (nutrition from outside of the gastrointestinal tract, such as nutrients given through intravenous treatment). The test also is used to monitor changes in nutritional status for patients who are receiving hemodialysis.

Depending on the exact levels, if pre-albumin is low, minor nutritional deficiencies can be the only problem or if pre-albumin is very low, then protein-calorie malnutrition has to be considered.

Conditions that may lead to lower levels of pre-albumin are the following:

- Severe or chronic illness, such as cancer
- Hyperthyroidism
- Liver disease
- Serious infections
- Digestive disorders
- Inflammatory disorders

When inflammation and malnutrition are both present, pre-albumin levels fall very far, very quickly. Higher levels of pre-albumin are common in patients with:

- High-dose corticosteroid therapy
- Hyperactive adrenal glands
- High-dose non-steroidal anti-inflammatory medications
- Hodgkin’s disease

If a patient is in renal failure, pre-albumin results may be falsely higher than they actually are.

Inflammation can interfere with the results of your pre-albumin test, causing it to be lower than it would be. Certain drugs can also lower your pre-albumin level, including amiodarone, estrogens, and oral contraceptives (birth control pills). Drugs that can cause your pre-albumin level to rise in your blood are anabolic steroids, androgens, and prednisolone.

Recent research has shown that the pre-albumin test can predict poor outcomes for hemodialysis patients. A low initial reading (baseline level) of pre-albumin predicts that a patient may have problems, and steadily dropping pre-albumin values are associated with low survival.

Pre-albumin is the best marker of malnutrition because it has a short serum half-life, it is less affected by liver disease than other proteins and is not affected by hydrations status or vitamin deficiency (except zinc).

Serum albumin levels measure visceral protein levels and therefore the body’s ability to manufacture protein. It is an adequate indicator of this ability for stable patients with a chronic medical condition, such as diabetes. If the patient is being evaluated during an acute illness, the urinary creatinine height index should be used. Serum albumin levels are often used to test for liver or kidney problems, or to learn if there is a lack of amino acid absorption. Because turnover time for albumin is 14 days, it is less sensitive than other measures. For instance, pre-albumin changes more quickly, making it more useful for detecting changes in short-term nutritional status than albumin.

**Albumin**

Albumin is the major protein synthesized by the liver. It maintains plasma oncotic pressure and transports nutrients in the blood stream. Low albumin levels may lead to edema in the lower extremities, skin breakdown and open wounds and increased infection, as well as increased morbidity and mortality. Decreased albumin levels correlate with poor clinical outcomes, increased length of hospital stay, increased risk for complications and death. It should be noted that hypoalbuminemia is an excellent marker for the stress response, but is considered to be a poor marker for overall nutritional status even though albumin levels are often used to monitor nutritional status. According to a recent study, those patients with diabetes and foot ulcers had significantly higher levels of fibrinogen and C-reactive protein. (This is a test that measures the concentration of a special type of protein in serum, produced by the liver, which is only present during episodes of acute inflammation. The most important role of CRP is its interaction with the complement system, which is one of the body’s immunologic defense mechanisms.) Diabetics also had lower albumin levels when compared to two groups of control patients, those with diabetes and no foot ulcers and those with neither diabetes nor foot ulcers. The decreased albumin levels results from a shift in the hepatic synthesis of proteins that result in an increase in acute-phase proteins and decreased production of homeostatic proteins. It is important to note that vascular permeability is increased because of this shift and proteins escape from the vascular space.

A common mistake made by clinicians in treating patients with diabetes and foot ulcers is to interpret hypoalbuminemia as a sign of malnutrition. When hypoalbuminemia shows up, calories are often increased significantly, leading to hyperglycemia and weight gain, both of which interfere with wound healing.

Total protein measurements can reflect nutritional status. In addition, low total protein levels can suggest a liver disorder, a kidney disorder, or a disorder in which protein is not digested or absorbed properly. More specific tests, such as albumin and liver enzyme tests, must be performed to identify which protein fraction is abnormal, so that a specific diagnosis can be made. High total protein levels can indicate dehydration or some types of cancer (e.g., multiple myeloma) in which an abnormal protein is accumulated, and further tests must be performed.

**Total iron binding capacity (TIBC)** is an indirect measurement of transferrin, a protein that binds and transports iron. It quantifies transferrin in terms of the amount of iron it can bind and is reported as percent saturation. Transferrin levels are generally depressed in patients who are malnourished or who have chronic disease states; however, it may be normal in many patients who are iron deficient.

Patients who are malnourished or protein-depleted benefit by early
It should be noted, however, that most wound healing patients, especially diabetics, require an increase in protein in their diet in conjunction with adequate calories. Research suggests that increasing protein intake to 20% or more of total calories may result in improved nitrogen balance in malnourished patients. Obtaining positive nitrogen balance is important to counter the effects of nitrogen losses, common in diabetics and patients under physiologic stress, and maximize the retention of nitrogen. At least 1 1/2-2 grams of protein and 25-30 calories per Kg. of body weight is recommended. For severely stressed or injured patients, as in burn patients, up to 2 1/2 grams of protein and 30-35 calories per Kg. of body weight is recommended. Some evidence exists that protein supplements (T) improve the healing process in any physiologically or metabolically stressed individual. This has a positive impact on all phases of wound healing, especially the critical initial phases. It should be noted that every patient’s needs are different. Protein requirements vary according to

**NUTRITIONAL ASSESSMENT**

**NORMAL REFERENCE LABORATORY VALUES**

<table>
<thead>
<tr>
<th>Determination Blood, Plasma, or Serum Values</th>
<th>Reference Range</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol</td>
<td>120-220 mg/100 mL (serum)</td>
<td>Fasting</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>40-150 mg/100 mL (serum)</td>
<td>Fasting</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.6-1.5 mg/100 mL (serum)</td>
<td>Fasting</td>
</tr>
<tr>
<td>Glucose</td>
<td>70-100 mg/100 mL (plasma)</td>
<td>Fasting</td>
</tr>
<tr>
<td>Glucose (1 hr postprandial)</td>
<td>180 mg/dL (plasma)</td>
<td>Values above this number are considered diagnostic for diabetes and require confirmation by other determinations.</td>
</tr>
<tr>
<td>Hemoglobin A1c</td>
<td>3.8-6.4% (plasma)</td>
<td></td>
</tr>
<tr>
<td>Potassium</td>
<td>3.5-5.0 mEq/L (serum)</td>
<td></td>
</tr>
<tr>
<td>Hematocrit</td>
<td>Male: 45-52% Female: 37-48%</td>
<td></td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>Male: 14-18 g/dl Female: 12-16 g/dl</td>
<td></td>
</tr>
<tr>
<td>Ferritin-iron deficiency</td>
<td>0-12 ng/mL 13-20 borderline (serum)</td>
<td></td>
</tr>
<tr>
<td>Prealbumin</td>
<td>16 to 35 mg/dl (serum)</td>
<td>Sensitive measure of nutritional status</td>
</tr>
<tr>
<td>Albumin</td>
<td>3.5-5.0 g/100 mL (serum)</td>
<td></td>
</tr>
<tr>
<td>Blood Urea Nitrogen</td>
<td>8-25 mg/100 mL (serum)</td>
<td></td>
</tr>
<tr>
<td>Urine Tests</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acetone plus acetoacetate</td>
<td>Quantitative 0</td>
<td></td>
</tr>
<tr>
<td>Protein</td>
<td>Quantitative &lt;150 mg/24 h May require more information in diabetes</td>
<td></td>
</tr>
<tr>
<td>Glucose</td>
<td>Quantitative 0</td>
<td>24 hour or other timed specimen</td>
</tr>
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</table>
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protein and 35 calories per Kg. of body weight may be needed. If the patient has nephropathy, a range of 1.0 to 1.5 gm of protein per Kg. of body weight is recommended. If this cannot be accomplished with increasing the amount of food a person eats, enteral formulas can be an alternative.

A standard enteral formula has 40 grams of protein per 1000 calories. The high-protein formulation, which is better equipped to meet the requirements of wound healing patients, has 60 grams of protein per 1000 calories. Studies suggest that for those patients who need a dietary alternative, high protein formulations have been recommended. This is because they have lower calorie-to-nitrogen ratios and therefore are associated with increased nitrogen retention and balance, improved serum protein levels and improved immunological function. Clinically, this leads to reduction in the size of large wounds and improved healing of smaller wounds. It is important to note that exceeding protein requirements will not cause the wound to heal faster.

An elevated BUN in elderly patients on a high-protein diet should not be of concern given that the patient does not have a pre-existing renal condition, has normal creatinine levels and the state of hydration on physical exam is normal. Urea is not a toxic molecule and the buildup of urea in this patient is of no consequence; and in a patient with a wound, the priority is healing the wound and not a normal BUN. The risk of underfeeding and sub-optimal protein consumption is non-healing and non-function. In patients who are adequately fed or fed slightly above what’s needed, elevated serum urea is a result of an extra amino acid being changed to glucose.

Hematocrit and hemoglobin values can be used as a gross indicator of iron status in individuals with diabetes. Low values are generally associated with chronic blood loss, heavy menstrual bleeding, or gastrointestinal bleeding. Diets low in saturated fat and cholesterol that are routinely prescribed for persons with diabetes often contain inadequate supplies of foods high in heme iron. The need for an iron supplement should be assessed.

A CBC with a differential will give an indication as to if there is a high white cell count, common in malnutrition and in infections. Protein intake should be monitored in clients at risk for renal disease. Modification of protein intake should become a decision reached by the physician, dietician and the patient.

There is suggestive evidence that several amino acids, particularly arginine and glutamine, appear to promote wound repair. Arginine’s effect is linked to enhanced wound collagen synthesis and pituitary hormone secretion; glutamine improves gut mucosal repair and serves as fuel for the immunocytes. No improvement in wound healing has been demonstrated using high-dose supplements of branched chain amino acid infusions.

Carbohydrate Requirements

The role of carbohydrates, as is the case with fats, is less well-defined than protein’s role. It is known, however, that the role of carbohydrates and fats is to provide the energy needed for cell proliferation that occurs in all phases of wound healing. Leucocytes, which are white blood cells that perform phagocytosis, utilize glucose as their primary fuel. Fibroblast proliferation, the key to collagen formation, also depends on glucose as their primary source of energy. It is clear that an abnormality in glucose metabolism would be expected to have an effect on these functions and therefore wound healing.

Fat Requirements

Fat in the diet is an absolute necessity for wound healing in a diabetic. However, because granulation tissue is an obligate glucose consumer, it follows that adherence to a high-carbohydrate diet can be of benefit. Some evidence exists in animal models that low-fat diets may be more beneficial to wound healing than an over-all higher fat intake. Reduction in total fat intake, especially saturated fats, is therefore recommended. Less than 30% of the calories consumed should be from fat and less than 10% should be from saturated fats. Fats, however, do help provide the fuel for all the phases of wound care as well as provide fatty acids. The precise role of fatty acids in wound healing is unknown. However, they are a key ingredient of triglycerides and phospholipids that are major components of cell membranes. Also, unsaturated fatty acids are precursors to prostaglandins and other regulators of the immune and inflammatory processes. Therefore, it is reasonable to assume that a deficiency in fatty acids likely results in sub-optimal wound healing.

A blend of fats has been shown to be more beneficial in wound healing than fats that come from a single source; and because various fats have different benefits than others, a fat blend can play an advantageous role in the healing of wounds where a high metabolic or physiologic stress situation exists or in wound healing.

For this reason, a lipid profile including essential fatty acids, especially omega 3 fatty acids, is critical. Why “essential?” Omega-3’s (and omega-6’s) are termed essential fatty acids (EFA’s) because they are critical for good health; and a deficiency in them has been shown to inhibit tissue regeneration. However, the body cannot make them on its own. For this reason, they must be obtained from food, thus making outside sources of these fats essential.

Although the body needs both omega-3’s and omega-6’s to thrive, most people consume far more 6’s than 3’s. Hardly a day goes by, however, without reports of another health benefit associated with omega-3’s. For this reason, many experts recommend consuming a better balance between these two EFA’s.

There are three key omega-3 fatty acids which include eicosapentaenoic acid (EPA) and docosahexanoic acid (DHA), both found primarily in oily cold-water fish such as tuna, salmon, and mackerel. Aside from fresh seaweed, a staple of many cultures, plant foods rarely contain EPA or DHA.

However, a third omega-3, called alpha-linolenic acid (ALA), is found primarily in dark green leafy vegetables, flaxseed and canola oil. Although ALA has different effects on the body than EPA and DHA do, the body has enzymes that can convert ALA to EPA. All three are important

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It is needed for the hydroxylation of lysine and proline, an essential step in collagen synthesis, as well as cross-linking. Wounds are metabolically more active than healthy connective tissue; therefore, increased concentrations of vitamin C are needed to create and maintain wound integrity. Studies suggest that pressure ulcer patients supplemented with very high doses of vitamin C had reduced pressure sore areas when compared with patients who had no vitamin C supplementation. (T). A vitamin C deficiency will cause the following complications:

1. Increased capillary fragility
2. Delayed wound healing
3. Decreased tensile strength of wounds and poor scar formation

These three factors are associated with a more common occurrence of all types of wounds as well as a higher incidence of wounds re-opening and reoccurring.

Vitamin A

Vitamin A is a fat-soluble vitamin that occurs in two forms in nature. It is found in its true form (also called retinol) in animal foods such as fish oils and liver. The body readily uses this form.

Vitamin A can be found in vegetables in the form of beta-carotene or provitamin A. This form is found in plants and is the precursor of the actual vitamin. Beta-carotene has to be converted in the body in order to be used by it. Fat and bile are needed for the conversion.

The liver regulates the blood level of vitamin A. It needs a protein carrier to be transported throughout the body. An adequate protein and fat intake is required for a good absorption of vitamin A.

Vitamin A is an anti-oxidant, a compound that may protect against disease by neutralizing unstable oxygen molecules, called free radicals, within the body. This vitamin is involved in cellular growth, moderates cell differentiation and reproduction as well as reverses the inhibitory effects on growth and wound healing by corticosteroids. It also maintains the health of the skin and surface tissues, especially those with mucous linings, an important factor in wound healing and prevention of infection. Vitamin A enhances tissue regeneration by aiding in glycoprotein synthesis. It is also a co-factor for collagen synthesis and cross-linkage. Therefore, even though it is somewhat pro-inflammatory, Vitamin A is still needed in wound healing primarily for:

1. Collagen formation
2. Epithelial integrity
3. Immune function

Vitamin A deficiency may decrease epithelialization, collagen synthesis, production of macrophages, and overall resistance to infection. Beta-Carotene, improves serum retinol levels and enhances immune function.

The B Vitamins

The B Vitamins also play a crucial role in wound healing. Generally, they assist in white blood cell function and aid the body in resisting infection.

Thiamine, Vitamin B₁, is important in collagen formation and is a cofactor in collagen cross-linking. Vitamin B₁ is found in Brewer’s yeast, unrefined cereal grains, organ meats, pork, legumes, nuts and seeds. A deficiency has been found to be associated with peripheral neuropathy.

Pantothenic Acid, Vitamin B₅, is a component of the coenzyme A molecule as well as being part of the carrier proteins involved in fatty acid metabolism. It helps release energy from fat, carbohydrate, and ketogenic amino acids. It is essential for the functioning of fibroblasts, the collagen-producing cells. A deficiency is associated with poor immune function, compromised wound healing and diminished graft take.

Vitamin B₂ is a co-factor in collagen cross-linking. It is found in broccoli, spinach, asparagus, meat, poultry, fish, yeast, egg whites, dairy products and fortified grain products.

Vitamin B₃ is a co-enzyme that stimulates wound healing and assists in activating protein synthesis. It is found in chicken, fish, kidney, liver, bananas, eggs, soy beans, oats, peanuts and walnuts.

Vitamin B₁₂ is a co-enzyme for protein and DNA synthesis and also stimulates wound healing and helps activate protein synthesis. It is found in meat, fish, poultry and eggs.

Folic Acid (Vitamin B₉) is needed for the metabolism of amino acids and in nucleic acid synthesis and thus for...
Nutrition...

the manufacturing of DNA. In wound healing, this translates to being a key factor in resisting infection.

Vitamins E & K

Vitamin E has antioxidant properties that promote cell membrane integrity. Supplementation has been shown in clinical studies to accelerate the healing of chronic stasis ulcers. It is found in wheat and rice germ, vegetable oil, dark green leafy vegetables, nuts and legumes.

Vitamin K is essential for coagulation, a necessary prerequisite for wound healing and is found in green leafy vegetables, dairy products, meat, eggs, cereals and fruit.

Trace Elements

Trace elements and micronutrients are lost through wound exudates and must be replaced for proper wound healing to occur. These include zinc, calcium, copper, iron, magnesium, chromium, phosphorus and selenium. Zinc is essential for wound healing. Similar to Vitamin C, zinc is not stored in significant amounts. It is found commonly in oysters, dark meat turkey, liver, lima beans and pork. Zinc is an essential trace element and important in wound healing due to the following:

1. It is a co-factor in about one hundred enzymatic reactions
2. It is essential for the transcription of RNA
3. It promotes protein synthesis, collagen formation and cellular replication
4. It mobilizes retinol-binding protein and albumin
5. It is essential in the synthesis of albumin
6. It plays a key role in tissue repair

Deficiency of zinc may occur suddenly and quickly, especially in patients that are medically, metabolically and/or physiologically compromised. Serum zinc may already be low in wound patients as a result of their being malnourished. When zinc is deficient, collagen synthesis and tensile strength of the wound is diminished and there are abnormalities in neutrophil and lymphocyte function. The end result is an increased risk for infection and delayed wound healing. Generally, if there is a zinc deficit, a wound will not heal.

Calcium, essential for collagen synthesis, is required for both the remodeling process and the degradation of collagen through the action of collagenases. Calcium is found in dairy products, sardines, oysters, kale, greens and tofu.

Copper promotes the cross-linking reactions of collagen and elastin synthesis. It also is involved in free radical elimination. These are critical factors in wound healing. Also, copper is required for the maintenance and repair of bones. Supplementation has been shown to potentially increase the rate of healing of bone fractures.

Copper is found in whole grain breads and cereals, shellfish, organ meats, poultry, dried peas and beans, and dark leafy vegetables. A copper deficiency can show up as impaired glucose tolerance and/or anemia.

Iron is necessary for the hydroxylation of lysine and proline in collagen synthesis and is needed to transport oxygen to the wound bed. Iron deficiency results in tissue hypoxia and therefore interferes with wound healing. If the deficiency is prolonged, anemia could develop, which further interferes with the wound healing process. Iron is plentiful in egg yolk, red meats, dark green leafy vegetables, enriched breads and cereals, legumes and dried fruits.

Magnesium is a co-factor for enzymes involved in protein and collagen synthesis. Low levels play a role in carbohydrate intolerance and resistance to insulin. Deficiency is rare. Magnesium is found in nuts, legumes, unmilled grains, green vegetables and bananas.

Chromium potentiates the action of insulin and therefore interplays with glucose, protein, and lipid metabolism. A chromium deficiency can lead to impaired glucose and amino acid utilization, increased plasma LDL-cholesterol levels, and peripheral neuropathy. Carbohydrate intolerance and insulin resistance is related to chromium deficiency, which is rare. To date, the only chromium deficiency reported has been in patients receiving parenteral nutrition without adequate chromium replacement.

Phosphorus is a critically important element in every cell. A component of membrane phospholipids, it influences affinity for oxygen, thus affecting tissue oxygenation. It also is involved in the metabolism of carbohydrates, protein and fat, and is essential for the maintenance of acid-base balance and required for normal nerve and muscle function. It is an essential component of many enzyme systems and many hormones are dependent on phosphorylation. Milk is an excellent source of phosphorus.

Selenium is a necessary part of collagen synthesis, as it protects the cell membrane lipids from oxidant damage. Selenium is found in seafood, kidney, liver, meats and grains.

Other Therapeutic Modalities

Pharmacologic modulation of cytokines, prostaglandins and the use of anabolic agents such as hormones and growth factors may prove to further enhance wound healing. The use of growth hormone is the best studied to date, but remains controversial. Recombinant growth hormone has been found to support enhanced wound healing, although there is evidence of increased infectious morbidity and mortality in critical care and burn patients that have used growth hormone. Alpha-lipoic acid is being researched as an antioxidant potential with its effect on glycemic control.

Malabsorption/Maldigestion

The condition of malabsorption (or maldigestion) has to be discussed as it can create a state of malnutrition. Malabsorption can be defined as impaired absorption of fat, carbohydrates, protein, vitamins, electrolytes, minerals, or water. Clinical manifestations include unexplained weight loss, steatoarrhea, diarrhea, anemia, tetany, bone pain and pathologic fractures, bleeding, dermatitis, neuropathy, glossitis, and edema. There are many tests available for determining the type and extent of the malabsorption problem.

The co-morbidities of diabetes, which may potentiate malabsorption of nutrients or accelerate their losses include gluten-sensitive or diabetic enteropathy with bacterial overgrowth, previous gastric surgery, large gaping wounds, Crohn’s disease, diverticular disease, radiation...
enteritis, enteric fistulas, HIV, any pancreatic insufficiency, short bowel syndrome, or prolonged use of total parenteral nutrition, where deficiencies of magnesium and/or chromium may become evident. These diseases may be associated with diarrhea which can precipitate or exacerbate the malabsorption. The patient with enteropathy complicated by bacterial overgrowth is at risk for vitamin B12 and folate deficiencies because the small bowel is unable to incorporate these vitamins. Gastric bypass surgery for obesity or a partial gastrectomy for peptic ulcer disease may increase a patient’s risk for vitamin B12, calcium and/or iron deficiencies. Short bowel syndrome with resection of any portion of the terminal ileum increases the likelihood of deficiency of any of the fat-soluble vitamins. Large gaping wounds can be a source of Vitamin C and/or zinc deficiency.

Knowledge of the patient’s medical history and selection of an appropriate supplement or enteral product may help diminish the effects of the malabsorption problem. However, depending upon the extent of the disease, parenteral nutrition may even be necessary in selected patients. Formulations composed of MCT’s (medium chain triglycerides) may control the diarrhea and other complications associated with malabsorption.

Medications the patient is taking can affect wound healing and/or control of glucose levels. Corticosteroids often inhibit wound healing by interfering with connective tissue formation, collagen synthesis, and wound retraction. Non-steroidal anti-inflammatory medication improves wound strength but may adversely affect the rate of wound re-infection due to its effect on a patient’s immunity. Cyclosporins, sympathomimetics, and corticosteroids may contribute to poor glycemic control. It is important to investigate all medications and supplements that the patient is taking because of the profound effect that they may have.

Control of Serum Glucose Levels

Glycemic control is an essential component to nutritional therapy as it applies to healing a wound in a diabetic patient, especially when planning an operative procedure. Poorly controlled diabetes contributes to poor wound healing and has deleterious effects on outcomes, including skeletal, neural, smooth muscle and immune dysfunction. Factors that may precipitate hyperglycemia, such as infection, overfeeding, volume depletion, medications, and inadequate insulin or oral medications, should be quickly addressed. Hypoglycemia can be harmful to the healing process as well. Gastroparesis, hepatitis, sepsis associated with nephropathy, discontinuation of nutritional support, resolution of the stress response, or weaning from steroid therapy can all contribute to a hypoglycemic response. Maintaining glucose levels between 100 and 150 mg/dl is a reasonable goal.

It is interesting to note that poor control of postoperative hyperglycemia in a recent study predicted the likelihood of serious infection. Patients with blood sugar levels over 220 mg/dl on the first day following surgery had a 24.6% incidence of serious infection, compared with 4.2% in patients with blood sugar levels under 220 mg/dl. Patients receiving total parenteral nutrition had higher mean glucose levels and required more insulin to maintain optimum serum glucose levels.

For any patient with diabetes on an oral diet, nutritional management, whether or not a foot ulcer is present, should be founded on an individualized meal plan based on recommendations set forth by a dietitian or the guidelines established by the American Diabetes Association. Meals should be at consistent times synchronized with the peak action of their insulin or oral medication. Focus on food choices and an optimal weight for the individual patient is recommended. Approximately 10 to 20% of calories should be from protein sources and less than 30% of the calories as fat (less than 10% from saturated fat). The remaining calories should be made up of carbohydrates. Ethanol intake should be restricted, substituting alcohol calories for fat exchanges and limiting intake to two alcoholic beverages a day to those on insulin.

In healing a diabetic foot wound, nutritional therapy may be the missing link when the wound is just not healing and the podiatric physician is seemingly doing everything right: ruling out all skin diseases, assuring glycemic control, maintaining adequate circulation, controlling infection, off-loading the wound, keeping the wound clean and free from contamination, debriding the necrotic and senescent tissue and using dressings that are creating an appropriate wound environment. In other words, the podiatric physician must not forget about the patient’s nutritional status.

In the final analysis, healing a wound in a person with diabetes can be as difficult as leading an orchestra made up of un-tuned instruments. Diabetes is a multi-system disease and all the systems have to be in harmony to achieve an optimal outcome. These systems need the appropriate fuel. Nutrition supplies that fuel, and therefore nutrition is the key to creating the energy that drives the process of wound healing.

References for Additional Information


Dr. Rehm, board certified in diabetic wound care, practices in San Diego, CA. He lectures nationally and offers seminars for podiatrists and other professionals. Dr. Rehm is Director of the Diabetic Foot and Wound Treatment Centers in San Diego.
1) Nutritional Management of a diabetic patient with or without a foot ulcer should be based on:
A) A high fat diet containing Omega 3 fatty acids
B) A low fat diet high in Omega 6 fatty acids
C) Recommendations set forth by the American Diabetes Association
D) Meals that are consistent with the patient’s appetite

2) All of the following are true statements except:
A) Meals should be at consistent times synchronized with the action of the patient’s medication
B) Meals should be based on an individualized meal plan
C) Focus should be food choices and the ideal weight for any person of the same height and weight
D) Ethanol intake should be limited to two alcoholic beverages per day to those on insulin

3) The basic principles of healing a diabetic foot wound include all of the following concepts except:
A) Keeping a wound dry until a scab is developed always allows optimal healing
B) A wound should be maintained with little or no pressure insult
C) Adequate circulation to the wound site is absolutely necessary
D) Contamination in a healing wound should be avoided

4) The ability of a patient to heal a foot ulcer is mostly affected by:
A) Hypoglycemia in the inflammatory phase of wound healing
B) Consuming foods that are high in DHEA
C) Avoiding foods that are abundant in alpha lipoic Acid
D) Choosing foods that are low in linoleic acid

5) Which of the following are the least instrumental in healing a diabetic foot wound?
A) Vitamin C
B) Vitamin A
C) Vitamin E
D) Trace boron

6) Zinc is an important trace element because:
A) It is a co-factor in catabolic reactions
B) It potentiates the action of DHA
C) It is essential for the transcription of RNA
D) It immobilizes the harmful effects of retinol-binding protein

7) Vitamin K is essential for the following reason:
A) It is needed for the metabolism of amino acids
B) It has anti-oxidant properties that promote cell membrane integrity
C) It is a coenzyme for DNA synthesis
D) It is essential for coagulation

8) A comprehensive nutritional assessment should evaluate all of the following except:
A) The ratio of complex vs. simple carbohydrates consumed
B) Macro- and micronutrient intake
C) Comorbidities
D) Medications

9) Basic principles of nutritional management of patients with diabetic foot wounds include the following:
A) Never force yourself to eat beyond your appetite
B) Never eat while watching T.V.
C) Never snack in between meals
D) Correction of chewing abnormalities

10) The four phases of wound healing are the following:
A) Hemostatic, catabolic, anabolic and reparative
B) Inflammatory, reparative, catabolic and remodeling
C) Catabolic, anabolic, homeostatic, maturation
D) Hemostatic, inflammatory, connective tissue, epithelial

11) A poor nutritional status in a diabetic patient most likely is due to all of the following except:
A) Poor appetite
B) Steatorrhea
C) Metabolic problem
D) Inability to digest or swallow properly

12) Which of the following statements is the least accurate?
A) Boron is a critical element in wound healing
B) Copper promotes the maintenance and repair of bones
C) Calcium is involved in the degradation of collagen
D) Deficiency of zinc may occur suddenly

13) Which of the following statements is not true?
A) Pharmacologic modulation of cytokines may enhance wound healing
B) The use of growth hormone has become part of the standard of care
C) The use of growth hormone is associated with increased risk of morbidity and mortality in burn patients
D) Alpha-lipoic acid is being researched for its role in diabetes and wound healing

Continued on page 210
14) Which of the following is the most likely cause of malabsorption and maldigestion:
   A) Marasmus
   B) Kwashlorkor
   C) Weight gain
   D) Pancreatic insufficiency

15) Vitamin A deficiency affects wound care in all of the following ways except:
   A) Decreases epithelialization
   B) Produces an increase in T-lymphocytes
   C) Decreases resistance to infection
   D) Decreases collagen synthesis

16) All of the following are important trace elements or micronutrients in wound healing except:
   A) Bismuth
   B) Zinc
   C) Copper
   D) Iron

17) Which of the following is not used for the diagnosis of protein malnutrition?
   A) Albumin
   B) Pre-albumin
   C) Total Protein
   D) BUN

18) Which of the following is not likely to cause an elevation in pre-albumin levels:
   A) Corticosteroid therapy
   B) Digestive disorders
   C) Hyperactive adrenal glands
   D) Hodgkin’s disease

19) All of the following are likely to interfere with pre-albumin levels except:
   A) Inflammation
   B) Amiodarone
   C) Estrogens
   D) Beta Carotene

20) Patients with diabetes and foot ulcers are likely to have all of the following except:
   A) Higher levels of fibrinogen
   B) Higher levels of C-reactive protein
   C) Higher levels of thyroid hormone
   D) Lower albumin levels

See answer sheet on page 211.
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and Answer Sheet
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Debride a Wound
(Johnson, Nixon, and Armstrong)

Circle:
1. A  B  C  D
2. A  B  C  D
3. A  B  C  D
4. A  B  C  D
5. A  B  C  D
6. A  B  C  D
7. A  B  C  D
8. A  B  C  D
9. A  B  C  D
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18. A  B  C  D
19. A  B  C  D
20. A  B  C  D

LESSON EVALUATION
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How much time did it take you to complete the lesson?
______ hours ______ minutes

How well did this lesson achieve its educational objectives?

_____ Very well  _______ Well

_____ Somewhat  _______ Not at all

What overall grade would you assign this lesson?
A   B   C   D

Degree____________________________

Additional comments and suggestions for future exams:
__________________________________________________
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EXAM #11/03
Nutrition
(Rehm)

Circle:
1. A  B  C  D
2. A  B  C  D
3. A  B  C  D
4. A  B  C  D
5. A  B  C  D
6. A  B  C  D
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19. A  B  C  D
20. A  B  C  D

LESSON EVALUATION
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_____ Very well  _______ Well

_____ Somewhat  _______ Not at all

What overall grade would you assign this lesson?
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Degree____________________________

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