

VitaMent™ key micronutrients:

Vitamin C is required for both collagen and glutathione synthesis. Adequate levels of vitamin C improves scar formation – Vitamin C is a cofactor in many enzymatic reactions involved in the metabolism of oxygen free radicals and has been shown to reduce free radical damage at the wound site. By reducing oxidative stress within the collagen matrix / wound bed, Vitamin C increases scar tensile strength. Glutathione, a tri-peptide of glutamine, cysteine and glycine, is a powerful antioxidant that reduces oxidative stress directly and by regulating other antioxidants. It also defends against infection and helps to regulate protein synthesis. Indirect benefits of Vitamin C supplementation on wound healing include: Participation in immune reactions and reduction in whole body stress. Additionally, therapeutic levels of Vitamin C have been shown to increase wound profusion by improving pulmonary function and increasing vascular density which reduces edema.

Carnitine, derived from an amino acid, is found in nearly all cells of the body. Carnitine plays a critical role in energy production and the preservation of lean body mass. It transports long-chain fatty acids into the mitochondria so they can be oxidized (“burned”) to produce energy. It also transports the toxic compounds generated out of this cellular organelle to prevent their accumulation. Carnitine deficiency is a metabolic state in which carnitine concentrations in plasma and tissues are less than the levels required for normal function of the organism. Medical conditions may affect carnitine homeostasis. Cirrhosis or chronic renal failure may impair the biosynthesis of carnitine. Malabsorption syndromes (e.g. Hypoproteinemia malnutrition, ostomies, fistulas, or chronic bowel diseases), or in conditions of increased catabolism (eg critical illness, surgery and pressure ulcers) may cause carnitine deficiency. Most vitamin and mineral supplements do not include carnitine.

Zinc is required for adequate immune efficiency (both innate and adaptive), wound healing, metabolic homeostasis (energy utilization and hormone turnover) and antioxidant activity (SOD enzyme). Zinc functions as a cofactor in numerous enzymatic reactions involved in acid-base balance, amino acid metabolism, protein and nucleic acid synthesis. Pertinent to wound healing, zinc deficiency can delay wound healing, decrease taste acuity, cause anorexia, diarrhea and hypogonadism. Risk for zinc deficiency include bowel disease, sickle cell anemia, diabetes, ileostomy/fistula, diarrhea, diuretics, chelating agents, thyroid disease, alcoholic cirrhosis, skin loss and draining wounds.

Drainage from chronic non-healing wounds contain 8 to 10 times the number of Matrix Metalloproteases (MMP) than the drainage from healing wounds. All of these MMPs contain protein and over 200 of them contain zinc and/or copper. Zinc is stored in various body tissues, but the epidermis contains 6 to 8 times the amount of zinc than any other tissue. So, individuals with large open wounds with heavy drainage are at particularly high risk for zinc, copper, and protein deficiency as well as dehydration. Adequate intakes of niacin and selenium are also required for proper zinc activity in the formation and function of metallothioneins and subsequent zinc homeostasis.

Zinc and copper compete for absorption, creating a risk for deficiency with supplementation. For example, copper deficiency has been shown to occur with 20mg/day of elemental zinc, resulting in copper deficiency anemia and poor wound healing. Zinc supplementation of 50mg/day for 4 to 6 weeks, or less if minimal wound drainage is present is recommended for wound healing. However, supplementation should be provided in a ratio of approximately 1:10 of copper to zinc to prevent deficiencies and a maximum of 4mg/d of copper to prevent toxicity. VitaMent provides 2mg of copper and 25mg of elemental zinc per pack.

Copper functions as a catalyst in the formation of hemoglobin; in the regulation of the expression of the genes for MMPs, and the cysteine-rich metallothioneins; mitochondrial function/cellular metabolism; connective tissue formation; the absorption, storage and metabolism of iron; in glucose oxidation for

energy release; balancing and secreting hormones of the thyroid; supplying the body's tissues with oxygen; nerve and brain function; and intestinal enzyme activity. All of these functions contribute to wound healing. Common causes of copper deficiency include: increased copper losses in wound drainage or diarrhea, increased utilization during metabolic stress, poor dietary intake or decreased absorption from supplemental zinc, and malabsorption syndromes (e.g. malnutrition, ostomies, fistulas, or chronic bowel diseases). Excess copper inhibits zinc absorption and supplementation should be provided as noted above.

As listed in the Micronutrients for Oxidative Stress and Wound Management Table, B Complex vitamins are involved in numerous body functions. However, one of the most critical functions of B Vitamins involves the reduction of homocysteine levels. Serum homocysteine is used as a diagnostic measure of inflammation in many chronic disease conditions. Specific to wound healing, at high serum levels, homocysteine binds to the fibronectin chain within the collagen matrix of the wound and acts as a physical barrier to necessary cross linking of proteins required to close the wound. Supplementation with folic acid and choline has been shown to reduce homocysteine levels and improve wound healing.

Micronutrients for Oxidative Stress & Wound Management (See www.Nap.edu.com for list of RDIs)

Micronutrient	Metabolic Function	Recommended	Upper Limit (UL)*
Fat-soluble Vitamins			
Vitamin A (retinal) and beta carotene	Synthesis of rhodopsin, epithelial cells, inflammatory stimulant for wound healing	5000 - 10,000 IU (1500 to 3000 ug RE)	Vitamin A: 10,000 IU (3000 ug RE) Beta Carotene: 25 mg Liver Disease: 5000 IU Vitamin A
Vitamin D	Regulation of calcium metabolism	400 IU	800 IU, current upper limits and RDI under review, increase likely.
Vitamin E	Antioxidant in cell membranes	200 – 400 IU	1,000 IU.
Water-soluble		B Complex - Cofactors in protein synthesis pathways	
Thiamin (B ₁)	Oxidative decarboxylation	50 mg	Not Determined (ND)
Riboflavin (B ₂)	Electron transfer	50 mg	ND
Niacin (B ₃)	Nicotinamide-adenine Dinucleotide; electron transfer; Supports zinc function.	50 mg Niacinamide (preferred form of supplemental Niacin)	1500 mg Niacinamide (Niacin has a lower safe uL – 35mg/day)
Pantothenic Acid	Part of Coenzyme A	50 mg	ND
Biotin	Carbon dioxide transfer	100 mcg	ND
Folic Acid	One carbon transfer reactions In conjunction with Choline acts to reduce homocysteine levels	1mg	1 mg
Choline	In conjunction with Folic Acid acts to reduce homocysteine levels; Liver function	400mg	ND
Cobalamine (B ₁₂)	Production of methionine coenzyme A reactions	50 mcg	ND
Ascorbic Acid (Vitamin C)	Antioxidant / free radical scavenger; collagen synthesis; carnitine production. Improves immune function and increases scar tensile strength.	500 to 1000 mg BID	3,000 mg, ASPEN CCG, 2009.

Minerals			
Chromium	Glucose and insulin utilization; enhances insulin action to help regulate glucose levels and utilization (for energy).	120 mcg	1000 mcg
Copper	Connective tissue development through collagen cross linking	2 mg per 25 mg of elemental zinc	10 mg
Iron	Hgb & O ₂ transport; electron transfer in O ₂ phosphorylation	Greater than RDI if anemia present	45 mg
Magnesium	Coenzyme, energy production, muscle and nerve cell function and bone formation	400 mg	400 mg
Manganese	Procollagen ground substance formation; fatty acid synthesis, brain & neuromuscular function;	4 mg	10 mg
Molybdenum	Metabolism of purines, pyrimidines; Redox reactions	80 mcg	350 mcg
Selenium	Antioxidant; fat metabolism; Vitamin E and zinc functions	100 mcg	400 mcg
Zinc	Immune function, wound healing, metabolic homeostasis & antioxidant activity. Enzyme functions, e.g. acid-base balance, amino acid metabolism, protein & nucleic acid synthesis & function. Coenzyme in over 200 Matrix-Metalloproteinases (MMPs) . .	Elemental Zinc: 50 mg for 4 to 6 weeks or until wound drainage is minimal.	40 mg. Higher doses of supplemental Zinc should be given with supplemental copper in a ratio of Cu:Zn = 1:10 to prevent an induced copper deficiency which can result in anemia & neutropenia, & impaired immune function.
L-Carnitine	Fatty acid transport for cellular energy and antioxidant activity. Tissue concentrations of carnitine decrease with aging.	500 mg	ND, At levels of 3000 mg/day can cause nausea, vomiting, abdominal cramps and diarrhea.
N-Acetyl Cysteine (NAC)	Antioxidant activity and protein synthesis. Required (precursor) for Glutathione & collagen synthesis	600 to 1200 mg	ND

Oxidative Stress:

The primary reactive species include reactive oxygen species (ROS) and reactive nitrogen species (RNS), levels of which increase with metabolic stress. These in turn react in the body and generate radical intermediates of lipids, proteins, and nucleic acids that ultimately form the chemical end products of oxidative stress. The physiological consequences of these end products are the causes of many chronic diseases as well as increased risk for skin breakdown post injury/illness and create a barrier to wound healing, leading to chronic non-healing wounds. In turn, chronic, non-healing wounds deplete nutritional stores resulting in malnutrition and further increase in oxidative stress. The protective mechanisms include protective enzymes, antioxidant or quenching compounds produced by the body and made available in the diet. Without adequate and appropriate nutritional intervention, the individual experiences severe malnutrition with overt nutrient deficiencies, perpetual wounding, loss of quality of life and eventual death.

For Metabolic Stress or Inflammation

Metabolic stress from illness, trauma or surgery triggers the inflammatory response which in turns

increases energy and nutrient utilization, resulting in malnutrition. Malnutrition is an independent risk factor for pressure ulcer development and poor surgical outcomes and is prevalent in patients with non-healing wounds. Patients with pre-existing inflammatory disease states with associated chronic oxidative stress are at highest risk for developing skin breakdown and non-healing wounds. Inflammatory-Malnutrition develops when there is underlying inflammatory process, injury, or condition. Levels of pro-inflammatory cytokines increase, creating a catabolic state and anorexia (at a time when increased intake is need). Amino acids are mobilized from muscle to the liver to meet increased energy needs. Subsequent erosion of body cell mass leads to impaired physiological function and GI integrity. Protein synthesis is suppressed as evident by increased positive acute phase proteins and decrease in negative acute phase proteins (egg. albumin and pre-albumin). Hypoalbuminemia causes collection of extracellular fluid due to changes in oncotic pressure. An obvious edema or anasarca result which masks weight loss, impairs skin integrity, restricts blood flow, further limits nutrient absorption and causes malabsorption diarrhea.

Examples of Inflammatory Conditions with Nutritional Implications

- Gut injury
- Inflammatory bowel disease
- Periodontal disease
- Wounds, Pressure Ulcers
- Trauma, Surgery
- Sepsis, ARDS, Infection
- Diabetes
- AIDS, HIV
- Arthritis
- Immobility
- Aging
- Organ failure, acute and chronic
- Obesity
- Metabolic syndrome
- Cardiovascular Disease
- Spinal Cord Injury

The connection between inflammatory- malnutrition (cachexia) and poor outcomes is well documented in the literature. Nutrition therapy for wound healing should attempt to optimize micro and macronutrient intake to modulate inflammation / reduce oxidative stress in order to restore homeostasis and proper utilization of nutrients; and to prevent or treat malnutrition associated with wounding. The American Society for Parenteral and Enteral Nutrition Critical Care Guidelines (publication pending JPEN. 2009) recommends therapeutic levels of key antioxidants for patients with metabolic stress to improve outcomes.

Antioxidant

A dietary antioxidant is a substance in foods that significantly decreases the adverse effects of reactive species. Different cells can be exposed to the same level of oxidants, but depending on the level of antioxidants or protective mechanisms available to the cell, they may or may not experience an oxidative stress. Oxidative stress is defined as an imbalance between the production of various reactive species and the ability of the organism's natural protective mechanisms to cope with these reactive compounds and prevent adverse effects.

Poor Appetite or Anorexia or Inflammatory Conditions

This chart can also be used for Xtracal Plus

Common Causes of Diminished Appetite in at Risk populations	
Effect	Possible Causes
Loss of Appetite	<ul style="list-style-type: none">• Disease related anorexia caused by the inflammatory response• Disease process/ complications, e.g. malnutrition, depression, dysphasia, dementia, Hypogonadism (males)• Medications, e.g. SSRI anti-depressants• Early satiety and volume sensitivity
Altered Taste	<ul style="list-style-type: none">• Dehydration• Medications, e.g. antibiotics, chemotherapy
Nausea/ Vomiting/ Diarrhea/ Dyspepsia	<ul style="list-style-type: none">• Disease process/ complications, e.g. C difficile, wound infection, glutamine depletion• Medications, e.g. antibiotics; Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) which may cause GI irritation
Constipation	<ul style="list-style-type: none">• Inadequate fluid intake to match increased needs• Medications, e.g. narcotics, iron supplements
Dehydration	<ul style="list-style-type: none">• Inadequate fluid intake to match increased needs• Medications, e.g. diuretics

Male Hypogonadism is a condition in which the body doesn't produce enough of the hormone testosterone — the hormone that plays a key role in masculine growth and development during puberty.

You may be born with male hypogonadism, or it can develop later in life from injury, infection, chronic illness (Diabetes, chronic kidney disease).

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