

## Arginine and Wound Healing: A Case Study

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Mr P, a 77-year-old man who resides at home with his wife, suffers from coronary heart disease, hypertension, glaucoma, an enlarged prostate, and involuntary weight loss. Clinical evaluation of the patient reveals a nonhealing surgical wound 8 weeks after coronary artery bypass grafting. The wound is located on the lower right leg, where a vein had been harvested for the procedure. The wound bed contains a significant amount of slough, with signs and symptoms of infection, including increased redness and exudate, and pain.

After a deep swab culture reveals the presence of *Staphylococcus aureus*, antibiotics and appropriate acute medical care are initiated for Mr P. The health care provider requests a consultation with the registered dietitian for nutrition evaluation and care.

### Nutritional Interventions

Mr P tells the dietitian that his wife prepares his meals. A typical day includes cold cereal for breakfast, a sandwich for lunch, and chicken for dinner. Mr P reports that he does not snack between meals, but does drink soda while watching television. He takes a multivitamin daily. Mr P notes that he has lost approximately 15 pounds over the last year, and is now 90% of his usual body weight.

Aggressive nutritional support to promote wound healing is indicated for this patient. The correlation between nutritional deficiencies and the development of chronic, nonhealing, or slow-healing wounds is well recognized.<sup>1-4</sup> Malnutrition caused by inadequate protein or caloric intake can lead to weight loss, a cycle of reduced appetite and illness, and diminished circulating proteins (prealbumin, transferrin, albumin, and others).<sup>5-7</sup> Protein-energy malnutrition has been reported to predispose patients to the development of chronic wounds because of reduced tissue regeneration and integrity, increased tissue catabolism, and altered inflammatory reaction and immune function.<sup>8</sup>

Patients with chronic wounds commonly have increased need for protein and calories. A protein intake of 1.2 to 1.5 mg/kg/day or more is recommended.<sup>2</sup> Mr P and his wife are educated about how to incorporate additional protein into his meals. Mr P is willing to replace his soda with another beverage if it will help his wound.

The registered dietitian recommends an arginine-enriched, powdered drink mix or a ready-to-drink, arginine-rich supplement with additional protein and calories. This type of drink can be consumed with meals as the beverage or enjoyed in between meals as a snack. Available arginine-enriched beverages include Resource Arginaid and Resource Arginaid Extra (Novartis Nutrition, Minneapolis, MN) and Juven (MTI Biotech, Ames, IA).

### Arginine: A Semi-Essential Amino Acid

Arginine is an amino acid. Amino acids are generally classified as essential or nonessential. Essential amino acids are those that the body cannot synthesize; a steady supply of amino acids must be provided through the diet. The body can manufacture nonessential amino acids, so an exogenous supply of them in the diet is unnecessary.

Arginine is a unique amino acid, generally referred to as *semi-essential*.<sup>9,10</sup> This noncommittal label indicates that although the body can manufacture arginine, at times it does so in an amount that is insufficient to meet physiologic needs. This often occurs during periods of growth, illness, and metabolic stress. In other words, arginine is a nonessential amino acid during periods of maintenance, but is an essential amino acid during periods of growth and healing.

Arginine regulates many metabolic and physiologic body functions and has several attributes that support wound repair, including the following:<sup>10-12</sup>

- Arginine is nitrogen-rich. The average amino acid is 16% nitrogen; L-arginine is 32% nitrogen.
- Arginine is a precursor to proline, which is converted to hydroxyproline, then to collagen.
- Arginine has a positive influence on the body's levels of insulinlike growth factor (IGF-I), a hormone that promotes wound healing.
- Arginine is a precursor to polyamines, the cell's building blocks, which are important for wound repair.
- Arginine is the only substrate for nitric oxide synthesis. Nitric oxide has a beneficial effect on circulatory status and increases blood supply to the wound.
- Arginine contains immune-enhancing properties that reduce the risk of wound complications.

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## In the Literature

A number of reports concerning the wound healing properties of arginine can be found in the literature. Benati et al<sup>13</sup> studied 36 hospitalized patients with severe cognitive impairment and pressure ulcers. Patients were randomized to receive a normal diet or a normal diet plus a standard high-protein, high-calorie supplement, or the same supplement enriched with 7.5 mg of arginine, 25 mg of zinc, and antioxidants over the 2-week study period. Patients on high-protein, high-calorie supplements had more rapid healing of their pressure ulcers than unsupplemented patients. The most rapid healing occurred in the group on enriched supplements.

Kirk et al<sup>14</sup> studied arginine supplementation in 30 healthy volunteers over age 65. A small catheter was placed subcutaneously and a 2 × 2 cm, split-thickness wound was created. Over the 2-week study period, half of the subjects received 17 grams/day of free arginine and half received placebo. Compared with the placebo group, the arginine-supplemented group demonstrated significantly higher protein and hydroxyproline catheter content, greater lymphocyte responses, and elevated levels of IGF-I. The investigators concluded that arginine supplementation improves wound healing and immune response in the elderly.

A study by Barbul et al<sup>15</sup> also suggests that supplemental arginine may promote wound healing. During their 2-week study, 36 healthy volunteers had a small catheter placed subcutaneously and were randomized to receive 24.8 grams/day of free arginine as arginine hydrochloride, 17 grams/day of free arginine as arginine aspartate, or placebo. Both arginine-supplemented groups displayed significantly enhanced collagen and hydroxyproline catheter deposition compared with the placebo group. Lymphocyte response was also greater in the arginine-supplemented groups versus the placebo group. Data from this study suggest that arginine may be of clinical benefit in improving wound healing and immune response.

Cui et al<sup>16</sup> studied arginine in scald-burned rats. Rats were inflicted with a 30% body surface area burn, then examined for the effects of supplemental arginine on protein metabolism. Nitrogen balance in the arginine group was markedly greater than in the control group. Whole-body protein turnover rates, fractional protein synthesis rates in tissue, and urinary excretion of polyamines were significantly higher in the arginine group. The investigators suggested that arginine's role as an important precursor to polyamines may further explain its importance in protein metabolism and wound healing. They concluded that an arginine-supplemented diet increases the level of polyamines, thereby promoting tissue repair.

## Conclusion

As more is learned about the role of nutrition in the treatment of wounds, practitioners are discovering that many different

types of supplements may help. Arginine supplementation is among the nutritional interventions that should be considered. It is inexpensive, noninvasive, and well tolerated. In addition, anecdotal reports of successful wound healing using Resource Arginaid, Resource Arginaid Extra, and Juven as part of a multi-disciplinary care plan have been reported in practice. ●

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