



# Glutamine: Indicated in Cancer Care?

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Little was known about L-glutamine (commonly referred to as glutamine) until research in the 1930s found it to be the most prevalent amino acid in the human body. Approximately 20 amino acids, classified as essential or nonessential, make up dietary protein (see Figure 1). Glutamine is a non-essential amino acid (i.e., the body is able to synthesize it) contained in most dietary proteins. A healthy person consumes 5–10 grams of dietary glutamine daily and, therefore, usually does not need supplemental glutamine (Lebow & Souba, 2000; Miller, 1999; Smith & Wilmore, 1990).

High concentrations of this amino acid are found in the skeletal muscle, liver, brain, lungs, and stomach (Miller, 1999; Souba, 1993). Glutamine has a role in multiple bodily functions and serves as a(n)

- Fuel source for small intestine enterocytes
- Nitrogen donor for certain synthetic pathways
- Precursor in both nucleic acid and nucleotide synthesis
- Regulator of acid-base balance
- Precursor of neurotransmitters
- Immune system cellular energy source for lymphocytes, macrophages, and fibroblasts (Lebow & Souba, 2000; Medina, 2001; Miller; Smith, 1999; Souba).

Glutamine becomes depleted during catabolic conditions that cause metabolic stress, including injury and infection (Lebow & Souba, 2000). Under such circumstances, intracellular glutamine levels may decrease by 50% or more (Lebow & Souba; Smith, 1999). Patients with cancer develop glutamine depletion because tumors use this amino acid, leading to protein catabolism. For example, depletion of skeletal muscle glutamine because of tumor growth results in cachexia (Klimberg & McClellan, 1996). Researchers believe that a tumor becomes a glutamine trap and worsens glutamine loss in patients with cancer and that glutamine has the potential to stall or halt tumor growth because of its immunomodulatory action (Klimberg & McClellan).

## Glutamine in Cancer Care

The use of glutamine in oncology has been researched in animals and humans, but the results often have conflicted (Miller, 1999). Researchers became concerned about an increase in tumor growth with glutamine supplementation in patients with cancer after *in vitro* studies revealed an increase in cellular growth with glutamine supplementation (Kang, Feng, & Hatcher, 1994). However, subsequent *in vivo* studies showed the opposite effect: a reduction in tumor growth (Bartlett, Charland, & Torosian, 1995; Fahr, Kornbluth, Blossom, Schaeffer, & Klimberg, 1994).

Early researchers were concerned about colon tumors absorbing glutamine. They theorized that because glutamine is absorbed in the gut, glutamine would be taken up faster in patients with diseases affecting the gut. However, glutamine uptake in patients with colon cancer, regardless of tumor size and cell type, is comparable to uptake in patients with healthy intestinal tissue (Souba et al., 1988; Van der Hulst, von Meyenfeldt, Deutz, & Soeters, 1997).

In early animal research studies, Klimberg, Souba, Dolson, et al. (1990) found that

an enteral diet containing glutamine increased muscle glutamine in rats by 60% without increasing tumor growth or tumor glutamine use. Glutamine supplementation in rats receiving methotrexate chemotherapy was found to increase tumor methotrexate concentration; reduce methotrexate-induced side effects, including mucositis; and improve survival (Fox et al., 1988). Glutamine supplementation also was found to prevent mucosal ulceration in rats subjected to abdominal radiation (Klimberg, Souba, Salloum, et al., 1990). Such promising results from laboratory and animal studies led to clinical studies of glutamine supplementation.

## Alleviating the Side Effects of Chemotherapy

Most studies of glutamine supplementation in patients receiving chemotherapy have focused on assessing its role in alleviating side effects. In a randomized, double-blind, crossover study, oral glutamine (16 g/day) or a placebo was given to 18 patients receiving 5-fluorouracil chemotherapy for gastrointestinal cancers. The glutamine was well tolerated with no apparent adverse effects but failed to have any significant effect on oral mucosa as assessed by the patients and researchers (Jebb et al., 1994). In a larger double-blind study, 66 patients were randomized to receive oral glutamine or a placebo in conjunction with oral cryotherapy and 5-fluorouracil chemotherapy. No significant differences were found in subjective and objective mucositis scores between the two groups (Okuno et al., 1999).

Other studies have found some benefits to glutamine supplementation. In a randomized,

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ESSENTIAL AMINO ACIDS	NONESSENTIAL AMINO ACIDS
Histidine	Alanine
Isoleucine	Arginine
Leucine	Asparagine
Lysine	Aspartic acid
Methionine	Cysteine
Phenylalanine	Glutamic acid
Theonine	Glutamine
Tryptophan	Glycine
Valine	Proline
	Serine
	Tyrosine

FIGURE 1. AMINO ACIDS

Note. Based on information from Whitney, Cataldo, & Rolfes, 1998.