

# IMMUNONUTRITION

## Abstract

Systemic inflammatory response, triggered by any kind of traumatic injury, surgical intervention or any microbial infection, can impose elevated metabolic requisites on diseased individuals, culminating in exhaustion of vital nutritional reservoirs.

Immunonutrition may be elucidated as the deliberate adjustment of immune system's efficacy or consequences of its activation, achieved through the consumption of nutrients or particular comestibles in quantities surpassing those customarily encountered in standard regimen. Immunonutrients refer to specific nutrients that have a notable impact on the immune system. Some essential immunonutrients include:

- Sulphur-containing amino acids
- Ω-3 fatty acids
- Anti-oxidants
- Glutamine
- Arginine
- Nucleotides

These immunonutrients play crucial roles in supporting and enhancing the immune system's functions, contributing to overall health and well-being.

Nutrient status has the potential to modulate cytokine biology and immune function. Inflammation may inhibit T lymphocyte function.

Thus any nutrient, which has an anti-inflammatory effect, may enhance T lymphocyte function by removing this inhibitory influence.

Nutrients may act at many cellular locations, affecting cytokine production and altering the response of target tissues to cytokines.

**Keywords:** Immunonutrition, Anti-oxidants, Glutamine, Arginine, Nucleotides.

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## I. BACKGROUND

1. Surgical procedures, traumatic incidents, or infections can induce a systemic inflammatory response, placing significant metabolic demands on patients. This can result in the depletion of crucial nutrient reserves.<sup>1</sup>
2. In the context of injury and infection, pro-inflammatory cytokines play a pivotal role in augmenting the host's response, a vital component for the proper functioning of the immune system.
3. However, the overproduction of pro-inflammatory cytokines can lead to an immunosuppressive effect despite their role in inflammation.
4. Moreover, individuals who are malnourished frequently undergo a decrease in immune function.

## II. WHAT IS IMMUNONUTRITION?

Immunonutrition can be described as the deliberate adjustment of either the immune system's activity or the outcomes of its activation, achieved through the consumption of nutrients or specific food items in quantities exceeding those typically found in the regular diet.<sup>2</sup>

**Immunonutrients:** Immunonutrients refer to specific nutrients that have a notable impact on the immune system. Some essential immunonutrients include:

Omega-3 fatty acids  
Glutamine  
Sulphur-containing amino acids  
Antioxidants  
Arginine  
Nucleotides

These immunonutrients play crucial roles in supporting and enhancing the immune system's functions, contributing to overall health and well-being.

Omega-3 fatty acids exhibit anti-inflammatory properties, effectively countering Immunosuppression is achieved by reducing the production of eicosanoids.

Sulfur-containing amino acids have a crucial function in the maintenance of antioxidant levels, particularly concerning glutathione, which serves as a pivotal antioxidant within the body.

Glutamine is an essential nutrient for quickly multiplying cells, including those within the immune system, thereby supporting enhanced gut barrier function. Additionally, it promotes the production of glutathione, fortifying antioxidant defenses.<sup>3</sup>

Arginine promotes the synthesis of nitric oxide and the production of growth hormone, resulting in an anabolic effect and an increase in T helper cell numbers.

Although nucleotides' role is not yet fully defined, they are believed to exert significant effects on T cell function.

### III. INFLUENCE OF OXIDANTS ON CYTOKINE PRODUCTION

Within the realm of cytokine production, oxidative molecules generated during the inflammatory response have a notable impact on the enhancement of cytokine production. This is achieved through the activation of nuclear transcription factors, including but not limited to nuclear factor kappa B (NFκB), nuclear factor IL-6 (NF-IL-6), and activator protein-1 (AP-1).<sup>4</sup>

NFκB, a transcription factor, remains in an inactive state in the cell cytoplasm due to its binding with an inhibitory subunit known as IκB. However, when cellular signals are triggered, IκB dissociates, revealing a nuclear recognition site. A series of phosphorylation steps then lead to the movement of the NFκB subunit into the cell nucleus, initiating gene transcription.

NFκB governs the regulation of a multitude of genes, leading to the synthesis of cytokines, adhesion molecules, enzymes, and various other inflammatory mediators. It's noteworthy that this process of dissociation and phosphorylation encompasses a redox-sensitive phase, in which oxidant molecules stimulate NFκB activation, while antioxidants act to impede it.

The up-regulation of NFκB governs many cytokines implicated in inflammatory responses observed during infections and injuries. In fact, several studies have revealed a direct association between increased NFκB activation in sepsis patients and higher mortality rates.

- 1. Antioxidants:** The human body boasts an intricate network of interconnected antioxidant defenses, providing protection against oxidative harm. These antioxidants are found in bodily fluids and various cellular compartments, including cell membranes.

Within the plasma, a number of dietary-derived antioxidants, including tocopherols (vitamin E), ascorbic acid (vitamin C), carotenoids such as β-carotene and lycopene, as well as catechins, can be identified. Additionally, endogenously synthesized proteins and peptides, such as glutathione, ceruloplasmin, albumin, and metallothionein, play crucial roles in antioxidant defense.<sup>5</sup>

While numerous substances serve as antioxidants in the aqueous portions of cells, vitamin E and carotene primarily operate as antioxidants within cellular membranes. Enzymes such as superoxide dismutase, catalase, and glutathione peroxidase/reductase transform oxidant molecules into benign by-products.

Nutrients with antioxidant properties, along with those serving as precursors for the mentioned molecules, bolster the body's antioxidant defenses, limiting the direct activation of NFκB by oxidants released during inflammation and protecting host tissue from damage.

Furthermore, these nutrients possess the capacity to alleviate the pathological aspects of cytokine-mediated responses during infection and injury. The synergistic interaction of multiple antioxidants in oxidation/reduction cycling further amplifies their efficacy.

Micronutrients also play a vital role in influencing antioxidant defenses, as some trace elements are essential components of antioxidant enzymes: copper for ceruloplasmin, copper/zinc/manganese for superoxide dismutases, and selenium for glutathione peroxidase. Together, this comprehensive antioxidant network contributes to the body's ability to counteract oxidative stress effectively.

- 2. Glutathione:** Concentrations of glutathione in different tissues often exhibit a decline following surgery and during infections. Notably, suboptimal levels of glutathione have been observed in various clinical conditions, encompassing human immunodeficiency virus infection, hepatitis C infection, cirrhosis, type II diabetes, ulcerative colitis, and myocardial infarction.

This suggests that the body's antioxidant defenses are depleted as a normal response to trauma and infection. However, there are multiple ways to enhance glutathione synthesis. One straightforward approach involves supplying patients with the three essential amino acids required for glutathione production: glycine, glutamic acid, and cysteine. Glutamine, which can be easily converted to glutamic acid, might contribute to its beneficial effects by supporting glutathione synthesis.

Delivering cysteine and methionine to patients poses a difficulty because these amino acids are not easily absorbed by cells. Nevertheless, cysteine can be provided in the form of n-acetylcysteine (NAC) or pro-cysteine. Multiple studies have illustrated the favorable impact of supplementing with glutamine on patient outcomes. This has led to reduced infection rates and shorter hospital stays, which can be attributed to glutamine's capacity to sustain glutathione levels while simultaneously nurturing both the gastrointestinal tract and the immune system.<sup>6</sup>

- 3. Fatty Acids:** Fatty acids can significantly impact cell cytokine production and tissue response to cytokines. Dietary fats consist of saturated, monounsaturated, and polyunsaturated fatty acids (PUFA), which can be classified as  $\omega$ -3 and  $\omega$ -6 based on their double bond position. Lipids exert an impact on the immune system by modifying the fatty acid composition of phospholipids within the membranes of both immune and target cells, resulting in the production of prostaglandins and leukotrienes when phospholipases are activated during trauma or infection. Different fatty acids in our diet lead to distinct profiles of released prostaglandins and leukotrienes, influencing the strength of the inflammatory response.

Numerous investigations have delved into the potential of fish oil, which is abundant in  $\omega$ -3 fatty acids, as an anti-inflammatory agent. These studies have primarily concentrated on chronic inflammatory conditions such as rheumatoid arthritis, psoriasis, asthma, multiple sclerosis, Crohn's disease, and ulcerative colitis. Fish oil has shown to improve inflammatory symptoms and reduce pro-inflammatory cytokine production in both healthy individuals and rheumatoid patients, potentially explaining its anti-

inflammatory effects. Moreover, fish oil has demonstrated protective effects against endotoxin, burn injury, and bacterial infection in animal studies. However, it's essential to note that most research has been conducted on chronic inflammatory conditions rather than acute inflammation.

Glutamine is the most abundant free amino acid in the body and plays a vital role in various functions.<sup>7</sup> During catabolic stress, muscle stores of glutamine can rapidly deplete. Glutamine is crucial for supporting rapidly dividing immune cells like lymphocytes and neutrophils, aiding in nucleotide synthesis, maintaining gut barrier function by providing fuel for enterocytes, and inducing the production of heat shock proteins. Additionally, it contributes to the synthesis of the endogenous antioxidant glutathione, which may be suboptimal in conditions like HIV, hepatitis C, type 2 diabetes, myocardial infarction, and cirrhosis.

- 4. Glutamine:** Supplementing with glutamine can protect against oxidative stress effects, especially in intensive care unit (ICU) patients who often exhibit low p-glutathione levels at admission, which correlates with illness severity and mortality rates. Studies have shown promising results of glutamine supplementation in various contexts. For example, in elective surgery patients, it reduced infectious complications and decreased hospital stay length. In critically ill patients, high doses of parenteral glutamine (>0.2g/kg/day) were associated with reduced complications and mortality rates.

To overcome glutamine's low stability in an aqueous environment, it is often combined with another amino acid like glycine or alanine to form a dipeptide. Different dosages of glutamine have been studied, and oral supplementation at 0.3mg/kg/day showed beneficial effects on intestinal integrity. A glutamine-enriched formula (containing 30.5g/100g protein) resulted in decreased infection rates in critically ill patients. However, parenteral administration of 0.4g/kg/day of glutamine decreased leukocyte and natural killer (NK) cell count, potentially suppressing inflammation. Overall, glutamine supplementation has shown promise in enhancing various aspects of health and well-being.<sup>8</sup>

#### IV. CONCLUSION

The nutritional status has the capacity to regulate cytokine biology and immune function. Inflammation can hinder the functioning of T lymphocytes.

1. Therefore, any nutrient with anti-inflammatory properties could potentially boost T lymphocyte function by alleviating this inhibitory impact.<sup>9</sup>
2. Nutrients can exert their effects at various cellular sites, influencing cytokine production and modifying how target tissues respond to cytokines.
3. Fatty acids can directly affect this by altering the composition of membrane phospholipid fatty acids.
4. Nutrients that impact antioxidant defenses have the potential to indirectly modify cytokine production. This occurs by regulating the degree of activation of transcription factors due to oxidant molecules generated during the inflammatory response.<sup>10</sup>

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