

proteinews

Issue 7



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Malnutrition and Infection

In developing countries, malnutrition is the most common risk factor for illness and death. It greatly increases the susceptibility to infectious agents. While, severe malnutrition is the most prevalent cause of immunodeficiency worldwide.¹

Malnutrition affects about -

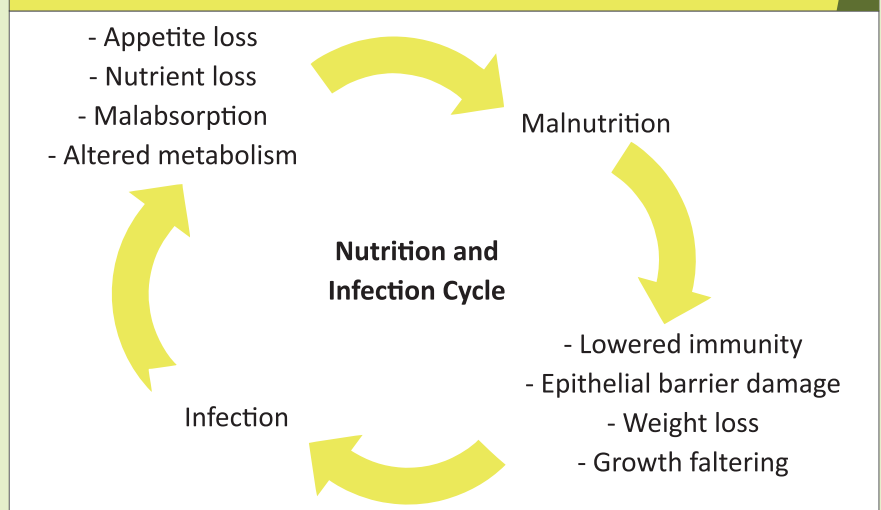
- Hundreds of millions of pregnant women and young children in developing countries.
- 50% of the population in some impoverished communities.¹

Increased susceptibility to infections occur due to the **impairment of immune function by** protein-energy malnutrition (**PEM**).²

In India, about 4% to 26% of the population are at risk of **protein deficiency**.³

Malnutrition can increase the susceptibility to infection, and infection can contribute to malnutrition, which leads to the vicious cycle (Figure 1).⁴

Figure 1: Nutrition and infection cycle.⁴



From Infection to Malnutrition

Infection can contribute to nutritional impairment through the multiple mechanisms including factors related to the -

- Decreased intake of nutrients
- Increased nutrient loss
- Malabsorption
- Altered metabolism⁴

It can develop from various associated mechanisms, these include the decreased intake of solids due to xerostomia, changes in the surface absorption of gastro intestinal lumen with destruction of intestinal villi due to the bacterial toxins, and the loss of nutrient through hypersecretion across the mucosa. These mechanisms directly affect the nutrient absorption or its retention capacity. It results in loss of nutrient through diet as well as through endogenous nutrients generated during normal cell turnover which, under normal conditions, would reabsorbed largely.⁴

Malnutrition can also affect the immune parameters as, without proper nutrition, the immune system is deprived of the components required to produce an effective immune response.^{5,6}

Malnutrition and the Immune System

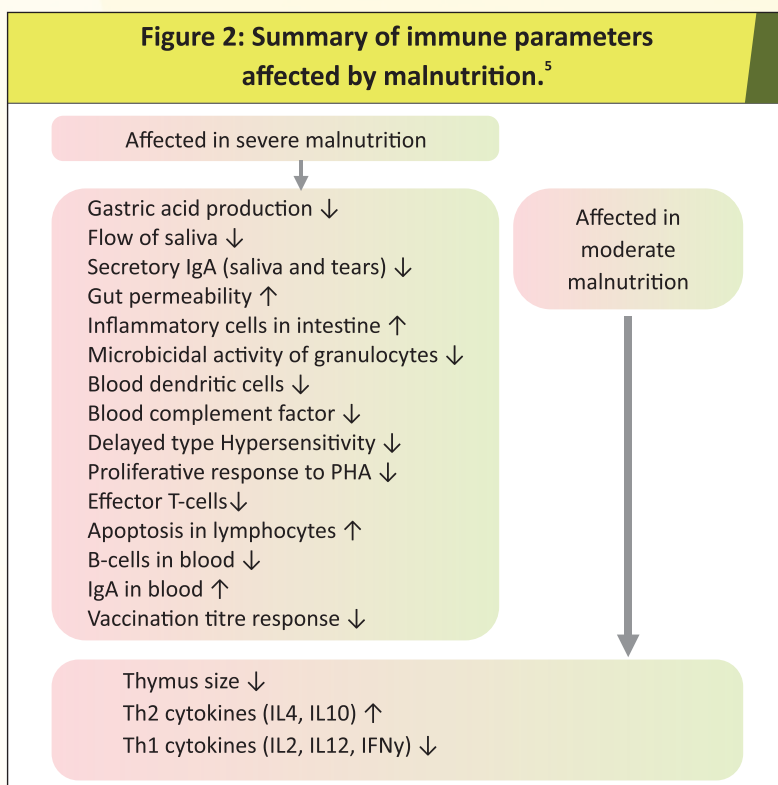
Most of the immune mechanisms depends on the production of active protein compounds (Figure 2). The functions of immune system reduces in protein deficiency. Adverse effect of protein deficiency on immunity may be related to the effect of immune system regulator for some amino acids.⁷

A deficiency of protein or amino acids is known to impair the immune function and increases the susceptibility to infectious disease.⁸ Latest evidences indicate that protein metabolism has an important role in formation of natural and acquired immunity against infections.⁷

Casein: Major Dietary Protein

Caseins is the major proteins in milk. It is classified of α -, β -, and κ -caseins which has nutritional value and have remarkably different immunomodulating properties (Table 1).^{9,10}

Casein proteins and its fragments are multifunctional and **possess** various physiological roles, such as **opioid-like features, immune-stimulation, anti-hypertensive, antibacterial and antiviral effect** and also **enhances calcium absorption**.^{11,12}



Casein proteins & its fragments possess various Immunomodulatory properties	
Stimulate proliferation of lymphocytes	
Release of cytokines	
Interleukin-1 production	
Generation of antibodies	
Stimulate phagocytic action of macrophages	
Inhibit cell growth	
Chemotactic properties	
Modulate leukocyte adhesion	
Modulates innate immune response	
Chaperone-like activities	

Table 1: Immune activities of peptides and protein hydrolysates from caseins.	
Casein	Function
α 1-Casein	Promotes antibody formation and accelerated phagocytosis <i>in vitro</i> ⁹
	Stimulates the expression of pro-inflammatory cytokine ¹¹
	Induce differentiation of monocytes toward macrophages ¹¹
	Inhibit matrix metalloproteinase 9 (MMP-9) activity, which involved in the induction of inflammatory cytokines ¹⁵
β -Casein	IgA-enhancing effect on B cells ¹⁶
	Upregulates MHC class II antigen expression on bone marrow-derived macrophages, increasing their phagocytic activity, and induces only a low level of cytokine release ⁹
	Suppresses the proliferation of lymphocytes ⁹
	Mitogenic effect on human T, B, and monocyte cells ¹⁶
K-Casein	Enhances mitogen-induced proliferation of human lymphocytes <i>in vitro</i> ⁹
	Has immuno-suppressive properties, such as reduces phagocytic function & suppresses production of reactive oxygen & nitrogen species ¹⁷
	Significantly suppressed cytokine production. ¹⁵
	Impair macrophages ability to release key inflammatory cytokine mediators; TNF- α and IL-10 in response to LPS. ¹⁵

Thus, dietary supplementation with high-quality protein would be effective in enhancing the protein nutritional status in malnourished subjects.⁸ Use of casein phosphopeptide is advantageous for the enhancement of mucosal immunity.¹⁴ A casein-derived bioactive nutraceutical which have immuno-modulatory properties would be of great importance.¹⁷

Casein also acts as a source of amino acids.¹⁴ Deficiency in essential amino acid can lead to the suppression on immune system.⁷

Amino acids

Amino acids are required for the synthesis of a variety of specific proteins (cytokines and antibodies).⁸ Changes in the amino acids concentrations can produce abnormal immune responses which can lead to malnutrition and certain pathological conditions such as infections, malignant neoplasm formation, autoimmunity, and inflammation.¹⁸

Amino acids regulate key metabolic pathways of the immune response to infectious pathogens.⁸

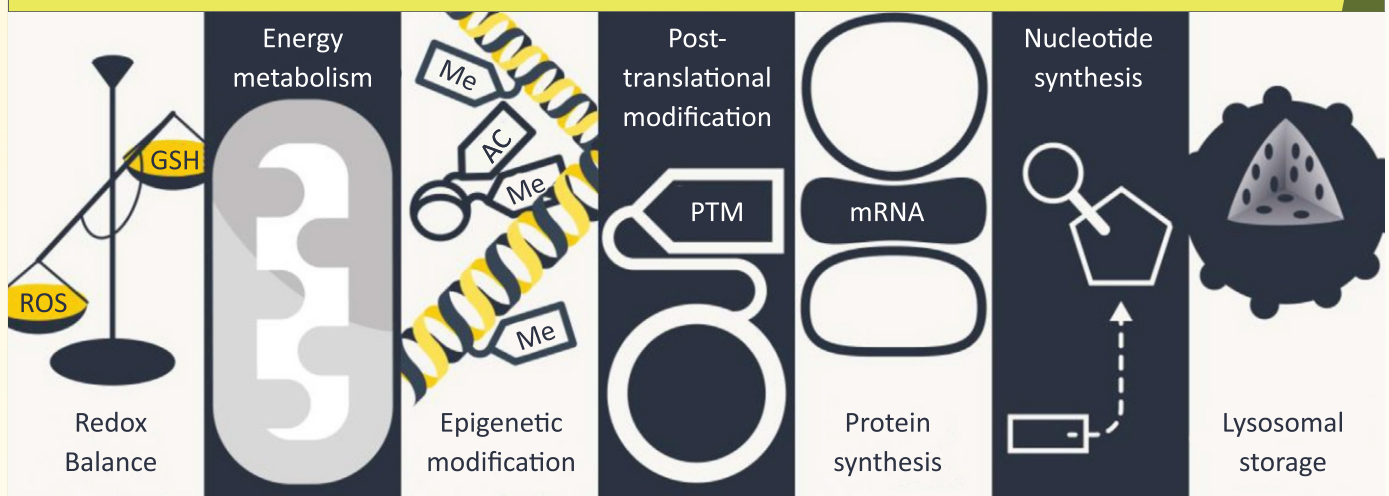


How Amino Acids Support Immune Cell Function by Multiple Mechanisms

Amino acids supports the immune cell function in multiple ways (Figure 3):

- **Supply intermediates** which drive metabolic refurbishing upon immune cell activation, and are used to **make antioxidants** such as glutathione, maintaining redox balance.
- Provide methyl and acetyl groups to modify DNA and histones epigenetically which facilitate specific gene expression programs in immune cells.
- These and other intermediates can also be used to modify proteins post-translationally and impact their function.
- **Fuel nucleotide synthesis** which drive proliferation and growth and drive translation, and can also be stored in lysosomes.
- **Drive autophagy** as a protective mechanism in times of stress.¹⁹

Figure 3: Mechanisms of Supporting Immune Cell Function by Amino Acids¹⁹



The immunological impairment can improve with several amino acids such as arginine and glutamine.¹⁸

Role of amino acids in the immune system

Amino acid	Role
Glutamine	<ul style="list-style-type: none"> • Used at a high rate by cells of the immune system.²⁰ • Support optimal lymphocyte proliferation.²⁰ • Regulate the rate of IL-2 production and IL-2 receptor expression.²¹ • Production of cytokines by lymphocytes and macrophages.²⁰
Arginine	<ul style="list-style-type: none"> • Improves lymphocytic progress and phagocytosis, and enhances wound healing. • Development of memory T-cells. • Normalizes T-cell response after serious surgical procedures & traumas.⁸
Tryptophan	<ul style="list-style-type: none"> • Enhances host immunity by inhibiting production of superoxide, scavenging free radicals and attenuating production of TNFα.⁸
Cysteine	<ul style="list-style-type: none"> • Important for T cells (precursor of the tripeptide glutathione). • Required for synthesis of proteins, glutathione and coenzyme A. • Rate limiting for cell growth and proliferation of lymphocytes.⁸



Histidine	<ul style="list-style-type: none"> Deficiency → decreases plasma concentrations of proteins → impairs the immune response. Supplementation can boost immune function, particularly in the skin.
Proline	<ul style="list-style-type: none"> Important for wound healing and injury recovery mediated by immune cells.⁸
Asparagine	<ul style="list-style-type: none"> Significant role in immune function.⁸
Glycine	<ul style="list-style-type: none"> A potent antioxidant, scavenging free radicals. Essential for proliferation and anti-oxidative defence of leucocytes. Novel anti-inflammatory, immunomodulatory and cytoprotective nutrient.⁸
Aspartate	<ul style="list-style-type: none"> Have versatile roles in the metabolism and function of leucocytes. Crucial for the proliferation of lymphocytes.⁸

Malnutrition is the most common risk factor for illness and death. Increased susceptibility to infections occurs due to the impairment of immune function by protein-energy malnutrition. The susceptibility to infection increases due to the malnutrition, and infection can contribute to malnutrition, which leads to the vicious cycle. A deficiency of protein or amino acids is known to impair the immune function and increases the susceptibility to infectious disease. Casein proteins and its fragments are multifunctional and possess various physiological roles, such as immune-stimulation, antibacterial, antiviral effect, etc. A casein-derived bioactive nutraceutical which has immuno-modulatory properties would be of great importance. Amino acids regulate key metabolic pathways of the immune response to infectious pathogens. The immunological impairment can improve with several amino acids such as arginine and glutamine. Amino acids are the cost-effective nutraceuticals for improving health and preventing infectious disease.

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