# proteinews

What's
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## Role of Proteins in Immune System

### Malnutrition and Immunodeficiency

Malnutrition is a serious health problem and is responsible for an enormous morbidity and mortality burden globally.[1,2] Around 45% of the global death in children <5 years of age is due to malnutrition.[2]

The relationship between malnutrition and death is mainly due to the resulting immunodeficiency and subsequently, greater susceptibility to infectious agents.[3] Malnutrition is the primary cause of immunodeficiency worldwide with infants, children, adolescents, and the elderly most affected.[4] It affects about 50% of the population in some impoverished communities.[3]

**Immunodeficiency is a hallmark of malnutrition.[2]**

Immune system needs its nutrition in order to function efficiently for protecting the body against infections. Infections are frequent and chronic in malnourished patients.[4]

Malnutrition increases susceptibility to infections while infections aggravate malnutrition by decreasing appetite, inducing catabolism, and increasing demand for nutrients. The increased susceptibility to infections may in part be caused by impairment of immune function by malnutrition (Figure 1).[5]

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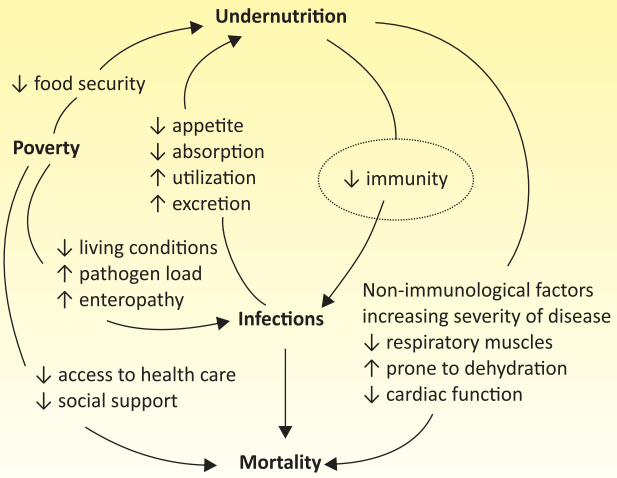
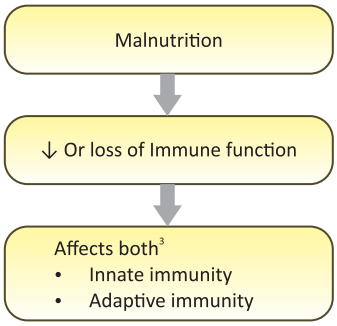
**Figure 1: Conceptual framework on the relationship between malnutrition, infections and poverty**




Malnutrition results in

- Haematopoiesis, anaemia, and leucopenia.
- Severe reduction in bone marrow.
- Significant decrease production of IL-6 and TNF-α by bone marrow cells.[3]


- Significant impairments of cell-mediated immunity, antibody concentrations, phagocyte function, complement system, and cytokine production.[4]

## Protein Energy Malnutrition

Protein energy malnutrition is the most common form of malnutrition affecting about 800 million people worldwide, including over 150 million children <5 years of age mostly in developing countries.[1]

Immunodeficiency due to protein energy malnutrition (PEM)

- Increases frequency and severity of infection
- Thymus atrophy
- Wasting of peripheral lymphoid tissue, with subsequent impairment of immune responses[6]
- Increases malaria morbidity and mortality in humans
- Increases M. tuberculosis infection[3]
- 2 fold decrease in the memory CD8 compartment
- Decrease in total lymphocyte numbers
- Dietary protein intake is critical for the maintenance of a functional CD8 memory pool. Thus, increase in protein intake can improve vaccine efficacy in malnourished individuals and decrease susceptibility to infections in chronically infected malnourished patients.[7]

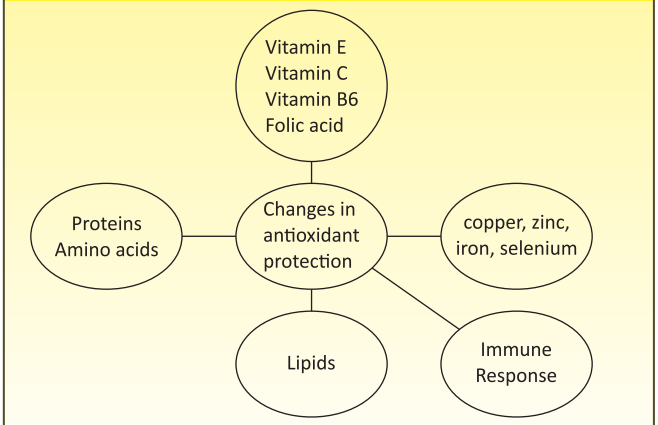
## Effects of nutrition: Macro- and Micronutrients on immune system

Malnutrition breaks down the immune functions by overwhelming the immune system. The factors that break down the immune functions are either deficient intake of macro-nutrients (fat, carbohydrate, protein) or micronutrients like vitamins and minerals. The nutrients which support and stimulate the immune system are called "Immuno nutritional elements" (Figure 2).[8]

Worldwide, around 6 million children die each year due to infections caused by the breakdown of immune system due to malnutrition.[8]

Both macro and micronutrients are essential in DNA, RNA and protein synthesis and development of immune

**Figure 2 : Immuno nutritional elements and Immune response**



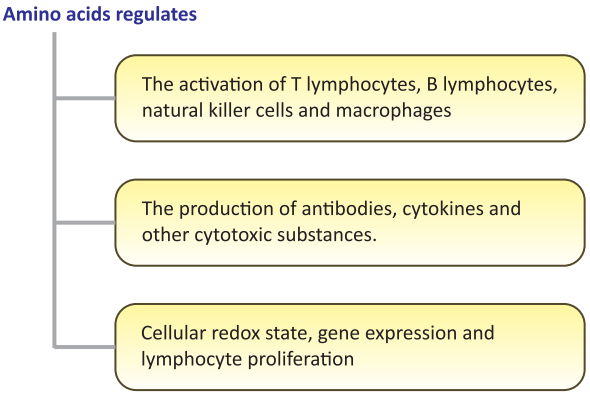

system.[9] Deficiency of single nutrient also results in altered immune responses and is observed even in the mild deficiency state.[10] Nutritional deficiency is commonly associated with impaired immune responses, particularly cell-mediated immunity, cytokine production, secretory antibody response and affinity.[9]

In order to reduce the risks of diseases and stay healthy, natural defence system or immunity of the body should be strengthen. To keep the immune system strong, the protein consumption should be adequate.[8]

Proteins make up the frame work of cells and also for the body defence systems, enzymes, and hormones. Most of the immune mechanisms depend on production of active protein compounds or cell replication.[8] Thus, proteins or amino acid plays an essential role in strengthening the immune system.

## Roles of amino acids in immune function

Dietary supplementation with amino acids enhances the immune status in humans with malnutrition and infectious disease thereby, reducing morbidity and mortality. Arginine, glutamine and cysteine are some of the amino acids which are known to enhance the immunity.[11]




### Arginine

- Arginine which improves the immune parameters during physiological stress.
- Immune enhancing diets including arginine were beneficial in moderate to severely malnourished patients undergoing gastrointestinal surgery and traumatic patients.[10]
- It enables normalization of T-cell response after serious surgical procedures and traumas.
- It enhances lymphocytic progress and phagocytosis, and speeds up the wound healing.[8]
- Supplementation enhances immune function in various models of immunological challenges.[11]

### Glutamate[11]

- Has versatile roles in the metabolism and function of leucocytes.
- Substrate for the synthesis of γ-aminobutyrate (GABA) which is present in both lymphocytes and macrophages.
- Plays an important role in the removal of oxidants and regulation of the immune response as it is a precursor for glutathione synthesis.
- It is necessary for maintaining an optimal immune status under conditions of immunosuppression.

**Glutamine**

It is the most freely amino acid in blood. Besides it is an important nutrient for prolific cells like blood cells.[8]

It is a critical nutrient for maintenance of the intestinal immune system and secretory IgA synthesis. It improves the immune response either by direct effect on lymphocyte proliferation or by acting indirectly on the antioxidant status. Any decrease in the availability of glutamine to lymphocyte decreases their rate of proliferation and their ability for rapid response to immune challenge.[10]

Role of glutamine in the immune system[11]

- Proliferation of lymphocytes in response to stimulation by T-cell mitogens and activation of protein kinase C.
- Prevent apoptosis, stimulate cell growth and promotes antibody production in lymphocytes.
- At or near physiological levels in plasma, glutamine modulates the production of cytokines by monocytes and macrophages.
- Influences the expression of various genes related to
  - Intercellular interactions
  - Production of cytokines by T lymphocytes.
  - Phagocytosis of immunoglobulin G or complement-opsonised particles
  - Antigen presentation
  - Opsonisation of human monocytes

Supplementing glutamine to patients after bone marrow transplant results in an increase in the number of lymphocyte, T-lymphocyte, CD4+ and CD8+.[8]

A randomised, double-blind study with 28 patients undergoing major abdominal surgery reported that pre-operative glutamine supplementation via TPN

- Improved nitrogen balance
- Increased lymphocyte function and augmented leukotriene production by neutrophils
- Reduced the incidence of infection and shortened hospital stay

Thus, a reduced availability of glutamine can increase the susceptibility of humans to infectious diseases by impairing immune function.[11] Glutamine, taurine, cysteine and arginine also enhances the immune response in critically ill patients.[10]

**Casein**

Caseins is the major proteins in milk composed of α-, ß-, and κ -caseins, each of which is important for nutritional value.[12] It is a principal source of amino acids.[13] Casein promote the release of cytokines, also linked to the regulation of haematopoiesis and immune response and inhibit the proliferation and induce the differentiation of leukaemia cells.[12] Bovine-casein significantly enhances interleukin-1 production.[13]

One of the study reported by Haq et al reported that A1-like variants of ß- casein had pro-inflammatory effects in the gut by

- Increasing the levels of inflammatory markers (myeloperoxidase, monocyte chemotactic protein-1, and interleukin-4) and immunoglobulins,
- Enhancing leukocyte infiltration and Toll-like receptor expression.[14]

The digestive process of caseins leads to the release of bioactive peptides which controls the expression of genes that exert epigenetic control by activating the immune response by serving as agonists or antagonists of opioid receptors. Later by binding to opioid receptor they block the nuclear factor κ-beta, increase the redox potential, and reduce oxidative stress and pro-inflammatory agents that favours an antioxidant and anti-inflammatory environment.

Caseins, both in complete and in fragment form produced by their enzymatic degradation enhances the different aspects of the immune system, such as

the

- Proliferation of lymphocytes
- Generation of antibodies.

Casein also regulate normal haematopoiesis via cytokine secretion, thereby inducing differentiation and enhancing proliferation.[12]

A tripeptide from κ-casein significantly increased the proliferation of human peripheral blood lymphocytes.[15] K-casein can suppress IgE mediated hypersensitivity responses by inhibiting histamine release.[10]

Oral use of the casein phosphopeptide is beneficial for the enhancement of mucosal immunity. Casein phosphopeptides can be used in enteral diets as an immunostimulator to enhance mucosal immunity and host defense.[13]

**Role of other amino acids in the immune system[11]**

| Amino acid | Role |
|---|---|
| Tryptophan (Serotonin, melatonin and N-acetylserotonin) | Enhances host immunity by –<br>• Inhibiting production of superoxide<br>• Scavenging free radicals<br>• Attenuating production of TNFα |
| Proline | Crucial for wound healing and injury recovery mediated by immune cells |
| Histidine | • Deficiency → decreases plasma concentrations of proteins → impairs the immune response.<br>• Supplementation can boost immune function, particularly in the skin. |
| Glycine | • A potent antioxidant, scavenging free radicals.<br>• Essential for proliferation and anti-oxidative defence of leucocytes.<br>• Novel anti-inflammatory, immunomodulatory and cytoprotective nutrient. |
| Asparagine | Has a significant role in immune function. |
| Alanine | • Influences immune system as it is a major substrate for leucocytes energy (glucose).<br>• Augmented antibody production in B-lymphocyte hybridoma. |
| Aspartate | • Has versatile roles in the metabolism and function of leucocytes.<br>• Crucial for the proliferation of lymphocytes. |

**Malnutrition is one of primary causes of immune deficiency which leads to various diseases and infections. Macro and micronutrients plays an essential for strong immune system. Various minerals and vitamins along with proteins and amino acids play a central role in normal immune functioning. Most of the components of immune system comprises of various proteins and amino acids. Casein, protein and amino acid like arginine and glutamine are vital for strengthening immune system and fighting various infections to stay healthy.**

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