# Forgotten Root: Nurturing Gut Flora for Optimal Host Immunity

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**Abstract**

*Immune system is a host defense system which protects the body from invading pathogens. When body is exposed to non-self-pathogens, this system activates innate or adaptive immunity by activating its physical, chemical and cellular mechanisms. Defense system functions optimally when there is an adequate supply of macro-micro-nutrients, and vitamins which strengthen the host immune response against foreign invaders. Gut flora is another indispensable entity that strengthens relationship between immunity and nutrition. This article outlines the role of nutrients and healthy gut flora in strengthening host immune system. It sensitises the clinicians to recommend appropriate nutrition in every prescription and to strike a balance between destruction of pathogens and retention of normal gut flora.*

Key words: Host immunity, nutritional deficiency, intestinal/gut flora, gut environment

Immune system is a vital system performing a highly vigilant function for the protection of our body from the invasion of pathogenic microbes. It executes an intellectual function of the cell through distinguishing self from non-self (Chapline, 2010). This system is programmed in itself not only to fight against the external threats but also to recognise and respond to threats that pop up internally (Paul, 2017). Most of the times, its function goes invisibly. However, it also produces signs while it is fighting hard to maintain body's homeostasis (Lorrie, 2009). Like any other system of body, immune system also requires adequate nutrition for functioning optimally.

Primarily, it procures nutrients from exogenous sources i.e. diet but in times of inadequate dietary sources, it utilises body's endogenous sources of nutrients (Childs et al, 2019). Competency of immune system largely depends on well balanced nutrition whilst nutritional deficiency results in impaired immune function (Maggini et al, 2018). Furthermore, the role of other important factors such as presence of infection or age of onset of nutritional deprivation cannot be overlooked (Chandra et al, 1986). This article elaborates the role of diet on host immune function by emphasising interlinks among nutrition, gut environment and host immunity.

**Immune System - Overview**

Immune system is an amazing network of cell, tissue and organ which communicate together to pass information back and forth to keep a surveillance to all body parts (USD HSS, 2003; Nicholson, 2016). Immune system is a defense system which protects the body from invading pathogens. When body is exposed to non-self-pathogens, the first line of defense i.e. innate immunity gets into action by activating its physical, chemical and cellular mechanisms (Marshall et al, 2018). Innate immune system consists of macrophages and neutrophils which interact each other to initiate phagocytic activity against foreign invaders (Huaang et al, 2018; Kumar et al, 2018). The second type of immune response is named adaptive immunity which is initiated against specific organisms by activating the clonal expansion of T and B lymphocytes (Nicholson, 2016).

These cells are originated from bone marrow and inhabit in lymphoid organs such as thymus, lymph node and spleen. Few of the pluripotent cells in the bone marrow become progenitor cells which travel to thymus via blood where they mature as a functional T cells. Then the matured T cells move from the thymus to different locations in the body depending upon the type of pathogen (Alberts et al, 2002; Cano et al, 2013). B cells are also produced by bone marrow and contribute a part of the adaptive immune response. Both B and T lymphocytes have a specific antigen to identify specific immune response. Immunoglobulin is produced by stimulation of B lymphocyte whereas T helper and T suppressor cells control the immune response and another cytotoxic T cells breakdown infected cell. Although the activation of immune response

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results in inflammation and damage to the tissues, the immune system itself brings the whole entity to an end.4

**Role of Macro and Micronutrient in Host Immunity**

Nutrition plays a vital role in strengthening body's immune system. Nutrients such as macro, micro nutrients, and vitamins strengthen the host immune response against foreign invaders and make the defense system competent Daily intake of micro nutrients such as vitamin A, C, D, E, B2, B6, B12, folic acid, iron, selenium and zinc is required for effective and integrated immune response. Amongst all micronutrients, Vitamin A, D and Zinc are found to be the strongest micronutrients to support immune function (Table 1).

**Protein:** Protein plays a crucial role in the immune function because immune system greatly depends on protein-based protectors such as antibodies, T-lymphocytes, leukocytes and a group of helper cells and related compounds.

**Vitamin A:** Vitamin A is a fat soluble vitamin acting as a key micronutrient for the growth, development and function of immune system, especially for the development of white blood cells. It has antioxidant and anti-inflammatory properties that play a vital role in immune function. Vitamin A is available in two forms: alpha carotene (preformed vitamin A) and beta carotene (preformed vitamin A) and gets converted into Retinol. While carotenes are responsible for lowering CRP levels, retinol is attributed to the maintenance of first line of defense through skin and mucosal lining in airway, digestive and urinary system. Deficiency of vitamin A impairs innate immunity and delay regeneration of mucosal barrier due to destruction of pathogens. Moreover, it reduces the function of macrophages, neutrophils and natural killer cells and it ultimately leads to increased morbidity and mortality.

**Vitamin C:** Vitamin C is a co-factor for various enzyme engage in biosynthesis of collagen, carnitine and neurotransmitters and a significant antioxidant which prevents protein, lipid and carbohydrate from damage by free radicals during metabolism and others toxic substances. It is crucial component for the function of innate and adaptive immunity system in combination of neutrophils to stimulate chemotaxis, phagocytosis reaction which destroy the pathogens. It is also needed in apoptosis function and has an impact on infection and degree of inflammation. It is also reported that deficiency of Vitamin C impairs the resistance against pathogens.

**Vitamin D:** The immune modulatory response of vitamin D takes place in two ways; antimicrobial activity as a part of innate immunity and T and B lymphocyte function of adaptive immunity. Immunologic effect of vitamin D has been found to be responsible for maintaining tolerance and for promoting protective immunity. Immune cells are capacitated to synthesize and respond to Calcidiol, an active form of vitamin D and vitamin D executes its paracrine and autocrine mechanism within the milieu of immune system. Macrophages and dendritic cells are able to respond to 25-hydroxyvitamin D, the major circulating vitamin D metabolite. 1,25 D promotes antibacterial response with help of antibacterial proteins and promoting autophagosome activity. Hence, inadequate intake of vitamin D may hamper the immune response in humans, and further leads to infectious disease and immune disorder.

**Vitamin E:** Vitamin E is a fat-soluble antioxidant; its substantial amount is available in immune cells as compared to other cells in blood. Vitamin E effectively modulates immune function. Vitamin E deficiency is extremely rare in humans and dietary deficiency does not attribute to this deficiency state. However, conditions such as intestinal malabsorption syndrome that tends to cause vitamin E deficiency must be considered as an inevitable component in the immunologic environment.

Besides these elements, magnesium, vitamin E, zinc and selenium also play key roles in the functional activity of immune system (Table 1).

**Magnesium:** This mineral has a strong association with immune system. It interacts with immune system for cell transformation, cell cycle regulation and effect of enzymatic and hormonal action. It also plays a role to keep up ionic gradients, cellular and tissue integrity, ATP production and activation, DNA, RNA, protein synthesis in body and also for various enzymatic activities. Magnesium deficiency occurs due to its loss from gastrointestinal tract or from urinary system. Patients with magnesium deficiency may have neuromuscular hyperexcitability, cardiac arrthymias and hypocalcemia.

**Table 1: Summary about role of nutrition in host immune system**

| Nutrients | Role in host immune system |
|---|---|
| Protein<br>Vitamin A<br>Vitamin C<br>Vitamin D<br>Vitamin E<br>Magnesium<br>Selenium<br>Zinc | • Basis for Antibodies, T-lymphocyte and a group helper cells-Protein based<br>• Maturation of white blood cells, lowering CRP levels and antioxidant<br>• Stimulation of chemotaxis, phagocytosis reaction and apoptosis<br>• Paracrine and autocrine mechanism in host immune system, Autophagosome activity<br>• Antioxidant<br>• Cell transformation and regulation, ATP production and Protein synthesis<br>• Regulation of oxidative stress in cells<br>• Antibody production, cellular proliferation and epithelial barrier |

**Selenium:** Alike other micronutrient, selenium also has a potent effect in both adaptive and innate immunity. It integrates with selenoproteins in managing oxidative stress in all tissues. Dietary selenium deficiency affects growth and development of a person and it also has a role in cardiovascular disease, infertility, myodegenerative disease and cognitive impairment.

**Zinc:** Zinc holds a central position in immune system through their involvement in proper functioning of both innate and adaptive immunity such as antibody production, proliferation of cellular activity and epithelial barrier. Zinc deficiency affects proliferation, maturation and survival of T and B lymphocytes, monocyte and polymorphonuclear antibody formation especially immunoglobulin G. Phagocytosis and cytokine production are also disturbed due to zinc deficiency. In addition it may incapacitate innate and adaptive immunity, cause thymic atrophy, lymphopenia and immune compromised state and ultimately leads to increase inflammation.

**Intestinal or Gut Flora – An Actor behind the Screen**

Intestinal flora or gut flora, a collection of body supporting microbes is formed by complex microorganism and are known as "indigenous microbiota". Normally human body consists of 1013 cell and nurture about 1014 bacteria. In a digestive tract, a limited number of bacteria exist in stomach (below 103g) due to acidity. The concentration enhances in small bowel (104 ml contents), to 106 –107 ml at the ileocecal region wherein colon has dense population of bacteria (1011-1012/g). Certain factors influence the formation of flora such as temperature, pH, water, oxygen whereas diet has an impact on intestinal flora.

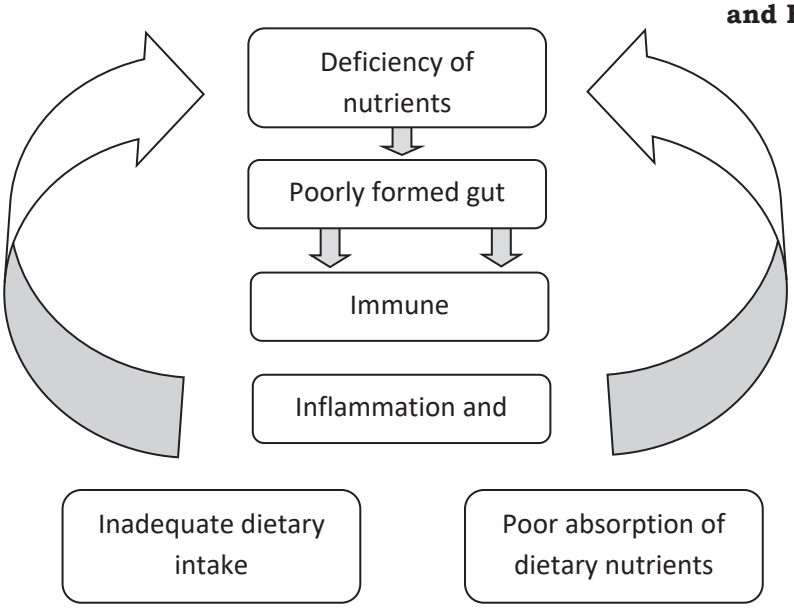


**Figure 1: Interplay between nutrition, gut environment and host immunity**

**Role of Gut Flora in Immunity**

Dietary intake of protein, fat, carbohydrate and fibre-rich diet affect different types of microbiota in the intestine. Colonic microbial growth depends upon the release of nitrogen from dietary proteins and plays a significant role in incorporation of carbohydrate and production of short chain fatty acid. Reduced intake of fibre-rich diet may cause low capacity of colonic mucosal barrier that make the host more susceptible to pathogen and inflammation.

On one side, gut flora is affected by nutritional intake, the other side a healthy gut flora has an important role in vitamin production, stimulation of immune system and intestinal movement regulation and are responsible for digestion of metabolised substrates. This demonstrates the coordinated effort between digestive system and gut microbiota in the effective utilisation of carbohydrate. The metabolic activity that takes place within the gut environment ensures production of bioactive compounds that can govern the health of a person.

Gut microbiota is essential part of gastro intestinal ecosystem which regulates homeostasis of human immune system and prevent unusual immune responses. Gut microbiota is involved in development of CD4+ T cell which is an important part of adaptive immune system. Microbiota enhances the growth of intestinal epithelial cell and development of mucosal immunity which facilitates in optimal macro and micronutrient absorption. Intestinal flora is also good source of vitamin B complex and vitamin K, and a strong link of gut bacteria in supply of triglycerides which is a major source of energy during serious condition and contributes to nitrogen balance.

**Interplay between Nutrition, Gut Environment and Host Immunity**

There is a complex interplay that takes place among three entities i.e. nutrition, gut environment and immunity is illustrated in the Figure 1. Recent research has suggested that diet exerts a greater influence on the gut's microbiota. Carbohydrates that are found in dietary fibre are highly involved in shaping microbiota when it becomes accessible to microbiota. Diet rapidly and reproducibly alters the human gut microbiome. Along way, a number of vitamins and minerals are also involved in the development and homeostasis of gut microbiome. Deficiency of these micro nutrients alters the immune function by perturbing innate and adaptive immune response leading to disruption of homeostasis. Inadequate intake of dietary nutrients compromises the immune mechanisms by allowing the pathogenic organisms into the

body and results in infection. The state of immune compromise may also cause poor absorption of digested nutrients contributing to malnourishment. Therefore, immune system requires vitamin A, iron and zinc, these nutrient improve the immune function in malnourished children and reduce children morbidity and mortality related to infectious disease.

**Nurture of Gut Flora**

Diet keeps up a major effect on the gut flora. Availability of accessible carbohydrate which is available in dietary fiber is an essential part for shaping of the colonic gut flora. Gut flora alteration happens with use of excessive plant-and animal-based diet, intestinal mucus is a source of carbohydrate to the gut flora. Throughout GI tract mucus is present which is thickest in colon and intervene host-gut flora relationship. The shaping of the gut flora depends upon mucus and mucin glyosylation which permits the most effective microbial species to intervene host health. Several studies result showed that impact of dietary Protein, fats, digestible and non-digestible carbohydrates, probiotics, and polyphenols all influence the modification of gut flora. Moreover, immune system also plays an important role for shaping gut flora.

## Conclusion

There is a complex, yet strong links functioning among nutrition, gut flora and immunity. Adequate nutrition and healthy intestinal flora determine the efficiency of host immune function. The nutritional demands of the body during non-normal states are always higher than normal requirements. Hence, clinicians must recommend appropriate nutrition in every prescription and must ensure appropriate strategies to retain the intestinal flora in the treatment process. In countries like India, discovering the simple and cost-effective nutritional measures is of greater scope in optimising host immunity in health as well as in illness.

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