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# Can food increase or decrease immunity? Article review

**Islam khalid kamal [1*], Atyaf Talal Mahmood [2], Alaa younis Al-Hamadany [3]**
[1, 2] Clinical Laboratory Sciences Department, College of Pharmacy, University of Mosul, Iraq
[3] Department of Anesthesia Techniques, Medical Techniques Institute, Northern Techniques University, Iraq

* Corresponding Author: **Islam khalid kamal**

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**Abstract**
This study searches at how nutrition, inflammation, and immune function are all closely related. It emphasizes how important macro- and micronutrients, phytochemicals, and dietary patterns are in regulating both innate and adaptive immune responses. Especially in areas with high rates of malnutrition, it highlights dietary inadequacies as a major factor in weakened immune systems and heightened vulnerability to infections. On the other hand, it talks about how wealthy nations deal with health issues brought on by a lack of nutrients in the face of high calorie intake. The study highlights the importance of certain nutrients, such as zinc, selenium, vitamins A, C, D, and E, in supporting immunological function while warning against the negative consequences of nutritional overconsumption. In contrast to Western diets, which are known to promote inflammation, it explores how dietary patterns like plant-based and Mediterranean diets might improve immune function. The effects of chronic inflammation brought on by obesity and starvation on immunological responses are also examined, as are the possible dangers of dietary additives. As a way to improve immunological resilience and prevent illness, the results indicate the need for tailored dietary treatments and emphasize the need of a well-balanced diet full of vital nutrients. Overall, this study urges more research on the importance of diet in preventing disease and enhancing health.

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## 1. Introduction

Nutrition has a profound impact on human health and the immune system. The innate immune system's inflammatory mechanisms are substantially modulated by nutrition, affecting disease development. The immune system eliminates antigens through innate and adaptive cells and antibodies 1. Research has focused on micro- and macronutrients, phytochemicals, and other nutrient-derived biocompounds as immune modulators. Nutrient-rich diets are essential for survival, cell proliferation, tissue development, growth, energy supply, and immune defense. Processed foods can negatively influence immunity. Nutritional deficiencies correlate with impaired immune responses and heightened susceptibility to infections. Malnutrition remains a major health problem in less developed regions, associated with higher morbidity and mortality from bacterial and parasitic infections. In contrast, developed countries often experience inadequate, low-nutrient diets combined with excess caloric intake 2.

Adequate nutrition is crucial for optimal immune cell function and effective pathogen responses. Activation of the immune system increases energy demand during infection, particularly with fever. Proper nutrition supports immune functions, facilitates rapid resolution of immune responses, and helps prevent chronic inflammation. When dietary intake is insufficient, nutrients can be mobilized from body stores. Micronutrients such as vitamin A, zinc, and amino acids like arginine have specific roles in immune development and maintenance 3. Under nutrition impairs immunity, with severity influenced by the extent of deficiency, nutrient interactions, presence of infection, and age.

Excessive intake of certain nutrients, notably iron, can also impair immunity, especially in malaria-endemic areas. Nutritional interventions address immune deficiencies and may enhance immune function to prevent infections and chronic diseases 4.

Nutrition is vital for the health and vigor of all living organisms. Dietary intake supplies nutrients essential for growth, cellular activities, tissue development, energy provision, and immune defense. The omnivorous human diet comprises animal and plant products that provide macronutrients (proteins, carbohydrates, fatty acids), micronutrients (vitamins, minerals, phytochemicals, antioxidants, probiotics), and dietary fiber, all fulfilling important biological functions. Nutritional immunology aims to elucidate how nutrients affect the immune system 1. Unhealthy diets or malnutrition characterized by macro- and micronutrient deficiencies can lead to ineffective immune responses and vulnerability to pathogens. Many diseases are associated with losses of essential nutrients, resulting in deficiencies. Nutrients can mediate both pro- and anti-inflammatory responses and modulate chronic inflammatory and autoimmune diseases. Nutrigenetics investigates nutrition as a target to prevent and reverse disease progression, striving to develop personalized dietary patterns that consider genetic predispositions influencing chronic diseases and the direct impact of food metabolites on gene expression 5.

## 2. Understanding Immunity

The human immune system is a combination of cells, tissues and organs that identify and attack dangerous microbes and substances. Protective immunity has two components: innate immunity and adaptive immunity. Innate immunity is the first line of defense and involves mechanisms that come into play immediately or within hours after an antigen's appearance in the body. Adaptive immunity is antigen-specific and develops only after the body's exposure to an antigen. Although innate and adaptive immunity have traditionally been viewed as separate, it is now widely recognized that their responses are totally integrated 6.

The ability to mount a protective immune response depends greatly on nutrition. Severe infections can result from deficiencies in nutrient intake and status, which compromise the immune system. Mild but widespread impairments of the immune system surrounding infections have been observed with inadequate intakes of some nutrients 7. Both macro- and micronutrients influence the two major components of the immune system, as well as the severity and duration of infections. Appropriate intake of key immune-enhancing nutrients can help maintain and improve immunity in the general population, enhance vaccination response, and contribute to the resolution and prevention of viral, bacterial, and parasitic infections 8.

### 2.1. Types of Immunity

The immune system protects the body from infections and harmful microorganisms. The primary types of immunity include innate, adaptive, humoral, and cellular immunity. Innate immunity provides an immediate nonspecific response to pathogens, while adaptive immunity represents a specific and more robust reaction upon re-exposure to the same pathogen. Humoral immunity relies on antibodies circulating in the serum, whereas cellular immunity depends on the activity of various immune cells, such as lymphocytes and phagocytes 9. The two main pathways of cellular immunity—general responses to pathogens and cytotoxic responses—aim to eliminate pathogenic microorganisms and cells infected by viruses. The functioning of humoral immunity involves neutralizing extracellular pathogens through antibodies secreted by B-lymphocytes. For the immune system to function effectively, a range of vitamins and trace elements is necessary; a deficiency in nutrients such as vitamins A, C, E, B6, B12, folic acid, as well as iron, selenium, and zinc can impair the immune response 10.

### 2.2. Factors Affecting Immune Response

Some individuals are extremely vulnerable to viral infections and severe symptoms, whereas others recover quickly or experience mild symptoms. A wide range of factors, including immune-related conditions, immunosuppressive drugs, age, and many other health issues, can significantly affect immune responses. Different age groups generally require different amounts of energy, macronutrients (carbohydrate, protein, and fat), and micronutrients that play an important role in influencing the immune response 8.

It is well known that elderly people are at greater risk of severe symptoms and mortality associated with covid-19 infection. Immune function deteriorates with ageing, a process known as immune senescence. Nutrition is one of the most important factors in maintaining immune function. Other factors, such as poor sanitation, poverty, and malnutrition, can cause immune deficiency, which results in increased susceptibility to infection and delayed recovery 11.

## 3. Role of Nutrition in Immune Health

Adequate and appropriate nutrition is required for all cells to function optimally, including immune cells. An activated immune system increases energy demand during infections, such as fever. Optimal nutrition supports immune functions by enabling immune cells to respond effectively against pathogens, resolve responses quickly, and avoid chronic inflammation. The immune system's energy and nutrient needs can be met through diet or body stores if dietary sources are inadequate 8. Some micronutrients, like vitamin A and zinc, are essential for immune cell development and function, while amino acids such as arginine are crucial for processes like nitric oxide production by macrophages. Under nutrition impairs immune function, whether from food shortages, malnutrition, or hospitalization 12. The severity of impairment depends on deficiency level, nutrient interactions, infection presence, and age. Excessive intake of some nutrients, like iron in malaria-endemic regions, can impair immune responses. Nutrition plays a role in treating immune deficiencies due to poor intake, and research continues into how specific nutrient interventions can boost immune function and prevent infections or inflammatory diseases 4.

### 3.1. Essential Nutrients for Immunity

Numerous nutrients are essential for the normal functioning of the immune response, including lipids, proteins, carbohydrates, fiber, vitamins, and minerals. Additionally, water, non-nutrient factors such as phytochemicals, and probiotic and/or prebiotic supplementation contribute to maintaining a healthy immune system. Immunity is particularly sensitive to deficiencies in zinc, iron, copper, selenium, and vitamins A, E, C, B6, and B12, and is directly affected by the quantity and quality of lipids, proteins, and carbohydrates in the diet 1. Inadequate intake of these constituents impairs many aspects of immune function and increases susceptibility to infections. Conversely, supplementing diets with selected specific nutrients above recommended dietary intake levels can enhance certain markers of immune function, particularly in subjects with suboptimal status. Infections, however, induce metabolic alterations that reduce levels of several nutrients important for immune function 87. During infections, both nutrient inadequacy and immune dysfunction increase morbidity and mortality, leading to a vicious cycle between nutritional deficiency and infection. Nutrition is therefore one of the most important factors influencing resistance to infection and affects all aspects of the immune response 8.

A wide variety of chemicals present in foods perform numerous functions other than simply offering calories for energy. Dietary lipids influence the immune response by affecting membrane fluidity, serving as precursors to eicosanoids, and modulating gene expression of cytokines and other mediators. High consumption of saturated fatty acids alters macrophage function and leads to the production of proinflammatory cytokines 13. In contrast, ω-3 polyunsaturated fatty acids exert anti-inflammatory effects. Various phytochemicals, such as carotenoids xanthophyll and carotenes, flavonoids, catechins, and curcumin, offer antioxidative and immunomodulation activities. High-protein diets can exacerbate the inflammatory response, while also playing a crucial role in building the immune system and facilitating infection recovery. Probiotic and/or prebiotic supplementation is often used for its immune modulatory effects in vulnerable populations. In addition to essential nutrients, these dietary components influence immune regulation 14.

### 3.2. Macronutrients and Immune Function

When a host is suffering from any severe disease, muscle protein is mobilized to provide precursor for acute-phase protein synthesis and the amino acids needed for cellular immune responses. Most amino acids are essential for cellular immunity, immunoglobulin synthesis, and lymphocyte activation and proliferation. Amino acid deprivation limits DNA and protein synthesis; therefore, the proper amino acid amount and composition are crucial for enhancing immune responses. Glutamine and arginine possess positive roles in immune processes 15.

Lipids affect immune responses in two ways: modulation of cellular membrane function and alterations in eicosanoid biosynthesis. Fatty acids can alter the function of cell membranes of lymphocytes, macrophages, and neutrophils. Arachidonic acid and its metabolites are involved in neutrophil chemotaxis and oxidative killing. Omega-3 fatty acids that replace arachidonic acid in cell membranes reduce the chemotactic ability of neutrophils as well as their oxidative killing. Lipid supplementation can counteract immunosuppressive effects of stress and the aging process 16.

## 4. Vitamins and Minerals

The role of nutrition in immune function is now recognised as largely supported; suboptimal nutritional status certainly can impair the immune response, ultimately affecting resistance to infection. Table 4 tabulates vitamins and minerals for which evidence suggests they can assist in reducing the risk of infection or its duration and in maintaining immune function. Functional markers of each micronutrient in the Table are broadly indicative of the respective micronutrient's roles within the immune system 17.

In addition to individual micronutrients, some multisubstance combinations have undergone evaluation with regard to immune function. The reported controlled trials in these areas, some double-blind, have featured combinations of five, six or over 20 micronutrients and other substances. Many include vitamin C, which has attracted substantial attention over many years. Table 5 summarises the outcomes of injury-related immune function studies in healthy volunteers after controlled supplementation with vitamin C alone or as part of a mixture. Several of the clinical studies relating to vitamin C and vitamin A are examined in more detail later in the review 18.

### 4.1. Vitamin C

Focusing on the nutritional impact on immune function, subsection 4.1 considers vitamin C. Adequate nutrition is essential to support the body's immune system and resistance to prevent pathogenic microorganism colonisation and infection. Micronutrient malnutrition impairs immune function, predisposing the individual to infection. Infection reciprocally impairs nutritional status by increasing requirements, reducing appetite, and impairing absorption. Immune function can be enhanced if a deficiency state is present by supplementation 19. Undernutrition increases susceptibility to infection, and although undernourished individuals may have an impaired immune response to some vaccination antigens, there is little evidence that supplementation improves vaccine efficacy. Several nutrients are involved in both innate and acquired immunity, but until relatively recently, the vitamin C immune connection was rarely mentioned in immunology textbooks. Although a large number of mechanistic studies show that vitamin C supports various cellular functions of both the innate and adaptive immune system, and that vitamin C deficiency results in impaired immunity and higher susceptibility to, and severity of infections, the role of vitamin C in immune function had not yet been reviewed systematically 20.

Vitamin C contributes to immune defence by supporting various cellular functions of the immune system. For example, vitamin C supports epithelial barrier function against pathogens and promotes the oxidant scavenging activity of the skin, thereby potentially protecting against environmental oxidative stress. Vitamin C accumulates in phagocytic cells, such as neutrophils, and can enhance chemotaxis, phagocytosis, generation of reactive oxygen species, and ultimately microbial killing. It is also involved in apoptosis and clearance of the spent neutrophils from sites of infection by macrophages, thereby decreasing necrosis/NETosis and potential tissue damage 1. The vitamin also supports differentiation and proliferation of B- and T-cells, probably due to its gene-regulating effects during their maturation induced by increased demand for vitamin C. Infections significantly impact vitamin C levels, with depletion of plasma and leukocyte vitamin C noted in both the common cold and more serious conditions such as pneumonia and sepsis. Moreover, infection susceptibility is increased when vitamin C status is inadequate. Supplementation in individuals with low or depleted vitamin C status generally appears to both prevent and treat respiratory and systemic infections 21.

### 4.2. Vitamin D

Vitamin D, a steroid hormone, was first recognized for its role in bone and mineral homeostasis. Evidence pointing to its immunomodulatory properties initially derived from the interrelationship between hypovitaminosis D and susceptibly to tuberculous infection. In addition to stimulating 1α-hydroxylase expression in the kidney, parathyroid hormone induces its expression in human macrophages. Stimulation of Toll-like receptors on macrophages results in enhanced expression of both 1α-hydroxylase and the vitamin D receptor, an effect that can be augmented with supplementation with 25(OH)D. The subsequent increase in the synthesis of 1,25(OH)2D enhances the expression of cathelicidins and ß-defensins, antimicrobial peptides with activity against M. tuberculosis 22.

Various forms of vitamin D are present in the diet; vitamin D2 (ergocalciferol), found in plants such as fungi and yeast, and vitamin D3 (cholecalciferol), produced endogenously in the skin and found in some foods such as egg yolk and fatty fish. Activated vitamin D, 1,25(OH)2D, is a secosteroid hormone that plays essential roles in bone and calcium metabolism, cell proliferation and differentiation, and immune system regulation. The main circulating form, 25(OH)D, is used clinically to assess vitamin D status, with deficiency generally defined as 25(OH)D < 20 nmol/L and insufficiency as 20–30 nmol/L. The dietary reference intake (DRI) for vitamin D established by the Institute of Medicine is 15 µg/day for adults; the upper limit is 100 µg/day for this age group 23.

### 4.3. Zinc

Zinc is necessary at all levels of the immune system, and it is critical for normal development and function of cells mediating nonspecific immunity, such as neutrophils and NK cells. The T-cell function is particularly sensitive to marginal zinc deficiency. Zinc regulates the balance between Th1- and Th2-cells, the production of Th1- and Th2-cytokines, and the generation of Treg cells. The immunological functions of zinc are probably involved in the pathogenetic processes in many chronic diseases, such as atherosclerosis, diabetes, and rheumatoid arthritis. Zinc modulates intracellular signaling cascades in innate and adaptive immune cells. As a signaling molecule, it modulates the activity of thymulin and the maintenance of thymic structure 24. Elderly subjects with low serum zinc concentrations had significantly reduced NK cytotoxicity compared with those with normal zinc concentrations, and NK cytotoxicity correlated positively with serum zinc and serum thymulin activities. Thymulin activity significantly correlated with serum zinc concentrations, supporting the view that zinc deficiency impairs thymic function. Zinc supplementation is effective in decreasing incidence rate, severity, and duration of infectious diseases in zinc-deficient populations 25.

The association between zinc deficiency and decreased immune function was underlined in a study performed in elderly subjects. In a subset of Basque elderly women, the association between the dietary intake of these nutrients and the natural killer cell cytotoxicity (NKCC) was evaluated. The results showed a lack of intake of zinc, selenium, and vitamin A. Vitamin A intake significantly correlated with the count of total leukocytes, while zinc intake correlated positively with CD19+ B cells and with NKCC in elderly in good health. Nevertheless, only the supplementation with selenium was able to improve NKCC after 6 months. It may be concluded that a regular and balanced intake of antioxidant vitamins and trace elements is necessary for maintaining the immune surveillance mechanism 26.

### 4.4. Selenium

The trace element selenium is fundamental for the correct functioning of the immune system as it acts as an antioxidant and plays vital roles in inflammation and immunity. Selenium is a key component of selenoproteins and selenoenzymes, including part of the catalytic center of glutathione peroxidase, responsible for antioxidant activity. It also participates in the metabolism of thyroid hormones by reducing their inactive forms to active ones and is involved in regulating the inflammatory response and in redox processes 27.

Adequate selenium status maintains a balanced Th1/Th2 immune response ratio and promotes effective cytotoxic T-cell and natural killer cell activity. Selenium deficiency can impair both innate and acquired immunity and is linked to increased virulence of certain viral strains (e.g., coxsackievirus and influenza virus) due to the generation of mutations within hosts with low selenium levels. Information on the functional consequences of selenium deficiency for human immunity remains limited. Although selenium deficiency is rare in Europe, selenium-poor regions do exist and the worldwide selenium distribution in food is heterogeneous 28.

## 5. The Impact of Diet on Immune Modulation

The Impact of Diet on Immune Modulation

Although the effects of nutrition on immunity have long been recognized, the extent to which diet can modulate the immune response is a relatively recent focus of research. Unlike macro- and micronutrient deficiencies, which cause immunosuppression, many dietary components can indeed modulate the immune system toward a more optimal response. Some of these components have been extensively researched, others less so, yet their actions are now better understood 29.

The overall effect of a particular food component on the immune system likely results from the additive or synergistic action of multiple components in the food. Because of the complexity of the immune system, relatively few *in vivo* studies have been able to pinpoint the actions and interactions of individual nutrients or food components. However, a more comprehensive understanding is emerging, now enhanced by new technologies such as transcriptomics, proteomics, and metabolomics. Recent reviews have provided a broader perspective on other modulators of inflammation and immunity, including the crucial role played by the gut microbiota 30.

### 5.1. Antioxidants and Immune Support

Antioxidants such as vitamin C, vitamin E, and zinc are critical for maintaining immune health. Vitamin C supports epithelial barrier function and enhances the ability of phagocytes to kill pathogens. It also accumulates in various immune cells and supports functions including neutrophil migration to infection sites, phagocytosis, oxidative burst, and apoptosis. Vitamin E maintains the integrity of the respiratory epithelial barrier and acts as an antioxidant protecting immune cells from free-radical damage 31. Zinc is vital for the development, differentiation, and function of both innate and adaptive immune cells. Deficiencies in either vitamins C or E can reduce the functions osf innate immune cells, including phagocytosis, oxidative burst, and natural killer-cell cytotoxicity, as well as adaptive immunity involving T and B lymphocytes. Similarly, inadequate zinc levels disrupt cellular signaling in neutrophils and monocytes and can lead to lymphopenia and lymphoid atrophy 32.

Nutritional factors have a profound influence on immunity. Both malnutrition and overnutrition impair immune cell metabolism and function, and subsequently affect the capacity to mount an effective immune response. Although protein is the key nutrient in supporting immune functions, some micronutrients, such as vitamins A, C, and D and zinc, are required to maintain the immune-cell metabolism needed for an effective response to harmful stimuli 33.

### 5.2. Probiotics and Gut Health

Probiotics and gut health contribute to the impact of nutrition on immune function.

The large dynamic metabolic interface of the gut exposes the body to massive numbers of commensal and pathogenic microorganisms, and profuse numbers of immunoregulatory and immune-activated cells, with which the probiotic lactic acid bacteria (LAB) interact 34. Animal models of inflammatory bowel disease suggest a role for probiotics in improving intestinal permeability and in reducing hyper-activation of the mucosal immune system in inflammatory bowel disease, primarily through decreasing IL-1β production. Probiotics are also reported to have a role in human studies in ameliorating the immunopathology seen in allergy and chronic inflammation, through increased levels of IL-10 and TGF-β, both of which regulate the activity of the proinflammatory Th1 cell population 35.

## 6. Food Patterns and Immune Function

Concepts of diet have evolved to encompass not only individual food items but also various dietary patterns. The Mediterranean diet is among the most studied; it is characterized principally by olive oil that supplies ample monounsaturated fatty acids and antioxidants, a relatively high intake of fruit and vegetables, a moderate-to-high intake of legumes and fish, a low intake of meat and dairy products and a moderate intake of alcohol (primarily wine) during meals 2. Vegetarian diets (including vegan diets) and palaeolithic diets have also received considerable attention. The specific influence of these patterns on immune function remains unclear. Other identified food patterns—high in fat or carbohydrate, exclusion of certain food groups, low FODMAP diet—predictably influence immune parameters. In addition to specific nutrients, other food components, including probiotics and phytochemicals, affect immune function 4. Of interest in relation to the central role of dietary fibre in supplying substrate to the gut microbiota is that its intake is suboptimal in many countries.

### 6.1. Mediterranean Diet

Throughout centuries, the Mediterranean Diet (MD) has been highly debated because of its impact on human health. Some evidence suggests that it could promote the amelioration of some diseases 36. Generally applied to two populations, one of which proceeded to follow a pro-inflammatory-life-style, MD was studied in the context of elderly subjects and the incoming effects of immune age-associated changes 37. Starting from low grade inflammation, to influenza vaccination response and the ex-vivo evaluation of innate immune function, all parameters seemed to be modulated by MD integration remarkably indicating its capability to reactivate more adequate immune defense mechanisms. In particular, aging-related parameters got a boost from this food style, a major contributor to the rejuvenated immune system. Although all other demographic and life-style-outcome variables were taken into consideration and were comparable between experimental clusters, anything but the nutritional habit assigned was able to focus and orientate the immunological investigation onto MD 38.

Research addressing immune alteration caused by aging identified a multidimensional process influenced by changing microenvironments and the interaction of immune and non-immune cells during extrinsic factors infiltration. The acronym inflammaging thus emerged to describe this phenomenon, and was found to be a major determinant of frailty and disease onset in humans. Representing a sterile, low-grade, and chronic inflammation, inflammaging resulted from the combination of endogenous damage-associated molecular pattern molecules (DAMPs) triggering an out of control pro-inflammatory status 39.

Therefore, inflammaging became a target of anti-aging strategies, including MD. Some evidence underlined the positive effect of vitamins and polyphenols contained in the Mediterranean formula. An experimental approach undertaken to study the immunomodulatory properties of MD prior to the onset of immune dysfunction came to light inside the NU-AGE project, recruiting 120 elderly individuals living independently in the community in the UK. The study conducted a one-year intervention involving a Mediterranean-like dietary pattern coupled with adequate vitamin D3 supplements, and assessed the impact on immune cells. As already known, nutrients are involved in the cascade of immune activation representing glycansuited energy and substrates. As suggested by the study results, they support the enhancement of immune capacity throughout pre-allocated nutrients to face future challenges 40.

### 6.2. Plant-Based Diets

Plant-based diets have been shown to have a positive impact on immune function. Nutritional components of abused drugs and addiction alter key host immune pathways, including inflammatory effectors and genes controlling processing of major histocompatibility complex (MHC) molecules, antigen presentation, and immune signaling 41.

Plant-based diets offer innovative interventions to influence systemic immunity through food. Dietary fiber—a characteristic component of plant-based eating—feeds the gut microbiome and promotes the production of several metabolites that regulate host immunity and inflammation 2. The diversity of plant-derived fiber has the potential to influence the spectrum of microbes and microbial products that, in turn, regulate immune cell generation or function. Plant-based diets also have high levels of anti-inflammatory and anti-oxidant nutrients such as polyphenols, antioxidants, carotenoids, and n3-rich fatty acids. Because of the difficulties in designing and conducting definitive placebo-controlled dietary intervention studies, much of the evidence for a protective effect of a plant-based diet on immune health is indirect but compelling; extensive epidemiological and experimental investigations have linked plant-based nutrients to the benefits reported in epidemiologic studies 42.

### 6.3. Western Diet

Diet has a substantial influence on the composition of the microbiome and systemic immune function. The Western pattern diet, characterised by high intakes of refined sugars, refined and processed grains, and high-fat dairy products, alongside an over-abundance of total fat and saturated fats, contributes to a pro-inflammatory state and exerts negative effects on immune function 2.

Intake of saturated fatty acids, particularly palmitic acid commonly found in palm oil and dairy products, can promote pro-inflammatory gene expression and TLR signalling. Conversely, saturated fatty acids such as lauric and capric acids, present in coconut oil and milk fats, foster anti-inflammatory effects and serve anti-microbial roles. Intake of trans fatty acids elevates cardiovascular risk and also aggravates inflammatory responses 4. Studies demonstrate that excessive consumption of the Western diet increases LPS levels in plasma in mice. This induces a chronic low-grade inflammatory response and heightened susceptibility to infection. The immunometabolic alterations induced by the Western diet can reactivate latent viral infections, such as Kaposi's sarcoma-associated herpesvirus, thereby increasing viral gene expression and production of infectious particles 43.

## 7. The Role of Inflammation

The role of inflammation in immune function is highly pertinent and becomes particularly evident when nutrition and immunity are considered. Inflammation, a complex process pivotal to an organism’s survival and homeostasis, originates as part of innate immunity and is normally self-limiting: it resolves as the immune system clears an insult. Before its restoration of homeostasis, inflammation initiates tissue repair, removes damaging stimuli, and restores the host to health 44. These functions are primarily accomplished through the migration of granulocytes and monocytes into affected tissues. Innate immune cells then, in turn, produce mediators that recruit nonimmune cells, such as endothelial cells and fibroblasts, as well as later-appearing adaptive immune cells, to the site of inflammation. When inflammation persists and fails to resolve, it becomes chronic, contributing to a host of diseases, including metabolic syndrome, cardiovascular disease, type 2 diabetes, and certain cancers 45.

Whether acute or chronic, the inflammatory process demands energy and nutrients, supplies of which often must be reallocated away from other functions to the immune system. Given its high metabolic cost, it is evolutionarily plausible that mechanisms exist to reduce inflammatory activity when food availability is limited. Although the attenuation of inflammatory responses with food restriction may not provide as obvious an osmotic benefit as does the modulation of complement activity, it nevertheless resembles that phenomenon in its paradoxical application to chronic inflammation 1. The inflammatory state of obesity and its associated chronic diseases can be viewed as a condition of positive energy balance undergoing uncontrolled amplification; therefore, the downregulation of inflammation during negative energy balance may offer an opportunity to restore homeostasis and disease regression 46.

### 7.1. Chronic Inflammation and Immunity

Chronic inflammation, allergy, and a compromised immune system are arising as common modern diseases. Until the mid-1960s, vitamin and trace element levels in human plasma were adequate, and immune system function was uncompromised. Since then, at least 50 percent of Americans have a low status of one or more essential nutrients, placing much of the US population at risk from the diseases harbored by a dysfunctional immune system. The clinical consequences of these deficiencies are not restricted solely to an increased risk of acute infections but also the growing potential for cancer exhibit less severe pathology due to the presence of the adequate levels of the essential nutrients in the immune system 47.

Numerous epidemiological studies have correlated increased body burden by pollutants with declining immune system function. Immune system function is necessary for host protection from not only pathogens but also from tissue damage. A healthy immune system will terminate immune reactions after completion of the protective process and also dispose of the dead cells and tissue debris produced by environmental insult. Human exposure to environmental pollutants such as mercury and cadmium is known to alter immune system function. The role of mercury, cadmium, vitamin A, and zinc can have a significant impact on wound healing in conjunction with other nutrients 48.

### 7.2. Anti-Inflammatory Foods

Macronutrient overconsumption precipitates a proinflammatory milieu associated with obesity. The inflammatory processes integral to innate immunity are markedly modulated by nutritional status. Conversely, specific nutritional interventions can attenuate inflammation and benefit immune function 8.

## 8. Food Additives and Immune Response

The immune system has developed mechanisms to distinguish pathogens from harmless agents and maintain self-tolerance under normal conditions. In the absence of infection, immune activation can lead to chronic inflammatory disorders whereby genetic predisposition, microbiota, and nutritional and environmental compounds are thought to play important roles in their aetiology 2.

Food additives have been reported to affect a number of physiological functions in the body such as neuroendocrine and neuroimmune regulation. For instance, carrageenans have been shown to induce a range of adverse effects such as ulcerations and vascular lesions in the stomach, large intestine and ileum 4. Food additives may function as inflammatory agents and disrupt the epithelial barrier resulting in pro-inflammatory immune activation both systemically and locally within the intestine. In a similar fashion, some food additives (vasodilators/anti-hypertensive drugs such as potassium chloride) have been shown to drive a significant change in bowel function and microbial composition. The term dinitrophenol-laden food refers to food additives that contain dinitrophenol, a chemical which has been used to aid in fat loss but is also very toxic and should be avoided 49.

### 8.1. Preservatives

Many factors influence immune function, including age, genetic makeup, diet, and stress level. Excessive chronic stress, for example, causes hypercortisolism that can cause immunosuppression. Lack of moderation in diet also alters immune response; obesity and also undemanding form of malnutrition. Lack of dietary vitamins and minerals and an impaired immune response is well documented 50.

Contrarily, the use of food preservatives can inhibit the growth of fungi or some parasite. For example, sorbate prevents the germination of *Toxoplasma gondii* oocysts in infected cat feces. The use of sodium benzoate has been associated with a decreased number of viable parasites in the presence of *Corcyra cephalonica* and in Diptheramelanogaster infected with the nematode parasite 51.

### 8.2. Artificial Sweeteners

Artificial sweeteners have been developed to replace sugar in foods and drinks without adding calories, providing consumers with alternatives for reducing calorie intake 52. Evidence indicates they do not increase the risk of obesity, cancer, diabetes, or cardiovascular disease 53. The consumption of artificial sweeteners may nonetheless have both benefits and drawbacks. They are used across four hobbies: maintaining an optimal weight, exercising to lose weight, following a low- or reduced-carbohydrate diet, and avoiding or managing diabetes. For individuals who previously indulged in excessive sugar consumption, artificial sweeteners may reduce their desire for sweetness. Yet, early exposure to these agents appears to produce long-term insensitivity to sweetness, necessitating greater amounts of sugar and contributing to increases in obesity, diabetes, cardiovascular disease, and related mortality. The risk/increase in blood glucose levels is dependent upon the individual and the particular artificial sweetener 54.

The effects also depend partly on the degree of initial restraint employed by the consumer and distinguish between abstainers, poorly restrained consumers, and highly restrained consumers. Research into gut bacteria and individual responses in the context of glucose regulation suggests a key role for the microbiome, the composition of which influences the effects of artificial sweeteners on blood glucose levels. A better understanding of the individual factors affecting the impact of these agents, including the gut microbiota, genetics, and epigenetics, will help to sharpen future risk analysis 55.

The consumption of artificial sweeteners stimulates the secretion of glucagon-like peptide-2 (GLP-2) in the gut. GLP-2 plays a vital role in intestinal nutrient absorption and maintenance of the intestinal mucosa, indicating potential benefits for patients with digestive disorders. Because their effects depend on individual differences and the type of sweetener, future evaluations should consider factors such as selection of sweetener form and duration of use. Subsequent research may reveal new applications for artificial sweeteners, including maintenance and enhancement of intestinal function 56.

## 9. Research Studies and Findings

Randomized clinical trials have investigated the correlation between nutritional status and immune functioning, and meta-analyses have examined individual nutrients as well as overall dietary patterns. Several interventions have reported specific immune changes, yet these alterations do not consistently translate into improved clinical outcomes. Some meta-analyses indicate that nutritional interventions may not exert a substantial effect on immune parameters 5. Little information has been published on the influence of food additives and contaminants on immune responses. The available data suggest that certain preservatives, such as sodium sulfites, may inhibit antigen processing by dendritic cells, and artificial sweeteners might affect bacterial species implicated in immune regulation 57. Although food components are capable of modulating immune variables, the wide inter-individual variation in immune responses complicates the generalizability of nutritional immunology studies 32.

### 9.1. Clinical Trials

Clinical trials often assess the ability of diet and dietary components to modify immune system measures *in vivo* and *in vitro*. Some nutrients and essential dietary components are crucial to carry out the cascade of events leading to an efficient immune response 58. Adequate intake of these nutrients supports the normal functioning of the immune system, an effect that can be enhanced by supplementation if the diet is restrictive. Every supplementary food or nutrient proposed as a treatment or preventive measure to enhance the immune response should be assessed for the potential to stimulate essential mechanisms or to exert a favourable modulation in a disordered immune system 10.

### 9.2. Meta-Analyses

Meta-analyses of clinical trials demonstrate that vitamin C supplementation shortens common cold durations. Explorations also assess whether vitamin D modifies susceptibility to upper respiratory tract infections and whether zinc lozenges alleviate the common cold. Investigations into the role of glutamine on immunity are likewise underway. The hypothesis that probiotics influence immunity has sparked substantial debate, with compelling evidence showing gut-associated lymphoid tissue supports the growth of beneficial bacteria. The probiotic concept proposes that disturbed gut flora increases susceptibility to disease, a condition correctable by probiotic interventions 59. A comprehensive review of functional foods on immune function concludes that specific antioxidants—vitamins A, C, E, and minerals zinc and selenium—are essential for immune defense maintenance. Deficiencies in any of these micronutrients impair resistance to infections. The article suggests that increasing intakes above recommended levels through supplementation might provide immune benefits. Analyses of dietary patterns identify the plant-based Mediterranean diet as most favorable for immune support, potentially due to its anti-inflammatory properties. Conversely, the Western-type diet may adversely influence immunity because of its pro-inflammatory effects. Emerging studies examine the impact of preservatives, coloring agents, and artificial sweeteners on immune function 60.

## 10. Practical Recommendations

A healthy and balanced diet is the cornerstone for supporting a coherent and adequate immune function. Harmonious food habits in the general population are the first recommendation to achieve a healthy immune response and defend against the risk of infection and other immune-related disturbances. Food variety is the guideline to avoid internal balance alterations and meet all nutrient demands, which will benefit infection risk and facilitate recovery after infection or vaccination 8.

When intake falls below recommendations, or when illness or stress increases nutrient requirements, maintaining an adequate nutritional status through proper nutrition may be difficult. In these challenging moments, specific nutrient supplementation may constitute a helpful strategy. Micronutrients such as vitamins A, B6, B12, C, D, E, folate, and minerals such as zinc, copper, iron, and selenium play vital roles in supporting the development and maintenance of the immune system. Their supplementation has been proven to reverse related immune dysfunctions and reduce the risk and severity of infections 61.

### 10.1. Dietary Guidelines

Dietary guidelines for maintaining immune function are designed to meet current nutritional needs, reflecting the appropriate nutrient mix and density. Nutrient recommendations are intended for maintaining health and normal function and for limiting oxidative and inflammatory damage. Currently, the US Recommended Dietary Allowances (RDA) define the amounts of specific nutrients that are sufficient to meet the nutritional requirements of 97% to 98% of healthy individuals in the population. These are compared with the Dietary Reference Intakes (DRI), which include the estimated average requirement (EAR) and adequate intake (AI) values. Reference Daily Intakes (RDIs) can also be used on food labels to summarize requirements for the majority of the population 62.

Food-based dietary guidelines provide recommendations concerning desirable amounts for food groups or for specific foods. These dietary guidelines are designed to reflect plausible dietary choices and incorporate epidemiological data relating diet to the epidemiology of chronic disease. However, such guidelines are usually designed to be refined periodically as new information from nutritional science and epidemiology becomes available 63.

### 10.2. Supplementation Advice

A multivitamin/mineral supplement that provides 100% of the RDA can bridge the nutrient gaps for most essential immune-supporting nutrients but might fall short of optimal intakes proposed for vitamin C (200 mg) and vitamin D (1500–2000 IU) 32. Older adults and individuals with suboptimal status may also require higher amounts of vitamin E and zinc. In the presence of vitamin D insufficiency or deficiency, elevated dosages could be necessary to increase serum 25(OH)D concentrations to at least 30 ng/mL. Micronutrients are fundamental to immune health and demand optimal levels for proper function, with the insufficiency or deficiency of a single nutrient capable of undermining immune competence and multiple inadequacies potentially leading to more pronounced impairments 64. The prevalence of inadequate intakes of vitamins A, C, D, E, and zinc remains considerable, particularly in vulnerable populations, underscoring the need for public health strategies to establish guidelines that ensure sufficient micronutrient intake. Supplementing nutritional deficiencies can improve immune function and infection resistance in malnourished subjects, with components such as vitamin C, vitamin E, β-carotene, zinc, and colostrum identified as contributors to enhanced immune parameters 65.

## 11. Limitations and Considerations

Several caveats merit consideration. The immunomodulatory effects of diet and nutrition depend upon baseline nutritional status 4. They will be smaller when a healthy diet is changed to an unhealthy diet than vice versa. Similarly, the quantitative effects of micronutrients are strongly dependent on initial status, and smaller in the better nourished 32. Chromium provides an example, with pronounced effects on the immune response of undernourished animals 66. Manganese is similarly effective when given to poultry fed a diet marginally deficient in this trace element but confers no benefits when animals are fed an adequate diet. Thus, the trajectory of nutrient status over the life course will have an important bearing on immune function 67.

### 11.1. Individual Variability

The diets and nutritional statuses of populations vary considerably across the globe, especially between regions of the world with differing levels of economic development, but also between individuals within a given population. Nutritional requirements and the impact of diet on the immune system will therefore also vary. Approaches to unraveling diet–immune relationships range from population-level surveys to detailed studies of the few key nutrients known to influence immune cell function, alongside intervention studies focused on particular nutrients or nutrient groups 1. The impact of diet on the inflammatory immune system is an area of intense interest because of the role that inflammation plays in immunity and the wide range of inflammatory conditions associated with diet alterations as well as the broader metabolic health of an individual 57. Interactions between individuals, the microbiome, diet and immune function are complex, and many of these relationships remain incompletely resolved.

### 11.2. Potential Risks of Over-Supplementation

The availability of dietary supplements has increased dramatically in recent years, as has the percentage of the population that uses supplementation (19, 20). The potential benefits of supplementation are essentially mirrored by a potential risk of overconsumption or overdoses. Supplements are often viewed as a compliance tool to increase intakes when current intakes from diet are inadequate. However, some consumers may use these products for disease prevention or treatment, assuming synergy with ongoing medications or other therapeutic processes 68. In this view, supplements are only effective when taken at the very high levels of commercial formulations on the market, such as >1 g/day of vitamin C or >500 mg/day of magnesium. However, there is often a controversy between the potential benefit and risk of a particular dose of a specific supplement 69.

Doses much higher than the estimated average requirement (EAR) or recommended daily allowance (RDA) are often associated with risks, and some nutrients, such as vitamin A, may accumulate in the body (for example, in the liver) over long-term exposure to high doses of supplement. In such cases, the tolerable upper intake level (UL) was established in the Dietary Reference Intake (DRI) report, mainly to avoid toxicity or other adverse effects (21, 22). Apart from vitamin A, which has an increased risk of toxicity when used at high doses, other nutrients such as vitamin B6, zinc, iron, manganese, and folate have ULs set up to protect the population from the adverse effects that may occur with excessive intakes. An overdosed nutrient may exert opposite effects in some biological functions, eventually suppressing the immune functions.

### 11.3. Emerging Areas of Study

Emerging areas of study involve immunonutrition, developing non-invasive approaches to improve immune system efficiency against specific diseases under varied environmental and physiological conditions 70. Diet can influence both the innate and adaptive arms of the human immune system. Insufficient nutrient intake can impair immune function and augment susceptibility to infection, contributing to the pathogenesis and progression of infectious and non-communicable diseases 5. Understanding the relationship between diet, nutrients, and immune function highlights targets for nutritional interventions aimed at supporting the immune system 4.

## 12. Conclusion

Nutrition plays a pivotal role in supporting a strong immune system. Various nutrients and specific foods provide key building blocks that help the immune system defend against pathogens. A balanced diet that includes a wide range of nutrient-rich foods from the five major food groups is critical in maintaining optimal immune function throughout the life cycle. Good nutrition reduces the risk of developing infections, even in people with chronic diseases associated with compromised immune function.

Nutritional support is especially important in the elderly because infections are often more severe and recovery is prolonged. Similarly, neonates and infants require adequate nutrition to build immunity both in early life and during periods of exposure to new and diverse environmental pathogens, such as starting nursery or school. A well-balanced diet thus supports a strong immune response, protecting the body from various infection-related chronic diseases.

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