ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Nutrition and Immunity in Elderly.

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ABSTRACT

Aging is associated with increase in chronic disease as well as infections and associated morbidity. This is often throughout to be secondary immunosenescene. Whether this decline in immune function with aging is due to the aging process per Se or is secondary to poor health, inflammation, and other life style factors particularly suboptimal nutritional status. With aging a variety of changes are observed in the immune system, which translate into less effective innate and adaptive immune responses and increased susceptibility to infections. Antioxidant vitamins and trace elements [vitamins C, E, selenium, copper and zinc] counteract potential damage caused by reactive oxygen species to cellular tissues and modulate immune cell function through regulation of redox-sensitive transcription factors and affect production of cytokines and prostaglandins. Adequate intake of vitamins B[6], folate, B[12], C,E, and of selenium, Zn, copper and iron supports a Th I cytokine-mediated immune response with sufficient production of proinflammatory cytokine. Vitamin A and D play important roles in both cell mediated and humoral antibody response. Nutrient supplementation is often accompanied by an improvement in immune function.

Keywords: Elderly, Immunity, Nutrition, chronic disease, macronutrients, micronutrients.

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ISSN: 0975-8585

INTRODUCTION

The older population among humans is increasing at unprecented rate. With recent advances in medical technology and better nutrition. People are living longer than ever especially in developed countries, where life expectancy will have nearly doubled. The aging process increases population risk for nutrient deficiencies[1]. Nutritional deficiencies are prevalent in the elderly people. This is associated with a variety of factors seen more frequently in this population, such as disability, physical, mental, dental, disease of digestive and metabolic disorders, disease and medicine – induced anorexia, poor food selection, and lower socio-economic status [2]

The immune system is one of the functions of the body profoundly affected by aging, and since the immune system interacts with every organ and tissue in the body. Aging is associated with a decline in immune function known as immunosenescence[3]

Disorders of the immune system can result in autoimmune diseases, inflammatory disease and cancer[4] Immunodeficiency occurs when the immune system is less active than normal, resulting in and life threatening infectious. Aging induces dysregulation of the immune system, mainly as a result of changes in cell mediated immunity[5].

Nutrition plays an important role in maintaining the vigor of the immune system ages, since nutrition deficits aggrevate the already weakened immune system in the elderly. Dietary supplements have been studied over the years and have been found to improve immune response in malnourished individuals.

This review initially describes structure and functions of the immune system, and then describe the critical role of nutrition in maintaining the immune response of the elderly people. Next we focous on supplementation studies that demonstrate the immunopotentiating effects of different nutrients on their potential application in improving the immune status in the elderly.

With aging a variety of changes are observed in the immune system, which translate into less effective innate and adaptive immune responses and increased susceptibility to infections. Also aging is associated with changes to the equilibrium of peripheral T and B-lymphocytes[6].

The structure of the immune system:

The Organs of the immune system are positioned throughout the body. They are called lymphoid organs because they are home to lymphocytes, small white blood cells that are the key players in the immune system.

Bone marrow, the soft tissue in the hollow center of bones, is the ultimate source of all blood cells including lymphocytes. The thymus is a lymphoid organ that lies above the heart behind the breastbone.

Lymphocytes known as T lymphocytes or T cells ["T stand" for thymus] mature in the thymus and then migrate to other tissues. B-lymphocytes also known as B. cells become activated and mature into plasma cells, which make and release antibodies.

Lymphnodes; which are located in many parts of the body, are lymphoid tissues that contain numerous specialized structures:

T cells from the thymus concentrate in the paracortex.
B cells develop in and around the germinal centers.
Plasma cells occur in the medulla.

Lymphocytes can travel throughout the body using the blood vessels. The cells can also travel through a system of lymphatic vessels that closely parallels the body's veins and arteries.

Cells and fluids are exchanged between blood and lymphatic vessels, enabling the lymphatic system to monitor the body for invading microbes. The lymphatic vessels carry lymph, a clear fluid that bathes the body tissues.

Immune, cells, microbes, and foreign antigens enter the lymph nodes via incoming lymphatic vessels or lymph nodes tiny blood vessels". All lymphocytes exit lymph nodes through outgoing lymphatic vessels. Once in the blood stream; lymphocytes are transported to tissue throughout the body. They patrol everywhere for foreign antigens then drift back into the lymphatic system to begin cycle all over again[7]

Spleen: The largest lymphatic organ in the body contain white blood cells that fight infection or disease. The spleen also helps control the amount of blood in the body and disposes of old or damaged blood cells[8]

The functioning of the immune system:

The immune system can be divided into innate and acquired immunity while the innate immunity is a first line of defence and a genetric response, the acquired immunity is a specific and requires continuous adaptation to foreign agents[9]. The main distinction between two lies in the cell types receptors and mechanisms involved in immune responses. The cross-talk between innate and acquired immunity through specific receptors and mediators enables a powerful host defence.
To perform the task of defending the host infection, the immune system features three extraordinary capabilities[10]

Major cells of the immune system:

The principle defensive "soldiers" of the immune system are class of mobile white blood cells called leukocytes. There are two distinct types of leukocytes, phagocytes including macrophages, neutrophilis. Phagocytes, engulf and destroy or other particles. They are part of the innate immune system and include monocytes, macrophages, neutrophils and dendtritic cells.

Monocytes circulate in the blood as precursors of macrophages and differentiate into macrophages after leaving in the circulation to migrate into tissues throughout the body.

Dendritic cells: are the primary line of immune cell defense against pathogens and toxins that invade the body. Representing the innate portion of the immune system, dendritic cells recognize and destroy invading bacterial, viral, protozoan, and fungal pathogens and other foreign molecules that escape the body's passive defenses. In innate immunity monoyctes recruited into inflammatory sites differentiate into dendtric cells under the influence of Th I cytokines[11]. The dentritic cell response comprises secretion of TNF: α and to aid in the clearing of pathogens[12]

The inflammatory cytokine TNF-α can bind to receptors on Gram-negative bacteria. Facilitating phagocytes by macrophages[13]. Dendritic cells may also activate NK cells through both contract a dependent and contact independent mechanism[14].When the pathogen load becomes excessive dendritic cell act primarily as antigen presenting cells by migrating to the spleen or peripheral lymph nodes and delivering portion of the invading pathogens to lymphocytes of the adaptive immune system to amplify the immune response.

Natural killer cells:

Natural killer cells [NK] cells are important in both innate and adaptive immunity. They are able to recognize and induce the killing of certain infected cells, cancer cells, and stressed cells. In addition, they produce a variety of cytokines including prion inflammatory cytokines, chemokines colony. Stimulating factors[15] and other cytokines that function as regulators of body defenses, including suppressing and or activating macrophages, suppressing and/or activating the antigen-presenting capabilities of dendritic cells, and suppressing and/or activating T-lymphocytes response[16].

NK cells use a dual receptor system in determining whether to kill or not kill or not kill human cells to which they bind. These dual receptors are termed the killer activating receptors [KAR] and the killer inhibitory receptor [KIR][17]

Immune system of the Gut:

This intestinal system is called the gut associated lymphoid tissue or [GALT]. GALT is rich in immune cells of both the innate and adaptive arm of your immune system. The innate system responds to novel pathogens that your immune system has never seen before. The adaptive system rembes post antigens and responds to them quickly when they are encountered again. The GALT system has a variety of organized lymphoid tissues called mesenteric lymph nodes and peyer patches.

Also diffused throughout the cells lining the digestive tract, as well as the connective tissue lying below these cells, are other immune vigilant cells or effector sites. Intraepithelial lymphocytes, dendritic cells, CD4+ T cells, CD8+ T cells, B cells and plasma cells[18].

The development of the immune system

The immune system is not constant but is subject to several changes during a person's life time changes are reduced by a number of environmental factors. The immune system in the elderly is often characterized by dysregulation of immune responses. Cellular may be decreased in the elderly, resulting in a higher sensitivity to infections. By contrast antibody production is comparable between the healthy elderly and younger adults. However, impairment of immunocompetence in the elderly may not be due to a primary decline of immune function, but rather due to latent nutritional deficits. Thus the dysregulation of immune responses in the elderly could be due to cumulative immunological processes throughout life, and any changes in nutrition, physical activity and general health may further contribute to this[10] .

Dietary factors which affect the immune response

There is much recent interest in and work on the effects of dietary intake and nutritional status on immunity and risk of illness in old age. It is well known that aging is often associated with dysregulation of immune response even among healthy elderly. Some of these changes may be secondary to deficiencies of macronutrients [energy and protein] and micronutrients notably, vitamins A, E, C, D and B6, B12 and folic acid as well as iron and zinc. Thus supplementation with a combination of these selected micronutrients can support the body's natural defense system by enhancing all three levels of immunity, epithelial barriers, cellular immunity, antibody production. Thus, nutrient supplements may be important for health promotion and prevention of certain chronic diseases[19].

Micronutrients in the elderly

Micronutrients consists of two components namely vitamins and minerals. Vitamins are organic substance that the body needs in minuscule amounts. Two classes of vitamins exist fat-soluble [A,D,E,K] and water soluble vitamins [B vitamins and vitamins C].

Minerals are inorganic elements, categorized as major minerals [sodium, calcium, phosphorus, magnesium, etc.] and trace element [iron, zinc, selenium iodine etc.] are essential minerals that the body needs in small amounts[20]. The function of minerals is involved in a variety of structural and regulatory of functions.

In the elderly, the body’s defense mechanisms begins low weaken, thus as a result the elderly are more susceptible than younger adults[21]. Several micronutrients are significant immune-modulators and thus are critical in determining the outcome of host microbe interaction[22]. Vitamin A, betacarotene, folic acid, vitamin B6,

B12, Vitamin C, Vitamin E, riboflavin, iron, zinc and selenium are some of the micronutrients that have been shown to influence host resistance mechanism, thus altering the susceptibility to infectious disease[23].

Antioxidants nutrients play a central role in maintaining the antioxidant or oxidant balance in immune cells and in oxidative stress protection, and preserving adequate function.

Vitamins:

Vitamin A: Vitamin A and its metabolites play critical role in both innate and adaptive immunity. Vitamin A helps to maintain the structural and functional integrity of these mucosal cells. Vitamin A is also important to the normal function of several types of immune cells important in the innate response, including natural killer [NK] cells, macrophages, and neutrophilis. Moreover vitamin A is needed for proper function of cells, that mediate adaptive immunity. Such as T and B cells, thus vitamin A is necessary for the generation of antibody responses to specific antigens[24]. Vitamin A deficiency increase the risk of infection disease. Vitamin A enhances the regeneration of damage mucosa epithelium and phagocytic activity of neturophils and macrophages. Additionally vitamin A supplementation restores the ability of gut immune cells to produce antibodies [IgA and IgG] against bacterial toxins, which is comprised in vitamin A deficiency.

Vitamin C:

The antioxidant vitamin C can also support the immune system and reduce the severity of allergic reaction[25]. Its mode of action on the immune system has been only partially researched. As a water soluble antioxidant it can prevent oxidative damage inside immune cells caused by reactive oxygen species which are released in greater quantities on activation of the immune response-[26]. Infection reduce the concentration of vitamin C in immune cells. Vitamin C also appears to act directly. On the cellular [immune cells] and humoral [plasma proteins such as antibodies] components of the immune system[27]. Hence the vitamin can promote activity by the white blood cells [Leukocytes, lymphocytes, T-cells], and macrophages, prolonging their function, and can stimulate the release of the signaling molecule interferon which is involved in the defense against viruses. Vitamin C also accelerates the decomposition of histamine in the blood. As a signaling molecule, histamine is substantially involved in the development of cold symptoms in terms of inflammatory reaction[28]. In particular vitamin C plays an important role in the function of phagocytes, and the failure of these cells may contribute to the impairment of the response to infection in vitamin C deficiency.

Vitamin D:

Vitamin D modulates the function of the innate and of the acquired immune system and is particularly effective in combating excessive infectious and inflammatory reactions[28]. Many immune cells appear to need vitamin for their development and function[29]. They posses vitamin D receptors[30].Vitamin D reinforces the activity of macrophages and monocytes brought into play by the body to fight microorganisms. Further, it appears to be crucial to the control of infection, because it increase the blood concentration of the body's own antimicrobial proteins [e.g. alpha and beta-defensin]. Moreover, vitamin D activates enzyme in T and B lymphocytes.

Vitamin E:

Vitamin E as a fat. Soluble antioxidant vitamin can protect lipids which are building block of cell membranes against attack by free radicals. These free radicals occur in the body as a result of metabolic processes like immunological reactions and the effect of environmental influences. Experimental findings indicate that vitamin E can also stimulate the immune system directly[31]. The vitamin acts as primarily on the mast cells [mastocytes], which belong to the leukocyte [white blood cell] group[28] and play a special role in wound healing, in warding off pathogens and in allergies. Most cells are activated by oxidized lipoproteins that occur under the influence of pro-inflammatory signaling molecules [cytokines]. These cells then release signaling molecules which in particular encourage allergic inflammatory processes. Vitamin E is thought to influence these processes on

several levels. Moreover vitamin. E reduces the formation of pro-inflammatory cytokines that are produced by macrophages [scavenger cells] and their precursor cells [monocytes]. Additionally, vitamin E appears to act directly on T cells [white helper cells] and is therefore able to reduce inflammation.

Vitamin B6

Vitmain B6 plays a major role in making proteins, hormones and neurotransimitters [chemicals that carry signals between nerve cells. Low vitamin B6 intake and nutritional status have been associated with impaired immune function, especially in the elderly. Decreased production of immune system cells known as lymphocytes, as well as decreased production of immune system cells known as lymphocytes as well as decreased production of an important immune system protein called inteleukin-2 have been reported in vitamin B6 deficient individuals[32]. Restoration of vitamin B6 status has resulted in normalization of lymphocyte proliferation and interleukin-2 production, suggesting that adequate vitamin B6 intake is important for optimal immune system function in older individuals[32,33]. However one study found that the amount of vitamin B6 required to reverse these immune system impairments in the elderly was 2.9mg/day for men and 1.9 mg/day for women, these vitamin B6 requirements are higher than the current RDA.

Folate:

Folate plays as crucial role in nucleic acid and protein synthesis by supplying in concert with vitamins B6 and B12 and therefore inadequate folate significantly alters the immune response. Folate deficiency modulate immune competence and reducing the proportion of circulating T lymphocytes and their proliferation in response to nitrogen activation. This effect in turn decreases resistance to infections[34]. Folate may affect the immune system by inhibiting the capacity of CD8+ T lymphocytes cells to proliferate in response to mitogen activation. This might explain the observation that folate deficiency enhances carcinogenesis next to increased damage to DNA and altered methylation capacity[35]. Folate supplementation of elderly individuals improves overall immune function by altering the age-associated decrease in NK cell activity supporting a ThI response thus providing protection against infections[36].

Zinc:

Zinc deficiency is widespread in many parts of the developing world. The immune related functions of zinc have been reviewed in the last few years[37-39]. Zinc is essential for highly proliferating cells, especially in the immune system and influences both innate and acquired immune functions. It is involved in the cytosolic defence against oxidative stress [superpoxide dismutase activity] and is an essential cofactor for thymulin which modulates cytokine release and induces proliferation. Zinc supplementation increases cellular components of innate immunity [e.g. phagocytosis by macrophages and neutrophils, NK cells activity, generation of oxidative burst, DTH activity antibody responses and the numbers of cytotoxic CD8+ T cells [ThI response].

Selenium:

Selenium is essential for an optimal immune response and influences both innate and acquired immune system. It has a key role in the redox balance, including the protection against DNA damage. Selenium is also an important cofactor of a group of enzyme that contribute to the protection of cells from oxidative damage because phagocytes generate large amounts of reactive oxygen. Selenium deficiency decreases immunoglobulin titers and aspects of cell-mediate immunity. Selenium supplementation can counteract these effects[40,41].

Copper:

Copper has been shown to have a role in the development and maintenance of the immune system and a large number of experimental studies have demonstrated that copper status alters several aspects of netrophils, monocytes and superoxide dismutase. Working together with catalase and glutathione peroxidase in the cytosolic antioxidant defence against ROS. Copper is essential in the dismutation of superoxide anion to oxygen and H2O2

and diminishes damage to lipids, protein and DNA. Both copper deficiency and high intakes over longer periods can modulate several aspects of the immune response[42,43].

Iron :

The immune related functions of iron have been subject to several reviews since 2001. Iron is essential for electron transfer reactions, gene regulation, binding and transport of oxygen, and regulation of cell differentiation and cell growth. Iron is a critical components of peroxide and nitrous oxide generating enzymes. It is involved in the regulation of cytokine production and mechanism of action and in the activation of protein kinase C, which is essential for phosphorylation of factors regulating cell proliferation. In addition, iron is necessary for myeloperoxidase activity which is involved in the killing process of bacteria by neutrophils through the formation of highly toxic hydroxyl radicals. Therefore any alteration in cellular iron homeostasis to either deficiency or overload has unfavourable functional consequences on the immune system[44]

Calcium:

As we ages, the body does not absorb calcium as easily as it used to increased calcium excretion accompanies decreased absorption. Age associated loss of bone density increases risk for fractures and osteoporosis. Losses of skeletal calcium in post menopausal women can reach more than 40%[45]. Because bone fractures are a significant contributor to morbidity and mortality in older people, achieving daily calcium needs is critical, yet only 5% of older women and 10% of older men consume the DRI recommendation[45].

Sodium :

Since many people will develop hypertension at some point during their lifetime and typically the higher their salt intake, the higher their blood pressure will be older adults should aim to consume no more than 1.500 [mg] of sodium per day. Further more, because potassium can counterbalance the harmful effects of sodium on blood pressure, older people should strive to meet the potassium recommendation [4.7 gram per day] with food. Consuming more potassium-rich foods may also help prevent the bone loss that occurs with aging.

Macronutrients :

They are essential nutrients that required by the body in relatively huge amounts or large quantities on a day to day basis in order to function properly. They contain calories unlike micronutrients. They include proteins, carbohydrates and fats. They are absolutely necessary for life and sustenance and cannot be ignored. They build the body, order biological functions, such as digestion and tissue repair, and provide strength, metabolism and vitality. Deficits or excess of any of these nutrients may compromise these processes, resulting in a variety of poor health outcomes that vary, depending on life stage of the affected individual.

Proteins and amino acids:

It has been proven that both quantitative and qualitative participation of proteins in a nutritional mixture is very important for the proper function of the immune system. It has been determined that the daily protein requirement for the healthy human is about 0.8g/kg which should be about 12% of the calorific value of the mixture. Deficiency of proteins leads to serious illnesses such as kwashiorkor, marasmus, impaired mental health, odema, failed organ, shrinkage of muscle tissues as well as weak immune system. Overdose of proteins can also adversely affect the health affect the health leading to kidney stress, fat gain, osteoporosis etc. In many publications the impact of certain amino acids on the immune system function was high lighted[46,47]. Arginine accelerates transformation and maturation of T cells, increases the activity of cytotoxic T lymphocytes and natural killer cells, and enhance the mitotic response of macrophages to inflammatory reaction[48]. Glutamine is an essential element supporting the natural intestinal barrer. Is it a precursor for biosynthesis of nucleotides, and an energy substrate for rapidly dividing cells, macrophages lymphocytes, endothelial cells, enterocytes[48]. Sulphur

amino acids [methionine, cysteine, procysteine] as donors of sulfhydryl groups and of glutathione synthesis stimulators exhibit antioxidant activity[46,49].

Lipids :

Lipids are components of cell membrane, a source of energy, and the precursors of many mediators. The groups of polyunsaturated fatty acids, which are no 3,6,9, fatty acids, is of particular importance. They are the most common constituent of cell membrane. It has been shown that dietary polyunsaturated fatty acids deficiency causes atrophy of lymphatic tissue and disturbance of the humoral response.Changing the proportion of fatty acids in nutrient leads to change in the release of phospholipase products – prosta glandine and leukotriense, which leads to modulation of immune system function[50].

Progress of nutrition research over the last decade clearly suggest that besides essential nutrients, non nutritive constituents such as phytochemical have a strong impact on human health. These phytochemicals are represented by a number of chemically diverse substances. So far mainly carotenoids and flavonoids have investigated for their immunodulatory potential.

Carotenoids:

Carotenoids are yellow arange and red compounds found in fruit and vegetables. Examples are β-carotene, which widely distributed in plants, and lycopene a carotenoid found in tomatoes. Like vitamins C and E, carotenoids are antioxidants and additionally β-carotene is a precursor of vitamin A.

The effect of beta-carotene on the immune system is based essentially on its properties as a fat soluble antioxidant. Reactive oxygen species are formed extensively during inflammatory processes intended to render germs harmless. Beta-carotene, working together with other antioxidants, can ensure balanced regulation of oxidative processes, so that infections germs can be fought without allowing an excess of free radicals to damage immune cells [51]. Beta-carotene and other carotenoids could directly streng-then cellular and humoral immune defense is as yet unclear and requires further research[52].

Some studies have shown that β-carotene supplementation may be beneficial for individuals with a compromised immune system. In particular, a recovery of decline natural killer cell activity in the elderly to normal levels was observed following β-carotene supplementation[10].

Flavonoids

Flavonoids are an important class of natural products. They are generally known to be present in plants and plant based products. These include various fruits, vegetables, herbs and beverages such as tea and red wide. Flavonoids are associated with a broad spectrum of health promoting effects. They are indispensable component in a variety of nutraceutical, pharmaceutical, medicinal and cosmetic applications. This is attributed to their anti-oxidative, anti-inflammatory, anti-mutagenic and anti-carcinogenic properties coupled with their capacity to modulate key cellular enzyme function. Work carried out in relation to health benefits of flavonoids suggest that certain flavonoids work as immune modualators. They are important chemical compounds having significant in vivo effect on homeostatis with the immune system and also affect the functions of inflammatory cells. Effect of flavonoids including quercetin on a variety of inflammatory processes and immune functions have been extensively reviewed[53,54]. For example, studies[55]. demonstrated significant anti-inflammatory activity of quercetin. It is shown to help inhibit several initial process of inflammation. Flavonoids play a role as nutritional supplements during treatment of cancer or during inflammatory disorders.

Probiotics, prebiotics and dietary fibre:

The bacteria of the gut play important roles in several functions related to the digestion of food and the establishment and maintenance of the gut immune defense barrier. They are the primary stimulus for the

intestinal immune system and are necessary for normal immune development. When the balance of organisms in the gut is disrupted or altered by disease or by the use of antibiotics, local immune defences are impaired.

Probiotics:

Probiotics are live microorganisms which provides a health benefit. Most probiotics are bacteria similar to the type normally found the people's guts, the "good" bacteria, which helps maintain a balance in the digestive tract and may confer natural protection against disease. The most common probiotics taken as supplements are lactobacilius and Bifidobacterium. Humans normally carry several pounds of bacteria in their intestines and they are key to digestion, immune system function and possibly play other beneficial roles. They can also out-compete "bad" bacteria that cause disease[56].

Probiotics and elderly immune function:

It has shown that probiotics interact with TLRs and other pattern recognition receptors on immune system cells and thus directly influence their functions. Furthermore, specific probiotics strains may induce beneficial changes in gut macrobiotics that have impact on immune status. It has been shown that probiotics [e.g.L. rhamnosus HN001], B. Lactis HNO19 or lactobacillus acidophilus NCFM] consumption enhances ex vivo cytotoxicity of NK cell against model tumor cells and phagocytic activity of neutrophils and monocytes against *Escherichia coli* [57-60].

In recent study, ingestion of lactobacillus delbrueckii subsp. Lulgarcius 8481 decreased inflammatory marker IL-8 level in the elderly[61].

In addition it was shown that intake of this probiotic could improve hallmarks of aging the number of recent thymus emigrant T-cells [CD8-CD31] was increased the number of senescent effector/memory type T.cells [CD8, CD 28] was decreased, and importantly CMV reactivation was prevented in probiotic group, indicating that probiotic consumption could counteract markers of immunesenescence.

Prebiotics and dietary fiber:

Prebiotics is a non-digestible selectively fermentable food constituent that beneficially affects the host be selectively stimulating the growth and/or activity of one or limited number of bacteria in the large intestine and confer benefits upon well-being and health.

Prebiotics are present in the normal diet at intakes of 2-10g/day. They include inulin, fructooligosaccharides, galactooligo-sacchrides and lactulose. Prebiotics alter the composition of the intestinal microbiota to one in which the proportions of bifidobacteria and lactobacilli are increased. The term dietary fibre describes plant food constituents such as cellulose and resistant starch, and includes some prebiotics. Prebiotics and dietary fibres have in common that they are not hydrolyzed in the small intestine and reach the colon. There, they serve as energy and carbon sources for the colonic microbiota and thus increase the bacterial mass in the intestine.

There is increasing interest in modulation of the immune system using prebiotics, which may be particularly useful inflammatory condition in the elderly. Evidence so far suggests that prebiotics can have significant effects on the immune system. It is however, unknown if these are direct or indirect effects resulting from stimulation by immune-modulatory bacteria, or production of SCFA, which are known to have immune-modulatory properties, and can bind to SCFA G protein coupled receptors on immune cells within gut-associated lymphoid tissue[62]..

Addition of FOS and lactulose to the diet has been shown to increase muscosal immunoglobulin production, mesenteric lymph nodes[63]

ISSN: 0975-8585

Synobiotics:

Products containing both probiotics and prebiotics have been termed synobiotics. A synobiotics is a mixture of probiotics and prebiotics that beneficially affects the host by improving the survival and implantation of live microbial dietary supplementation in the GI tract, by selectively stimulating the growth and/or activating the metabolism of one or limited number of health promoting bacteria, and the improving host[64]. Trials demonstrating the application of synobiotics in elderly people are limited. Bartosch et al. [2005] performed study with a synobiotic product containing two bifidobacterum strains [B. Lactis BL 0.1 and Bifidum BB-02] and inulin-based prebiotic. The consumption of synobiotic product increased the size and diversity of fecal bifidobacteria and increased lactolbacilli numbers. The characterization of bifidobacterial species revealed that the rise of total bifidobacterial numbers was most likely due to the consorted effect of both ingested probiotic strains and the stimulation of indigenous bifidobacteria by prebiotic compounds.

Role of immunity in some disease :

Respiratory infection:

Infections, particularly respiratory infections are common in older individuals. Infections can interfere with daily activities, prolong recovery time from illnesses and result in more frequent complications. Contributing to that greater susceptibility to respiratory infections is the decline in immune response that occurs as we grow older.

Good nutrition plays an important role in keeping the immune system functioning efficiently, especially getting adequate amounts of protein and a variety of nutrient such as zinc and vitamins B6, A, C, D and E.[10]. Vitamin A restores the integrity of the mucosa in the pulmonary tract, and vitamin D fosters the production of the endogenous antibiotic cathlicialin. Both mechanisms could protect the body from colonization and proliferation of pathogens. Vitamin E significantly reduces upper respiratory infections. The protective effect of vitamin E against colds is noteworthy for a number of reasons. First colds were the most common upper respiratory infection. Cold are also frequently seen in the elderly population a whole and often lead to increased disease in this age group[66] Vitamin E and selenium protect immune cells from oxidative damage and hence could reduce the risk of contracting respiratory infections or alleviate the symptoms.

Cancer:

Cancer is a term used for diseases in which abnormal cell divides without control and are able to invade other tissues. Cancer cells can spread to other parts of the body through the blood and lymph systems. It has long been thought that the immune system could play a role in the recognition of and the reaction to tumors. Several studies have revealed that subject with a low natural killer cell activity had an increased cancer risk.

Food plays an important role both carcinogenic inhibition, i.e. the formation of neoplastic or cancerous cell, and the promotion and progression of cancer once it is initiated. The putative role that food plays in the development of cancer requires that we have a basic understanding of the cell replication and proliferation process.

Nutrient in the diet interact with the immune system in cancer disease. The diet is an important determinant of some type of cancer and nutrient play a role both by influencing the normal cell cycle and also through the presence of carcinogenic agents in the diet. Micronutrient like vitamin A and carotenoids, vitamin E, D, C and minerals like selenium play an important role in immune function. Many of these micronutrients function as potent antioxidants they not only prevent or reduce oxidative damage but also provide the important antioxidant defence, thus reducing the potential for cell and DNA damage and thus cancer[67].

Heart disease :

Numerous dietary factors have been correlated with increases or decrease in the risk of heart diseas. Atherosclerois is a major cause of mortality from heart disease. It is an inflammatory disease of the arteries resulting in the deposition of arterial plaques. The immune system is involved in the pathogenesis of atherosclerosis-through interaction between its white blood cells [monocytes and macrophages] and cells of the arterial wall. Dietary factors influence the immunological processes underlying the pathogenesis of atherosclerosis[10].

Several studies indicate that the risk of heart disease can be reduced by increased intake of PUFA and dietary antioxidants and anti-inflammatory effect of vitamin C. Wannamethee et al., 2006 tochopherols [Vitamin E], and B-carotenes in fruit and vegetables are well recognized[69]. Adequate intake of vitamin K in green vegetables can be protective against cardiovascular disease by its role in regulation of blood coagulation[70]. Vitamin D supplement given to patients with congestive heart failure reduce inflammation of cytokine profile. Vitamin D may serve as an anti-inflammatory agent in this disease[71]. Folate in green leafy vegetables reduces blood homocyteine concentration. Dietary components such as phytochemicals, polyphenols, flavonoids , and alcohol also reduce blood homocysteine

Alzheimer's Disease:

Alzheimer's is a degenerative brain disease that affects cognition memory and social abilities. The disease is not a normal part of growing old, it is a disorder that gets worse with age. Currently there is no known cure . Available treatments focus on reducing the rate of cognitive define and on improving the quality of life for those suffering from the disease[72]. Scientists are also investigating ways to prevent the onset of Alzheimer. Many nutrients play a key role in the metabolism of neuronal cells and their appendages. Their actions may be mediated by their catalytic role in numerous enzymes, antioxidant action, and various other processes. In vitro, micronutrients potentiate the ability of immune cells withstand the toxic effect inclusion bodies found in brains of patients with Alzhimer's disease[73]. Furthermore micronutrients may reduce the amount of amyloid material in brain biopsies patients with Alzhimer's disease. The role of good nutrition in helping to reduce the risk of Alzhimer's. Certain antioxidant-rich foods may help prevent the build up of harmful molecules in brain tissue, causing brain inflammation, damaging nerve cells and forming the destructive clumps associated with brain plaques. Eating a high fat diet essentially hits the brain with a "double whammy". First, it contributes to high blood cholesterol and high blood pressure, which hamper healthy blood flow to the brain, and second, it likely contributes to the production of free radicals. The good news is that we can take charge of our brain health by maintaining a healthy diet. Good nutrition involves maintaining a low sugar, low fat diet that consists eating whole grains, fruits and vegetables, lean meats and fish. Foods that contain high levels of antioxidants or anti-inflammatory components are believed to greatly improve brain health and functioning. For example, eating green leafy and cruciferous vegetables, such as broccoli and cauliflowers, provide the brain with powerful chemicals to boast brain health[74]. Other nutritional solutions which research suggest can affect cognitive decline or Alzheimer's risk include omega 3s [DHA], antioxidants such as vitamin E [due to the inflammatory nature of AD] and acetylcholine which is a key part of memory function [which is often deficient in Alzheimer's cases[75].

CONCLUSIONS

As we have seen, aging affects many components of the immune system, and since the immune system interacts with every organ in the body.

The immune system consists of an intricate array of defence mechanisms that protect the body against potentially harmful foreign agents. Nutritional factors can influence immune functional factors can influence immune functioning in many ways and at many levels. Dietary factors that influence immune responses include total energy intake, total fact intake, the type of fatty acids ingested [especially n-3 LCPUFA] several vitamins [especially vitamins A, D,E, B6 and C], carotenoids, flavonoids, trace minerals especially zinc and selenium],

prebiotics and probiotics. However, vitamins and minerals supplements have been shown to improve immune function in the elderly.

Research suggests that altering the immune response by dietary means might be of value in the reduction of risk and/or the treatment of a wide variety of disorder including inflammatory diseases, heart disease, viral and bacterial infections and cancer.

Abbreviations :

NK	: Natural killer cells.
GALT	: Gut associated lymphoid system.
RDA	: Recommended dietary allowance.
DTH	: Delayed type hypersensitivity skin test.
ROS	: Reactive oxygen species.
DRI	: Dietary Recommended intake.
TLRs	: Toll-like receptors in the innate immune system.
CMV	: Cytomegalovirus
FOS	: Fructooligosaccharides.
SCFA	: Short chain fatty acids.
PUFA	: Polyunsaturaed Fatty acids.
AD	: Alzheimer's diseases.
DNA	: Deoxyribonucleic acid.
DHA	: Docosahexaenoic acid

REFERENCES

[1] Meydani, A., Ahmed T., Meydani SN. [2005]Aging nutritional status and infection in the developing world. Nutr. Rev., 63, 233-246.

[2] Munkyong, Pea, Simin Nibkin, Meydani and Dayong Wu [2012]. The role of nutrition in enhancing immunity in aging Aging Dis., 3[1], 91-129.

[3] Pawelec, G. [2012]. Hallmark of human "immnosenescence" Adaptation or dysregulatlion? Immune Aging, 9,15.

[4] Pawelec, G, Akbar A, Caruso C, Effres R, Grubeck Loebenstein B, Wikby. A [2004]. Is immunosensececne Trends Immunol, 25, 406-410.

[5] Nicdwiecki, A., Rath M [2005]. Malnutrition: The leading cause of immune deficiency disease worldwide, DRRI Brochure.

[6] Chinn, IK, Blackburn CC, Manley NR, Sepowski GD [2012] Changes in primary lymphoid organ with aging. Semin Immunol. 24, 309-320.

[7] www.naid-nih gov/topics/immune system Oct. 2008.

[8] Kim, Ann. Zimmermann [2013]. Immune system: Disease , Disorder and Fucntion. Live Science www.live science.com.

[9] Van, den Biggelaar AH., Huzinga TW., de Craen Aj., Gussekleo, J., Heijmans BT, Frolich M. Westendrop RG [2004]. Impaired innate immunity predicts Frailly in old age. The leiden 85-plus study. Exp. Gerntol, 39, 1407-1414.

[10] Lillian, L., Sandra G. [2011]. Nutrition and Immunity in man ILSI Europe concise monograph series.

[11] Trez, De C, Magez, S., Akira S, Ruffel, Y, Carlier, Y and Muraille, E. [2009]. INOS – Producing inflammatory dendritic cells constitute the major cell type during the chronic leishmania major infection phase of C57BL16 resistance mice-Plos Pathogens Vol. 5, No. 6.

[12] Serbina, N.V., Salazer-Mather, T.P., Biron, C.A., Kuziel, W.A., Pamer, E.g. [2003]. TNF/INOS – producing dendritic cells mediate innate immune defence against bacterial infection. Immunity, Vol. No. 1, 59-70.

[13] Luo, G., Niesel, D.W., Shaban, R.A., Grimm, E.A., Klimpel, G.R. [1993]. Tumor necrosis factor alpha binding to bacteria. Evidence for a high – affinity receptor and alteration of bacterial virulence properties, "Infection and Immunity, 61, 3, 830-835.

[14] Barreiva, R., Silva, Da. and Münz, C. [2011]. Natural Killer cell activation by dendritic cells. Balancing inhibitory and activating signals. Cellular and molecular life sciences 68, 21, 3505-3518.
[15] Kovacs, ES., Palmer, J.L. , Fortin, CF., Fulop, T., Goldstein, DR., Linton, PJ. [2009]. Aging and Innate immunity in the mouse : impact of intrinsic and extrinsic factors. Trneds Immunol, 30, 319-324.
[16] Vivier, E. et al., [2011]. Innate or adaptive immunity, The example of natural killer cells. Science, 331,44-49.
[17] Shaw, AC., Joshi S., Greenwood H., Panda A., Lord J.M. [2010]. Aging of the innate immune system curr opin. Immunol, 22, 507-513.
[18] Your Gut and Immune system connection [Recipe and Give away]. www.Food Matters.tv.2014.
[19] Ranjit, Kummar Chandra [1997]. Graying of the immune system.can nutrient supplements improve immunity in the elderly. JAMA.227 [17], 1398-1399.
[20] Ahuwalia, N. [2004]. Aging, nutition and immune function J. Nutr. Health Aging, 8, 2-5.
[21] Yoshikawa, T.T. [1977]. Perspective aging and infection disease. J. Infact Dis., 176, 53-57.
[22] Bhaskaram, P. [2002]. Micronutrient malnutrition infection, and immunity an overview. Nutr. Rev., 60, 540-555.
[23] Grimble, RR. [1997]. Effect of anioxidative vitamins on immune functions with clinical application. Int. J. Vit. Nut. Res., 67, 512.
[24] Semba, R.D. [2004]. Vitamin A. In: Hughes DA, Darlington LG, Bendic A., eds. Diet and Human immune function. Totowa, New Jersy, Human Press Inc., 105-131.
[25] Chambial, S. et al. [2013]. Vitamin Cin disease prevention and cure. An overview. Indian J. Clin. Biochem., 28[4], 314-328.
[26] Holmannova, D.et al. [2012]. Vitamin C and its physiological role with respect to the components of the immune system vnitr lek, 58[10], 743-744.
[27] Hemilä, H. [2003]. Vitamin C respiratory infections and the immune system . Trends immunol, 24[11] 579-580.
[28] Shaik, Dasthagrisheb, Y.B. et al. [2013]. Role of vitamins D,E, C in immunity and inflammation. J. Biol. Regul Homeost Agents, 27[2], 291-295.
[29] Prietl, B. et al. [2013]. Vitamin D and immune function Nutrients. 5[7], 2502-2521.
[30] Peelen, E. et al. [2011]. Effects of vitamin D. on the peripheral adaptive immune system : a review. Autoimmun Rev., 10[12], 733-743.
[31] Mocchegiani, E. et al. [2014]. Vitamin E gene interaction in aging inflammatory age-related diseases : implications for treatments systematic review. Aging Res. Rev.
[32] Meydani, SN, Ribaya – Mercado JD, Russell RM, Sahyoun N, Morrow FD, Gersshoff SN [1991]. Vitamin B6 defciency impairs interleukemia 2 production and lymphocytes proliferation in elderly adults. Am. J. Clin. Nul., 53[5], 127-1280.
[33] Talbott, MC, Miller, LT, Kerkuliet, NI. [1987]. Pyridoxine supplementation: Effect on lymphocyte response in elderly Persons. Am. J. Clin. Nut. 46[4], 659-664.
[34] Dhar, A., Gahla, P., and Hercbergs [1991]. Folate status and the immune system. Progr Food Nutr. Sci., 15, 43-60.
[35] Courtemanche, C., El-Son-Schwab I., Mashiyuama ST., Kerry N and Ames BN [2004]. Folate deficiency inhibits the proliferation of primary human CD8+ T lymphocytes in Vitro. J. Immunol, 173,3186-3189.
[36] Troen, AM., Mitchell, B., Sorensen, B., Wener, MH., Jchston A., Wood B., Selhub J. Mc, Tieman, A., Yousui Y, Oral E Potter J. D and Ultrich CM [2006] unmetablized folic acid in plasma is associated with reduced natural killer cell cytotoxicity among postmenopausal women J. Nutr., 136, 189-194.
[37] Wintergerst, ES., Magginis and Hornig DH [2006]. Immune enhancing role of vitamin C and effect on clinical conditions. Ann Nutr., Met, 50, 85-94.
[38] Prasad, AS. [2000]. Effects of zinc deficiency on immune functions . J. Trace Elem. Exp. Med. [13], 1-30.
[39] Ilbs, KH and Rink, L. [2003]. Zinc altered immune function J. Nutr. 133, 14525-14565.
[40] Wintergerst, E.S., Maggini S., Horning DH. [2007]. Contribution of selected vitamins and trace elements to immune function. Ann Nutr. Metab, 51[4], 301-333.
[41] Arthur, JR., Mckenzie, R and Beckett GJ [2003]. Selenium in the immune system J. Nutr. 133, 145955-145975.

[42] Klotz, LO., Kroencke, KD., Buchczyk DP and Sies H [2003]. Role of copper, Zinc, Selenium and tellurinm in the cellular defence against oxidative and nitrosative stress. J Nutr, 133, 14485-14515.
[43] Pan, YT and Loo, G. [2000]. Effect of copper deficiency on oxidative DNA damage in Jurkat T. Lymphocytes. Free Rad Biol. Med., 28, 824-830.
[44] Oppenheimer, SJ. [2001]. Iron and its relation to immunity and infections disease J. Nutr., 131, 6165-6355.
[45] Tucker, L.K. [2003]. Dietary intake and bone status with aging. Current pharmaceutical Design, 9, 2687-2704.
[46] Grimble, RF. [2005]. Immunonutrition. Curr opin Gastroenterol 21, 216-222.
[47] Krenitsky, J. [1996]. Nutrition and the immune system AACN clinical issues, 7, 359-369.
[48] Tepaske, R. [1997]. Immunutrition.curr opin Anaesthesiol 10, 86-91.
[49] Sobotks, L. [2007]. Basics in clinical nutrition 3rd ed. [Polish] Korta T [ed]. PZWL, Warsaw.
[50] Wum, Shaji, Y., Chuang, P, Tsai, S. [2007]. Endometriosis disease pathophysiology and the role of prostaglandins Expert Rev. Mol. Med., 9, 1-20.
[51] Puertollano, M.A. et al. [2001]. Dietary antioxidants: immunity and host defence curr top Med. Chem. 11[14] 1752-1766.
[52] Chew, B.P. and Park, J. S. [2004]. Carotenoid on the immune response. J. Nutr. 134[1], 257-261.
[53] Comalada, M.D. et al. [2005]. Eur. J. Immunol., 35,584-592.
[54] Wang, J. et al. [2002]. J. Agric. Food chem., 50, 4183-4189.
[55] Park, HJ., et al. [2009]. Int immunopharmacoly, 9[3], 261-267.
[56] www. Probiotic Prebiotic info, 2014.
[57] Gill, HS., Cross, M.L., Rutherfurd, K.J. and Global, P.K. [2001]. Dietary probiotics supplementation to enhance cellular immunity in the elderly. British Journal of biochemical science 58, 94-96.
[58] Gill, H. S., Rutherfurd, K.J. and Cross, M.L. [2991b]. Dietary Probiotic supplementation enhance natural killer cells activity in the elderly: an investigation of age related immunological changes. Journal of clinical immunology, 21,264-271.
[59] Ibrahim, F., Ruviol, S., Granulund, L., Saliminen S., Viitanene M and ouwehand, A.C [2010]. Probiotics and immunosensences cheese as a carrier – FEMS immunology and medical microbiology 59, 53-59.
[60] Sheih, Y.H., Chang, B.L., Wang, L.H., Liao, CK., and Gill, H.S [2001]. Systemic immunity enhancing effects in healthy subjects following dietary consumption of the lactic acid bacterium lactobacillus rhamnosus H NOO1. Jorunal of the American College of Nutrition 20, 149-156.
[61] Moro-Garcia, M.A., Alonso-Arias, R., Baltadjieva, M., Fernandez Benitez, Fernandex Barrial M.A., Diaz, E., Ruisanchez, R., Alonso Santos, M., Alvarez Sanchez, J., Savendra Mijan and Lopez Larrea C. [2012].
[62] Brown, A.J., Goldsworthy, SM., Barnes AA., Eilert MM, Tcheang, I., Daniels D., Mvir., AI., Wigglesworth, MJ., Kinghorn, I., Fraser, N.J., Pike NB., Strum JC., steplewiski, KM., Murdock, P.R., Holder, JC., Marshall FH., Szekeres, PG., Wilson, S., Ignar DM., Foord SM., Wise, A, Dowell SJ. [2003]. The orphran G protein coupled receptor GPR41 and GPR43 are activated by propionate and other short chain carboxylic acids.
[63] Schley, P.D., Field C.J. [2002]. The immune enhancing effects of dietary fibres and prebiotics, Br. J. Nurt., 87, 5221-5230.
[64] Gibson, G.R. and Roberfroid, M.B. [1995]. Dietary modulation of the human colonic microbiota. Introducing the concept prebiotics. J. Nutr. 125, 1402.
[65] Bartosch, S. et al. [2005]. Microbiological effects of consuming a synobiotics containing bifidobacterium bifidum, bifidobacterium lactis, and oligorfructose in elderly persons, determined by real-time polymerase chain reaction and counting of viable bacteria clin. Infec. Dis., 40, 28.
[66] Blumberg, J. and Heber, D., Eds [2004]. Multivitamins and Public Health: Exploring the evidence, Washington De New York, NY: Bioscience communications.
[67] Books google.com.eg./books/2003.
[68] Wannmethee, SG., Lowe, GDO, Rumley, A. [2006]. Association of vitamin C status, fruit and vegetables intake and markers of inflammation and homeostasis. Am. J. Clin. Nutr., 83, 567-74.
[69] Watzel, B., Kulling, S.E., Mosender J. [2005]. A 4-week intervention with high intake of carotenoid-rich vegetables and fruit reduces plasma c-reactive protein in healthy, non-smoking men. Am. J. Clin. Nutr., 82, 1052-1058.
[70] Geleigose, JM., Vermeer, C., Grobbee D.E. [2004]. Dietary intake of menaquinone is associated with a reduced risk of coronary heart disease: the Rotterdam study. J. Nutr, 134, 3100-3105.

[71] Schleithoff, S.S., Zittermann, A., Tenderich G. [2006]. Vitamin D supplementation improves cytokine profiles in patients with congestive heart failure: a double-blind-randomized placebo-controleld trial. Am J. Clin. Nutr., 83, 754-759.
[72] Nandy, K., Sherwin, I. eds. [1997]. The aging brain and senile dementia. New York: Plenum Plenum Press.
[73] Chandra, RK. [1997]. Graying of immune system. Can nutrient supplements improve immunity in the elderly JAMA, 277, 1398.
[74] WWW. Bacweb.org/alzheimers. Php. Alzheimer's disease posjetili ste ovu stranicu [2014].
[75] www.food forthebrain.org/nutrition. Dementia/Alzheimer's disease food for the brain [2014].