Nutrition and immune system in the elderly

Rina K. Kusumaratna a

Department of Community Medicine, Medical Faculty, Trisakti University

ABSTRACT

The number of individuals aged 60 years or older is projected to double as a proportion of the world’s population and to more than triple in number over the next 50 years. Aging is often associated with a dysregulation in immune function, particularly in T-cell responses, even in the healthy elderly. Adequate nutrition is important for optimal immune function. Specific nutrient deficiencies can aggravate the age-associated dysfunction in immune function and increase the risk of illness. Several micronutrients such as iron, zinc, and selenium are essential to specific and non-specific immune function and thus influence the susceptibility of the elderly to infectious diseases. Free radicals and oxidative stress have been recognized as important factors in the biology of aging and of many age-associated degenerative diseases. Therefore, dietary components with antioxidant activity have received particular attention because of their potential role in modulating oxidative stress associated with aging and chronic conditions. The nutritional deficiency impairs the immune response, exposure to viral pathogens, and will result in an increase in the severity of diseases. Nutritional deficiency in the elderly must be treated to reduce the risk of infection and possibly slow the aging process.

Keywords : Nutrition, aging, immunity

Zat gizi dan sistem kekebalan pada lanjut usia

ABSTRAK


Kata kunci : Zat gizi, penuaan, kekebalan
INTRODUCTION

The proportion of age individuals has rapidly increased in the second half of the twentieth century in both Western and Developing Countries\(^1\) The number of individuals aged 60 years or older is projected to double as a proportion of the world’s population and to more than triple in number over the next 50 years. The United Nations Population Division estimated that this age group represented ~10% of the world’s population, or ~600 million people, in 1999. They project that by the year 2050, this proportion will increase to 20% and will include >2 billion people.\(^2\)

These changes will be most dramatic in the less developed countries, where the population age structure will change rapidly from one that is predominantly young, with few elderly, to one with more balanced numbers across age groups. One of the mayor consequences of this growing elderly population is the significant increase in health care expenses due to their susceptibility to infection. The aging process has been described to be associated with decreased immune functions, mainly with important decreases in cell-mediated immunity (CMI) and lower effect of non-specific and humoral immunity. To support the immune system the body requires nutrients, defined as substances in food that the body can use to obtain energy, synthesize tissues or perform regulatory functions. Our body needs nutrients for normal growth and development, maintenance of cells and tissues, providing fuel for physical activity and metabolic processes, as well as regulation of daily body processes. There are six classes of nutrients in food, such as carbohydrates, lipids, proteins, vitamins, minerals and water. The six classes of nutrients serve three general functions: (i) provide energy, (ii) regulate body processes and (iii) contribute to body structures.

Our body needs large quantities of carbohydrates, proteins and lipids to serve the general functions, these substances are called macronutrients; the vitamins and minerals are called micronutrients, because the body requires it in relatively small quantities for cellular metabolic processes.

Nutritional status plays an important role in the functions of the immune system. Impaired immune response in aging may be partly due to underlying nutritional deficiency. The aging process increases population risk for nutrient deficiencies because of various physiological, social and economic factors. Epidemiological and clinical data suggest that nutritional deficiency is a risk to immune competence and increases the risk of infection, especially in the elderly.\(^3\)

Nutrition in the elderly

Aging is associated with physiological and economical changes that compromised nutritional status. Environmental, pharmacological and psychological stresses often increase age-related changes in body composition, sensory abilities, organ system and immune function. The clinical outcome of impaired immunity is an increased incidence of common infections affecting the upper and lower respiratory, urinary and genital tracts. Changes in immunity, which is associated with aging, include decreased delayed-type hypersensitivity (DTH) responses, reduced IL-2 production and proliferation of lymphocytes, reduction in serum IgA as well as decreased antibody titer after vaccination.\(^4\)

Human growth hormone stimulates skeletal and muscle growth, and its production declines with age. It also contributes to loss of bone, muscle mass and strength.\(^5\) Also declining with age is the perception of taste. It requires a higher concentration of a flavor to detect it, and may contribute to loss of appetite and poor intake. Changes that occur along the gastro-intestinal
(GI) tract affect GI function that could interfere with food intake, absorption and elimination of waste products.\(^6\)

Under-nutrition is common in the elderly population that indicates poor dietary practices caused by age-related decline, especially eating disorders.\(^7\) However, the requirement for dietary energy and most micronutrients (vitamins and minerals) does not decrease, and a well-balanced diet is important to prevent an inadequate intake of macro and micronutrients. Human malnutrition is usually a complex syndrome of multiple nutrient deficiencies.\(^3,8\) A study included 3,885 people of 65 years of age and over in the US showed that older people who reported food insufficiency: lower mean intake of several nutrients; lower intake of the vegetable and meat groups; lower dietary variety; lower mean serum levels of certain nutrients; higher risk of being underweight, and in poor or fair health.\(^9\)

Considering that older people are at risk of malnutrition, this study indicates that food insufficient elderly people are an especially vulnerable population. If all older people are to maintain or acquire a healthy lifestyle, then outreach to the food insufficient elderly must be developed and implemented. Also, gaps in the safety net must be identified and remedied and food assistance and nutrition education efforts improved.

**Micronutrients in the elderly**

Micronutrients consist 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, and K) and water-soluble vitamins (B vitamins and vitamin 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.\(^10\) The function of minerals is involved in a variety of structural and regulatory functions.

In the elderly, the body’s defense mechanisms begin to weaken, thus as a result the elderly are more susceptible than younger adults to infections and illness. Moreover, elderly people are two to 10 times more likely to die of a variety of infections than younger adults.\(^11\) Several micronutrients are significant immuno-modulators and thus are critical in determining the outcome of host microbe interactions.\(^4\) Vitamin A, beta-carotene, folic acid, vitamin B\(_6\), vitamin B\(_{12}\), 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.\(^12\)

Antioxidant nutrients play a central role in maintaining the antioxidant or oxidant balance in immune cells and in oxidative stress protection, and preserving adequate function. Dietary supplements protect the body from accelerated aging process in various ways. The supplements enhance metabolic functions, help to detoxify harmful substances, antioxidant activity or recycle antioxidants after quenching free radicals. Some supplements are important as cofactors for antioxidant enzyme activity.

**Immune system in the elderly**

The most basic defense mechanism of the human body is the immune system. There are two types of immune function, innate and acquired immunity. Dysregulation of immune function on humans may contribute to increasing the incidence of infection, inflammatory and cancerous diseases in the elderly and prolonged recovery period of illness. The increase in disease frequency associated with aging suggests that immune responsiveness is decreased in the elderly; aging is associated with higher incidence
of infections and subsequently, a higher mortality related to infections. Aging is also associated with other pathologies related to immune dysfunction, i.e. higher incidence of cancer, increased monoclonal immuno-globulins and increased autoantibody levels.\(^{(1)}\)

Numerous studies have investigated the age-related changes in immune responses. The ability of stem cells decreases with age; their ability to mature in lymphoid tissues also decreases with age, in relation to decreased thymus function.\(^{(13)}\) Lesourd\(^{(14)}\) examined the effect of aging (healthy elderly) with or without PEM, found that age-associated with decline in total-T and T-helper cells occurred only in the presence of protein energy malnutrition (PEM). Similar adverse findings on immune function also were reported for elderly deficient in vitamins B6, B12, iron and zinc. Bogden\(^{(15)}\) also reported that deficiency of zinc impairs cell-mediated immunity by reduced lymphocyte proliferation response.

Scrimshaw and Giovanni\(^{(16)}\) showed evidence of adverse effects on immunity in several macro and micronutrients deficiencies. The results suggested that even mild infections could adversely affect nutritional status and deficiency of almost any nutrient will impair immunity and resistance to infection. Thus, it is not surprising that some aspect of immunity was strongly influenced by nutritional deficiencies. Some studies had summarized that undernutrition in the elderly appeared as one of the main factors that could influenced low immune response in the elderly.\(^{(8)}\)

Catabolic response occurs with all infections including sub-clinically and not accompanied by fever. Under the stimulus of interleukin-I released by leukocytes, endocrine changes are initiated that lead to the mobilization of amino acids from the periphery, primarily from skeletal muscle. During infection, amino acids as an anabolic response are diverted from normal pathways for the synthesis of immuno-globulins, lymphokines, C-reactive proteins and a variety of other proteins.

Barringer\(^{(17)}\) showed that a multivitamin and mineral supplement reduced the incidence of participant-reported infection and related absenteeism in participants with type-2 DM and high prevalence of sub-clinical micronutrient deficiency. Nutrition had strong influence on the immune system of the elderly. Aging induced dysregulation of the immune system, mainly changes in cell-mediated immunity that is associated with changes to the equilibrium of peripheral T and B lymphocyte subsets. It decreased the ratios of mature to immature, naïve to memory, T helper 1 subset (TH-1) to TH-2, and CD5- to CD5+ cells.

**Effect of protein-energy malnutrition on immune responses in the elderly**

Infections are more common in undernourished than in well-nourished persons. Both protein energy malnutrition (PEM) and aging had cumulative effects on immune responses that induced a sharp decline in immunity in aged, both animal trials and humans, with low protein intakes. Increases in immature CD2+, CD3-, T cell subsets were observed in both healthy and well-nourished elderly, although low serum folate concentrations was found in Lesourd study.\(^{(18)}\) On the other hand, malnourished elderly, showed alterations in T lymphocyte subsets together with lowered T lymphocyte proliferation and IL-2 release, compared with healthy elderly without any nutritional deficiencies. It has been reported that undernourished elderly subjects are more likely to have pulmonary infection. In many pulmonary-infected elderly individuals, CD4+ concentrations have been reported as low as those found in patients with AIDS.\(^{(19)}\)

In elderly subjects with PEM, all parameters of cell mediated immunity are
decreased beyond the levels found with “normal” aging: T cell number (CD3+, CD4+), lymphocyte proliferation, and cytokine synthesis. PEM induces not only low lymphocyte counts and functions but also low polymorphonuclear and monocyte function. Therefore, PEM can modify the clinical symptoms of inflammation in undernourished elderly individuals, for example, there is a low release of IL-1 in the undernourished during infection and although these patients are really infected, but in some no signs of fever are shown. Antibody response also is lowered in the undernourished elderly population. Seroconversion rates after tetanus toxoid or influenza vaccine are shown to be lower in elderly people suffering from malnutrition. After vaccination, not only are antibody levels lowered in the elderly suffering from malnutrition, but antibody affinity is also reduced.

The role of nutrition in immunity in the elderly

Immunological vigor declines with age, contributing to increase morbidity and mortality in the elderly. In addition, the elderly are at greater risk for low intake of several vitamins and minerals known to influence the immune response. The fact that nutrient-nutrient interactions and multiple nutrient deficiencies often occur in the elderly. Adequate protein status is important for determining lymphocytes counts, lymphocyte proliferation, and antibody response. Recent studies have shown that supplementing the elderly with single nutrients or mixture of vitamins and minerals at levels that exceed the Recommended Dietary Allowances (RDA) significantly improves certain indices of the immune response. Harshman et al studied supplementation with trace element selenium acted both as an antioxidant and anti-inflammatory agent. Selenium deficiency could impair both cell-mediated immunity and B cell function, also may be linked to the transition of harmless viruses to virulent ones and may have an impact on viral disease. By acting as scavengers, gluthione peroxidases (selenoproteins) hinder the propagation of free radicals and reactive oxygen, diminishing the production of inflammatory prostaglandin and leukotrien from hydroperoxide intermediate. Selenium supplementation showed enhanced proliferation of activated T cell, enhanced the response to antigen stimulation of lymphocyte, increased the ability of lymphocytes to become cytotoxic for tumor cell destruction, and increased natural killer-cell activity. Another study used four-leg supplementation, trace element (Se & Zn) or Vitamin (E, C, β-carotene) or a combination of both, or placebo. Antioxidant levels in the supplementation were of physiologic doses: 1 to 3 times the RDAs, and the study was conducted over 2 years with institutionalized elderly in “apparently good health” with a priori life expectancy of 3 years. Selenium and vitamin deficits were corrected with supplementation within 6 months, but a longer period (1 year) was needed to restore zinc deficit. The supplementation induced decreases in lipid peroxidation. The group treated with antioxidant vitamins showed increased monocyte functions (IL-1 production). In contrast, the increase in antibody titers after influenza vaccine was higher in the trace-element group and reduced the incidence of infection. Meydani have conducted several studies using a large range of vitamin E supplements for several months. The result showed that in “healthy” elderly, vitamin E supplements increased delayed type hypersensitivity, lymphocyte proliferation and IL-2 production. The optimal dose level of vitamin E per-day that caused this immune response was 200 mg. An epidemiological study indicate that the antioxidant properties of vitamin E and polyphenols present in green tea may contribute to reducing the risk of cardiovascular disease, in part by reducing the susceptibility of...
low density lipoproteins to oxidation, decreasing the vascular endothelial cell expression of pro-inflammatory cytokines, and decreasing the expression of adhesion molecules and monocyte adhesion.\(^{(25)}\)

Thus, five general concepts have been advanced that value the effect of micronutrient on immune responses, namely (i) alterations in immune responses occur early in the course of reduced micronutrient intake, (ii) the extent of immunology impairment depends on the type of nutrient involved, its interaction with other essential nutrients, the severity of deficiency, the presence of concomitant infection, and the age of the subject, (iii) immunology abnormalities predict outcome, particularly the risk of infection and mortality, (iv) for many micronutrients excessive intake is associated with impaired immune responses, and (v) test of immuno-competence are useful in assessment of safe lower and upper limits of micronutrient intake. However, in elderly individuals, diet is restricted and the absorption of nutrients is reduced in metabolic function that might need supplementation of certain nutrients.\(^{(26)}\)

Without adequate nutrition, the immune system is clearly deprived of the components needed to generate an effective immune response. Nutrition deprivation, such as protein energy malnutrition (PEM), often causes immunodeficiency leading to increased frequency and severity to infection. (Table 1)\(^{(22)}\)

Table 1. Physiological and pathological situations in which nutrition acts as a primary or secondary determinant of immune function impairment\(^{(22)}\)

<table>
<thead>
<tr>
<th>Physio/pathological</th>
<th>Effect on immunity</th>
<th>Nutritional advice</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEM</td>
<td>Thymus atrophy, leukopenia, ↓CD4/CD8</td>
<td>Reversible with refeeding</td>
</tr>
<tr>
<td>Aging</td>
<td>↑frequency of infections, ↓IL-2 production, ↓Lymphocyte proliferation</td>
<td>Beneficial nutrient supplementation</td>
</tr>
<tr>
<td>Obesity</td>
<td>Immunosuppression, ↑frequency of infections, poor antibody response</td>
<td>Rationally controlled weight loss &amp; then weight stability</td>
</tr>
<tr>
<td>Eating disorders</td>
<td>Leukopenia, relative lymphocytosis, ↓DTH response, altered pattern of cytokine secretion</td>
<td>Nutritional rehabilitation Nutritional education &amp; correction of dietary habit</td>
</tr>
<tr>
<td>Sports requiring low body weight</td>
<td>Leukopenia, lymphopenia, ↓DTH response altered pattern of cytokine secretion</td>
<td>Nutritional rehabilitation Nutritional education &amp; correction of dietary habit</td>
</tr>
<tr>
<td>Food allergy</td>
<td>Hyper-response of immunologic mechanism Leading to asthma, atopic eczema &amp; other allergic manifestations</td>
<td>Strict avoidance of allergenic food</td>
</tr>
<tr>
<td>Gastro-intestinal disorders</td>
<td>Those secondary to nutrient deficiencies Failure of mucosal mechanisms of defense (altered IgA-mediated protection) Impairment of the homeostatic response to limit epithelial inflammation</td>
<td>Administration of probiotics with adequate bacteria strains</td>
</tr>
</tbody>
</table>
Older and obese individuals tends to have high prevalence of common infections. The effect of exercise on immune response is multifaceted, depending upon the type of exercise and the intensity of training. In general, it is accepted that while moderate exercise enhances immune functions, high-intensity and heavy training can suppress various immune response parameters. The primary activity of mucosal immune response is to protect the mucosa by blocking microbial, toxin and antigen. Commensal bacteria may exert a dual function: the stimulation of mucosal mechanisms of defence and the maintenance of homeostasis of the immune response. Probiotics have proved helpful in prevention of infectious diarrhea and shortening of the episodes.

CONCLUSION

The importance of adequate macronutrient and micronutrient intake throughout the life course to maintain health is essential. Under nutrition strongly influences immune response in the elderly since many nutrients interact with immune system. Because the immune response needs rapidly dividing cells and highly activated secreting cells to be efficient, all nutrients that interfere with cell division and metabolism may influence immune response. The nutritional deficiency impairs the immune response, exposure to viral pathogens, and will result in an increase in the severity of diseases. The multiple effects of nutritional deficiencies on immune function also increase the frequency and severity of infections. This indicates that aging and the undernourished had cumulative effects on immune response of the elderly that could be detectable both in cell-mediated and humeral immunity. Supplementation with micronutrients, including minerals such as selenium and zinc, could reduce morbidity from respiratory infections among the aged. Therefore, nutritional deficiency must be treated in the elderly to reduce risk of infection and possibly slow down the aging process.

Reference