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Concept of Immuno-Nutrition

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Introduction

Proper nutrition offers one of the most effective and least costly ways to decrease the burden of numerous diseases and their associated risk factors. Modern nutritional research significantly contributes to improving health of both current and future generations. An important part of nutrition and health is immuno-nutrition, which can be defined as the effect of the provision of specific nutrients on immune function. Another explanation of this term is the description of enteral feeding formulas that have been supplemented with some combination of amino acids, nucleic acids, oils, herbs, and additional vitamins and minerals. We can also understand nutrition as the science of food, particularly in relation to health and disease.

The potential to modulate the activity of the immune system by interventions with specific nutrients is the true concept of immuno-nutrition. This concept may be applied to any situation in which an altered supply of nutrients is used to modify inflammatory or immune responses. However, immuno-nutrition has lately become associated most closely with attempts to improve the clinical course of critically ill and surgical patients, who will often require an exogenous supply of nutrients through the parenteral or enteral routes. Unfortunately, this rather narrow focus forgets the fact that with optimal nutrition it is possible to modulate health status of all individuals. Three potential targets exist for immuno-nutrition-mucosal barrier function, cellular defense, and local or systemic inflammation. Many trials used different compositions, but there are also trials which have shown some benefit from the single immuno-nutrient approach. For example, enteral provision of glutamine decreased the incidence of sepsis in premature neonates and the incidence of pneumonia, and severe sepsis in critically ill patients.

Many of the protective functions of immune cells depend on membrane fluidity, which adversely affects immune response. Therefore, the relevance of antioxidants is particularly critical for the functionality of immune system. Nutritional status represents an important factor contributing to immuno-competence and to optimal cooperation among nutrition, infection and immunity. It is now clearly established that nutritional deficiency is closely related to an inadequate function of immune response, including phagocyte function, cytokine and antibody production, and anti-infection immunity. In addition, we have to remember that antioxidants represent our first line of defense and are crucial for maintaining optimal health therefore we need an optimal intake of components with anti-oxidative properties. We also have to remember that nutrition and the respective antioxidants may be important for the development of other diseases which are not related to the immune system. Several studies show that antioxidant constituents may be important in the development of eye disease and significantly lower glaucoma risk.

The effects of diets on the development of some diseases are well documented. A stroke can serve as an example. Scientific literature covers 152 research papers on this subject. A systematic review and meta-analysis of relevant papers suggested that adherence to healthy dietary patterns (such as Mediterranean or DASH diets) was associated with reduced risk for stroke incidence and mortality [1].

The immune system is the body's primary defense against invading pathogens, non-self-components and cancer cells. Inflammatory processes, including the release of pro-inflammatory cytokines and formation of reactive oxygen and nitrogen species, are an essential part of these processes. Although such actions are usually followed rapidly by anti-inflammatory effects, excessive production of pro-inflammatory cytokines, or production in the wrong biological context may lead to situations of chronic inflammation. Whether such conditions arise as a result of exogenous chemicals, invading pathogens or disease processes, the long-term implications include an increased risk of cancer. A number of nutrients have the ability to modulate immune response and counter inflammatory processes. Prostate cancer can serve as another example. There is no doubt that there are hereditary and environmental factors contributing to prostate carcinogenesis, but at present, only age, race, and family history are established risk factors. However, increasing evidence from epidemiologic surveys and case-control studies suggests that diet and lifestyle plays a crucial role in prostate cancer development. Numerous nutrients and supplements have shown benefits in helping to slow progression and to reduce recurrence, as well as complementing conventional treatment improving quality of life. Detailed review confirmed that whereas consumption of red meat, dietary fat and milk should be reduced, fruit, vegetables and most of all polyphenols may be preventive in prostate cancer [2].

Intestinal tract represents the largest interface between human body and external environment. Its role in nutrient uptake has no substitution. Nutritional components are extremely important for the integrity of the intestinal epithelial barrier [3].

Nutrition and infections are intimately related, which is particularly important for young children who frequently suffer respiratory problems and diarrheal disease. The link between malnutrition and impaired immune functions is well described [4]. The subsequent research into specific nutritional components that might improve immune functions has stimulated the development of commercial enteral products designed to improve both the outcomes of hospitalized patients and the general public. Treatments involving food and supplements include nutrition and lifestyle changes, herbal medicine and biological treatments that encompass multivitamin use. We have to keep in mind that we can hardly change our health by changes in food alone. It is both impractical and impossible to just increase the consumption of specific food and hope for the best. Currently, there is inadequate information available to provide detailed

information on these effects, but it is always better to use well-established and well-tested supplements than large quantities of food which might contain this or that particular component. Resveratrol, often considered to be the responsible part of the healthy benefits of the Mediterranean diet, was repeatedly shown to have health benefits. However, the amounts in red wine (which is supposed to be the real reason behind these benefits) are so small that in order to have the benefits documented with supplements, we would have to drink several bottles of red wine every single day. Potentially beneficial effects of immuno-nutrients on innate and adaptive immunity, with an emphasis on cancer related properties, are well-established [5]. However, most of the current knowledge on links between immunity and nutrition is focused on innate immunity [6] and more attention on the specific immunity is clearly necessary.

The most common additions to the general nutrition are arginine (increasing T lymphocyte functions), glutamine (serving as an oxidative fuel for rapidly dividing cells), omega-3 fatty acids (reduction of proinflammatory mediators in stressed people), nucleotides (improvements of immune reactions), antioxidants (such as vitamin E, vitamin C, selenium, copper, iron, β-carotene and zinc), and glucan. These antioxidants commonly included in our diet, improve different immune functions exhibiting an important protective role in infections caused by bacteria, viruses and parasites. As a result, dietary antioxidants have been related to modulate the host susceptibility or resistance to numerous infectious pathogens. With so many different antioxidants available, we must remember, that to have "only" antioxidative properties does not necessary result in health benefits. Further investigations need to be performed to evaluate the interaction between different antioxidant nutrients and to establish the real level of supplementation necessary to optimize immune responsiveness in different groups of population.

All of these components are important for our health and their effects were demonstrated by improvements after consuming these additives, as well as by health problems when fed diets without these components. Trials of these immuno-nutrients indicate several beneficial clinical effects, particularly in surgical patients.

One of the most commonly recognized immuno-nutrient is zinc. Zinc is required as a catalytic, structural and regulatory ion for enzymes and proteins and is therefore a key trace element in many homeostatic mechanisms of the body, including immune responses. It is also a critical component of many of the enzymes involved in DNA replication and transcription. Since immune cells are rapidly dividing, especially during infection, they have heightened sensitivity to impaired DNA replication. Zinc plays a structural role in the formation of zinc fingers that are exploited by transcription factors for regulating the activity of genes. It is also a component of proteins involved in signal transduction during T lymphocytes activation and interaction with B lymphocytes.

Zinc deficiency is characterized by depressed immune functions, lymphopenia and reduced numbers of circulating T and B lymphocytes, and impaired chemotactic responses of neutrophils, monocytes and macrophages. A zinc deficiency raises blood glucocorticoid levels, decreases thymulin activity and affects many cytokine concentrations. In general, cytokines affecting lymphocytes are suppressed and inflammatory cytokines are enhanced. Prolonged zinc deficiency may result in a substantial reduction of the thymus size, depletion of T lymphocytes from periphery organs and reduced formation of B lymphocyte precursors in bone marrow. In combination with retinoic acid, zinc promotes protection against Listeria [7].

Low zinc ion bioavailability results in reduced resistance to infection in older people. Supplementation of zinc to physiological levels for 1-2 months restores immune responses, reduces the incidence of infections and prolongs survival. While zinc supplementation is beneficial in prevention and treatment of infection of zinc-compromised people, zinc supplementation of the diet should be adjusted to the particular zinc status in view of the great variability in habitat conditions, health status and dietary requirements. The list of the effects of some nutritional supplements on immune reactions is given in Table 1.

Supplement	Effect
Zn	Lower infection with sickle-cell disease
Zn+Se	Lower number of infections
Glucan+Se	Stimulation of immunity
Vitamin E	Lower kidney infections
Fe	Stimulation of immunity

Table 1: Effects of nutritional components on immunity.

To discover if a nutritional supplement would decrease the number of infections and positively affect the immune system, the proper tests are necessary. We did a series of clinical trials using children with chronic respiratory problems and coming from areas of heavy pollution and/or indoor smoking and compared the control group with a group consuming food supplemented with glucan for 30 days. We found significant improvements in production of secretory antibodies, improvement in the production of lysozyme, C-reactive protein and calprotectin. In addition, strong improvements in endurance were observed [8-12].

In many diseases, nutrition might be an important key in recovery. But every patient has unique metabolic needs, so some need more of this nutrient, some more of the other one. In addition, nutrition also plays an important role in exercise and heavy training [13]. One has to remember that poor nutrition leads to poor immune defense, which can allow the infection or cancer cell to thrive. Proper diet also affects chronic diseases and life span [14].

Although a considerable amount of the currently-available literature on immuno-nutrition focuses on cancer patients, the greatest potential of modulating immune function may be in chemoprevention of cancer. Health professionals must better educate both the general public and their colleagues in the judicious use of these substances. In most cases, the data are still sketchy. At the same time, some changes have to occur at the medical training level. In many medical schools the future physicians receive only very limited nutritional training, often during their biochemistry course. The rest of medical school is completely pharmaceutically focused.

On the other hand, some of the immuno-modulators were already studied so extensively and the progress of our knowledge of their action is so substantial, that there are no doubts about their benefits [15]. Beta glucan, with over 10,000 peer-reviewed scientific studies, can serve as the best example. It took 70 years for the scientific community to accept that vitamin C cured scurvy. It may take repetitious studies and more time before flavonoids, vitamin C, beta-carotene, NSAIDs,

selenium, vitamin A (retinoids), mannose, beta glucan, fatty acids or antioxidants are credited for their roles in the battle against cancer.

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