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Mini Review

Nutritional Factors Versus Immunity

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Diet and lifestyle factors become visible to encompass a crystal-clear influence on innate and adaptive immunity, influencing development of non-communicable diseases (NCDs). As oxylipins, derivatives of EFA, have a critical role in the development of immunity and inflammatory responses, and are derived from polyunsaturated fatty acids (PUFA), it becomes clear that PUFA can influence immunity and inflammation. PUFA bound to membrane phospholipids are released on stimulation by hormones, cytokines, and other stimuli, like viral infection, from cell membranes, and become substrates for production of dodecanoic, eicosanoid and oceanids. Deficiency of PUFA and other micronutrients in the Western type diets may decrease these eicosanoids resulting in decline in T-lymphocyte function and immune defense, predisposing to infection. There is evidence that Indo-Mediterranean style diets, omega-3 fatty acids, flavonoids and herbs as well as moderate intake of alcohol, may have beneficial effects and ultimately acting as immune-modulators [1,2]. This 'Mini review' aims to highlight the functionally enriched diet to be most significant nutritional modulators of immunological function likely to providing protection from diseases as follows. Western diet, characterized with high energy and low micronutrients is known to generate free radical induced oxidative stress, leading to systemic inflammation. The effect of Western diet is largely blunted by dietary changes, but myeloid cell-induced innate immune responses remain augmented and predispose to pro-inflammatory NCDs, if prevented measures are not undertaken. Western diet triggers innate immunity, the nucleotide-binding oligomerization (NOD)-like receptors (NLRs), and IFN signaling pathways. It is important to understand the mechanisms of the role of diet and lifestyle factors in the development of immunity to explain their role in the pathogenesis and prevention of COVID-19. It is proposed that diet and lifestyle induced immunological protection provided to host should be recognized as trained immunity. It is an emerging new concept highlighting a long term hyperactivation of the innate immune system after exposure to certain antigenic stimulations. However, upon continuation of energy rich, nutrient deficient diet, there may be immunosuppression predisposing to increased susceptibility from free radical induced damage to tissues. The progression of disease is associated with inflammatory processes involving cells of the innate immune system, mainly monocyte-derived macrophages. Hence, it is of fundamental and translational importance to understand explicitly the mechanisms that link to the consumption of energy rich diets to increase in inflammation.

Among dietary factors, flavonoids have specific immunomodulatory effects that might be of importance in the development of many diseases in which immunity is reduced [3]. Among several types of immune cells, T lymphocytes play a critical role in protecting the immune system as well as in the pathogenesis of specific autoimmune diseases. In the immune system, mTOR, particularly, in T-lymphocytes is an important mediator of metabolism. Polyphenolics and flavonoids can suppress mTOR activity and may induce the T-regulatory subset. There is evidence that several of the dietary flavonoids including quercetin, naringin, hesperidin, and

catechin can influence virulence and replication of herpes simplex virus type 1 (HSV-1), polio-virus type 1, parainfluenza virus type 3, and respiratory syncytial virus (RSV) [4]. It seems that dietary flavonoids may have variable spectrum of antiviral activity against certain RNA and DNA viruses which may inhibit infectivity and/or replication, indicating that flavonoids might also inhibit these markers in COVID-19. Polyunsaturated fatty acids are known to exhibit a range of immunomodulatory functions that progress through T-cell mediated events, although the molecular mechanisms of these actions have not yet been fully elucidated. It seems that some of these immune functions are linked to polyunsaturated fatty acid-induced alteration of the composition of cellular membranes and the consequent changes in signaling pathways linked to membrane raft-associated proteins. Some experts have suggested that significant aspects of the polyunsaturated fatty acid bioactivities are mediated through their transformation to specific lipid mediators, products of cyclooxygenase, lipoxygenase, or cytochrome P450 enzymatic reactions. It is possible that appreciation of the mode of action of these lipids presents opportunities for the design and development of therapeutic strategies aimed at regulating T cell function. It is clear that fatty acids are involved in T cell biology both as nutrients important for energy production as well as signaling molecules [4].

Omega-3 fatty acids induce immune response, apart from decrease in inflammation [5].There is evidence that omega-3 and omega-6-derived metabolites have important immune-regulatory functions. These metabolites are generally known as pro-resolving mediators. These mediators may be classified in different families; prostaglandins, leukotrienes, thromboxane's, maresins, protections, and resolving. The synthesis of these molecules is orchestrated by certain enzymes; lipoxygenase, cyclooxygenase, or cytochrome P450. Omega-3 and omega-6 substrates compete for these enzymes, as well as for the above mentioned elongates and elastases. In the presence of omega-3 fatty acids, the competition for the enzymes reduces the synthesis of omega-6-derived metabolites, which also have effects on immune cells. There have been significant advances in understanding the mechanisms of action of n-3 fatty acids over the last 10 years [6,7]. These include the identification of new actions of lipid mediators that were already described and of novel interactions among those mediators and the description of an entirely new family of lipid mediators, resolving and protections that have anti-inflammatory actions and are critical to the resolution of inflammation. It is also recognized that EPA and DHA can inhibit activation of the prototypical inflammatory transcription factor NF-κB. Recent studies suggest three alternative mechanisms by which n-3 fatty acids might have this effect. Within T-cells, as well as other cells of relevance to immune and inflammatory responses, EPA and DHA act to disrupt very early events involving formation of the structures termed lipid rafts which bring together various proteins to form an effective signaling platform [8]. Several effects of n-3 fatty acids EPA and DHA on functional responses of cells involved in inflammation and immunity have been described. Fatty acid-induced modifications in membrane order and in the availability of substrates for eicosanoid synthesis are long-standing mechanisms that are considered important. Arachidonic acid is which is rich in muscle and eggs acts as a chemical messenger first released by the muscles during intense weight training, controlling the core physiological response to exercise and regulating the intensity of all growth signals. If there is any tissue injury, inflammation is involved in healing of the wound mediated by arachidonic acid present in cell membranes that produces eicosanoids. T cell, also called T lymphocyte, type of leukocyte which is an essential component of the immune system. The eicosanoids may be pro-inflammatory and anti-inflammatory, competing with each other. Arachidonic acid is the substrate to PGE2 and PGF2a. There is evidence that PGF2a, specifically, as being the prostaglandin most closely tied to increased synthesis of protein in the skeletal muscle. That has no capacity to actually store prostaglandins, so the only local source for PGF2a is the arachidonic acid that is retained in the outer phospholipids layer of each cell [6,7].

The intake of consumption of n-6 polyunsaturated fatty acids greatly exceeds that of n-3 polyunsaturated fatty acids in most of the dietary patterns. Arachidonic acid; a type of The n-6 polyunsaturated fatty acid present in egg, meat, fish and mushroom, arachidonic gives rise to the eicosanoid family of inflammatory mediators such as prostaglandins, leukotrienes and related metabolites. It is possible that and through these mediators regulates the activities of inflammatory cells, the production of cytokines and the various balances within the immune system [9]. It is possible that increased intake of fish oil and oily fish are good sources of long chain n-3 polyunsaturated fatty acids as well as arachidonic acid which is in fish meat. Consumption of these fatty acids liberates decreases the amount of arachidonic acid forming cell membranes increasing its and so availability for eicosanoid production. It is possible that these fatty acids might elicit some of their effects by eicosanoid-independent mechanisms. Such *n*-3 fatty acid-induced effects may be of use as a therapy for acute and chronic inflammation, and for disorders which involve an inappropriately activated immune response [5-7]. The occurrence of corona virus infection has become a public health problem in India, according to Ministry of Health, Government of India. Half of the deaths occur among subjects above 60 years and one third deaths occur, among subjects between 34 to 60 years, in India. The death rates are greater among subjects with co-morbidities, diabetes mellitus, heart failure, coronary artery disease and chronic kidney disease (78%). The death rate is lower (14%) among subjects below 45 years. It seems that COVID-19 has already crossed the epidemiological criteria to be declared as Pandemic, having infected more than 213 countries around the Globe [10,11]. Since COVID-19 infection is associated with marked decline in immunity, it poses the possibility that diet and lifestyle factors related with immune function may influence rate of infection, complications and deaths.

Increasing evidence suggests that light to moderate amounts of polyphenol-rich alcoholic beverages like wine or beer could have health benefits. The effects of alcohol on immune function, showing on the one hand, that high doses of alcohol consumption can directly suppress a wide range of immune responses, and that alcohol abuse

is associated with an increased incidence of a number of infectious diseases. On the other hand, moderate alcohol [12,13]. Therefore, the link between alcohol consumption, immune response, as well as infectious and inflammatory processes remains completely understood. With this in mind, it is important to realize that other factors, unrelated or indirectly related to immune function, like drinking patterns, beverage quality, amount of alcohol, or gender differences, will entail that alcohol consumption may have on the immune system. It is possible that light to moderate amounts of polyphenol-rich beverages like wine or beer seem to have beneficial impacts.

Conclusion and Future Perspectives

In brief, Mediterranean type diets rich in polyphenols and flavonoids, omega-3 fatty acids and arachidonic acids, moderate alcohol intake, physical activity and sleep may be vital immune-modulators. It is possible that vitamins; A,E,C,D and beta carotene and minerals, zinc, copper, selenium, chromium and magnesium may have beneficial effects on immunity. However, Western type foods such as sugar, excess of salt, trans fat, refined foods, processed and red meat, tobacco and alcoholism, short sleep and infections may have adverse effects on immunity. This editorial provides new insights or clues to develop nutritionally fortified food products likely to be immunity modulators or boosters.

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