

Nutrition and Immunity: A Co-Relative Case

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ABSTRACT:-

Many macronutrients, including certain fatty acid, cholesterol, and amino acid, as well as variety of micronutrients, including minerals, vitamins, and other micronutrients, have been shown to have a very significant and focused effect on healthy immunological function. Although nutrition knowledge is crucial, health care training pays little emphasis to it. Health requires a number of specific vitamins, minerals, and other nutrients. By giving immune cells the right nutrients in the right amounts, nutrition is key in the control of an optimum reaction. Dietary health can also be influenced by the fluids that are crucial to our vital hydration. The host is shielded from harmful organisms by the immune system (bacteria, viruses, fungi, parasites). The immunity has developed to incorporate a variety of specific cell verities, communication element, and function response to deal with the variety of the threats. Although the immunity is constantly engaged in monitoring, it becomes more active when a person contracts an infection. As a result of this increased activity, the body requires more sources of energy, regulatory chemical and substrate for biosynthesis, all of which are finally obtained from the food. An autoimmune condition known as Hashimoto (HT) causes the thyroid to be destroyed as result of lymphocyte attack. The brought on a rise in the antibody titters against Thyroglobulin and Thyroid peroxidase. As a result, alterations is thyroid hormone levels and metabolism are seen in HT patients, which cause a variety of vague physical and psychological symptoms.

KEYWORDS: vitamins, minerals, amino acids, immunity, health, and nutrition.

I. INTRODUCTION: -

In particular, pathogenic organisms, which might take the shape of protozoa, fungi, viral, microorganisms, are what the immunity service's role is to protect the host. The immunity of humans has develop to comprise a variety of types of cell, molecules used for communication, and functional responses after counteract such an expansive of dangers. ([1])Theimmunity is constantly engaged in monitoring, but when a person is sick, it becomes more activity. Together with this heightened activity comes a heightened rate of metabolism, which requests sources of energy, and biosynthetic substrate. The substrate regulatory molecules ultimately and energy source originated from food. Thus, a sufficient quantity of a variety of nutrition is necessary to maintain the immune system and ensure that it performs at its best. ([2])

One strategy for enhancing immunological health is to have a well-balanced, healthy diet. Recovery from illness will be greatly aided by healthy eating and safe food handling habits. One strategy to safeguard ourselves against the severity of this sickness is to strengthen our immune systems. Our ability to fight off viral infection and develop a healthy immune system is aided by proper diet. Whether is consumed either fresh produce, whole grains, or cereals, human systems absorb the nutrients and utilise them to create the antibodies and cells that make up our immune system. The minerals and foods that help boost immunity are listed below.

- 1 Vitamin C: It has outstanding anti-oxidant qualities that are beneficial in preventing infections. White blood cell synthesis, a key component of our body's defence system, is aided by this vitamin. Oranges, strawberries, kiwi, assorted tangerines, lime, and lemons, as well as broccoli, red bell pepper, kale, and red bell peppers are some fruits and veggies that are abundant in vitamin C.([4])
- 2 Zinc: The immune system in our bodies is largely dependent on this mineral to function properly. We are more prone to infections if we don't get enough zinc. Zinc is incredibly abundant in oysters. Crab, lobster, chicken, turkey, and red meat are all excellent sources of zinc, as are fortified cereals, breads, and beans.([3])
- **3** Vitamin B6: The development of the brain and nerve normally also a strong immune system depend on this vitamin. Creation of fresh Red Blood Cells is also aided by it. This vitamin is found in foods including chickpeas,



bananas, poultry, and seafood like salmon and tuna.([4])

- 4 Vitamin A: Food beta-carotene is transformed into vitamin A. It has anti-inflammatory properties and aids in the immune system's reaction to poisons like viruses. Most yellow and orange vegetables and fruit are rich in vitamin A. Excellent sources of vitamin A include carrots, squash, cantaloupe, papaya, apricots, sweet potatoes, spinach, kale, and other fruits and vegetables.([4])
- 5 Vitamin D: The body needs this vitamin to operate properly and to control immunological responses. For healthy bones, joints, and muscular function, vitamin D is also essential. Three times a week, 15 minutes of sun exposure is all that is required for the human body to produce enough vitamin D. Other sources of vitamin D include sun-dried mushrooms, tomatoes, eggs, dairy products, and seafood like salmon and tuna.([4])
- 6 Green tea: A strong source of antioxidants, it boosts our immune system and helps us fight infections. It also decreases inflammation. The beverage comes in a variety of flavours and is minimal in calories. Three to five cups of green tea each day should be included in your diet.([4])
- 7 Water: Water aids in the removal of poisons from our bodies. It is a key component of both blood and lymph and is crucial for the movement of immune system cells, white blood cells, and other nutrients throughout the body. To maintain our bodies well hydrated, it is crucial to drink 2 to 3 litres of water each day. Water content is high in many fruits and vegetables, including watermelon, cucumbers, and oranges. A tasty and refreshing method to keep healthy is to add slices of fruit and veggies to your water.([4])

II. THE IMPACT OF DIET ON OPTIMUM IMMUNOLOGICAL RESPONSE:

As previously discussed, nutrition plays a crucial part in controlling optimum immunological responses by giving immune cells enough nutrients in the right amounts. Hence, a powerful defence against infections can be mounted by the immune system. In order to prevent chronic inflammation, dietary components are crucial in causing this quick response.([5]) The immune system's cells are severely depleted of some nutrients when food

intake is insufficient or ineffective, which compromises immunity.

It's been established that a number of macronutrients, including amino acids, have significant and focused impacts on immunological modulation. For macrophages to function properly as immune cells, amino acids like L-arginine & Ltryptophan are crucial. According to alterations in the intracellular environment, macrophages exhibit variations in plasticity and polarisation. Depending on the intracellular milieu and various signalling molecules, they can transform into several subtypes. L-arginine is linked to established immune regulatory systems that M2 macrophages use to their advantage. ([6])Arginase 1, which breaks down Larginine, & the genes in charge of both M1 inhibition and M2 stimulation are involved in this pathway. Aside from that, the creation of polyamines involves both methionine and arginine working together. By maintaining DNA homeostasis and cell membrane stability, it promotes cell proliferation (Figure 2). Also, numerous studies have demonstrated the role of these types of amino acids in the metabolic processes of tumour cell growth and anti-tumour immune system responses.([7])Several amino acids act as the building blocks for enzymes, for a variety of biological processes once they have been broken down.([8])For insulin growth hormone and insulinlike growth factor-I, arginine can be a powerful secreted ligand for these molecules. Type 2 Diabetes & the metabolic syndrome are serious public health issues that are closely linked to diet. The synergistic activation of insulin release form the pancreas' βcell involves a number of amino acids. At neutral pH, arginine can reduce the activity the plasma membrane. When there is glucose involved, which is one of the best-known mechanisms. Cationic refers to this gating mechanism. ([9])

The initial rate-limiting step in the degradation of L-tryptophan is catalysed by Indolamine-2,3-dioxygenase 1, а strongimmunosuppressant enzyme. Tumour necrosis factor, interferon-g and II-1 are immune modulatory molecules that are produced in response to IDO1 depleting L-tryptophan reserves. ([10]) IDO1 is highly expressed and active catalytically by Dendritic Cell (DCs) in response to IFN-g. The creation of NAD+, a cofactor capable of redox reaction, is a result of the metabolism of tryptophan. Nuclear factor kappa-light-chain enhancer (NFkB)pathway activation in activated B cell may be influenced by arginine catabolism in immunological tolerance. In addition to serving as a substrate for



cell growth and survival, arginine is crucial for differentiation and the [deletion] of the proper genes. ([8])

Endoplasmic reticulum (ER) stress is caused by reductions in protein metabolism linked to a decline in the concentration of a particular amino acid. T cells are then activated, producing cytokines that promote inflammation.([11]) A lack of average is correlated with cells' diminished capacity to stimulate tumour immunity.([7])

Carotenoids & retinyl ester, which are known to affect healthy immunological function, are produced through the production of vitamin A. If it interacts to retinoic acid receptors, it can also function as a transcription factor (RARs). By controlling the expression of particular gene, it may therefore be in charge of maintaining lipid homeostasis as well as cell division, growth, and specialisation. ([12]) Immune system processes are impacted by vitamin A insufficiency, including neutrophil dysfunction, NK cell activity suppression, and reduced macrophage population and phagocytosis. ([13])

Zinc is one more instance of a micronutrient. ([14]) Zinc can suppress the NF-kB transcription factor (Figure 1). Zinc also controls certain pro-inflammatory Th17 & Th9 cells development pathways. ([15], [16]) Impaired lymphoproliferation, Natural killer cell activity and delayed type hypersensitivity are some of the specific consequences.([17])



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Fig 1:- The Relationship between nutrition and the immune system

III. ILLNESS AND DIETARY PATTERNS: RELEVANCE OF ESSENTIAL NUTRIENTS

Vitamins and minerals: - Ancient Egyptians used liver, which is high I vitamin A as a treatment for blindness, and there have been records of links between nutrition and disease dating back to 1500 BC. ([18]) The middle. Ages are when the word "scurvy," which refers to a swollen mouth, first appeared. Indeed, the eighteenth century saw a significant advance in the understanding of the significance of keeping citrus fruits separate to fight against scurvy. ([19])The 11 different vitamins were isolated, thoughtheir chemical formula weren't discovered until the first decade of the 20th century. By 1948, every vitamin has been recognised chemically and discovered. Table 1 provides a summary of all vitamins. ([20])

blue represent the fat-soluble vitamins and B vitamins, respectively. ([20])					
Vitamin	A sign of vitamin deficiency				
Vitamin A (retinol)	Blindness at night and xerophthalmia				
Thiamine (Vitamin B1)	Wernicke's encephalopathy, polyneuropathy, and Beriberi				
Riboflavin (Vitamin B2)	Dermatitis and glossitis				
Niacin(Vitamin B3)	Pellagra, diarrhoea, and mental illness				
Vitamin B6 (pyridoxine)	Macrocytic anaemia, seizures, and depression				
Vitamin B12 (cobalamin)	Spinal cord deterioration, peripheral neuritis, and macrocytic anaemia				
Biotin(Vitamin B7)	Anorexia, muscular discomfort, and dermatitis				
acid pantothenic Vitamin (B5)	Intestine and nervous system issues				
Vitamin B9 (Folic acid)	Macrocytic anaemia, anaemia				
(Ascorbic acid) Vitamin C	Scurvy, bleeding capillaries, and painful gums				
Vitamin D (cholecalciferol)	Bone malformation, tetany, and rickets				
Vitamin E (tocopherol)	Haemolytic anaemia and neuromuscular impairment				
Vitamin K (phylloquinone)	Haemorrhage and a reduction in blood clotting				

 Table 1:- Vitamins and the main signs of diseases caused by vitamin deficiencies. Red and blue represent the fat-soluble vitamins and B vitamins, respectively.([20])

Table 2:- Common minerals and the symptoms of their insufficiency([21])				
Mineral	Deficiency symptom			
Fe	Anaemia			
I	Congenital hypothyroidism in children with possible cognitive impairment thyroid goitre in adults			
Zn	Growth retardation, hypogeusia, and acrodermatitis enteropathica			
Mg	Tremor, muscle spasm, nystagmus, seizures			
Se	Cardiomyopathy in Keshan illness			
Ca	Osteoporosis			

Essential fats: -Necessary fats there was a great need to find out if there were other crucial elements needed in the human diet as it became evident that dietary deficits of vitamin were causing major health problems, even death. In the 1930s, clinical nutritionists investigated the relationship between symptoms of deficiencies and the appearance of scaly skin, infertility, stunted growth, & kidney



deterioration in animal model. The omega-3adipose, omega-6 with the omega-6 greasy omega-3, were found to be two more necessary nutrients. These are the fundamental components of all other fatty acids, which the body can produce in variable amounts.These are the fundamental components of all other fatty acids, which the body can produce in variable amounts.([22])

Essential amino acids: -These are 9 other important nutrient for human, which are consisting of the following 9 amino acid: lysine, valine, threonine, phenylalanine, tryptophan, isoleucine and methionine. In addition to the 15mineral, 2fatty, and 11 vitamins. The essential building block of all proteins isamino acids. 13 specific amino acids, some of which are necessary, have special uses that are not related to protein production. There are 21 amino acids in all, with humans being able to generate 12 of them, while the remaining nine must be ingested. Protein, especially animal protein are balanced amino acid delivery, is the principal natural supply of essential amino acids. There source are protein out there they don't have all the essential amino acids and if people, specific growing children & infants, eat protein sources that don't have all the essential amino acids, they won't thrive. ([23])

Carbohydrates: -When it comes to being necessary for a healthy human diet while not meeting the concept of an essential "nutrient" according to conventional wisdom, carbohydrates present a clinical contradiction. Monosaccharides, such as glucose, disaccharides, such as lactose, and polysaccharides make up carbohydrates (Such as starch, glycogen & plant-fibre).Polysaccharides, like starch in a cracker, can be broken down quickly, while fibre, which is a carbohydrate, is inconsistent with the digestive enzymes present in the human stomach.

There are populations that live on diets that are almost entirely devoid of carbohydrates, despite the fact that adult humans have an RDA for carbohydrates of 130 g/d. Before the arrival of Western diets and illnesses, the historical Inuit Eskimos of Greenland relied nearly exclusively on a diet heavy in meat and little to nothing in carbs, and they hardly ever suffered cardiovascular disease (CVD) or diabetes.([24])The Canadian Inuit have a 37-year life expectancy at birth between 1951 and 1961, which was 33 years less than the national average and it may not come as a surprise that their low-carb diet may have prevented the development of cardiovascular disease in them given that they may not have lived long enough to do so. ([25]) Unquestionably, long-term use of high levels of refined dietary carbohydrates has regularly been linked to a number of illnesses, including as obesity, diabetes, cancer, & cardiovascular disease. Ironically, people who lack whole grains and dietary fibre are also more prone to get ailments like colon cancer and cardiovascular disease. If we are to feed the world in a way that is environmentally sustainable, as it takes at least 10 pounds of grain to produce one pound of meat. ([26])

Increasing carbohydrate intake has been connected with an increases risk obesity, &there is no universally accepted top safe limit. BMI is calculated by dividing either multiplying the body mass (weight) by the square of the body weight in pounds or dividing by the body height inches. Adults are classified by their Body Mass Index into four categories: less than 18.5 kg/m2, between the range of 18.5-24.9, between 25 and 29.9, & over that (30 or more). By predicting BMI/age for kids ages 2 to 20, the CDC developmental milestones (http://www.cdc.gov/growthcharts) help to track growing and varying nutritional intake from birth throughout ([**27**])While maturity. being straightforward and simple to use, BMI screening may only accurately predict obesity 50% of the time. ([28][30])Person fitness level, such as VO2 max, is more expensive while also providing a more accurate prediction of health and overall mortality. Although BMI is a good predictor of overall mortality, it is not ideal. BMI changes are not necessarily reflected by changes in diet and exercise habits. ([29])

Water or other liquid forms for hydration:-The body loses water through normal physiological processes including perspiration, urine, and healthy bowel movements, thus it is important to drink enough water each day to make up for these losses. The daily appropriate consumption requirement for people who do not exercise is 2.7 L for women, drink 91 ounces or 3.7 L (or 125 oz or 15.6 cup) of all food and drink, and 11.3 cups (11.3 cups) for males.([30])A more accurate estimate of water requirements is 35 to 45 mL/kg/d, with demands rising by roughly 1 mL water for every calorie burned when exercising.([31])Care must be taken when calculating an individual's water needs due to the significant variations in body weight, level of exercise, overall health (water loss through perspiration or diarrhoea), as well as the water content of a food consumed.



Consuming a green tea beverage related at a lower risk of cardiovascular disease &cancer.([32],[33]) According to a new green meta-analysis of tea by Wang and associates, black tea is just marginally more protective than green tea in terms of health benefits .([34])

Drinking coffee is regarded as safe and may have various health advantages. Compared to non-coffee drinkers, In fact, drinking coffee may help avoid the onset of hypertension.([35]) Drinking 3 to 5 cup per day of caffeinated coffee reduces the risk of cardiovascular disease development, with utilization of greater than 6 cups per day remaining basically neutral.([36])

Dairy milk has been shown to enhance bone health and calcium absorption, & vitamin D fortification helps to improve the efficacy. Containing a lot of calcium and having a lipid makeup that makes it easier for fat-soluble vitamins to be absorbed, milk is the perfect food to fortify with vitamin D. Protein, magnesium, and potassium are all abundant in milk. Low-fat dairy consumption may low BP, according to the (DASH) DIETARY APPROACHES TO STOP HYPERTENSION research.([37]) Milk canlower to the danger ofheartdisorder but does not appear to have an impact on total mortality; this effect is likely to be stronger for low-fat milk.([38])

Patients who avoid dairy milk product do so for a variety of reasons, such as dietary, lactose intolerance choices, flavour, natural occurring protection, or health problems that may or may not be substantiated by clinical findings. Non-dairy milk is a popular choice among these patients. Consumers have mostly accepted plants- based milk made from palm, almond, oats, and other plant, while soy milk is still the most widely consumed. By 2020, plant-based milks are anticipated to account for up to 13% of the United States milk market. ([39])

Juice fruit are a well-liked method of increasing fruit consumption due to their wide availability, simplicity of storage, affordable price, and hedonistic motivations (taste). According to the USDA's My Plate standards, a serving of fruit should be considered to be equal to one cup of 100% fruit juice.([40]) Apple juice and orange juice have an energy content that is roughly 6% more than that of cola beverages (110 kcal/240 mL serving). White grape juice has an even higher caloric density, with about 150 kcal/240 m.

The average daily intake of soft drinks and fruit juices for teenagers aged 13-19 years, as determined by National Health and Nutrition Examination Survey (NHANES) 2005–2006 data collection, was 242 kcal/d, or almost 17% of total daily calorie intake. ([41]) Although the exact cause of the rise in adult & adolescent obesity in the US is likely complex, intake of Sugar Sweetened Drinks (SSBs) is likely one contributor. Type 2 diabetes risk, metabolic syndrome risk, and weight gain risk are all highly and favourably correlated with adult SSB use. ([42])

Artificial sweeteners used in beverages have grown in popularity as a caloric sweetener replacement in SSBs, despite the fact that their potential health effects on even common conditions like obesity or weight reduction are yet unknown. Furthermore, the general populace still has a limited ability to recognise them. ([43]) Given these facts, even though avoiding soda totally is undoubtedly the best choice, it might make sense to advise restricting consumption to a maximum of 1 or 2 cups each day.

Alcohol: -Although determining "drink equivalent" is not always straightforward, moderate alcohol consumption is typically defined at two drink per day for man & 1day for women. Except for the clear link between consuming alcohol or a significantly mild alcohol drinkingdoesn't often greater the risk of cancer, but greater the risk of breast cancer in women & is protective against myocardial infarction.([44],[45],[46]) In an analysis plank and assistant (2008) investigated the outcome of alcohol on life excitement across 83 prospective support research studies with 788,000 participants.([47]) According to their research, individuals between the ages of 40 and 50 had the longest life expectancy when their weekly alcohol consumption was less than 100 gram or between 0 and one drink per day. The risk of miscarriage and stillbirth is also significantly elevated when pregnant women engage in binge drinking and/or regular alcohol consumption. ([48])





Fig 2:-Equivalent drink sizes that meet the US standard for one "drink" at 14 grimes of alcohol ([49])

IV. THE IMMUNE SYSTEM:-

After a person is exposed to an infectious pathogen, their immune system becomes crucial. The immune system must use various strategies to deal with various infectious agent types since the nature of infectious agents differs. While the broad strategies used by these various methods-which all attempt to find and eliminate-are similar, the precise immune systems that are activated can vary. While the majority of bacteria don't enter host cells, the majority are still vulnerable to the immunological response of the host; frequently, innate phagocytic cells (typically macrophages, monocytes, neutrophils, and accessory cell) engulf these bacteria, which are then digested after being killed inside intracellular phagocytic vacuoles. The remainder of the bacterial population (antigens) can then be seen on the phagocyte's surface thanks to Major Histocompatibility Class (MHC) II. When such antigens are recognized by antigen-specific CD4+ helping T cells, the adaptive immune response to the bacterium begins. T cells are controlled this immunological in response.Producing antigen-specific antibodies from B lymphocytes, and further activating innate immune cells. It is apparent that the goal of this reaction to extracellular bacteria is to eliminate those organisms. MHC I can display antigens on the surface of infected cells when viruses (and some bacteria) enter host cells rather than staying entirely extracellular. The host cell that is producing the antigen is killed when CD8+ cytotoxic T lymphocytes recognise it. In a manner similar to cytotoxic T lymphocytes, natural killer cells may identify and destroy virally infected cells. Natural

killer cells are able to identify virally infected cells and, like when in touch with infected cells, cytotoxic T lymphocytes kill them. Hence, the goal of this reaction to virally infected cells is to eradicate the virus-carrying host cells. Naturally, killing host cells unleashes viruses, escalating the struggle between virally-infected cells and the host's immune system. ([50])

Effective host defence is made possible by the immune system's four general functions, which are as follows:

- 1. Barrier function: Infections cannot enter the body from the outside environment thanks to the immune systems. Examples of biological barriers include the complement system, commonly found commensal microbes on the skin and in the digestive system, IgA-producing release in saliva and tears, and commensal proteins in the gastrointestinal tract. Examples of sensible drawback include the mucosal layer and skin. Among the syntheticdrawback is the stomach of pH acid.([50])
- identification: 2. Pathogen -Macrophages, monocytes, and dendrites cells of the innate immunity can recognise pathogens. This is made possible by the existence of pattern recognition receptors (PRRs), which recognize common chemical features that many different groups pathogen share. MAMPs. or microbeassociated molecular patterns, are the name given to these structures. The 1st line of the host defence responses is initiated when PRRs identify MAMPs. Among PRRs are Tool like receptor (TLRs). Humans contain More



than 10 functioning TLRs, each of which is capable of identifying a different MAMP from a variety of fungi, virus, bacteria and parasites. The two that are well explained are TLR4 and TLRs2, which recognise the lipopolysaccharides and lipoteichoic acid, respectively, from the cell walls of gram positive & negative bacteria. Because the pathogens that innate immune cells recognise, primarily germ, are extracellular, many TLRs are expressed on their cell surfaces. ([51]-[55])

3. Pathogen removal: It has been demonstrated that phagocytic cells like macrophages and dendritic cells can take in extracellular bacteria. Peptide fragments known as antigens are shown to CD4+ helper T cells that are antigen-specific on the surface of phagocytic cells after internalised bacteria have been digested (through MHC II). Interleukin (IL)-2 and interferon are produced by the proliferating T helper 1 phenotype of activated helper T cells

(IFN). IFN-y encourages B cell to produce antigen-specific antibodies. By coating the bacteria, these antibodies neutralise them and increase the effectiveness of phagocytosis. the production of well-known inflammatory cytokines such tumour necrosis factor (TNF), interleukin (IL)-1, and interleukin (IL)-12, as well as the stimulation of transcription factors such nuclear factor a-light-chain-enhancer of activated β cells (NF-kB) occur as a result of innate immune cells' recognition of pathogens via PRRs in addition to phagocytosis. Certain virus-infected cell types promote the production IFNs type 1 (IFN- α & IFN- β), which lead to antiviral resistance by, among other things, activating natural killer cells.([55],[56])Also, as was previously said, Natural killer cells are immediately activated by virally infected cells and kill the infected cell. Moreover, PRR signalling promotes dendritic cell maturation, which starts acquired immunity.



Fig:-3 and overview of antiviral defences. The text explains the events depicted in the illustration.Blood cells include B-lymphocytes, CTLs (cytotoxic T lymphocytes), Igs (immunoglobulins), ILs (interleukins), MHCs (major histocompatibility class), and nuclear factors (NF-B). Other terms mentioned include "t Helper lymphocytes," "tumournecrosis factor" "toll-like receptor" "alpha-light-chain-enhancer of activated beta cell," "natural killer cell."([50])



- 4. Immunological memory: -Itis the immunity capacity to correctly & rapidly identify an antigen that the body has previously seen and generate the appropriate immune response to it.The concept of immunological memory has two components. First, antibodies that provide protection against reinfection can stay in use for several weeks to several years. Second, when a modest proportion of T memory (both CD4+ and CD8+) and B cell remain after an active immune response has finished. Cells persist. Even though they are in a resting condition, they can react immediately if the same antigen that formed them comes into contact with them, which can speed up the removal of the antigen's source. ([50])
- 5. Aging's impact on the immune system:-Immunosenescence, a phenomenon related with ageing, is a decline of immunological competence. Reduced immune cell production from bone marrow, where all immune cells originate, is one factor associated with immunosenescence. ([57]-[61]) Also, as we age, the thymus changes, producing fewer naive T cells, which limits their capacity to react to novel antigens. Immunosenescence refers to the

fact that older adults have decreased immune responses to vaccinations and greater vulnerability to illnesses including pneumonia and respiratory tract infections.([57], [58], [62], [63])The biggest site of immunological tissue in humans is found in the gut, and studies using mice models have shown that the gut mucosal immune system ages, as shown, among other things, by changes in mucosal dendritic cell function, decreased secretory IgA response, and Reduced oral tolerance to new antigens. ([64], [65]) Older adults are more prone to COVID19 because of immunosenescence, for example, which is more severe. Inflammation refers to the paradoxical relationship between aging and elevated blood levels of several inflammatory mediators. The risk of chronic aging disorders such as heart disease, metabolic diseases (diabetes, non-alcoholic fatty liver disease), neurodegeneration, and many types of cancer are thought to be increased by this syndrome. When infected, it can also be predisposed to producing an excessive inflammatory response. ([66])

Some si	gnificant signs of aging-relate	ed immunological decrease (immunosenescence)
	T	Τ

ininunological cell	Immunosenescence				
	• A decline in circulation numbers.				
	• Unbalances between various phenotypes.				
	• A greater in memory T cells that are not active.				
	Poor response time				
Lymphocytes T	• A decline in circulation numbers.				
	Decrease in the amount and formation of native T				
	lymphocytes.				
	• Less variety in antigen receptors.				
	• Poor proliferative capacity.				
	• Reduced production of interleukin (IL) 2 and				
	interferon (IFN).				
	• Reduction in the number of naive B lymphocytes.				
	Modified immunoglobulin chemistry				
B lymphocytes	Reduced receptivity				
	• A build-up of inactive memory B cells				
	A build-up of inactive memory B cells				
	 A build-up of inactive memory B cells A reduction in phagocytosis 				
Dendritic cells	 A build-up of inactive memory B cells A reduction in phagocytosis A Decreased ability to respond 				
Dendritic cells	 A build-up of inactive memory B cells A reduction in phagocytosis A Decreased ability to respond Decreased expression of Toll-like receptors (TLR). 				
Dendritic cells	 A build-up of inactive memory B cells A reduction in phagocytosis A Decreased ability to respond Decreased expression of Toll-like receptors (TLR). Decreased generation of type 1 IFN 				



Neutrophil	 The circulation of numbers is maintained. Impaired bacterial killing and oxidative burst. Deteriorated chemotaxis Defective phagocytosis. Lessening of neutrophil extracellular trap formation. A reduction in responsiveness.
Monocytes	 A reduction in responsiveness Modified expression of TLR Modified cytokine production patterns
Macrophages	Defective phagocytosisModified expression of TLR
Native killer cells	 A rise in circulation numbers Decreased cytotoxicity Reduced cytokine production. Unbalances between various phenotypes Poor response time

V. HOW OBESITY AFFECTS THE IMMUNE SYSTEM:-

Obesity has been linked to decreased antibody and IFN- production,([67],[68]) as well as immune system impairments including helper T lymphocyte, cytotoxic T lymphocytes, neutral killer в lymphocytes and activity deficiencies.([69],[71])This indicates that obese people are more susceptible to a variety of bacteria, fungi, infection and viral and have less effective immune responses to vaccinations than people of healthy weight.([67],[69],[72]-[74]) The effects of obesity on influenza infection and influenza vaccine have been thoroughly studied. During the 2009 H1N1 influenza a virus pandemic, obese individuals exhibited delayed and impaired antiviral responses to infection as well as a worsening of their disease recovery when compared to those of healthy weight. ([69]) Obesity is linked to prolonged influenza virus shedding in humans and animals, which suggests a breakdown in viral control & killing as well as the formation of dangerous minor variations. ([69]) Its examined that in vitro response of immune cells from healthy, overweight, and obese individuals to influenza vaccination. Activated cytotoxic T lymphocytes, granzyme-expressing cytotoxic T lymphocytes, amount of cytotoxic T lymphocytes generating interferon (IFN) increased after the immune blood cell were exposed to the immunisation. Nevertheless, 40%, about 60%, and 65% less responses were observed in the cells of obese persons. Cells from obese and overweight individuals had similar responses. Similar results on

blood cell responses to pandemic H1N1 influenza a virus have been reported by many authors. ([75])

VI. THYROIDITIS WITH HASHIMOTO'S

One of the most common autoimmune disorders, Hashimoto (HT) disease is characterised by lymphocyte infiltration, thyroid tissue damage and scarring, and Proliferation of antibodies to thyroid peroxidase and thyroglobulin.([76])The term was coined by Dr. Hashimoto, a Japanese physician, who first identified four cases of the disease as "Hashimoto's disease" in 1912. In an article published in the Archives of Clinical Surgery, Dr. Hashimoto described the clinical and histologic features of four cases.Referring to them as "the lymphocytic goitre, in which the thyroid parenchyma develops lymphoid follicles along with a significant infiltrate of lymphocytes."([77])

Males are less likely than females to contract the condition, and women between the ages of 30 and 60 are most at risk for developing it. The fact that this condition can be detected in individuals of any age, including youngsters, is crucial to keep in mind. ([78])The incidence of Hashimoto's disease is increasingly Hashimoto's, which is believed to affect 5% of Caucasians. Clinically obvious gland dysfunction can occur in 0.1-2% of people or can be subclinical in 10-15% of people. ([79])Overproduction of antibodies to thyroid antigens such as thyroid peroxidase and thyroglobulin controls the progression of Hashimoto's disease. That occur when the immune system is impaired. The iodine addition to the



tyrosine residues of thyroglobulin is catalysed by the first protein.Resulting in the formation of triiodothyronine, which has three iodine atoms, or thyroxin, which has four. ([80])

Elucidation of the etiology of Hashimoto's disease-related factors. Hashimoto's illness has existential, environmental, and genetic causes such gender, parenting, and age. Some of the genetic components include some thyroid genes, immune system-regulating proteins, and Major Histocompatibility Genes, which encode antigens on human leukocytes. When impacted by outside

stimuli, they lead the immunity to overproduce antibody to thyroid antigens.([81]) Among the natural factors are nutrient excess or deficiency, exposure to chemicals and heavy metals, including endocrine disruptors like bisphenols and phthalates, pharmaceuticals, and others.([81],[82]) Mood swings, sadness, attention issues, brain fog, and biological abnormalities including loss of hair, dry skin, Persistent fatigue, weight changes, and irregular bowel movements despite adequate sleep are a few examples.([83])

Table 3:- Hashimoto's disease-related factors.([81], [84], [85])						
Genetic	Existential Factors:	Nutritional and environmental factors:				
component:						
Thyroid-	Female gender	Smoking	Insufficiency	Infections		
specific genes						
Immune-	Age	Alcohol	Selenium	Environmental		
modulating	-	use	inadequacy	stress		
genes						
The major	Parenthood	Iodine	Vitamin D	Medication		
histocompatibi		excess	deficiency			
lity complex						
(MHC)						

VII. CONCLUSION:-

In order to defend from such a wide range of dangers, the immune system of humans has developed to consist of a diversity of cell varitey, interaction elements, and function responses. Hence, a suitable amount of the range of micronutrients is required to keep the immunity in good shape and to ensure that it functions at its peak. Vitamin A may be found in abundance in the majority of yellow and orange fruits and vegetables. It is a key component of both blood and lymph and is crucial for the movement of immune system cells, white blood cells, and other nutrients throughout the body. In addition to serving as a substrate for cell growth and survival, arginine is crucial for differentiation of the proper genes. The Canadian Inuit have a 37-year life expectancy at birth. years between 1951 and 1961, which was 33 years less than the national average and it may not come as a surprise that their low-carb diet may have prevented the development of cardiovascular disease in them given that they may not have lived long enough to do so. With a high calcium content and a lipid composition that enhances the absorption of fat-soluble vitamins. milk is the perfect food to fortify with vit D. The four instances were defined by Hashimoto as having "Lymphocytic goiter in which focal lymphocytic

infiltration occurs in the thyroid parenchyma with formation of testicular tubules on the basis of clinicaland histological findings. The development of Hashimoto's disease is determined by the overproduction of anti-thyroid antibody, such as those against thyroid peroxidase & thyroglobulin, whichoccurs when the immune system is impaired.

REFERENCE:-

- [1]. Calder PC. Feeding the immune system. Proc. Nutr. Soc. 2013; 72:299–309.
- [2]. Gombart AF, Pierre A, Maggini S. A review of micronutrients and the immune System–Working in harmony to reduce the risk of infection. Nutrients 2020; 12:E236.
- [3]. Shankar AH, Prasad AS. Zinc and immune function: the biological basis of altered resistance to infection. Am J Clin Nutr. 1998 Aug; 68(2 Suppl):447S-463S. Doi: 10.1093/ajcn/68.2.447S. PMID: 9701160.
- [4]. <u>https://www.health.harvard.edu/staying-</u> healthy/how-to-boost-your-immune-system
- [5]. Childs C, Calder P, Miles E. Diet and immune function. Nutrients. (2019) 11:1933. doi:10.3390/nu11081933
- [6]. Sica A, Mantovani A. Macrophage plasticity and polarization: in vivo veritas. J



Clin Invest. (2012) 122:787–95. doi: 10.1172/JCI59643

- [7]. Szefel J, Danielak A, Kruszewski W. Metabolic pathways of L-arginine and therapeutic consequences in tumors. Adv Med Sci. (2019) 64:104–10. doi: 10.1016/j.advms.2018.08.018
- [8]. Grohmann U, Mondanelli G, Belladonna M, Orabona C, Pallotta M, Iacono A, et al. Amino-acid sensing and degrading pathways in immune regulation. Cytokine Growth Fact Rev. (2017) 35:37–45. doi: 10.1016/j.cytogfr.2017.05.004
- [9]. Newsholme P, Brennan L, Rubi B, Maechler P. New insights into amino acid metabolism, b-cell function and diabetes. Clin Sci. (2005) 108:185–94. doi:10.1042/CS20040290
- [10]. Mellor AL, Munn DH. IDO expression by dendritic cells: tolerance and tryptophan catabolism. Nat Rev Immunol. (2004) 4:762–74. doi: 10.1038/nri1457
- [11]. Rubio-Patiño C, Bossowski J, De Donatis G, Mondragón L, Villa E, Aira L, et al. Low-protein diet induces IRE1a-dependent anticancer immunosurveillance. Cell Metab. (2018) 27:828.e–42.e. doi: 10.1016/j.cmet.2018.02.009
- [12]. Al Tanoury Z, Piskunov A, Rochette-Egly C. Vitamin A and retinoid signaling: genomic and nongenomic effects: thematic review series: fat-soluble vitamins: vitamin A. J Lipid Res. (2013) 54:1761–75. doi: 10.1194/jlr.R030833
- [13]. Maggini S, Pierre A, Calder P. Immune function and micronutrient requirements change over the life course. Nutrients. (2018) 10:1531. doi: 10.3390/nu10101531
- [14]. Liu M, Bao S, Gálvez-Peralta M, Pyle C, Rudawsky A, Pavlovicz R, et al. ZIP8 regulates host defense through zincmediated inhibition of NF-kB. Cell Rep. (2013) 3:386–400. doi: 10.1016/j.celrep.2013.01.009
- [15]. Kitabayashi C, Fukada T, Kanamoto M, Ohashi W, Hojyo S, Atsumi T, et al. Zinc suppresses Th17 development via inhibition of STAT3 activation. Int Immunol. (2010) 22:375–86. doi: 10.1093/intimm/dxq017
- [16]. Maywald M, Wang F, Rink L. Zinc supplementation plays a crucial role in T helper 9 differentiation in allogeneic immune reactions and non-activated T

cells. J Trace Elements Med Biol. (2018) 50:482–8. doi: 10.1016/j.jtemb.2018.02.004

- [17]. Rosenkranz E, Maywald M, Hilgers R, Brieger A, Clarner T, Kipp M, et al. Induction of regulatory T cells in Th1-/Th17-driven experimental autoimmune encephalomyelitis by zinc administration. J Nutr Biochem. (2016) 29:116–23. doi: 10.1016/j.jnutbio.2015.11.010
- [18]. Olsen JA, Vitamin A. Handbook of vitamins.In: MachlinLJ, editor.2nd Edition. New York: Marcel Dekker; 1991.p.2–57.
- [19]. Moser U, Bendich A. Vitamin C In: Handbook of vitamins. In: Machlin LJ, editor. 2nd Edition. New York; 1991. p. 196–232.
- [20]. Vitamin intake and health, edited by Gaby S.K, Bendich A., Singh V. N., et al, 1991, pp 1-16
- [21]. Stephenson T, Sanctuary MR, Passerrello CW. Human nutrition: science for healthy living. New York City, New York: McGraw-Hill; 2022
- [22]. Lands, W.E.M. Polyunsaturated fatty acid effects on cellular interactions. In: Micronutrients in health and in disease prevention, edited by Bendich A and Butter- worth C E, New York: 1991, pp 9-34.
- [23]. Rose WC, Haines WJ, Warner DT. The amino acid requirements of man. III. The role of isoleucine; additional evidence concerning histidine. J Biol Chem 2016; 193:605–12.
- [24]. Dinicolantonio JJ. Increase in the intake of refined carbohydrates and sugar may have led to the health decline of the Greenland Eskimos. Open Heart 2016; 3(2): e000444.
- [25]. Statistics Canada. Health reports. modified 2015 82-003-x 19(1). Available at: https://www150.statcan.gc.ca/n1/pub/82-003-x/2008001/article/10463/4149059eng.htm. Accessed January 10, 2022.
- [26]. Schulz R, Slavin J. Perspective: defining carbohydrate quality for human health and environmental sustainability. Adv Nutr 2021;12:1108–21.
- [27]. National Center for Health Statistics. Growth charts. centers for disease control and prevention. Available at. https://www.cdc.gov/growthcharts/. Accessed February 22, 2022.



- [28]. Romero-Corral A, Somers VK, Sierra-Johnson J, et al. Accuracy of body mass index in diagnosing obesity in the adult general population. Int J Obes (Lond) 2008;32:959–66.
- [29]. Barry VW, Baruth M, Beets MW, et al. Fitness vs. fatness on all-cause mortality: a meta-analysis. Prog Cardiovasc Dis 2014;56(4):382–90.
- [30]. National Academies of Sciences, Engineering, and Medicine. Dietary reference intakes for water, potassium, sodium, chloride, and sulfate. Washington (DC): The National Academies Press; 2005. https://doi.org/10.17226/10925.
- [31]. Vivanti AP. Origins for the estimations of water requirements in adults. Eur J Clin Nutr 2012;66:1282–9.
- [32]. Carlson JR, Bauer BA, Vincent A, et al. Reading the tea leaves: anticarcinogenic properties of (-)-epigallocatechin-3-gallate. Mayo Clin Proc 2007;82:725–32.
- [33]. Basu A, Lucas EA. Mechanisms and effects of green tea on cardiovascular health. Nutr Rev 2007;65:361–75
- [34]. Wang ZM, Zhou B, Wang YS, et al. Black and green tea consumption and the risk of coronary artery disease: a meta-analysis. Am J Clin Nutr 2011;93:506–15.
- [35]. Miranda AM, Goulart AC, Bensen or IM, etal. Coffee consumption and risk of hypertension: a prospective analysis in the cohort study. Clin Nutr 2021;40:542–9.
- [36]. Ding M, Bhupathiraju SN, Satija A, et al. Long-term coffee consumption and risk of cardiovascular disease: a systematic review and a dose-response meta-anal- ysis of prospective cohort studies. Circulation 2014;129:643–59.
- [37]. Appel LJ, Moore TJ, Obarzanek E, et al. A clinical trial of the effects of dietary patterns on blood pressure. N Engl J Med 1997;336:1117–24.
- [38]. Soedamah-Muthu SS, Ding EL, Al-Delaimy WK, et al. Milk and dairy consumption and incidence of cardiovascular diseases and all-cause mortality: dose– response meta-analysis of prospective cohort studies. Am J Clin Nutr 2011;93: 158–71.
- [39]. GoodFoodInstitute.U.S.Retailmarketdatafo rtheplant-basedindustry.Avail- able at. https://gfi.org/marketresearch/#:w:text5Pla nt%2Dbased%20milk%20is

%20the,%2C%20growing%2045%25%20s ince%202019. Accessed:January 18, 2022.

- [40]. MyPlate. US. Department of Agriculture. Available at: https://www.myplate.gov/ eat-healthy/fruits.
- [41]. Popkin BM. Patterns of beverage use across the lifecycle. Physiol Behav 2010; 100:4–9.
- [42]. Malik VS, Popkin BM, Bray GA, et al. Sugar-sweetened beverages and risk of metabolic syndrome and type 2 diabetes: a meta-analysis. Diabetes Care 2010;33:2477–83.
- [43]. Wilson T, Murray B, Price T, et al. Nonnutritive (Artificial) sweetener knowledge among university students. Nutrients 2019;11:E2201.
- [44]. Mukamal KJ, Jensen MK, Grønbaek M, et al. Drinking frequency, mediating biomarkers, and risk of myocardial infarction in women and men. Circulation 2005; 112:1406–13.
- [45]. Cao Y, Willett WC, Rimm EB, et al. Light to moderate intake of alcohol, drinking patterns, and risk of cancer: results from two prospective US cohort studies. BMJ 2015;18:351, h4238. 45.
- [46]. Willett WC. Public health benefits of preventive nutrition: global perspective. In: Bendich A, Deckelbaum RJ, editors. Preventive nutrition. 5th edition. New York: Humana Press, Springer/Nature; 2015. p. 25–46.
- [47]. Wood AM, Kaptoge S, Butterworth AS, et al. Risk thresholds for alcohol consumption: combined analysis of individual-participant data for 599 912 current drinkers in 83 prospective studies. Lancet 2018;391:1513–23.
- [48]. Gosdin LK, Deputy NP, Kim SY, et al. Alcohol consumption and binge drinking during pregnancy among adults aged 18–49 years — United States, 2018–2020. MMWR Morb Mortal Wkly Rep 2022;71:10–3.
- [49]. National Institute of Standards and Technology. How do you know your food's nutrition label is accurate? National Institute on Alcohol Abuse and Alcoholism. National Institutes of Health. US Department of Health and Human Services. Rethinking Drinking. Available at:

http://rethinkingdrinking.niaaa.nih.gov/Ho



wmuch-is-too-much/What-counts-as-adrink/Whats-A-Standard-Drink.aspx. Accessed: January 7, 2022.

- [50]. Calder PC. Nutrition, immunity and COVID-19. BMJ Nutrition, Prevention & Health 2020;0. doi:10.1136/ bmjnph-2020-000085
- [51]. Dosch SF, Mahajan SD, Collins AR. Sars coronavirus spike proteininduced innate immune response occurs via activation of the NF- κ B pathway in human monocyte macrophages in vitro. Virus Res 2009;142:19–27.
- [52]. Hu W, Yen Y-T, Singh S, et al. Sars-Cov regulates immune functionrelated gene expression in human monocytic cells. Viral Immunol 2012;25:277–88.
- [53]. Wang Y, Liu L. The membrane protein of severe acute respiratory syndrome coronavirus functions as a novel cytosolic pathogenassociated molecular pattern to promote beta interferon induction via a toll-like-receptor-related TRAF3independent mechanism. mBio 2016;7:e01872–15.
- [54]. Al-Qahtani AA, Lyroni K, Aznaourova M, et al. Middle east respiratory syndrome corona virus spike glycoprotein suppresses macrophage responses via DPP4-mediated induction of IRAK-M and PPARγ. Oncotarget 2017;8:9053–66.
- [55]. García-Sastre A, Biron CA. Type 1 interferons and the virus-host relationship: a lesson in Detente. Science 2006;312:879– 82.
- [56]. Sallard E, Lescure FX, Yazdanpanah Y, et al. C-20-15 discovery French Steering Committee (2020) type 1 interferons as a potential treatment against COVID-19. Antiviral Res;178:104791.
- [57]. Pawelec G, Larbi A, Derhovanessian E. Senescence of the human immune system. J Comp Pathol 2010;142:S39–44.
- [58]. Pera A, Campos C, López N, et al. Immunosenescence: implications for response to infection and vaccination in older people. Maturitas 2015;82:50–5.
- [59]. Agarwal S, Busse PJ. Innate and adaptive immunosenescence. Ann Allergy Asthma Immunol 2010;104:183–90.
- [60]. Montgomery RR, Shaw AC. Paradoxical changes in innate immunity in aging: recent progress and new directions. J Leukoc Biol 2015;98:937–43.

- [61]. Ventura MT, Casciaro M, Gangemi S, et al. Immunosenescence in aging: between immune cells depletion and cytokines upregulation. Clin Mol Allergy 2017;15:21
- [62]. Fulop T, Pawelec G, Castle S, et al. Immunosenescence and vaccination in nursing home residents. Clin Infect Dis 2009;48:443–8.
- [63]. Goodwin K, Viboud C, Simonsen L. Antibody response to influenza vaccination in the elderly: a quantitative review. Vaccine 2006;24:1159–69
- [64]. Fujihashi K, Kiyono H. Mucosal immunosenescence: new developments and vaccines to control infectious diseases. Trends Immunol 2009;30:334–43.
- [65]. Ogra PL. Ageing and its possible impact on mucosal immune responses. Ageing Res Rev 2010;9:101–6.
- [66]. Calder PC, Bosco N, Bourdet-Sicard R, et al. Health relevance of the modification of low grade inflammation in ageing (inflammageing) and the role of nutrition. Ageing Res Rev 2017;40:95–119.
- [67]. Milner JJ, Beck MA. The impact of obesity on the immune response to infection. Proc Nutr Soc 2012;71:298–306.
- [68]. Andersen CJ, Murphy KE, Fernandez ML. Impact of obesity and metabolic syndrome on immunity. Adv Nutr 2016;7:66–75.
- [69]. Honce R, Schultz-Cherry S. Impact of obesity on influenza A virus pathogenesis, immune response, and evolution. Front Immunol 2019;10:1071.
- [70]. Frasca D, Diaz A, Romero M, et al. Ageing and obesity similarly impair antibody responses. Clin Exp Immunol 2017;187:64–70.
- [71]. O'Shea D, Hogan AE. Dysregulation of natural killer cells in obesity. Cancers 2019;11:E573.
- [72]. Huttunen R, Syrjänen J. Obesity and the risk and outcome of infection. Int J Obes 2013;37:333–40.
- [73]. Dobner J, Kaser S. Body mass index and the risk of infection - from underweight to obesity. Clinical Microbiology and Infection 2018;24:24–8.
- [74]. Frasca D, Blomberg BB. The impact of obesity and metabolic syndrome on vaccination success. Interdiscip. Top. Gerontol. Geriatr 2020;43:86–97.
- [75]. Paich HA, Sheridan PA, Handy J, et al. Overweight and obese adult humans have a



defective cellular immune response to pandemic H1N1 influenza A virus. Obesity 2013;21:2377–86.

- [76]. Krysiak R, Szkróbka W, Okopień B. The Effect of Gluten-Free Diet on Thyroid Autoimmunity in Drug-Naïve Women with Hashimoto's Thyroiditis: A Pilot Study. Exp Clin Endocrinol Diabetes. 2018 Jul 30. <u>https://doi.org/10.1055/a-0653-7108</u>.
- [77]. Hiromatsu Y, Satoh H, Amino N. Hashimoto's thyroiditis: history and future outlook. Hormones (Athens, Greece). 2013; 12(1): 12–18.
- [78]. Monaco F. Thyroid Diseases. Taylor and Francis; 2012, p. 78.
- [79]. Pyzik A, Grywalska E, Matyjaszek-Matuszek B, Roliński J. Immune disorders in Hashimoto's thyroiditis: what do we know so far? J Immunol Res. 2015; 2015: 979167. https://doi.org/10.1155/2015/979167.
- [80]. Ott J, Promberger R, Kober F, Neuhold N, Tea M, Huber JC et al. Hashimoto's thyroiditis affects symptom load and quality of life unrelated to hypothyroidism:
 - a prospective case-control study in women undergoing thyroidectomy for benign goiter. Thyroid 2011; 21: 161–167.
- [81]. Wiersinga WM. Clinical Relevance of Environmental Factors in the Pathogenesis of Autoimmune Thyroid Disease. Endocrinol Metab. 2016; 31: 213–22. <u>https://doi.org/10.3803/EnM.2016.31.2.213</u>
- [82]. Boas M, Feldt-Rasmussen U, Main KM. Thyroid effects of endocrine disrupting chemicals. Mol Cell Endocrinol 2012; 355: 240–148. https:// doi.org/10.1016/j.mce.2011.09.005
- [83]. Kawicka A, Regulska-Ilow B. [Metabolic disorders and nutritional status in autoimmune thyroid diseases]. Postepy Hig Med Dosw (online) 2015; 69: 80–90 (Polish).

https://doi.org/10.5604/17322693.1136383.

- [84]. Lizis-Kolus K. Ocena wpływu niedoboru witaminy D na przebieg choroby Hashimoto u chorych w województwie świętokrzyskim [praca doktorska]. Kraków; Uniwersytet Jagielloński; 2015 (Polish).
- [85]. Virili C, Fallahi P, Antonelli A, Benvenga S, Centanni M. Gut microbiota and Hashimoto's thyroiditis. Rev Endocr Metab

Disord. 2018; 19(4): 293–300. https://doi.org/10.1007/s11154-018-9467-y