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Review Article

Nutrition, a Primary Prevention of Communicable Disease?

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Abstract

This article is a reminder that, in addition to the classic hygienic anti-epidemic measures, communicable (infectious) and non-communicable (chronic) diseases can possibly be prevented by purposefully focusing on nutritional programs.

In ancient times, nor antibiotics, the only way to prevent and treat diseases was to adjust the patient's diet.

Many times over the years, nutritional health promotion has proven itself to be effective even though, as typical of the history of medicine, it has sometimes been forgotten. Even Hippocrates (460-337 BC) was aware of the importance of nutrition for health as he stated: "If you know nothing about a person's diet, how can you understand his illness?"

The authors have tried to point out the importance of nutrition, which always contains antigens that directly induce immunological memory, in both specific (adaptive) immunity and as recently demonstrated, non-specific immunity, within our largest organ of immunity, the Intestinal Lymphoid Tissue (GALT).

In essence, in addition to its nutritional value, food intake could also be considered as an ongoing form of "vaccination".

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Keywords

Nutrition; Communicative Diseases; GALT; Specific and Non-Specific Immunity; Immunological Memory; Trained Immunity

Abbreviations

COVID-19: Coronavirus; SARS: Severe Acute Respiratory Syndrome; PAMP: Pathogen-Associated Molecular Patterns; DAMP: Danger Associated Molecular Patterns; PRR: Pattern Recognition Receptors; GALT: Gut Associated Lymphoid Tissue

Introduction

The current coronavirus pandemic still places an emphasis on conventional sanitary-anti-epidemic measures and, in particular, on vaccination programs, which have in the past been proven to be effective means in the prevention the spread of many infectious diseases [1].

Looking at the history of the human race, it appears that, unlike non-communicable diseases such as various types of malignancies, cardiovascular diseases or nervous diseases, communicative or infectious diseases usually appeared unexpectedly and suddenly, affecting particularly populations exposed to either prolonged stress, such as food shortages during periods of crop failure or war, short-term stress, immediately caused by unforeseen climatic causes (floods, tsunamis, typhoons) or other disasters (volcanic eruptions, earthquakes) [2,3].

Although life expectancy has significantly increased in many countries over the last 150 years thanks to the introduction of hygienic measures (sewerage, disinsection, deratization, safe drinking water and food), the discovery of effective drugs, including antibiotics, the availability of a healthier diet and, last but not least, the introduction of mass vaccination programs, resulting in a halt to the spread of pandemics and epidemics of the most dangerous infections (smallpox, cholera, typhoid fever, measles, etc.), it is noted that none of the above measures, nor new drugs, have completely prevented the recurrence of infections caused by already known pathogens or previously unknown communicative diseases caused by new, unknown pathogens.

Recently emerging diseases such as filovirus-induced hemorrhagic fevers - Marburg (1967), Ebola (1976) -, severe acute respiratory diseases after infection with Betacoronavirus viruses such as SARS (2002) and MERS (2012) and in particular the current COVID-19 pandemic represent a constant challenge in the development of effective preventive and treatment measures [4].

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We must admit that, once again, only traditional preventive measures, hygiene regulations and vaccination to prevent their occurrence and further spread, are available to us.

Belief in the Possibility of Eradicating Communicable Diseases

In the 1960s, optimistic epidemiologists and the general public became almost convinced that in the foreseeable future, within twenty to thirty years, the most serious infectious diseases would be eradicated. After all, new antibacterial and antiviral drugs, effective antibiotics, reliable vaccination programs and sets of hygiene measures had been available and had proven to be successful in preventing the spread of diseases in the past. However, the premise of eradicating communicable diseases had only been met for smallpox, which has not been vaccinated worldwide for more than 40 years.

However, as clear as they are, the conclusions from the experience of eradication with only one disease (smallpox) cannot be applied to other infectious diseases caused by other pathogens. Therefore, to date, other communicable diseases have not been completely eradicated. What is worse is that far greater risks could arise from new diseases caused by new pathogens that humanity has not encountered in its history and against which the above-mentioned preventive measures and therapies may not be fully effective.

Other unexpected and unknown infections await beyond the horizon, just as no one expected the emergence and spread of the current coronavirus pandemic. Almost a century ago, the French bacteriologist Ch. JH Nicolle (1866 - 1936), Nobel Prize 1928, became famous for his discovery of the louse of the locker room being carrier of typhus, which no one thought until then. “Nature's efforts to create new diseases are continuous: successful, doesn't change anything. What has happened in the distant past, when her efforts have exceptionally met with success, is happening at every moment of the present and will continue indefinitely in the future, as it is an inevitable natural process. Unfortunately, the fact that their development is fully completed by the time we register these diseases remains equally inevitable".

This warning must be kept in mind at all times. In the future, it will be particularly important for those responsible, whether politicians or medical professionals, to anticipate the emergence of new diseases. Steps based on their course, spread and health severity, will be taken such as conventional preventive measures, i.e. hygiene measures and vaccination programs, reliable diagnostic tests, effective medicines as well as the improvement of the organization of traditional hygiene measures.

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Do we have other options? What is often forgotten, or the importance of nutrition in the prevention of communicable diseases

Significantly, old knowledge and experience have often been forgotten for centuries, especially in regards to the relationship between nutrition and health as it had forgotten that it was known from ancient times that diet affected a person's health. Hippocrates (5th century BC) thought quite modernly that the "health lies in the proper mixing of body juices of different species, which is achieved by a proper diet" [5]. In this context, it should be recalled that "diathetics" was the study of the right way to live life (including hygiene and gymnastics). In the treatise “Peri archaias étrikás’ (on old medicine) the history of medicine was described as a history of understanding the effects of diets on the health of the patient. It follows that the treatment of the diseases at that time consisted mainly in prescribing special diets. They further advice, if we provide each individual with the right amount of food and exercise, not too little and not too much, we will provide him with the safest way to health.

Four centuries later, Aulus Cornelius Celsus’ words conveyed the same meaning. According to modern criteria, he recommended an unsalted diet for kidney disease, eating liver for night blindness and drinking milk for poisoning. The doctor of Emperor Marcus Aurelius, Claudius Galenus of Pergamum, who lived from 129 (130) to 201 (210) AD, most strongly promoted the treatment of diseases with diets. He claimed that the best medicine is good food (“optimum medicamentum cibus bene datus is”) [6]. Only after a thousand years of oblivion, Philippus recalled the same wisdom as Aureolus Theophrastus Bombastus von Hohenheim, known as Paracelsus (1493-1541) in essentially the same words, "our medicines must be food and our food must be medicine. “As for the diet, he is said to have advised "Eat as much as you can, until you have as much as fifty, as much as you have to and as little as you can when you are fifty ".

So didn't this centuries-old medical experience essentially provide us with the mean to prevent and treat nutritional diseases?

Again, a lot of time has passed during which these recommendations have been forgotten. The idea of using diets to prevent and treat disease was out of the question. During the middle Ages, any thought of improving the treatment of disease was unacceptable and was even considered heresy as diseases were considered to be God's punishment [7].

James Lind (1716-1794), an English Navyship's physician, later considered to be the founder of marine hygiene in England, is said to have been the first to apply appropriate nutrition in the prevention and treatment of disease in practice. In 1747, without any knowledge of the health benefits of vitamin C, he recommended the use of fresh citrus fruits and their juices to eradicate scurvy, a disease affecting sailors practically all over the world. It was one of the first large-scale clinical trials to prevent and treat the disease by dietary modification. He published his results in 1757 in the essay "Essay on the most effective means of protecting the health of

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seafarers in the Royal Navy" providing necessary tools to those treating or visiting patients with fevers as well as an appendix on the treatment of diseases in hot climates [8]. It took 70 years for the scientific community to take note of this success.

A hundred years later, Takaki Kanehiro (1849-1920), a naval physician of the Japanese Imperial Navy, cured beriberi disease (avitaminosis B1) by adjusting his patients' diet [9]. It is worth noting that it took years for medical science to take note, as this treatment was in stark contrast to the views of doctors at the time, considering beriberi to be an infectious disease.

It should be noted that the importance of vitamins as basic food ingredients in the prevention of diseases (not only infectious) was gradually discovered and convincingly documented only in the first half of the 20th century [10].

History of cognition of the relationship between nutrition and immunity

In 1810, which is considered the year of the emergence of nutritional immunology, JF Menkel described thymic atrophy as a result of malnutrition and starvation [10,11]. The thymus is the main organ of specific (adaptive) immunity, which is inhabited by hematopoietic stem cells from the bone marrow during adolescence. In it, they then differentiate into functional subpopulations of immunocompetent cells. 35 years later, Her Majesty Queen Victoria's First Chief Medical Officer, Victoria J Simon (1816-1904), published a detailed study of the thymus and without knowing its importance in maturing immunity, she described the thymus as a "malnutrition barometer."

It is again remarkable, however, that a hundred years later, doctors did not think that nutrition played a role in the prevention and treatment of infections, perhaps only in the case of tuberculosis [13]. It was not until 1936 that Aide-Mémoire sur l´Alimentation, et., l´ Hygiène states: "Based on advances in physiology, nutrition is now considered not one of the functions necessary to sustain life, but the basis of physical and mental health, the main means of prophylactic defense against disease and an important factor in Improving individuals and society as a whole. Nutritional hygiene can no longer be satisfied with supplying the body with the bare minimum of mineral salts and vitamins. Its task is to directly ensure health through optimal nutrition".

And it was not until 1941 that the Food and Nutrition Council Board at the US National Academy of Sciences (founded in 1940) determined the standards for proper nutrition i.e. the recommended dietary allowance (RDA, Recommended Dietary Allowances), the first edition of which was not published until 1943 [14].

And again, much later, in 1968, the World Health Organization acknowledges, for the first time in history, that malnutrition increases the susceptibility to infectious diseases and states that inadequate nutrition is the cause of up to 75% of infectious diseases [15]. It turned out that the

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stress resulting from malnutrition accompanying the disease, induces a catabolic state, which again leads to further worsening of the infection course. This creates a vicious cycle that can only be broken by supplying a suitable nutrition composition.

The relationship between nutrition and immunity was fully acknowledged only after 2000, almost two hundred years after the discovery of the nutritional atrophy of the thymus in 1810. It is finally concluded that "nutrition is an important determinant of immunity, especially at both ends of the human age range, in early childhood and old age" [14,15].

How nutrition affects immunity

To maintain a normal metabolism in the body i.e. to maintain health, it is important to maintain a certain amount of nutrients in the diet as well as its biological value, which is given by the content of basic nutrients such as proteins, carbohydrates and fats, but also vitamins, minerals, trace elements and other biological important components.

After centuries of examining the optimal composition of a diet, it is almost forgotten that our diets do not only contain these components, but also substances of immunogenic, or molecular structure, occurring on the surfaces of pathogenic organisms representing antigens and inducing an immune response. These substances are referred to as Pathogen-Associated Molecular Patterns (PAMPs), possibly with a certain hazard (DAMPs- Danger Associated Molecular Patterns) [16-18].

These structures then bind to so - called cellular receptors recognizing foreign patterns (PRRs - Pattern Recognition Receptors) which carry on their surfaces specific (adaptive) immunity (mainly lymphoid cells), non-specific (natural) immunity (NK cells, macrophages, monocytes, basophils, neutrophils and epithelial dendritic cells), as well as some subpopulations of immunocompetent immune cells acquired (adaptive) specific [19-21].

The Gut Associated Lymphoid Tissue (GALT) lying through the intestines represents a large portion of the immune system. Since the food products pass through the digestive tract, its low molecular weight (indigestible i.e. enzymatically non-degradable) antigenic determinants pass directly through the intestinal wall directly into the GALT, where they act primarily on natural, non-specific immune cells present there from the earliest stages of human ontogenetic development and then develop their effector functions long before cells of specific (adaptive) immunity develop throughout life.

Natural, nonspecific immunity also has an immunological memory

For decades, immunologists have assumed that innate immunity, unlike specific immunity, was not endowed with any type of immunological memory. However, recent discoveries have

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supported the presence of an immunological memory in innate immunity. In effect, cells providing natural defense mechanisms are also equipped with adaptive ability, i.e. they remember foreign molecular patterns such as the ones of PAMPs and DAMPs, which they have encountered before and are able to specifically recognize and therefore adequately respond to the presence of these molecules [22].

Invertebrates, unlike vertebrates, do not have specific, adaptive immunity. They however have a similar immunological memory and so they are able to produce immunoglobulin antibodies that exactly bind the antigen triggering their production [23-26]. In plants, this type of immunological memory is referred to as SAR (Systemic Acquired Resistance) [27].

Even prokaryotes have a certain type of adaptive immunity, which is mediated by the CRISPR-Cas9 system (Clustered Regularly Interspaced Short Palindromic Repeats-Crispr associated protein 9). This latter protects them from plasmid infections, virophages and bacteriophages carrying foreign genetic information [28]. It follows that immunological memory must also be added to the basic attributes of life.

CISPRs are repetitive, regularly spaced stretches of nucleotides in prokaryotic DNA (palindromes) [29-31]. Currently, technologies based on the CRISPR-Cas9 principle (sometimes referred to as "molecular scissors") are used for targeted interventions in the genome of living organisms i.e. prokaryotes, plants and animals.

Virophages are small viral phages relying on the viral replication factory of the co-infecting giant virus for their own replication. An example would be the "satellite" single-stranded RNA virus Sputnik (described in 2008), which is able to replicate only with the help of giant viruses of the genera Mimivirus and Mamavirus, attacking protozoa (Acanthamoeba) and leading to acanthamoebic keratitis , a corneal inflammation, acanthamoebic keratitis. Virophage labeling has been adopted for these viral parasites [32,33].

The ability of vertebrate innate immunity to show a certain degree of immunological memory was referred to, by MG Netea in 2011, as “trained immunity”. It has gradually been shown that trained immunity arises from epigenetic reprogramming in innate immunity effector cells (especially macrophages and so-called Natural Killer (NK) cells) and that it can persist for a relatively long time after the initial stimulus, even when the pathogen is already absent. It is also less specific than the immunological memory of adaptive immunity cells, so it could protect against infectious agents other than those that caused it.

Comparing specific and non-specific immunity, it can noted that non-specific immunity is evolutionarily much older. It would therefore be quite strange that this latter would not develop some type of immunological memory in such a long time.

The advantage of trained immunity (and thus non-specific immunity) is its faster response to infection. It can be said that it responds to the pathogen (antigen) almost immediately, as its

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effector cells do not have to go through several lengthy processes of differentiation in immunocytes.

Trained immunity can also be induced not only by antigen, but also by vaccines such as BCG by various microbial products (lipopolysaccharides, beta- glucans) or by various Biological Response Modifiers (BRM) [34-38].

On the other hand, trained immunity also has certain disadvantages. It has a shorter lifespan than the classical immunological memory of adaptive immunity and is also, as already mentioned, less specific.

Conclusion

In conclusion, we should acknowledge the recommendations of antiquity astute doctors based on their observations and experiences. Despite their lack of insight about microbes, metabolic processes, mechanisms of immunological processes or substance/content of a healthy diet, their advice on how to prevent and treat nutritional diseases was only confirmed by the development of modern medicine. This latter revealed that nutritional health promotion can be an important factor in the prevention and treatment of current and future communicable diseases.

Recent discovery of trained immunity, a confirmation that even natural, nonspecific immunity has a specific immunological memory, provides us with further evidence that a rational healthy diet containing, in addition to nutrients, immunogenic substances directly affecting GALT.

When consumed from an early age, an healthy diet can be perceived as a “preventive vaccination”, a real mean to effectively support a person’s immunological status, one’s resistance to current community-based infections and to a significant extent, a way to prevent not only recurrent epidemics and pandemics, but also future diseases to come.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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