NUTRITIONAL SOLUTIONS WHITE PAPER • JANUARY 2020

Nutritional solutions to optimize your immunity

BRIGHT SCIENCE. BRIGHTER LIVING.™



Contents

3 Foreword

4 Why immunity is more important today than ever before

The innate immune system The adaptive immune system

6 How the immune system changes throughout life

Key nutrients impacting the immune system

- 8 What do consumers think?
- 9 How can we boost our immune system?

10 Nutrients and immunity: evidence and mechanism

Vitamins Omega-3 LCPUFAs Trace elements Applicable and approved claims

- 15 Gut health and immunity
- 15 Solutions to deliver immune health
- 16 Conclusions and takeaway messages





Foreword

by Dr Manfred Eggersdorfer, Professor of Healthy Aging at the University Medical Center Groningen and Scientific Advisor to the DSM Nutrition Academy

The global population is growing rapidly year-on-year, and people are living longer than ever before. Our living environment has also changed substantially in recent decades, placing new and increased stress on our body.

Both factors mean there is a greater need to support health and wellbeing throughout life. The question of how to protect our body effectively against disease is, therefore, an ever more prominent concern for individuals worldwide. There are a wide range of factors that can have a negative impact on the function and performance of the body's natural defense system – also known as the immune system – and as a result, steps must be taken to ensure that its integrity can be maintained throughout life.

While there are natural variations in individual immune performance, which can be the result of age or environmental factors, a growing body of research suggests that measures can be implemented to support and optimize immunity. There is, for instance, increasing evidence that nutrition may help to enhance the immune system and ensure that the body is well equipped to defend itself against pathogens, allergens and other immune triggers.¹ Although further research is needed to harmonize a nutritional approach and fine-tune nutrient recommendations, more must be done to raise awareness of the role of nutrition in supporting our immune system and the important relationship between immunity, inflammation and gut health in enabling optimal health throughout life.

This white paper will explore the role nutrition can play in maintaining a healthy immune system, as well as how nutritional solutions can help to optimize immune responses for population groups and individuals worldwide.

Why immunity is more important today than ever before

The human body is exposed to a wide range of stimuli every day that have the potential to compromise our health and wellbeing.

Exposure to harmful bacteria, viruses and allergens, but also other stimuli such as stress and air pollution, can all contribute to an increased risk of infection and disease. When these factors are compounded by one another, individuals are at an increased risk of immune dysfunction. Consumers are exposed to a greater number of these risks in the current environment, and their growing awareness is driving a demand for solutions to manage them. The immune system – the body's natural defense mechanism – plays an important role in helping to protect the body against disease and infection, modulate inflammation and maintain good health throughout life.

The immune response involves a complex system of molecules, cells and tissues designed to defend the host against infectious agents, as well as other harmful substances and the damage they cause. When encountering infectious agents, such as viruses, harmful bacteria or substances such as allergens, the immune system employs two lines of defense: the innate immune system and the adaptive immune system.

The innate immune system

As the body's first line of defense, the innate immune system provides an immediate, non-specific response to environmental stressors and pathogens.² This system offers both physical and chemical protection. The skin, for instance, can act as a physical barrier to airborne microorganisms and the gastrointestinal tract is the first point of contact for food. Epithelial barriers, including skin, respiratory and gastrointestinal mucosa, then help to prevent pathogens from taking hold if they enter the body – for example, through an open wound or orifice. Stomach acid and tears are also able to guard the body against pathogens.³ However, if these defenses are weakened or unable to prevent the entry of pathogens, an innate immune response is triggered, and a cascade of immune molecules begin to take action.

The body responds rapidly to pathogens by inducing an inflammatory response, causing blood to rush to the site of infection. This enables white blood cells, such as neutrophils, monocytes and macrophages, to engulf the invading pathogen through phagocyosis and destroy it by producing defense molecules such as digestive enzymes. This is supported – or complemented – by the complement system during inflammation and in response to some bacterial infections. Other important components of the innate immune system include natural killer cells (NKCs), which can detect abnormal cells and eliminate them, and dendritic antigen-presenting cells, which relay information about the pathogen from the innate system to the adaptive system.

The adaptive immune system

In comparison to the innate immune system, the adaptive system can utilize information about the invading pathogen to develop a targeted, specific response. Antigens, or substances capable of eliciting an immune response — such as proteins or other molecules — can be detected by dendritic cells of the innate system and relayed to the adaptive immune system. This process is called antigen presentation; here, a phagocyte moves parts of the ingested material back to its surface, where it can then be displayed to other immune cells, such as lymphocytes, to take action.

There are two broad types of adaptive immune response; the antibody-mediated and cell-mediated immune responses, both of which can be supported by optimal intake of nutrients. All adaptive responses are performed by white blood cells called lymphocytes, although there are several lymphocytes which all perform slightly different functions.⁴ In antibody responses, B lymphocytes, also known as B cells, recognize antigens and trigger the production of antibodies. Antibodies are proteins that travel via the bloodstream to the site of the intruding antigen and bind to it, potentially inactivating the antigen's function and marking it for destruction by phagocytes.

In a cell-mediated response, however, T cells are activated. Cytotoxic T cells can identify and eliminate an infected host cell through the viral antigens on its surface, to prevent the virus from replicating. Helper T cells generate signalling molecules called cytokines that activate macrophages and facilitate engulfment of infected cells. They also support the maturation of B lymphocytes in the production of highly efficient antibodies and help to activate cytotoxic T cells.⁵

The B and T cells of the adaptive immune system also store information about antigens, creating a so-called 'memory' of a previously encountered pathogen. This allows the body to respond more quickly to that pathogen upon future re-exposure.



How the immune system changes throughout life

An effective, fully functioning immune system is essential to help protect the body against infection and disease.⁶ However, as with many functions of the body, this system changes significantly throughout life, and understanding how it evolves over time is essential to optimally support specific requirements for each age group.⁷

- **Infants:** At birth, the immune system is relatively immature, with the cells in the innate and adaptive systems rapidly developing in order to respond to external stimuli after birth. Critical early protection against many infectious diseases previously experienced by the mother is given by the passive IgG antibody transferred from the mother transplacentally and in milk.
- **Childhood to adolescence:** Exposure to an increasing variety of pathogens and other harmful substances during childhood causes the immune system to evolve and mature over time. The risks are now much reduced by vaccinations, which stimulate protective immune responses in the maturing immune system. However, children may still acquire viral, bacterial and parasitic infections that must be fought off and controlled by immune responses. The protection provided by the immune response increases, and young adults typically suffer fewer infections.
- Adulthood: When an individual reaches adulthood, their immune system is fully matured and functional. The B and T cells in the adaptive system typically have an extensive bank of information from previous exposure to infective agents, allergens and vaccinations, enabling the body to react quickly and efficiently when exposed to these pathogens or substances.
- Aging adults: With aging, the efficiency of the immune system gradually declines, which consequently impacts health, longevity and quality of life.

With the immune system changing as we get older (figure 1), it is essential to look for ways to optimally adapt the responses to infections and diseases on an individual basis – particularly during early and later life, when the immune system is either immature or declining with age. Research is currently ongoing into the potential role of nutrition in supporting the body's defense mechanism.

AGE	FUNCTIONALITY	STAGE
Birth / infants	Immune system development	The immune system is immature at birth, but develops rapidly in order to respond to external stimuli after birth and throughout infancy. Impaired development of the immune system in infancy can have a major impact on immune function later in life.
Childhood / adolescence	Immune system development and maturation	The immune system evolves and matures following exposure to pathogens and other harmful substances during childhood. Vaccination and immunization at this stage supports more sophisticated immune responses in adolescence.
Adulthood	Mature immune system	At this stage, the immune system is fully matured and functional. The body can react quickly and efficiently when exposed to pathogens or substances as a result of previous exposure to infective agents, allergens and vaccinations.
Aging adults	Immune system decline	Older adults are exposed to an increased risk of infection and allergies as the immune system begins to decline.

Figure 1: The evolution of the immune system over the lifetime⁸



Key nutrients influencing the immune system

Micronutrients, such as vitamins, trace elements, omega-3 LCPUFAs and bioactive substances such as polyphenols, have been shown to support the immune system.

Individuals with imbalanced dietary habits are at risk of inadequate nutrient status, which may result in malnutrition and a phenomenon known as 'hidden hunger'. Hidden hunger is increasingly prevalent across age groups in Western societies and occurs as a result of energy-dense, but nutrient-poor diets. Inadequate status of and deficiency in essential micronutrients, such as vitamins A, C, D, E, the vitamin B family, selenium, zinc and omega-3 LCPUFAs, can have a negative effect on the immune system and lead to reduced resistance against disease and infection.

Scientific data, and in particular clinical evidence, has established a relationship between malnutrition and immune responses, with malnutrition reported to be one of the leading causes of immunodeficiency disorders worldwide.⁹ Immunodeficiency disorders result in full or partial impairment of the immune system, and leave individuals unable to defend themselves effectively against infection or disease.¹⁰ Primary immunodeficiency disorders (PID) are typically inherited, while secondary disorders, such as protein-energy malnutrition, are acquired as a result of disease or other factors, such as malnutrition.

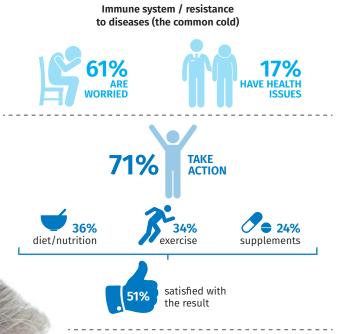
Studies have also revealed that nutritional interventions were able to resolve secondary immunodeficiency disorders associated with nutrient deficiencies.¹¹ These findings demonstrate that nutritional supplementation can effectively improve the immune system function of individuals with impaired immunity, and consequently their longevity and quality of life.

What do consumers think?

With information on health and wellbeing becoming increasingly accessible to all, individuals are more aware of factors that may compromise their immunity and health. In a recent consumer survey, 61% of respondents reported being worried about the health of their immune system – making it one of the leading consumer health concerns across the globe, particularly in Latin American countries and the Asia-Pacific region (figure 2).¹² 28% of respondents believed that they get more colds than they used to get.

These concerns have led to more consumers exploring ways to boost their immune system, especially through diet (36%) and dietary supplements (24%). Over half of those surveyed also believed that a cleaner environment can help to improve their immunity. As a result, more and more people are taking action to address their concerns; 71% of respondents reported implementing measures to improve their diet and nutrition, increase levels of physical exercise or consume dietary supplements to boost their health and immunity, with just over half of those surveyed reportedly satisfied with the result. 76% of concerned parents also reported implementing dietary or supplementation measures to address their worries regarding their children's immune system and resistance to disease.¹³ The immune system and its functionality are a concern for individuals throughout life – 64% of parents in the survey reported being concerned about their children's immune system and resistance to disease.¹⁴

Figure 2: Global consumer survey on leading global health concerns¹⁵



Do not take action

29%

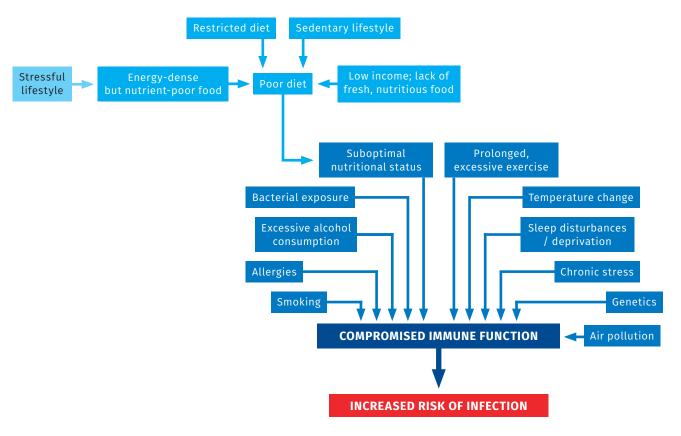
How can we boost our immune system?

Immunity and resistance against disease are key concerns for consumers of all ages around the globe, with many becoming more aware of the factors that may imbalance the immune system (figure 3). Studies have demonstrated that, in addition to malnutrition, non-modifiable factors, such as genetics and food allergies, as well as modifiable factors such as smoking, stress, sedentary lifestyles, medication, bacterial exposure and temperature change, all have the potential to negatively impact the immune system and immune responses.

Furthermore, a growing body of evidence also indicates that pollutants in the air may be more damaging to our immune system than previously realized. Air pollution is a global challenge, responsible for an estimated seven million deaths worldwide every year, with 91% of the world's population reportedly living in regions not compliant with World Health Organization (WHO) air quality guidelines.¹⁶ It is widely recognized that some population groups, such as older adults, children and those already suffering from illnesses like asthma and diabetes, are especially vulnerable to the harmful effects of air pollution.¹⁷

Recent scientific data, however, suggests that nutritional solutions, such as supplementation with vitamin E and omega-3 LCPUFAs, can help to reduce levels of reactive oxygen species which interact with cellular DNA to cause oxidative stress that can trigger cell damage. Increasing dietary consumption of key nutrients, thus reducing nutrient inadequacies, may also help to improve our body's immune responses and its ability to defend against the damaging effects of air pollution.

Figure 3: Overview of factors influencing infection risk¹⁸



Nutrients and immunity: evidence and mechanism

There is a growing body of evidence indicating that nutrition and immune responses are closely interrelated, highlighting the role that nutrient-rich diets or dietary supplementation may play in supporting our immune system (figure 4).

While research is ongoing, the totality of scientific evidence supports the role of nutritional intervention as an effective approach to improving the body's immune response against disease and infection.

Figure 4: Overview of the key role played by micronutrients in the immune system¹⁹

MICRO- NUTRIENT	NUTRITIONAL BENEFIT	INNATE IMMUNE FUNCTION	ADAPTIVE IMMUNE FUNCTION	SCIENTIFIC EVIDENCE
Vitamin C	 Helps to reduce the duration and severity of the common cold Works with vitamin E to protect omega-3 PUFAs and their structures 	 Boosts plasma neutrophil concentration Promotes neutrophil function and mobility to accelerate immune cell response Helps to reduce presence of radicals and oxidants and protects against oxidative stress Promotes phagocyte activity 	 Promotes the maturation of T lymphocytes Accelerates the decomposition of histamine 	
Vitamin D3	 Supports overall health and wellbeing and bone health Facilitates normal immune function May reduce risk of autoimmune disorders 	 Helps to reduce susceptibility to pathogens 	 May suppress excessive adaptive immunity responses 	
Vitamin B6	 Supports healthy functioning of the nervous system and red blood cell formation Facilitates normal immune function 	 Supports overall immune system function Contributes to production of DNA and proteins in the immune system Boosts NKC activity 	 Supports antibody production and metabolism Boosts lymphocyte proliferation 	
Vitamin A	 Supports normal function and development of both the innate and adaptive immune systems Mediates functions required for growth and development 	 Enhances the body's ability to shield itself against the threat of pathogens Modulates innate immune responses 	 Contributes to the proliferation and differentiation of antibody- producing lymphocytes Modulates T cell response 	
Selenium	 Required for optimal immune function Helps to reduce risk of susceptibility to bacterial or viral infections 	 Acts as an antioxidant to protect against oxidative damage, through the reduction in reactive oxygen species Regulates inflammatory processes 	 Regulates immune responses 	
Zinc	 Protects against the effects of reactive oxygen compounds Supports optimal immune function, particularly in athletes 	 Promotes growth, maturation and activity of innate cells, like NKCs 	 Promotes growth, maturation and activity of adaptive cells, like B and T lymphocytes 	
Vitamin E	 Works with vitamin C to protect omega-3 PUFAs and their structures Supports overall improved immune health and function Improves wound healing 	 Protects omega-3 PUFAs against attack from reactive molecules Supports defense against oxidative damage Reduces inflammation 	 Increases resistance against pathogens 	Emerging scientific evidence
Omega-3 LCPUFAs	 Supports optimal immune function Supports early life immune system development 	 Modulates eicosanoid production 	 Modulates eicosanoid production 	
Polyphenols	 Reduces the symptoms of the common cold and influenza 	 Acts as an antioxidant to protect against oxidative damage 	 Boosts the number of T lymphocytes involved in the adaptive response 	

Vitamins

Vitamin A

Vitamin A is widely recognized for its role in a number of physiological processes in the body, including the normal functioning and development of both the innate and adaptive immune system.²⁰ Research suggests that vitamin A contributes to the proliferation and differentiation of antibody-producing lymphocytes in the adaptive response, while also improving the innate immune response by enhancing the body's ability to shield itself against the threat of pathogens.²¹

Vitamin A can be obtained via dietary sources such as the carotenoid beta-carotene, an antioxidant that is found in fruits and vegetables and is a natural precursor to the vitamin. A metabolite of vitamin A, retinoic acid, has also been shown to mediate the functions of the vitamin that are required for growth and development, as well as playing a role in modulating T cell and innate immune responses.²² Long-lasting deficiencies of vitamin A can have a strong negative impact on the immune system, with some individuals – particularly children – reported to demonstrate impaired phagocytic activity and antibody-mediated immunity.²³

Vitamin B6

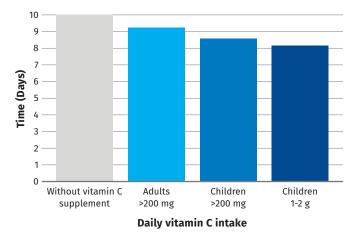
Vitamin B6, part of the B-complex vitamin, is a naturallyoccurring nutrient found in a wide range of animal and plant food products that supports healthy functioning of the nervous system and red blood cell formation.^{24,25} It is required as a coenzyme in the metabolism of antibodies and cytokines.²⁶ Furthermore, studies have highlighted a link between deficiencies in vitamin B6 and reduced proliferation of lymphocytes and decreased antibody production following immunization, as well as a reduction in the activity of NKCs.^{27,28}

Vitamin C

While vitamin C is known to contribute to the functioning of a number of tissues and organs in the body, such as the brain, heart and kidneys, it is also particularly well recognized for its role in the human immune system.²⁹ It is, for instance, highly concentrated in white blood cells because it is actively accumulated in leukocytes, resulting in a concentration that is up to 20 times higher than in the plasma, underscoring its important role in immune defense.³⁰

Vitamin C has been shown to promote the maturation of T lymphocytes and stimulate white blood cell function, while also promoting phagocyte activity. Regular vitamin C consumption also helps to reduce the duration and severity of the common cold by helping to replenish vitamin C resources that have been diminished by infection (figure 5). Furthermore, studies show that vitamin C may accelerate the decomposition of histamine, a cell signaling molecule involved in the development of cold symptoms, in the blood.³¹

Figure 5: The effects of vitamin C on common cold duration³²



Vitamin C is a powerful antioxidant and forms an important line of defense in the body, capable of essentially reducing all physiologically relevant radicals and oxidants and protecting against the effects of oxidative stress.³³ This includes the cooperation of vitamin C and vitamin E to protect omega-3 PUFAs and their structures, like cell membranes, against peroxidation where vitamin C recycles vitamin E.³⁴ Daily intake of vitamin C has also been shown to promote neutrophil function and mobility, helping to provide greater protection by accelerating immune cell response and subsequently increasing the speed at which pathogens can be eliminated from the body.³⁵ A growing body of evidence also indicates that vitamin C in higher doses may serve as an effective tool in some cancer therapy treatments, although further research is required.³⁶

Vitamin D

Vitamin D, often referred to as the 'sunshine vitamin', has been found to play an important role in the function of the immune system. Immune cells possess vitamin D receptors, which enable this nutrient to contribute to a wide range of essential actions in both the innate and adaptive immune systems, including the development of stem cells into all types of blood cells. Its antibacterial effects help to reduce susceptibility to pathogens and may also play a role in suppressing excessive adaptive immunity responses, although more research exploring this in further detail is currently underway.^{37,38}

Vitamin D is rarely found in food or beverage products and deficiency in this vitamin is highly prevalent worldwide. Lack of exposure to natural sunlight can also contribute to this issue. Vitamin D deficiency has been associated with an elevated risk of autoimmune disorders, such as multiple sclerosis, and respiratory tract infections.³⁹ Increasing intake of vitamin D supplements or foods fortified with vitamin D may help to address nutritional shortfalls.

Vitamin E

Vitamin E is a fat-soluble antioxidant that helps to protect lipid cell membranes against attack from reactive molecules like free radicals, which are generated during the innate immune response and can lead to oxidative damage.⁴⁰ Higher intake of vitamin E, which is commonly found in dietary sources, such as vegetable oils and nuts, has also been associated with overall improved immune health and function, with studies reporting increased resistance against pathogens – particularly in elderly populations.⁴¹ Other benefits include its contribution to reduced inflammation and improved wound healing.⁴²

Omega-3 LCPUFAs

Adequate dietary intake of omega-3 LCPUFAs, such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), is also essential for optimal immune function. In addition to helping to trigger the inflammatory cascade of immune modulating molecules, omega-3 LCPUFAs have also been shown to modulate the production of eicosanoids (active metabolites of omega-3 and omega-6 LCPUFAs), which can impact the immune system. Moreover, omega-3 LCPUFAs play a role in the development of the immune system in early life.^{43,44} Benefits of omega-3 LCPUFAs supplementation have also been observed in patients with rheumatoid arthritis, as well as those living with asthma and allergic respiratory diseases.^{45,46,47}

Trace elements

Selenium

Selenium is a trace element present at higher doses in immune tissues, such as lymph nodes and the spleen, and is required for optimal immune function. Its role is multifaceted; on the one hand, it acts as an antioxidant to protect against oxidative damage, while on the other hand it can also help to regulate immune responses and inflammatory processes.⁴⁸ Selenium deficiencies have been found to contribute to an increased risk of susceptibility to bacterial or viral infections, particularly in older adults, as well as an elevated risk of complications from these infections.⁴⁹

Zinc

Like selenium, the antioxidant properties of zinc help to protect immune cells against the effects of reactive oxygen compounds. It also helps to promote the growth, maturation and activity of both innate and adaptive immune cells, such as NKCs and B and T lymphocytes.⁵⁰ Increased zinc intake may be of particular benefit to individuals undertaking intense physical exercise. Athletes often face decreased concentrations of trace elements such as zinc, which can lead to a greater risk of decreased immune function and infection.⁵¹

Polyphenols

Polyphenols are plant-based bioactive substances found in many dietary sources, and are the most abundant antioxidants in the human diet.⁵² They have been shown to significantly reduce the symptoms of the common cold and influenza by increasing the number of T lymphocytes involved in the adaptive response, thus helping to improve resistance to pathogens.⁵³



There is extensive research highlighting the potential that vitamins, trace elements and polyphenols have in supporting immune health. However, there is ongoing debate within the scientific community and governments alike regarding the recommended intake of these respective nutrients, and how much is required to benefit human health and wellbeing. As a result, there are significant variations in current recommendations across the globe; for instance, while current Food and Agriculture Organization (FAO) and WHO guidelines advise a daily vitamin C intake of 45 mg, these values often vary between countries and most countries advise levels of up to 100-110 mg for women and men, respectively. These recommendations can be influenced by other factors such as age and gender.⁵⁴ In the US, higher intake is also recommended for cigarette smokers, pregnant women and lactating mothers.

Recent research, however, suggests that while the current Recommended Dietary Allowance (RDA) is set to prevent scurvy, which is the clinical demonstration of vitamin C deficiency, these guidelines may be too low to provide optimal health benefits associated with vitamin C. For this reason, some countries – including China, New Zealand and Australia – have set a revised target for vitamin C consumption, with a proposed intake of 200 mg vitamin C per day.^{55,56} Studies exploring the role of vitamin C in immune health have provided further support for this recommendation, with evidence indicating that 200 mg/day vitamin C intake may reduce the duration of the common cold and promote neutrophil function.⁵⁷

To streamline recommendations and implement a worldwide consensus on the RDA of nutrients that contribute to optimal immune performance, it is essential that key stakeholders and decision makers across the globe collaborate to harmonize reference values. This is particularly important when considering essential nutrients such as vitamins C and D, which have been shown to play a crucial part in optimizing both innate and adaptive immunity responses and may be integral in supporting better immune health worldwide.



Gut health and immunity

The human gut is home to trillions of microorganisms, with each individual harbouring a unique composition of different bacterial species. Most of these microorganisms are bacteria, however others, such as viruses and fungi, are also present.

The microbial communities in the gut aid the host to acquire energy from non-digestible food and produce short chain fatty acids, which are important for human health. The gut microbes also play a critical role in the development of a robust and balanced immune system. They enable, for instance, the host to develop a tolerance to the large number of antigens passing through the gut, and also act as a barrier to invading pathogens by competing for space to prevent harmful microorganisms taking hold.⁵⁸ Certain alterations to the composition of the gut microbiota, known as dysbiosis, are often associated with gastrointestinal and systemic disease, however there is also evidence to suggest that malnutrition can have a negative impact on gut microbial composition.⁵⁹ It is for this reason that nutritional concepts to target microbiota composition, such as probiotics and prebiotics, have been explored as potential solutions to support optimal gut and immune health.

In fact, probiotics and prebiotics are two of the most widely studied interventional approaches in the field of gut microbiota. They both can be used to restore the balance of the gut microbiota in dysbiosis. Beneficial effects of probiotic supplementation include reducing the risk of diarrhea, necrotizing enterocolitis, acute upper respiratory tract infections, pulmonary exacerbations in children with cystic fibrosis and eczema in children.⁶⁰

Solutions to deliver immune health

With a wide variety of factors capable of negatively impacting immunity, there is a growing need for solutions that can support immune function.

As a result, there is an increased demand for nutrients that support our immunity, such as vitamins C and D (see figure 4), which can help to defend against infection and neutralize harmful free radicals, pollutants and toxins. However, while many essential nutrients are found naturally in animal or plant products and may be consumed as part of a healthy lifestyle, it is not always possible to get the required nutrition from diet alone. Dietary supplements are popular among those looking for solutions to support immunity, with almost half of consumers globally choosing supplements as an easy, convenient way to bolster their immune system.⁶¹ Other preferred formats include on-the-go drinks like tea, juice and drinking yogurts.⁶² Food and beverage manufacturers may also fortify their products with essential nutrients, enhancing the nutritional value of a product and facilitating easier access to nutrition for consumers looking to support their immune system.

Conclusions

While the variety of factors capable of disrupting the immune system, such as air pollution and stress, have increased in recent decades, developing and maintaining an effective immune system throughout life is possible. Lifestyle changes, such as adopting more active routines and taking steps to reduce exposure to harmful bacteria, can play an important role in protecting the body against infection and disease. However, other factors - such as malnutrition, which can contribute to the development of immunodeficiency disorders - must also be taken into consideration. Globally, many individuals have an inadequate or deficient nutrient status and, as such, addressing the issue of malnutrition will only be possible if there is collaboration between scientific and medical communities, industry and governments. Agreement, for instance, on global reference values for nutrient intake will be essential in driving forward nutritional intervention as an effective approach to maintaining immune health.

Further research on the link between immunity and gut health is also vital in order to demonstrate how poor diet can impact overall health and wellbeing. As such, implementing measures to encourage individuals to make healthier lifestyle choices, including incorporation of a variety of nutrients in optimal ranges, and introducing frameworks to combat malnutrition could be integral to optimizing immune health and enable people to lead longer, healthier lives.

Takeaway messages

- Protecting the body against infection and disease is increasingly important as the world's population lives longer and consumers are more aware than ever before of the factors that may imbalance their immunity.
- The immune system is the body's natural defense mechanism, designed to protect the body against disease and infection, modulate inflammation and maintain good health throughout life.
- The immune system is composed of two lines of defense: the innate immune system, providing a rapid, non-specific response; and the adaptive immune system, generating a strong, long-lasting specific response.
- The immune system evolves throughout life, with infants and elderly adults particularly susceptible as a result of weak or under-developed immune systems.
- Nutrient gaps and deficiencies are highly prevalent across the globe. Extensive research has shown that nutritional intervention using key nutrients, such as vitamins A, B6, C, D and E, omega-3 LCPUFAs, selenium, zinc and polyphenols, may be an effective approach to strengthen and support immunity.
- Gut and immune health are closely connected, and disruption to microbiota in the gut can have a negative impact on immunity, and therefore overall health and wellbeing. Research has shown that certain probiotics and prebiotics may be an effective solution to restoring gut microbiota and gut homeostasis.
- Collaboration between scientific and medical communities, industry and governmental agencies is needed to establish harmonized, global frameworks to support nutritional intervention and recommendations as an approach to optimizing immune health.

DSM: your preferred partner

DSM is a global purpose-led, science-based company active in Nutrition, Health and Sustainable Living. We offer high quality ingredients, customized premixes and expert services to solve the challenges we face in keeping the world's growing population healthy.

With unparalleled scientific heritage and our deep consumer insights, we help to differentiate products and drive consumer appeal. We continue to invest in our market-ready solutions, premix capabilities, innovation, R&D and strategic partnerships to discover new formats and product applications that inspire consumers to rethink health as a priority in their life.

Inspired by people, delivered by experts.

For more information about how DSM can support you in the development of innovative nutritional solutions, visit *www.dsm-humannutrition.com*

References:

- E. S. Wintergerst et al., 'Contribution of selected vitamins and trace elements to immune function', *Annals of Nutrition and Metabolism*, vol. 51, no. 4, 2007, p. 301-323.
- 2. Ibid.
- 3. Ibid.
- B. Alberts et al., 'The adaptive immune system' in Molecular Biology of the Cell, 4th ed, New York, Garland Science, 2002.
- 5. Ibid.
- A. K. Simon, G. A. Hollander & A. McMichael, 'Evolution of the immune system in humans from infancy to old age', Proceedings. Biological Sciences, vol. 282, no. 1821, 2015, p. 1-9.
- 7. Ibid.
- S. Maggini et al., 'Immune function and micronutrient requirements change over the life course', Nutrients, vol. 10, no. 1531, 2018, p. 1-27.
- 9. Op. cit. (Wintergerst et al.).
- British Society for Immunology, Immunodeficiency, [website], 2017, https://www.immunology.org/ policy-and-public-affairs/briefings-and-positionstatements/immunodeficiency (accessed 29 November 2018).
- 11. Op. cit. (Wintergerst et al.).
- 12. DSM, 'Global health concerns', [report], 2017.
- 13. Ibid.
- 14. Ibid.
- 15. Ibid.
- World Health Organization, Air pollution, [website], 2018, http://www.who.int/airpollution/en/ (accessed 30 November 2018).
- 17. DSM, 'Air pollution and cardiovascular health: new evidence on nutritional solutions', [report], 2017.
- 18. Op. cit. (Maggini et al.).
- 19. Ibid.
- 20. European Food Safety Authority, 'Scientific opinion on the substantiation of a health claim related to vitamin A and contribution to normal development and function of the immune system pursuant to Article 14 of Regulation (EC) No 1924/2006', EFSA Journal, vol. 11, no. 7, 2013, p. 1-11.
- C. J. Field et al., 'Nutrients and their role in host resistance to infection', *Journal of Leukocyte Biology*, vol. 71, no. 1, 2002, p. 16-32.
- 22. M. Raverdeau et al., 'Modulation of T cell and innate immune responses by retinoic acid', *Journal of Immunology*, vol. 192, no. 7, 2014, p. 2953-2958.
- 23. Op. cit. (EFSA, 2013).
- J. D. Fernstrom et al., 'Brain and nervous system' in B. Caballero et al. (eds), *Encyclopedia of Human Nutrition*, 2nd ed., Elsevier Academic Press, 2005, p. 225-232.

- A.D. Mackey et al., 'Vitamin B6' Modern Nutrition in Health and Disease, 10th ed, Baltimore, MD; Lippincott Williams and Wilkins, 2006, p. 194-210.
- 26. European Food Safety Authority, 'Scientific opinion on the substantiation of health claims related to vitamin B6 and protein and glycogen metabolism (ID 65, 70, 71), function of the nervous system (ID 66), red blood cell formation (ID 67, 72, 186), function of the immune system (ID 68), regulation of hormonal activity (ID 69) and mental performance (ID 185) pursuant to Article 13(1) of Regulation (EC) No 1924/2006, EFSA Journal, vol. 7, no. 9, 2009, p. 1-20.
- 27. Op. cit. (Mackey et al.).
- 28. Op. cit. (Wintergerst et al.).
- S. Chambial et al., 'Vitamin C in disease prevention and cure: an overview', *Indian Journal of Clinical Biochemistry*, vol. 28, no. 4, 2013, p. 314-328.
- S. M. Bozonet et al., 'Enhanced human neutrophil vitamin C status, chemotaxis and oxidant generation following dietary supplementation with vitamin C-Rich SunGold kiwifruit', Nutrients, vol. 7, no. 4, 2015, p. 2574-2588.
- V. Elste et al., 'Emerging evidence on neutrophil motility supporting its usefulness to define vitamin C intake requirements', *Nutrients*, vol. 9, no. 5, 2017, p. 1-16.
- 32. Ibid.
- G. R. Buettner et al., 'The pecking order of free radicals and antioxidants: lipid peroxidation, a-tocopherol and ascorbate', Archives of Biochemistry and Biophysics, vol. 300, no. 2, 1993, p. 535-543.
- 34. Ibid
- J. Schwager et al., 'Ascorbic acid modulates cell migration in differentiated HL-60 cells and peripheral blood leukocytes', *Molecular and Nutritional Food Research*, vol. 59, no. 8, 2015, p. 1513-1523.
- H. Fritz et al., 'Intravenous Vitamin C and Cancer: A systematic review', *Integrative Cancer Therapies*, vol. 13, no. 4, 2014, p. 280-300.
- F. Sassi, C. Tamone and P. D'Amelio, 'Vitamin D: nutrient, hormone and immunomodulator', *Nutrients*, vol. 10, no. 11, 2018, p. 2-14.
- D. D. Bikle, 'Vitamin D and the immune system: role in protection against bacterial infection', *Current Opinion in Nephrology and Hypertension*, vol. 17, no. 4, 2008, p. 348-352.
- A. Ascherio et al., 'Vitamin D and multiple sclerosis', Lancet Neurology, vol. 9, no. 6, 2010, p. 599-612.
- 40. D. Raederstorff et al., 'Vitamin E function and requirements in relation to PUFA', *British Journal of Nutrition*, vol. 114, no. 8, 2015, p. 1113-1122.
- S. N. Meydani et al., 'Vitamin E supplementation and in vivo immune response in healthy elderly subjects. A randomized controlled trial', *JAMA*, vol. 277, no. 17, 1997, p. 1380-1386.
- C. Winkler et al., 'Vitamin C and E suppress mitogenstimulated peripheral blood mononuclear cells in vitro', Arch. Allergy Immunol., vol. 142, no. 2, 2007, p. 127-132.

43. Op. cit. (Maggini et al.).

- 44. P. C. Calder et al., 'Session 5: Early programming of the immune system and the role of nutrition: is there a role for fatty acids in early life programming of immune system', Proceedings of the Nutrition Society, vol. 69, 2010, p. 373-380.
- A. A. Berbert et al., 'Supplementation of fish oil and olive oil in patients with rheumatoid arthritis', *Nutrition*, vol. 21, no. 2, 2005, p. 131-136.
- 46. T. D. Mickleborough et al., 'Dietary polyunsaturated fatty acids in asthma- and exercise-induced bronchoconstriction', European Journal of Clinical Nutrition, vol. 59, no. 12, 2005, p. 1335-1346.
- L. C. Echeverri Tirado & L. M. Yassin, 'B cell interactions in lipid immune responses: implications in atherosclerotic disease', *Lipids in Health and Disease*, vol. 16, no. 30, 2017, p. 1-11.
- Z. Huang, 'The role of selenium in inflammation and immunity: from molecular mechanisms to therapeutic opportunities', *Antioxid Redox Signal*, vol. 16, no. 7, 2012, p. 1325-1336.
- P. Iglesias et al., 'Selenium and kidney disease', J Nephrol, vol. 26, no. 2, 2013, p. 266-272.
- D. Konig et al., 'Zinc, iron and magnesium status in athletes – influence on the regulation of exerciseinduced stress and immune function', *Exercise Immunol Review*, vol. 4, 1998, p. 2-21.

51. Ibid.

- T. R. Neyestani, 'Polyphenols and immunity' in F. De Meester & R.R. Watson (eds) Wild-Type Food in Health Promotion and Disease Prevention, Humana Press, Totowa, 2008, p. 413-434.
- 53. C.A. Rowe et al., 'Specific formulation of Camellia sinensis prevents cold and flu symptoms and enhances gamma delta T cell function: a randomized, double-blind, placebo-controlled study', Journal of the American College of Nutrition, vol. 26, 2007, p. 445-452.
- 54. Food and Agriculture Organization; World Health Organization, Human Vitamin and Mineral Requirements; Training Materials for Agricultural Planning, Bangkok, Thailand, 2002.
- German Nutrition Society (DGE), 'New reference values for vitamin C intake', Annals of Nutrition and Metabolism, vol. 67, no. 1, 2015.
- Australian Government Department of Health, 'Nutrient reference values for Australia and New Zealand' Ministry of Health, 2005.
- 57. Op. cit. (Elste et al.).
- A. M. Valdes et al., 'Role of the gut microbiota in nutrition and health', British Medical Journal, vol. 361, 2018, p. 36-44.
- M. I. Smith et al., 'Gut microbiomes of Malawian twin pairs discordant for kwashiorkor', Science, vol. 339, 2013, p. 541-548.
- 60. Op. cit. (Valdes et al.).
- 61. Op. cit. (DSM, 2017).
- 62. Mintel Nutrition Insight, 'Immunity', [report], 2016.



Although DSM has used diligent care to ensure that the information provided herein is accurate and up to date, DSM makes no representation or warranty of the accuracy, reliability, or completeness of the information. This white paper only contains scientific and technical information on nutritional solutions to support the immune system. Any explicit and/or implied claims included within this document may not necessarily be appropriate for immunity support marketing purposes. Please consult with your independent legal, science and regulatory professionals accordingly. Country or region-specific information should also be considered when labeling or advertising to final consumers. This publication does not constitute or provide scientific or medical advice, diagnosis, or treatment and is distributed without warranty of any kind, either expressly or implied. In no event shall DSM be liable for any damages arising from the reader's reliance upon, or use of, these materials. The reader shall be solely responsible for any interpretation or use of the material contained herein. The content of this document is subject to change without further notice. Please contact your local DSM representative for more details. All trademarks listed in this white paper are either registered or licensed trademarks of DSM group of companies in the Netherlands and/or other countries, unless explicitly stated otherwise.