



Supporting the Immune System through Diet

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As many still await full vaccination, it's worth considering what we can do to support our own natural immunity. The first step is reversing some of the less healthy habits developed during the various lockdowns.

A worldwide survey explored the consequences of COVID-19 restrictions.¹ Food tended to be less healthy, more snacks and comfort foods were consumed, and some people felt their eating was out of control. The British Nutrition Foundation surveyed 2,067 adults and found that 27% had eaten less healthily during lockdown.² Sixty-three per cent of those eating less healthy meals attributed the change to 'boredom', whereas 45% said the problem was 'stress, anxiety and tiredness'. When the COVID-19 restrictions are lifted, the priority for 43% was to lose weight, whereas for 29% the aim was to eat more healthily.

One way to develop optimal immunity is by improving diet, since it is well accepted that poor nutrition adversely affects the immune system.³ EU authorised health claims, now adopted in UK law post-BREXIT, state that vitamins A, B6, B12, C, D, and folate, as well as zinc, iron, selenium and copper '*contribute to the functioning of the immune system*'.⁴

What is immunity?

The immune system can be divided into two parts – innate and acquired – with the antibodies produced by a vaccine being an example of acquired immunity.⁵ However, developing acquired immunity takes days or weeks, necessitating a short-term first line of defence. This is provided by innate immunity, which responds in a general manner to foreign cells. A distinction between innate and acquired immunity is that the efficiency and speed of the former does not increase with repeated exposure to a pathogen.⁵

Innate immunity

There are various aspects of the innate immune system:⁵

- Physical barriers, such as the skin or gut epithelium, which prevent the entry of pathogens⁵
- Leukocytes are types of white blood cells, including neutrophils, eosinophils and basophils. Neutrophils are amongst the first white blood cells to arrive when damaged cells release a messenger, called interleukin-8⁶
- Macrophages engulf material and release cytokines to reduce the spread of infection⁵
- Natural killer cells are lymphocytes best known for targeting cells that have been infected by a virus⁵
- The complement cascade is a complex system of over thirty proteins that cause lysis (bursting) and phagocytosis (ingestion) of foreign cells⁷
- Inflammation of surrounding tissue is triggered during an immune response, playing a key role in destroying invading cells.^{5, 6}

“There is a need for a wide ranging and varied diet to ensure that all nutrients associated with immune function are consumed.³”

Acquired immunity

Key terms are antigen and antibody. An antigen is a molecule that can stimulate the immune system to produce antibodies. Such a response results when the immune system does not recognise a bacterium, virus, pollen or chemical. Each antigen has a distinctive feature so that the immune response is specific to a particular antigen. The acquired immune system responds to an antigen by producing antibodies (immunoglobins) that are Y-shaped proteins. Each antibody is specific to a particular antigen and marks a cell to be killed.⁵

Acquired immunity relies on T-cells and B-cells,^{5,6} lymphocytes produced in the thymus and bone marrow. The role of B-cells is to make antibodies that are specific to each pathogen and attach themselves to the surface of a foreign cell, marking it for destruction. T-cells are divided into two main types, helper and killer T-cells. The helper cells stimulate B-cells to produce antibodies and encourage the development of killer T-cells. In turn, killer T-cells destroy cells that have been infected by the relevant pathogen.⁵

Diet & immunity

It is accepted that many aspects of diet play a role in the functioning of the immune system, such that a sub-optimal nutritional status has adverse consequences.³ Some of these functions are briefly noted:

Vitamin A: Plays a role in the development and distribution of T-cells; it is anti-inflammatory; encourages the production of interferon and prevents the infection of uninfected cells.⁸

Vitamin C: An antioxidant, is important as the immune system is susceptible to oxidative stress; neutrophils contain high levels of vitamin C; increases the production of B- and T-cells.⁹

Vitamin B6: Co-enzyme in the tryptophan-kynurenine pathway that regulates cytokines; deficiency reduces the delayed hypersensitivity response (inflammatory reaction 2 to 3 days after exposure to an antigen); deficiency inhibits growth of lymphocytes and functioning of T-cells; deficiency reduces size of the thymus.¹⁰

Vitamin B12: Influences provision of natural killer and T-cells; maintains balance between helper and killer T-cells; deficiency reduces the release of immunoglobulins.¹¹

Folate: Deficiency reduces antibody response; supports cytokine-mediated immune response; aids survival of regulatory T cells that regulate other immune system cells.¹²

Vitamin D: Cells in the immune system convert 25-hydroxyvitamin D to the active form, 1,25-dihydroxyvitamin D – important in the macrophages' antimicrobial response. Without vitamin D, 'naïve' T-cells do not become either killer or helper T-cells.^{13,14}

Vitamin E: Increases lymphocytes, natural killer cells, immunoglobulin, interleukin and antibody response; reduces production of prostaglandin (a pro-inflammatory chemical); increases the creation of T-cells in the thymus and maintains the balance between different T-helper cells.¹⁵

Iron: Deficiency decreases vaccine-induced antibody production and increases susceptibility to infection.¹⁶

Zinc: Involved in development of cells for innate and adaptive immune system; deficiency disturbs communication via cytokines and increases inflammation.¹⁷

Selenium: Part of the enzyme glutathione peroxidase, an antioxidant which reduces inflammation; deficiency increases susceptibility to infection and is associated with higher levels of inflammatory cytokines.¹⁸

One meta-analysis found that an increased intake of fruit and vegetables improves biomarkers of inflammation, such as C-reactive protein (CRP) which increases following interleukin-6 secretion by macrophages and T-cells.¹⁹ Boosting fruit and vegetable intake also enhanced the profile of immune cells. Chronic inflammation has been associated with a high white blood cell count, as well as a lower habitual intake of vegetables, and a higher intake of processed foods.²⁰ A recent review of intervention studies found that hesperidin – a polyphenol found in 100% orange juice – was linked to significant reductions in CRP.²¹

Role of the gut

It is now recognised that the gut epithelium and microbiota work together to create a hostile environment for potential pathogens.²² The immune system promotes beneficial species of bacteria which, in turn, help the growth and activation of immune cells and repel potential pathogens by lowering the pH of the gut and blocking potential sites for colonisation.

Habitual diet influences the makeup of the microbiota, with a diet rich in fibre and prebiotic compounds, such as polyphenols, helping to maintain a healthy immune system. A study of 10,000 samples of gut bacteria found that three main types, *Faecalibacterium*, *Ruminococcus* and *Akkermansia*, were associated with the white blood cells involved in the initial response to infection.²³

As one example of the many foods that influence gut bacteria, the beneficial *Akermansia* and *Ruminococcus* species increased when women consumed 100% orange juice rather than a 'no juice' control.²⁴

Polyphenols also have antioxidant properties and, therefore, supports immune cells as they are sensitive to oxidative stress.²⁵ Another bioactive plant compound, carotenoids, are a vitamin A precursor and also have antioxidant properties.²⁶

Dietary advice

There is a clear impression that immunity is complex and influenced in a multitude of ways by many aspects of diet. Hence, it is improbable that an isolated change in the diet is going to have a significant impact, other than on the very rare occasions when there is a clinical deficiency of a single nutrient. Many nutrients play a role, but they act in synchrony, such that one in isolation is unlikely to have a large impact. It follows that any media claim that there is a superfood that boosts immunity is unlikely to stand examination.

There is, however, a large body of research that associates inadequate nutrition to a weaker immune response.³ In particular, there has been considerable interest in the role of vitamin D in the COVID-19 pandemic. A review of seven studies²⁷ found that people with vitamin D deficiency had poorer clinical outcomes while, in four studies, a supplement improved the outcome. Updated UK advice is for everyone to take a daily vitamin D supplement during the winter and spring,²⁸ yet most people don't comply.²⁹

There is a need for a wide ranging and varied diet to ensure that all nutrients associated with immune function are

consumed.³ The foods providing the nutrients described here will be familiar to healthcare professionals, although there is little point in concentrating on one nutrient in isolation, irrespective of its importance, there is much more going on.

It is clear that the traditional '5-a-day' message should be reinforced as there are many good reasons for at least this amount. An important factor is helping individuals interpret their ability to deal with the perceived inconvenience, impracticality and effort of eating more fruit and vegetables.³⁰ Thus, offering a range of options, such as fresh, frozen, dried and 100% juice can help with compliance. In the UK, the consumption of fibre is less than recommended.³¹ Indeed, a minority of people eat the recommended 5-a-day and the recommended 30 g of fibre daily.³¹ Yet the consumption of fibre is fundamental to a healthy microbiota and a well-functioning immune system.³²

Summary

As poor nutrition disrupts the immune system, changing the diet can be part of a healthier lifestyle, including exercise, getting sufficient sleep, not smoking and drinking alcohol in moderation. Such changes are likely to be even more important as we age, since the immune system becomes less efficient.

A safe conclusion is that rarely will a single nutrient or food have a major influence on immunity. At best, any improvement would be further enhanced if the provision of other nutrients were optimal. Certainly, there can be no suggestion that a healthy diet will stop us being infected by viruses, although if you start with a robust immune system, the impact will be decreased.

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Disclaimer: Professor David Benton is a member of the Fruit Juice Science Centre 'Scientific Expert Panel'.