THE CARB-APPROPRIATE REVIEW

THE IMMUNITY ISSUE

A MONTHLY RESEARCH REVIEW BY

CLIFF HARVEY PHD

In association with The Holistic Performance Institute

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ABOUT CLIFF

Cliff Harvey PhD is an author, clinician, and researcher. He was one of the first clinical nutritionists to begin working with ketogenic and low-carb diets, way back in the 1990s and is also considered a pioneer in the area of mind-body integrative healthcare.

Cliff's early post-graduate work was in mind-body healthcare, while his master's research focussed on the use of medium-chain triglycerides to mitigate 'keto-flu' and encourage faster induction of nutritional ketosis.

His doctoral thesis continued to investigate keto-flu and ketogenesis, and the effects of different types of low-carbohydrate diets along with the individualisation of dietary prescription and how 'carbohydrate tolerance' varies from person-to-person.

He is a former world champion strength athlete, submission grappler, and author of several best-selling books, including *The Carbohydrate Appropriate Diet*, *Carb-Appropriate 101*, *Time Rich Cash Optional* and *The Credo.*

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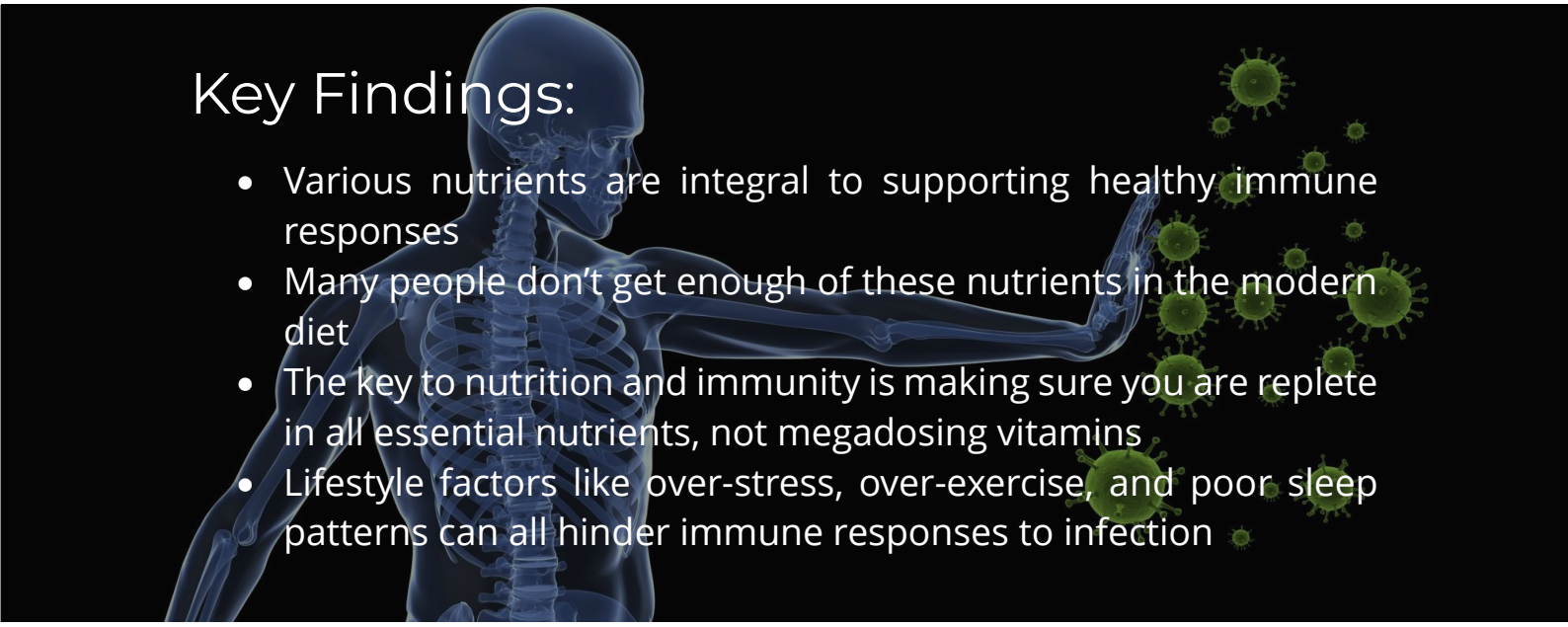
THIS MONTH

ALL ABOUT: IMMUNITY



Key Findings:

- Various nutrients are integral to supporting healthy immune responses
- Many people don't get enough of these nutrients in the modern diet
- The key to nutrition and immunity is making sure you are replete in all essential nutrients, not megadosing vitamins
- Lifestyle factors like over-stress, over-exercise, and poor sleep patterns can all hinder immune responses to infection

The immune system is the body's defence system. It protects us against *pathogens* which are micro-organisms like viruses, bacteria, protozoa, and fungi, that can cause disease. The immune system fights off these disease-causing microbes, keeping them in balance with the health-promoting microbes of our microbiota (the 'friendly' bacteria, yeasts, and fungi occurring throughout the body that are beneficial to health).

Because pathogens rapidly mutate and evolve, our defence system needs to be responsive and have multiple defences. The first line of defence is the *innate response.* This response is non-specific meaning that it will not discriminate against specific bacteria, viruses, or parasites. Inflammation is one of the key innate responses. People think of inflammation as 'bad' or undesirable but when you the cardinal signs of inflammation: redness, swelling, warmth, along with pain, there is a complex interplay of cells and molecules working to prevent pathogens from causing damage and clearing out waste products of the healing process.

Conversely, the adaptive response adapts to specific pathogen threats, allowing us to better defend ourselves against future infection. It includes a range of different cells and systems that identify specific patterns on the surface of pathogens and builds a large, targeted response specifically against them. Therefore for many illnesses, exposure when young, or vaccination, will provide lifelong, or long-term immunity to the illness.

Disorders of the immune system can result in autoimmune diseases, inflammatory diseases and cancer. Immunodeficiency occurs when the immune system is less active than normal, resulting in recurring and life-threatening infections. In humans, immunodeficiency can either be the result of a genetic disease such as severe combined immunodeficiency, or acquired conditions such as HIV/AIDS, or the use of immunosuppressive medication.

Autoimmunity results from a dysfunction of the immune system in which self-cells (or non-pathogenic microbes residing on tissue) are targeted by the immune system and result in damage to our tissue.

What is it made up of?

The immune system includes cells that help to recognise pathogens and differentiate them from 'self' tissue and beneficial microbes, along with proteins that help to regulate the inflammatory response (*inflammasomes*). It also includes many of the more commonly known immune components; white blood cells (*leukocytes*) that engulf and destroy pathogens, along with lymphocyte B and T-cells which identify, mark, and target pathogens and cells infected with pathogens for destruction. The various components of the inflammatory systems work to help encourage healing by encouraging increased blood flow to areas of infection (transports immune cells to the area), swelling and pain (which results from the increased flow and slow clearance, but also helps immobilise the area to prevent further damage).

Signs your immune system is not as healthy as it should be:

- Frequent or persistent colds or flu-like viruses
- Severe hay-fever or other allergies
- Autoimmune conditions

Note: Many serious conditions can result in these signs and symptoms. If you are experiencing any of these, consult with your doctor for proper diagnosis and treatment.

Nutrients for a healthy immune system

The foundation for a healthy immune system is a good diet that provides sufficient energy, essential fats, protein, and micronutrients.

Conversely, diets that are high in processed and refined foods, and especially those high in trans-fats and sugar are likely to worsen responses to infections.

Also, many nutrients have been shown to help support immunity, such as:

- Omega 3 fats help us to regulate immunity and inflammation in conjunction with the 'pro-inflammatory' omega 6 fats. Omega 3 fats are found in fatty fish and vegan sources like flaxseeds and algae.
- Vitamin A is intricately involved in immunity, [1] and sufficient Vitamin A is associated with immunity to illness and infections.[2, 3]
- Vitamin C, contrary to popular belief, probably won't cure the common cold but research suggests that it might help to reduce symptoms of colds and shorten their duration,[4] and might even help to prevent the occurrence of colds in athletes and others prone to higher levels of stress when taken regularly.[5, 6]
- Vitamin E also has immunomodulatory effects.[7]
- Vitamin D is a key immune regulator and has also shown promise for aiding several auto-immune conditions like systemic lupus and rheumatoid arthritis.[8]
- Zinc is also a key co-factor for immune responses. Evidence suggests that zinc supplementation might help reduce the duration and severity of the common cold.[9, 10]
- Research shows that bioflavonoids from plants reduce upper-respiratory-tract infections.[11] Other antioxidant-rich foods like grapeseed, rosehips, and cacao improve antioxidant status and immunity and reduce inflammation.[12-17]
- Adaptogens are herbs that are stress 'tonics' that help us to respond to stressors more effectively. Among the adaptogens, ginger, ginseng, gotu kola, ashwagandha and astragalus have demonstrated a range of antioxidant, anti-inflammatory and immune-boosting properties.[18-26]

- Common herbs like rosemary are anti-inflammatory and anti-microbial and may benefit immune status.[27]
- Spices such as turmeric are likely to improve immune function.[28]
- Many mushrooms help to provide immunity against infections. For example, shiitake mushroom is thought to aid immunity by increasing white blood cell activation.[29, 30]
- Probiotics supplementation reduces the incidence and severity of respiratory infections,[31-36] and probiotics are suggested for use to reduce inflammation and infection following several types of surgeries.[37-40]
- Spirulina might reduce the effects of seasonal allergies, along with reducing oxidation and inflammation.[41-43]
- Chlorella has demonstrated the capacity to provide a short-term 'boost' to immunity by increasing levels of natural killer cells.[44]

NOTE: It must be remembered that typically, these nutrients (especially the essential vitamins and minerals) work to **support** immunity by supporting the diet. In other words, many people don't eat enough pre-formed vitamin A and zinc, and these are integral to the modulation of immune function. Therefore, the use of these is to restore us to sufficiency and there may be no benefits from mega-dosing (which may worsen outcomes...)

Treat all claims of 'cures' and 'preventatives' with caution, especially in the current climate of emerging threats like novel flu viruses and other similar viruses like the current COVID-19 novel coronavirus pandemic.

> Treat all claims of 'cures' and 'preventatives' with caution

Lifestyle and immunity

Exercise

Exercise is known to improve health overall, and specifically the functions of the immune system. However, excessive amounts of exercise, leading to over-stress and overtraining, can result in impaired immune function and greater risk of infections, especially colds and flu-like viruses.[45]

> Excessive exercise may result in a greater risk of infections

Stress

Stress, in particular work-related stress, is known to impact the immune system and reduce resistance to infections.[46] Interestingly, the effort-to-reward ratio (how much we value the benefits from our job versus the effort it requires) has a greater effect on immunity than overwork.[47]

How much we value the benefits from our job versus the effort it requires has a greater effect on immunity than overwork

Other factors that can affect immunity:

- Poor sleep
- Smoking
- Excessive alcohol use

HOW TO SUPPORT IMMUNITY

Eat 6 servings of vegetables per day

Vegetables help to provide many essential and non-essential, yet health-promoting nutrients...and most of us don't eat enough of them.

Make sure you are eating enough, and enough protein

Being consistently 'under-fuelled' is a sure-fire way to put yourself at risk of colds and flu-like infections. Make sure that you are eating enough and always base your meals on a serve of a quality protein food. Amino acids like glutamine from protein are also associated with reducing infection rates in athletes.

Consider supplementing with a good-quality multi-nutrient

The key consideration for immunity is not to get massive doses of particular nutrients to 'boost' immune function, but instead to make sure you have all the nutrients your immune system needs to function correctly. A quality multi-nutrient can help you to fill in the gaps in your nutrition and supply some of the nutrients you may not always take in each day.

Exercise, but not too much

If you're new to exercise, start at a level you can do relatively easy and build from there. Work up to taking at least 7,500 steps per day and doing 2 sessions of weight-training or resistance work (like bodyweight workouts or progressive yoga if you don't want to hit the gym). Add on extra cardio if you can.

Get 8 hours of sleep per night

Sleep is critical to health. Try to get to bed a little bit earlier if you're not getting at least 7 hours of quality sleep per night. Also, try shutting off your phone and other devices around 2 hours before bedtime.

Reduce your life and work stress

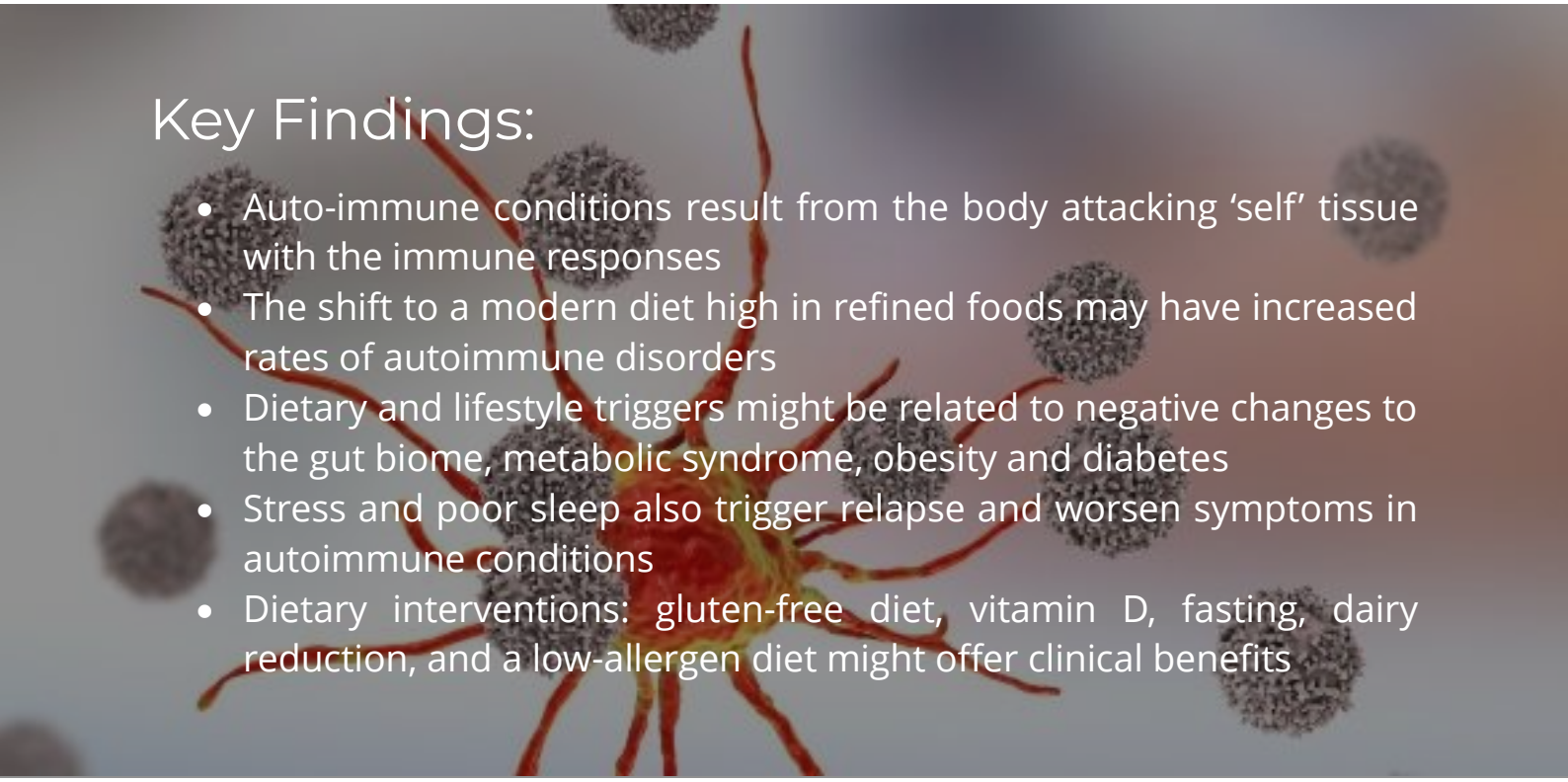
Stress can impact immune function. If you have stressful relationships or environments (like work) try to change them to more fulfilling ones if able.

Meditation is also a great way to reduce the impacts of life's stresses on how we think and feel. As with exercise, start with just a little (even as little as 1 minute of meditation on day one!) and build over time until you are doing around 20min or more per day.

Conclusion

A healthy, well-functioning immune system is a function of having a healthy, well-balanced life! There are no pills or potions that will magically 'boost' your immune system, but you can help to support the best functioning immune system *you* can have by following some simple guidelines of good food, movement, intelligent supplementation, and mindfulness.

IN BRIEF: AUTO-IMMUNITY



Key Findings:

- Auto-immune conditions result from the body attacking 'self' tissue with the immune responses
- The shift to a modern diet high in refined foods may have increased rates of autoimmune disorders
- Dietary and lifestyle triggers might be related to negative changes to the gut biome, metabolic syndrome, obesity and diabetes
- Stress and poor sleep also trigger relapse and worsen symptoms in autoimmune conditions
- Dietary interventions: gluten-free diet, vitamin D, fasting, dairy reduction, and a low-allergen diet might offer clinical benefits

Autoimmunity refers to the situation in which the immune system launches a response against its healthy cells instead of against a foreign 'invader' like a bacteria, virus, fungi, protozoa or helminth. The diseases that can result from this type of response are collectively known as autoimmune diseases. Autoimmune conditions include diseases such as myocarditis, systemic lupus, autoimmune hepatitis, dermatitis herpetiformis, psoriasis, vitiligo, Addison's disease, autoimmune pancreatitis, type 1 diabetes, Hashimoto's thyroiditis, multiple sclerosis, and many more.

Autoimmune conditions usually result from a mixture of 'nature and nurture' with a strong genetic basis, amplified by environmental and lifestyle factors. For example, in some individuals, infectious parasites might help to protect people against autoimmune conditions (*hygiene theory*) whereas in others, different parasites can trigger autoimmune reactions, likely as a result of molecular mimicry (in which the pathogen carries markers similar to self-tissue) or because the pathogen becomes inextricably linked to tissue in the body.

Diet and lifestyle could also play a role in the development of autoimmune conditions. A healthy diet can help the immune system to better recognise self vs non-self but the exact effects of specific nutrients on autoimmune conditions are at this time, not clear.[48]

> The shift to a western-style diet high in processed and refined foods could be a risk factor for the development of autoimmune conditions

It has been suspected that the shift to a western-style diet high in processed and refined foods could be a risk factor for the development of autoimmune conditions.[49] The modern diet and its effect on the gut microbiome have also been suggested as one of the myriad reasons why people might develop AI diseases, and one of the reasons that fasting is beginning to show efficacy for the treatment of AI conditions.[50] The modern diet also predisposes people to fat gain and obesity. Fat tissue (adipose tissue) produces pro-inflammatory *adipokines* that have been linked to autoimmune diseases and obesity is considered a risk factor for conditions like multiple sclerosis,[51] while insulin resistance (metabolic syndrome) is considered a risk factor for AI conditions including autoimmune hepatitis.[52]

> Fat tissue produces *adipokines* that have been linked to autoimmune diseases

What do we know about diet and lifestyle, and AI conditions?

Stress

The onset of around 50% of autoimmune conditions has been attributed to 'unknown triggers', and stress (psychosocial, emotional, and physical) is thought to play a primary role in the development of autoimmunity.[53-56] It is presumed that the stress-triggered hormones lead to altered regulation of the immune system which can ultimately result in autoimmune disease,[53] stressful life events are associated with increased risk of developing an autoimmune disease.[57]

> ~50% of autoimmune conditions has been attributed to 'unknown triggers', and stress

However, 'stressors' can be positive or negative.[58] For example, exercise can be 'stressful' to the body but results in positive adaptations. Similarly, fasting can promote stress reactions in the body that are beneficial. In both cases though, a positive stressor can easily become a negative one if carried out to the extreme.

Sleep

One of the effects of stress (and a cause of it) is poor sleep. Poor sleep has been associated with increased inflammation,[59] and increases the symptoms or risk of developing autoimmune diseases such as multiple sclerosis,[60] rheumatoid arthritis, scleroderma, and lupus.[61] Sleep apnoea has also been suggested as a risk factor for autoimmune diseases,[62] and Chrono insomnia (with sleeping pill prescription) has been linked to a 70% increased risk of autoimmune disease.[63]

> Poor sleep increases the symptoms, or risk of developing autoimmune diseases

Sleep is thought to have a 'bidirectional' relationship with the immune system (poor sleep can affect our immune control and poor immune function can affect sleep). In a study of a mouse model of lupus, the results indicated that mice submitted to sleep deprivation exhibited an earlier onset of the disease, as reflected by the increased number of antinuclear antibodies. However, no statistical difference was found in the other parameters analysed. According to these results, sleep deprivation could be considered as a risk factor for the onset but not for the evolution of the disease.[64]

Gluten-free diet

The gluten-free diet is an obvious intervention for the autoimmune disease of gluten intolerance, Coeliac disease, but it is also potentially linked to other non-Coeliac autoimmune diseases too and may increase the risk of other diseases due to a range of factors including; shared genes (with Coeliac disease), increased intestinal permeability, and increased intestinal and systemic inflammation.[65]

It is known that a gluten-free diet reduces zonulin (which is responsible for modulating intestinal permeability) and reduces 'leaky gut' and auto-antibodies, further suggesting a role for a gluten-free diet for autoimmune conditions.[66] There is, for example, a higher incidence of autoimmune thyroid disease amongst those with Coeliac disease,[67] and the risk for someone with Coeliac disease developing another autoimmune disease is more than double if they have not been compliant with a gluten-free diet.[68] Several cases have noted reductions in systemic symptoms or comorbidities in people with autoimmune conditions, suggesting a wider benefit in autoimmunity from a gluten-free diet.[69-71] In another series of case studies, improvements were seen in a range of autoimmune conditions (including Crohn's

disease and type 1 diabetes) from the implementation of a wheat-free Paleo-style diet.[72]

Improvements were seen in a range of autoimmune conditions from a Paleo-style diet

Dairy?

While diary is typically *anti-inflammatory* dairy is a relatively common allergen and the incidence of dairy allergies appears to be rising.[73]

A review of 52 clinical trials evaluated the inflammatory score of diets containing dairy. The overall evidence suggested an anti-inflammatory effect of dairy whether low-fat, high-fat, or fermented. However, when the subjects in the studies were analysed according to health status, dairy was found to be inflammatory for those with underlying allergies to dairy proteins,[74] and elimination diets that include the reduction or complete elimination of dairy have shown efficacy for autoimmune conditions such as Crohn's disease,[75] ulcerative colitis,[76] and asthma,[77] and clinical experience suggests that dairy elimination should be trialled in those with autoimmune conditions.

The reduction or complete elimination of dairy has shown some efficacy for autoimmune conditions

Improved gut health

Changes to the gut microbiota and the production of bacterial metabolites (like short-chain fatty acids) have been suggested as a possible reason for the rising incidence of autoimmune conditions.[50, 78] In one of the broadest autoimmune conditions, *systemic lupus erythematosus*, which can affect many organs and tissue throughout the body, there is a high rate of dysbiosis, and the microbiota is being considered as a promising therapeutic target.[79]

Vitamin D

Industrialised countries further from the equator (New Zealand, Australia, the UK) have some of the highest prevalence of autoimmune conditions and this has been linked to vitamin D levels from sun exposure.[80]

Fasting

Dietary energy restriction helps to modulate inflammatory and immune responses and offers promise as part of the adjunctive treatment for autoimmune conditions.[81, 82]

Cocoa and other flavonoids?

While feeding cocoa did not reduce swelling in a mice model of autoimmune arthritis, it did reduce reactive oxygen species production, and the inflammatory marker tumour necrosis factor-α (a common marker of inflammation in autoimmune conditions).[83]

The autoimmune diet?

In a 'leaky gut' increased intestinal permeability leads to the entry into the body of larger molecules (than are usually absorbed) and these can be mistakenly identified as pathogens, leading to immune dysfunction. Leaky gut is intricately tied to the health of the microbiome and gut-health in general and increased intestinal permeability may result from a diet that is excessively high in sugar, low in nutrients such as zinc and omega-3 fatty acids, and resultant 'dysbiosis' (distorted microbe levels in the gut) resulting from poor diet and lifestyle habits (along with genetic components). The Autoimmune Protocol Diet has been suggested as a way to reduce leaky gut and inflammation and help to treat autoimmune conditions.

The Autoimmune Protocol Diet

Allowed foods	Disallowed foods
meat and fish, preferably not factory raised vegetables (but not nightshades, such as tomatoes, eggplants, peppers, and potatoes) sweet potatoes fruit (in small quantities) coconut milk avocado, olive, and coconut oil dairy-free fermented foods, such as kombucha, kefir made with coconut milk, sauerkraut, and kimchi honey or maple syrup (but only to be used occasionally, in small quantities) fresh non-seed herbs, such as basil, mint, and oregano green tea and non-seed herbal teas bone broth vinegar, such as apple cider and balsamic	all grains, such as oats, rice, and wheat all dairy eggs legumes, such as beans and peanuts nightshade vegetables (tomatoes, eggplants, peppers, and potatoes) all sugars, including sugar replacements (except for occasional use of honey) butter and ghee all oils (except for avocado, coconut, and olive) food additives alcohol

Does it work?

In studies of the autoimmune protocol diet for autoimmune inflammatory bowel diseases, improvements were seen for quality of life, markers of inflammation and healing of the intestinal mucosa, along with reduced disease activity.[84-88] In Hashimoto's thyroiditis, both symptoms overall health were observed to improve with the AIP, along with decreased inflammation but there were no significant changes in thyroid hormones or antibodies.[89]

So, there do seem to be meaningful benefits from the AIP diet but we can't be exactly sure why (could it be the elimination of an allergen like gluten, dairy proteins etc.) and we cannot rule out that less restrictive, healthy diets could result in similar benefits.

Reduced carbohydrate diets

A Low-carb diet resulted in reduced anti-thyroid antibodies compared with a control group in a pilot study.[90]

Conclusion

I have seen in clinical practice that only moderately restrictive diets have been very effective for my patients with autoimmune conditions. These typically involve a focus on high-quality protein, increasing vegetable intake, and a focus on healthy fats and increasing omega-3 fat intake, while reducing or eliminating gluten, dairy, grains, corn, and intestinal irritants like carrageenan.

NOTE: People with autoimmune conditions are not necessarily at greater risk of contracting infectious conditions (like SARS viruses for example). However, those using immune-suppressing drugs as part of their treatment, those with extra-system effects like autoimmune-related respiratory illnesses, and those with comorbidities like type 2 diabetes and insulin resistance could have a greater risk of infection and more serious effects of illnesses like COVID-19.

RESEARCH IN BRIEF

Does lack of sleep affect immunity?

It's likely that sleeping too little, or having poor sleep, and possibly sleeping too long impact immunity. There are strong associations between sleep length and quality and a range of long-term health outcomes, such as[91]:

- Diabetes mellitus
- Hypertension
- Cardiovascular diseases
- Coronary heart diseases
- Obesity

Over 70 studies featuring more than 50000 participants have evaluated the effects of sleep deprivation on markers of immunity and inflammation. Sleep disturbance was associated with higher levels of c-reactive protein, and the inflammatory cytokine interleukin 6 (IL-6). Shorter sleep duration was associated with higher levels of c-reactive protein, but not IL-6. Long sleep durations (>9 hours) were also associated with increased inflammation marked by higher c-reactive protein, and IL-6. Interestingly, neither long nor short sleep or sleep disturbance were associated with increased levels of tumour necrosis factor-α, one of the key markers of autoimmune inflammatory conditions like Crohn's disease.[59] C-reactive protein in particular also has an association with over-reaching and over-training in athletes, who also experience frequent colds and flu-like viruses and excessive stress-markers like this suppress some of the normal immune responses. In summary, poor-quality sleep will likely reduce our ability to properly modulate our immune function.

Exercise and immunity

It's widely accepted that exercise improves health and is, by extension, a valuable contributor to proper immune functioning and resistance to infection. However, excessive exercise is a stressor that can dampen immune functions and as a result, over-training can lead to increased rates of infection with colds and flu-like viruses, a situation commonly seen in athletes. Over-exercise or over-stress from any cause is pro-inflammatory and over half of all sports injuries are also secondary to overuse.[92] Markers of antioxidant status such as glutathione concentration and inflammatory markers such as interleukin 10 are affected by long periods of intense training.[93]

So, exercise helps to mitigate stress and fatigue and helps us to modulate inflammatory/immune and antioxidant pathways, BUT too much (over-reaching) can be just as detrimental as too little.

Overreaching and over-training syndrome in athletes is depicted as a continuum, this is also likely to be the case for generalised

'stress'. So, excessive exercise (or any other stressor) can be depicted as stress → fatigue → greater incidence of infection (and burnout).

Moderate amounts of exercise improve immune system functions and reduce the risk of infection. On the other hand, athletes engaged in regular prolonged and intensive training can experience acute (and possibly chronic) exercise-induced changes in immune function resulting in higher than normal incidence of minor infections, especially of the upper respiratory tract (e.g. the common cold and influenza).[45]

Progressive exercise, within the bounds of someone's ability to recover increases white blood cell counts.[94] However, acute strenuous exercise can decrease innate immune response in both competitive athletes and healthy 'non-athletes'.[95]

Also, moderate-intensity exercise is suggested to improve the function of the intestinal mucosal barrier (a key barrier to infection), while higher intensity exercise could cause intestinal barrier disruption.[96] Low-intensity exercise forms like Tai Chi might also improve antioxidant activity and improve immune responses.[97]

Does carbohydrate supplementation protect against exercise-induced reductions in immunity?

It has long been suggested that carbohydrate supplementation improves immune responses to exercise. However, in a 2016 randomised controlled trial, while carbohydrate supplementation during a 2-hour exercise test (at 60% VO2max) reduced cortisol (one of the key 'stress' hormones and an inhibitor of immune function), it did not affect immune responses to a test antigen (an 'antigen' is a structure on the cell wall of an infectious agent that the immune system recognises and responds to.)[98] In another study, carbohydrate supplementation significantly reduced the immune/inflammatory marker TNF-a post-exercise at simulated altitude conditions, an effect not seen for placebo or glutamine (with no significant effect seen in other markers of inflammation/immunity – IgA, IL-10, IL-6).[99]

> Energy sufficiency (i.e. eating enough!) is more important than macronutrient intake for immunity.

Can caffeine increase immune function with exercise?

In a 2016 randomised controlled trial, ingestion of 6 mg/kg of caffeine one hour before 20 min of high-intensity interval exercise, resulted in increased natural killer cell counts before and after exercise (after N.S.) without any significant effect on adaptive immune cells ($CD4^+$ and $CD8^+$ T cells).[100] Bear in mind this is a large dose... 6 mg per kilo of bodyweight for me would be the equivalent of around 5 cups of coffee!

Take home message

Exercise is part of the foundation of health and has enormous benefits to overall resilience and particularly our resistance to infection. However, like anything else, *the dose defines the poison*! Excessive amounts of exercise are likely to reduce immunity and encourage a greater likelihood of infections, especially respiratory infections and possibly gut-related infectious disturbances too.

It is therefore important to:

- Begin any exercise routine at a level that is comfortable for you
- Increase volume and intensity slowly
- Back off the intensity and/or volume if you are feeling run-down, are getting repeated cold or flu-like viruses and if your sleep is suffering
- Consider starting with: Move for at least 20 min per day
    - Do some resistance training – start with low-volume strength training. I.e. 2-3 exercises for 1-2 sets of 3-6 reps, 2-6 x per week at a load that you can handle easily (but increase this by small increments as often as possible!)

It's important to remember that we can habituate ourselves to increased levels of exercise and if we start at a level at which we are comfortable and not over-reacting with excessive stress responses and then incrementally increase volume and/or intensity of our training, we can increase our work threshold.

It is best to start with an almost ridiculously easy volume and intensity and then incrementally increase that to build your overall work-tolerance rather than 'smashing' yourself at each session. Important considerations for fatigue are that 'grind' lifts with a slower velocity may be preferable to explosive or 'metabolic-style' workouts during times of recovery from fatigue or sickness, due to the reduced volume required for neuromuscular adaptations, reduced eccentric loadings and better overall neuromuscular adaptations post-exercise.[101] Longer rest periods (more than 2 min rest between sets) also preferred for those in the recovery phase from fatigue and these facilitate an improved free-testosterone to cortisol ratio.[102]

The effects of stress on immunity

Stress has an undeniable and large effect on health and is a less commonly discussed, but extremely important part of encouraging the greatest human resilience and resistance to infections.

A systematic review of 56 studies showed that stress had a significant impact on measures of immunity (reduced natural killer cell activity, NK and T cell subsets,

CD4+/CD8+ ratio, and increased inflammatory markers).

In particular, the following psychosocial factors of stress were implicated[46]:

- Job-stress
- Low job control
- High job strain
- Job dissatisfaction
- High effort and low reward work \
- Overcommitting
- Burnout
- Unemployment
- Organizational downsizing
- Economic recession

The effort-reward imbalance, in other words, the reward you receive in comparison to the effort required at work, is particularly associated with much higher stress levels, with a demonstrable effect on immunity. Overcommitment or overwork are also associated with reduced immunity, For example, caregivers of dementia patients suffer poorer immune responses and this is considered to be as a result of the demands of their workplace stress.[103] but a lower reward-to-effort ratio results in a greater reduction in immunity than overcommitment.[47]

Prenatal stress is also reported to increase the risk of nervous, endocrine and metabolic diseases, along with immune dysfunction. The influence of prenatal stress on the immune system is complicated and includes changes to immune cells, cytokines, and immune organs.[104]

Effect of stress-reduction

A systematic review of 75 studies was conducted to look at the effect of psychological interventions for optimising immune function. Small-to-medium effects were found for the effects of psychological interventions on optimization of immune function. Large effects on immune function were shown for in vivo immune-related challenges in studies which included skin-tests and wound healing, while studies incorporating psychophysiological challenges and in vitro immune-related stimulations also demonstrated better immune responses among those receiving stress-reducing interventions. These findings support the effectiveness of stress-reducing psychological interventions in improving immunity.[105]

Take-home message

Stress reduces our ability to optimally respond to immune threats. The biggest impact on stress is likely to come from the psychosocial environment and in particular job stress. Out of the subsets of job stress, how much reward we receive for our efforts is the biggest impactor of our stress levels and we should strive to be improving how much reward and perceived value we receive from our work. Also, stress-reduction, in particular mindfulness and meditation, and exercise are keys to improving our relationship with life stress and can mitigate the effects of stress on our immunity.

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