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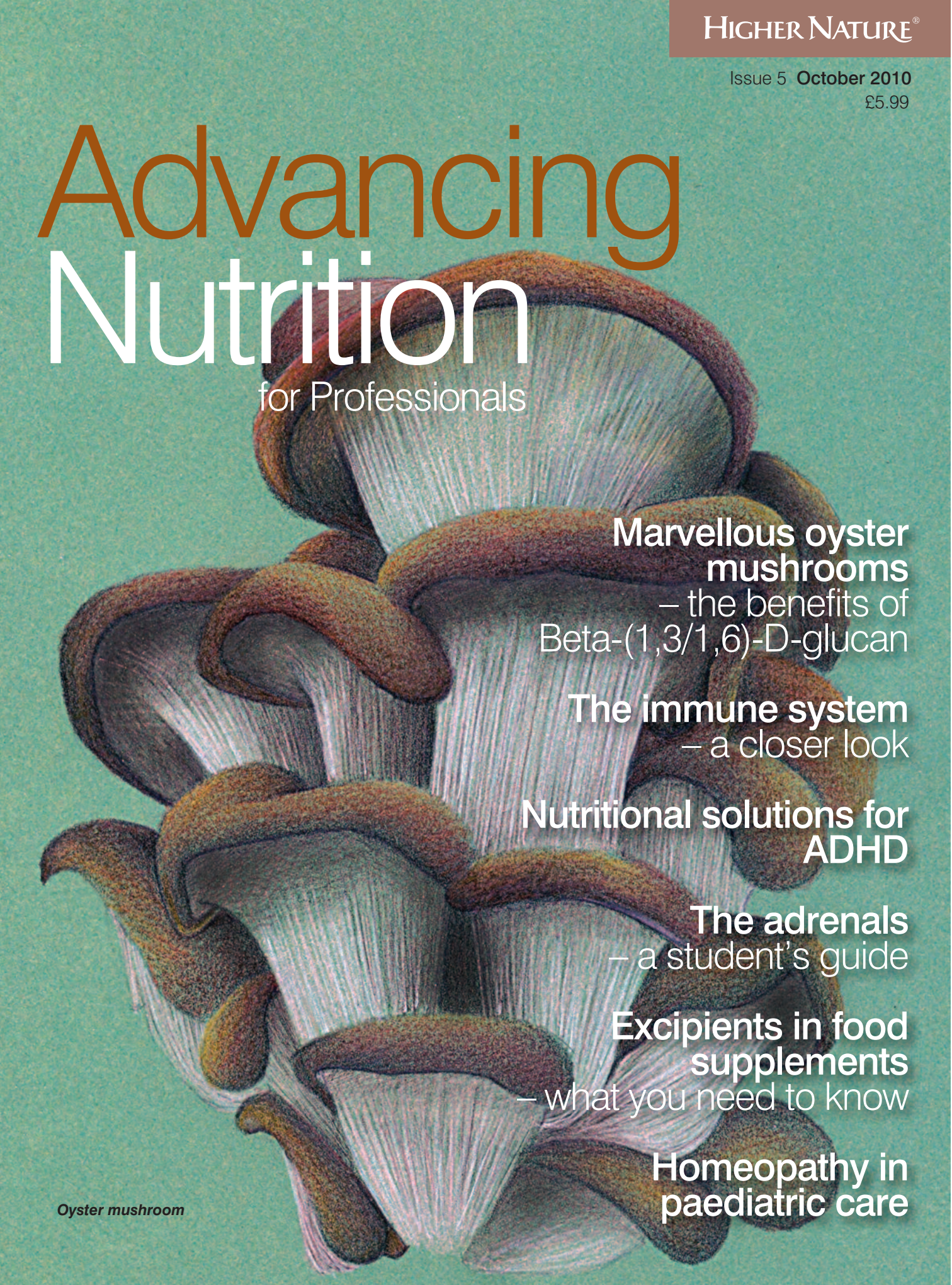

Marvellous oyster mushrooms – the benefits of Beta-(1,3/1,6)-D-glucan

The immune system – a closer look

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The adrenals – a student's guide

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Oyster mushroom

Taking a closer look at the immune system

We all know the immune system is complicated and appropriate treatments depend on the specific condition. However, there are still common and important key areas to target. We'll outline these areas, along with some key nutrients, based on the latest research.

by Shannon Feely BSc ND

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Treating the immune system

There are five major areas to consider when balancing the immune system, bearing in mind that these areas do overlap. The key word here is 'balance'. Because we don't fully understand how the immune system works as a whole, it's important not to use a reductionist approach and focus solely on a single area. Rather, the focus should be on multiple and synergistic nutrients that target the major areas of the immune system. These are:

1. **Immune cell modulation**
2. **Intestinal health**
3. **Inflammation**
4. **Antimicrobial**
5. **Nutritional deficiency**

There are certainly other areas to consider within immune health, such as liver support, adrenal health, specific cancer and autoimmune pathophysiology, to name a few, but the focus of this article is general immune support and building the foundation of a healthy immune system.

1. Immune cell modulation

This involves balancing the production and function of immune cells that may be either hyper-functioning or under-functioning.

Vitamin D: Based on what we currently know about vitamin D, its main function within the immune system is prevention of a variety of conditions, including cancer (especially colon, breast and prostate), and protection against autoimmune disease. For example, vitamin D supplementation may inhibit an autoimmune reaction that targets the pancreatic beta cells in Type I diabetes[1]. There is interest, however, in using vitamin D for improving more acute conditions, such as respiratory disorders (COPD and bronchitis). Evidence suggests that higher 25-hydroxy vitamin D serum levels are associated with increased pulmonary function[2]. Vitamin D may also be involved with improving lung function, by decreasing immune-mediated inflammation of the air passages. A population-based study found that patients with low 25-hydroxy vitamin D serum levels are 27-55% more likely to have upper respiratory tract infections, compared to people with normal levels[3]. However, another study (a randomised control trial) found no benefit of vitamin D3 supplementation in decreasing the incidence or severity of upper respiratory tract infections. Further studies are needed to determine the role of vitamin D in infection[4].

Mushrooms: One of the powerful compounds in many mushrooms is beta glucans. Beta glucans are polysaccharides that can activate the immune system, enhance macrophages and natural killer cell function and inhibit tumour growth[5]. For example, the Th2 interleukins, which are responsible for the allergic inflammatory response in allergic rhinitis, are decreased in the presence of beta glucans, while levels of Th1 interleukins are increased[6]. In addition, eosinophils, which are part of the inflammatory response in allergic rhinitis, are decreased.

Different mushrooms have varying types of beta glucans that may make specific mushrooms suited to supporting different conditions. Current research shows the beta glucans from the oyster mushroom (*Pleurotus ostreatus*) support a variety of immune functions[7,8]. One study found that oyster mushroom beta glucans reduced the mucosal damage and reduced inflammation in rats with ulcerative colitis[9]. Other mushrooms that also have promising potent immune effects are the red reishi mushroom (*Ganoderma lucidum*) and maitake mushroom (*Grifola frondosa*).

Lactoferrin: This is an iron-binding protein in human and bovine milk, found in mucosal secretions of the intestinal tract, vagina, saliva and intestinal mucus. It is also released by neutrophils at sites of inflammation.

Deficiency of lactoferrin is associated with altered neutrophil function and recurrent bacterial infections and autoimmune diseases[10]. Lactoferrin production is increased in response to inflammation and it binds with epithelial cells at the site of infection and prevents inflammatory cytokine

production. It may also increase phagocytic activity of leucocytes and increase natural killer cells.

Its antibacterial activity is through sequestering iron (therefore preventing bacterial growth) and binding to bacterial cell surfaces and causing cell lysis. Some research shows that lactoferrin has activity against *Helicobacter pylori*, by preventing its attachment to the stomach wall[11]. One meta-analysis found lactoferrin supplementation was more effective (than no lactoferrin) at increasing the eradication rate of *H. pylori*, especially in patients with eradication failure[12]. Bovine lactoferrin may have more activity against *H. pylori* than human lactoferrin[13].

Lactoferrin has antiviral activity against herpes simplex virus (HSV) 1 and 2, cytomegalovirus, human immunodeficiency virus (HIV), human papillomavirus and hepatitis B and C viruses[14]. Lactoferrin may also have antifungal activity. Preliminary research suggests that it is active against *Candida albicans*[15].

Nucleotides: These are molecules that make up RNA and DNA. Dietary nucleotides provide important nutrition for making new cells and particularly for immune and intestinal cells, that need to quickly multiply during times of stress[16].

Dietary nucleotides affect lymphocyte maturation, activation and proliferation[17]. They enhance macrophage phagocytosis, delayed hypersensitivity and tumour responses. However, the exact mechanisms of how dietary nucleotides modulate the immune system are still unknown.

One interesting area of research is using nucleotide supplements for immune system support in people who exercise. One study found that a chronically-ingested nucleotide supplement blunts the response of the physiological stress hormone, cortisol, as well as raising secretory IgA, during short-term, high-intensity exercise[18].

Plant sterols: Plant sterols naturally occur in some plants, such as soya beans, and are well known for their ability to lower LDL cholesterol. Plant sterols can also play a strong role in immune health. For example, beta sitosterol and sitosterolin, given together, appear to enhance production and growth of T-cells (in vitro)[19]. These sterols may also reduce the immune suppression and inflammation seen in marathon runners after a race. Plant sterols may increase the Th1 immune response[20]. Results on inflammation markers and plant sterols, so far, have been inconsistent but there is enough promising evidence to warrant further research.

2. Intestinal health

Intestinal health plays a large role in immune health through the gut-associated lymphoid tissue (GALT), balanced ratios of 'good' and 'bad' micro-organisms, intestinal pH, mucus and IgA antibodies, enzymes in saliva and bile, and detoxification.

Probiotics: We know that probiotics affect the immune system through:

- Synthesis of vitamins (biotin, B12, folic acid, pantothenic acid, pyridoxine, riboflavin, vitamin K, butyric acid and amino acids)[21].
- Production of short-chain fatty acids in the colon, producing fuel for intestinal epithelial cells. The short-chain fatty acids also acidify the environment and a lower colon pH is associated with a lower incidence of colon cancer[22].
- Metabolism of environmental and internal toxins. This includes reducing pro-carcinogenic enzymes such as beta-glucuronidase[23].
- Prevention and neutralisation of pathogenic overgrowth of other microbes and bacterial toxins. This may play an important role in preventing pathogens from developing antibiotic resistance.
- Increasing antibody production and anti-cancer compounds such as n-butyrate[24].
- Reducing inflammatory cytokines.

Lactobacilli: These species generally stabilise the mucosal barrier and decrease intestinal permeability. Lactobacilli latch on and colonise the intestinal and urinogenital mucosa and, thus, increase epithelial mucus production and compete with pathogens for mucosal binding sites. Lactobacilli produce lactic acid and some produce hydrogen peroxide, which inhibits bacterial pathogens and maintains the pH of the intestinal tract. They also synthesise antibodies against pathogens, particularly secretory IgA.

The way the Lactobacilli affect immune function may depend on the health status of the patient. In people with hypersensitive immune systems, Lactobacilli seem to down-regulate immune function. In healthy people, without immune system hypersensitivity, Lactobacilli may stimulate the immune system. Factors such as hormone levels also influence adherence and effectiveness of Lactobacilli. Their ability to attach to epithelial cells can change during the menstrual cycle, due to changing hormone levels. In post-menopausal women, balancing low oestrogen levels can help restore Lactobacilli colonisation, without supplementation.

- ***Lactobacillus acidophilus*** has been shown to decrease the incidence of infant diarrhoea and decrease levels of toxic amines in the blood of dialysis patients with small intestine bacterial overgrowth[25].
- ***Lactobacillus casei*** has been found to increase serum IgA response in Crohn's disease. *Lactobacillus casei* may adhere better to urinogenital cells than other *Lactobacillus* species[26].
- ***Lactobacillus sporogenes*** has been found to be more resistant, than other probiotics, to most antibiotics and contaminated food and drink. *Lactobacillus sporogenes* with FOS (fructo-oligosaccharide prebiotic) given prophylactically can significantly reduce the number of days and the duration of events in children with antibiotic-induced diarrhoea[27]. Research also shows *Lactobacillus sporogenes* survives through stomach acid in spore form and becomes active in the intestines. This is because some bacteria form spores during times of stress and re-emerge when conditions improve. This is unlike many other *Lactobacillus* probiotics that are destroyed by stomach acid and can lose their potency before reaching the intestines[28].

Probiotics are increasingly being found to benefit acute viral and bacterial respiratory infections. For example, a daily combination of *Lactobacillus acidophilus* and *Bifidobacterium lactis* was a safe and effective method to reduce fever, rhinorrhea and cough occurrence and duration of antibiotic prescription use[29]. In particular, one study found that regular, long-term intake of various probiotics (*Lactobacillus plantarum*, *Lactobacillus rhamnosus* and *Bifidobacterium lactis*), as well as lactoferrin and prebiotics, may improve health by reducing the incidence and severity of respiratory diseases during the flu season[30].

An additional study found a combination of *Lactobacillus rhamnosus* and *Bifidobacterium lactis* may be an effective way to reduce the risk of otitis media, antibiotic use and recurrent respiratory infections in infants under a year old[31].

Glutamine: Recent research shows that glutamine may become 'essential' during inflammatory conditions such as infection (and injury). Under stressful conditions, glutamine is vital for cell proliferation and acts as a fuel for the respiratory system. Lymphocyte production and cytokine production, and macrophage, phagocytic and neutrophil bacteriocidal activity all require a high level of glutamine[32].

3. Inflammation

While inflammation is necessary for a short period of time in various conditions, chronic inflammation is generally destructive.

Fish oil: The potent anti-inflammatory effects of fish oil have been well documented. One interesting piece of new research shows that we also need to consider the direct effects that fish oil can have on the immune cells. For example, the phagocytic activity of various immune cells is increased by fish oil[33].

Proteolytic enzymes: Proteolytic enzymes, such as bromelain, serrapeptidase, trypsin, chymotrypsin and papain, reduce inflammatory cytokines and circulating immune complexes and increase antioxidant enzymes (SOD, catalase and glutathione peroxidase)[34]. This may be of help in auto-immune conditions, such as rheumatoid arthritis (RA). One study found RA patients' symptoms were significantly improved with six months of proteolytic enzyme treatments[35]. Proteolytic enzymes also help improve the frequency and severity of respiratory tract infections[36].

Antioxidants: One of the most negative side effects of chronic inflammation is the production of reactive oxygen species (ROS). These are released by phagocytic leucocytes at the site of inflammation, which create an imbalance of ROS and lower levels of antioxidants[37]. In addition, ROS then prevent proper function of the immune cells and stimulate inflammatory processes.

Antioxidants are also important for the thymus gland. The thymus gland plays a large role in immune health, through its production of the T-lymphocyte white blood cells, and the hormones that control the T-lymphocyte activities and other immune system activities. As we age, the thymus gland shrinks because it is very sensitive to free-radical damage. Many health conditions, such as autoimmune diseases, have high ROS, which cause further damage to the thymus gland. Some of the antioxidants that are important for the thymus gland are the carotenes, vitamins C and E, zinc and selenium[38].

- **Astaxanthin:** This is a reddish pigment and is the main carotenoid in aquatic animals, including salmon, trout, shrimp, lobster and the algae *Haematococcus pluvialis*. One of its most important qualities is as an antioxidant. In animal studies, astaxanthin enhances antibody production and restores decreased humoral immune responses in elderly mice[39]. It has also been found to reduce *H. pylori* symptoms and plays a role in supporting tumour-fighting immune cells.
- **Elderberry:** Black elderberry-based immune formulae are also strong antioxidants and have been found to be effective in preventative and prophylactic treatment of influenza[40]. The therapeutic effects of black elderberry are based on the high flavonoid content.
- **Vitamin C:** One of its main functions for immune support is as an antioxidant against ROS[41]. There is mixed research on whether vitamin C can reduce influenza occurrence and duration. A Cochrane review found that, in prophylaxis trials, vitamin C has consistently shown a reduction in the duration of common colds and alleviated symptoms[42]. However, therapeutic trials have not been able to replicate this evidence. This may indicate that supplementing chronically with vitamin C will not decrease the amount of colds one receives, but that supplementing chronically (rather than only supplementing during infection period) may reduce the duration of the cold and the symptoms.
- **Other potent and important antioxidants:** CoQ10, green tea, curcumin, quercetin (with bromelain), vitamin E, N-acetyl-L-cysteine and nutrients that support antioxidant reactions, such as selenium and zinc.

4. Antimicrobial

Grapefruit seed extract: Grapefruit seed extract (GSE) testing (in vitro) shows that it is anti-bacterial against a wide range of gram-negative and gram-positive bacteria[43]. GSE appears to destroy the bacteria, by disrupting the bacterial membrane and causing the cytoplasmic contents to leak out. GSE, in vitro, is also antifungal, particularly against two strains of *Candida albicans*, *Candida krusei* and *Saccharomyces cerevisiae*[44].

Blackcurrant: The antiviral activities of *Ribes nigrum*, or blackcurrant, against influenza A and B may work by inhibiting the release of the virus from infected cells[45]. Blackcurrant also shows antiviral action against the herpes virus (HSV type 1). With HSV, it inhibits viral replication in cells, by inhibiting protein synthesis in infected cells from the early stage of infection[46]. It also seems to prevent HSV type 1 attachment to cell membranes. Blackcurrant also contains a polysaccharide-rich substance that stimulates macrophage activity. In mice, blackcurrant juice was found to shrink the growth of a solid tumour by 45%[47].

Other strong antimicrobials: Olive leaf extract (calcium-D-elenoate), oregano, berberine, *Glycyrrhiza glabra*, St John's wort, garlic, echinacea.

5. Nutritional deficiencies

Protein-energy malnutrition is associated with impaired immune functions, including cell-mediated immunity, phagocyte function, complement system, secretory immunoglobulin A antibody concentrations and cytokine production[48].

Whey: This is an excellent choice of protein because it has antioxidant activity and it contains, among other nutrients, lactoferrin and immunoglobulins, which are in high enough concentrations to carry immunity to humans[49]. For people with strong milk allergies, whey products may not be suitable. However, many people sensitive to dairy produce find that, because whey is low in the casein protein and contains almost no lactose, they can tolerate whey[50].

Hemp: This has been around for many thousands of years and is unique, in that it is a complete vegetable protein with a high amino acid content and is, therefore, a superb choice for vegetarians, vegans, those with strong allergies to dairy produce or people who simply want a non-animal alternative source of protein.

Deficiency of single nutrients also causes an altered immune response[51]. This is found even when the deficiency state is relatively mild. Of the micronutrients, zinc, selenium, iron, copper, vitamins A, C, E and B6 and folic acid have important roles in immune responses. For example, low-birth-weight babies have impaired immunity that can be partly restored by providing extra amounts of dietary zinc. These nutrients are particularly important for the function of the thymus and its hormone actions. Zinc, vitamin B6 and vitamin C are among the most important for the thymus and supplementation with these minerals improves thymic hormone function and immunity[52].

Zinc: Zinc is involved in all aspects of immunity and considered the most critical mineral in thymus gland function. For example, when zinc is low, the amount of T cells are reduced, thymic hormone levels are lower and important white blood cell responses are lowered. These effects are reversible with adequate amounts and absorption of zinc[53].

Conclusion

Using a comprehensive approach in treating immune conditions allows you to establish the foundation of a healthy immune system. From there, you can then build on your treatment plan, using additional nutrients to target the specific pathophysiology of your client's condition.

REFERENCES:

1. Therapeutic Research Faculty. *Vitamin D. Natural Medicine Comprehensive Database.* [Online] 2010. Available at www.naturaldatabase.com [Accessed 2nd July 2010].
2. Therapeutic Research Faculty. Vitamin D. *Natural Medicine Comprehensive Database.* [Online] 2010. Available at www.naturaldatabase.com. [Accessed 2nd July 2010].
3. Therapeutic Research Faculty. Vitamin D. *Natural Medicine Comprehensive Database.* [Online] 2010. Available at www.naturaldatabase.com. [Accessed 2nd July 2010].
4. Li-Ng M, Aloia JF, Pollack S, Cunha BA, Mikhail M, Yeh J et al. A randomized controlled trial of vitamin D3 supplementation for the prevention of symptomatic upper respiratory tract. *Epidemiology and infection.* [Online] 2009; 137(10): pp 1396-404. Available at www.cochrane.org [Accessed 2nd July 2010].
5. Akramiene D, Kondrotas A, Didziapetriene J, Kevelaitis E. Effects of beta-glucans on the immune system. *Medicina* (Kaunas). 2007; 43(8) pp: 597-606. Available at: www.journals.indexcopernicus.com [Accessed 2nd July 2010].
6. Kirmaz C, Bayrak P, Yilmaz O, Yuksel H. Effects of glucan treatment on the Th1/Th2 balance in patients with allergic rhinitis: a double-blind placebo-controlled study. *Eur Cytokine Netw.* 2005 Jun;16(2) pp:128-34.
7. Paulík S, Svrcek, Mojzisová J, Durove A, Benísek Z, Húska M. The immunomodulatory effect of the soluble fungal glucan (Pleurotus ostreatus) on delayed hypersensitivity and phagocytic ability of blood leucocytes in mice. *Zentralbl Veterinarmed B.* 1996 May;43(3) pp:129-35.
8. Bobek P, Galbavy S. Effect of pleuran (beta-glucan from Pleurotus ostreatus) on the antioxidant status of the organism and on dimethylhydrazine-induced precancerous lesions in rat colon. *Br J Biomed Sci.* 2001;58(3) pp:164-8.
9. Nosál'ová V, Bobek P, Cerná S, Galbav_ S, Stvrtina S. Effects of pleuran (beta-glucan isolated from Pleurotus ostreatus) on experimental colitis in rats. *Physiol Res.* 2001;50(6), pp:575-81.
10. Therapeutic Research Faculty. Lactoferrin. *Natural Medicine Comprehensive Database.* [Online] 2010. Available at www.naturaldatabase.com [Accessed 2nd July 2010].
11. Therapeutic Research Faculty. Lactoferrin. *Natural Medicine Comprehensive Database.* [Online] 2010. Available at www.naturaldatabase.com [Accessed 2nd July 2010].
12. Zou J, Dong J, Yu XF. Meta-analysis: the effect of supplementation with lactoferrin on eradication rates and adverse events during Helicobacter pylori eradication therapy. *Helicobacter.* [Online] 2009;14(2):119-127. Available at www.cochrane.org *Database of Abstracts of Reviews of Effects 2010 Issue 2.* [Accessed on 2nd July 2010].
13. Zou J, Dong J, Yu XF. Meta-Analysis: The effect of supplementation with lactoferrin on eradication rates and adverse events during Helicobacter pylori eradication therapy. *Helicobacter.* 2009 March;14(2). Pp: 119-127.
14. Therapeutic Research Faculty. Lactoferrin. *Natural Medicine Comprehensive Database.* [Online] 2010. Available at www.naturaldatabase.com [Accessed 2nd July 2010].
15. Therapeutic Research Faculty. Lactoferrin. *Natural Medicine Comprehensive Database.* [Online] 2010. Available at www.naturaldatabase.com [Accessed 2nd July 2010].
16. Gil, A. Modulation of the immune response mediated by dietary nucleotides. *European Journal of Clinical Nutrition.* 2002; 56(3) pp: S1-S4.
17. Gil, A. Modulation of the immune response mediated by dietary nucleotides. *European Journal of Clinical Nutrition.* [Online] 2002; 56(3) pp: S1-S4. Available at www.nature.com [Accessed 30th June 2010].
18. McNaughton L, Bentley D, Koeppel P.The effects of a nucleotide supplement on the immune and metabolic response to short term, high intensity exercise performance in trained male subjects. J Sports Med Phys Fitness. 2007 Mar;47(1) pp:112-8.
19. Therapeutic Research Faculty. Plant Sterols. *Natural Medicine Comprehensive Database.* [Online] 2010. Available at www.naturaldatabase.com Accessed 2nd July 2010.
20. Brüll F, Mensink R, Plat J. Plant sterols: functional lipids in immune function and inflammation? *Clinical Lipidology.* [Online] 2009; 4(3). Pp: 355-365. Available at www.futuremedicine.com [Accessed 3rd July 2010].
21. Jones D, ed. *Textbook of Functional Medicine.* Washington: The Institute for Functional Medicine; 2005.
22. Donaldson, M. Nutrition and cancer: A review of the evidence for an anti-cancer diet. *Nutrition Journal.* [Online] 2004; 3(19). Available at: www.nutritionj.com/content/3/1/19 [Accessed 29th June 2010].
23. Donaldson, M. Nutrition and cancer: A review of the evidence for an anti-cancer diet. *Nutrition Journal.* [Online] 2004; 3(19). Available at: www.nutritionj.com/content/3/1/19 [Accessed 29th June 2010].
24. Jones D, ed. *Textbook of Functional Medicine.* Washington: The Institute for Functional Medicine; 2005.
25. Jones D, ed. *Textbook of Functional Medicine.* Washington: The Institute for Functional Medicine; 2005.
26. Therapeutic Research Faculty. Lactobacillus acidophilus. *Natural Medicine Comprehensive Database.* [Online] 2010. Available at www.naturaldatabase.com [Accessed 2nd July 2010].
27. La Rosa M, Bottaro G, Gulino N, Gambuzza F, Di Forti F, Inì G et al. Prevenzione della diarrea associata ad antibiotici con Lactobacillus sporogenes e frutto-oligosaccaridi. Studio pediatrico multicentrico in doppio cieco vs placebo. *Minerva pediatrica.* 2003;55(5) pp: 447-52.
28. Thorne Research. Lactobacillus sporogenes product review. 2009. Available at: www.thorne.com [Accessed 2nd July 2010].
29. Leyer GJ, Li S, Mubasher ME, Reifer C, Ouwehand AC. Probiotic effects on cold and influenza-like symptom incidence and duration in children. *Pediatrics.* 2009; 124(2) pp: e172-9.
30. Pregliasco F, Anselmi G, Fonte L, Giussani F, Schieppati S, Soletti L. A new chance of preventing winter diseases by the administration of synbiotic formulations. *Journal of Clinical Gastroenterology.* 2008; 42(3.2) pp: S224-33.
31. Weiss G, Rasmussen S, Nielsen Fink L, Jarmer H, Nøhr Nielsen B, Frøkiaer H. Bifidobacterium bifidum actively changes the gene expression profile induced by Lactobacillus acidophilus in murine dendritic cells. *PLoS One.* [Online] 2010; 5(6). Available at: www.plosone.org [Accessed 2nd July 2010].
32. Newsholme P. Why is L-Glutamine Metabolism Important to Cells of the Immune System in Health, Postinjury, Surgery or Infection? *J Nutrition.* [Online] 2001; 131 pp: 2515S-2522S. Available at www.jn.nutrition.org [Accessed 3rd July 2010].
33. Turini ME, Crozier GL, Donnet-Hughes A, Richelle MA. Short-term fish oil supplementation improved innate immunity, but increased ex vivo oxidation of LDL in man - a pilot study. *European Journal of Nutrition.* 2001 April;40(2) pp: 56-65.
34. Collins J. Clinical Efficacy of Systemic Enzyme Support. *Townsend Letter.* 2009 June. Available at www.townsendletter.com [Accessed 3rd July 2010].
35. Collins J. Clinical Efficacy of Systemic Enzyme Support. *Townsend Letter.* 2009 June. Available at www.townsendletter.com [Accessed 3rd July 2010].
36. Collins J. Clinical Efficacy of Systemic Enzyme Support. *Townsend Letter.* 2009 June. Available at www.townsendletter.com [Accessed 3rd July 2010].
37. Pizzorno J, Murray M. *Textbook of Natural Medicine.* 3rd Edition. [Online] St. Louis: Churchill Livingstone; 2009. Available at www.mdconsult.com. [Accessed on 4th July 2010].
38. Pizzorno J, Murray M. *Textbook of Natural Medicine.* 3rd Edition. [Online] St. Louis: Churchill Livingstone; 2009. Available at www.mdconsult.com [Accessed on 4th July 2010].
39. Guerin M, Huntley M, Olaizola M. Haematococcus astaxanthin: applications for human health and nutrition. *Trends in Biotechnology.* 2003;21(5). pp: 210-216.
40. Rones-Zakay Z, Thom E, Wollan T, Wadstein J. Randomized Study of the Efficacy and Safety of Trial Elderberry Extract in the Treatment of Influenza A and B Virus Infections. *The Journal of International Medical Research.* 2004;32 pp:132-140.
41. Osiecki H. *The Physician's Handbook of Clinical Nutrition.* 7th Edition. Australia: Bio Conepts Publishing; 2008.
42. Hemilä H, Chalker E, Douglas B. Vitamin C for preventing and treating the common cold. *Cochrane Database of Systematic Reviews.* 2007; 3. Available at www.cochrane.org Accessed 1st July 2010.
43. Heggers J, Cottingham J, Gusman J, Reagor L, McCoy L, Carino E, et al. The effectiveness of processed grapefruit seed extract as an antibacterial agent: II. Mechanism of action and in vitro toxicity. *The Journal of Alternative and Complementary Medicine.* 2002; 8(3) pp:333-340.
44. Cvetnic Z and Vladimir-knezevic S. Antimicrobial activity of grapefruit seed and pulp ethanolic extract. *Acta Pharm.* 2004;54 pp: 243-250.
45. Knox Y, Tatsuo S, Itsuro Y, Masanobu A. Anti-influenza virus activity of crude extract of Ribes nigrum. *Phytotherapy Research.* 2003;Feb 17(2). pp: 120-2.
46. Suzutani T, Ogasawar M, Yoshida I, Azuma M, Knox Y. Anti-herpes virus activity of an extract of Ribes nigrum. *Phytotherapy Research.* 2003 June;17(6). pp: 609-13.
47. Takata R, Yamamoto R, Yanai T, Konno T, Okubo T. Immunostimulatory effects of a polysaccharid-rich substance with antitumor activity isolated from black currant. *Biosci. Biotechnol. Biochem.* 2005; 69(11) pp: 2042-2050.
48. Chandra RK. Nutrition and the immune system: an introduction. *Am J Clin Nutr.* 1997 Aug; 66(2) pp 460S-463S.
49. Marshall, K. Therapeutic Applications of Whey Protein. *Alternative Medicine Review.* 2004; 9(2) pp: 136-156.
50. Marshall, K. Therapeutic Applications of Whey Protein. *Alternative Medicine Review.* 2004; 9(2) pp: 136-156.
51. Chandra RK. Nutrition and the immune system: an introduction. *Am J Clin Nutr.* 1997 Aug; 66(2) pp 460S-463S.
52. Pizzorno J, Murray M. *Textbook of Natural Medicine.* 3rd Edition. [Online] St. Louis: Churchill Livingstone; 2009. Available at www.mdconsult.com. [Accessed on 4th July 2010].
53. Pizzorno J, Murray M. *Textbook of Natural Medicine.* 3rd Edition. [Online] St. Louis: Churchill Livingstone; 2009 Available at www.mdconsult.com. [Accessed on 4th July 2010].