

Immune Boosting Components to Arrest Colds and Flu

By: Rachel Olivier, MS, ND, PhD

During this time of the year our nutritional focus typically spotlights the cold and flu season. Nutrients to support the ramifications of such immune disturbances are an important component of the nutritional arsenal. This topic becomes especially pertinent this year in light of the new H1N1 flu. It is well known in the alternative healthcare industry that keeping the immune system healthy contributes significantly to the prevention of seasonal illnesses. In light of this, components noted to have a beneficial effect on the immune response, and to aide in keeping the immune system healthy are discussed.

Larch Arabinogalactans

Arabinogalactans derived from the Western Larch, *Larix occidentalis* consist of highly branched nondigestible polysaccharides, composed primarily of galactose and arabinose in a 6:1 ratio. In addition to the Larch, many edible plants are also a rich source of arabinogalactans, including among others carrots,^{1,2} pear,³ tomato,⁴ and maize.⁵

The immune-enhancing properties of Larch arabinogalactans suggest that it possesses an array of clinical applications, both in preventive medicine, due to its ability to build a more responsive immune system, and in clinical medicine, as a therapeutic agent in conditions associated with lowered immune function, decreased NK activity, or chronic viral infection.⁶ Its use has also been demonstrated to enhance the cytotoxicity of natural killer (NK) cells,⁷ implying an additional benefit in immune support. In one cell culture study, the pretreatment of cells with arabinogalactan from *Larix occidentalis* was demonstrated to induce a moderately increased release of TNF α , interleukin 1 β (IL-1 β), interferon gamma (IFN- γ) and interleukin 6 (IL-6).⁸

Vitamin D

The cells involved in both innate and adaptive immune responses, including macrophages, dendritic cells, T cells and B cells, are known to express the vitamin D receptor (VDR) on the cell surface, and can both produce and respond to vitamin D (1,25(OH)₂D₃).⁹ Additionally, the comprehensive vitamin D system exerts a cumulative effect on the immune response. Consequently, immune responses are exceedingly dependent upon an adequate vitamin D status. Vitamin D has also been associated with the activation of toll-like receptors (TLRs), specifically TLR2. Toll-like receptors provide defense against pathogens, by virtue of their response to “conserved pathogen-associated molecular patterns derived from bacteria, mycoplasma, fungi or viruses.”¹⁰ In light of epidemiological data, Cannell and colleagues have proposed

that the production of vitamin D elicits a “seasonal stimulus” which underlies the seasonality of epidemic influenza.^{11, 12, 13} Cumulatively, vitamin D’s specific response has been correlated with an enhancement of innate immunity, coupled with multifaceted regulation of adaptive immunity.¹⁴

Neonatal Thymus Glandular

The thymus gland is the initial migratory place of the T lymphocytes following their origination in the bone marrow. In the thymus the T lymphocytes gain further specificity, forming either helper T-cells (CD4) or cytotoxic T-cells (CD8). The helper T-cells function in aiding other cells of the immune system by promoting their activation, while the cytotoxic T-cells act directly on infected or diseased cells. Epithelial cells of the thymic cortex express both class I and class II MHC antigens,^{15,16} which function in the development of T lymphocytes within the thymus.¹⁷

In a study with children, oral consumption of thymus glandular was demonstrated to result in a significant decrease in the frequency of recurrent respiratory infections. Additionally, in the supplemented group a statistically significant increase in the level of salivary IgA (P<0.02) was observed.¹⁸ The beneficial attributes of thymus glandular in this capacity was attributed to a “restorative” effect.¹⁹ Other studies have concurred the beneficial attributes of thymus glandular extract, which included accelerated bone marrow recovery and normalization of the peripheral blood count.^{20, 21, 22, 23} Intake has also been shown to benefit recurrent respiratory tract infections, resulting in a lowered frequency of infection, a shortened time of infection (mean = 3 days), and a diminished severity of recurrences.²⁴

Neonatal Bovine Trachea

Trachea tissue is a powerful immune modulator, whose use was historically examined by John Prudden, MD of Harvard University. Trachea tissue has been specifically referred to as an “immunoregulator,” functioning to both stimulate the immune system, as well as to repress it, as in instances of an overactive immune response. It is said to resemble fetal mesenchyme, which is the primordial tissue from which muscle, bone, bone marrow, tendons, ligaments, and skin develop.²⁵ The antigen presenting capacity (APC)²⁶ of trachea tissue is well established, with it demonstrating the ability to secrete IL-1 and to express MHC class II antigens.²⁷ Its action was also observed to result in an increase in the activation of both macrophages and cytotoxic T cells, along with a stimulation of B cells, resulting in an increase in immunoglobulins A, G and M, with an overall increase in antimitotic activity.²⁵ An immuno-stimulatory response to viruses has also been demonstrated, resulting in viral resistance.²⁸ Given the fact that the entire respiratory tract contains dendritic cells, capable of functioning in antigen presentation, it is hypothesized that these cells play an important role in the immune responses of

the entire respiratory system,²⁹ including the thoracic cavity, the nasal cavity, the pharynx, the larynx, as well as both the bronchi and alveoli.

Vitamin A

Vitamin A is directly involved in protein synthesis, both at the transcriptional and translational level.³⁰ In addition to these roles, it is also known to play a functional role in gene activation.³¹ The immune supporting properties of vitamin A are well established, including its ability to enhance natural killer (NK) cell activity,³² as well as its ability to decrease bacterial adhesion to the respiratory epithelium.³³ In addition to these attributes, it is also speculated that vitamin A contributes to the immune response by virtue of its “anti-infective” properties, specifically by contributing to both the maintenance and differentiation of the intestinal and respiratory epithelium.³⁴ In animals a deficiency in Vitamin A was demonstrated to drastically impair the secretory IgA (sIgA) response to influenza infection, with a corresponding modest increase in the serum IgG.³⁵ The sIgA-mediated response is considered a “crucial step in achieving efficient protection of the epithelial barrier,”³⁶ while IgG aids in the preparation of the antigen to the phagocytic cells, thus enhances phagocytosis.³⁷

Vitamin C

Leukocytes are known to contain a high concentration of vitamin C. Preventative trials utilizing 1 gram of vitamin C have shown that daily use reduces the duration of colds in adults by 8% and in children by 14%.³⁸ In a review of trials by Hemilä *et al.*, it was determined that supplemental vitamin C (average dose of 1g/day) reduced the duration of colds by about 23%, and ameliorated symptoms, although consistent effects were absent.³⁹ A separate long-term trial (five years) reported evidence of a 66% decrease in the common cold with a daily 500 mg dose of vitamin C, compared to a daily low dose (50 mg).⁴⁰

Echinacea

Echinacea use for upper respiratory tract infections is well recognized. As a member of the aster family (Asteraceae), its primary components include polysaccharides, glycoproteins, alkamides, volatile oils, and flavonoids. The roots contain a high concentration of volatile oils, while the above-ground parts of the plant tend to contain a higher percentage of polysaccharide components, which serve in triggering an immune activation. The above ground components are approved in Germany for the treatment of colds, upper respiratory tract infections, urinary tract infections, and slow-healing wounds, while the root components are approved for the treatment of flu-like symptoms.⁴¹ In a meta-analysis examining the effect of Echinacea on the deterrence and management of the common cold, a 58% decrease in the odds of developing the common

cold was demonstrated ($p < 0.001$), in addition to a decrease in the duration by 1.4 days ($p = 0.01$).⁴² It is also approved by the German Commission E expert panel as an adjunct therapeutic in influenza-like infections.⁴³

Broad Spectrum Vitamin/Mineral Combination

In addition to the products discussed above, immune protection may also be accomplished by the use of a broad spectrum multi vitamin/mineral supplement, containing immune supporting nutrients. Immune supporting components, which provide beneficial attributes, include citrus bioflavonoids, Echinacea, *Capsicum annuum*, chlorophyllins and a source of methyl donors and acceptors, which serves to assist with various metabolic conversions, including free radical conversion. Glandular components including adrenal, thymus, spleen, liver, pancreas, parotid, lymph and placenta also serve to provide both organ and immune support.

It is well documented that multiple factors, including age, stress, and dietary insufficiencies can negatively impact the immune system. Inadequate nutrition along with a poor diet makes one more susceptible to succumbing to illnesses. The combined use of select nutrients or combination thereof, as noted above, provides support to strengthen the immune system, and subsequently the immune response, making one less susceptible to seasonal illnesses.

References

- Pennell RI, Knox JP, Scofield GN, Selvendran RR, Roberts K. A family of abundant plasma membrane-associated glycoproteins related to the arabinogalactan proteins is unique to flowering plants. *J Cell Biol.* 1989 May;108(5):1967-77.
- Baldwin TC, McCann MC, Roberts K. A Novel Hydroxyproline-Deficient Arabinogalactan Protein Secreted by Suspension-Cultured Cells of *Daucus carota* (Purification and Partial Characterization). *Plant Physiol.* 1993 Sep;103(1):115-123.
- Chen CG, Pu ZY, Moritz RL, Simpson RJ, Bacic A, Clarke AE, Mau SL. Molecular cloning of a gene encoding an arabinogalactan-protein from pear (*Pyrus communis*) cell suspension culture. *Proc Natl Acad Sci USA.* 1994 Oct 25;91(22):10305-9.
- Related Articles, Links Pogson BJ, Davies C. Characterization of a cDNA encoding the protein moiety of a putative arabinogalactan protein from *Lycopersicon esculentum*. *Plant Mol Biol.* 1995 May;28(2):347-52.
- Kieliszewski MJ, Kamyab A, Leykam JF, Lamport DT. A Histidine-Rich Extensin from *Zea mays* Is an Arabinogalactan Protein. *Plant Physiol.* 1992 Jun;99(2):538-547.
- Kelly GS. Larch arabinogalactan: clinical relevance of a novel immune-enhancing polysaccharide. *Altern Med Rev.* 1999 Apr;4(2):96-103.
- Hauer J, Anderer FA. Mechanism of stimulation of human natural killer cytotoxicity by arabinogalactan from *Larix occidentalis*. *Cancer Immunol Immunother.* 1993;36(4):237-44.
- Hauer J, Anderer FA. Mechanism of stimulation of human natural killer cytotoxicity by arabinogalactan from *Larix occidentalis*. *Cancer Immunol Immunother.* 1993;36(4):237-44.
- Adorini L, Penna G. Control of autoimmune diseases by the vitamin D endocrine system. *Nat Clin Pract Rheumatol.* 2008 Aug;4(8):404-12. Epub 2008 Jul 1.
- Liu PT, Krutzik SR, Modlin RL. Therapeutic implications of the TLR and VDR partnership. *Trends Mol Med.* 2007 Mar;13(3):117-24. Epub 2007 Feb 5.
- Cannell JJ, Vieth R, Umhau JC, Holick MF, Grant WB, Madronich S, Garland CF, Giovannucci E. Epidemic influenza and vitamin D. *Epidemiol. Infect.* 2006 134:1129-1140.
- Cannell JJ, Zasloff M, Garland CF, Scragg R, Giovannucci E. On the epidemiology of influenza. *Virology.* 2008 5:Art 29.
- White JH. Vitamin D Signaling, Infectious Diseases, and Regulation of Innate Immunity. *Infection and Immunity.* Sept. 2008 76(9):3837-3843
- Bikle DD. Vitamin D and immune function: understanding common pathways. *Curr Osteoporos Rep.* 2009 Jul;7(2):58-63.
- Rouse RV, Parham P, Grumet FC, Weissman IL. Expression of HLA antigens by human thymic epithelial cells. *Hum Immunol.* 1982 5:21.
- Van Ewijk W, Rouse RV, Weissman IL. Distribution of H-2 microenvironments in the mouse thymus, Immunoelectron microscopic identification of I-A and H-2K bearing cells. *J Histochem Cytochem.* 1980 28:1089.
- Jenkinson EJ, van Ewijk W, Owen JTT. Major histocompatibility complex antigen expression on the epithelium of the developing thymus in normal and nude mice. *J Exp Med.* 1981 153:280.
- Fiocchi A, Borella E, Riva E, Arensi D, Travaglini P, Cazzola P, Giovannini M. A double-blind clinical trial for the evaluation of the therapeutical effectiveness of a calf thymus derivative (Thymomodulin) in children with recurrent respiratory infections. *Thymus.* 1986 8(6):331-9.
- Longo F, Lepore L, Agosti E, Panizon F. [Evaluation of the effectiveness of thymomodulin in children with recurrent respiratory infections]. [Article in Italian] *Pediatr Med Chir.* 1988 Nov-Dec;10(6):603-7.
- Skotnicki AB, Dabrowska-Bernstein BK, Dabrowski MP, Gorski A, Czarnecki J, Aleksandrowicz J. Biological properties and clinical use of calf thymus extract TFX-Polfa, in Goldstein A L (ed): *Thymic Hormones and Lymphokines*, pp. 545-564, New York, Plenum Press (1984).
- Aleksandrowicz J, Blicharski J, Janicki K, Lisiewicz J, Skotnicki A B, Sliwczynska B, Turowski G, Szmigiel Z, Wazewska-Czyzewska M: Effect of the thymus extract on congenital hypogammaglobulinaemia and immunological deficiency accompanying the proliferative and aplastic haematological diseases, in van Bekkum D K (ed). *Biological Activity of Thymus Hormones*. Rotterdam, Kooyker. 1975 pp. 37-39.
- Skotnicki A B, Blicharski J, Lisiewicz J, Sasiadek U, Janik J, Wolska T, Zdunczyk A, Aleksandrowicz J: Calf thymus extract TFX-Polfa in the treatment of patients with secondary leukopenia. *Ther Drugs.* 1987 37(95).
- Zeromski J, Siowik-Gabryelska A, Krzysko R. The preliminary evaluation of TFX administration in advanced bronchogenic carcinoma, in Seminar on Cellular and Humoral Immunity in Lung Diseases. *Poznan* (1976). pp. 44-46.
- Stankiewicz-Szymczak W, Moszynski B, Dabrowski MP, Dabrowska-Bernstein BK, Stasiak A. The initial results of TFX-Polfa application in patients with chronic recurrent infections of upper respiratory tract. *Pol J Otolaryng.* 1986 2:350.
- Kriegel H. Dr. John Prudden and Bovine Tracheal Cartilage Research. *Alternative & Comp Therapies.* April/May 1995. pp. 187-189.
- Holt P, Schon-Hegrad MA, Oliver J. MHC class II antigen-bearing dendritic cells in pulmonary tissues of the rat. *J. Exp. Med.* 1988 167:262-274.
- Sertl K, Takemura T, Schachler T et al. Dendritic cells with antigen presenting capability reside in airway epithelium, lung parenchyma and visceral pleura. *J Exp Med* 1986;163:436-451
- Rosen J, Sherman WT, Prudden JF, Thorbecke GJ. Immunoregulatory effects of catrinx. *J Biol Response Modifiers.* 1998 7:498-512.
- Sertl K, Takemura T, Tschachler E, Ferrans VJ, Kaliner MA, Shevach EM. Dendritic cells with antigen presenting capability reside in airway epithelium, lung parenchyma, and visceral pleura. *J. Exp. Med.* 1986 163 :436.
- Berdanier CD. Advanced Nutrition Micronutrients. *CRC Press.* 1998 p. 33.
- Semba RD. Vitamin A, immunity, and infection. *Clin Infect Dis.* 1994 Sep;19(3):489-99.
- Goldfarb RH, Herberman RB. Natural killer cell reactivity: regulatory interactions among phorbol esters, interferon, cholera toxin, and retinoic acid. *Journal of Immunology.* 1981 126:2129-2135.
- Chandra, RK. Increased bacterial binding to respiratory epithelial cells in vitamin A deficiency. *British Medical Journal.* 1988 297:834-835.
- Stephensen CB, Blount SR, Schoeb TR, Park JY. Vitamin A deficiency impairs some aspects of the host response to influenza A virus infection in BALB/c mice. *J Nutr.* 1993 May;123(5):823-33.
- Stephensen CB, Moldoveanu Z, Gangopadhyay NN. Vitamin A deficiency diminishes the salivary immunoglobulin A response and enhances the serum immunoglobulin G response to influenza A virus infection in BALB/c mice. *J Nutr.* 1996 Jan;126(1):94-102.
- Phalipon A, Cardona A, Kraehenbuhl JP, Edelman L, Sansonetti PJ, Corthésy B. Secretory component: a new role in secretory IgA-mediated immune exclusion *in vivo*. *Immunity.* 2002 Jul;17(1):107-15.
- <http://pathmicro.med.sc.edu/mayer/IgStruct2000.htm>
- <http://lpi.oregonstate.edu/infocenter/vitamins/vitaminC/>
- Hemilä H, Chalker E, Treacy B, Douglas B. Vitamin C for preventing and treating the common cold. *Cochrane Database of Systematic Reviews 2007, Issue 2.* Art. No.: CD000980. DOI: 10.1002/14651858.CD000980.pub3
- Sasazuki I, Sasaki S, Tsubono Y, Okubo S, Hayashi M, Tsugane S. Effect of vitamin C on common cold: randomized controlled trial. *EJCN.* 2006 60:9-17.
- <http://www.umm.edu/altmed/articles/echinacea-000239.htm>
- Shah SA, Sander S, White CM, Rinaldi M, Coleman CI. Evaluation of echinacea for the prevention and treatment of the common cold: a meta-analysis. *Lancet Infect Dis.* 2007 Jul;7(7):473-80.
- <http://www.naturalstandard.com/monographs/>