

Reversing Immunosenescence: The Key to Anti-Aging?

BY FRED PESCATORE, M.D., MPH

MEDICAL DIRECTOR, THE CENTERS FOR INTEGRATIVE AND COMPLEMENTARY MEDICINE
NEW YORK

Immunosenescence describes the deterioration of immune response that occurs with age and is the cause of increased frequency and severity of autoimmune, infectious and noninfectious diseases that afflict the elderly. Evidence has accumulated from several studies suggesting an association between immune function and individual longevity. Studies on various natural and nutritional therapies show that many aspects of impaired immune response are correctable and that immunosenescence can be prevented and, in some cases, reversed.

For instance, a hybridized mushroom extract called active hexose correlated compound (AHCC) has proved extremely effective for activating vital parts of the immune system leading to both prevention and treatment of serious diseases associated with aging such as hepatocarcinoma and hepatitis C. Treatments such as this provide an essential aspect of anti-aging medicine that not only offers improved quality of life by preventing diseases that debilitate the aging patient, but also slows or reverses the progression of cancer, hepatitis, diabetes, atherosclerosis, Alzheimer's disease, osteoporosis and other chronic diseases.

What Causes Immunosenescence?

Immunosenescence is the result of continuous exposure to a variety of potential antigens (viruses, bacteria, pollution, food, self molecules and others). This exposure is accelerated by atrophy of the thymus in early adulthood, increased levels of cortisol and

decreased levels of DHEA and other hormones after age 50. In addition, contributions to immunosenescence occur through the sedentary lifestyles and undernutrition of the elderly. Much of the decrease in immunoresponsiveness related to immunosenescence is linked to decreased functioning of natural killer (NK) cells, T cells and macrophages, suppression of IL-2, and the overproduction of IL-6 and other inflammatory cytokines.

NK cells play a key role in preventing immunosenescence because of their dual functions as a cytotoxic destroyer and immunoregulator. As the sentinel cell in the immune system, NK cells provide the first line of defense against invasive pathogens such as bacteria, viruses and emerging malignancies. The NK cell participates either directly or indirectly in multiple developmental, regulatory and communication networks of the immune system. NK cell-initiated cytokines prevent the overproliferation of precursor cell populations, thereby exerting more discriminating control over antigen-specific T- and B-cell responses. In many chronic and degenerative diseases, levels of NK cell function prove to be an important indicator of disease progression and patient prognosis.

Building Up the Sentinel Cell

Enhancing NK cell function, restoring lost function or preventing functional decline is a central mechanism of anti-immunosenescence. Many therapies that stimulate the immune system in general also stimulate NK cell function, but not of the magnitude necessary to provide a therapeutic effect. Conversely,

some pharmaceuticals that sufficiently stimulate NK cell function have diminishing effect over time and/or have such severe side effects that they are not appropriate for use in the management of chronic diseases.

One natural compound in particular offers an effective balance between high levels of stimulation and nontoxicity. Research on an extract of hybridized medicinal mushrooms called active hexose-correlated compound documents its ability to increase NK cell function by 300-fold or more, also stimulating T-cell, macrophage and cytokine activity. This level of immune stimulation can be a very effective therapy for patients whose age-weakened immune systems have succumbed to a number of catastrophic illnesses.

For instance, a study recently presented at the 1999 European Surgical Research Meeting demonstrated both treatment and preventative effects for hepatocarcinoma patients using this compound. The goal of this five-year study was to evaluate the efficacy of AHCC as a biologic response modifier and to determine a correlation between immune stimulation and time to treatment failure (disease recurrence or death). Of 151 patients participating in this study, 70 were given AHCC after having their liver cancer surgically removed, and the remaining 81 acted as the control.

The results show a definite correlation between immune stimulation and positive therapeutic outcome:

- Patient survival was significantly longer in the treatment group (average 23 months).

- Patient disease recurrence was 18 percent lower in the treatment group.
- Patient mortality was significantly lower in the treatment group (28 percent).
- No side effects were associated with treatment.

The Impact of Hepatitis C

While cancer remains one of the unfortunate, yet perfect, examples of immunosenescence, another very difficult-to-treat disease is approaching epidemic proportions as the majority population in the United States reaches its 40s and 50s. Hepatitis C virus is the most common chronic blood-borne infection in the United States. It is estimated that 3.9 million Americans (1.8 percent) have been infected with hepatitis C. Most of these people are chronically infected and can serve as a source of transmission to others and are at risk for chronic liver disease or other hepatitis C-related chronic diseases during the first two or more decades following initial infection.

Chronic liver disease associated with hepatitis C is the 10th-leading cause of death among adults in the United States and accounts for approximately 25,000 deaths annually in the United States. Because most hepatitis C-infected people are aged 30 to 49 years, the number of deaths attributable to hepatitis C-related chronic liver disease could increase substantially during the next 10 to 20 years as this group of infected people reaches ages at which complications from chronic liver disease typically occur.

Currently, interferon-alpha is the treatment of choice by conventional medical standards even though its long term effectiveness is estimated at only 10 to 20 percent. Also, interferon-alpha has been reported to create flulike symptoms in 60 percent of the people taking it for hepatitis C and anemia in 80 percent. Because of its lack of effectiveness and side effects, the growing population of

hepatitis C sufferers need a fast improvement on their treatment options.

Immune system stimulation, particularly NK cell, T cell and macrophage enhancement, could be a viable treatment option for hepatitis C given the effectiveness of immune stimulants on many viral infections.

Testing Immune Stimulation

To test the effectiveness of immune stimulation on hepatitis C, three patients with chronic hepatitis C were chosen. Once again, AHCC was used because of its ability to activate NK cells, T cells and macrophages and its previous research on liver disorders.

The first patient was a 64-year-old female who was diagnosed with hepatitis C two to three years before starting AHCC treatment. After four months, the patient's hepatitis viral load decreased 89 percent (1,475,000 RNA down to 167,000 RNA), and only three months later, her viral load was normal (2,000). Also, the patient reported a significant increase in energy and was able to return to a normal, pre-hepatitis C lifestyle.

Next was a 35-year-old woman with hepatitis C who was originally diagnosed in July 1992. The patient started AHCC treatment in November 1998. Within four months, the hepatitis C viral load was reduced by 27 percent (2,160,900 RNA to 1,573,400 RNA). This case is particularly exciting because the patient has a history of intravenous drug abuse. The third patient is a 47-year-old who was originally diagnosed with hepatitis C in 1974. In December 1998, his hepatitis C viral load was 2,498,200. After six months of AHCC treatment, the patient's viral load was reduced by 80 percent (down to 499,600).

Obviously, these cases show how a stimulated immune system has the ability to lower viral loads and decrease symptoms of hepatitis C, such as lack of energy and jaundice. Also, by keeping hepatitis C viral loads reduced, you are

lowering the possibility of future complications such as cirrhosis of the liver and liver cancer.

However, what could be most important about this research is what the treatment didn't do—AHCC did not cause any side effects. Remember, the leading conventional treatment for hepatitis C causes flulike symptoms and anemia, and it is only effective in 10 to 20 percent of the cases it treats.

This is very significant for people diagnosed with hepatitis C and for people exhibiting the symptoms of hepatitis C who are unable to confirm their diagnosis through laboratory testing. Thousands of people fit this description. Unfortunately, while they wait to confirm their illness, their liver is already deteriorating.

We cannot ignore our immune systems simply because we do not feel sick or don't anticipate getting sick. We need to follow the old adage, "by the time you feel it ... it may be too late." By keeping your immune system strong, you may be able to deter cancer or heart disease or any other illness that seems to strike as we age.

Additional Therapies

Besides AHCC, a complete protocol includes additional natural and nutritional therapies that support and enhance other aspects of the immune system. Research and my own clinical experience show the benefits of N-acetyl-L-cysteine, thymic peptides, and specific antioxidants and minerals. The anti-immunosenescence approach to anti-aging medicine is the core of preventative medicine, strengthening the body's own defenses. The effects can be measured quantitatively through the standard biometric criteria of aging, and in improved quality of life for patients.

References:

1. Kitade H., Matsui Y., Takai Y., Imamura A., Kawaguchi Y., Kamiyama Y., Sun B., Kosuna K., *Preventive Effect of Active Hexose Correlated Compound (AHCC) on the Recurrence of Postoperative Hepatocellular Carcinoma Patients*.

- 33rd Congress of the European Society for Surgical Research, 1998 p. 74.
2. Ghossein M, Winkley M, Salem E, McKlein A, Atallah N, Gill G, *Immunomodulatory and Anti-Cancer Effects of Active Heretichalides Compound (AHCC)*, International Journal of Immunotherapy, 1995; XI(1) 23-28.
 3. Masuzawa K, Kuramitsu Y, Ohno Y, Obara M, Kobayashi M, Li Y, Hoshikawa M, *Combination Therapy of Active Hexose Correlated Compound Plus UFT Significantly Reduces the Metastasis of Rat Mammary Adenocarcinoma*, Anti-Cancer Drugs, 1998; 9:343-50.
 4. Wakame K, Department of Biochemistry, Dokkyo University School of Medicine, *Protective Effects of Active Hexose Correlated Compound (AHCC) on the Onset of Diabets Induced by Streptozotocin in the Rat*, Biomedical Research, 1999; 20 (3):145-52.
 5. Matsumoto T, Sun B, Tomama K, *Active Hexose Correlated Compound (AHCC) Protects Against Glycose Aminoxidase Induced Abpexia in the Nephrotic Rat Animal Model*, Japanese Journal of Cancer Research, 89:2405
 6. Sun B, Wakame K, Matsumoto T, Tsubokawa A, Kamazawa T, *Protective Effects of AHCC on Carbon Tetrachloride Induced Liver Injury in Mice*, Natural Medicine, 1997; 51:10-15.
 7. Malnick SD, Beerghel M, Lurie Y, Department of Internal Medicine C, Kaplan Medical Center, Rehovot Israel, *Treatment of Chronic Hepatitis C Virus Infection*, Ann Pharmacother, 2006; Oct. 34(10):1156-64.
 8. Vargas H.E, Whitcomb D.C., *Hepatitis for Half a Century*, Gastroenterology, 2006; Nov. 119(5):1405-07.
 9. Gaster B, Janson A., Department of Medicine, University of Washington, Seattle, *Chronic Hepatitis C: Common Questions, Practical Answers*, J Am Board Fam Pract. 2000; Sept.-Oct. 13(5):59-63.
 10. Ry D.E., Department of Surgery, University of New Mexico School of Medicine, Albuquerque, *The ABCs of Hepatitis*, Adv Surg. 1999; 33:423-37.
 11. Reisman J.P., Palladino S., Kay I.D., Cheng W.S., *The Role of Viral Load Monitoring in Predicting Which Patients With Hepatitis C Virus Will Respond to Interferon Therapy*, Med J Aust. 1999; Sept. 20171(6):334.
 12. Oketani M, Aoshima Y, Wu CH, Wu G.Y., Department of Medicine, University of Connecticut Health Center, Farmington, *Inhibition of Hepatitis C Virus-Derived Gene Expression by a DNA Ribonuclease*, J Hepatol 1999; Oct. 31(4):623-34.
 13. Whiteside TL, Herberman RB., *Role of Herpesviral Natural Killer Cells in Health and Disease*, Clin Diagn Lab Immunol. 1994; March 1(2):125-33.
 14. Hanna N., *Role of Natural Killer Cells in Control of Cancer Metastasis*, Cancer Metastasis Rev. 1982.
 15. Ben-Bryghon S, Page G.G, Yarnira R, Shalika G., *Evidence That Stress and Surgical Interventions Promote Tumor Development by Suppressing Natural Killer Cell Activity*, Int J Cancer. 1999; March 15, 80(6):880-88.
 16. Shorle I., Jishi N., Adyani S., Nishimura J., *Impaired T Lymphocyte Function and Differential Cytokine Response Pattern in Members From Cancer Families*, Natural Immun. 1998; 1:64:146-56.
 17. Ben-Bryghon S, Page G.G, Yarnira R, Thaler A.N., *Acute Alcohol Intoxication Suppresses Natural Killer Cell Activity and Promotes Tumor Metastasis*, Nat Med. 1996; April 2(4):457-60.
 18. Whiteside TL, Herberman R.B., Pittsburgh Cancer Institute, University of Pittsburgh, *Role of Herpesviral Natural Killer Cells in Health and Disease*, Clin Diagn Lab Immunol. 1994; March 1(2):125-33.