Nutrition — The Immune System and Viruses

Introduction: The immune system represents an elaborate, finely tuned defense to destroy and counter the effects of microorganisms and foreign substances. When the immune system is healthy, it destroys foreign elements without causing symptoms. The immune system can remember previous invaders and mount a rapid response when they reappear. An imbalanced immune system can set the stage for disease and chronic conditions when foreign substances and microorganisms are not recognized or destroyed. Therefore, maintaining a healthy immune system is key to host resistance.

Among foreign invaders attacked by the immune system are viruses, which can be regarded as the ultimate parasites of cellular life forms. Virions are mature virus particles. They are characterized from other life forms by the following properties: They possess primarily one type of nucleic acid; replication of the viral genome is directed by viral nucleic acid; they lack binary fission and metabolic machinery that generate energy typical of cells; and they depend entirely on host protein synthesizing machinery for production of viral proteins. In typical extracellular viruses, both intracellular and extracellular phases occur in the life cycle and the immune system counters both. The extracellular phase involves mature infective viral particles. The virion possesses a characteristic structure with protein coat surrounding an inner core of nucleic acid. Several animal viruses, such as the Herpes simplex, develop an outer coat ("envelope") derived from the host cytoplasm or nuclear membrane. Most viruses are either single stranded RNA or double stranded DNA; the genomes may consist of double stranded DNA or single stranded DNA in some instances. The immune system is normally able to attack each of these types.

As a general rule, animal virions attach to specific chemical receptor sites on the host cell surface. Projections on the virions serve as attachment points. Viruses then enter host cells either by pinocytosis or by phagocytosis. Once inside the cell, the virus resides in a membrane-bound vacuole, while it becomes uncoated, baring its nucleic acid. This allows transcription of the viral genome, permitting first the replication of viral nucleic acid, which may be required for the formation of viral directed enzymes, followed by the synthesis of viral coatproteins. Alternatively, the viral genome may become integrated into the host genome indefinitely until localized stimuli can trigger gene replication and viral production. In terms of immune response, the incorporation of the viral genome into the host cell can alter its metabolism and antigenicity.

Many viruses can inhabit the upper respiratory tract. The common cold is certainly one of the most common viral infections; in fact, less than 10 percent of the population manages to avoid colds. About half of all colds are due to the rhino viruses which enter mucous membranes of the eye, nose or lung. Common mode of transmission is the air due to coughing, nose blowing and sneezing. The virus can also be transmitted by a handshake; 40% of people with rhino virus colds have viruses on their hands, where they can last for up to 3 hours. The respiratory syncytial virus (RSV) can survive for hours on surfaces and infection is often transmitted by direct contact. Influenza virus is

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also commonly spread through the air. This virus survives only 10 minutes on the skin but can survive up to 3 days on hard surfaces, thus it can be spread indirectly.

Both humoral and cell mediated immunity are important antiviral defense mechanisms. The thymus gland produces T-lymphocytes required for cell-mediated immunity and are extremely important for resistance to viruses and other microorganisms. In a typical scenario, macrophages engulf a viral particle and degrade it and release cytokines. Processed antigens on its surface are recognized by T-lymphocyte (T-helper cells) which are stimulated to proliferate and to produce lymphokines that activate other defensive cells. Stress, whether physical or emotional, is believed to be important in reducing such resistance. For example, the stress response products for the adrenal glands reduce the activity of the thymus gland and promote hypertrophy. Lifestyle factors profoundly affect host resistance to viruses. Alcohol consumption, tobacco use, excessive sugar consumption, exposure to environmental chemicals and chronic allergies are other factors to consider in considering resistance to viruses. On the other hand, a variety of nutrients can enhance immune system function, and several botanical preparations have proven useful in maintaining normal cell and humoral immunity. The following are noteworthy:

Nutrients for Immune Support

Vitamin C: Vitamin C plays many roles in helping support immune function. White blood cells contain very high levels of vitamin C, which enhances T-cell function and increases phagocytosis[1,2]. Vitamin C also enhances antibody production and B-cell function2. Vitamin C possesses antihistamine-like properties and reduces inflammation. Additionally, vitamin C increases immunoglobulin synthesis in B-cells. It also seems to enhance nonspecific immune responses, such as increasing the production of interferon[3].

Vitamin A: Vitamin A plays a key role in the development and maintenance of mucosal surface and their secretions which represent a primary, nonspecific barrier to microorganisms. Additionally, vitamin A stimulates and supports natural killer cell activity, phagocytosis, and antibody production[4]. Evidence suggests that vitamin A counters stress-induced inhibition of thymic function and that it enhances antiviral activity[5].

Natural mixed carotenoids: Beta carotene is often the most prevalent carotenoid in foods; however, foods supply an abundant mixture of carotenoids, including carotenes such as lycopene and alpha carotene, as well as oxidized carotenoids such as lutein, zeaxanthin and cryptoxanthin. Carotenoids complement tocopherols as antioxidants and their distribution is tissue specific. Although lycopene is more prevalent in the blood, lutein and zeaxanthin are the only two carotenoids that occur in the macula of the retina. Natural mixed carotenoids appear to be more readily absorbed and more effective as antioxidants in humans than synthetic beta carotene[6]. Beta carotene supplementation enhanced certain aspects of immunity in healthy nonsmokers and in elderly subjects [7,8].

Copper: Ceruloplasmin is the major copper protein of serum. The enzyme is involved in the acute phase of inflammation, in addition to transporting copper and the binding and storage of iron[9]. Ceruloplasmin synthesis is regulated by inflammatory cytokines, Interleukin-1, Interleukin-6 and tissue necrosis factor.

Propolis: Bees produce a "glue" derived from plant materials and which is isolated from bee hives. Propolis has been used in folk traditions. Propolis contains caffeic acid, phenethyl ester and other antioxidants. When added to the diet of rats, they were shown to support normal production of eicosanoids[10]. Propolis was found to inhibit cocci and Gram-positive bacteria with little effect on Gram-negative bacteria[11].

Zinc: As a cofactor for DNA and RNA polymerase, alcohol dehydrogenase, and over a hundred other enzymes, zinc plays an essential role in the proliferation of immune cells. Zinc is a cofactor for copper/zinc superoxide dismutases, required to inactivate the free radical, superoxide. Zinc deficiency is known to impair the efficiency of the immune system[12]. Cells with rapid turnover rates, such as those involved in cell-mediated immunity, are vulnerable to zinc deficiency.

Flavonoids

Rutin *(quercetin rutinoside)*: Orally ingested quercetin as well as its glycoside, rutin, are bioavailable forms of flavonoids[13]. Quercetin influences the immune system in a variety of ways. As an effective antioxidant, quercetin can neutralize reactive oxygen species generated by phagocytic cells during excessive inflammation. In addition, quercetin and other flavonoids inhibit mast cell and basophil degranulation, which limits the release of lysosomal degraditive enzymes, as well as inflammatory agents. Flavonoids inhibit the formation of proinflammatory leukotrienes, for example, by

blocking the arachidonic acid cascade and by inhibiting lipoxygenase. Quercetin possesses significant antiviral activity in vitro as well[14]. Quercetin and other flavonoids can stabilize connective tissue and help maintain the integrity of capillaries, thus reducing capillary hyper-permeability[15].

Hesperidin: Hesperidin is the rutinoside of the flavanone, hesperitin. Animal experiments have demonstrated that the hesperidin can normalize reduced capillary resistance and lower increased capillary permeability[16]. Like quercetin, hesperidin seems to reduce vascular permeability. Hesperidin, quercetin and other flavonoids are believed to protect vitamin C, thus helping the body economize this essential nutrient.

Botanical Support for Immune System

Astragalus membranaceous: a traditional Chinese herb with a long history of folk use. Extracts of this herb tonify the spleen and blood and increase qi[17]. Major ingredients include D-asparagine, isoflavone, calycosin, formononetin, cycloastragenol, astragalosides, choline, betaine, kumatakenin, glucuronic acid and beta sitosterol. Radiation treated rats, or aged rats injected with extracts, increased their responses to T-cell dependent antigens[18]. Incubation of phagocytes with Astragalus extracts increased chemiluminescent oxidative bursts, which indicated increased phagocytic activity[19].

***Forsythia suspensa*:** This herb is used in Oriental traditions, which describe it as expelling wind heat[20]. Major ingredients include forsythol, forsythin, matairesinoside, betulinic acid, phyillygenin, pinoresinol. Forsythol and forsythin possess antioxidant and anti-bacterial properties. Pinoresinol modulates the immune system[21].

***Stillingia sylvatica*:** a Chinese herb with a history of traditional use in balancing body systems. Stillingia contains an essential oil, which possesses tocopherols (gamma tocotrienal) and terpenoids called estolides, believed to be active ingredients[22].

Wheat grass powder: Wheat grass is a source of trace minerals and plant pigments including chlorophyll. Chlorophyll possesses antioxidant activity and protects lymphocytes, thus supporting cell-mediated immune function[23].

***Hamamelis virginiana*:** This herb had a long history of use by Native Americans before it was subsequently adopted by European colonists. *Hamamelis virginiana* contains 3 to 10% tannic acid, which is partially responsible for its astringent properties. Other compounds have been identified: gallic acid, hamamelose, saponins together with glycosides of myricetin, quercetin, and kaempferol. Extracts are reported to improve blood vessel tone in animal studies[24].

***Bupleurum falcatum*:** Bupleurum is a traditional herb long used in China where it is considered bitter and cool. Bupleurum supports gastrointestinal and liver function and helps normalize inflammatory responses. Roots of bupleurum species provide a group of terpenoid saponins (saiko-saponins). The highest level of these saponins occurs in *Bupleurum falcatum*[25]. Other ingredients include pectin-like polysaccharides (bupleurans) and other phytosterols (alpha-spinasterol). In experimental animals saiko saponins potentiated the hormonal response of the adrenal cortex. Mouse macrophages exposed to saiko saponins showed increased phagocytic activity[26] and mice pretreated with the saponins demonstrated an increased immune function after immunization with red blood cells from sheep[27].

Maitake mushroom: a source of complex carbohydrates (glucans) and other fiber, calcium, potassium, magnesium, niacin and vitamin C. Feeding lab animals standard chow fortified with maitake mushroom powder lowered serum lipids; the level of HDL was unchanged[28]. In other experiments, the administration of 1gm of maitake to rats helped normalize blood glucose and triglycerides[29]. An acidinsoluble, alkali-soluble fraction was characterized as a 1,6-beta glucan with 1,3 branched carbohydrate chains with a molecular weight of 1,000,000 ("maitake D fraction"). When injected or administered orally to experimental animals, the glucan activated immune competent cells[30].

***Phyllanthus amarus*:** Hydrolyzable tannins purified from this source inhibited calcium dependent-protein kinase activity more effectively than other plant-derived inhibitors[31]. *Phyllanthus amarus* extracts were shown to inhibit hepatitis B virus polymerase activity in cultured HepG2 2.2.15 cells. When *Phyllanthus amarus* was administered to transgenic mice carrying the G26 hepatitis virus, hepatic HbsAg mRNA levels decreased[32].

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