Immunology and treatment of asthma by Chinese medicine

T.C.M.Anti-Cancer Centre & Acuouncture Clinic

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1. The human immune system

T- and B- lineage cells both arise from a subset of hematopoietic stem cells in the bone marrow of fetal liver that become committed to the lymphoid pathway of development. Human B-lymphocyte development takes place entirely within the bone marrow. T cells on the other hand, develop from immature precursors that leave the marrow and travel through the bloodstream to the thymus, where they proliferate and differentiate into mature T lymphocytes. no more than 1% of the total lymphocyte population can be found in the blood. Most of the remaining cells are contained in specialized lymphoid organs, such as the lymph nodes, thymus, tonsils, and white pulp of the spleen, where they carry out most of their functions.

2. B lymphocytes make humoral antibody responses and T lymphocytes make cell-mediated immune responses

Antibodies are made by plasma cells derived from B-lymphocytes, each of which is programmed to make only one antibody which is placed on the cell surface as a receptor. Antigen binds to the cell with a complementary antibody, activates it and causes clonal proliferation and finally maturation to antibody-forming cells and memory cells. Thus the antigen brings about clonal selection of the cells making antibody to itself. Antibodies differentiate between antigens because recognition is based on molecular shape complementarity. Thus memory induced by one antigen will not extend to another unrelated antigen. The immune system differentiates self components from foreign antigens by making immature self-reacting lymphocytes unresponsive through contact with host molecules; lymphocytes reacting with foreign antigens are unaffected since they only make contact after reaching maturity. the antibody molecule evolved as a specific adaptor to attach to microorganisms which either fail to activate the alternative complement pathway or prevent activation of the phagocytic cells.

The T-cell is concerned with control of intracellular infections, Like the B-cell, each T-cell has its individual antigen receptor which recognizes antigen and undergoes clonal expansion to form effector and memory cells providing specific acquired immunity. The T-cell recognizes cell surface antigens in association with molecules of the MHC. T-helper cells (CD4+)which see antigen with class II MHC on the surface of macrophages, release cytokines which in some cases can help B-cells to make antibody and in others, activate macrophages and enable them to kill intracellular parasites. Cytotoxic T-cells have the ability to recognize specific antigen plus class I MHC on the surface of virally infected cells which are killed before the virus replicates. They also release r-interferon which can make surrounding cells resistant to viral spread.

Antibody and complement give protection against most extracellular organisms, while T-cells, soluble cytokines, and macrophages deal with intracellular infections.

The immune system is clearly 'a good thing', but like mercenary armies, it can turn to bite the hand that feeds it, and cause damage to the host. Immunopathologically mediated tissue damage to the host can occur as a result of:

Inappropriate hypersensitivity reactions to exogenous antigens.

Loss of tolerance to self-giving autoimmune disease.

Immunodeficiency leaves the individual susceptible to infection.

3. Autoimmune diseases

The induction of immunological tolerance is necessary to avoid self-reactivity, include high avidity T-cells which react with self-antigens presented by macrophages and dendritic cellos are eliminated by negative selection, lack of class II on the antigen-presenting cell or low concentration of peptide/MHC, T-suppression is probably more concerned in reversing autoimmunity rather than preventing it. B-cell tolerance is induced by clonal deletion, clonal anergy, receptor editing and 'helplessness' due to preferential tolerization of T-cells needed to cooperate in B-cell stimulation.

Autoimmunity is associated with certain diseases which form a spectrum. At one pole, exemplified by Hashimoto's thyroiditis, the autoantibodies and the lesions are organ-specific with the organ acting as the target for autoimmune attack; at the other pole are the nonorgan-specific or systemic autoimmune diseases such as Systemic lupus erythematosus (SLE) where the autoantibodies have widespread reactivity and the lesions resemble those of serum sickness relating to deposition of circulating immune complexes.

4. Type of hypersensitivity

Excessive stimulation of the normal effector mechanisms of the immune system can lead to tissue damage and we speak of hypersensitivity reactions of which several types can be distinguished.

Type I-anaphylactic hypersensitivity: Anaphylaxis involves contraction of smooth muscle and dilatation of capillaries. This depends upon the reaction of antigen with specific IgE antibody bound through its Fc to the mast cell. leads to release from the granules of mediators including histamine, leukotrienes and platelet activating factor, plus eosinophil and neutrophil chemotactic factors and the cytokines IL-4, 5 and GM-CSF. IL-4 is involved in isotype switch to IgE. Atopy stems from an excessive IgE response to extrinsic antigens which leads to local anaphylactic reactions at sites of contact with allergen. Hay fever and extrinsic asthma represent the most common atopic allergic disorders resulting from exposure to inhaled allergens. many food allergies involve type I hypersensitivity.

Type II -antibody-dependent cytotoxic hypersensitivity: This involves the death of cell bearing antibody attached to a surface antigen. The cells may be taken up by phagocytic cells to which they adhere through their coating of IgG or C3b or lysed by the operation of the full complement system. Cells bearing IgG may also be polymorphs and macrophages or by K-cells. Examples are: transfusion reactions, hemolytic disease of the newborn through rhesus incompatibility, antibody-mediated graft destruction, autoimmune reactions directed against the formed elements of the blood and kidney glomerular basement membranes, and hypersensitivity resulting from the coating of erythrocytes or platelets by a drug.

Type III - complex-mediated hypersensitivity: This results from the effects of antigen-antibody complexes through activation of complement and attraction of polymorphonuclear leukocytes which release tissue-damaging mediators on contact with the complex, and aggregation of platelets to cause microthrombi and vasoactive amine release. where circulating antibody levels are high, the antigen is precipitated near the site of entry into the body. The reaction in the skin is characterized by polymorph infiltration, edema and erythema maximal at 3-8 hours. Examples are: Complex glomerulonephritis, Farnmer's lung etc..

Type IV - cell-mediated or delayed - type hypersensitivity: This is based upon the interaction of antigen with primed T-cells and represents tissue damage resulting from inappropriate cell-mediated immunity reactions. A number of soluble cytokines including IFNr are released which activate macrophages and account for the events which occur in a typical delayed hypersensitivity response such as the Mantoux reaction to tuberculin, that is the delayed appearance of an indurated and erythematous reaction which reaches a maximum at 24-48 hours and is characterized histologically by infiltration with mononuclear phagocytes and lymphocytes. Examples are: tissue damage occurring in bacterial (tuberculosis) infections, contact dermatitis from exposure to chromates and poison ivy, insect bites and psoriasis.

5. Immunology of asthma

Inflammation of mucosa and epithelial damage of the bronchi are characteristic pathological features of asthma. Infiltration of Th2 lymphocytes and eosinophils into mucosa followed by their activation and release of cytokines including interleukin 4 (IL-4) and interleukin 5 (IL-5) seem to be a contributing process.

6. Immunomodulatory action of chai hu hou pu tang

In order to study the pathogenic roles of IL-4 and IL-5 in asthma and the mechanisms of reduction of the bronchial hyperresponsiveness by macrolides, and chai hu hou pu tang. we have examined serum IL-4 and IL-5 levels, spontaneous production of IL-4 and IL-5 by peripheral blood mononuclear cells (PBMC) and the effect of macrolides or chai hu hou pu tang on the production of IL-4 and IL-5 by PBMC. The serum levels IL-4 and IL-5 were significantly higher in patients with bronchial asthma than in normal controls. IL-4 and IL-5 production by Concanavalin A (Con A)-stimulated PBMC was significantly higher in atopic asthma than in normal controls.

Addition of Erythromycin (EM) into culture medium resulted in suppression of IL-4 and IL-5 production from Con A-stimulated PBMC in a dose-dependent manner. Interestingly, addition of chai hu hou pu tang into culture medium preferentially suppressed the IL-4 production by Con A-stimulated PBMC in a dose-dependent manner, but did not suppress the IL-5 production.

7. Determination and treatment of asthma by Chinese medicine

1) Asthma of Cold Type: A feeling of fullness and distress in the chest, dyspnea with wheezing sound in the throat, cough with thin sputum, frequent attacks in cold seasons or caused by cold, whitish, moist and glossy fur of the tongue, taut and tight pulse. Recipe: Belamcanda and Ephedra Decoction.

2) Asthma of Heat Type: Dyspnea with wheezing, irritable oppressed sensation in the chest even gasping for breath, yellowish mucoid sputum, thirst, frequent occurrence in hot seasons or onset closely associated with heat, reddened tongue with yellow greasy fur, slipper and rapid pulse.

Recipe: Ephedra, Apricot Kernel, Gypsum and Licorice Decoction.